P

P: Parental generation.

P: ►probability

P (Polyoma): A regulatory DNA element in the viral basal promoter. ►Simian virus 40, ►polyoma

^{32}P: Phosphorus isotope. ►isotopes

P1: Double-stranded DNA, temperate *E. coli* phage. It is also a vector used DNA sequencing with a load capacity of ~80 kb.

P_1, P_2: Designations of the parents, homozygous for different alleles, at the critical locus (loci) in a Mendelian cross. ►Mendelian laws, ►gametic arrays, ►genotypic segregation, ►allelic combinations

p (petit): Short arm of chromosomes, also denote frequencies. ►q

π: ►diversity

π: 22/7 ≈ 3.132857, Ludolf number, indicates the ratio of the circumference to the diameter of a circle.

ϕ (phi): The symbol of some phages.

ψ (psi): ►pseudouridine (see Fig. P1), formula. Also, packaging signal for virions. The packaging signal is located at the 5′ LTR repeat and reaches over into the upstream end of the gag gene. It is not translated. ►retroviruses

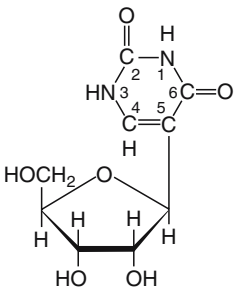

Figure P1. Pseudouridine

p13suc1: The yeast cell cycle activating enzyme binding to the cyclosome. ►cyclosome, ►cell cycle; Simeoni F et al 2001 Biochemistry 40:8030.

p14: ►ARF

$p15^{INK4B}$: An inhibitor of CDK4 (encoded in human chromosome 9p21) appears to be an effector of TGF-β, a protein known to control the progression from G1 phase of the cell cycle to S phase. ►cell cycle, ►TGF, ►$p16^{INK4}$, ►p18, ►p19, ►cancer; Seoane J et al 2001 Nature Cell Biol 3:400.

p16 (*MTSI* [multiple tumor suppressor], CDKN2): A cell cycle gene (in human chromosome 9p21) that has a major role in tumorigenesis. In 50% of the melanoma cells, it is deleted and in 25%, it is mutated. Over 70% of the bladder cancer cases are associated with deletions of 9p21 in both homologous chromosomes, in head and neck tumors 33%, in renal and other cells usually this tumor suppressor gene is lost. It normally restrains CDK4 and CDK6. ►melanoma, ►pancreatic adenocarcinoma, ►CDK4, ►CDK6, ►cell cycle, ►ARF; Serrano M et al 1993 Nature [Lond] 366:704.

p16: A weak ATPase and a packaging protein of φ29 bacteriophage. It interacts with the viral packaging RNA (pRNA) and the phage portal protein and assists in pumping the double-stranded DNA into the phage head. p16 and other packaging components are not found within the head. ►packaging of DNA; Ibarra B et al 2001 Nucleic Acids Res 29:4264.

$p16^{INK4}$ (CDKN2A): A protein inhibitory to CDK4/CDK6 and thus appears to be a tumor suppressor because it inhibits the progression of the cell cycle from G^1 to S. Thus, it may also direct the cell toward senescence rather than neoplasia. $p16^{INK4a}$ induces age-dependent decline in cell regenerative capacity (Krishnamurty J et al 2006 Nature [Lond] 443:453). Absence of $p16^{INK4a}$ may reduce aging of hematopoietic stem cells and acts similarly to ARF in tumor suppression. The two proteins share coding sequences but ARF does not seem to affect stem cell aging (Janzen V et al 2006 Nature [Lond] 443:421). Both $p16^{INK4}$ and $p19^{INK4}$ are transcribed from the same 9p21 locus but from alternative alleles. ►CDK4, ►tumor suppressor, ►PHO81, ►cell cycle, ►cancer, ►p18, ►p19, ►Ets oncogene, ►Id protein, ►senescence, ►mole, ►centrosome; Quelle DE et al 1995 Cell 83:993; Wang W et al 2001 J Biol Chem 276:48655; Reinolds PA et al 2006 J Biol Chem 281:24790.

$p18^{INKC}$: Cell cycle inhibitors that block cell cycle kinases CDK4 and CDK6. ►cell cycle, ►cancer, ►p15, ►p16, ►p19; Blais A et al 2002 J Biol Chem 277:31679.

$p19^{Arf}$: ►Arf, ►$p16^{INK4}$

$p19^{INK4d}$: Cell cycle inhibitor of CDKs. ►p15, ►p16, ►p18, ►cell cycle, ►cancer, ►ARF

p21: A transforming protein of the Harvey murine sarcoma virus. A Ras-gene encoded 21 kDa protein binds GDP/GTP and hydrolyzes bound nucleotides

and inorganic phosphate. This protein is involved in signal transduction, cell proliferation and differentiation and p21 controls the cyclin-dependent kinases (Cdk4, Cdk6, Cdk2), and binds to DNA polymerase δ processivity factor and it inhibits in vitro PCNA-dependent DNA replication but not DNA repair. In the absence of p21, cells with damaged DNA are arrested temporarily at the G2 phase and that is followed by S phases without mitoses. Consequently hyperploidy arises and apoptosis follows. Gene *p21* is under the control of p53 protein and the retinoblastoma tumor suppressor gene RB. MyoD regulates expression of the p21 Cdk inhibitors (p21Cip/WAF1, 6p21.2) during differentiation of muscle cells and non-muscle cells, and then withdrawal from the cell cycle does not require the participation of p53. Experimental evidence indicates that telomere dysfunction induces p21-dependent checkpoints in vivo that can limit longevity at the organismal level (Choudhury AR et al 2007 Nature Genet 39:99). RAF and RHO activate protein $p21^{Cip/Waf}$, leading to inhibition of the transition of the cell cycle into the S phase. Actually, RAS activates the serine/threonine kinase Raf that may facilitate the transition to the S phase but upon excessive stimulation by RAF and RHO, $p21^{Cip/Waf}$ has the opposite effect. Also, p53 is an independent activator of $p21^{Cip/Waf}$. After mitosis, p21 is expressed at the onset of differentiation but it may again be down-regulated at later stages of differentiation due to proteasome activity. In addition, p21 may not have an absolute requirement for induction by MyoD. The N terminal domains of p27 and p57 provide other antimitogenic signals. $P21^{SNFT}$ is a 21 kDa nuclear factor of T lymphocytes. Its overexpression represses transcription from the interleukin-2 and AP1-driven promoters. ►cell cycle, ►Cdk, ►mitosis, ►cancer, ►hyperploidy, ►apoptosis, ►p53, ►PCNA, ►p27, ►p57, ►MyoD, ►cell cycle, ►RAS, ►RASA, ►proteasome, ►interleukin, ►AP1, ►NF-AT, ►epigenesis; Prall OWJ et al 2001 J Biol Chem 276:45433; Wu Q et al 2002 J Biol Chem 277:36329; Bower KE et al 2002 J Biol Chem 277:34967.

p23: A component of the steroid receptor complex with Hsp90. ►Hsp, ►steroid hormones, ►molecular chaperone interacting complex, ►telomerase; Knoblauch R, Garabedian MJ 1999 Mol Cell Biol 19:3748; Munoz MJ et al 1999 Genetics 153:1561.

p24: A family of evolutionarily conserved small integral membrane proteins, which form parts of the COP transport vesicles or regulate the entry of cargo into the vesicles. It also mediates viral infection. ►protein sorting, ►COP transport vesicles; Blum R et al 1999 J Cell Sci 112(pt 4):537; Hernandez M et al 2001 Biochem Biophys Res Commun 282:1.

p27 ($p27^{Kip1}$): A haplo insufficient tumor suppressor protein, which inactivates cyclin-dependent protein kinase 2. Its mutation (homo- or heterozygous) results in increased body and organ size and neoplasia in mouse. p27 in cooperation with RAS controls metastasis (Bessom A et al 2004 Genes Dev 18:862). The wild type allele as a transgene may retard cancerous proliferation. Germ-line mutations in p27*Kip1* can predispose to the development of multiple endocrine tumors in both rats and humans (Pellegata NS et al 2006 Proc Natl Acad Sci USA 103:15558). Inactivation of $p27^{Kip1}$ is triggered by phosphorylation and mediated by the proteasome complex. Non-receptor tyrosine kinases phosphorylate $p27^{Kip1}$ and decrease its stability leading to entry into the cell, cycle (Kaldis P 2007 Cell 128:241). ►Cdk2, ►p21, ►cell cycle, ►cancer, ►KIP, ►Knudson's two-mutation theory of cancer, ►cancer gene therapy, ►metastasis, ►RAS, ►transgene, ►proteasome, ►p38, ►SKP, ►dyskeratosis, ►MEN; Mohapatra S et al 2001 J Biol Chem 276:21976; Malek NP et al 2001 Nature [Lond] 413:323.

$p27^{BBP}$: ►eIF-6

$p34^{cdc2-2}$: The gene coding for the catalytic subunit of MPF in *Schizosaccharomyces pombe* (counterparts, *CDC28* in *Saccharomyces cerevisiae*, *CDCHs* in humans have 63% identity with *cdc2*; these genes are present in all eukaryotes). The gene product is a serine/tyrosine kinase and its function is required for the entry into M phase of the cell cycle. If prematurely activated, it may cause apoptosis. ►cell cycle, ►MPF; Shimada M et al 2001 Biol Reprod 65:442; Nigg EA 2001 Nature Rev Mol Cell Biol 2:21.

p35 (Cdk5 regulatory subunit): A homolog of the baculoviral (survival) protein and cyclin-dependent regulator of neural migration and growth and which blocks apoptosis in a variety of eukaryotic cells. It co-localizes in the cells with RAC and Pac-1. Truncation of p35 results in a very stable p25 protein that is present in Alzheimer disease tangles. ►baculoviruses, ►RAC, ►Pac-1, ►Alzheimer disease, ►CDK; Tarricone C et al 2001 Mol Cell 8:657; Lin G et al 2001 In Vitro Cell Dev Biol Anim 37(5):293.

p38 (MPK2/CSBP/HOG1): A stress-activated protein kinase of the MEK family. It accelerates the degradation of $p27^{Kip1}$, and it phosphorylates H3 histone. p38 is one of the factors required for the initiation of G2/M checkpoint after UV radiation. The down-regulation of E-cadherin during mouse gastrulation requires p38 and a p38-interacting protein (Zohn IE et al 2006 Cell 125:957). The p38-activated protein (PRAK) is essential for RAS-induced senescence and tumor suppression (Sun P et al 2007 Cell 128:295). The mitogen-activated protein kinase

(MAPK) p38 controls inflammatory responses and cell proliferation. Using mice carrying conditional *Mapk14* (also known as *p38α*) alleles, when specifically deleted in the mouse embryo, fetuses developed to term but died shortly after birth, probably owing to lung dysfunction. Fetal hematopoietic cells and embryonic fibroblasts deficient in p38 showed increased proliferation resulting from sustained activation of the c-Jun N-terminal kinase (JNK) pathway (Hui L et al 2007 Nat Genet 39:741). p38 is a lung tumor suppressor (Ventura JJ et al 2007 Nat Genet 39:750). ►MEK, ►MEF, ►MAP kinase, ►JNK, ►cadherins, ►gastrula, ►checkpoint, ►UV; Schrantz N et al 2001 Mol Biol Cell 12:3139; Bulavin DV et al 2002 Curr Opin Genet Dev 12:92.

p40: A tumor suppressor encoded in human chromosome 3q, produced by alternative splicing of p51. Also an L1 RNA transcript (of ORF II) binding protein required of retrotransposon movement. ►p51, ►p53, ►L1, ►retrotransposon, ►ORF; Hess SD et al 2001 Cancer Gene Ther 8(5):371; Henning D, Valdez BC 2001 Biochem Biophys Res Commun 283:430.

p42: ►MAPK

p50: The N-terminus of the p105 light chain of NF-κB encoded at 4q23-q24. ►NF-κB; Yamada H et al 2001 Infect Immun 69:7100.

p51: A cell proliferation inhibitor protein related to p73 and encoded at 3q28. p51A is 50.9 kDa and p51B is 71.9 kDa. ►p73, ►p40, ►p53; Guttieri MC, Buran JP 2001 Virus Genes 23:17.

p52^{SHC}: A RAS G-protein regulator protein; it is regulated through CTLA-4–SYP associated phosphatase. ►CTLA-4, ►SYP, ►RAS; Joyce D et al 2001 Cytokine Growth Factor Rev 12:73.

p53 (TP3, 17p13.1): A tumor suppressor gene when the wild type allele is present but single base substitutions may eliminate suppressor activity and the tumorigenesis process may be initiated.

p53 is a tetramer with separate domains for DNA binding, transactivation and tetramerization (see Fig. P2).

The transcriptional coactivator p300 binds to and mediates the transcriptional functions of the tetrameric tumor suppressor p53. In the four domains of the complex between tetrameric p53 and p300, the latter wraps around the four transactivation domains of p53 (see Fig. P3) (Teufel DP et al 2007 Proc Natl Acad Sci USA 104:7009). Protein p53 as tetramers of tetramers binds to different DNA sites and in case of stress activates the expression of genes involved in apoptosis. Wild type alleles of oncogenes and DNA damage, both activate tumor suppressor activities of p53 although through separate metabolic routes (Efeyan A et al 2006 Nature [Lond] 443:159; Christophorou MA et al 2006 Nature [Lond] 443:214). New information is available for the structural framework in interpreting mechanisms of specificity, affinity and cooperativity of DNA binding as well as regulation by regions outside the sequence-specific DNA-binding domain (Kitayner M et al 2006 Mol Cell 22:741). Protein p53 recognizes specific DNA sequences, activates transcription from promoters with p53 protein binding sites and represses transcription from promoters lacking p53-binding sites; p53 regulates more than 160 genes. Recent data based on chromatin immunoprecipitation and paired end ditag sequencing identified 542 binding sites for p53 (Wei CL et al 2006 Cell 124:207). After DNA damage, the level of p53 increases by new translation and increased half-life of its mRNA. Ribosomal protein L26 binds to the 5′-untranslated region of mRNA and enhances its translation. Protein nucleolin binds to the same region and decreases translation (Takagi M et al 2005 Cell 123:49). Tumor suppressors p53, p63 and p73 express multiple splice variants and can use different promoters, thereby determine tissue-specificity of their expression (Bourdon J-C et al 2005 Genes Dev 9:2122; Murray-Zmijewski F et al 2006 Cell Death Differ 13:962). It promotes annealing of DNAs, inhibits replication, controls G1 and G2 phase checkpoints, leads to apoptosis or just blocks cytokinesis if the DNA is damaged, interferes with tumorous growth, maintains genetic stability, reduces radiation hazards by its regulatory role in the cell cycle. For the maintenance of G2 arrest after DNA damage it also requires the presence of p21. Protein p53 binds to a somewhat conserved consensus and it is phosphorylated at serine 315 residues by CDK proteins during S, G2 and M phases of the cell cycle but not at G1 although p53 controls an important G1

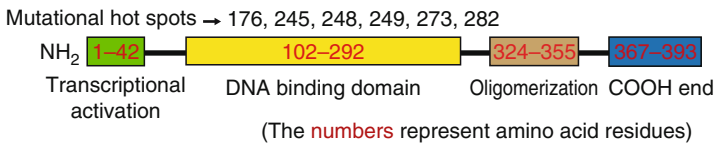

Figure P2. Structure of the p53 protein

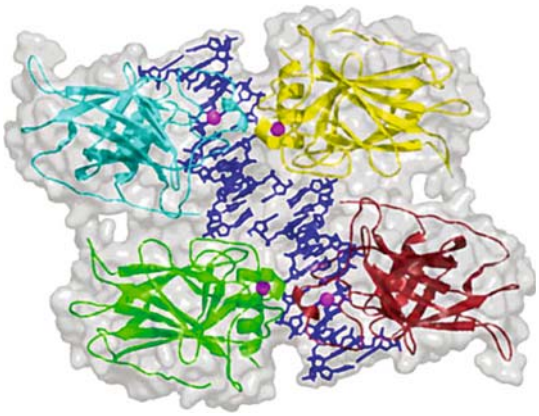

Figure P3. Ribbon diagram of the four core domains of p53 (light blue, green, yellow, maroon) interacting with DNA (dark blue). The Van der Waals surface is shown in gray; the four Zn irons are represented by mangenta spheres. (Courtesy of Professor Z. Shakked, Weizmann Institute of Science)

checkpoint. Binding subunits may have ubiquitin-conjugating role. Histone H3, methylated at lysine 79, targets 53BPP to DNA double-strand breaks (Huyen Y et al 2004 Nature [Lond] 432:406). p53 also controls proteins p21, p27 and p57. The p53 protein binds to the four copies of its consensus in DNA (5′-PuPuPuGA/T-3′). The C-terminal domain controls tetramerization and the N-terminal domain is responsible for transcriptional activation and for the regulation of down-stream genes. Small-angle x-ray scattering information in solution defined its shape, and NMR identified the core domain interfaces and showed that the folded domains had the same structure in the intact protein as in fragments. The combined solution data with electron microscopy on immobilized samples provided medium resolution 3D maps (Tidow H et al 2007 Proc Natl Acad Sci USA 104:12324).

One study indicated that at least 34 different transcripts were induced by p53 more than ten-fold although there was heterogeneity in the response. Co-activators TAFII40, TAFII 60 and other TATA box binding factors mediate its transcriptional activation. When the first six exons of the gene are deleted, the mRNA is still translated into a C-terminal protein fragment. Such a mutation enhances tumor suppression but leads to premature aging in mice (Tyner SD et al 2002 Nature [Lond] 415:45). p53 is encoded in human chromosome 17p13.105-p12; in about half of the human tumors the normal allele is altered. p53 regulates mitochondrial respiration through cytochrome oxidase c (SCO2) and may account for glycolysis in cancer cells and aging versus the respiratory pathway in normal cells (Matoba S et al 2006 Science 312:1650). Protein 53 plays a central role in cellular metabolism and its expression is induced by many factors such as oncogene expression, chemotherapy, oxidative stress, hypoxia, etc. Topoisomerase I is a p53-dependent protein. A p53-induced apoptosis may require transcriptional activation or it may occur in the absence of RNA or protein synthesis. The activation of p53 may be followed by FAS transport from Golgi intracellular stores without a need for synthesis of FAS. Tumor suppressor p53 product in the nucleus regulates pro-apoptotic genes such as *FAS, BAX, Bid, Noxa* and *PUMA*. In the cytoplasm, the p53 protein activates Bcl-2 and facilitates the permeability of the mitochondria for the release of pro-apoptotic molecules such as cytochrome c. In the cytoplasm, p53 is dislodged from Bcl-2 by PUMA to act on the mitochondrial permeability and apoptosis; thus PUMA interconnects the nuclear and cytoplasmic functions of p53 (Chipuk JE et al 2005 Science 309:1732).

The activity of p53 is also regulated by methylation of lysine 4 residues of histone-3 by Set9 methyltransferase and thereby the protein is better stabilized (Chuikov S et al 2004 Nature [Lond] 432:353). The Smyd2 protein mediates methylation of Lys370 in p53 and represses its activity; Set9 mediated methylation at Lys372 reduces methylation at Lys370 (Huang J et al 2006 Nature [Lond] 444:629). Acetylation of lysines 373 and 382 increases its DNA binding (Luo J et al 2004 Proc Natl Acad Sci 101:2259). Single nucleotide polymorphism in the promoter of MDM2 increases the affinity of the Sp21 transcriptional activator and attenuation of the p53 resulting in accelerated tumorigenesis (Bond GL et al 2004 Cell 119:591).

The ASPP family member regulatory proteins bind to the proline-rich region of p53, which contains the most common p53 polymorphism at codon 72. iASPP (inhibitory ASPP) binds to and regulates the activity of p53Pro72 more efficiently than the alternative amino codon p53Arg72. Hence, escape from negative regulation by iASPP is a newly identified mechanism by which p53Arg72 activates apoptosis more efficiently than p53Pro72 (Bergamaschi D et al 2006 Nature Genet 38:1133).

The calcium-binding proteins S100B and S100A4 bind preferentially to the tetramerization domain at lower oligomerization states, disrupt tetramerization and control intracellular movement of the p53 protein (Fernandez-Fernandez, M.R et al. 2005 Proc Natl Acad Sci USA 102:4735).

Protein p73 has functions similar to those of p53. $p33^{INGI}$, encoded at human chromosome 13q34, cooperates with p53 by protein-protein interaction in

repressing cellular proliferation and the promotion of apoptosis.

The DNA-dependent protein kinase (DNA-PK) activates p53 in case the DNA is damaged. When amino acid site 376 is dephosphorylated by ionizing radiation protein 14-3-3 binds to p53 and increases its ability for DNA binding (see Fig. P4). Still other proteins such as IRF may be involved with p53 and other cooperating proteins. p53 activity may also be affected by oncoproteins RAS and MYC. Chemotherapeutic agents, UV light and protein kinase inhibitors may also activate p53. p53 is reversibly blocked by pifithrin-α (2[2-imino-4,5,6,7-tetrahydrobenzothiazol-3-yl]-1-polyethanone) and may protect from the undesirable side effect of anticancer therapy without causing new tumors in the absence of p53 function. When 33,615 human unique genes were tested by cDNA microarrays, 1,501 genes responded one way or another to p53 (Wang L et al 2001 J Biol Chem 276:43604).

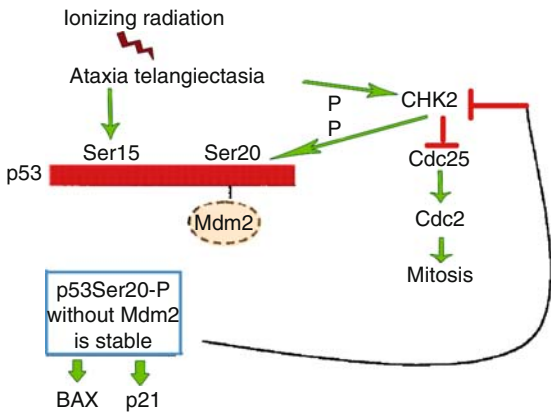

Figure P4. Some of the circuits of p53. Ionizing radiation damage to the ataxia telangiectasia protein results in the phosphorylation of the serine 15 residue of p53 and checkpoint 2 (CHK2), which in turn phosphorylates residue 20. The latter point is normally occupied by Mdm2/HDM2 a negative regulator of p53 that is now dislodged by the phosphorylation of site 20. The p53 ser20-p protein is now stabilized, despite the radiation and can induce BAX (a porin with anti-apoptosis function) and p21, a suppressor of mitosis. The blocking of CHK2 than prevents its inhibition of cell division cycle proteins (Cdc25 and Cdc2). The process to mitosis is then facilitated

Pharmacological compounds (CP-31398, CP-257042, etc.) have been selected by large-scale screening that could stabilize the DNA-binding domain of mutant p53 and activate its transcription as well as to slow tumor development in mice. In some cancers, p53 may increase sensitivity to chemotherapeutic agents but in others, it does not affect them. NADH quinone oxidoreductase may stabilize the p53 protein. Synthetic siRNA with single base difference may suppress the expression of mutation in p53 and may selectively block tumorigenesis by restoring wild type function (Martinez LA et al 2002 Proc Natl Acad Sci USA 99:14849). Using RNAi technology p53 function can be reactivated in murine liver carcinomas by triggering cellular senescence and innate immunity and consequently leading to tumor clearance (Xue W et al 2007 Nature [Lond] 445:656). Blocking p53 expression by introducing a stop cassette into the gene or removing it by the use of the Cre/loxP system, lymphomas and sarcomas of mice could be induced and then regressed after restoration of p53 function (Ventura A et al 2007 Nature [Lond] 455:661). The antiviral and anticancer effects of p53 is mediated by interferons (α and β), which boost the response to stress signals and thus promote apoptosis (Takaoka A et al 2003 Nature [Lond] 424:516).

Germline mutations occur in about 1×10^3 of the Caucasian populations but in about half of the sporadic cancers, it is somatically mutated. (Science magazine declared p53 the molecule of year 1993). ►tumor suppressor gene, ►annealing, ►apoptosis, ►PUMA, ►BCL, ►TAF, ►TBP, ►transactivator, ►nucleolin, ►cancer, ►Sp1, ►cell cycle, ►p21, ►p27, ►p40, ►p51, ►p57, ►p63, ►p73 substitution mutation, ►DAP kinase, ►MDM2, ►lactacystin, ►ARF, ►IRF, ►papilloma virus, ►DNA-PK, ►protein 14-3-3, ►E2F, ►ribonucleotide reductase, ►ataxia telangiectasia, ►CHK, ►Cdc, ►porin, ►p21, ►GADD45, ►RNAi, ►interferon, ►paired-end diTAG; Vogelstein B et al 2000 Nature [Lond] 408:307; Vousden KH 2000 Cell 103:691; Asher G et al 2001 Proc Natl Acad Sci USA 98:1183; Johnson RA et al 2001 J Biol Chem 276:27716; Olivier M et al 2002 Hum Mut 19:607; minireview: Kastan MB 2007 Cell 128:837; p53 mutation database: http://www-p53.iarc.fr/index.html; http://p53.free.fr.

p55 (TNFR1): A tumor necrosis factor receptor of Fas. ►Fas, ►TNF; Dybedal I et al 2001 Blood 98:1782; Longley MJ et al 2001 J Biol Chem 276:38555.

p56chk1: A protein kinase and a checkpoint for mitotic arrest after mutagenic damage inflicted by UV, ionizing radiation or alkylating agents. The DNA damage results then in the phosphorylation of this protein in yeasts. The phosphorylation may prevent the mitotic arrest yet the cells may die later; p56 is not involved in DNA repair. Phosphorylation is required so that other checkpoint genes become/stay functional. ►cell cycle, ►DNA repair; Feigelson SW et al 2001 J Biol Chem 276:13891.

p57 ($p57^{Kip2}$): An antimitogenic protein; its carboxyl end assures nuclear localization and the amino end is involved in the inhibition of CDK proteins. ►CDK, ►p21, ►p27, ►cell cycle, ►KIP; Thomas M et al 2001 Exp Cell Res 266:103.

$p58^{IPK}$: A heatshock protein 40 family member that inhibits interferon-induced, double-stranded RNA-activated eukaryotic translation initiation factor eIF2α protein kinase, PERK. Stress in the endoplasmic reticulum (ER) caused by unfolded proteins activates the translation of the gene and thereby reduces protein overload in the ER. ►heat-shock proteins, ►eIF2; Yan W et al 2002 Proc Natl Acad Sci USA 99:15920.

p60: Binds to Hsp70 and Hsp90 and chaperones the assembly of the progesterone complex. ►Hsp70, ►Hsp, ►progesterone, ►animal hormones, ►chaperone; Mukhopadhyay A et al 2001 J Biol Chem 276:31906.

p63: A member of the p53 tumor suppressor gene family, encoded at 3q27-q29. The gene expresses at least 6 transcripts, involved with transactivation of p53 and p73, DNA binding and oligomerization. It controls ectodermal (limb, craniofacial and epithelial) differentiation. Protein p63 regulates also the commitment to prostate cell lineage development (Signoretti S et al 2005 Proc Natl Acad Sci USA 102:11355). The first direct target of p63 appears to be the Perp protein localized in the desmosomes. Absence of Perp leads to post-natal death in mice (Ihrie RA et al 2005 Cell 120:843). Although p63 belongs to the p53 tumor suppressor family, its function seems to be different. Mouse heterozygotes for p63 were not prone chemically induced tumorigenesis (Keyes WM et al 2006 Proc Natl Acad Sci USA 103:8435). p63 protects female germ line—by apoptosis—during meiotic arrest (Suh E-K et al 2006 Nature [Lond] 444:624). Epithelial stem cells require p63 for proliferation (Senoo M et al 2007 Cell 129:523). ►p53, ►p73, ►desmosome, ►EEC syndrome, ►Hay-Wells syndrome; van Bokhoven H et al 2001 Am J Hum Genet 69:481; van Bokhoven, Brunner HG 2002 Am J Hum Genet 71:1.

p65: A component of the NF-κB complex. It can be exploited advantageously for gene activation in a chimeric construct with a mutant progesterone-receptor-ligand binding domain of gene GAL4. ►NF-κB, ►GAL4, ►gene-switch, Burcin MM et al 1999 Proc Natl Acad Sci USA 97:355.

p70/p86: The Ku autoantigen. ►DNA-PK, ►Ku

$p70^{s6k}$: Phosphorylates S6 ribosomal protein at serine/threonine residues before translation. Also called S6 kinase. ►translation initiation, ►$p85^{s6k}$, ►S6 kinase, ►signaling to translation; Harada H et al 2001 Proc Natl Acad Sci USA 98:9666.

p73: It has homology in amino acid sequence to p53 protein and is encoded in human chromosome 1p36.3. Similarly to p53, it regulates apoptosis and anti-tumor activity (upon E2F1 induction), hippocampal dysgenesis, hydrocephalus, immune reactions and pheromone sensory pathways. It affects proliferation, although in a somewhat different manner, but its loss does not lead to tumorigenesis in mice. p73 may compete with p53. This protein may have antiapoptotic effect in neurons. ►p53, ►apoptosis, ►p63, ►E2F; Sasaki Y et al 2001 Gene Ther 8:1401; Stiewe T, Putzer BM 2001 Apoptosis 6:447; Melino G et al 2002 Nature Rev Cancer 2:605.

p75: A non-tyrosine kinase receptor protein, TNFR 2 (tumor necrosis factor receptor 2). It is a Fas receptor. ►Fas, ►TNF; Hutson LD, Bothwell M 2001 J Neurobiol 49(2):79; Wang X et al 2001 J Biol Chem 276:33812.

$p80^{sdc25}$: A protein phosphatase that activates $p34^{cdc2}$-cyclin protein kinase complex by dephosphorylating Thr^{14} and Tyr^{15}. ►cell cycle, ►Ku; McNally KP et al 2000 J Cell Sci 113[pt 9]:1623.

$p85^{s6k}$: Phosphorylates S6 ribosomal protein before translation at serine/threonine sites; also called S6 kinase. p85 protein is also involved in a p53-dependent apoptotic response to oxidative damage and activation of natural killer. p85 phosphoinositide 3-kinase also mediates developmental and metabolic functions. ►translation initiation, ►$p70^{s6k}$, ►S6 kinase, ►phosphoinositides; Fruman DA et al 2000 Nat Genet 26:379.

p95: is Fas and is involved in apoptosis; its mutation leads to the Nijmegen breakage syndrome and other double breakage of the chromosomes. ►acrosomal process, ►Fas, ►APO, ►Nijmegen breakage syndrome, ►apoptosis

p97 (Cdc48): About M_r 600 ATPase and mediates membrane fusion. ►endoplasmic reticulum-associated degradation; Hirabayashi M et al 2001 Cell Death Differ 8(10):977.

p105: ►p50

p107: A retinoblastoma protein-like regulator of the G1 restriction point of the cell cycle. ►restriction point, ►tumor suppressor, ►retinoblastoma, ►cell cycle, ►pocket; Charles A et al 2001 J Cell Biochem 83:414.

p110α: The catalytic subunit of PIK. It has a critical role in insulin signaling and with TOR it controls the

development of gliomas. ►PIK/PI(3)K, ►insulin, ►glioma

p110^{Rb}: The protein encoded by the retinoblastoma (Rb) gene. When not fully phosphorylated it interferes with the G_0 and G_1 phases of the cell cycle by inhibition of the E2F transcription factor. ►retinoblastoma, ►cell cycle, ►tumor suppressor, ►E2F, ►killer cells; DeCaprio JA et al 1988 Cell 54:275.

p115: A monomeric GTPase with a specific guanine exchange factor (GEF) for RHO (p115 Rho GEF). ►GTPase, ►RHO, ►GEF; Wells CD et al 2001 J Biol Chem 276:28897.

p125^{FAK} (focal adhesion kinase): A non-receptor tyrosine kinase. ►CAM; Yurko MA et al 2001 J Cell Physiol 188:24.

p130: A retinoblastoma protein-like regulator of the G1 restriction point of the cell cycle. p130^{Cas} is involved in the organization of myofibrils, actin fibers, anchorage-dependence of cultured cells. ►restriction point, ►tumor suppressor, ►retinoblastoma, ►CAS, ►pocket; Tanaka N et al 2001 Cancer 92:2117.

p160: A family of transcriptional co-activators such as SRC-1, GRIP1/TIF2 and p/CIP. They modify chromatin structure by methylating some of the histones. ►chromatin remodeling, ►nuclear receptors, ►p/CIP; Mak HY 2001 Mol Cell Biol 21:4379.

p300 (CBP): A cellular adaptor protein preventing the G_0/G_1 transition of the cell cycle, it may activate some enhancers and stimulate differentiation. It is also a target of the adenoviral E1A oncoprotein. Its amino acid sequences are related to CBP, a CREB-binding protein. Nuclear hormone-receptors interact with CBP/p300 and participate in gene transactivation. PCAF is a p300/CBP-associated factor in mammals, and it is the equivalent of the yeast Gcn5p (general controlled nonrepressed protein), an acetyltransferase working on histones 3, 4 (HAT A) and thus regulating gene expression. p300 functions also as a co-activator of NF-κB. p300 also binds PCNA. In several human cancers, p300 mutations were identified indicating that the protein is a tumor suppressor. p300 may show ubiquitin ligase activity for p53. ►adenovirus, ►CREB, ►NF-κB, ►PCNA, ►histone acetyl-transferase, ►E1A, ►bromodomain, ►chromatin remodeling, ►histone methyltransferases, ►p53; Lin CH et al 2001 Mol Cell 8:581; ►CARM

p350: A DNA-dependent kinase, it is a likely basic factor in severe combined immunodeficiency and it may also be responsible for DNA double-strand repair, radiosensitivity and the immunoglobulin V(D)J rearrangements. In association with the KU protein, it forms a DNA-dependent protein kinase. ►severe combined immunodeficiency, ►kinase, ►KU, ►DNA-de-pendent protein kinase, ►immunoglobulins; Chan DW 1996 Biochem Cell Biol 74:67.

P450 (CYP): A family of genes coding for cytochrome enzymes involved in oxidative metabolism. They are widely present in eukaryotes and scattered around several chromosomes. All mammalian species have at least eight subfamilies. The homologies among the subfamilies are over 30% whereas the homologies among members of a subfamily may approach 70%. These cytochromes possess monooxygenase, oxidative deaminase, hydroxylation, sulfoxide forming, etc., activities. *Aspergillus oryzae* has ~149 cytochrome P450 genes in multiple copies. The proteins are generally attached to the microsomal components of homogenized cells (endoplasmic reticulum [fragments]), often called S9 fraction. Some of these enzymes (subfamily IIB) are inducible by phenobarbital. Their expression may be tissue-specific, predominant in the liver, kidney or intestinal cells. Mammalian P450 cytochrome fraction is generally added to the *Salmonella* assay media of the Ames test in order to activate promutagens. The pregnane X receptor (PXR) is activated by a variety of compounds and is thus responsible for the activation of different drugs involved in mutation, cancer and interaction with other drugs. One member of the P450 series is involved in the regulation of the synthesis of the 6th class of plant hormones, brassinosteroids. P450 enzymes require the cofactor NAD or NADPH and their activity is favored by the presence of peroxides as oxygen donors. By mutagenesis, industrially more useful P450 variants are being produced. The P-450 (CYP1A1) dioxin and aromatic compound-inducible P450 maps to human chromosome 15q22-qter. CYP1A2 is phenacetin O-deethylase. Phenacetin is an analgesic and antipyretic carcinogen. CYP2D (22q13.1) is a debrisoquin 4-hydroxylase. Debrisoquine is a toxic anti-hypertensive drug. CYP51 (7q21.2-q21.3) is lanosterol 14-α-demethylase is a sterol biosynthetic protein. ►Ames test, ►cytochromes, ►hypoaldosteronism, ►steroid hormones, ►brassinosteroids, ►peroxide, ►NAD, ►analgesic, ►antipyretic, ►cyclophilin; Fujita K, Kamataki T 2001 Mutat Res 483:35; Ingelman-Sundberg M 2001 Mutat Res 482:11; crystal structure of p450 3A4: Williams PA et al 2004 Science 305:683.

P Blood Group: Controlled by two non-allelic loci. The non-polymorphic P blood group is located in human chromosome 6 and it is encoding globoside whereas the polymorphic P1 locus in human chromosome 22 encodes paragloboside. The frequency of the P gene in Sweden was found to be 0.5401 and that of P1 0.4599. According to other studies, the frequency of

P among caucasoids is about 0.75. The P1 blood type facilitates bacterial attachment to the epithelial cells of the urinary tract and kidney. Therefore, infections are more common. Some P alleles raise the risk of abortions, and others may increase the chances of stomach carcinomas. Some of the literature calls P as P1 and P1 as P2. ►blood groups, ►globoside; Stroud MR 1998 Biochemistry 37:17420.

P Body (processing bodies, cytoplasmic body): A small number of specific sites in the cytoplasm involved in the decapping of mRNA after deadenylation of the polyA tail. At this location, mRNAs occur at various stages of degradation mediated by several proteins. Argonaute 2 of the RISC complex of RNAi is also localized in the P bodies (Sen GL, Blau HM 2005 Nat Cell Biol 7:633). The mammalian protein elongation factor eIF4E, its transporter (eIF4E-T) as well as the DEAD-box helicase rck/p54 are also located at these cytoplasmic sites (Andrei MA et al 2005 RNA 11:717). P bodies can recycle to the polysomes and when conditions are favorable can be translated (Brengues M et al 2005 Science 310:486). ►decapping, ►mRNA, ►RNAi, ►microRNA, ►eIF-4E, ►DEAD-box, ►RNA surveillance; Sheth U, Parker R 2003 Science 300:805; review: Parker R, Sheth U 2007 Mol Cell 25:635.

P1 Cloning Vectors: They have a carrying capacity up 100 kbp DNA; thus they fall between Lambda and YAC vectors. ►vectors, Park K, Chattoraj DK 2001 J Mol Biol 310:69; Grez M, Melchner H 1998 Stem Cells 16(Suppl. 1):235.

P Cytotype: ►hybrid dysgenesis

P Element: ►hybrid dysgenesis

P Element Vector: Constructed from the 2.9 kb transposable element P of *Drosophila* equipped with 31 bp inverted terminal repeats. The gene to be transferred is inserted into the element but in order to generate stable transformants the transposase function located in the terminal repeats is disabled. Functional transposase is provided in a separate helper plasmid (pπ25.7wc). Such a binary system permits the separation of the two plasmids and the screening of the permanent transgenes if a selectable marker is included. Both plasmids are mixed in an injection buffer and delivered into pre-blastoderm embryos. The various P vectors have been widely used in for gene tagging, induction of insertional mutation and for exploration of functional genetic elements in *Drosophila* and in some other insects. A newer type of vector, Pacman contains the P transposase and the phage φC31 integration site. The φC31 integrase mediates recombination between the engineered phage *attP* in the *Drosophila* genome and a bacterial *attB* site in an injected plasmid. Such a system permits integration of large tracts of DNA (up to 133 kb) at specific sites. Such a targeted transgenesis can rescue much larger lethal mutations than it would be possible with only P element (Venken KJT et al 2006 Science 314:1744). ►hybrid dysgenesis, ►transposon vector, ►*att* sites; Sullivan W et al 2000 *Drosophila* Protocols, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York.

P Granule: Serologically definable elements in the cytoplasm of animal cells at fertilization that segregate to the posterior part of the embryo where stem cell determination takes place. During embryogenesis, the P granules (RNA) may segregate asymmetrically into the blastomeres that produce the germline. (See Harris AN, Macdonald PM 2001 Development 128:2823).

P Nucleotides: ►immunoglobulins

P1 Phage: An *E. coli* transducing phage and vector with near 100 kb carrying capacity. (See Lehnherr H et al 2001 J Bacteriol 183:4105).

P22 Phage: The temperate bacteriophage of *Salmonella typhimurium*; its genome is about 41,800 bp. (See Vander Byl C, Kropinski AM 2000 J Bacteriol 182:6472).

P1 Plasmid: A cloning vector with a carrying capacity of about 100 kb. ►vectors, ►P1 phage; Bogan JA et al 2001 Plasmid 45(3):200.

P Region of GTP-Binding Proteins: Shares the G-X-X-X-X-G-K-(S/T) motif (►amino acid symbols) and is suspected to involve the hydrolytic process of GTP-binding and several nucleotide triphosphate-utilizing proteins. ►GTP binding protein superfamily

P Site: The peptidyl site on the ribosome where the first aminoacylated tRNA moves before the second charged tRNA lands at the A site as the translation moves on. The binding of the tRNA to the 30S ribosomal subunit appears to be controlled by guanine residues at the 966, 1401 and 926 positions in the 16S rRNA. ►A site, ►protein synthesis, ►ribosome; Feinberg JS, Joseph S 2001 Proc Natl Acad Sci USA 98:11120; Schäfer MA et al 2002 J Biol Chem 277:19095.

PABp: The poly(A) binding protein (~72 kDa) is the major protein that binds to the poly A tail of eukaryotic mRNA and converts it to mRNAP. Pab1p connects the mRNA end to the eIF-4H subunit of the eukaryotic peptide initiation factors eIF-4G and eIF-4F. It contains four RRM motifs. PABp also interacts with PAIP a translational co-activator protein in mammals. ►binding proteins, ►mRNAP, ►mRNA

tail, ►polyadenylation signal, ►mRNA decay, ►eIF-4F, ►eIF-4G, ►Xrn1p, ►ribosome scanning, ►translation initiation, ►translational termination, ►RRM, ►mRNA circularization; Kozlov G et al 2001 Proc Natl Acad Sci USA 98:4409.

PAC (phage artificial chromosome): P1 phage PAC carries about 100–300 kb DNA segments. Most PAC vectors lack selectable markers suitable for mammalian cell selection but can be retrofitted by employing the Cre/loxP site-specific recombination system. ►BAC, ►YAC; Poorkaj P et al 2000 Genomics 68:106.

pac: A site in the phage genome where terminases bind and cut during maturation of the DNA before packing it into the capsid. ►terminase, ►packaging of the DNA

PAC-1: Dephosphorylates Thr^{183} and Tyr^{185} residues and thus regulates mitogen-activated MAP protein kinase involved in signal transduction. The Pac1 nuclease removes the 3′ external transcribed spacers from the nascent rRNAs in cooperation with RAC. PAC1 is activated by p53 protein during apoptosis and suppresses carcinogenesis. ►MAP, ►MKP-1, ►apoptosis, ►p53; Boschert U et al 1997 Neuroreport 8:3077; Spasov K et al 2002 Mol Cell 9:433.

PACAP (pituitary adenylyl cyclase-activating polypeptide-like neuropeptide): A neurotransmitter at the body-wall neuromuscular junction of *Drosophila* larvae. It mediates the cAMP-RAS signal transduction path. ►signal transduction, ►RAS, ►RAF; Kopp MD et al 2001 J Neurochem 79:161.

Pacemaker: Maintains rhythmic balance like the pulse of the heart or circadian rhythm.

Pachynema: Literally "thick thread" of chromosomes at early meiosis when the double-stranded structure of the chromosomes is not distinguishable by light microscopy because the chromatids are tightly appositioned (see Fig. P5). Also, the two homologous chromosomes are closely associated, unless structural differences prevent perfect synapsis. If a pair of chromosome is not completely synapsed by pachytene, they will not pair later either. In pachytene the chromosomal knobs and chromomeric structure is visible and can be used for identification of individual chromosomes. After pachytene, the synaptonemal complex is dismounted and the chromosomes progressively condense. In case the chromosomes are defective at this stage the Red1 (required for chromosome segregation) and Mek1 proteins serve as checkpoint control by preventing further progress of meiosis. Normally MEK kinase phosphorylates Red. Phosphatase Glc7 dephosphorylates Red. More than two dozens of other proteins (named differently in different organisms) are also involved in pachytene controls. ►meiosis, ►pachytene analysis, ►synapsis, ►chiasma, ►chromomere, ►MEK; Bailis JM, Roeder GS 2000 Cell 101:211; Roeder GS, Bailis JM 2000 Trends Genet 16:395.

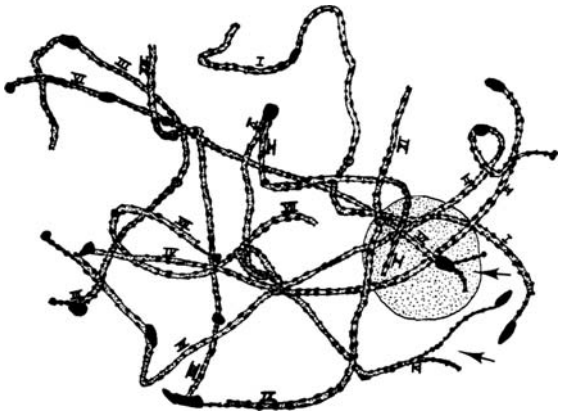

Figure P5. Naturalistic drawing of the 10 pachytene chromosome pair of a teosinte x maize hybrid. Note (←) unpaired ends of chromosomes V, VII. And some terminal and near-terminal knobs (Courtesy of Dr. A. E. Longley, see also 1937 J Agric Res 54:835)

Pachyonychia: A rare autosomal dominant keratosis of the nails and skin. ►keratosis

Pachytene Analysis: The study of meiotic chromosomes at the pachynema stage when cytological landmarks, chromomeres, and knobs are distinguishable by the light microscope, and chromosomal aberrations (deletions, duplications, inversions, translocations, etc.) can cytologically be identified and correlated with genetic segregation information. The pachytene analysis of plants is analogous to the study of giant chromosomes in dipteran flies and other lower animals. The bands of the (somatic) salivary chromosomes are tightly appositioned chromomeres in these endomitotic chromosomes. ►meiosis, ►salivary gland, ►chromomere, ►endomitosis, ►recombination nodule; McClintock B 1931 Missouri Agric Exp Sta Bull 163; Carlson WR 1988 In: Corn and Corn Improvement, Agricultural Monograph 18, ASA-CS-SSA, Madison, Wisconsin, p 259.

Pachytene Stage: The chromosomes form pachynema. pachynema.

Packaging Cell Lines (For Retroviral Vectors): For the replication of the vector the viral proteins gag, pol, env are required but these are deleted from the vectors to prevent the production of disease-causing virions. The packaging signal ψ is however retained in the vector. Another solution is to insert these viral genes

into host chromosomes or remove from the helper virus the packaging signal (Ψ [psi]) and delete the 3′-LTR. In neither case could the production (by two recombinations) of replication-competent virions be completely eliminated. Thus, the nucleic acid (with the transgene) can be packaged although the virions are defective. An improved construct removed LTRs from the structural genes and replaced them with heterologous promoters and polyadenylation signals. The *gag* and *pol* genes are placed on a plasmid different from the one that carries the *env* gene. Thus, in the packaging cell lines, these two are inserted at different chromosomal sites. Also, if the number of cell divisions is limited, the chance of recombination between vector and helper is reduced. In an improved packaging system, a stop codon is engineered into *gag* reading frame to prevent the assembly of a fully competent virus. In the packaging cell lines, the appropriate envelope protein for the intended target (ecotropic or amphotropic) should be present in the helper virus (pseudotyping) to insure optimal transfection. The envelope protein may need modification in order to ensure the proper targeting to the intended types of cells. Antibodies, specific for certain cell surface antigens or against particular receptors may be employed. Although some of these procedures appear very attractive, they may not always be equally efficient. These technical problems are obviously attracting serious research efforts. ►retroviral vectors, ►ecotropic retrovirus, ►amphotropic retrovirus, ►pseudotyping, ►viral vectors; Thaler S, Schnierle BS 2001 Mol Ther 4(3):273.

P

Packaging of Phage DNA: λ phage gene A recognizes the cos sites, gene D assists in filling the head (capsid) and genes W, F, V ILK and GMH assemble the phage from prefabricated elements and act in the processes shown diagrammatically in Fig. P6.

The DNA that first enters the phage capsid has the Nu end and the opposite end (the last) is the R end. The organization of the DNA in the phage head is not random; the geometry of the arrangement is determined by writhe of the DNA (Arsuaga J et al 2005 Proc Natl Acad Sci USA 102:9165). ►lambda phage, ►p16, ►development, ►writhing number, ►heedful rule; Smith DE et al 2001 Nature [Lond] 413:748, Kindt J et al 2001 Proc Natl Acad Sci USA 98:13671.

Packaging Signal (ψ): Allows the stuffing of the viral genome into the viral capsid.

Packing Ratio: The DNA molecule is much-much longer than the most extended chromosomes fibers. The packing ratio was defined as the proportion of the DNA double helix and the length of the chromosome fibers. In the human chromosome complement, the packing ratio was estimated to be more than 100:1 at metaphase. The length of the *Drosophila* genome at meiotic metaphase was estimated to be 7.8 μm and the length of a chain of 3000 nucleotides is approximately 1 μm. The *Drosophila* genome contains about 9×10^7 bp, hence the total length of DNA within the *Drosophila* genome is about 30,000 μm and that would indicate a packing ratio of 3846:1. The packing ratio indicates some of the problems the eukaryotic chromosomes encounter in condensing an enormous length of DNA to a small space and still replicating, transcribing and recombining it in an orderly manner. To illustrate the problems in a trivial way: many eukaryotes have the same packing problem as folding a 2.5 km (1.6 mi) long thread into a 2.5 cm (1″) skein. Prokaryotic type DNA—such as without nucleosomal structure—the excessive amount of plasmid DNA forms liquid crystalline molecular supercoils. ►Mosolov model, ►supercoiled DNA; see photo of bacterial chromosome at lysis, p. 1,150; DuPraw EJ 1970 DNA and Chromosomes. Holt, Rinehart and Winston, New York; Holmes VF, Cozzarelli NR 2000 Proc Natl Acad Sci USA 97:1322; Cook PR 2002 Nature Genet 32:347.

Pack-MULEs: The abundant (3000/rice genome) transposable elements in different plant species that carry fragments of cellular genes (~1000 in rice) derived from all chromosomes. These fragments can have multiple chromosomal origins, and can be functional. During millions of years, the fragments could be rearranged, amplified and contributed to evolution of plant genes. ►transposable elements plants; Jiang N et al 2004 Nature [Lond] 431:569.

Paclitaxel: ►taxol

Pac-Man Model: Kinetochores induce depolymerization of the microtubules of the kinetochore at their plus end and that allows the sister-chromatids to move toward the poles during mitosis by, so to say, chewing

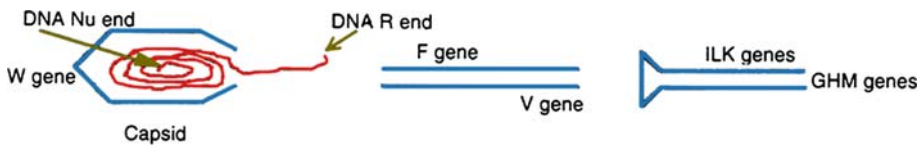

Figure P6. Packaging of phage DNA

up spindle fiber tracks. ►anaphase, ►spindle fibers, ►microtubules, ►kinetochore; Rogers GC et al 2004 Nature [Lond] 327:364; Liu J, Onuchic JN 2006 Proc Natl Acad Sci USA 103:18432.

PACT (p53 associated cellular protein): A negative regulator of p53. ►p53

Pactamycin: An inhibitor of eukaryotic peptide chain initiation (see Fig. P7).

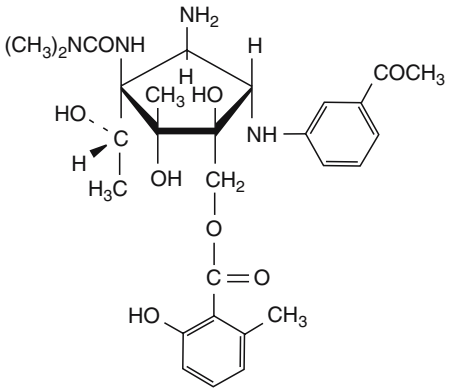

Figure P7. Pactamycin

PAD4: peptidylarginine deiminase. It converts methylarginine to citrulline and releases methylamine. It targets also multiple sites in histones H3 and H4. ►arginine, ►citrulline, ►methylation of DNA, ►histones, ►epigenesis; Wang Y et al 2004 Science 306:279.

Padlock Probe: Contains two target-complementary segments connected by linker sequences (see Fig. P8). Hybridization to target sequences brings the two ends close to each other and can be covalently ligated. The so circularized probes are thus catenated to the DNA (≈) like a padlock (OO). Such probes permit high-specificity detection and distinction among similar target sequences and can be manipulated without alterations or loss. By using circularizable or circularized allele-specific probe, primers and rolling circle, amplification can detect mutations in short genomic sequences (see Fig. P9). The principle of the procedure is shown modified after Lizardi PM et al 1998 Nature Genet 19:225.

Figure P8. Padlock

Alternatively, for the rolling circle amplification two primers were used (see Fig. P10). After the first primer (P1) initiated the replication the second (P2) primer is bound to the tandem repeats and both primers generate repeats in opposite directions ⮌ or ⮎ using either the (+) or (−) strands, respectively. In 90 min, at least 10^9 copies of the circles are generated making it possible to detect very rare somatic mutations. Rolling circle amplification can detect gene copy number single base mutations and can quantify the transcribed mRNA (Christian AT et al

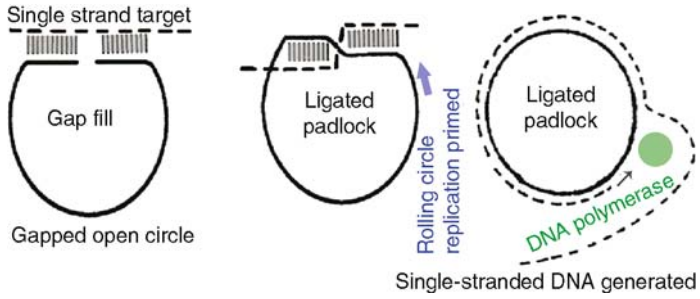

Figure P9. The probe at left, interrupted by a 6- to 10-base gap, hybridizes to the target DNA. The gap is filled with an allele-specific or DNA polymerase-generated sequence. After ligation, it generate a closed duplex padlock. A complementary (18-base) primer was then employed with a DNA polymerase. The original target DNA is not shown

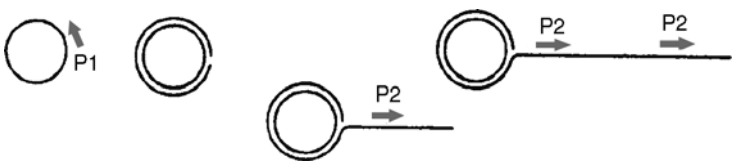

Figure P10. Padlock primers

2001 Proc Natl Acad Sci USA 98:14238). The procedure generated replication products, which were hybridized to either fluorescein- or Cy3-labeled deoxyribonucleoprotein-oligonucleotide (DNP) tags, respectively. The tag was anti-DNP immunoglobulin M (IgM). This process of condensation of amplification circles after hybridization of encoding tags is called CACHET. The procedure permits also the identification of single-copy genes by epifluorescence microscopy. ►probe, ►rolling circle, ►fluorochromes, ►immuno-globulins, ►DNA polymerases, ►microscopy, ►mutation detection; Baner J et al 2001 Curr Opin Biotechnol 12:11; Roulon T et al 2002 Nucleic Acids Res 30 (3):e12.

Padumnal Allele: Derived from the male. ►madumnal allele

PAF (population attributable fraction): PAF represents the fraction of the disease that would be eliminated if the risk factor were removed. High risk alleles generally show PAF > 50% whereas in rare alleles in common diseases it is generally <10%. The common modest-risk alleles account for greater PAF in common diseases than the rare high-risk alleles. This hypothesis is called the common disease/common variant (CDCV). ►complex disease, ►QTL, ►correlation, ►association, ►HapMap; Carlson CS et al 2004 Nature [Lond] 429:446.

PAF: A positive and negative regulator of RNA polymerase II mediated transcription (Shi X et al 1996 Mol Cell Biol 16:669). The Paf complex has a role also in polyadenylation of mRNA.

PAF-AH: platelet activating factor acetylhydrolase coupled with dynein affects neural migration in lissencephaly. ►lissencephaly, ►dynein; Tarricone C et al 2004 Neuron 44:809.

Page: An acronym for polyacrylamide gel electrophoresis. ►gel electrophoresis

Paget Disease: Two autosomal dominant forms have been described involving cancer of the bones or of the anogenital region (the region of the anus and genitalia) or the breast. The disease is an anomaly of osteoclastogenesis. BDB1 gene was located to 6p21.3 and PDB2 (also called familial expansile osteolysis, FEO) to 18q21-q22. Mutations in the tumor necrosis factor receptor, TNFR seem to be involved and affect the signaling by NF-κB (RANK, receptor activator of nuclear factor κB). Additional loci mapped to 5q35-qter (PDB3), to 5q31 (PDB4), to 2q36 (PDB5) and 10p13 (PDB6). ►osteoclast, ►osteoporosis, ►NF-κB, ►TNFR; Laurin N et al 2001 Am J Hum Genet 69:528.

PAH (polyaromatic hydrocarbon): The majority of PAH are carcinogenic (see Fig. P11).

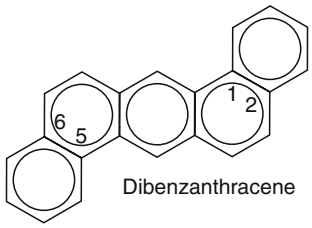

Figure P11. PAH

PAH (paired amphipathic helix motif): It may mediate protein-protein interactions in regulating enzyme functions. ►amphipathic

PAI: plasminogen activation inhibitor. ►plasminogen activator; Eilers AL et al 1999 J Biol Chem 274:32750.

Pain-Insensitivity: Controlled by defects causing hereditary sensory neuropathies. In the dominant form, the dorsal ganglia are degenerated. In the recessive neuropathy, the loss of myelinated A-fibers cause touch insensitivity. The congenital pain insensitivity with anhidrosis (CIPA, 1q21-q22) involves a defect of the nerve growth factor receptor (TRKA), and in the congenital insensitivity to pain without anhidrosis, the small myelinated A-delta fibers are defective. Mutation in the Na-channel subunit (SCN9A, encoded at 2q24.3) leads to pain-insensitivity (Cox JJ et al 2006 Nature [Lond] 444:894). The apparent insensitivity to the self-torture of the fakirs (Hindu ascetics) may be based on such genetic condition. ►neuropathy, ►Riley-Day syndrome, ►TRK, ►sensory neuropathy 1, ►anhidrosis; Mardy S et al 2001 Hum Mol Genet 10:179; Cheng H-YM et al 2002 Cell 108:31.

Pain-Sensitivity: May be traditionally treated with analgesics. Gene therapy by introduction of genes producing analgesic substances (catecholamines, enkephalins) or antinociceptive peptides are potential molecular approaches. The capsaicin or vanilloid receptor (VR1) control heat-gated ion channel with response to low temperature (~43°C) stimuli whereas the VRL-1 receptor responds to about 52°C. The vanilloid channel receptor is induced by protein kinase C. The transcriptional repressor DREAM constitutively suppresses prodynorphin in the neurons of the spinal chord. When DREAM is knocked out, there is still sufficient expression of dynorphin but there is a strong reduction in pain-sensitivity. Single amino acid substitutions (val^{158}/met) in catechol-*O*-methyltransferase (COMT) may modulate pain sensitivity/insensitivity. Simultaneous, two synonymous and one

non-synonymous, divergence in the human haplotype of the gene modulate COMT protein expression by altering mRNAs secondary structure (Nackley AG et al 2006 Science 314:1930). Prostaglandin E^2 is a mediator of inflammatory pain-sensitization via glycine receptor α3 (Harvey RJ et al 2004 Science 304:884). Expectation of pain reduced the subjective feeling of pain as well as activation of pair-related areas of the brain (Koyama T et al 2005 Proc Natl Acad Sci USA 102: 12950). Covalent modification of reactive cysteines within TRPA1 (Transient Receptor Potential family of ion channels) by noxious compounds causes channel activation, rapidly signaling potential tissue damage through the pain pathway (Macpherson LJ et al 2007 Nature [Lond] 445:541). ►analgesic, ►nociceptor, ►catecholamines, ►enkephalins, ►endorphin, ►dynorphin, ►DREAM, ►protein kinase, ►prostaglandins, ►allodynia, ►temperature-sensitive mutation; Samad TA et al 20001 Nature [Lond] 410:471; Costigan M, Woolf CJ 2002 Cell 108:297; Mantyh PW et al 2002 Nature Rev Cancer 2:201; Zubieta J-K et al 2003 Science 299:1240.

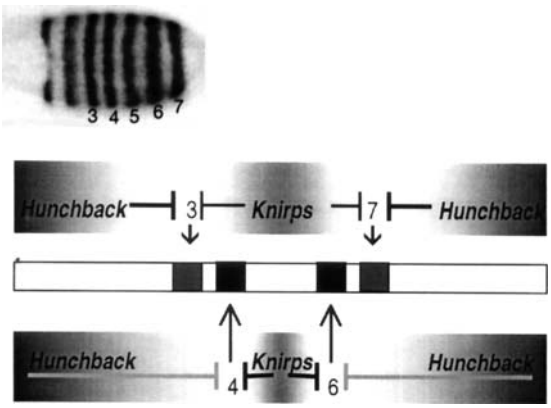

Figure P12. Pair rule genes. The banding pattern on the body of the Drosophila embryo is under the control of several regulatory genes. In the case of the *even-skipped* gene (chromosome 2.58) the seven stripes in the syncytial blastoderm are under the control of five enhancers. Three of them #1, #2, #3) drive the expression of single stripes and the remaining two control the expression of pairs of stripes (3 + 7 and 4 + 6). The stripes are formed at the boundary of interactions of the suppressor gradients of genes *Hunchback* (encoded at 3.48) and *Knirps* (encoded at 3.46) and the *even-skipped* enhancers. It is assumed that binding-site affinity and distribution on the enhancers determine the sensitivity to the repressors as illustrated on the diagram. The four bands in the middle represent body stripes (not chromosome bands!) brought about by the interactions of the suppressor gradients. (Modified after Clyde DE et al 2003 Nature [Lond] 426:849)

Pair Rule Genes: Determine the formation of alternating segments in the developing embryo as shown in Figure P12. Similar segment pattern, although with variations, occurs in other insects too. ►morphogenesis in *Drosophila*, ►metamerism, ►*fushi tarazu*, ►*knirps*, ►*engrailed*, ►*Runt*

Paired Box Genes: ►PAX

Paired t-Test: ►matched pairs test, ►Student's *t* distribution, ►*t* value

Paired-End diTAG (PET): PET uses chromatin immunoprecipitation to enrich DNA fragments for the mapping transcription factors across the genome. It separates signature sequences from the 5′ and 3′ ends of the fragments, concatenates them and maps them (Ng P et al 2005 Nat Methods 2:105). ►immunoprecipitation, ►transcriptome, ►transcription factor map

Paired-End Sequence: The product of the first sequencing of both ends of a cloned DNA tract. (See Zhao S et al 2000 Genomics 63:321).

Paired-End Sequence Method: The method used to identify structural alterations in the DNA. The standard genome sequence is compared with another genome represented by fosmid paired-end sequences (see Fig. P13). The procedure detects fine-scale variations in the genome that may be important for disease. ►fosmid; Tuzun E et al 2005 Nature Genet 37:727.

Pairing (synapsis): The intimate association of the meiotic chromosomes mediated by several protein factors. In prokaryotes, the RecA and the RecT protein have important role and in yeast and humans, the Rad52 protein carries out similar functions. ►meiosis, ►zygotene, ►pachytene analysis, ►somatic pairing, ►hydrogen pairing, ►base pair, ►tautomeric shift, ►synapsis,

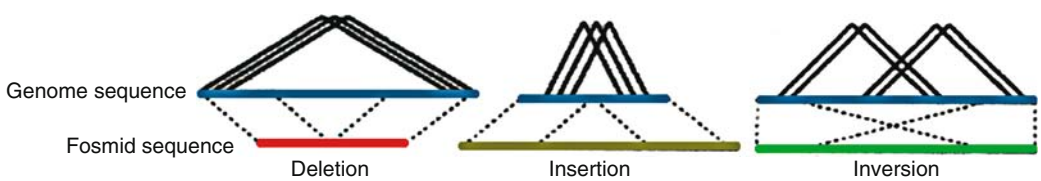

Figure P13. Paired-ed sequence method

►RecA, ►RecT, ►Rad, ►*Ph* gene; Kagawa W et al 2001 J Biol Chem 276:35201.

Pairing Alkylated Bases: ►alkylation

Pairing Centers: The cis-acting sites required for accurate segregation of homologous chromosomes during meiosis of *Caenorhabditis elegans* (MacQueen AJ et al 2005 Cell 123:1037). The *HIM-8* gene, encoding a zinc-finger protein, concentrates at the pairing centers on the X chromosome mediates chromosome-specific synapsis (Phillips CM et al 2005 Cell 123:1051).

Pairing-Sensitive Repression: Polycomb (PC) proteins bind to Polycomb-response elements (PREs) and thus cause repression. Repression is enhanced when two such elements are present. There are other similar elements like Mcp. ►Polycomb

Pair-wise Likelihood Score: Estimates the potential relationship between pairs of individuals on the basis of allele sharing. (See Smith BR et al 2001 Genetics 158:1329).

PAK (p21 activated kinase): The serine/threonine kinases activated by GTPases, Rac and Cdc42. Pak3 regulates Raf-1 by phosphorylating serine 338 in rats. Paks regulate the actin cytoskeleton, cell motility, neurogenesis, angiogenesis, signal transduction, apoptosis, metastasis, etc. A non-syndromic mental retardation (human chromosome Xq22, yeast homolog is *STE20*) prematurely terminates PAK3 transcription. ►GTPase, ►Rac, ►raf, ►Cdc42, ►p21, ►p35, ►PDK, ►actin, ►cytoskeleton, ►apoptosis, ►mental retardation, ►non-syndromic; Xia C et al 2001 Proc Natl Acad Sci USA 98:6174; Bokoch GM 2003 Annu Rev Biochem 72:743.

PAL: Phenylalanine ammonia lyase.

Palea: The inner, frequently translucent, bract around the grass flower (see Fig. P14).

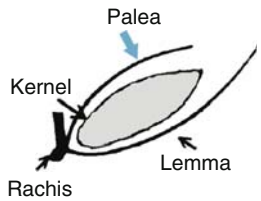

Figure P14. Palea

Paleogenomics: ►ancient DNA

Paleolithic Age (Old Stone Age): More than 20,000 years ago it marked the beginning of human tool formation and cave artistry by the Cro-Magnon humans. ►neolithic, ►mesolithic, ►geological time periods, ►Lascaux, ►Neanderthal

Paleologous Loci: Include ancient duplications.

Paleontology: Deals with the relics of past geological periods. Its methods and materials are used for the study of the evolution of biological forms. ►paleolithic age, ►geological time periods; Eurasian Miocene and Pleistocene land mammals and excavation sites: http://www.helsinki.fi/science/now/.

Paleozoic: The geological period between about 225 to 570 million years ago. During the later part of this period land plants, amphibians and reptile appeared. ►geological time periods

Palindrome: The region of a DNA strand where complementary bases are in opposite sequence, such as ATGCAC*GTGCAT (see Fig. P15). Palindromes may come about by inverted repeats of sections of the double-stranded DNA where these sequences of the opposite strands read the same forward and backward. Upon folding of these sequences in a single strand, they can assume structures with paired bases.

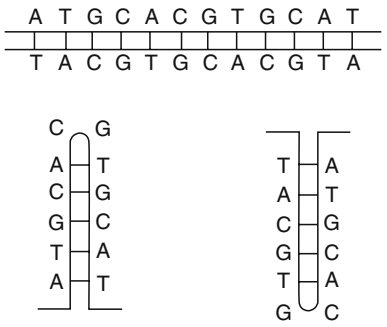

Figure P15. Palindromic DNA and possible pairing within single strands of it. (From Flavell RB, Smith DB 1975 Stadler Symp 7:47)

Palindromic sequences in the DNA reassociate very rapidly because of the complementary bases are in close vicinity. A simple palindromic word is MADAM, it reads the same from left to right or from right to left. Palindromic sequences are often unstable; recombination within palindromes results in deletions and duplications. The restriction enzyme recognition sites are palindromic. Palindromes are common in cancer cells and provide a platform for gene amplification and chromosomal aberrations (Tanaka H et al 2005 Nature Genet 37:320). ►stem and loop, ►inverted repeats, ►insertion elements, ►restriction enzyme, ►RecA independent recombination; Leach DR 1994 Bioessays 16:893; Nasar F et al 2000 Mol Cell Biol 20:3449; Zhu Z-H et al 2001 Proc Natl Acad Sci USA 98:8326; short

palindromic repeat detection: http://crispr.u-psud.fr/Server/CRISPRfinder.php.

Palingenesis: The regeneration of lost organs and parts or the reappearance of evolutionarily ancestral traits during ontogeny. According to Ernst Haeckel (1834–1914) the ontogeny recapitulates the phylogeny. ►ontogeny, ►phylogeny

Palisade Cells: Oblong cells and arranged in a row; the large palisade parenchyma cells are below the upper epidermis of plant leaves and loaded with chloroplasts (see Fig. P16).

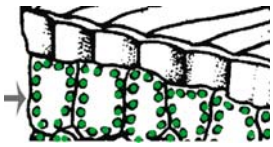

Figure P16. Palisade cells in a leaf

Pallister-Hall Syndrome: postaxial polysyndactyly (PAPA1), encoded in human chromosome 7q13, at the same location as the Greig syndrome. The gene is also called GLI3 and its product has a homology to the *Drosophila* Krüppel Zn-finger protein. The clinically distinct phenotypes of the two diseases are due to different allelic mutations of the same gene (Johnston JJ et al 2005 Am J Hum Genet 76:609). A similar syndactyly was recorded by French scientist, Maupertuis, in the Prussian royal court in Berlin in 1756. ►polydactyly, ►Greig cephalopolysyndactyly, ►DNA-binding protein domains, ►EEC syndrome, ►Smith-Lemli-Opitz syndrome

Palmitoylation: The covalent attachment of fatty acids (mainly palmitate) to cysteine residues to membrane proteins by creating a thioester link. This process tethers protein reversibly to cellular membrane surfaces. The enzymes involved belong to the protein acetyltransferase (PAT) family (e.g., Akr1, Erf2) and share a common domain of DHHC (aspartate-histidine-histidine-cysteine; see Mitchell DA et al 2006 J Lipid Res 47:1118). Palmitoylated proteins play key roles in cell signaling, membrane traffic, cancer and synaptic transmission, heterotrimeric G proteins and many non-receptor tyrosine kinases (Fyn, Lck, Yes) and the epithelial nitric oxide synthase are palmitoylated. By proteomic analysis, 35 new PAT proteins have been identified in budding yeast (Roth AF et al 2006 Cell 125:1003). ►fatty acids, ►G proteins, ►Fyn, ►Lck, ►Yes, ►nitric oxide

Palmprint: ►fingerprint, ►Down's syndrome, ►simian crease

Palomino: A horse with light tan color fur and flaxen mane and tail. The genetic constitution is *AAbbCCDd* (see Fig. P17).

Figure P17. Palomino

PALS: ►alternative splicing

Palsy (paralysis): Cerebral palsy may be caused by physical injuries or may be part of the symptoms of diverse genetic syndromes. ►syndrome, ►tau

PAM: ►evolutionary clock

PAMAM (polyamidoamine): The dendrimers can carry chemotherapy compounds (methotrexate) to the cancer cell, especially if connected with folate hooks that attach preferentially to the abundant folate receptors of cancer cells. ►dendrimer, ►methotrexate, ►nanotechnology; Najlah M et al 2007 Bioconjug Chem 18:937.

PAMP: pathogen-associated molecular pattern recognition is an important step in developing reaction in animals and plants against infection. ►vaccine

PAN: The genus of chimpanzees. ►primates, ►hominidae; Gagneux P 2002 Trends Genet 18:327.

PAN Editing: Adding of U residues to the primary transcripts of mtDNA and thus causing extensive post-transcriptional changes in RNA. ►kinetoplast, ►RNA editing

Pancreas: A large gland behind the stomach, between the spleen and the duodenum. It secretes insulin, glucagons, and protein-digesting enzymes. ►spleen, ►duodenum, ►insulin, ►glucagons, ►diabetes, ►Langerhans islets, diabetes: http://www.cbil.upenn.edu/EPConDB.

Pancreatic Adenocarcinoma: The cancer of the pancreas is frequently associated with loss or defect of DCC, or p53 or MTS1 oncogene suppressors. One study revealed an average of 15 annotated gene alterations (amplifications, deletions, tumor suppressors) in 24 adenocarcinoma lines (Aguirre AJ et al 2004 Proc Natl Acad Sci USA 101:9067). It was also attributed to mutations in codon 12 of the c-K-ras

(Kirsten RAS) gene encoded at human chromosome 12p12. A dominant susceptibility locus was assigned to 4q32-q34. Chromosomal aberrations, telomere shortening, methylation of CpG islands and point mutation may be the underlying cause. Silencing of cancer suppressors by hypermethylation at multiple genes may be involved. HER2/NEU overexpression is also a frequent cause. Tyrosine-kinase growth factor receptors may be involved. It may be associated with the Peutz-Jeghers syndrome (66%) and other syndromes such as hereditary pancreatitis (40%), BRCA2 (5–10%), etc. Its prevalence in the USA is $\sim 3 \times 10^{-5}$, and its prognosis is bad. ►DCC, ►p53, ►p16, ►Kirsten-Ras, ►p21, ►Peutz-Jeghers syndrome, ►HER2, ►NEU; Eberle MA et al 2002 Am J Hum Genet 70:1044; Hansel DE et al 2003 Annu Rev Genomics Hum Genet 4:237.

Pancreatitis, Hereditary: Autosomal dominant (7q35) gene (80% penetrance and variable expressivity) has an onset before the teen years, appearing as abdominal pain and other anomalies. The basic defect is in a cationic trypsinogen. ►trypsin, ►Johanson-Blizzard syndrome

Pancytopenia: Low blood cell number.

Panda (*Ailurus fulgens*): 2n = 36.

Pandemic: The infection by a microbe or virus spread over large areas (countries, continents).

Paneth's Cells: The secretory intestinal epithelial cells expressing defensin and other antimicrobial peptides. In the Paneth cells of mice, 149 transcripts expressed 2 to 45-fold by microbial colonization. Among them was very abundant (31-fold increase) a bactericidal lectin (RegIIIγ) that may represent a primitive evolutionary form of innate immunity (Cash HL et al 2006 Science 313:1126). ►defensin, ►microbiome; Ghosh D et al 2002 Nature Immunol 3:583.

Pangenesis: An ancient misconception about heredity that originated in the Aristotelian epoch and periodically revived during the centuries. Charles Darwin has also interpreted inheritance as pangenesis. Accordingly, all the information expressed during the life of the individuals is transported to the gametes from all parts of the body. Thus, pangenesis is the means of the inheritance of all, including the acquired characters. ►lysenkoism, ►acquired characters

Pangenome: The essential, shared sequences among all representatives of a species (Tettelin H et al 2005 Proc Natl Acad Sci USA 102:13950).

Panic Disorder (PD): Episodic panic attacks involving palpitations, sweating, shortness of breath, feeling of choking, chest pain, false touch sensations usually in the absence of physical contact (such as burning, prickling), nausea, etc. The heritability appeared 0.48. Panic disorder may be associated with a number of physical diseases. Chromosome 13q appears to harbor several genes responsible for PD and chromosome 22 may carry some susceptibility factors. ►psychoses, ►panic obsessive disorder, ►anxiety; Hamilton SP et al 2003 Proc Natl Acad Sci USA 100:2550.

Panicle: An inflorescence of a compound raceme structure such as of oats. ►raceme

Panmictic Index: ►fixation index, ►panmixis

Panmixis (panmixia): Random mating; in a population there is equal chance for each individual to mate with any other of the opposite sex. ►Hardy-Weinberg theorem

Panning: The use of antibody affinity chromatography or ELISA for the separation of specific molecules (in analogy to the gold-washing pans of the gold hunters). ►affinity chromatography, ►ELISA, ►phage display; Chen G et al 2001 Nature Biotechnol 19:537.

Panspermia: The theory claiming that life has originated at several places in the universe and spread to earth by meteorites or by other means. ►origin of life

Panther (*Panthera pardus*, leopard): 2n = 38: A feline species; in captivity may be crossed with lion but no mating is known to take place in the wild where conspecific sexual partners are available.

Panther: The database for functionally related proteins, signaling pathways. http://panther.appliedbiosystems.com.

Pantothenic Acid: A precursor of Coenzyme A (see Fig. P18).

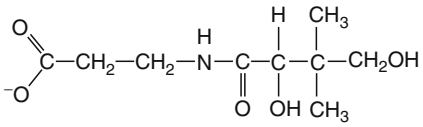

Figure P18. Panthotenate

Pantropic: Can affiliate with many different types of tissues.

PAP (purple acid phosphatases): Ubiquitous metallophosphoesterase proteins with phosphatase, exonuclease, 5′-nucleotidase, etc. functions. (See Li D et al 2002 J Biol Chem 277:27772).

Pap (Papanicolaou) Test: A cytological test for premalignant or malignant conditions (used primarily on smears obtained from the female urogenital tract). It detects also papilloma virus infections. ►malignant growth, ►papilloma virus

PAPA Syndrome (pyogenic sterile arthritis and acne and familial recurrent arthritis, 15p): It may involve also ulcerative skin lesions (pyoderma gangrenosum). It may be caused by defects in the 15-exon CD2-binding protein1 (CD2BP1). ►CD2; Wise CA et al 2002 Hum Mol Genet 11:961; Shoham NG et al 2003 Proc Natl Acad Sci USA 100:13501.

Papain: A member of a family of proteolytic enzymes with an imidazole group near the nucleophilic SH group, and the former plays a role as a proton donor to the cleaved-off part. Papain cleaves immunoglobulin G into three near equal size fragments and this helped in clarifying the structure of antibodies. ►proteolytic, ►calpain, ►immunoglobulins, ►antibody

Papanicolaou Test: ►PAP test

Papaver: ►poppy

Papaya (*Carica papaya*): A melon-like, edible fruit, latex-producing small tree with four genera and all 2n = 2x = 18; it is the source of the proteolytic enzyme papain. ►papain

PapD: Gram-negative bacterial chaperone (28.5 kDa) delivers the components of the pilus from the periplasm. ►periplasma, ►chaperones, ►pilus, ►Gram negative/Gram positive

Paper Chromatography: A technique for the separation of (organic) molecules in filter paper by applying the mixture in a spot or band at the bottom of the paper and allowing an appropriate solvent to be sucked up and thus carry the components at different speed (to different height) so they can be separated (see Fig. P19). The components become visible by their natural color or by the application of specific reagents. A large variety of different modifications were worked out in one or two dimensions, in ascending and descending ways. Nowadays paper chromatography is not used very much. ►chromatography, ►thin layer chromatography, ►Rf value, ►column chromatography, ►high performance liquid chromatography, ►affinity chromatography, ►ion-exchange chromatography

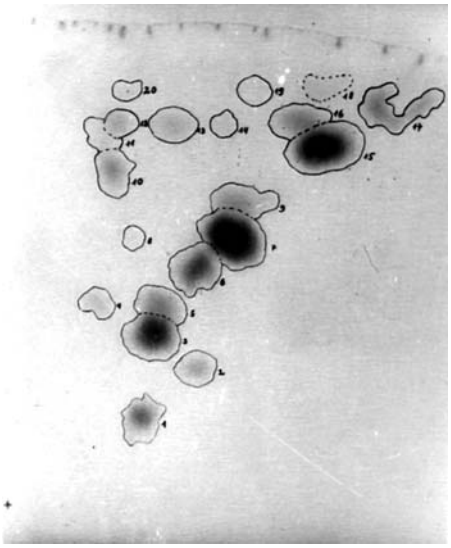

Figure P19. Two-dimensional separation of 20 amino acids in a plant extact

Papillary Renal Cancer, Hereditary: Based on the MET oncogene at human chromosome 7q31, encoding a hepatocyte growth factor receptor. ►MET, ►HGF, ►receptor tyrosine kinase

Papillary Thyroid Carcinoma: Caused by the RET oncogene. It accounts for about 80% of the thyroid cancers that have prevalence in the 10^{-5} range. Its incidence is higher in females than males. ►RET

Papillation, Bacterial: Secondary colonies develop on the colonies of bacteria.

Papilloma: Pre-malignant neoplasia displaying epithelial and dermal finger-like projections.

Papilloma Virus (HPV, human papilloma virus): A double-stranded DNA (≈5.3 × 10^6 Da or ~8 kb) virus causing animal and human warts and squamous carcinomas in mice. The HPV-16 and 18 are frequently present in cervical cancer. The E6 viral protein of HPV-16—through a ubiquitin path—is prone to degrade the p53 tumor suppressor if at amino acid position 72 there is an arginine rather than a proline. The E7 protein of strain HPV-18 degrades another tumor suppressor protein RB. The E1 protein is a hexameric helicase (Enemark EJ, Joshua-Tor L 2006 Nature [Lond] 442:270). Apparently, highly effective vaccines have been developed against HPV strains 16 and 18 that most commonly cause viral cervical cancer. HPV is a critical factor in the majority of cases of cervical cancer that which allowed development of strategies to prevent this form of oncogenesis. It is important to note that several other cancers are also associated with HPV infection, including head and neck cancers. Cancer prevention will require the long-term observation of a large number of treated women and it is necessary in the meantime to monitor for unintended adverse consequences of vaccination (Baden LR et al 2007 N Engl J Med 356:1990). There is also an unresolved moral and ethical problem regarding the age of vaccination of adolescent, sexually not active girls. HPV has about 100 different strains and some pose cancer risk whereas some others do not seem to be carcinogenic. HPV is one of the most common causes of sexually transmitted disease and condom use does not offer perfect protection because the transmission is through

the skin. HPV has been used as a genetic vector. ►papova viruses, ►p53, ►retinoblastoma, ►tumor suppressor, ►cervical cancer, ►Pap test, ►condom, ►helicases; Wolf JK, Ramirez PT 2001 Cancer Invest 19:621.

Papillon-Lefèvre Syndrome: ►periodontitis

Papova Viruses: A large class of (oncogenic) animal viruses of double-stranded, circular DNA includes the polyoma viruses, the bovine papilloma virus and simian virus 40 (SV40), etc. that have been used as genetic vectors for transformation of animal cells. Also, they have been extensively studied by molecular techniques to gain information on structure and function. ►polyoma, ►Simian virus 40, ►papilloma virus; Soeda E, Maruyama T 1982 Adv Biophys 15:1.

PAPS: 3′-phosphoadenosine-5′-phosphosulfate is a sulfate donor in several biochemical reactions, involving cerebrosides, glycosaminoglycans and steroids. It is generated by the pathway: ATP + sulfate → adenosine-3′-phosphosulfate (APS) + pyrophosphate, APS + ATP → PAPS + ADP. Mutations at 10q23-q24 (spondyloepimetaphyseal dysplasia, SEMD) locus encoding the PAPSS2 cause short bowed limbs, large knee joints, brachydactyly, curved spinal column (kyphoscoliosis). ►bone diseases

PAR (pseudoautosomal region): Where recombination may take place between the X and Y chromosomes. The ends of both of the short arm (PAR1) and the long arm (PAR2) have pseudoautosomal regions. ►pseudoautosomal, ►X chromosome, ►Y chromosome, ►lyonization; Dupuis J, Van Eerdewegh P 2000 Am J Hum Genet 67:462.

PAR (protease-activated receptors): The seven-transmembrane G protein-coupled receptors that mediate thrombin-triggered phosphoinositide hydrolysis. Pars are involved in thrombosis, inflammation and vascular biology. Matrix metalloprotease (MMP-1) is an agonist of Par1 (Boire A et al 2005 Cell 120:303). Pars may also activate proteases and protect the airways. Par1 has a role in invasive and metastatic cancers. PAR is a cofactor of PAR4. Binding and phosphorylation of PAR4 by Akt is essential for the survival of cancer cells. Inhibition of the PI3K-Akt pathway leads Par-4—dependent apoptosis (Goswami A et al 2005 Mol Cell 20:33). Par2 is a trypsin receptor. ►thrombin, ►phosphoinositides, ►metalloproteinases, ►AKT, ►apoptosis; Kamath L et al 2001 Cancer Res 61:5933.

Parabiosis: Two animals joined together naturally such as Siamese twins or by surgical methods and can be used to study the interaction of hormones, transduction signals, etc., in-between two different individuals. Intrauterine parabiosis develops immune tolerance.

Paracellular Space: The intercellular space in the tissues.

Paracentric Inversion: ►inversion paracentric

Paracentrotus lividus: Sea urchin; extensively studied by embryologists. ►sea urchins

Paracrine Effect: A ligand (e.g., hormone) is released by a gland and affects neighboring cells.

Paracrine Stimulation: When one type of cell affects the function (such as proliferation) of another (nearby) cell. ►autocrine; Janowska-Wieczorek A et al 2001 Stem Cells 19:99.

Paracytosis: Passing bacteria through cell layers without disruption of the cells (See van Schilfgaarde M et al 1995 Infect Immun 63:4729).

Paradigm: A model or an example to be followed.

Paradox: A statement or phenomenon, which is apparently contradictory to current knowledge but may actually be true.

Paraesthesia (paresthesia): Peripheral nerve damage, disease-caused itching, burning and tickling sensation.

Paraganglioma: ►mitochondrial diseases in humans

Paraganglion: Cells originating from the nerve ectoderm flanking the adrenal medulla, and darkly stained by chromium salts. These cells may form a type of phaeochromocytoma tumors that secrete excessive amounts of epinephrine and norepinephrine. ►SHC oncogene

Paragenetic: phenotypic alterations not involving hereditary mutation.

Parahemophilia: Determined by homozygosity of semidominant autosomal genes. The symptoms involve bleeding similar to the conditions observed in hemophiliacs, bleeding from the uterus (menorrhagia) several days following childbirth. The physiological basis is a deficiency of proaccelerin, a protein factor (V) involved in the stimulation of the synthesis of prothrombin. The therapy requires blood or plasma. ►antihemophilia factors, ►hemophilia, ►pro-thrombin deficiency, ►hemostasis

Parahox Genes: The hox-like genes in clusters, separate from the hox genes, and has originated by duplication from an ancestral protohox gene. ►homeotic genes

Parainfluenza Viruses: A group of immunologically related but distinguishable pathogens responsible for some respiratory diseases. ►Sendai virus

Paralinin: ►karyolymph

Parallel Cascade Identification: Non-linear systems modeling approach. In biology, it can be used to predict long-term treatment response for cancer on the basis of small differences of gene expression levels. (See Korenberg MJ 2002 J Proteome Res 1:55).

Parallel Substitution: Various organismal lineages may display similar or different nucleotides at a number of sites. The chance of these substitutions at a site (p) in (n) lineages can be predicted on the basis of the binomial distribution, $(p + [1 - p])^n$ and upon expansion, e.g., for n = 5 it becomes $p^5 + 5p^4(1-p) + 10p^3(1-p)^2 + 10p^2(1-p)^3 + 5p(1-p)^4 + (1-p)^5$ and the same change per any two lines is p^2. ►evolution and base substitutions, ►evolutionary substitution rate, ►evolutionary tree, ►parallel variation

Parallel Synthesis: An approach commonly applied in drug development. Several similar compounds are generated simultaneously rather in a sequence, one after the other in order to speed up the process of discovery of effective drugs. ►combinatorial chemistry

Parallel Variation: Within taxonomically closely or even distantly related groups of organisms similar mutations may occur during evolution. Mutation in regulatory switches may be the basic cause of these alterations. ►parallel substitution; Vavilov NI 1922 J Genet 12:47; Pagel M 2000 Brief Bioinform 1(2):117.

Paraloci: They have the same properties as pseudoalleles. ►pseudoalleles

Paralogon: A pair of genes evolutionarily derived from common ancestral sequences.

Paralogous Loci: Originated by duplication that was followed by divergence. However, Paralogs may provide backup in case of defect or damage of one of the pairs (Kafri R et al 2005 Nature Genet 37:295). ►orthologous loci, ►isolocus, ►evolution of proteins, ►non-orthologous gene displacement, ►gene family, ►duplication, ►subfunctionalization, ►tetralogue, ►outparalog, ►inparalog; Yamamoto E, Knap HT 2001 Mol Biol Evol 18:1522.

Paralogy: Evolution by duplication of a locus. ►orthologous loci, ►orthology, ►homolog

Paramecium: Unicellular Protozoon. Normally reproduces by binary fission, i.e., a single individual splits into two. Each cell has two diploid micronuclei and a polyploid macronucleus. At fission, the micronuclei divide by mitosis while the macronucleus is simply halved. These animals also have sexual processes (*conjugation*). Two of the slipper-shaped cells of opposite mating type attach to each other and proceed with meiosis of the micronuclei (see Fig. P20). Only one of the four products of meiosis survives in each of the conjugants. Each of these haploid cells divides into four cells (gametes). One of these gametes (male) is passed on into the other conjugating partner through a *conjugation bridge* and fuses with a haploid gamete (female).

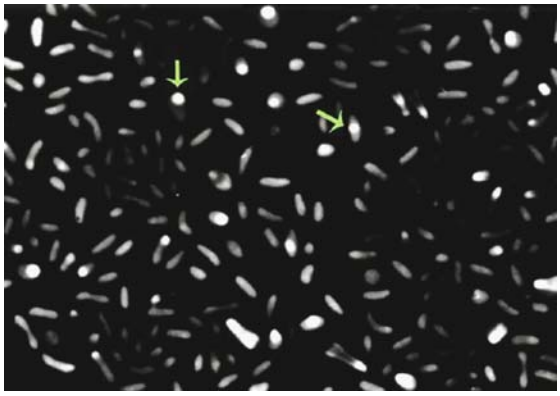

Figure P20. *Paramecium aurelia* (500 X) cells with bright and non-bright kappa particles symbionts (1,650X). The symbionts are bacteria. The bright particles contain the so-called R (refractive) bodies, which are bacteriophages. The non-bright kappa can give rise to bright indicating lysogeny. The kappa-free (*kk*) paramecia are sensitive to the toxin produced by the bright particles and may be killed. The K, killer stocks are immune to the toxin. (From Preer JR et al 1974 Bacteriol Rev 38:113 [Photo by C. Kung]; courtesy of Dr. J. R. Preer)

This is a reciprocal fertilization, resulting in diploid nuclei in the conjugants. Subsequently the pair separates into two *exconjugants*. The macronucleus disintegrates then in both. The diploid zygotic nuclei undergo two mitoses and form four diploid nuclei each. Two of the four nuclei function as separate micronuclei of the cells whereas the other two fuses into a macronucleus that become polyploid, and that is responsible for all metabolic functions and for the phenotype. Besides this sexual reproduction (conjugation), *Paramecia* may practice self-fertilization (*autogamy*).

Meiosis takes place and the one surviving product divides twice by mitoses. Two of these identical cells then fuse and form two diploid, isogenic micronuclei.

If the conjugation lasts longer, cytoplasmic particles may also be transfered through the conjugation bridge. Chromosome numbers may be 63–123; in the macronuclei there may be 800 or more chromosomes. *P. tetraurelia* genome includes 39,642 genes and 80% carry introns of mean 25 bp. The large gene number is apparently the result of whole genome duplication (Aury J-M et al 2006 Nature [Lond] 444:171). ►killer

strains, ►symbionts hereditary, ►*Ascaris*, ►macronucleus, ►chromosome diminution, ►duplication, ►polyploidy, ►internally eliminated sequences, ►cortical inheritance, ►conjugation paramecia; Sonneborn TM 1974 In: King RC (Ed.) Handbook of Genetics, vol. 2, Plenum, New York, p. 469; Prescott DM 2000 Nature Rev Genet 1:191; *Paramecium tetraurelia* database: http://paramecium.cgm.cnrs-gif.fr.

Parameter: A quantity that specifies a hypothetical population in some respect or a variable to which a constant value is attributed for a specific purpose or process. Statistics usually denotes parameters by Greek letters and Latin letters indicates the computed values.

Parameter Alpha: ►alpha parameter

Parametric Methods in Statistics: Involves explicit assumptions about population distribution and parameters such as the mean, standard deviation of the normal distribution, the *p* parameter of the *Bernoulli process*, etc. ►Bernoulli process, ►normal distribution, ►non-parametric statistics, ►robustness

Parameter Space: In a dynamic system the values of the various parameters of a model are constrained within this limit.

Paramyxoviruses: Negative-sense retroviruses of 15–19 kb RNA containing 6–10 genes. They are infectious to a wide range of mammals. In humans, they cause influenza-like respiratory diseases. (See Gotoh B et al 2002 Rev Med Virol 12:337).

Paramutation: A *paramutable* allele becomes a *paramutant* (paramutated) in response to a *paramutagenic* allele if the two are in heterozygous condition. The alteration is similar but not identical to the paramutagenic allele. Both *paramutability* and paramutagenic functions are allele-specific. In contrast to gene conversion, paramutation may take place at low frequency and also in the absence of a paramutagenic allele. At the *R* locus of maize partial reversion of the paramutant may happen but this has not been observed at the *B* locus of maize. The paramutant phenotype at the *R* locus may vary but at the *B* locus, the phenotype appears to be uniform. The exact mechanism of this heritable alteration is not fully understood.

Apparently at the *R* locus of maize hypermethylation is involved, at the *B* locus involvement of methylation has not been detected. Distant upstream sequences play regulatory role in the expression and paramutation of the *B′* locus (Stam M et al 2002 Genetics 162:917). At the *pl* locus the paramutation seems to results in a genetic alteration of the chromatin structure, which affects the regulation of the expression of the gene during development. It appears that the level of transcription is reduced at the paramutant allele compared to that in the paramutable. one.

Although paramutation has been considered an endogenous mechanism, it appears that in the promoter region of the two *r* alleles in the homozygotes the *doppia* (CACTA) transposable elements are present within the 387 bp σ region that is intercalated between the two S elements in opposite orientation. (These elements are called S because they are responsible for anthocyanin coloration of the seed by this complex locus. The elements responsible for coloration of the plant were named P). Paramutation of the *b1* locus of maize depends on an RNA polymerase encoded by the *mop1* gene (*mediator of paramutation*). Paramutation at the *b1* locus involves the presence of non-coding tandem repeats of an

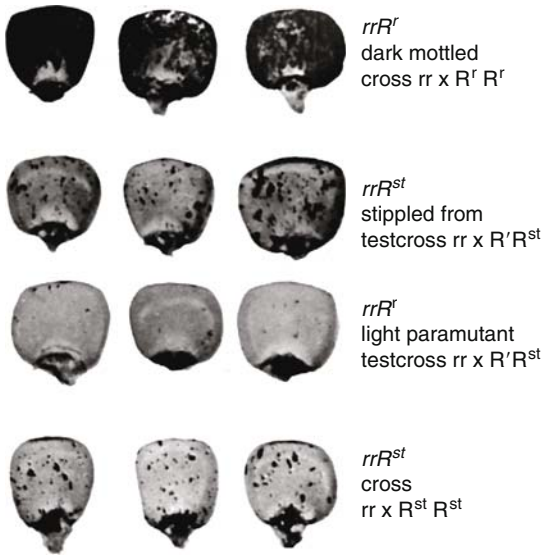

Figure P21. Paramutation results in reduced pigmentation in the triploid aleurone of maize. The R^r homozygotes are fully colored (when all other color-determining alleles are present). The r homozygotes are colorless. The rr^r genotype is responsible for the dark mottled aleurone. R^{st} causes paramutation (stippling) of the R^r paramutable allele that may be manifested in different grades. In the crosses the pistillate parents are shown first, left. (Courtesy of Brink RA see also 1956 Genetics 41:872)

853 bp sequence 100 kb upstream. The number of repeats may be 7 to 1. The strength of the paramutation is correlated with the number of these repeats and a single copy is not sufficient for paramutation. The RNA polymerase transcribes both strands of the repeats (Alleman M et al 2006 Nature [Lond] 442:295).

Paramutation is not a general property of all genes although similar phenomena have been observed at

a few other genes in maize and other plants. This phenomenon seems to violate the Mendelian principle that alleles segregate during meiosis independently and during the process, no "contamination" takes place. Paramutation in the broad sense involves several types of gene silencing in various organisms. Paramutation-like phenomenon attributed to transmethylation was observed in mouse (Herman H et al 2004 Nature Genet 34:199). A new mechanism of paramutation was reported in mouse. Insertion of a 3 kilobase *LacZ-neomycin* cassette into the *Kit* gene downstream of initiator ATG site resulted in mutation involving white spots in the animals because inactivation of a tyrosine kinase receptor and defect in melanogenesis (►phenotype on the reconstructed image of an animal). Although the homozygotes were lethal, the heterozygotes expressed the phenotype as illustrated. The proven wild type individuals (lacking the insertion) among the progeny of heterozygotes displayed the white patches on the tail and feet as did the heterozygous mutants. This phenotype was transmitted by male and female to the offspring and there was a reduced level of *Kit* mRNA and an accumulation of abnormal size non-polyadenylated RNA molecules. The paramutant condition was transmitted though meiosis for several generations but eventually it was diluted out. Injection into fertilized eggs either the total RNA from $Kit^{tm1Alf/+}$ or *Kit*-specific microRNA also induced the white tail (see Fig. P22). The observations indicate a particular type of epigenetic inheritance of RNA molecules (Rassoulzadegan M et al 2006 Nature [Lond] 441:469). This phenomenon bears similarities to the case in the plant *Arabidopsis* claiming that a cache of RNA can be maintained in the nuclei and cause the reappearance of an atavistic trait (Lolle S et al 2005 Nature [Lond] 434:505). Newer information indicates, however, that the apparent "atavism" is due to contamination by pollen of the *Arabidopsis* mutant *HOTHEAD*, which has protruding stigma making unexpected cross-pollination easier (Pennisi E 2006 Science 313:1864). ►gene conversion, ►copy choice, ►directed mutation, ►localized mutagenesis, ►pangenesis, ►blending inheritance, ►presence-absence hypothesis, ►graft hybrid, ►co-suppression, ►RIP, ►epigenesis, ►position effect, ►transvection, ►tissue specificity, ►atavism; Brink RA 1960 Quart Rev Biol 35:120; Hagemann R, Berg W 1978 Theor Appl Genet 53:113; Chandler VL 2000 Plant Mol Biol 43 (2–3):121; Lisch D et al 2002 Proc Natl Acad Sci USA 99:6130; Chandler VL, Stam M 2004 Nature Rev Genet 5:532; Chandler VL 2007 Cell 128:641.

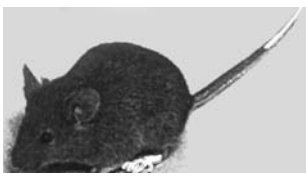

Figure P22. Kit^{tm1Alf}

Paramyotonia: Periodic paralysis (gene located in human chromosome 17). ►myotonia

Paramyxovirus: Single-stranded RNA viruses with a genome of 16–20 kb. Members of this group cause human mumps, respiratory diseases in human and other animals, including birds and reptiles. ►RNA viruses

Paranemic Coils: The two components of the coil can be separated from each other without any entanglement as one can easily pull apart two spirals that were pushed together after they were wound separately, i.e., they are not interlocked. ►plectonemic coils

Paraneoplastic Neurodegenerative Syndrome: ►autoimmune diseases

Paranoia: A psychological disorder in more (paranoia) or less severe (paranoid) state. The major characteristics are delusions of persecution (delusional jealousy, erotic delusions) or less frequently by feeling of grandiosity. It differs from schizophrenia in that, the rest of the personality and mental capacity may remain normal. Frequently, however, paranoid schizophrenia may occur. The precipitating factors are insecurity, frustration, physical illness, drug effects, etc. There is also an apparently undefined genetic component. ►schizophrenia, ►affective disorders

Paranome: Genes within gene families; the entire sets of duplicated genes. ►gene family

Paranormal: Beyond the normal biological expectation, e.g., extrasensory perception. It has been reported (Cha KY et al 2001 J Reprod Med) that prayer for success of in vitro fertilization approximately doubled the success of pregnancy in an international, randomized, double-blind clinical trial involving 219 women. More recently, experts questioned the outcome of this study and suspected inappropriate handling of the experiment (Nature [2004] 429:796). In the nineteenth century, Francis Galton, the father of biometrics, concluded that prayer has unlikely influence on worldly events because the number of shipwrecks was not effected by the fact that praying missionaries were aboard or royalties, for whom their subjects regularly prayed, did not live longer than other citizens. In some instances, when prayer provides comfort, beneficial psychological effects may result (Handzo G et al 2004 N Engl J Med 351:192; ►creationism

Paraoxonase (PON1, 7q21.3): May be associated with high-density lipoproptein in the blood plasma. It may

protect against coronary heart disease by destroying oxidized lipids, responsible for inflammation. It may detoxify organophosphate pesticides (parathion, chloropyrifos [Dursban]). ►arylesterase, ►cholinesterase, ►pseudocholinesterase, ►HDL, ►Kupffer cell; Brophy VH et al 2001 Am J Hum Genet 68:1428.

Parapatric Speciation: Groups of organisms inhabiting an overlapping region become sexually isolated. ►allopatric, ►sympatric

Paraphyletic Group: Does not include all descendants of the latest common ancestor.

Paraplegia: The paralysis of the lower part of the body; it may be hereditary. ►Pelizaeus-Merzbacher disease, ►Silver syndrome, ►spastic paraplegia, ►Mast syndrome, ►ALS

Paraplegin: ►mitochondrial disease in humans

Paraptosis: A programmed neuronal cell death different from apoptosis in as much it is mediated by a caspase-9, which is independent of Apaf-1 and it does not respond to Bcl-X. ►apoptosis, ►Apaf-1, ►BCL; Sperandio S et al 2000 Proc Natl Acad Sci USA 97:14376.

Paraprotein: An abnormally secreted normal or abnormal protein, e.g., the Bence-Jones protein in myelogenous myeloma. It is also called M component. ►Bence-Jones protein

Paraquat: An artificial electron acceptor of photosystem I and a lung toxicant. It may produce oxidative stress by indirect production (through cellular diaphorases) of superoxide radicals. ►diquat, ►photosystem I, ►diaphorase, ►superoxide, ►ROS

Pararetrovirus: The genetic material is double-stranded DNA but it is replicated with the aid of an RNA molecule, e.g., in hepadnaviruses and caulimoviruses. They may occur in many copies in higher eukaryote genomes. ►animal viruses, ►plant viruses, ►retroviruses, ►hepatitis B virus, ►cauliflower mosaic virus; Richert-Poggeler KR, Shepherd RJ 1997 Virology 236:137; Gozuacik D et al 2001 Oncogene 20:6233.

Parascaris: A group of nematodes. ►*Ascaris*

Parasegment: The unit of a metameric complex consisting of the posterior part of one segment and the anterior part of another in insect larval and subsequent stages. ►morphogenesis

Paraselectivity: An apparent (but not real) selectivity in pollination among plants.

Parasexual Mechanism of Reproduction: The somatic-cell fusion and mitotic genetic recombination. The processes bear similarities to those common at sexual reproduction but do not involve sexual mechanisms. ►mitotic recombination, ►cell fusion, ►somatic cell genetics; Pontecorvo G 1956 Annu Rev Microbiol 10:393.

Parasitemia: The blood contains parasites, e.g., *Plasmodium*. ►thalassemia, ►*Plasmodium*

Parasitic: That which lives on and takes advantage of another live organism. ►biotrophic, ►parasitoid; http://www.ebi.ac.uk/parasites/parasite-genome.html; various parasites' database: http://fullmal.ims.utokyo.ac.jp.

Parasitic DNA: same as DNA selfish.

Parasitoid: Lives on another organism and eventually destroys it like some wasps and viruses. Some plants—upon attack and wounding by some insects—synthesize and emit host and parasite specific volatile compounds that attract parasitoid wasps that in turn may destroy the insects. The parasitoid wasp *Cotesia congregata* of the lepidopteran host *Manduca sexta* harbors Polydnavirus. The virus is injected into the host along with the parasitoid egg. The viral genome controls the host immune system and protects the wasp progeny development inside the host. The virus genome is 567,670 bp contained by 30 DNA circles of 5–40 kb, including 156 coding sequences of 66% AT; 69% of the viral genes has introns. The rest of the viral DNA is non-coding (Espagne E et al 2004 Science 306:286). ►parasitic, ►biological control, ►aphid

Paraspeckles: Formed from RNA-binding proteins in the cell nucleus within the interchromatin nucleoplasmic space, usually at the periphery of the nucleolus and in the vicinity of the nuclear speckles. ►speckles; Fox AH et al 2002 Curr Biol 12:13.

Parasterility: Caused by incompatibility between genotypes that may be fertile in other combinations. ►self-incompatibility alleles, ►Rh blood group

Parastichies: The imaginary helical line in phyllotaxis. ►phyllotaxis

Parathormone (parathyroid hormone, 11p15.3-p15.1): Produced by the parathyroid gland next to the thyroid gland. It is a regulator of calcium and phosphate metabolism (mediated by cAMP) primarily in the bones, kidneys and the digestive tract. A recessive hypoparathyroidism was mapped to Xp27. ►hypercalcemia-hypocalciuria, ►hyperpara-thyroidism, ►enchondromatosis; Healy KD et al 2005 Proc Natl Acad Sci USA 102:4724.

Parathyroid Hormone: Regulates Ca^{2+} level in animals. ►parathormone

Paratope: The epitope-binding site of the antibody Fab domain. ►antibody, ►epitope

P

Paratransgenic: An insect, which has transgenic symbionts inhabiting its gut. *Rhodnius prolixus* carries the actinomycete bacterium *Rhodococcus rhodnii* with which it has a symbiotic relationship. *R. prolixus* is a blood-sucking arthropod, vector of *Trypanosoma cruzi*, responsible for Chagas disease. When *R. rhodnii* is transformed by cecropin A, a 38-amino acid antimicrobial peptide derived from the moth *Hyalophora cecropia*, the peptide diffuses into the insect and lyses *Trypanosoma cruzi* within the insect without serious damage to *R. rhodnii* and thus effectively curtails the propagation of the protozoon. This is a more attractive defense than using chemical pesticides. ►transgenic, ►*Trypanosoma*, ►Chagas disease, ►CRUZIGARD; Beard CB et al 2001 Int J Parasitol 31:621.

Parcelation: The relative lack of pleiotropic effects between two sets of non-overlapping traits.

Parenchyma: In plant biology it means storage cells, either near isodiametric, *spongy parenchyma*, closer to the lower surface of the leaves or the *palisade parenchyma* consisting of one or two layers of columnar cells with their long axis perpendicular to the upper epidermis. Both types of tissues contain conspicuous intercellular space. In zoology, the parenchyma cells mean the functional units, rather than the network of an organ or tissue. ►palisade cells

Parens Patriae: The state or community right to intervene against individual rights or beliefs and protect the interest of a person against potentially serious or actually life-threatening conditions, e.g., compulsory immunization, genetic screening, prohibition of incest, etc.

Parental Ditype: ►tetrad analysis

Parental Histone Segregation: In front of the DNA replication fork the existing nucleosome structure is temporarily and reversibly disrupted to make nascent DNA readily accessible to the replication protein machinery (see Fig. P23).

Parenteral: The application of a substance by injection rather than by oral means.

Parent-of-Origin Effect: May be due to the differences in the cytoplasm, differential transmission of defective chromosomes through the two sexes, differences in trinucleotide-repeat expansions, endosperm: embryo chromosomal differences in the reciprocal crosses in case of polyploids and imprinting. ►imprinting, ►trinucleotide repeats, ►uniparental disomy, ►uniparental inheritance; Morrison IM, Reeve AE 1998 Hum Mol Genet 7:1599; Haghighi F, Hodge SE 2002 Am J Hum Genet 70:142.

Pareto Distribution: $f(x) = \frac{\gamma\alpha^{\gamma}}{x^{\gamma+1}}$ Applicable for the gene expression profiles. Some genes are expressed at very high level other transcripts occur once or even less per cell thus the distribution is highly skewed by the low-abundance transcripts (see Fig. P24). The Pareto probability distribution is: $\alpha \leq x < \infty, \alpha > 0, \gamma > 0$, mean $= \gamma\alpha/(y-1, \gamma > 1$ and variance $= \gamma\alpha^2[(\gamma-1)^2(\gamma-2), \gamma > 2$ (See Kuznetsov VA et al 2002 Genetics 161:1321).

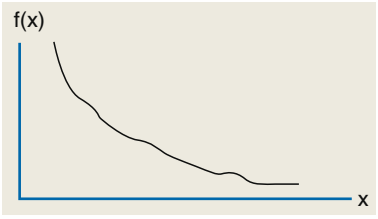

Figure P24. A hypothetical Pareto distribution

Parietal: Situated on the wall or attached to the wall of a hollow organ.

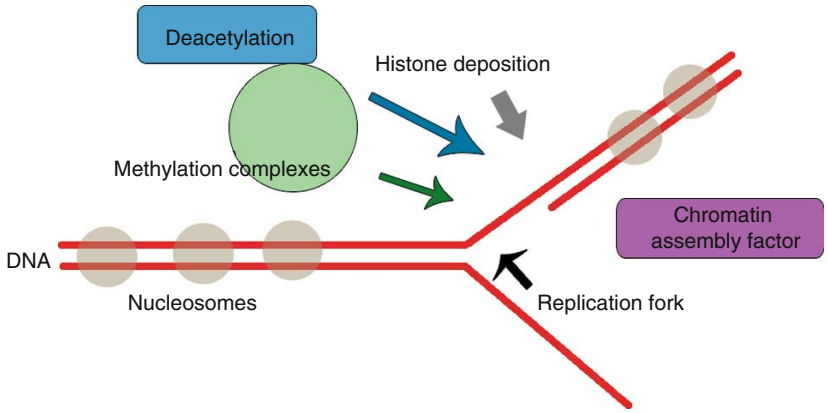

Figure P23. Nucleosome remodeling—Parental histone segregation

Periodontal Disease: Involves inflammation of the tissues surrounding teeth such as gingiva, ligaments, gum, etc. ►point-of-care test

Paris Classification: Paris classification of human chromosomes standardized (in 1971) the banding patterns and classified them by size groups; it is very similar to what is used today. Current maps show, however, only one of the two chromatids. ►human chromosomes, ►Denver classification, ►Chicago classification

Parity: Parity in gene conversion the process can go equally frequently in the direction of one or the other allele. ►gene conversion; Fogel S et al 1971 Stadler Symp 1–2:89.

Parity: In human biology, it is the condition that a woman had borne offspring. Natural selection does not necessarily favor maximal reproduction because reproduction imposes fitness costs, reducing parental survival, and offspring quality. Parents in a pre-industrial population in North America incurred fitness costs from reproduction, and women incurred greater costs than men. The survivorship and reproductive success (Darwinian fitness) of 21,684 couples, married between 1860 and 1895, identified in the Utah Population Database showed that increasing number of offspring (parity) and rates of reproduction were associated with reduced parental survivorship, and significantly more for mothers than fathers. Parental mortality resulted in reduced survival and reproduction of offspring, and the mothers' mortality was more detrimental to offspring than the fathers' were. Increasing family size was associated with lower offspring survival, primarily for later-born children, indicating a tradeoff between offspring quantity versus quality (Penn DJ, Smith KR 2007 Proc Natl Acad Sci USA 104:553). ►fitness, ►reproductive rate, ►fecundity, ►fertility

Parity Check: In a digital system it reveals whether the number of ones and zeros is odd or even.

Parkin: ►Parkinson's disease

Parking: A set of rules for seeding in which no seed overlaps with any other seedings. It is an iterative procedure that may be used at the early phase in genome sequencing. Each iteration sequences a new portion of non-overlapping piece of the DNA. Aside for non-overlaps, the sequences are chose at random. ►seeding, ►genome projects; Roach JC et al 2000 Genome Res 10:1020.

Parkinsonism: A secondary symptom caused either by drugs, or inflammation of the brain (encephalitis), or Alzheimer's disease, or Wilson's disease, or Huntington's chorea, etc. ►Parkinson's disease and the conditions named above, ►tau

Parkinson Disease (PD, PARK): A shaking palsy (bradykinesis) generally with late onset, however juvenile forms also exist. PD may include mental depression, dementia, reduced olfactory abilities and deficiency of several different substances, notably dopamine, from the nervous system. The genetic determination of the heterogeneous symptoms is unclear; autosomal dominant, recessive, X-linked, polygenic and apparently only environmentally caused phenotypes have been observed. The prevalence of PD is 0.001 and it may be 0.01 over age 50 but perhaps no more than 10% of the cases are familial.

Defects in the mitochondrial complex I resulting in oxidative stress favor the development of PD (Canet-Avilés RM et al 2004 Proc Natl Acad Sci 101:9103). Conditional knockout mice (termed MitoPark mice), with disruption of the gene for mitochondrial transcription factor A (*Tfam*) and in progressive degeneration of the nigrostriatal dopamine system (DA) neurons have reduced mtDNA expression and respiratory chain deficiency in midbrain DA neurons, which, in turn, leads to a parkinsonism phenotype with adult onset of slowly progressive impairment of motor function, accompanied by formation of intraneuronal inclusions and dopamine nerve cell death. Confocal and electron microscopy show that the inclusions contain both mitochondrial protein and membrane components demonstrating that respiratory chain dysfunction in DA neurons may be of pathophysiological importance in PD (Ektrand MI et al 2007 Proc Natl Acad Sci USA 104:1325). Endocannabinoids may have beneficial effects on motor deficits in PD and Huntington chorea (Kreitzer AC, Malenka RC 2007 Nature [Lond] 445:643).

A PTEN-induced putative kinase (*PINK1*) mutation in *Drosophila* that has high similarity to human PINK1 also encodes a mitochondrially located protein and it is complemented by parkin (Park J et al 2006 Nature [Lond] 441:1157; Clark IE et al 2006 Nature [Lond] 441:1162). Loss-of-function mutations in a previously uncharacterized, predominantly neuronal P-type ATPase gene, *ATP13A2*, underlying an autosomal recessive form of early-onset Parkinsonism with pyramidal degeneration and dementia (PARK9, Kufor-Rakeb syndrome) were observed. The pyramidal cells are excitatory neurons in cerebral cortex. The wild-type protein was located in the lysosome of transiently transfected cells; the unstable truncated mutants were retained in the endoplasmic reticulum and degraded by the proteasome (Ramirez A et al 2006 Nature Genet 38:1184).

The herbicide paraquat, the fungicide maneb, the insecticide rotenone and other environmental toxins may contribute to PD by inhibiting complex I (Dawson TM, Dawson VL 2003 Science 302:819).

Mitochondrially coded nicotinamide adenine dinucleotide dehydrogenase complex plays a role in reduced susceptibility (van der Walt JM et al 2003 Am J Hum Genet 72:804).

An early onset PD was located to human chromosome Xq28 and another (PARK6) to 1p35-p36. Mitochondrially localized PTEN-induced kinase 1 (PINK1, 1p35) mutations are involved in PARK6 (Valente EM et al 2004 Science 304:1158). PINK contains a serine-threonine protein kinase domain; it localized in mitochondria. An autosomal dominant form is in chromosome 22. Another locus encoding spheres of protofibrils of α-synuclein was assigned to human chromosome 4q21-q23. The α-synuclein gene is apparently responsible for only a minor fraction of Parkinsonism. A susceptibility gene (SNCA) has been located also to human chromosome 17q21. Multiple copies of SNCA may occur in a single nucleus. A low penetrance (40%), late onset (∼60 years) gene is at 2p13. Autosomal dominant juvenile Parkinsonism gene (1395 bp ORF) encoding the 465-amino acid *parkin* protein was located to 6q25.2-q27. Parkin is an E3 ubiquitin protein ligase and ubiquitin-proteasome deficit favors the development of PD and its S-nitrosylation inhibits its normal protective action (Kung KKK et al 2004 Science 304:1328). Parkin disease is Parkinsonism without the formation of Lewy bodies. Several other loci are also involved with the developmental of this disease. Protein DJ-1 (1p36)—situated in the mitochondria—is a protein regulating mRNA stability and its defect can cause Parkinsonism.

The parkin gene appears to be a suppressor of ovarian cancer and adenocarcinoma (Cesari R et al 2003 Proc Natl Acad Sci USA 100:5956). In some cases a missense mutation in the carboxy terminal hydrolase L1 (UCH-L1, 4p14), component of the ubiquitin complex, localized in the Lewy bodies, is responsible for PD. Not all forms of PD shows Lewy bodies. Loss of dopaminergic neurons in the substantia nigra is usually associated with the disease. Glial cell line-derived neurotrophic factor (GDNF) has nutritive effects on the dopaminergic nigral neurons. In an autosomal recessive juvenile PD parkin-associated endothelin receptor-like (Pael-R) accumulates apparently because a misfolded Pael-R is not degraded if there is a defect in parkin. LRRK2 (PARK8, 12p12) is a leucine-rich repeat kinase gene involving Lewy body disease of advanced adult age.

Parkin has several other substrates and that explains the complicated etiology of the different forms of PD (Imai Y et al 2001 Cell 105:891; Shimura H et al 2001 Science 293:263).

Various tomography techniques facilitate detection of susceptibility to PD before the appearance of clinical symptoms. The imaging can measure the integrity of dopamine in the substantia nigra of the brain. The procedure is based on the conversion of 18F-DOPA into 18F-dopamine or by the use of DOPA transporter (DAT) ligands. The reduction in DAT ligand uptake correlates with the loss of dopamine in the corpus striatum (the striped gray substance in front and beside the thalamus in the brain) and this is characteristic for aging and particularly for incipient PD. Also, loss of fluorodeoxyglucose distinguishes PD from other neurodegenerative diseases. Dopamine dysfunction may be indicated also by olfactory impairment (see DeKosky ST, Marek K 2003 Science 302:830).

Gene therapy using lentivirus vector carrying the GDF gene, injected into the brain (striatum and substantia nigra) of old monkeys or young monkeys pretreated with a nigrostriatal degeneration inducing agent (1-methytl-4-phenyl-1,2,3,6-tetrahydropyridine [MPTP]) reversed the functional deficits and prevented degeneration, respectively. Anticholinergics (blocking choline) and dopamine, glial-cell-derived neurotrophic factor (GDNF) treatments may be somewhat beneficial. An alternative approach may be using gene therapy by expressing transfected tyrosine hydroxylase or aromatic amino acid decarboxylase in the striated muscle cells. These enzymes can produce dopamine yet the response is below expectation. New approaches appear more promising (▶gene therapy). Transplantation of fibroblasts equipped for secretion of BDNF and GDNF into the brain appears promising in animal models. Inhibition of cyclooxygenase (COX-2) seems to prevent the formation of the oxidant dopamine-kinone, which has been implicated in Parkinsonism (Teismann P et al 2003 Proc Natl Acad Sci USA 100:5473). Electric shocks localized to the globus pallidus (a medial part of the brain) had beneficial effects in some cases. Caspase-3 may be a conditioning factor in the apoptotic death of dopaminergic neurons in PD. Embryonic stem cells may develop into dopamine-producing neurons in the brain of the mouse and seem to be promising for cell-replacement therapy of PD (Kim J-H et al 2002 Nature [Lond] 418:50; Barberi T et al 2003 Nature Biotechnol 21:1200). Midbrain proteins Lmx1a and Msx1 mediate dopamine neuron differentiation of proneural protein NGN2 and seem important for cell replacement therapy in PD (Andersson E et al 2006 Cell 124:393). Activation of intracellular neurotrophic signaling pathways by vector transfer is a feasible approach to neuroprotection and restorative treatment of neurodegenerative disease. Adeno-associated virus 1 transduction with a gene encoding a myristoylated, constitutively active form of the oncoprotein Akt/PKB had pronounced trophic effects on dopamine neurons of adult and aged mice, including increases in neuron size, phenotypic markers, and sprouting. Transduction confers almost complete

protection against apoptotic cell death in a highly destructive neurotoxin model (Ries V et al 2006 Proc Natl Acad Sci USA 103:18757). Nix, a pro-apoptotic BH3-only protein, promotes apoptosis of non-neuronal cells. Using a yeast two-hybrid screen with POSH (plenty of SH3 domains, a scaffold involved in activation of the apoptotic JNK/c-Jun pathway) as the bait, identified an interaction between POSH and Nix and contributed to cell death in a cellular model of Parkinson disease (Wilhelm M et al 2007 J Biol Chem 282:1288). The disease-linked processes are detectable in peripheral blood by 22 unique genes differentially expressed in patients with PD versus healthy individuals. Such an approach may provide biomarkers for early clinical detection of the disease (Scherzer CR et al 2007 Proc Natl Acad Sci USA 104:955). Multiple axon-guidance pathway genes may predispose to PD (Lesnick TG et al 2007 PloS Genet 3(6):e98). ►parkinsonism, ►neuromuscular diseases, ►dopamine, ►adeno-associated virus, ►Akt, ►tyrosine hydroxyls, ►Lewy body, ►Kufor-Rakeb syndrome, ►GDNF, ►BDNF, ►dopamine, ►mitochondrial disease in humans, ►subtantia nigra, ►synuclein, ►caspase, ►ubiquitin, ►tau, ►stem cells, ►brain human, ►tomography, ►PTEN, ►argyrophilic grains, ►BAK, ►cannabinoids, ►axon guidance; Dawson TM 2000 Cell 101:115; Kordower JH et al 2000 Science 290:767; Valente EM et al 2001 Am J Hum Genet 68:895; Vaughan JR et al 2001 Ann Hum Genet 65:111; Lansbury PT Jr, Brice A 2002 Curr Opin Genet Dev 12:299; Betarbet R et al 2002 BioEssays 24:308; Cookson MR 2005 Annu Rev Biochem 74:29; Farrer MJ 2006 Nature Rev Genet 7:306.

Paromomycin ($C_{23}H_{45}O_{14}N_5$): An aminoglycoside antibiotic. It may cause translational errors by increasing the initial binding affinity of tRNA. Oral LD^{50} in mice is 1625 mg/kg. ►phenotypic reversion, ►aminoglycoside antibiotics, ►LD50

Parotid Gland: The salivary gland; the proline-rich parotid glycoprotein is encoded in human chromosome 12p13.2.

Paroxysm: Recurring events such as convulsions (but most commonly normal conditions in between), sudden outbreak of disease.

Paroxysmal Nocturnal Hemoglobinuria: A dominant human chromosome 11p14-p13 susceptibility of the erythrocytes to destruction by the complement because of a deficiency in protectin (HRF20/CD59) and DAF. ►complement, ►membrane attack complex, ►DAF, ►angioneuritic edema, ►CD59, ►protectin, ►hemoglobin

PARP (poly[ADP-ribose] polymerase): An enzyme involved in surveillance and base excision repair of DNA and NAD^+-dependent chromatin remodeling (Kim MY et al 2004 Cell 119:803). PARP is involved in puff formation of *Drosophila* gene loci (Tulin A, Spradling A 2003 Science 299:560). It is cleaved by an ICE-like proteinase. Its deficiency increases the sensitivity to radiation damage, recombination and sister chromatid exchange. PARP is required also for the assembly and structure of the spindle (Chang P et al 2004 Nature [Lond] 432:645). PARP-deficient mice are viable and free of tumors and inhibitors of PARP/DNA repair activity can selectively kill BRCA2 defective tumor cells (Bryant HE et al 2005 Nature [Lond] 434:913). PARP deficiency prevents homologous recombination repair of damaged BRCA1 and BRCA2 eventually apoptosis eliminates the mutant cells (Farmer H et al 2005 Nature [Lond] 434:917). ►ICE, ►apoptosis, ►puff, ►tankyrase, ►telomeres, ►spindle, ►DNA repair, ►breast cancer, ►Kif; Bauer PI et al 2001 FEBS Lett 506(3):239; Lavrik OI et al 2001 J Biol Chem 276:25541.

PARS (poly[ADP-ribose] synthetase): PARS attaches ADP-ribose units to histones and to other nuclear proteins. It is activated when DNA is damaged by nitric oxide.

Parser: A software for reading flat files for further processing. ►flat file

Parsimony: ►maximal parsimony, ►evolutionary tree

Parsing: Resolve it to parts or components. ►exon parsing, ►pars means part in Latin

Parsley (*Petroselinum crispum*): The roots and leaves of parsley are used for flavoring; 2n = 2x = 22 (see Fig. P25).

Figure P25. Parsley

Parsnip (*Pastinaca sativa*): A root vegetable; 2n = 2x = 22 (see Fig. P26).

Figure P26. Parsnip

Parsonage–Turner Syndrome (Feinberg syndrome/Tinel syndrome/Kiloh-Nevin syndrome): The syndrome is most likely to be identical with hereditary amyotrophic neuralgia; it is also very similar to the Gillain-Barré syndrome. ►amyotrophy hereditary neuralgic, ►Guillain-Barré syndrome

Parthenocarpy: The development of fruit without fertilization. It may have horticultural application by producing seedless apple varieties such as Spencer Seedless or Wellington Bloomless. The gene responsible in these apples is homologous to *pistillata* of *Arabidopsis*. ►parthenogenesis, ►apomixia, ►seedless fruits, ►flower differentiation in *Arabidopsis*; Yao J et al 2001 Proc Natl Acad Sci USA 98:1306.

Parthenogenesis: Embryo production from an egg without fertilization. Parthenogenesis may be induced in sea urchins by hypotonic media or in some amphibia by mechanical or electric stimulation of the egg. In some fish, lizards and birds (turkey) it occurs spontaneously. Parthenogenesis in animals is most common among polyploid species. Parthenogenetic individuals produce only female offspring. On theoretical grounds, parthenogenesis may be disadvantageous because it deprives the species of elimination of disadvantageous mutations on account of the lack of recombination available in bisexual reproduction. Parthenogenesis may cause embryonic lethality in mouse if the imprinted paternal genes are not expressed. Parthenogenesis is not known to occur in humans (or generally in mammals but deletion of imprinting may yield viable parthenogenetic mouse), however it may exist as a chimera when after fertilization, the male pronucleus is displaced to one of the blastomeres and then the maternal chromosome set in the other blastomere is diploidized. The failure of parthenogenetic development of mammalian offspring is due to the requirement for imprinting (Kono T et al 2004 Nature [Lond] 428:860). Fusion of two oocyte nuclei can produce, however, viable, fertile mouse. Many plant species successfully survive by asexual reproduction as an evolutionary mechanism. Parthenogenesis in plants is called apomixis or apomixia. Asexually reproducing plant populations appear to be preponderant under conditions marginally suitable for the species is called *geographic parthenogenesis*. ►apomixia, ►gynogenesis, ►parthenocarpy, ►RSK, ►imprinting, ►oocyte; Mittwoch U 1978 J Med Genet 15:165; Cibelli JB et al 2002 Science 295:819; Krawetz SA 2005 Nature Rev Genet 6:633.

Parthenote: An egg stimulated to divide and develop to some extent in the absence of fertilization by sperm. Parthenotes may offer possibilities for stem cell production for therapeutic purposes when embryonic stem cells are prohibited. ►parthenogenesis, ►apomixia; Kiessling AA 2005 Nature [Lond] 434:145.

Partial Digest: The reaction is stopped before completion of nuclease action and thus the DNA is cut into various size fragments some of which may be relatively long because some of the recognition sites were not cleaved. ►restriction enzyme

Partial Diploid: ►merozygote

Partial Dominance: An incomplete dominance, semidominance.

Partial Linkage: The genes are less than 50 map units apart in the chromosome and can recombine at a frequency proportional to their distance. ►crossing over, ►recombination

Partial Trisomy: Only part of a chromosome is present in triplicate. ►trisomy

Particulate Inheritance: The modern genetic theory that inheritance is based on discrete particulate material (written in nucleic acid sequences) transmitted conservatively rather than according to the pre-Mendelian theory of pangenesis, which claimed that the hereditary material is a miscible liquid subject to continuous changes under environmental effects. According to the particulate theory of genetics, genes are discrete physical entities that are transmitted from parents to offspring without blending or any environmental influence, except when mutation or gene conversion

or imprinting occurs. ►pangenesis, ►gene conversion, ►mutation, ►imprinting, ►blending inheritance

Particulate Radiation: ►physical mutagens

Partington Syndrome (Xp22.13): Primarily mild or moderate mental retardation accompanied by developmental anomalies caused by polyalanine expansion in the *aristaless-like* homeobox gene. (*al, aristaless* alleles were discovered early in *Drosophila* and mapped to chromosome 2.4; some involved cytologically detectable inversions. Mammalian homologs exist.) At this chromosomal area several other similar mental retardation genes occur. Some have recessive expression others are dominant. ►homeotic genes, ►mental retardation, ►mental retardation X-linked

Partitioning (segregation): The distribution of plasmids and/or the bacterial chromosome(s) into dividing bacterial cells. It may be a passive process mediated by the attachment of the DNAs to the cell membrane. The partition depends on ParA and ParB proteins by the P1 plasmid. ParB recognizes at the partition site a dimeric B box and at the opposite ends two A boxes with helix-turn-helix (HTH) domains (see Fig. P27). The HTH domains emanate from the dimerized DNA-binding modules composed of a six-stranded β-sheet coiled coil that binds the B boxes (Schumacher MA, Funnell BE 2005 Nature [Lond] 438:516). A bacterial tubulin-like protein FtsZ may carry out the separation. Plasmid and bacterial genes control the process. The bacterial chromosome or some of the plasmids seem to have a centromere-like protein that may bind to the cell poles and to 10 copies of a sequence situated along a 200 kb region near the replicational origin. The loss of the chromosome in the new cells is less frequent than 0.003. The segregation of plasmids present in multiple copies is more complex. Mechanisms ("addiction" system) exist to resolve plasmid dimers and to ensure that each cell would have at least one copy of a plasmid. The two-component addiction module include a stable toxin and a labile antitoxin. The plasmid-free cells may be eliminated (Engelberg-Kulka H, Glaser G 1999 Annu Rev Microbiol 53:43). ►segregation, ►cell division, ►addiction module, ►plasmid maintenance; Hiraga S 2000 Annu Rev Genet 34:21; Gordon GS, Wright A 2000 Annu Rev Microbiol 54:681; Draper GC, Gober JW 2002 Annu Rev Microbiol 56:567.

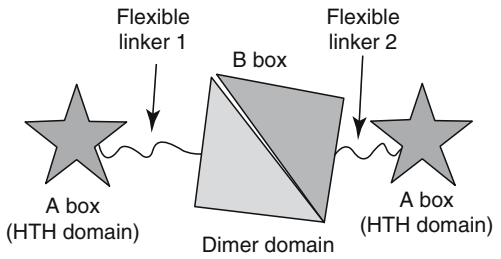

Figure P27. Partitioning

Partitioning: In statistics, breaking down the variances among the identifiable experimental components or in a compound chi square to reduce the quantity of the residual or error variance. ►analysis of variance

Parturition: The labor of child delivery.

Parvoviruses: Non-enveloped, icosahedral (18–25 nm), single-stranded DNA (~5.5 kb) viruses. The group includes the densoviruses of arthropods, the autonomous, lytic parvoviruses and the adeno-associated viruses. ►icosahedral, ►adeno-associated virus, ►autonomous parvovirus, ►oncolytic viruses; Lukashov VV, Goudsmit J 2001 J Virol 75:2729.

Parvulin: A very small monomeric 92-amino acid prolyl isomerase of *E. coli* involved in protein maturation. Similar proteins occur in yeast (Ess1, 19.2 kDa) and humans (Pin1, 18 kDa) and *Drosophila* (dodo, 18.3 kDa). Ess1 may not have isomerase activity, but Pin1 does. In the absence of Ess1 the nuclei fragment and growth ceases, dodo has apparently similar function as Ess1 and it is interchangeable. Pin regulates mitotic progression by interacting with CDC25 and NIMA. ►PPI, ►peptidyl-prolyl isomerases, ►CDC25, ►NIMA; Rulten S et al 1999 Biochem Biophys Res Commun 259:557.

PAS Domain (Per-Arnt-Sim): A shared motif of proteins involved in the regulation of the circadian rhythm of the majority of eukaryotes. PAS domain serine/threonine kinases also regulate several different signaling pathways including drug response. ►circadian rhythm; Rutter J et al 2001 Proc Natl Acad Sci USA 98:8991.

PASA: A special PCR procedure by which chosen allele(s) can be amplified if the primers match the end of that allele. ►PCR; Smith EJ, Cheng HH 1998 Microb Comp Genomics 3:13; Shitaye H et al 1999 Hum Immunol 60:1289.

Pascal Triangle: Represents the coefficients of individual terms of expanded binomials: $(p + q)^n$:

$$1p^n + \frac{n}{1!(n-1)!}p^{n-1}q + \frac{n!}{2!(n-2)!}p^{n-2}q^2 + \ldots + \frac{n!}{(n-1)!1!}p^{n-(n-1)}q^{n-1} + 1q^n$$

Since genetic segregation is expected to comply with the binomial distribution, the coefficients indicate the frequencies of the individual phenotypic (or in case of trinomial distribution) genotypic frequencies. ►binomial distribution, ►trinomial distribution, see Table P1.

Table P1. The Pascal triangle represents the coefficients of individual terms of expanded binomials. The exponent of the binomial is n. The figures display a symmetrical hierarchy. The frequency of a particular class can be readily calculated because of the sum of the coefficients is displayed at the bottom of the columns. Mendelian segregation follows the binomial distribution

n →	1	2	3	4	5	6	7	8	9	10
	1	1	1	1	1	1	1	1	1	1
	1	2	3	4	5	6	7	8	9	10
		1	3	6	10	15	21	28	36	45
			1	4	10	20	35	56	84	126
				1	5	15	35	70	126	210
					1	6	21	56	126	252
						1	7	28	84	210
							1	8	36	120
								1	9	45
									1	10
										1
SUMS	2	4	8	16	32	64	128	256	512	1024

n →	11	12	13	14	15	16	17	18	19	20
	1	1	1	1	1	1	1	1	1	1
	11	12	13	14	15	15	17	18	18	20
	55	66	78	91	105	120	136	153	171	190
	165	220	286	364	455	560	680	816	969	1140
	330	495	715	1001	1365	1820	2380	3060	3876	4845
	462	792	1287	2002	3003	4368	6188	8568	11682	15504
	462	904	1716	3003	5005	8008	12376	18564	27132	38760
	330	792	1716	3432	6435	11440	19448	31824	50388	77520
	165	495	1287	3003	6435	12870	24310	43758	75582	125970
	55	220	715	2002	5005	11440	24310	48620	92378	167960
	11	66	286	1001	3003	8008	19448	43758	92378	184756
	1	12	78	364	1365	4368	12376	31824	75582	167960
		1	13	91	455	1820	6188	18564	50388	125970
			1	14	105	560	2380	8568	27132	77520
				1	15	120	680	3060	11628	38760
					1	16	136	816	3876	15504
						1	17	153	969	4845
							1	18	171	1140
								1	19	190
									1	20
										1
SUMS	2048	4096	8192	16384	32768	65536	131072	262144	524288	1048576

Passage: The transfer of cells from one medium to another.

Passenger DNA: A DNA inserted into a genetic vector.

Passenger Proteins: Include the inner centromeric protein (INCENP), which is a substrate for Aurora, the Aurora B kinase, the TD-60 autoimmune antigen, the inhibitor-of-apoptosis protein Survivin/BIR-1. These proteins are situated at the centromeres and move the spindle at late metaphase and anaphase. ►centromere, ►mitosis, ►Aurora, ►Survivin; Bishop JD, Schumacher JM 2002 J Biol Chem 277:27577.

Passive Immunity: Acquired by the transfer of antibodies or lymphocytes

Passive Transport: Does not require special energy donor for the process. ►active transport

Pasteur Effect: The fast reduction of respiration (glycolysis) if O_2 is added to fermenting cells.

Pasteurella multocida: A pathogenic bacterium causing cholera in birds, bovine hemorrhagic septicemia, atrophic rhinitis (inflammation of the nasal mucosa) in pigs, and humans may be infected by it through cat or dog bites. The sequenced genome of 2,257,487 bp contains ~2014 coding sequences. ►*Yersinia*; May BJ et al 2001 Proc Natl Acad Sci USA 98:3460.

Pasteurization: Reducing (killing) the microbe population in a material by heating at a defined temperature for a specified period of time. ►aseptic, ►axenic, ►autoclaving

PAT1 (Ran1): A protein kinase required for the continuation of mitotic division in fission yeast. Its inactivation triggers the switch to meiosis. ►meiosis, ►Ran1

Patatin: A glycoprotein like storage protein in potato with lipid acid hydrolase and esterase activity. It inhibits pests' larvae. It constitutes ~40% of the soluble proteins in the tubers. ►potato; Hirschberg HJ et al 2001 Eur J Biochem 268:5037.

Pätau's Syndrome: Caused by trisomy for human chromosome 13. This is one of the few (X, Y, 8, 18, 21, 22) trisomies that can be carried to term but it generally leads to death within six months because of severe defects in growth, heart, kidney and brain failures. It is accompanied by face deformities (severe hare lip, cleft palate), polydactyly, clubfoot, defects of the genital systems, etc. (see Fig. P28). Definite identification is carried out by cytological analysis, including FISH with the available chromosome-13-specific probes. An old designation of trisomy 13 was trisomy D because chromosome 13 belonged to the D group of human chromosomes. ►trisomy, ►aneuploidy, ►polydactyly, ►hare lip, ►clubfoot

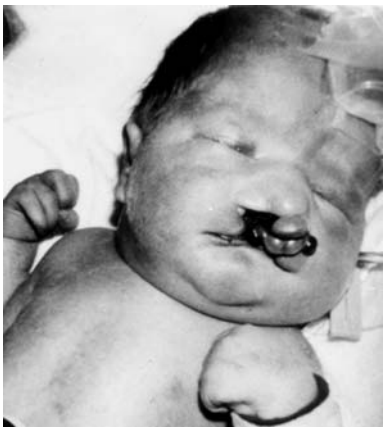

Figure P28. Pätau syndrome. (Courtesy of Dr. Judith Miles)

Patch (*Ptc*): ►sonic hedgehog, ►hedgehog

Patch (patched duplex): The resolution of a recombination intermediate (Holliday junction) without an exchange of the flanking markers (can be gene conversion). ►Holliday model L

Patch Clamp Technique: The method to measure the flow of current through a voltage gated ion channel by tightly pressing an electrode against the plasma membrane. It is used also for the sensitive in situ study of neurotransmitters. ►ion channels

Patch Mating: Actin patches of the cytoskeleton can be used in yeast to quantify the number of viable diploid cells in the presence of silencer genes, which regulate the expression of mating types. Actin patches are detectable for duration about 10 seconds at sites of polarized growth and then rapidly disappear. ►mating type determination in yeast; Smith MG et al 2001 J Cell Sci 114(pt 8):1505.

Patella Aplasia-Hypoplasia (PTLAH, 17q21-q22): The absence or reduction of the size of the knee cap. The symptoms occur also in various syndromes such as the Coffin-Siris syndrome, trisomy 8 syndrome. ►Coffin-Siris syndrome, ►nail-patella syndrome

Patent: The so-called gene patents do not protect the DNA (or ESTs) sequence itself, rather the process of manipulation is the object. The gene "ownership" only prevents the use or selling a particular sequence without permission. In general, according to US patent laws, the patent is protected for 17 years from date of issue. A requisite for patenting is that the

subject of the patent application would be new and non-obvious and practically useful, e.g., a probe for a gene. Natural DNA sequences are not patentable, but purified or isolated recombinant molecules or parts of a vector are patentable. Legal patentability requirements: (i) usefulness, (ii) novelty, (iii) being non-obvious, and (iv) definiteness of description. A further requirement is "enablement," i.e., a trained person after reading the patent description can use the "invention" without further research. In October 1998, USA, the first patent was awarded to an EST. Once a patent is issued, even further, originally undisclosed applications are protected. Also, another person after isolating a full-length open reading frame using an STS may obtain a patent but not without the permission of the "inventor" of the patented STS. During the period of patent, the patent-holder can prevent anybody from using it, including those who invented the same independently or even those who improved on the procedure to such an extent that the second invention meets the requirements for patenting. However, the inventor is obligated by law to disclose the invention in sufficient technical detail so that anybody with proper expertise can use it. The fact that an invention was arrived at under federal financial support does not exclude patentability but the inventor must report the patentable invention to the sponsoring agency. The intention of the government is that the invention would be used at maximum benefit to the public that can be achieved most effectively by commercial private enterprises. Laboratory assays, reagents and procedures, including computer programs may also be patentable. By 2005, more than 4000 genes were patented and three-fourths of them by single individuals. Presenilin gene (PSN2) has 8 patent owners for 9 patents and breast cancer gene (BRCA1) has 12 owners for 14 patents. Of the 292 cancer genes reported by 2004, 131 are patented (Jensen K, Murray F 2005 Science 310:239).

The patenting of the outcome of genetic research may be harmful to science if the investigators keep the ongoing work a secret until it becomes patentable. Patenting basic research products (upstream inventions) is detrimental to society because it may prevent the development of new useful (commercial) products. The Bayh–Dole Act allows the "exemption for research" to facilitate the use of the results of basic research. Unfortunately, this exemption is difficult to define and is subject to controversy (Holman C 2006 Cell 125:629). The exemption can be applied to the patent (effectiveness, usefulness) itself but does not permit application of the patent (Kaye J et al 2007 Nature Biotechnol 25:739). If the discovery is published through proper means of scientific communications prior to the patent application, it is disqualified from patenting. It is generally easier to patent a product than a process. Natural products (e.g., proteins) are usually not patentable unless they are modified in some way and are different from the natural product in structure or function and these properties were not generally known. A DNA sequence, identified as the coding unit for a genetic disease or a genetic marker in its vicinity, may be patentable but a cloned gene that may be used for translating a protein may be not. DNA markers are patentable only if their direct use can be determined. The concept of patenting biological material raises several moral objections but it is defended by the biotechnology industry because it takes 100s of millions of dollars for the completion of such projects, and without the financial means, these investigations cannot be maintained. Between 1981 and 1995, a total of 1175 human DNA sequences were patented. If the subject of the patent has been published or in use for more than one year prior to the date of the patent application, it will not be approved. If another person can prove that he/she invented the object before the date of publication by others, the person may still be entitled to a patent. The patent laws vary in different countries, and new legislation may take place any time. The European Union is now approving patents for human genes and transgenic animals and plants. An alternative to patenting is Trade Secret Protection. One way of preventing another person from patenting an invention is public disclosure, e.g., publication in sufficient details (e.g., in a scientific journal). This ensures that another party would not be able to claim priority for the invention, which is one of the requisites for patenting. Publications may not necessarily provide an effective and lasting protection. Patent infringement usually does not entitle the patentee for more financial compensation than the reasonably calculated loss of royalty or profit caused by the infringement. It must also be verified that the original patent description do not include deceptive assertions.

The justification of an existing patent may be challenged administratively by *inter partes* re-examination request to the US Patent and Trademark Office (USPTO, Washington DC, USA). The claim must prove substantial new question of patentability based on a "prior art" document and requires a fee of $8800. This procedure has monetary advantages vis-à-vis litigation (Derzko NM, Behringer JW 2003 Nature Biotechnol 21:823). The patent regulations are subject to changes and it is advisable to seek consent from the owners of the patent even when the invention is used only for laboratory research. A recent analysis revealed many problems with patents granted by USPTO. The patents examined had problems with description (37.5%), enablement/utility (42.4%) novelty/non-obviousness (6.9%) and

definiteness (13.1%). The conclusion faulted insufficient educational background of the examiners with most of the problems (Paradise J et al 2005 Science 307:1566). ►STS, ►EST, ►SNP, ►Herfindahl index, ►presenilin, ►breast cancer, ►cancer, ►Cohen-Boyer patent on recombinant DNA; Eisenberg RS 1992 p 226. In: Annas GJ, Elis S (Eds.) Gene Mapping, Oxford University Press, New York, DNA-based patents: Robertson D 2002 Nat Biotechnol 20:639; Arnold BE, Ogielska-Zei E 2002 Annu Rev Genomics Hum Genet 3:415; patented genetic sequence information retrieval: Dufresne G et al 2002 Nature Biotechnol 20:1269; ethical issues of DNA patenting: Resnik DB 2004 Owning the Genome: A Moral Analysis of DNA Patenting, State University New York Press, Albany, New York; Eisenberg RS 2003 Science 299:1018; Robertson JA 2003 Nature Rev Genet 4:162; property rights in plant breeding: Fleck B, Baldock C 2003 Nature Rev Genet 4:834; Paradise J, Janson C 2006 Nature Rev Genet 7:148; Van Overwalle G et al 2006 Nature Rev Genet 7:143; stem cell lines: Loring JF, Campbell C 2006 Science 311:1716; http://geneticmedicine.org or patents in general: http://www.uspto.gov; http://scientific.thomson.com/derwent; http://www.bioforge.org; http://www.bustPATENTS.COM/; gene and sequence patents for various organisms: http://www.patome.org/; ftp://ftp.ebi.ac.uk/pub/databases/embl/patent; ftp://ftp.wipo.int/pub/published_pct_sequences.

Patent Ductus Arteriosus (6p12): The ductus arteriosus connects the lung artery and the aorta and shunts away blood from the lung of the fetus. Normally it fades away after birth. In ~1/2000 cases, this does not happen and the duct stays open and causes heart defect. The disease may be caused by fetal rubella infection and apparently by autosomal dominant gene(s). The 6p12-p21 dominant *Char syndrome* involves patent ductus, facial anomalies and abnormal fifth digit of the hand (see Fig. P29).

Figure P29. Char syndrome. In the Char syndrome the middle phalanx of the fifth digit is missing

The basic problem is traced to TFAP2B neural crest-related transcription factor that does not bind properly to its target. Risk of recurrence in an affected family is about 1–2%. General incidence is less than 10% of that. ►risk, ►aneurysm; Zhao F et al 2001 Am J Hum Genet 69:695.

Paternal Leakage: The transmission of mitochondrial DNA through the males. Generally, mitochondria are not transmitted through the animal sperm because mitochondrial DNA of spermatozoon is destroyed by ubiquitination in the oocytes (Sutovsky P et al 2000 Biol Reprod 63:582). In mice, apparently the male transmission of mitochondria is within the range of 10^{-5}. In interspecific mouse crosses, paternal mitochondria are transmitted but they are eliminated during early embryogenesis or later during development (Kaneda H et al 1995 Proc Natl Acad Sci USA 92:4542). Heteroplasmy is rare. The role of transmission of mitochondria in humans is not clear. Some cytological observations may indicate the incorporation of the midpiece of the sperm (containing mitochondria) into the egg. Genetic evidence for human paternal transmission of mitochondria is rare (Schwartz M, Vissing J 2002 N Engl J Med 347:576).

In some molluscans (mussel), there is a strong biparental inheritance of mtDNA. In *Mytilus* the paternal and maternal mtDNA displays 10–20% nucleotide divergence. The females transmit just one type of mitochondria to sons and daughters whereas the males transmit a second type of mtDNA genome to the sons. Biparental transmission of mtDNA may also occur in interspecific crosses of *Drosophila*. In *Paramecia*, mitochondria may be transmitted through a cytoplasmic bridge. In fungi, the transfer is maternal although in some heterokaryonts cytoplasmic mixing may take place. In some slime molds, mtDNA transmission is also mating type dependent. In *Physarum polycephalum* different *matA* alleles regulate the mtDNA transmission but a plasmid gene may also be involved and recombination can take place between mtDNAs. In *Chlamydomonas* algae, several genes around the mating type factors were implicated. In the contact zone of hybridizing conifers (*Picea*) recombinant mtDNA was observed as apparent result of paternal leakage (Jaramillo-Correa JP, Bousquet J 2005 Genetics 171:1951). ►mtDNA, ►plastid male transmission, ►Eve foremother, ►mitochondrial disease in humans, ►mitochondrial genetics, ►plastid genetics, ►doubly uniparental inheritance, ►*Paramecium*, ►heteroplasmy; Eyre-Walker A 2000 Philos Trans R Soc Lond B Biol Sci 355:1573; Shitara H et al 1998 Genetics 148:851; Yang X, Griffith AJ 1993 Genetics 134:1055; Meusel MS, Moritz RF 1993 Curr Genet 24:539.

Paternal Transmission: Imprinting causes paternal transmission of certain genes. Some of the human insulin and the insulin-like growth factor alleles may be preferentially inherited through the paternal chromosome and cause early-onset obesity. ►imprinting, ►obesity, ►paternal leakage; Le Stunff C et al 2001 Nature Genet 29:96.

Paternity Exclosure: Based on genetic paternity tests. ►paternity testing, ►DNA fingerprinting, ►Y chromosome, ►alternate paternity

Paternity Testing: Frequently required in civil litigation suits, it might have significance for medical, population, immigration, archeological and other cases. The laboratory procedures are generally the same as used for DNA fingerprinting. Here, as in DNA fingerprinting in general, the exclusion of paternity is simple and straightforward. However, the determination of identity may pose more difficulties because in the multilocus tests more than 10% of the offspring may show one band difference and 1% may show two, due to mutation. Therefore, Penas and Chakraborty (Trends Genet 10:204 [1994]) recommended the formula shown in Figure P30.

$$PI = \frac{\binom{N}{U}\mu^{U}(1-\mu)^{N-U}}{\binom{n}{U}X^{n-U}(1-X)^{U}}$$

Figure P30. Penas-Chakraborty formula

PI = paternity index, μ = mutation rate, X = band-sharing parameter, N = total number of bands per individual, n = number of test bands, U = number of bands not present in the alleged father. In rare instances (mistakes at maternity wards) similar test may be necessary to test maternity. The biological father of a child—even if the paternity can be accurately proven—cannot assert paternal rights against the will of the mother if she was/is married to another man (Hill JL 1991 N Y Univ Law Rev 66:353). When "the child is born to a mother who is single or part of a lesbian couple, law does permit the biological father to assert his paternal rights, even if he clearly stated his intention prior to conception to have no relation" (Charo RA 1994 In: Frankel MS, Teich A (Eds.) The Genetic Frontier. Ethics, Law and Policy, American Association of Advance Science, Washington DC). ►Y chromosome, ►forensic genetics, ►DNA fingerprinting, ►forensic index, ►utility index, ►surrogate mother, ►microsatellite typing

Path Coefficient: This method of Sewall Wright was worked out for studying mathematically and by diagrams, the paths of genes in populations and genetic events determining multiple correlations. Here it is not possible to discuss meaningfully the mathematical foundations but one type of graphic application for determining some relations between offspring and parents can be found under *F* and inbreeding coefficient. ►inbreeding coefficient, ►correlation; Wright S 1923 Genetics 8:239; Wright S 1934 Ann Math Stat 5:161.

Pathogen: An organism (microorganism) capable of causing disease on another. (See pathogen database: http://www.nmpdr.org; ►vectors for pathogens, ►*Brucella*, ►*Rickettsia*, ►*Coxiella* and viruses: https://patric.vbi.vt.edu).

Pathogen Identification: The food industry may need rapid and highly sensitive methods for the detection of live pathogens in various products. In case of viable *E. coli* cells, this is feasible by infection with compatible bacteriophages carrying bacterial luciferase inserts. The genes in the phages are expressed only in live bacteria and if such are present, with a high-powered luminometer or by a microchannel plate enhanced image analyzer, even a single bacterial cell emitting light may be detected. Immunoassays and PCR are also useful for the detection of the presence of pathogens. An apparently very fast procedure is based on B lymphocyte sensors (CANARY: cellular analysis and notification of antigen risks and yields), which are engineered with the potential to express green fluorescent protein (GFP, aequorin) and membrane-bound antibodies specific for the pathogen of interest. GFP is a calcium-activated light emitter. When the antibody binds the pathogen, the intracellular calcium concentration is elevated within seconds and fluorescence is readily detectable. A bio-conjugated nanoparticle-based fluorescence immunoassay for in situ pathogen quantification detects single bacteria within 20 min (Zhao X et al 2004 Proc Natl Acad Sci USA 101:15027). For epidemic surveillance of respiratory pathogens, identification and strain typing can employ electrospray ionization mass spectrometry and polymerase chain reaction amplification from highly conserved genomic regions even from polymicrobial mixtures (Ecker DJ et al 2005 Proc Natl Acad Sci USA 102:8012). ►luciferase bacterial, ►immunological test, ►B lymphocytes, ►bioterrorism, ►PCR, ►aequorin, ►electrospray MS, ►polymerase chain reaction, ►quenched autoligation probe, ►quantum dot; Rider TH et al 2003 Science 301:213; GeneDB, bacterial, protozoa, fungal gene sequences: http://www.genedb.org/.

Pathogen-Derived Resistance: The protection of plants against certain pathogens by the transgenic expression of viral coat proteins, other proteins, antisense sequences, satellite and defective viral sequences. ►host–pathogen relations, ►plantibody

Pathogenesis Related Proteins (PR): A variety of acidic or basic proteins synthesized in plants upon infection

with pathogens. The chitinases and glucanases apparently act by damaging the cell wall of fungi, insects or even bacteria. ►host–pathogen relations, ►SAR

Pathogenic: Capable of causing disease. (See Hill, A,V. S. 2001 Annu Rev Genome Hum Genet 2:373).

Pathogenicity Island (PAI): A group of genes in a pathogen involved in the determination and regulation of pathogenicity. In *Helicobacter pylori*, these islands are delineated by 31 bp direct repeats (DR), and indicate that horizontal transfer acquired these. Commonly the same genes are present between the ends of this large insert and the chromosomal genes in both pathogenic and non-pathogenic species of the same group of bacteria. Frequently, the insert is adjacent to a tRNA 3′ sequence or a codon for an unusual amino acid. The DNA inserts encode a rather specific secretory system (type III) and elements of transport and bacterial surface effectors located then next to host cell receptors. The PAI may carry insertion elements, integrases and transposases and their sequences may be unstable. Their location may change within the same bacterium. This organization is conducive to effective subversion the host defense system. The size of the pathogenicity islands may vary from 10 to 200 kb or more. The base composition of the islands and the codon usage may differ from that of the core DNA. In some bacteria only a single PAI occurs, in others there are several. Similar mechanisms operate in both animals and plants. ►transmission, ►cholera toxin, ►host–pathogen relations, ►integrase, ►transposase, ►secretion system, ►codon usage, ►*Helicobacter pylori*, ►symbionts; Hacker J, Kaper JB 2000 Annu Rev Microbiol 54:641; http://www.gem.re.kr/paidb.

Pathogenicity Islet: These are similar in some functions to pathogenicity islands but their size is much smaller, 1–10 kb.

Pathovar: Plant varieties or species, which share disease susceptibility/resistance genes. Alternatively, a plant pathogen that is specific for a taxonomic group of plants.

Pathway Tools (http://bioinformatics.ai.sri.com/ptools/): Software for determining metabolic and signaling pathways and database. ►EcoCyc, ►MetaCyc, ►BioCyc

Pathways: Guide to metabolic, molecular, immunological and many other processes and interactions: http://www.pathguide.org/; network tools: http://visant.bu.edu/.

Patrilocality: An anthropological term indicating that males more frequently bring in mates from outside their location than moving to the location of the females.

Patristic Distance: The sum of the length of all branches connecting two species in an evolutionary tree. ►evolutionary tree

Patroclinous: Inheritance through the male such as the Y chromosome, androgenesis, fertilization of a nullisomic female with a normal male, through nondisjunction the chromosome to be contributed by the female is eliminated, some of the gynandromorphs, sons of attached-X female *Drosophila*, etc. ►gynandromorph, ►nondisjunction, ►attached-X

Patronymic: A designation indicating the descent from a particular male ancestor, e.g., Johnson, son of John or O'Malley descendant of Malley. Common family names may assist in isolated populations to establish relationships. This analysis may be improved by studies of Y-chromosomal molecular markers. ►isonymy, ►Y chromosome

Pattern Formation during Development: Pattern formation specifies the arrangement of the cells in three dimensions. Developmental patterns may begin by intracellular differentiation (animal pole, vegetal pole, yolk), positional signals between cells and intracellular distribution of the receptors to various signals. Fibroblast growth factor and transforming growth factor-β have apparently major roles as epithelial and mesoderm induction signals. The *Drosophila* gene *fringe* (*fng*) is involved with mesoderm induction and in wing embryonal disc formation. Juxtaposition of *fng*-expressing and non-expressing genes is required for establishing the dorsal ventral boundary of wing discs. The gene *fng* is expressed in the dorsal half of the wing disc whereas *wingless* (*wg*, 2-30) is limited to the dorsal-ventral boundary. Gene *hedgehog* (*hh*, 3-81) is expressed in the posterior half, and *decapentaplegic* (*dpp*, 2-40) is detected in the anterior-posterior boundary. Anterior-posterior patterning in *Drosophila* is affected by the *trithorax* (*trx*), *Polycom* (*Pc-G*) family members such as *extra sex combs* (*esc*). The homolog of the latter, *eed* (embryonic ectoderm development) controls anterior-posterior differentiation in mouse. Homologs to these genes have been identified in other animals and humans as well. In *Xenopus*, it appears that the FNG protein is translated with a signal peptide (indicating that it is secreted), in the proFNG, peptide is terminated with a tetrabasic site for proteolytic cleavage and after this processing it is ready for the normal function. *Wingless* of *Drosophila* is homologous to *Wnt1* mouse mammary tumor gene. The branching pattern of trachea and lung, respectively in *Drosophila* and mammals is controlled primarily by the fibroblast growth factor

signaling pathway. This is used reiteratively in repeated sequences of a branching. At each stage different feedback and other control signals provide the specifications (Metzger RJ, Krasnow MA 1999 Science 284:1635). In mice, mutation of the *Foxn1* gene causes follicular development to terminate just after it starts accumulating pigments. Then the immature follicles restart the developmental process and the skin color of the animal displays the striped pattern (Suzuki N et al 2003 Proc Natl Acad Sci USA 100:9680). Vascular mesenchymal cells can differentiate into specific embryonic structures and in adult diseases the process may be restarted again and bone osteoblasts may arise in the walls of the arteries or in the cardiac walls under the influence of morphogens. The process may be mathematically modeled (Garfinkel A et al 2004 Proc Natl Acad Sci USA 101:9247). In bacteria pattern formation can be programmed in a synthetic system by acyl-homoserine chemical signals emitted by labeled "sender" cells to "receiver" cells in Petri plate cultures (see Fig. P31).

Figure P31. Pattern formation induced by the sender cells (darker color) in the receiver cells (lighter color) lawn of bacteria. In the experiments the two types of cells were distinguished by flourescence. (Redrawn after Basu, S. et al. 2005 Nature [Lond] 434: 1130)

A newer idea posits that the mechanical control of form precedes pattern formation (Ingber DE 2005 Proc Natl Acad Sci USA 102:11571). Using microfabrication for controlling the organization of sheets of cells revealed the emergence of stable patterns of proliferative foci. Concentrated growth corresponded to regions of high tractional stress and could be measured by micromechanical force sensor. Inhibiting actomyosin-based tension or cadherin-mediated connections between cells disrupted spatial pattern of proliferation. The conclusion is that contraction of cells, an existence of pattern of mechanical forces, is due to multicellular organization and the tissue form is an active regulator of tissue growth (Nelson CM et al 2005 Proc Natl Acad Sci USA 102:11594).

Developmental pattern formation is under genetic control also in plants (Lee MM, Schiefelbein J 1999 Cell 99:473). The progress has been much slower, however, because the plant tissues and cells are more liable to dedifferentiation and redifferentiation. Mutants have been obtained with clear differences in morphogenesis, with the exception of flower differentiation and photomorphogenesis, much less is known about the molecular mechanisms involved. Down-regulation of the MYB transcription factor gene (*PHANTASTICA*) changes compound pinnate (left) leaves into palmate compound (right) leaves (see Fig. P32) (Kim M et al 2003 Nature [Lond] 424:438). ►morphogenesis, ►morphogenesis in *Drosophila*, ►RNA localization, ►flower differentiation, ►photomorphogenesis, ►MADS box, ►signal transduction, ►homeotic genes, ►cell lineages, ►fibroblast growth factor, ►actomyosin, ►cadherin; reaction–diffusion model of leaf venation as a mechanism of pattern formation: Dimitrov P, Zucker SW 2006 Proc Natl Acad Sci USA 103:9363; Malakinski G, Bryant P (Eds.) 1984 Pattern Formation: A Primer in developmental biology, Macmillan, New York; Comparative Pattern Formation in Plants and Animals: Willemsen V, Scheres B 2004 Annu Rev Genet 38:587.

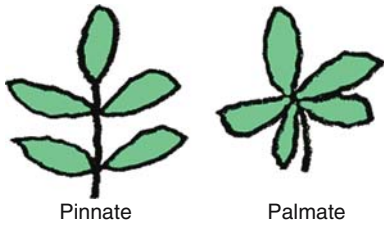

Figure P32. Pinnate (left); palmate (right)

Pattern Recognition Receptors (PRR): These are tools of the innate immunity system. They recognize pathogen-associated molecular patterns (PAMPs) that are essential for the survival of the pathogen and are therefore stable. PRRs are hereditary, are conserved across phylogenetic categories, expressed constitutively and do not require immunological memory. PRRs recognize pathogen-associated molecular patterns such as exist in lipopolysaccharides, proteoglycans or double-stranded RNA. (See Qkira S et al 2006 Cell 1214:763; innate immunity, Toll, host–pathogen relationship, downstream pathways: Lee MS, Kim Y-J 2007 Annu Rev Biochem 76:447.

PAU Genes: ►seripauperines

pauling: ►evolutionary clock

PAUP (phylogenetic analysis using parsimony): A computer program for the analysis of evolutionary descent on the basis of molecular data. ►evolutionary distance, ►evolutionary tree

Pause: RNA polymerase, I, II and III do not operate continuously at the same rate but due to various causes, their transcription may hesitate and then

resume synthesis. A minimal functional element of PAUSE-1 is $TCTN_xAGAN_3T_4$ where x = 0, 2 or 4. Various elongation proteins such as ELL, Elongin, and transcription factor TFIIF may mediate pausing. The pause may facilitate the binding of regulatory factors. Pausing and backtracking allows the binding of the RfaH suppressor factor of early termination (Artsimovich I, Landick R 2002 Cell 109:193). Pausing may allow for proofreading and elimination of misincorporated bases (Shaevitz JW et al 2003 Nature [Lond] 426:684). Sequence-specific pause sites have been revealed (Herbert KM et al 2006 Cell 125:1083). ►attenuator region, ►Nus [►lambda phage], ►σ; Ogbourne SM, Antalis TM 2001 Nucleic Acids Res 29:3919.

Pausing, Transcriptional (hesitation): The discontinuity of the transcriptional process by all RNA polymerases. As a consequence there is a heterogeneity of the transcripts because of the differences in recognition of modulating factors such as attenuation, transcription factors TFIIF, ELL, silencers, nus (λ phage), antitermination signal, etc. Paucity of a nucleotide(s) or too high concentration of it may slow down transcription. RNA polymerase often pauses before a GTP is incorporated. Pause signals have been detected in both the template and the non-template DNA strands. Generally, hairpin structures (RNA base-pairing) favor pausing although secondary structure may not be the sole cause of it. DNA sequences 16–17 bp downstream of the pause may alter the conformation of the polymerase and the pause. Even the non-template strand may have an effect. ►arrest transcriptional, terms named under separate entries; Davenport RJ et al 2000 Science 287:2497.

PAX (paired box homeodomains): They are so called because they include two helix-turn-helix DNA-binding units. Several PAX proteins are known to be encoded in at least five different chromosomes and they mediate the development of the components of the eyes in insects (compound eyes) and humans, teeth, the central nervous system, the vertebrae, the pancreas and tumorigenesis. The 130-residue paired domain binds DNA and functions as a transcription factor for B cells, histones and thyroglobulin genes. The *Pax5* gene encodes the BSAP transcription factor. Mutation in *Pax5* arrests B cells at the pro-B stage. BSAP may also promote the expression of CD19 and indirectly IgE synthesis. BSAP may block the immunoglobulin heavy chain 3′-enhancer and isotype switching and the formation of the pentameric IgM antibody. The activator motifs of BSAP display about 20 times higher binding affinity to the DNA than the repressor motif yet the activator or repressor function depends primarily on the context of the motif. The level of BASP is high in the pre-B and immature B cell stages and after the antigen signal has arrived its level greatly diminished by signals from IL-2 and IL-5. Overexpression of BSAP results in its repressor activity. PAX6 (11p13) mutations cause absence of the iris of the eye (aniridia) without elimination of vision but other general neurodevelopmental problems. ►Waardenburg syndrome, ►DiGeorge syndrome, ►aniridia, ►Wilms tumor, ►renal-coloboma syndrome, ►hypodontia, ►rhabdosarcoma, ►animal models, ►B cell, ►immunoglobulins, ►histones, ►thyroglobulin, ►hox, ►homeotic genes, ►isotype switching, ►FKP, ►goiter familial, ►helix-turn-helix motif, ►integrin, ►PTIP, ►myoblast, ►neural crest; Balczarek KA et al 1997 Mol Biol Evol 14:829; Chi N, Epstein JA 2002 Trends Genet 18:41; Pichaud F, Desplan C 2002 Curr Opin Genet Dev 12:430; http://pax2.hgu.mrc.ac.uk/; http://pax6.hgu.mrc.ac.uk/.

PAZ Domain (Piwi/Argonaute/Zwille): In Argonaute 1 protein it consists of a left-handed, six-stranded β-barrel capped at one end by two α-helices and wrapped on one side by a distinctive appendage, which comprises a long β-hairpin and a short α-helix. The PAZ domain binds a 5-nucleotide RNA with 1:1 stoichiometry. It plays a role in RNAi function and it is present in both Argonaute and Dicer proteins. ►Argonaute, ►Dicer, ►RNAi; Yan KS et al 2003 Nature [Lond] 426:469; Lingel A et al 2003 Nature [Lond] 426:465; Ma J-B et al 2004 Nature [Lond] 429:318; PIWI domain structure: Parker JS et al 2005 Nature [Lond] 434:663; Ma J-B et al 2005 Nature [Lond] 434:666.

PBAF: An ATP-dependent chromatin remodeling complex. ►chromatin remodeling; structure of PBAF: Leschziner AE et al 2005 Structure 13:267.

Pbp74: ►Hsp70

pBR322: A non-conjugative plasmid (constructed by Bolivar & Rodriguez) of 4.3 kb, can be mobilized by helper plasmids because (although it lost its mobility gene) it retained the origin of conjugal transfer (see Fig. P33). It is one of the most versatile cloning vectors with completely known nucleotide sequence and over 30 cloning sites. It carries the selectable markers ampicillin resistance and tetracycline resistance. Insertion into these antibiotic resistance sites permit the detection of the success of insertion because of the inactivation of these target genes results in either ampicillin or tetracycline sensitivity. Although its direct use of this 20-year old plasmid has diminished during the last years, pBR322 components are present in many currently used vectors. ►plasmid, ►vectors, ►Amp, ►tetracycline; Bolivar, F., Rodriguez RL et al 1977 Gene 2:95.

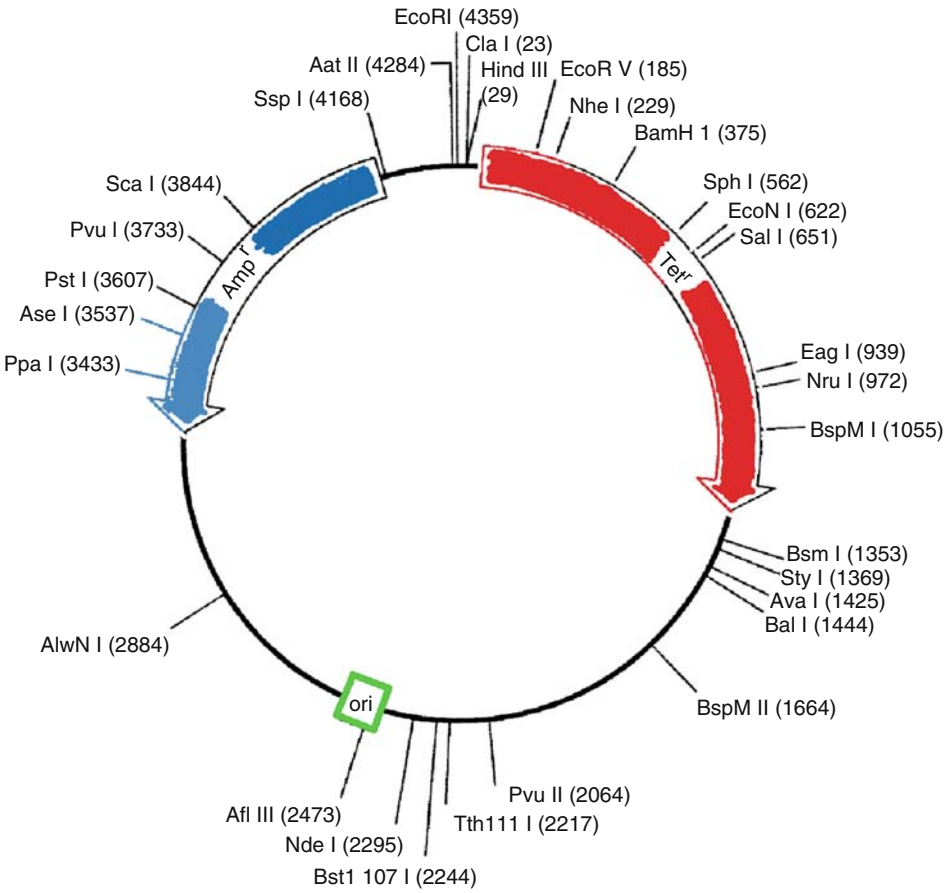

Figure P33. pBR vector (4361 bp), From Pharmacia Biotech Inc., by permission

PBS: Phosphate buffered saline. ►saline

PBSF (pre-B cell growth-stimulating factor): A ligand of CXCR controlling B cell development and vascularization of the gastrointestinal system. ►CXCR, ►lymphocytes; Egawa T et al 2001 Immunity 15:323.

PBX1, PBX2: Transcription factors involved in B cell leukemias, encoded in human chromosomes 1q23 and 3q222, respectively. ►leukemia

p. c.: ►post coitum

PC4 (positive co-activator of transcription): PC4 interacts with activator protein-1 (AP-2) and facilitates transcription, and may relieve the self-interference of AP-2. ►transcription, ►AP1; Zhong L et al 2003 Gene 320:155.

PCA (principal component analysis): A multivariate statistical method that separates the original variables into independent variables and associated variances. It may be useful for the interpretation of microarray data. (See Méndez MA et al 2002 FEBS Lett 522:24).

PCAF: A human acetyltransferase of histones 3 and 4. ►p300, ►$TAF_{II}230/250$, ►histone acetyltransferases, ►nucleosome, ►signal transduction, ►chromatin remodeling, ►bromodomain, ►INHAT; Blanco JC et al 1998 Genes Dev 12:1638.

PCB: Polychlorinated biphenyl is an obnoxious industrially employed carcinogen. A *Pseudomonas* enzyme may break it down. ►environmental carcinogens, ►sperm

PCD: ►apoptosis

pCIP: A co-activator protein, interacting with p300 (CREB) and regulates transcription and somatic growth of mammals. ►signal transduction, ►nuclear receptors; Wang Z et al 2000 Proc Natl Acad Sci USA 97:13549.

PCL: Putative cyclin. ►cyclin

PCNA (proliferating cell nuclear antigen): An auxiliary protein (a processivity factor) in pol δ and pol ε functions in eukaryotes. It has a similar role in DNA replication in general, and in the cell cycle and repair. Its function is similar to that of the β subunit of the prokaryotic pol III, it provides a "sliding clamp" on the DNA to be replicated. Binding to p21 may inhibit

PCNA replicative function. PCNA also binds other proteins such as cyclin D, FEN1/Rad27/MF1, DNA ligase 1, GADD, DNA methyltransferase, DNA repair proteins XPG, MLH and MSH. The protein interaction (PIP-box) provides a dock for interaction with replication and repair proteins (Bruning JB, Shamoo Y 2004 Structure 12:2209). The PCNA-interacting mutations in PCNA alter the conditions for nucleosomal assembly by interacting with CAF. Under such conditions, silencing by heterochromatin is reduced or lost. Some mutations in RFC may compensate for defects in PCNA. If the DNA is damaged, PCNA is modified by mono-ubiquitination at lysine residue 164 or a lysine 63-linked multi-ubiquitin chain to allow error-free or error-prone replication bypass of the damaged site. Ubiquitination of PCNA at lysine 164 specifically activates DNA polymerase η and Rev1, a deoxycytidyl-transferase in mutagenic replication of DNA (Garg P, Burgers PM 2005 Proc Natl Acad Sci USA 102:18361). In addition, SUMO-modified PCNA may recruit Srs2 helicase, which disrupts recombination by affecting Rad51 protein (Pfander B et al 2005 Nature [Lond] 436:428). ►DNA replication, ►eukaryotes, ►cell cycle, ►DNA polymerases, ►ligase DNA, ►p21, ►cyclins, ►ABC excinuclease, ►excision repair, ►mismatch repair, ►sliding-clamp, ►methylation of DNA, ►Rad27/Fen1, ►RFC, ►CAF, ►heterochromatin, ►ubiquitin, ►SUMO, ►Srs, ►Rad51; Karmakar P et al 2001 Mutagenesis 16:225; Ola A et al 2001 J Biol Chem 276:10168; López de Saro FJ, O'Donell M 2001 Proc Natl Acad Sci USA 98:8376; Lau PJ, Kolodner RD 2003 J Biol Chem 278:14; crystal structure of binding domains: Kontopidis G et al 2005 Proc Natl Acad Sci USA 102:1871; review: Moldovan G-L et al 2007 Cell 129:665.

PCR: ►polymerase chain reaction

PCR, Asymmetric: By using unequal amounts of amplification primers, an excess of single-strand copies of DNA can be obtained (Gyllensten UB, Erlich HA 1988 Proc Natl Acad Sci USA 85:7682). ►polymerase chain reaction, an improved procedure: Pierce KE et al 2005 Proc Natl Acad Sci USA 102:8609.

PCR, Allele-Specific: Used to screen a population for a particular allele-specific mutation, e.g., mutations responsible for MELAS in the aging human mitochondrial DNA. One of the most common mutations in this anomaly involves the transition A→G at site 3243. If the primer containing the complementary base C is used, the mutant sequence from appropriate tissues is successfully amplified and can be detected by gel electrophoresis. The same C primer does not generate substantial quantity of the fragment using the wild type template. Thus, by this procedure, the approximate frequency of this allele-specific mutation or recombination can be determined. ►polymerase chain reaction, ►mitochondrial disease in humans, ►transition mutation, ►hot-start PCR; Ugozzoli L, Wallace RB 1992 Genomics 12:670.

PCR, Broad-Based: Uses primers, which amplify a broad base of genes, e.g., the microbial rRNA genes or a group of viral genes common to the majority of related species in order to facilitate molecular identification of same pathogens. RDA and other procedures may supplement the analysis. ►RDA

PCR, Competitive: Used for quantifying DNA or RNA. The competitor nucleic acid fragment of known concentrations in serial dilutions is co-amplified with another (the experimental) nucleic acid of interest using a single set of primers. The beginning quantity of the experimental molecules is estimated from the ratio of the competitor and experimental amplicons obtained during the PCR procedure that are supposedly amplified equally. The quantity of the unknown DNA is determined by the equivalence-point (EQP) where the experimental and the competitor show the same signal intensity indicating that their amounts is the same. A simplified new version is described by Watzinger F et al 2001 Nucleic Acids Res 29(11):e52.

PCR, Discriminatory: A method to detect small mismatches or point mutations (see Fig. P34). It is a much easier method than sequencing larger sequences to distinguish, e.g., phylogenetic differences within taxonomic groups. (See Picard FJ et al 2004 J Clin Microbiol 42:3686).

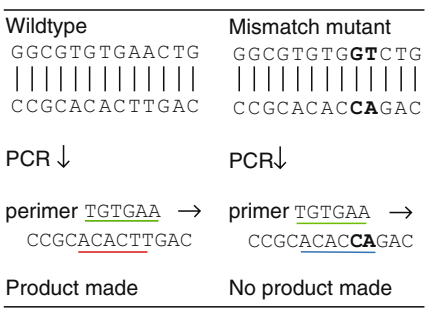

Figure P34. Discriminatory PCR

PCR, DOC (degenerate oligonucleotide-primed polymerase chain reaction and capillary electrophoresis of DNA): A random amplification technique combined with analysis on microchips. ►capillary electrophoresis, ►PCR, ►DOP-PCR; Cheng J et al 1998 Anal Biochem 257:101.

PCR, Electronic: ►electronic PCR

PCR, Methylation-Specific: ►methylation-specific PCR

PCR, Multiplex: Employs multiple sets of primers for amplification in a single reaction batch. (See Broude NE et al 2001 Proc Natl Acad Sci USA 98:206).

PCR, Nested: The use of two different internal primers to thus identify overlapping transcripts.

PCR, Overlapping: The use of two sets of primers; each has complementary sequences at the 5′-end. Two separate PCRs are carried out and then the products purified by gel to remove the unincorporated primers. A second PCR process uses only the outside primer pairs and the two primary products are joined. ►PCR

PCR, Quantitative: Determine gene expression quantitatively by optimized primers: http://primerdepot.nci.nih.gov/; http://mouseprimerdepot.nci.nih.gov/.

PCR, Real-Time Reverse Transcription: see Seeger K et al 2001 Cancer Res 61:2517.

PCR, Single Molecule: ►polony

PCR Targeting: ►targeting genes

PCR, Transcriptionally Active (TAP): 1. Specific primers amplify the gene of interest. 2. Mixtures of DNA fragments are equipped with promoter and terminator elements and then can be used for transfection in a suitable plasmid. They can be inserted into plasmids also by homologous recombination. TAP products can be used as DNA vaccines and generate antibodies against the encoded genes. The procedure is suitable for the generation of hundreds or thousands of transcriptionally active genes for genomic/proteomic studies. (Liang X et al 2002 J Biol Chem 277:3593).

PCR-Based Mutagenesis: Any base difference between the amplification primer will be incorporated in the future template through polymerase chain reaction. Actually only half of the new DNA molecules would contain the alteration present in the original amplification primer unless a device is used, e.g., the undesired strand would be made unsuitable for amplification and therefore lost from the reaction mixture. The method may include multiple point mutations, small insertions or deletions too. The amplification may also result in other nucleotide alterations as a result of the error-prone Taq polymerase. ►local mutagenesis, ►primer extension, ►polymerase chain reaction, ►DNA shuffling, ►VENT, ►small-pool PCR; Nelson RM, Long GL 1989 Anal Biochem 180:147.

PCR-LSA (polymerase chain reaction amplification): A method for the localization of SNIPS. ►SNIPS, ►RRS

PCR-Mediated Gene Replacement: The procedure replaces—by mitotic recombination—particular genes with an identifiable marker of a neutral phenotype. A 20 bp unique sequence tract tags each of these lines. On the basis of hybridization of the PCR products to a tag sequence, it is possible to quantitate the altered cell lines in a population. When one of the target genes is deleted in diploid yeast, the other is still expected to be functional. Some of them, however, due to haplo-insufficiency, will display a defective phenotype. These "heterozygotes" may also display increased sensitivity to drugs and may be used for pharmaceutical research. ►haplo-insufficiency; Giaever G et al 1999 Nature Genet 21:279.

PC-TP: phosphatidylcholine transfer protein mediating transfer of phospholipids between organelles within cell.

PD-1: An inhibitory immune receptor (2q37.3) on B, T lymphocytes and natural killer cells.

PDB (Protein Data Bank): http://www.rcsb.org/pdb/cgi/explore.cgi?pdbld.

PDECGF: Platelet-derived endothelial cell growth factor.

pDelta: γδ

PDF: An electronic publishing software readable with the aid of Adobe Acrobat reader. Frequently used by journals available through the Internet.

PDGF: ►platelet derived growth factor

PDGFR: Platelet derived growth factor receptor

PDI (protein disulfide isomerase): A co-factor of protein folding mediated by chaperones. ►chaperone, ►PPI, ►Eug, ►Mpd, ►Erp61

PDK (phosphoinositide-dependent kinase): A part of the MAPK, RSK signaling pathway. ►MAPK, ►RSK, ►phosphoinositides, ►PIK, ►Akt; Toker A, Newton AC 2000 Cell 103:185.

PDS: An anaphase inhibitory protein that must be degraded with the assistance of CDC20 component of APC before the cell cycle can exit from mitosis regulated also by the activity of the Cdc14 phosphatase. ►cell cycle, ►APC, ►Esp1, ►sister chromatid cohesion, ►checkpoint, ►mitotic exit, ►Cdc14, ►Cdc20; Salah SM, Nasmyth K 2000 Chromosoma 109:27.

pDUAL: γδ

PDZ Domains (post-synaptic density, disc-large, zo-1): Approximately 90 amino acid repeats involved in ion-channel and receptor clustering, and linking effectors and receptors. PDZ domain proteins are involved in the regulation of the Jun N-terminal

kinase pathway, in the post-synaptic density (PSD) proteins at glutamatergic synapses, Rho-activated citron protein function, visual signaling, etc. The *Drosophila* gene, *scribble* (*scrib*) encodes a multi PDZ domain protein and in cooperation with a leucine-rich protein controls apical polarization of the embryo. ►ion channels, ►tight junction, ►protein folding, ►Van Gogh, ►receptor, ►effector, ►signal transduction, ►AMPA, ►HOMER, ►citron, ►Jun, ►Rho, ►NMDAR, ►mesenchyma, ►Fraser syndrome; Harris BZ, Lim WA 2001 J Cell Sci 114(pt 18):3219; Hung AY, Sheng M 2002 J Biol Chem 277:5699.

Pea (*Pisum* ssp): Several self-pollinating vegetable and feed crops: the Mendel's pea is *P. sativum*, and others are 2n = 2x = 14 (see Fig. P35). *Pisum*, photograph shows normal Mendelian segregation for smooth and wrinkled within a pod.

Figure P35. Pea

PEA: Death effector domain proteins.

Pea Comb: Comb characteristic of poultry of *rrP*(*P/p*) genetic constitution. ►walnut comb

Peach (*Prunus persica*): x = 7, the true peaches are diploid.

Peacock's Tail: An evolutionary paradigm when a clear disadvantage (like the awkward tail) turns into a mating advantage because of the females' preference for the fancy trait and thus increasing the fitness of the males that display it. ►fitness, ►selection, ►sexual selection

Peanut: ►groundnut

Pear (*Pyrus* spp): About 15 species; x = 17 and mainly diploid, triploid or tetraploids. It is very difficult to hybridize it with apples but can be crossed with some *Sorbus*. ►apple

Pearson Marrow Pancreas Syndrome: ►mitochondrial disease in humans

Pearson's Product Moment Correlation Coefficient: ►correlation

Pebble: ►scaffolds in genome sequencing

Pectin: The polygalacturonate sequences alternated by rhamnose and may contain galactose, arabinose, xylose and fucose side chains. Molecular weight varies from 20,000 to 400,000. Its role is intercellular cementing of plant cells. Acids and alkali may cause its depolymerization.

Pedicel: The stalk of flowers in an inflorescence. ►peduncle

PEDANT (protein extraction, description and analysis tool): See http://pedant.gsf.de/.

Pedigree Analysis: Generally carried out by examination of pedigree charts used in human and animal genetics where the family sizes are frequently too small to conduct meaningful direct segregation studies (see Fig. P36). The pedigree chart displays the lines of descent among close natural relatives. Females are represented by circles, males by squares and if the sex is unknown a diamond (◇) is used (see Fig. P37). The same but smaller symbols or by a vertical or slanted line indicates abortion or still birth over the symbol. For spontaneous abortions, triangles (q) may be used. Individuals expressing a particular trait are represented by a shaded or black symbol, and in case they are heterozygous for the trait, half of the symbol is shaded.

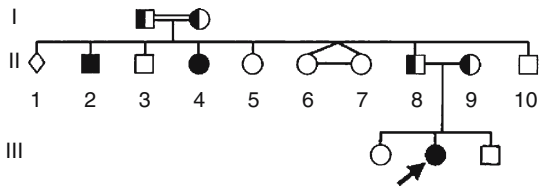

Figure P36. Pedigree chart

When an unaffected female is the carrier of a particular gene, there is a dot within the circle. In case segregation for traits needs to be illustrated in the pedigree, the individual displaying both traits may be marked by a horizontal and vertical line within the symbol or only by a horizontal or vertical line, respectively. Horizontal lines connect the parents and if the parents are close relatives, the line is doubled. The progeny is connected to the parental line with a vertical line and the subsequent generations are marked by Roman numerals at the left side of the chart, I (parents), II children, (III (grandchildren), and so on. Twins are connected to the same point of the generation line and if they are identical, a horizontal line connects them to each other. The order of birth of the offspring is from left to right and may be numbered accordingly below their symbol. An arrow to a particular symbol indicates the proband, the individual who first became known to the geneticist as expressing the trait. The appropriate symbols of

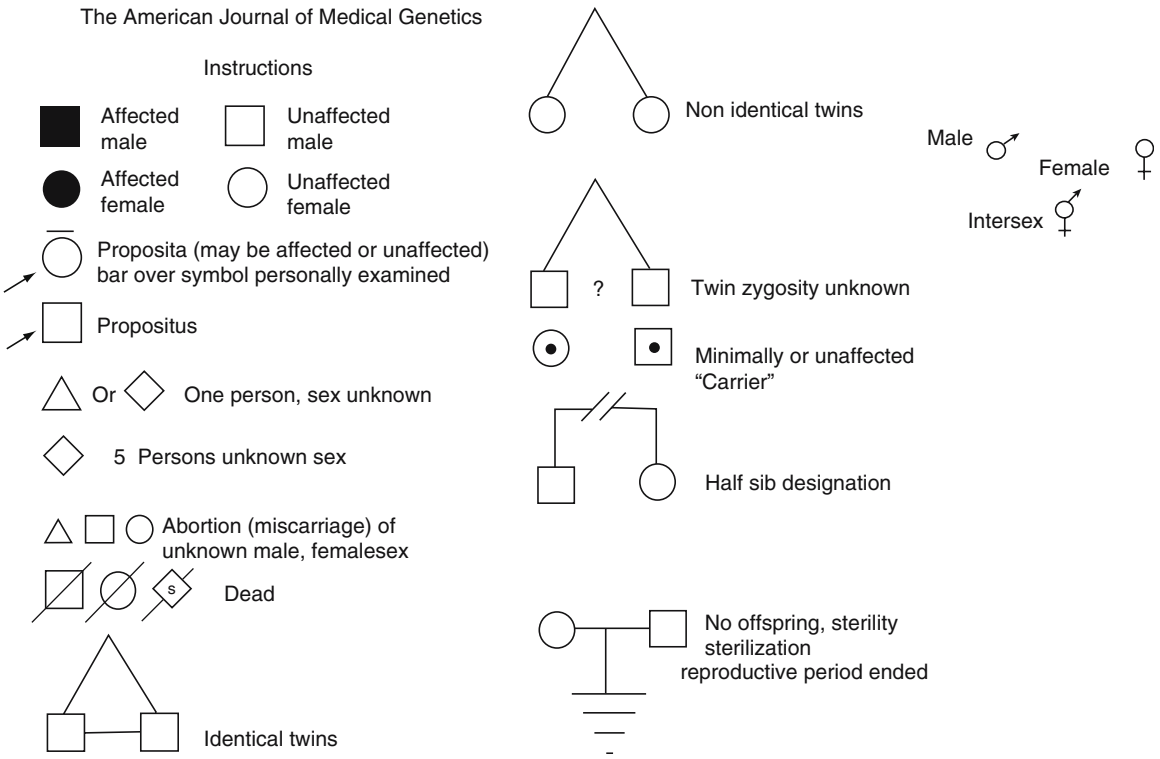

Figure P37. Pedigree symbols

adopted children may be bracketed. If a prospective offspring is considered at risk, broken lines draw the symbol. A horizontal line connected by a vertical line to the "parental" line may indicate lack of offspring by a couple.

Infertility may be represented by doubling a horizontal line under and connected to the male or female symbol, respectively. Egg or sperm donors (in case of assisted reproductive technologies [ART]) are indicated by a D and surrogate mothers by S within the symbols. *Mars shield* represents males and a *Venus mirror* represents females, and the sign in the box shown above at right indicates intersexes. ►ART; Bennett RL et al 1995 Am J Hum Genet 56:745; Am J Med Genet pedigree chart is reprinted by permission of John Wiley & Sons, Inc.

Pedogenesis: Egg production by immature individuals such as larvae.

PEDRo (Proteomics Experiment Data Repository): A model for the collection of information in proteomics. ►proteomics; Taylor CF et al 2003 Nat Biotechnol 21:247.

Peduncle: The stalk of single standing flowers (→); bundle of nerve cells (see Fig. P38). ►pedicel

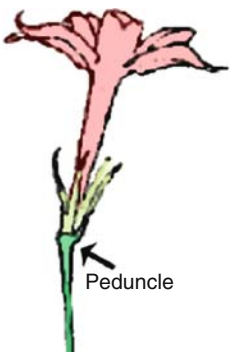

Figure P38. Peduncle

PEG (polyethylene glycol): May be liquid or solid and comes in a range of different viscosities (200, 400, 600, 1500, etc.). It facilitates fusion of protoplasts, uptake of organelles, precipitation of bacteriophages, plasmids and DNA, promoting end-labeling, ligation of linkers, reduction of immunogenicity when attached to humanized antibody, etc.

PEG-3 (progression elevated gene-3): In nude mice up-regulates carcinogenesis in progress via activation of VEGF. It can be blocked by antisense technology. ►VEGF, ►antisense technology

PEG (paternally expressed gene): ►imprinting

PEGylation: Attaches polyethylene glycol (PEG) to the polypeptide backbone of a protein drug, and renders it less liable to clearance from the body, and thus does not have to be supplied so frequently. PEGylated interferons have about 24 h half-life in the plasma whereas native interferons display only 4 h half-life. Interferon-α-2b (a recombinant product) when PEGylated is administered only once a week whereas without PEGylation it needs three dosing per week. ►interferon; Walsh G 2003 Nat Biotechnol 21:865.

PEK: ►HRI

Pelargonidine: ►anthocyanin

Pelargonium zonale (geranium): An ornamental plant. Some variegated forms transmit the non-nuclear genes also through the sperm whereas in the majority of plants the plastids are transmitted only through the egg. ►uniparental inheritance, ►chloroplasts, ►chloroplast genetics

Pelger(-Huet) Anomaly: An autosomal dominant condition in humans as well as in rabbits, cats, etc., characterized by fewer (1.1–1.6) than normal (2.8) nuclear lobes in the granulocytic leukocytes. Mutations may involve the lamin B receptor. It may be a mild anomaly but it may be associated with other more serious ailments. The prevalence varies from 1×10^{-3} to 4×10^{-4}. Similar phenotypes were described also as autosomal recessive or X-linked. ►laminopathies; Shultz LD et al 2003 Hum Mol Genet 12:61.

Pelizaeus-Merzbacher Disease: An Xq22 chromosomal recessive leukodystrophy that accumulates a proteolipoprotein (PLP, a 276-amino acid integral membrane protein) of the endoplasmic reticulum and the surface protein DM20 (26.5 kDa). The defect involves alternative splicing of the same mRNA. Duplications and deletion may be responsible for the disorder. The clinical symptoms are defective myelination (dysmyelination) of the nerves and defective interaction between oligodendrocytes and neurons, pathogenesis of the central nervous system and impaired motor development with an onset before age one. Mutation in the same gene encoding PLP is responsible also for X-linked spastic paraplegia type 2 (SPG-2) and the difference is in the degree of hypomyelination and motor dysfunction. Hereditary spastic paraplegia alleles were assigned to 8p, 16p, 15q and 3q27-q28. The corresponding defect in mouse displays *jimpy* and the myelin deficient (*msd*) phenotype. ►myelin, ►Charcot-Marie-Tooth disease, ►leukodystrophy, ►spastic paraplegia

Pelle: Serine/threonine kinase, involved in dorsal signal transduction. ►IRAK

Peloric: The circular symmetry of the flower in contrast to the bilateral symmetry of the wild type first described in *Linaria* by Linnaeus. Homologous mutations occur in *Antirrhinum* as shown in Figure P39. This variation of floral symmetry of *Linaria* is due to the different methylation of a gene, *Lcyc* (Cubas P et al 1999 Nature [Lond] 401:157). It is thus an epimutation. The first figure is the wild type *Antirrhinum* flower of bilateral symmetry. The second figure is the *cycloidea* mutant with radial symmetry (pelory). (Illustration is the courtesy of Professor Hans Stubbe; ►methylation of DNA, ►epigenesis, ►superman, ►snapdragon, ►cycloidea)

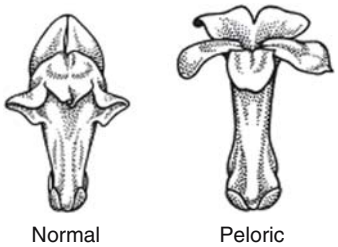

Figure P39. Normal and peloric snapdragon flowers

pelota: *Drosophila* gene involved in sperm function. ►azoospermia

Pemphigus: A collection of skin diseases with the general features of developing smaller or larger vesicles of the skin that may or may not heal and in extreme cases may result in death. The autosomal dominant familial pemphigus vulgaris is an autoimmune disease of the skin and mucous membranes. In the majority of cases, HLA-DR4 is involved. This anomaly is particularly common among Jews in Israel. In mice pemphigus vulgaris, inhibitor of MAPK (p38) can reduce the autoimmune blisters (Berkowitz P et al 2006 Proc Natl Acad Sci USA 103:12855). ►Hailey-Hailey disease, ►HLA, ►skin diseases, ►desmosome, ►autoimmune disease

Pena-Shokeir Syndrome: A fetal akinesis caused by brain malformations; X-chromosomal inheritance is suspected. ►akinesis

Pendred Syndrome: A recessive (7q31, PDS) thyroid anomaly and neurosensory deafness. The locus encodes *pendrin* an anion transporter, a presumed sulfate transporter localized in the cell membrane and a bicarbonate secretion in the kidney. Recent evidence indicates chloride and iodide transport too. This locus is responsible for about 1–10% of the genetically determined hearing loss. ►deafness, ►goiter; Royaux IE et al 2001 Proc Natl Acad Sci USA 98:4221.

Penetrance: The percentage of individuals in a family that express a trait determined by gene(s) they contain. The genetic basis of this phenomenon is poorly understood, and may cause serious problems in genetic counseling. ►expressivity

Penicillin: An antibiotic originally obtained from *Penicillium* fungi (see Fig. P40). The arrow points to the reactive bond of the β-lactam ring. ►antibiotics, ►*Penicillium*, ►lactam, ►β-lactamase

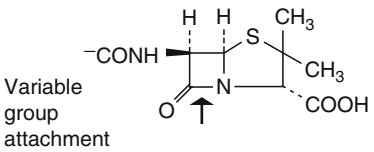

Figure P40. Basic structure of penicillins

Penicillin Enrichment: ►penicillin screen

Penicillin Screen: Used for mass isolation of auxotrophic microbial mutations that failed to grow in basal media (in contrast to the wild type) and the presence of the antibiotic therefore did not lead to their death (in contrast to the wild type). After transfer to complete (or appropriately supplemented) media the auxotrophs grew and thus were selectively isolated. ►selective medium, ►replica plating, ►mutant isolation; Davis BD 1948 J Am Chem Soc 70:4267; Lederberg J, Zinder N 1948 J Am Chem Soc 70:4267.

Penicillinase: β-lactamase

Penicillin Binding Proteins: ►PBP

Penicillium notatum (fungus): x = 5 (see Fig. P41).

Figure P41. Penicillium conidiophore with conidia

Penis: The male organ of urinary excretion and insemination (homologous to the female clitoris). It contains the *corpus spongiosum* through which the urethra and sperm passes. Above that are the *corpora cavernosa* that become extended when erection takes place due to enhanced blood supply to this elastic tissue as a consequence of NO (nitrogen-monoxide) gas flows to the muscles of the blood vessel wall, initiated by acetylcholine. The release of acetylcholine is controlled by steroid hormones. Cyclic GMP-dependent kinase is an essential enzyme for the maintenance of the extended state of the *corpus cavernosum*. Injection of prostaglandin E1 blocks cGMP-degrading phosphodiesterase and facilitates erection. The penis of canines (and most other mammals including primates except humans and spider monkeys) contains a small bone (*baculum* or *os penis*). In all humans, the gulonolactone oxidase (EC 1.1.3.8) gene on chromosome 8p21 is defective and no baculum is formed. The lack of this enzyme also makes humans dependent on dietary ascorbic acid. (It has been suggested that God created Eve not from a rib but from the baculum of Adam.) The baculum of mammals assists quick penetration of the vagina. During sexual intercourse of dogs, the male first penetrates the vulva of the female and erection takes place only in a second phase. At the base of the dog's penis the oval *bulbus glandis* then expands and locks the penis in position and the mating pair cannot separate until the ejaculation is terminated. Some animals (snakes, lizards, crustaceans and insects) have two penises (*virgae*). In *Euborellia plebeja* (Dermatoptera) both are functional. ►animal hormones, ►acetylcholine, ►acetylcholine receptors, ►hypospadias, ►nitric oxide, ►cGMP, ►prostaglandin, ►baculum, ►erectile dysfunction, ►clitoris; Kamimura Y, Matsuo Y 2001 Naturwiss 88:447; insect penis evolution review: Palmer AR 2006 Nature [Lond] 444:689.

Pentaglycines: ►bacteria

Pentaploid: Its cell nucleus contains five genomes (5x). Pentaploids are obtained when hexaploids (6x) are crossed with tetraploids (4x). The pentaploids are generally sterile or semi-fertile because the gametes generally have unbalanced number of chromosomes. ►polyploids, ►*Rosa canina*

Pentatrico: A ~35 unit sequence of amino acids, generally repeated several times in some proteins. Pentatricopeptide repeat (PPR) proteins form one of the largest families in higher plants and are believed to be involved in the posttranscriptional processes of gene expression in plant organelles and RNA editing in the chloroplasts (Okuda K et al 2007 Proc Natl Acad Sci USA 104:8178). ►RNA editing, ►retrograde regulation

Penton: Capsomer with five neighbors in the viral capsid. ►capsomer, ►hexon; Zubieta C et al 2005 Mol Cell 17:121.

Pentose: A sugar with 5-carbon-atom backbone, such as ribose, deoxyribose, arabinose, xylose.

Pentose Phosphate Pathway: glucose-6-phosphate + 2 NADP + H_2O → ribose-5-phosphate + 2 NADPH +

2 H + + CO2, i.e., the conversion of hexoses to pentoses generates NADPH, a molecule that serves as a hydrogen and electron donor in reductive biosynthesis. ►Embden-Meyerhof pathway, ►Krebs-Szent-györgyi cycle

Pentose Shunt: Same as pentose phosphate pathway.

Pentosuria: An autosomal recessive non-debilitating condition characterized by excretion of increased amounts of L-xylulose (1–4 g) in the urine because of a deficiency of the NADP-linked xylitol dehydrogenase enzyme. In Jewish and Lebanese populations, the frequency of the gene was about 0.013–0.03. ►gene frequency, ►allelic frequencies

PEPCK (phosphoenolpyruvate carboxykinase): A regulator of energy metabolism.

Pepper (*Capsicum* spp): It exists in a great variety of forms but all have 2n = 2x = 24 chromosomes. Some wild species are self-incompatible and the cultivated varieties yield better if they have a chance for xenogamy. ►self-incompatibility, ►xenogamy

Pepsin: An acid protease, formed from pepsinogens. It has preference for COOH side of phenylalanine and leucine amino acids.

Pepstatin ($C_{34}H_{63}N_5O_9$): A protease (pepsin, cathepsin D) inhibitor.

Peptamer: The exposed loop on the surface of a carrier protein; it is thus protected from degradation and its conformational stability is improved.

Peptidase (protease): Hydrolyzes peptide bonds. In humans, the peptidase gene PEPA is in chromosome 18q23, PEPB in 12q21, PEPC in 1q42, PEPD in 19cen-q13.11, PEPE in 17q23-qter, PEPS in 4p11-q12, and the tripeptidyl peptidase II (TPP2), a serine exopeptidase is in 13q32-q33. (See http://merops.sanger.ac.uk).

Peptide Bond: Amino acids are joined into peptides by their amino and carboxyl ends ↑ (and they lose one molecule of water) (see Fig. P42).

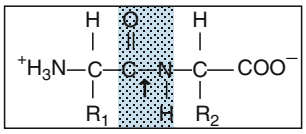

Figure P42. Peptide bond

Peptide Elongation: ►protein synthesis, ►aminoacylation, ►aminoacyl-tRNA synthetase, ►elongation factors (eIF), ►ribosome, ►tmRNA, ►cycloheximide

Peptide Initiation: ►protein synthesis, ►pactamycin

Peptide Mapping: The separation of (in)complete hydrolysates of proteins by two-dimensional paper chromatography or by two-dimensional gel electrophoresis for the purpose of characterization. The distribution pattern is the map or fingerprint, characteristic for each protein.

Peptide Mass Fingerprints: The protein is first cleaved by a sequence-specific protease such a trypsin and analyzed by MALDI-TOF and compared with protein sequences with similar lysyl or arginyl residues of the same mass. On this basis matching proteins even in a mixture can be identified. Modified proteins are detectable on the basis of peptide sequence with an incremental mass due to, e.g., a phosphogroup. ►proteomics, ►MALDI, ►trypsin; Mann M et al 2001 Annu Rev Biochem 70:437; Pratt JM et al 2002 Proteomics 2:157; Giddings MC et al 2003 Proc Natl Acad Sci USA 100:20; http://www.peptideatlas.org/.

Peptide Nucleic Acid (PNA): A nucleic acid base (generally thymine) is attached to the nitrogen of a glycine (or other amino acids) by a methylene carboxamide linkage in a backbone of aminoethylglycine units (see Fig. P43). Such a structure can displace one of the DNA strands and binds to the other strand.

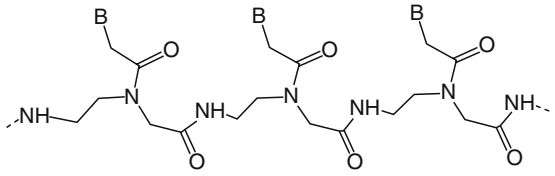

Figure P43. PNA backbone resembles that of DNA. The letter B stands for nucleic acid bases

They are DNA mimics. This highly stable complex has similar uses as the antisense RNA technology. PNA may be used to inhibit excessive telomerase activity in cancer cells. Homopyrimidine PNA may invade homopurine tracts in double-stranded DNA and may form triplex DNA and interfere with transcription. Peptide nucleic acid can target the polyguanine tract of HIV-1 and can arrest translation elongation (Boutiah-Hamoudi F et al 2007 Nucleic Acids Res 35:3907). PNA may also be used to screen for base mismatches and small deletions or base substitution mutations. Peptide nucleic acid complementary to mutant mtDNA selectively inhibits the replication of mutant mtDNA in vitro. PNA has been suggested to be the first pre-biotic genetic molecule rather than RNA. PNA may be useful for delivering genes to the mitochondria. PNA–DNA hybrids may be identified by binding of the dye 3,3′-diethylthiadicarbocyanine and used for the rapid detection of

mutations of clinical importance. Site-specific recombination may be substantially enhanced by PNA. ►antisense RNA, ►antisense DNA, ►TFO, ►mtDNA, ►Hoogsteen pairing, ►RNA world, ►mitochondrial gene therapy, ►acquired immunodeficiency; Corey DR 1997 Trends Biotechnol 15:224; Chinnery PF et al 1999 Gene Ther 6:1909; Wilhelmsson LM et al 2002 Nucleic Acids Res 30(2): e3; Rogers FA et al 2002 Proc Natl Acad Sci USA 99:16695.

Peptide Processing: ►post-translational processing

Peptide Sequence Tag: ►electrospray MS

Peptide Transporters: ►TAP, ►ABC transporters

Peptide Vaccination: Synthetic polypeptides corresponding to CTL epitopes may result in cytotoxic T cell-mediated immunity but in some instances, it may enhance the elimination of anti-tumor CTL response. ►vaccination, ►CTL, ►epitope, ►cancer prevention, ►immunological surveillance; Vandenbark AA et al 2001 Neurochem Res 26:713.

Peptidoglycan: The heteropolysaccharides cross-linked with peptides constituting the bulk of the bacterial cell wall, especially in the Gram-positive strains. ►Gram negative; see chemical formula in Fig. P44.

Peptidomimetics: These are polymer analogs containing unnatural amino acids. The non-natural amino acids are incorporated by the translation machinery using suppressor amino acid-transfer RNAs or nonsuppressor tRNA in a modified system. Peptidomimetics may facilitate the study of translation, enable directed evolution of small molecules with desirable catalytic and pharmacological properties, and are potential blocking agents of carcinogenesis by promotion of apoptosis. ►translation, ►aminoacyl-tRNA synthetase, ►suppressor tRNA, ►genetic code, ►alloproteins; Forster AC et al 2003 Proc Natl Acad Sci USA 100:6353.

Peptidyl Site: ►P site, ►ribosome, ►protein synthesis

Peptidyl Transferase: Generates the peptide bond between the preceding amino acid carboxyl end (at the P ribosomal site) and the amino end of the incoming amino acid (at the A site of the ribosome). It is a ribozyme and the catalytic function resides in the 23S ribosomal RNA. Essential function is attributed to adenine 2451. ►ribosome, ►protein synthesis, ►macrolide

Peptidyl-Prolyl Isomerases (PPI): PPI mediate the interconversion of the cis and trans forms of peptide bonds preceding proline. PPI genes are in human chromosomes 4q31.3, 6p21.1, 7p13 and the mitochondrially located at 10q22-q23. This family includes cyclophilins, FKBs and parvulins. ►FK506, ►cyclophilins, ►parvulin; Shaw PE 2002 EMBO Rep 3:521; Wu X et al 2003 Genetics 165:1687.

Peptoid: A peptide-like molecule that results from the oligomeric assembly of N-substituted glycines. Peptoids have various biological applications.

per *(period)* locus: In *Drosophila* (map location 1-1.4, 3B1-2), *per* locus controls the circadian and ultradian rhythm, thus affecting eclosion, general locomotor activity, courtship, intercellular communication, etc. The mutations do not seem to affect the viability of the individuals involved, only the behavior is altered. When per^{S} (caused by a base substitution mutation in exon 5) in the brain is transplanted into per^{01} mutants (nonsense mutation in exon 4) causing short ultradian rhythm and multiple periods, some flies may be somewhat normalized. The locus has been cloned and sequenced and seems to code for a proteoglycan. Gene NONO of mammalian cells apparently positively modulates PER and gene WDR5 (involving a histone-methyltransferase subunit) controls methylation/expression of PER (Brown SA et al 2005 Science 308:693). The Per protein forms a heterodimeric complex with the Tim (*timeless* gene) protein

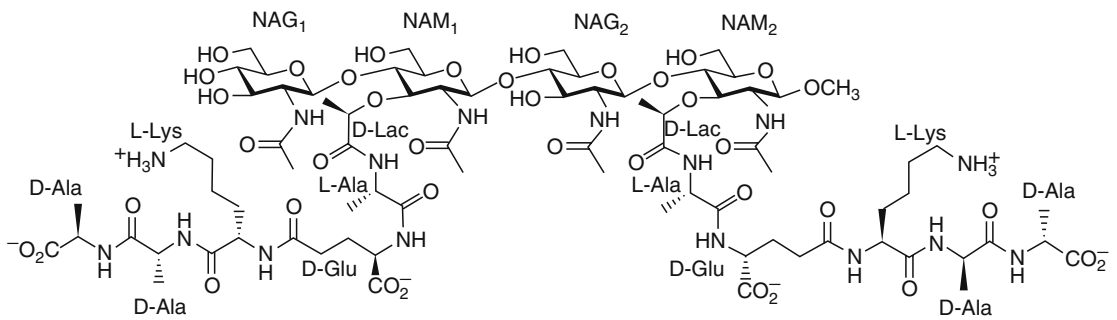

Figure P44. Chemical structure of a segment of peptidoglycan. (NAG): N-acetylucosamine-N-acetyl muramic acid disaccharide (NAM) and attached pentapeptide. See Meroueh SO et al. 2006 Proc Natl. Acad. Sci. USA 103:4404

and jointly autoregulate transcription. Tim is degraded in the morning in response to light and that results in the disintegration of the complex that is reformed again in dark in a circadian oscillation. In mammals, three *mPer* loci have been identified controlling the circadian clock. ►circadian, ►ultradian, ►proteoglycan

Percent Identity Plot (PIP): A macromolecular sequence map displaying the percentage of identity between two sequences. (See http://bio.cse.psu.edu).

Percentile: The percentage of the distribution of variates. More than 50 percentile indicates a value higher than 50% of the variates.

Perdurance: The persistence and expression of the product of the wild type gene even after the gene itself is no longer there.

Perennial: Lasts through more than one year.

Perfect Flower: Has both male and female sexual organs, i.e., it is hermaphroditic (see Fig. P45). ►hermaphrodite, ►flower differentiation

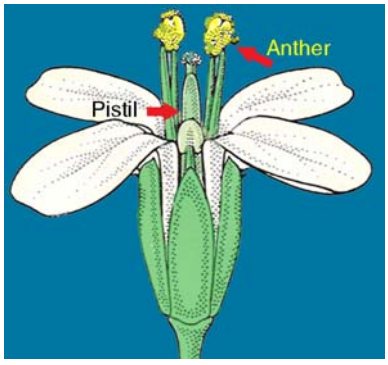

Figure P45. Perfect flower

Perforin (encoded at 10q22): Pore-forming protein (homologous to component 9 of the complement) that establishes transmembrane channels; it is stored in vesicles within the $CD8^+$ cytotoxic T cells (CTL). These vesicles contain also serine proteases. Perforin mediates apoptosis by permitting killer substances (granzyme) slowly enter the cell. Perforin may have a role in T cell-mediated destruction of pancreatic β-cell in diabetes mellitus type I. ►apoptosis, ►complement, ►T cells, ►fragmentin-2, ►granzymes, ►caspase, ►histiocytosis, ►diabetes mellitus; Keefe D et al 2005 Immunity 23:249.

Perfusion: Adding liquid to an organ through its internal vessels in vitro or in vivo.

Perianth: Designates both sepals and petals of the flowers. ►flower differentiation

Pericarp: The fruit wall (maternal tissue), developed from the ovary wall such as the pea pod, the outer layer of the wheat or maize kernels. The *Arabidopsis* silique, the peel of the citruses, and the skin of apple, the shell of the nuts, etc., are also similar but are exocarps. The outer layer of the common barley "seed" is not part of the fruit wall but it is a bract of the flower.

Pericentric Inversion: ►inversion pericentric

Pericentromeric Region: A highly redundant tract (<1 kb to ~85 kb), a transition zone, between the genic region of the chromosomes and the satellite heterochromatin. ►heterochromatin, ►centromere, ►satellite DNA; Horvath JE et al 2001 Hum Mol Genet 10:2215.

Perichromatin Fibers: Active genes occupy the surface of specific compartments in the interphase nucleus (chromosome territories) and represent the perichromatin fibers. ►SR motif, ►chromatin, ►chromosome territories; Cmarko D et al 1999 Mol Biol Cell 10:211.

Periclinal Chimera: Contains genetically different tissues in different cell layers. ►mericlinal chimera, ►chimera

Pericycle: The (root) tissue between the endodermis and phloem. ►root, ►endodermis, ►phloem

Peridium: The covering of the hymenium or the hard cover of the sporangium of some fungi. ►hymenium, ►sporangium

Perinatal: The period after 28 weeks of human gestation⇔four weeks after birth.

Perinuclear Space: A ~20 to 40 nm space between the two layers of the nuclear membrane. ►nucleus

Periodic Acid-Schiff Reagent (PAP): The tests for glycogen, polysaccharides, mucins, and glycoproteins. It breaks C-C bonds by oxidizing near hydroxyl groups and forms dialdehydes and generates red or purple color.

Periodic Paralysis (PP, KCNE): A group of autosomal dominant human diseases manifested in periodically recurring weakness accompanied by low blood potassium level (hypokalemic periodic paralysis, defect in the α subunits of Ca^{2+} channel) or in other forms with high blood potassium level (hyperkalemic periodic paralysis, paramyotonia). The latter types were attributed to base substitution mutations in a highly conserved region of the αsubunit of a transmembrane sodium channel protein. In another type of the disease, the blood potassium level appeared normal and the patients responded favorably to sodium chloride. The MiRP2 potassium

channel defect is also associated with PP. ►ion channel, ►Moebius syndrome, ►myotonia, ►hyperkalemic periodic paralysis; Abbott GW et al 2001 Cell 104:217.

Periodicity: The number of base pairs per turn of the DNA or the number of amino acids per turn of an α-helix of a polypetide chain. ►protein structure, ►Watson and Crick model

Periodontitis: Several diseases involving inflammation of the gingiva, especially at the base of the teeth and the alveolae, the bone support of the teeth. It is usually associated with keratosis of the palms and soles. About 30% of the human population is affected by it. In the juvenile form (encoded at 4q11-q13) both milk and permanent teeth may be lost in early childhood. The disease is the result of bacterial infections (~500 different species may inhabit the human mouth). The Papillon-Lefèvre syndrome (11q14, prevalence $1–4 \times 10^{-6}$) is based on deficiency of cathepsin C, a dipeptidyl peptidase I. In the similar autosomal recessive periodontitis deficiency of IL-1 is suspected. Similar symptoms may occur also in the Ehlers-Danlos syndrome Type VIII. ►keratosis, ►cathepsin, ►IL-1, ►Ehlers-Danlos syndrome, ►dentinogenesis imperfecta; Travis J et al 2000 Adv Exp Med Biol 477:455.

Peripheral Nervous System: Resides outside the brain and the spinal chord.

Peripheral Proteins: These are bound to the membrane surface by hydrogen bonds or by electrostatic forces. ►membrane proteins

Peripherin (retinal degeneration slow protein): ►retinal dystrophy

Periplasma: The cell compartment between cell wall and cell membrane. In *E. coli* the Sec family of proteins mediate the translocation across the periplasmic and the outer membrane. The extracellular stress response factor σ^E regulates the assembly of the outer membrane. The two-component Cpx seems to be involved in the assembly of the pilus. ►Sec, ►two-component regulatory system, ►pilus; Danese PN, Silhavy TJ 1998 Annu Rev Genet 32:59; Raivio TL, Silhavy TJ 2001 Annu Rev Microbiol 55:591.

Peristalsis: The contraction of muscles of a tubular structures (e.g., intestines) propelling the content.

Peristome: A fringe of teeth at the opening of the sporangium of mosses or the buccal (mouth) area of ciliates.

Perithecium: A fungal fruiting body of disk or flask shape with an opening (ostiole) for releasing the spores (see Fig. P46). A perithecium of *Neurospora* contains about 200 asci. Its primordium is called protoperithecium. ►ascogonium, ►apothecium, ►cleistothecium, ►gymnothecium, ►*Neurospora*, ►ascus, ►tetrad analysis

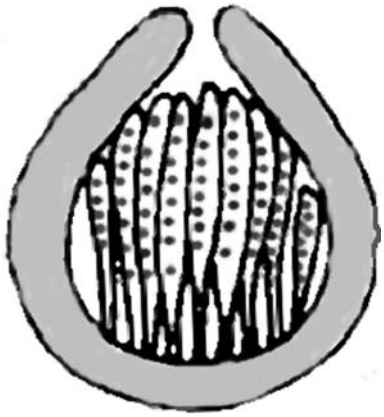

Figure P46. Perithecium

Periventricular Heterotopia: A human X-chromosomal mental retardation and seizures caused by anomalies of the brain cortex. The neurons destined for the cerebral cortex fail to migrate. The mutation involves the filamin gene (FLN1, Xq28) encoding an actin-cross-linking phosphoprotein. ►double cortex; Sheen VL et al 2001 Hum Mol Genet 10:1775.

PERK (PKR-like ER kinase): A phosphorylating enzyme in the endoplasmic reticulum, similar to the mammalian RNA-dependent protein kinase (PKR). It is interferon-inducible and activated by double-stranded RNA. PERK and the phosphorylation of eIF2α inhibit the initiation of translation. ►PKR, ►eIF2α, ►Ire, ►unfolded protein response, ►S6; Kumar R et al 2001 J Neurochem 77:1418.

Perl Script: Assembles and merges sequences from different DNA libraries. ►DNA library, ►PHRAP

Perlecan: Heparan sulfate proteoglycan that interacts with the extracellular matrix, growth factor receptors and affects signal transduction. ►proteoglycan, ►heparan sulfate, ►Schwartz-Jampel syndrome; Knox S et al 2002 J Biol Chem 277:14657.

Perlegen Sciences: Perlegen sciences have genotyped over 1.5 million unique genetic variants (SNPs), in 71 individuals of European American, African American, or Han Chinese ancestry. In total, more than 112 million individual genotypes were determined, with an average distance between adjacent SNPs of 1871 base pairs. The genotype browser permits accession to virtually all the SNP, linkage disequilibrium, and haplotype data reported in the study. ►SNIPs, ►linkage disequilibrium, ►haplotype;

expanded data: Hinds DA et al 2005 Science 307:1072; http://genome.perlegen.com/.

Permafrost: The soil layer in cold regions that remains permanently frozen even when the top may thaw.

Permanent Hybrid: ►complex heterozygote

Permease: The enzymes involved in the transport of substances through cell membranes. ►membrane transport, ►membrane channels, ►membrane potential, ►ion channels; Abramson J et al 2003 Science 301:610.

Permissible Dose: ►radiation hazard assessment

Permissive Condition: The condition at which a conditional mutant can survive or reproduce. ►conditional mutation

Permissive Host: A cell permits (viral) infection and/or development.

Permutation: Generating all possible orders of n numbers, and it can be obtained by the factorial: n!, e.g., the factorial of 4, $4! = 4 \times 3 \times 2 \times 1 = 24$. ►combination, ►variation

Permutation Test (randomization test): The test used to assess the association of QTLs with multiple (molecular) markers in a randomized array. ►QTL, Edington ES 1995 Randomization tests, Marcel Dekker, New York.

Permuted Redundancy: At the termini of phage DNA a collection of redundant sequences occur in the phage population that start and end with permuted sequences of the same nucleotide sequence, e.g., 1234…1234, 2341…2341, 3412…3412, etc. This arrangement is characteristic for T-uneven phages, e.g., T1, T3, T5, etc. ►non-permuted redundancy

Perodictus: ►*Lorisidae*

Peroxidase: Heme protein enzymes, which catalyze the oxidation of organic substances by peroxides. Glutathione peroxidase (and selenium) deficiency may cause hemolytic disease. Several peroxidase genes have been located in the human genome: GPX1 in 3q11-q12, GPX2 in 14q24.1, GPX3 in 5q32-q33, GPX4 (in testes) in chromosome 19, a rare eosinophil peroxidase (EPX) may compromise the immune system, a thyroid peroxidase deficiency (2p25) interferes with thyroid function. ►immune system, ►eosinophil, ►hemolytic disease, ►oxidative stress

Peroxidase and Phospholipid Deficiency: An autosomal recessive anomaly of the eosinophils involving the enzyme defects named. ►microbody, ►Refsum disease, ►Zellweger syndrome

Peroxides: They display the — O — O — linkage. Organic peroxides participate in activation and deactivation of promutagens, mutagens, procarcinogens and carcinogens and in many other physiological reactions. Peroxides are formed by the breakdown of amino acids and fatty material in the cell and may inflict serious damage. According to some views, spontaneous mutation may be caused to a great extent by these regular components of the diet. Therefore, eating rancy food may pose substantial risk. ►environmental mutagens, ►peroxidase, ►catalase peroxisomes, ►promutagen, ►ROS, ►P450

Peroxins: Peroxisome proteins. PEX1 (7q21-q22), PEX10, human chromosome 1) is a peroxisome biogenesis protein, PEX13 (2p15) in another peroxisome biogenesis protein. ►peroxisome, ►PEX, ►Zellweger syndrome, ►Refsum disease, ►microbodies; Walter C et al 2001 Am Hum Genet 69:35.

Peroxiredoxins: Antioxidant enzymes present in prokaryotes and eukaryotes and control signal transduction, apoptosis, tumor formation, HIV infection, etc. (See Wood ZA et al 2003 Science 300:650; Neumann CA et al 2003 Nature [Lond] 424:561).

Peroxisomal 3-Oxoacylcoenzyme A Thiolase Deficiency (pseudo-Zellweger syndrome): Autosomal recessive disease assigned to human chromosome 3p23-p22. ►microbody, ►Zellweger syndrome, ►adrenoleukodystrophy

Peroxisome: Peroxisome are ~0.15–0.5 μm diameter bodies, surrounded by single-layer membrane, in eukaryotic cells containing about 50 proteins, including oxidase and catalase enzymes. The peroxisomes synthesize ether phospholipids by dihydroxyacetonephosphate acetyltransferase (DHAPAT, human chromosome 1q42) and alkyl dihydroxyacetonephosphate synthase (ADHAPS, 2q31). In a human cell, the number of peroxisomes vary from less than 100 to more than 1000. In yeast either over expression or lacking the Inp 1 protein (inheritance of peroxisome protein 1) are detrimental for the right amount and the proper distribution of peroxisome. Inp binds several proteins involved in peroxisome division (Fagarasanu M et al 2005 J Cell Biol 169:765). The peroxisomes have indispensable roles in fatty acid β oxidation, phospholipid and cholesterol metabolism. Fatty acid granules are also named microbodies. The peroxisome biogenesis disorders (PBD) are recessive lethal diseases in variable forms. The extreme form is the Zellweger syndrome, the Refsum disease and the adrenoleukodystrophy are milder and the rhizomelic chondrodysplasia punctata (RCDP) involves bone defects. Peroxisome mutations have been identified also in yeast (PAS). Some rodent carcinogens increase the number of peroxisomes but in humans, these agents did not appear to be carcinogenic. Peroxisomal protein Pex2 controls photomorphogenesis in *Arabidopsis*. ►glyoxisome,

►microbodies, ►PPAR, ►peroxin, ►Zellweger syndrome, ►Refsum disease, ►adrenoleukodystrophy, ►chondrodysplasia, ►oxalosis, ►peroxidase and phospholipid deficiency, ►peroxisomal 3-oxo-acyl-coenzyme A thiolase deficiency, ►PPAR, ►micropexophagy, ►pexophagy, ►PEX; Gould SJ, Valle D 2000 Trends Genet 16:340; Sacksteder KA, Gould SJ 2000 Annu Rev Genet 34:623; Titorenko VI, Rachubinski RA 2001 Trends Cell Biol 11:22; Thai T-P et al 2001 Hum Mol Genet 10:127; Titorenko VI, Rachubinski RA 2001 Nat Rev Mol Cell Biol 2:357; Purdue PE, Lazarow PB 2001 Annu Rev Cell Dev Biol 17:701; Hu J et al 2002 Science 297:405; Matsumoto N et al 2003 Am J Hum Genet 73:233; Weller S et al 2003 Annu Rev Genomics Hum Genet 4:165; Wanders RJA, Waterham HR 2006 Annu Rev Biochem 75:295; http://www.peroxisomeDB.org.

Peroxynitrite ($ONOO^-$/ONOOH): The diffusion-limited product of nitric oxide with superoxide. It is strongly oxidizing and toxic. ►nitric oxide, ►superoxide, ►peroxides; García-Nogales P et al 2003 J Biol Chem 278:864.

Perp: ►p63

Persistence, Bacterial: A phenocopy-like phenomenon in bacteria. When the culture is exposed to strong stress (e.g., antibiotics), the majority of the cells die but a small fraction survives although without a heritable resistance. When they re grow the population become sensitive to the antibiotic. ►phenocopy; Balaban NQ et al 2004 Science 305:1622.

Personal Genomics: ►DNA fingerprinting, ►DNA sequencing

Personality: Can be characterized by five main groups of features: (1) *extraversion* (being outgoing) or the lack of it, ability to lead and sell their ideas versus reticent and avoiding company [heritability about 0.71]; (2) *neuroticism* (emotional versus stable) worrisome or self-assured, [heritability about 0.21]; (3) *conscientiousness* (well-organized versus impulsive) responsible or irresponsible, reliable or undependable, [heritability 0.38–0.32); (4) *agreeableness* (empathic or unfriendly) warm versus cold, cooperative versus quarrelsome, forgiving versus vindictive, [heritability about 0.49], and (5) *openness* (insightful or lacking intelligence) imaginative versus imitative, inquisitive or superficial). These heritability estimates vary a great deal, however, and may be very different in some populations. Based on twin studies, several investigators concluded that overall close to 50% of the variance could be attributed to additive or non-additive genetic determination. ►behavior in humans, ►behavior genetics, ►human intelligence, ►affective disorders, ►heritability in humans

Person/Year: Used as, for e.g., incidence of an event a (symptoms of a disease) per person per year.

Persyn: ►synuclein-γ

Perturbogen: Short peptides or protein fragments that can disrupt specific biochemical function in the cell.

Pertussis Toxin: Produced by the Gram-negative *Bordatella* bacteria, responsible for whooping cough. The toxin stimulates ADP-ribosylation of the $G\alpha_1$ subunit of a G-protein in the presence of ARF and thus GDP stays bound to the G-protein and adenylate cyclase is not inhibited and K^+ ion channels do not open. As a consequence, histamine hypersensitivity and reduction of blood glucose level follows. ►whooping cough, ►signal transduction, ►ARF, ►G-protein, ►ADP, ►GDP, ►cholera toxin, ►adenylate cyclase; Alonso S et al 2001 Infect Immun 69:6038.

PERV (porcine endogenous retrovirus): Exists in >50 copies/pig chromosome complement and has been feared to endanger humans with xenotransplantation of pig organs. So far, the limited information indicates minimal risk relative to the potential benefits. PERVs can be transferred to mice by xenotransplantation. ►xenograft, ►xenotransplantation, ►nuclear transplantation; Specke V et al 2001 Virology 285:177.

PEST (proline [P]-glutamate [E]-serine [S]-threonine [T]-rich motif): PEST in the carboxyl domain of IκB and other proteins (Ubc) is involved in the stimulation of proteolysis. ►IκB, ►NF-κB, ►proteasome, ►Ubc, ►ubiquitin

Pest Eradication by Genetic Means: ►genetic sterilization, ►*Bacillus thüringiensis*, ►host–pathogen relations (see Fig. P47).

Figure P47. *Bacillus thüringiensis* toxin transgene is lethal to worms (right) but the wild type plants (left) were destroyed. (Courtesy of Professor Marc Van Montagu, Rijksuniversiteit, Gent)

Pesticide Mutagens: ►environmental mutagens

Pesticin: The toxin of *Pasteurella* bacteria

Pestilence: An infectious epidemic of disease.

PET: ►tomography

PET: ►transcriptome, ►paired-end diTAG

Petaflop Computer: An extremely powerful supercomputer. "Peta" comes from the Latin word *peto* (I move forward) and in computer jargon, "flops" designate floating operations. This new hardware may be capable of performing one quadrillion flops/second, that are more than 10^6 times the efficiency of the best desktop computers.

Petals: Generally the second whorl of modified leaves from the bottom of the flower (see Fig. P48).

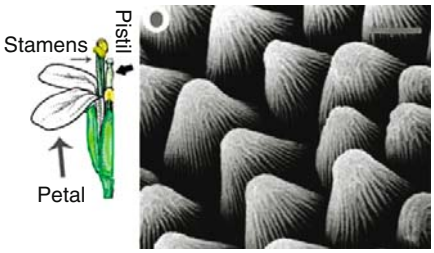

Figure P48. Petals of *Arabidopsis* are shown at left. At right: The adaxial ridge of the petal as viewed by scanning electronmicrography and reveal the beauty, which the naked eye cannot see. (From Bowman JL, Smyth DR 1994 In: Bowman JL (ed) Arabidopsis: An Atlas of Morphology and Development. By permission of Springer-Verlag, New York)

Frequently, they are quite showy because of their anthocyanin or flavonoid pigmentation. The petal number is a taxonomic characteristic, although petal number may be altered by homeotic mutations converting the anthers and/or pistils into petals and appearing as sterile double flowers of floricultural advantage. MicroRNA may have a role in the regulation of petal number (Baker CC et al 2005 Curr Biol 15:303). ►flower differentiation, ►flower pigments, ►homeotic mutants; Roeder AHK, Yanofsky MF 2001 Dev Cell 1:4.

PETCM (α-[trichloromethyl]-4-pyridineethanol): Stimulates caspase-3 activity and thereby apoptosis. ►caspase, ►apoptosis; Jiuang X et al 2003 Science 299:223.

Petiole: The stalk of a leaf (see Fig. P49).

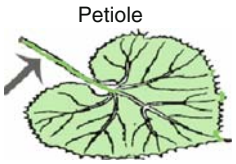

Figure P49. Petiole

Petite Colony Mutants: Petite colony mutants of yeast forms small colonies because they are deficient in respiration (OXPHOS minus) and lethal under aerobic conditions. The *vegetative petites* (ρ^-) are caused by (large) deletions in the mitochondrial DNA, the *segregational petites* are controlled by nuclear genes at over 200 loci. The mitochondrial mutations occur at high (0.1 to 10%) frequency and using ethidium bromide as a mutagen their frequency may become as high as 100%. The mitochondrial petites fail to transmit this character in crosses with the wild type except one special group the *suppressive petites* that may be transmitted at a low frequency in outcrosses with the wild type. In yeast, the A + T content of the normal mitochondrial DNA is about 83%, in some of the mitochondrial mutants the A + T content may reach 96% because the coding sequences were lost and only the redundant A + T sequences were retained and amplified so the mtDNA content is not reduced. The *hypersuppressive petite* mutants have short (400–900 bp) repeats that share 300 bp (*ori* and *rep*) sequences with the wild type, necessary for replication. *Neutral petites* produce wild type progeny when outcrossed to the wild type. Yeast cells that have normal mitochondrial function make large colonies and are called *grande*. Cells that can dispense with mitochondrial functions are sometimes called petite-positive whereas that absolutely need mitochondria are called petite-negative. Inactivation of an ATP and metal-dependent protease (Yme1p) associated with the inner membrane of the mitochondrium can convert the "positives" to "negatives" and the presence of the Yme1p function may have the opposite effect. Yme is not universally present in all yeasts. ►mitochondria, ►mtDNA, ►mitochondrial mutations, ►oxidative phosphorylation; Sager R 1972 Cytoplasmic Genes and Organelles, Academic Press, New York; MacAlpine DM et al 2001 EMBO J 20:1807; Chen XJ, Clark-Walker GD 2000 Int Rev Cytol 194:197.

Petri Plate: A (flat) glass or disposable plastic culture dish for microbes or eukaryotic cells (see Fig. P50).

Figure P50. Petri plate

Petunia hybrida (2n = 28): *Solanacea*e; predominantly self-pollinating but allogamy also occurs. It has been used extensively for cell, protoplast and embryo culture, intergeneric and inter-specific cell fusion, genetic transformation and the genetic control of pigment biosynthesis. It has a good number of related species.

Peutz-Jeghers Syndrome: ►polyposis hamartomatous

PEV (position effect variegation): ►position effect, ►heterochromatin, ►RPD3

PEX: Proteins import the peroxisome-targeting signals (PTS) to the peroxisomes. The various PEXs play roles in peroxisome biogenesis. ►peroxisome; Braverman N et al 1988 Hum Mol Genet 7:1195.

Pexophagy: Sequestration to and engulfing peroxisomes into vesicles and their destruction. ►peroxisome

Peyer's Patches: Aggregated lymphatic nodes. The Peyer's patches mediate the uptake of macromolecules, antigens and microorganisms through the epithelium of the gut. These plaques are instruments of mucosal immunity. B cells are required for the normal functions of the Peyer's patches. *Salmonella typhi* infection may cause perforation of the Peyer's patches. Tyrosine kinase receptor RET is a regulator of Peyer's patch formation (Veiga-Fernandes H et al 2007 Nature [Lond] 446:547). ►mucosal immunity, ►RET oncogene

Peyronie Disease: An apparently dominant autosomal disorder, it may be caused by a variety of acquired and genetic conditions. Its exact prevalence has not been determined but it may occur at ~1 to 8% of the human males. It involves fibrous, thickened collagen plaques on most commonly on the dorsal part of the penis and causes its curvature under painful conditions of erection. The condition may be transient. It occurs generally after age 40. Several drugs and in severe conditions surgical intervention have been used for treatment. (See Usta MF, Hellstrom WJG 2004 In: Seftel AD et al (Eds.) Male and Female Sexual Dysfunction, Mosby, St. Louis, Missouri, p 191).

PFAM: A database of over 3000 protein families and domains, multiple sequence alignments and profile hidden Markov models. ►alignment; Bateman A et al 2002 Nucleic Acids Res 30:276; http://pfam.wustl.edu; http://www.sanger.ac.uk/Software/Pfam/; http://pfam.jouy.inra.fr; http://pfam.cgb.ki.se/.

Pfeiffer Syndrome: The syndrome includes autosomal dominant bone malformation affecting the head, thumbs and toes (acrocephalosyndactyly) (see Fig. P51), the autosomal recessive head-bone (craniostenosis) and heart disease. The origin is primarily paternal. The latter type seems to co-segregate with fibroblast growth factor receptor 1 (FGFR1) in human chromosome 8p11.2-p11.1.

Figure P51. Short and broad thumb in Pfeiffer syndrome

Another locus in chromosome 10q26 represents also a fibroblast growth factor receptor, FGFR2. FGFR3 is located in chromosome 4p16.3 and its mutation is concerned with hypo-chondroplasia. Mutations in all three genes involve Pro→Arg replacements at identical sites, 253. This syndrome is allelic to the Crouzon and to the Jackson-Weiss syndromes. Some of the mutations represent gain-of-functions. ►fibroblast growth factor, ►Alpert's syndrome, ►Crouzon syndrome, ►Jackson-Weiss syndrome, ►craniosynostosis syndromes, ►hypochondroplasia, ►achondroplasia, ►gain-of- function, ►receptor tyrosine kinase

PfEMP1: A group of *Plasmodium falciparum* protein ligands expressed on the surface of infected red blood cells and mediate cell adhesion (virulence factors) but may incite host immune reaction. PfEMP displays antigenic variation to evade this response. Other pathogenesis proteins of the parasite are rifins. ►Plasmodium, ►antigenic variation, ►rifin; Flick K et al 2001 Science 293:2009.

PFGE (pulsed field gel electrophoresis): PFGE separates very large nucleic acid fragments or even small chromosomes. The megabase size fragments can be used for physical mapping of large chromosomal domains (PFG mapping). ►pulsed field gel electrophoresis

pfu (p.f.u.): The plaque forming unit. The number of phage particles/mL that can invade a bacterial lawn and then after reaching about 10^7 particle numbers

a clear spot appears on the Petri plate where the bacterial cells had been lysed. ►plaque, ►pu, ►CFU

PG: ►prostaglandins

PGA: Phosphoglyceric acid, a 3-carbon product of photosynthesis. ►photosynthesis, ►Calvin cycle, ►C3 plants

PGC (primordial germ cells): Gynogenetic/parthenogenetic cell, the primordial cell of female gonads. ►gonad, ►gynogenesis, ►parthenogenesis

PGC1 (PPAR-γ-coactivator): A regulator of transcription, body heat production, mitochondrial biogenesis and other processes. PGC-1β is a transcriptional coactivator for the production of cholesterol and triglycerides. PGC1α regulates both the gluconeogenetic and glycolytic pathways during fasting. PGC1α is also a regulator of the expression of several transcription factors required for the biogenesis of mitochondria and it is down regulated in Huntington disease (McGill JK, Beal MF 2006 Cell 127:465). Sirtuin interacts with and deacetylates PGC in a NAD-dependent manner as part of energy homeostasis, diabetes and lifespan (Rodgers JT et al 2005 Nature [Lond] 434:113). ►PPAR, ►nuclear receptor, ►sirtuin, ►gluconeogenesis, ►glycolysis, ►aging, ►resveratrol, ►Huntington's chorea; Tsukiyama-Kohara K et al 2001 Nature Med 7:1102.

PGD (preimplantation genetic diagnosis): PGD can be carried out for some human genetic disorders, for e.g., PCR or FISH (for fragile X, aneuploidy, etc.) examining polar bodies or blastomeres at the stage of a few cells in the embryo. The disorders that have been identified by PCR included cystic fibrosis, Tay-Sachs disease, Lesh-Nyhan syndrome, Huntington chorea, Marfan syndrome, ornithine transcarbamylase deficiency, Fanconi anemia, etc. The diagnosis may permit—by using in vitro fertilization—to develop a human offspring of a certain (disease-free) genetic constitution. Misdiagnosis is rare but varies somewhat in different laboratories. It seems likely that all cells in a single eight-cell embryo may not be identical. (See diseases mentioned under separate entries, ►PCR, ►FISH, ►ART; Bickerstaff H et al 2001 Hum Fert 4(1):24; Simpson JL 2001 Mol Cell Endocrinol 183(Suppl. 1):S69; Findlay I et al 2001 Mol Cell Endocrinol 183(Suppl. 1):S5; PGD tests carried out according to international survey: Sermon K et al 2005 Hum Reprod 20:19).

PGK-neo: A commonly used transformation cassette for gene knockout where the neomycinphos photransferase gene (*neo*) is fused to the phosphoglycerate kinase (PGK) promoter. ►knockout, ►vector cassette; Scacheri PC et al 2001 Genesis 30(4):259.

P-Glycoprotein: The 170 kDa product of the human multidrug resistance gene (MDR-1, 7q21.1) that exports different (mainly hydrophobic) toxic substances from the cells in an ATP-dependent manner. ►multidrug resistance

PGM: ►phosphoglucomutase

PGRS (polymorphic GC-rich repetitive sequences): Mycobacterium tuberculosis proteins (~70) with glycine-glycine doublets that have few charged amino acids and essentially contain no cysteine. These proteins are apparently involved in pathogenesis. ►*Mycobacteria*; Karlin S 2001 Trends Microbiol 9:335.

PgtB: Bacterial kinase that phosphorylates regulator protein PgtA. ►kinase, ►protein kinases

PH: Pleckstrin homology domain. ►pleckstrin

pH: = $-\log (H_3O^+)$, negative logarithm of the hydrogen ion concentration; pure water at 25°C contains 10^{-7} mole hydrogen ions; solutions of acids could contain 1 mole and solution of bases 10^{-13} moles per liter.

The pH meters measure the electrical property of solutions which is proportional to pH; pH 7 is neutral and below it is acidic above it is alkalic (basic) (see Fig. P52). The pH of body fluids and tissues is regulated by the function of the ion channels.

The pH of plant tissues is generally below 7 because of the presence of organic acids and the majority of plant tissues can be cultured best in media around pH 6. Most animal tissues display neutral pH (~7). In the human blood, the pH is normally within the narrow range of 7.3 to 7.5. If the blood pH approaches 7, acidosis may result causing coma and at about pH 7.8 alkalosis may cause tetany

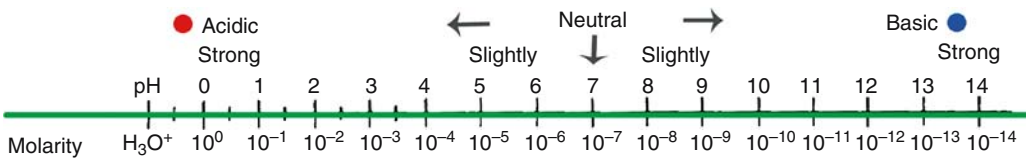

Figure P52. ph scale

(dangerous spasms) but the stomach secretions may be pH 0.9. The pH optima of enzymes vary a great deal but most commonly, it is in the range of 6 to 9. The preferred pH of microbes is also variable; the euryarchaeon bacterium, *Picrophilus torridus* thrives well at pH 0.7 and 60°C. (Fütterer O et al 2004 Proc Natl Acad Sci USA 101:9091). ►ion channels, ►buffer

Ph1 Chromosome: ►Philadelphia chromosome

***Ph*Gene** (pairing high): An approximately 700 Mb sequence that controls selective pairing in hexaploid wheat. In its presence, homoeologous chromosomes do not pair. It is in chromosome 5B. Plants nullisomic for this chromosome display multivalent associations in meiosis. A similar gene *Ph2* is in chromosome 3D. A *Ph* gene is present also in the A genome. Additional less powerful genes regulate chromosome pairing also. The *Ph* gene is absent from the genome of diploids but it is present in the B and G genomes in tetraploids. This observation indicates that *Ph* originated after polyploidization. ►*Triticum*, ►homoeologous, ►nullisomic; Sears ER 1969 Annu Rev Genet 3:451; Martinez-Perez E 2001 Nature 411:204; Griffith S et al 2006 Nature [Lond] 439749; Dvorak J et al 2006 Genetics 174:17.

PHA (phytohemagglutinin): A lectin of bean (*Phaseolus vulgaris*) plants; agglutinates erythrocytes and activates T lymphocytes. ►lectins, ►agglutination, ►erythrocyte, ►lymphocytes

Phaeochromocytoma (pheochromocytoma): A bladder-kidney carcinoma, over-producing adrenaline and noradrenaline. The disease may be caused by mutation in the von Hippel-Lindau gene or the neurofibromatosis 1 or the RET protooncogenes or by the multiple endocrine neoplasia gene MEN2. Mutations in the subunits of mitochondrial succinate dehydrogenase in the long arm of human chromosome 11 also may be involved. ►animal hormones, ►von Hippel-Lindau syndrome, ►neurofibromatosis, ►MEN, ►RET, ►succinate dehydrogenase; Astuti D et al 2001 Am Hum Genet 69:49; MaherER, Eng C 2002 Hum Mol Genet 11:2347.

Phaeomelanin: A mammalian pigment. ►pigmentation of animals

Phage (bacteriophage): A virus of bacteria. ►bacteriophages, ►development, ►phage life cycle

Phage Conversion: The acquisition of new properties by the bacterial cell after infection by a temperate phage. ►temperate phage

Phage Cross: ►rounds of matings

Phage Display: Filamentous bacteriophages (M13, fd) have a few copies (3–5) of protein III gene at the end of the particles (see Fig. P53). This protein controls phage assembly and adsorption to the bacterial pilus. When short DNA sequences are inserted into gene III (g3p), the protein encoded may be displayed on the surface of the particles. In case variable region fragments of antibody genes are inserted into the protein III coding sequences, specific antigens may be screened. The peptides can be separated with antibody affinity chromatography (panning). By repeated screening enormous arrays of recombinant libraries become available. The g3p product and the Fvs (fragments of variability) can be separated proteolytically or by inserting a stop codon between g3p and Fv. By the insertion of a large array of nucleotide sequences, a huge combinatorial library of soluble epitopes may be generated. The specificity of the antibodies can be further manipulated by mutation (random or targeted), by error-prone polymerase chain reactions, recombination, by chain shuffling, i.e., trying out various light and heavy chain combinations, synthetic CDR sequences, etc. Similarly, a variety of different antigens may be displayed on the surface of protein III and can be used to screen for cognate antibody. Phage display may be of applied significance for the pharmaceutical industry because extremely large number of variants (up to 10^8 to 10^{10}) of monoclonal antibodies can be selectively isolated and tested. For in vitro testing the two-hybrid method may be employed. The protein-protein interaction may then be studied in mammalian cells and screening techniques can be developed to isolate the cells that can neutralize the cytotoxic virus. The use of phagemid vectors may enhance the efficiency of the procedure. This procedure may facilitate the isolation of novel receptors, ligands, antibodies, anti-cancer reagents, transport proteins, signal transduction molecules, transcription factors, etc. Phage display technique may substitute for the construction of hybridomas (see Fig. P54). It can be used also for typing blood, for various diagnostic procedures, etc. A T7 phage display system permits the selection of RNA-binding regulatory proteins.

By screening large phage libraries for select tissue-specific organ antibodies, luminal endothelial cell

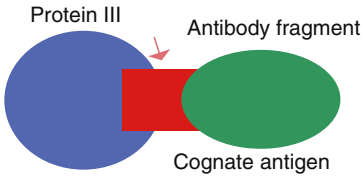

Figure P53. Protein III recognition

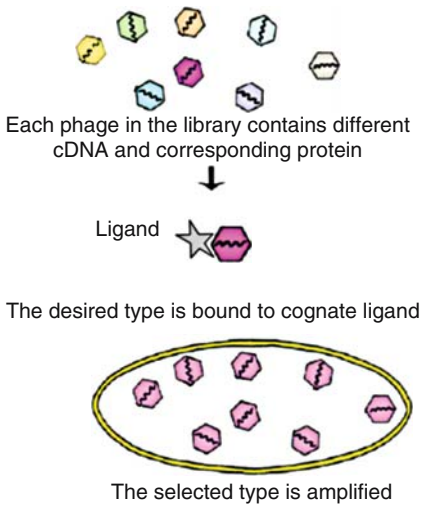

Figure P54. Phage display. (Note that the filamentous phage is represented as 'globular' only for the convenience of drawing).

plasma membranes were enriched from the bloodstream. The phage-displayed antibodies were converted Fv-Fc fusion proteins and monitored target selection by whole-body γ-scintigraphic imaging. Mass spectrometry identified the antigen targets. The procedure permits monitoring the vascular route of specific substances (Valadon P et al 2006 Proc Natl Acad Sci USA 103:407). ►filamentous phages, ►affinity chromatography, ►epitope screening, ►combinatorial library, ►pilus, ►antibody engineering, ►CDR, ►monoclonal antibody, ►mRNA display, ►two-hybrid method, ►monoclonal antibody, ►hybridoma, ►phagemid, ►anchored periplasmic expression; Smith GP, Petrenko VA 1997 Chem Rev 97:391; Danner S, Belasco JG 2001 Proc Natl Acad Sci USA 98:12954; Arap W et al 2002 Nature Med 8:121.

Phage Ghost: The empty protein shell of the virus.

Phage Immunity: A lysogenic bacterium carrying a prophage cannot be infected by another phage of the same type. ►prophage, ►zygotic induction

Phage Induction: Stimulates the prophage to leave a site in the bacterial chromosome and become vegetative. Physical and chemical agents may be inducive (UV light, mutagens, zygotic induction).

Phage Lifecycle: See Fig. P55, Böhm J et al 2001 Curr Biol 11:1168.

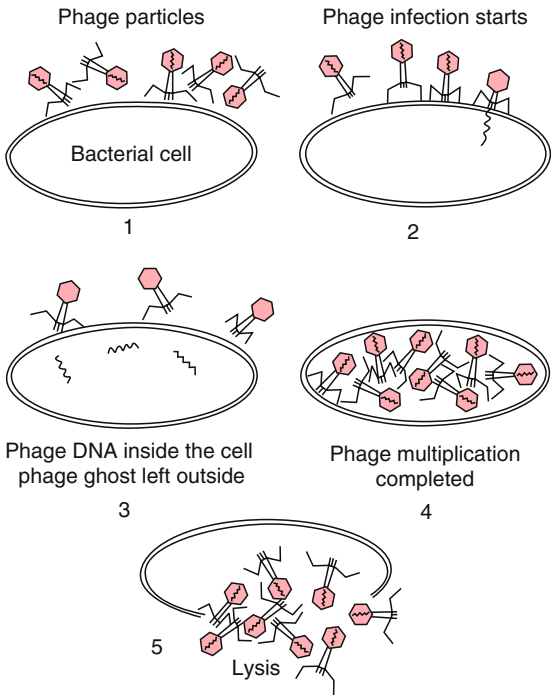

Figure P55. Phage lifecycle. (Redrawn after the illustration provided by Drs. Simon LD, Anderson TF Institute of Cancer Research, Philadelphia, PA, USA

Phage Morphogenesis: ►one-step growth, ►development, ►phage life cycle

Phage Mosaic: May be generated by phage display, expressing different molecular structures on the surface of a filamentous phage. ►phage display

Phage Therapy: The bacteriophages are bacteria-eating systems. D'Hérelle, the discoverer of phages, already attempted their therapeutic use in poultry as well as for humans with considerable success. With the discovery of antibiotics, the interest in phage therapy ebbed. Another cause for the decline of interest was the discovery of phage resistance in bacteria.

Also, bacteria encode restriction/modification systems of defense. The human body may also react immunologically against the phages. Recent studies, despite some technical problems indicate feasibility of this type of therapy. (See Summers WC 2001 Annu Rev Microbiol 55:437; Schuch B et al 2002 Nature [Lond] 418:884).

Phagemids: Genetic vectors that generally contain the ColE1 origin of replication and one or more selectable markers from a plasmid and a major intergenic copy of a filamentous phage (M13, fd1). When cells carrying such a combination are superinfected by a filamentous phage, it triggers a rolling

circle type replication of the vector DNA. This single-stranded product is used then for sequencing by the Sanger type DNA sequencing system, for oligonucleotide-directed mutagenesis and as strand-specific probes. The phagemids can carry up to 10 kb passenger DNA. Their replication is fast (in the presence of a helper), and they can produce up to 10^{11} plaque-forming units (pfu)/mL bacterial culture. Their stability is comparable to conventional plasmids. They obviate subcloning the DNA fragments from plasmid to filamentous phage. The most widely used phagemids contain parts of phage M13 and pUC, πVX^c, and pBR322 vectors. ►phasmid, ►vectors, ►plasmovirus, ►vectors, ►pfu, ►pUC, ►DNA sequencing; Sambrook J et al 1989 Molecular Cloning, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York; O'Connell D et al 2002 J Mol Biol 321:49.

Phagocytosis: A special cell (phagocyte) engulfs a foreign particle (microorganism, cell debris) and eventually exposes it to lysosomal enzymes for the purpose of destroying it. Dendritic cells and macrophages have important roles. In lower animals, this mechanism substitutes for the immune system. Phagocytosis pathway is controlled by a battery of *Ced* genes (and homologs, e.g., Dock180 in humans) during apoptosis. The CD14 human glycoprotein on the surface of macrophages recognizes and clears apoptotic cells (see Fig. P56). The major phagocyte receptors are CR3 (binds opsonized C3bi complement fraction) and the Fc gamma receptor, FcγR (binds immunoglobulin G). Both processes require the reorganization of the cytoskeleton under the control of RAC or RHO G proteins, respectively. ►pinocytosis, ►apoptosis, ►macrophage, ►complement, ►antibody, ►opsonins, ►RAC, ►RHO, ►lysosomes, ►cross presentation, ►cell fusion; Underhill DM, Ozinsky A 2002 Annu Rev Immunol 20:825; Stuart LM, Ezekowitz RAB 2005 Immunity 22:539.

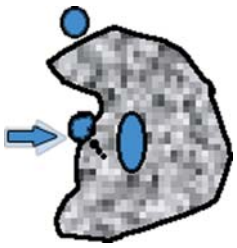

Figure P56. Phagocytosis

Phagosome: A body (vesicle) surrounded by plasma membrane of a phagocyte. They are fused with endosomes and lysosomal compartments to become degradative organelles (Touret N et al 2005 Cell 123:157). In *Drosophila* phagosomes 617 interactive proteins have been detected that are involved in immune reactions (Stuart LM et al 2007 Nature [Lond] 445:95). ►phagocytosis, ►endocytosis, ►endosome, ►lysosomes, ►macrophage

Phakomatoses (neurocutane syndromes): Hereditary and congenital diseases, which are of ectodermal origin and display spots on the body, such as neurofibromatosis, epiloia/tuberous sclerosis, FAP, von Hippel-Lindau syndrome, nevoid basal cell carcinoma, Cowden disease, Peutz-Jeghers syndrome, polyposis. (See separate entries; Tucker M et al 2000 J Natl Cancer Inst 92:530).

Phalange(s): The three bones in fingers and toes (at left) with the metacarpal bone (at right) (see Fig. P57).

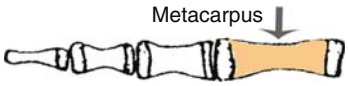

Figure P57. Phalange

Phalloidin: An amanotoxin, similar to, but faster in action than amanitin. When labeled with fluorescent coumarin phenyl isothiocyanate it is suitable to identify filamentous actin in the cells. It is extremely toxic. ►amatoxins, ►α-amanitin; Vetter J 1998 Toxicon 36:13.

Phallus: The penis, a symbol of generative power, also the fetal anlage of the penis and clitoris. ►penis, ►clitoris, ►anlage

Phantom Mutation: Artifacts of the DNA sequencing. They can be filtered out by statistical procedures. (Bandelt, H-J et al 2002 Am J Hum Genet 71:1150).

Pharate: The larva/adult emerging from the puparium.

Pharmaceuticals: The chemical agents used for medical purposes. Data collected on 352 marketed drugs (excluding anti-cancer agents, nucleosides, steroids and peptide-based formulations, which are known to affect DNA); 101 (28.7%) had at least one positive indication for genotoxicity. Four types of tests were used: bacterial mutagenesis, in vitro cytogenetics, in vivo cytogenetics and mouse lymphoma assay. One must keep in mind that carcinogenicity may involve routes that are not testable by these methods. Also, the laboratory assays are not 100% reliable. ►genotoxic chemicals, ►combinatorial chemistry, ►bioassays in genetic toxicology; Snyder RD, Green JW 2001 Mutat Res 488:151.

Pharmacogenetics: The study of the reaction of individuals of different genetic constitution to various drugs and medicines. Most of the differences are monogenic. Polymorphic genes frequently determine drug metabolism, drug transporters and drug responses of the body. Pharmacogenetics studies also study simultaneous drug responses by many genes. Based on these responses drugs with special, selective effect can be developed. Certain drugs have special side effects for individuals of particular genetic constitution ►cytochromes, ►SADR; Roses AD 2001 Hum Mol Genet 10:2261; Kuehl P et al 2001 Nature Genet 27:383; Roses AD 2002 Nature Rev Drug Discov 1:541; Goldstein DB et al 2003 Nature Rev Genet 4:937; Evans WE, Relling MV 2004 Nature [Lond] 429:464; problems and goals in pharmacogenetics/genomics: Need AC et al 2005 Nature Genet 37:671); variation in human genes and drug responses: http://www.PharmGKb.org; key therapeutic targets in proteins and nucleic acids: http://xin.cz3.nus.edu.sg/group/ttd/ttd.asp; pharmacogenetic substances [proteins, drugs]: http://bidd.cz3.nus.edu.sg/phg/.

Pharmacogenomics: The study of drug response of the entire genome of an organism. ►pharmacogenetics, ►SADR

Pharmacokinetics (pharmacodynamics): The study of absorption, tissue distribution, metabolism, and elimination (ADAME) as a function of time of biologically relevant molecules.

Pharmacoproteomics: The study of the proteins in sera or urine as a consequence of disease and/or drug therapy.

P

Pharmacodynamics: ►pharmacokinetics

Pharming: The production of pharmacologically useful compounds by transgenic organisms. ►transgenic, ►biopharming, ►molecular breeding, ►plantibody

PHAS-1: A heat stable protein ($M_r \approx 12{,}400$); when it is not phosphorylated it binds to peptide initiation factor eIF-4E and inhibits protein synthesis. Its Ser^{64} site is readily phosphorylated by MAP and then no longer binds to eIF-4E and protein synthesis may be stimulated. ►eIF-4E, ►MAP

Phase Diagram: A graphic representation of the equilibrium between/among components of a system. The phase is an identifiable part of a system. Phase diagrams are used in several scientific fields for the elucidation of the behavior of the phases of the components under dynamic conditions. In biology, phase diagrams can shed light on the mechanisms of interaction within a system, e.g., in a genetic network. Figure P58 represents three hypothetical internal (metabolic) components of the cell and two external factors (e.g., temperature and light) that determine in an interactive manner the node (red dot). ►networks, ►genetic networks; Park J, Barabási A-L 2007 Proc Natl Acad Sci 104:17916.

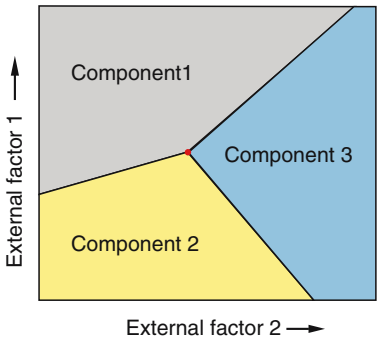

Figure P58. Phase diagram

Phase Variation: A programmed rearrangement in several genetic systems. The flagellin genes of the bacterium *Salmonella* display it at frequencies of 10^{-5} to 10^{-3}. The flagellar protein has two forms, H1 and H2. The *H1* gene is a passive element. When *H2* is expressed no H1 protein is made. When *H2* is switched off the H1 antigen is made. The expression of *H2* is regulated by the expression of the *rh1* repressor (repressing the synthesis of the H1 protein) and the promoter of *H2*. This promoter is about 100 bp upstream from the gene and it is liable to inversion, and then *H2* and *rh1* are turned off. Such an event then switches on the synthesis of H1 protein. Reversing the inversion flip switches back to H2. The Hin recombinase that is very similar to the invertases or recombinases of phage Mu or Cin from phage P1 catalyze the inversions. They can functionally substitute for each other. Hin binds to the *hixL* and *hixR* recombination sites. Additional genes are also involved in the fine-tuning. Defect in type III methyltransferase in restriction modification systems can cause phase variation of different genes in several bacterial species (Srikhanta YN et al 2005 Proc Natl Acad Sci USA 102:5547).

Somewhat similar mechanisms control the host-specificity genes of phage Mu and the mating type of budding yeast. ►cassette model, ►regulation of gene activity, ►antigenic variation, ►mating type determination in yeasts, ►*Trypanosoma*, ►flagellin, ►DNA uptake sequences, ►SSR; Hughes KT et al 1988 Genes Dev 2:937; Snyder LA et al 2001 Microbiology 147:2321.

Phase-Contrast Microscope: It alters the phase of light passing through and around the objects and this permits its visualization without fixation and/or

staining. ►Nomarski, ►fluorescence microscopy, ►microscopy light, ►confocal microscopy, ►electronmicroscopy

Phaseolin (C_{20} $H_{18}O_4$): An antifungal globulin in bean (*Phaseolus*).

Phasing Codon: Initiates translation (such as AUG) and determines the reading frame. ►genetic code, ►reading frame

Phasmid (phage-plasmid): A plasmid vector equipped with the *att* site of the lambda phage and thus, enables the plasmid to participate in site-specific recombination with the λ genome resulting in incorporation of plasmid sequences into the phage (*lifting*). Because it contains both λ and plasmid origins of replication it may be replicated either as a plasmid or as λ. ►lambda phage, ►phagemid, ►vectors; Briani F et al 2001 Plasmid 45:1.

Phenacetin ($C_{10}H_{13}NO_2$): An analgesic and antipyretic drug and a carcinogen.

Phene: An observable trait that may or may not have direct genetic determination. ►gene

Phenetics: The taxonomic classification based on phenotypes.

Phenocopy: The phenotypic change that mimics the expression of a mutation. ►phenotype, ►epigenetic, ►epimutation, ►morphosis, ►genocopy

Phenodeviate: An individual of unknown genetic constitution displaying a phenotype attributed to various genic combinations within the population.

Phenogenetics: The attempts to correlate the function of genes with phenotypes.

Phenogram: ►character matrix

Phenolics: Compounds containing a phenol ring such as acetosyringone, hydroxyacetosyrin-gone, chalcone derivatives, phenylpropanoids, and some phytoalexins. The mentioned compounds may excite or suppress the *vir* gene cascade of *Agrobacterium* and may affect the response to plant pathogenic agents. Capsaicin, ginger, resveratrol may be anticarcinogens due to their antioxidative properties and may promote apoptosis. Phenylpropenes such as chavicol, *t*-anol, eugenol and isoeugenol repel animals and microorganism but may attract some pollinators (see Fig. P59). Humans use these compounds as spices, food preservatives and medicine. Coniferyl acetate and NADPH may form as a precursor for enzymatic synthesis of eugenols (Koeduka T et al 2006 Proc Natl Acad Sci USA 103:10128). ►*Agrobacterium*, ►virulence genes of *Agrobacterium*, ►phytoalexins, ►chalcones, ►acetosyringone, ►resveratrol, ►ginger, ►capsaicin, ►apoptosis, ►wound response; Nicholson RL, Hammerschmidt RE 1992 Annu Rev Plant Path 30:369.

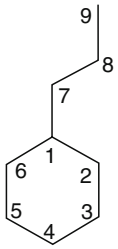

Figure P59. Phenylpropene backbone

Phenology: The study of the effects of the environment on live organisms.

Phenome: The collection of phenotypes; a group of organisms with shared phenotypes. (See Freimer N, Sabatti C 2003 Nature Genet 34:15; ►SNIPs; http://www.jax.org/phenome; http://www.phenomicdb.de.

Phenome Analysis: The attempts to determine the expression of genes at the RNA and protein level under different conditions, involving the environment and/or the prevailing genetic system (network). This may be an extremely difficult undertaking because gene expression may vary from complete silence to very variable and great complexity. ►phenotype, ►phenotype MicroArray; Bochner BR 2003 Nature Rev Genet 4:309.

Phenomenology: The description of facts as observed without metaphysical interpretation. The concept that behavior depends on how a person interprets reality rather than what is the objective reality.

Phenoptosis: An apoptosis-like phenomenon in unicellular organisms. ►apoptosis

Phenotype: The appearance of an organism that may or may not represent the genetic constitution. The proteins encoded by the DNA (the genotype) represent the phenotype. The 1014 human (disease) genes displayed 1429 distinguishable phenotypes (~141%). Microarray hybridization data can provide most comprehensive information on phenotype. In budding yeast, similar morphology indicates functional similarity of the coding genes. Triple-stained mutants facilitate the analysis of the morphology as a quantitative trait and can attribute function to many genes with previously unknown function (Ohya Y et al 2005 Proc Natl Acad Sci USA 102:19015). Mutation in the DNA is largely responsible for altered phenotypes. Alterations in transcription and translation also affect the phenotype and generally, as shown, there are more phenotypes than the number of

genes (Bürger R et al 2006 Genetics 172:197). ►gene ontology, ►microarray hybridization, ►cell comparisons, ►endophenotype; Phenomic Data Base facilitates the identification of genes involved in a phenotype or gives the phenotype caused by genes in major organisms: http://www.phenomicDB.de; muse phenotypes and relevance to human disease: http://www.eumorphia.org/

Phenotype MicroArrays: An automated analysis of phenotypic expression of hundreds of genes on microplates and can be used to monitor the consequences of knockouts or other genetic alterations. ►microarray hybridization, ►knockout; Bochner BR et al 2001 Genome Res 11:1246.

Phenotypic Assortment: ►macronucleus

Phenotypic Knockout: It means somatic gene therapy that neutralizes intracellular harmful mechanisms. ►gene therapy, ►knockout

Phenotypic Lag: A period of time may be required for gene expression after transformation or mutagenic treatment. ►transformation genetic, ►premutation; Ryan FJ 1955 Am Nat 89:159.

Phenotypic Mixing: The mixed assembly of viral nucleic acids and proteins upon simultaneous infections by different types of viruses. Therefore, the coat protein properties of the virions do not match the viral genotype by serological or other tests. (See Hayes W 1965 The genetics of bacteria and their viruses. Wiley, New York).

Phenotypic Plasticity: An adaptive property of an organism enabling it to take advantage of local conditions without evolving a particular function and at the expense of another function. ►homeostasis genetic, ►canalization, ►plasticity

Phenotypic Reversion: An apparent restoration of the normal expression of a mutant gene; it is not, however, inherited. Aminoglycoside antibiotics (paromomycin, geneticin, etc.) may successfully compete with the translation termination factors in eukaryotes in cases when the mRNA carries a stop codon mutation. As a result, some of the polypeptide chains are not terminated/truncated but completed in the presence of the drug. Transposable elements may also alter gene function without causing mutation in the gene. Phenotypic reversion may be exploited for correcting the genetic defects in some diseases. ►phenocopy, ►amino-glycosides, ►G418, ►paromomycin, ►suppressor tRNA, ►translation termination; Gause M et al 1996 Mol Gen Genet 253:370; Franzoni MG, De Castro-Prado MA 2000 Biol Res 33:11; Biedler JL et al 1975 J Natl Cancer Inst 55:671.

Phenotypic Sex: It may not reflect the expectation based on the sex-chromosomal constitution. ►testicular feminization, ►hermaphrodite

Phenotypic Stability Factor: A measure of developmental homeostasis; it is calculated by the ratios of the quantitative expression of a parameter (gene) under two different environmental conditions. ►homeostasis, ►logarithmic stability factor; Lewis D 1954 Heredity 8:334.

Phenotypic Suppression: An apparently normal but non-hereditary phenotype brought about by translational error due to environmental effects and/or drugs. ►error in translation

Phenotypic Switch: Alters phenotypes more frequently than expected by point mutation and may be caused by epigenetic methylation or by protein folding. (See Lim HN, van Oudenaarden A 2007 Nature Genet 39:269).

Phenotypic Value: In quantitative genetics, it is defined as the mean value of a population regarding the trait under study and it is generally represented as P value. ►breeding value

Phenotypic Variance: ►genetic variance

Phenylalanine ($C_9H_{11}NO_2$): An essential water-soluble, aromatic amino acid (MW 165.19). Its biosynthetic path (*with enzymes involved in parenthesis*): Chorismate → (*chorismate mutase*) → Prephenate → (*prephenate dihydratase*) → Phenylpyruvate → (*aminotransferase*, glutamate NH_3 donor) → Phenylalanine. ►chorismate, ►tyrosine, ►phenylketonuria

Phenylalanine Ammonia Lyase (PAL): PAL deaminates phenylalanine into cinnamic acid and it is thus involved in the synthesis of plant phenolics. ►phenolics

Phenylalanine Hydroxylase (PAH, 12q24.1): The deficiency of PAH leads to phenylketonuria.

Phenylhydrazine ($C_6H_9ClN_2$): A hemolytic compound but it is also used as a reagent for sugars, aldehydes, ketones and a number of industrial purposes (stabilizing explosives, dyes, etc.). ►hemolysis

Phenylketonuria (PKU, PAH, Fölling disease): This gene was located to human chromosome 12q24.1. It is a recessive disorder that has a prevalence of about 1×10^{-4} (carrier frequency is about 0.02) in white populations. Thus, an affected person has about 0.01 chance to have an affected child in case of a random mate but the recurrence rate in a family where one of the partners is affected and the other is a carrier it is nearly 0.5 (see Fig. P60).

Figure P60. Mentally retarded heterozygous children of a phenylketonuric mother (indirect epistasis). Courtesy of Dr. C. Charlton Mabry 1963; by permission of the New England Journal of Medicine 269:1404

Its incidence is substantially lower among Asian and black people (one-third of that in whites). PKU is more frequent in European populations of Celtic origin than in the other Europeans. This has been interpreted as the result of natural selection because PKU heterozygosity conveys some tolerance to the mycotoxin, ochratoxin A, produced by *Aspergillus* and *Penicillium* fungi, common in humid northern regions. Before the nature of this disorder and the method of treatment were identified, about 0.5 to 1% of the patients in mental asylums were afflicted by PKU. A deficiency of the enzyme phenylalanine hydroxylase and consequently the accumulation of phenyl pyruvic acid and a deficiency of tyrosine cause the disease:

$$\text{PHENYL PYRUVIC ACID} \rightleftarrows$$
$$\text{PHENYLALANINE} \Rightarrow \text{TYROSINE}$$

For the identification of the condition the Guthrie test has been used to cultures of *Bacillus subtilis* containing blood of the patients, β-2-thienylalanine was added. This phenylalanine analog is a competitive inhibitor of tyrosine synthesis. In the presence of excess amounts of phenylalanine, the bacterial growth does not stop. Since in the different families the genetically determined defect in the enzyme varies, so does the severity of the clinical symptoms. The accumulation of phenyl pyruvic acid is apparently responsible for the mental retardation and the musty odor of the urine of the patients.

The reduced amount of tyrosine prevents normal pigmentation (melanin) and thus results in pale color. The good aspect of this condition is that relative normalcy can be established if it is diagnosed early and dietary restrictions for phenylalanine are implemented. The restriction of phenylalanine must start as early as possible (before birth if feasible), and continue at least until age 10. Restriction should be observed before pregnancy, during pregnancy and during breast-feeding or during the entire life to avoid harm to the nervous system. Phenylketonuria of the mother may damage the nervous system of genetically normal fetus through placental transfer (indirect epistasis). Because of the multiple metabolic pathways involving phenylpyruvic acid, besides the deficiency of phenylalanine hydroxylase, other genes and conditions may cause similar clinical symptoms. Phenylalanine hydroxylase activity requires the availability of the reduced form of the co-factor 5,6,7,8-tetrahydrobiopterin that is made by the enzyme *dihydrobiopterin reductase* from 7,8-dihydrobiopterin. The dihydrobiopterin reductase enzyme is coded in human chromosome 4p15.1-p16.1. Defect in this enzyme also causes phenylketonuria symptoms but lowering the level phenylalanine in the diet does not alleviate the problems. Another form of phenylketonuria is based on a deficiency in dihydrobiopterin synthesis. Using the φBT1 integrating phage vector (containing a site-specific recombinase), equipped with the murine phenylalanine hydroxylase cDNA, PKU could be completely and persistently cured after three injections to the mouse liver (Chen L, Woo SLC et al 2005 Proc Natl Acad Sci USA 102:15581).

Prenatal diagnosis can be carried out by several methods. Mutations at various related metabolic sites in the mouse may serve as a model for studying phenylketonuria. ►epistasis, ►mental retardation, ►one gene-one-enzyme theorem, ►genetic screening, ►Guthrie test, ►tyrosinemia, ►alkaptonuria, ►phenylalanine, ►hyperphenylalaninemia, ►amino acid metabolism, ►prenatal diagnosis, ►enzyme replacement therapy, ►integrase, ►targeting genes; Ledley FD et al 1986 N Engl J Med 314:1276; Gjetting T et al 2001 Am J Hum Genet 68:1353.

Phenylpropanoid: ►phenolics, ►phytoalexins

Phenylthiocarbamide Tasting (PTC): A major incompletely dominant gene appears to be in human chromosome 7q35-q36 (Conneally PM et al 1976 Hum Hered 26(4):276). A major bitter testing locus is assigned to human chromosome 5p15 (Reed DR et al 1999 Am J Hum Genet 64:1478). The TAS2R10 PTC receptor appears to be in the short arm of chromosome 12. A single G protein coupled receptor with allelic variants may account for the taste perception (Bufe B et al 2005 Curr Biol 15:322). In humans and chimpanzees, two alleles at the TAS2R38 locus control bitter tasting but the human and chimpanzee alleles are different (Wooding S et al. 2006 Nature [Lond] 440:930). About 30% of North-American Whites and about 8–10% of Blacks cannot taste the

bitterness of this compound. Persons affected by thyroid-deficiency (athyreotic) cretenism (mental deficiency) are non-tasters. Phenylthiocarbamide (syn. phenylthiourea) has been used for classroom demonstration of human diversity but it should be kept in mind that it is a toxic compound (LD_{50} oral dose for rats 3 mg/kg and for mice 10 mg/kg). ►taste, ►LD_{50}; Guo SW, Reed DR 2001 Ann Hum Biol 28(2):111; Kim U-K et al 2003 Science 299:1221.

Phenylthiourea: ►phenylthiocarbamide tasting (see Fig. P61).

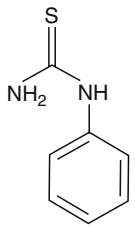

Figure P61. Phenylthiourea

Pheochromocytoma (phaeochromocytoma): An adrenal tumor induced by the SHC oncogene. ►paraganglion, ►SHC, ►adenomatosis endocrine multiple, ►endocrine neoplasian neuroendocrine cancer

Pheresis (apheresis): The medical procedure of withdrawal of blood; after fractionation, some fraction(s) are reintroduced. Such a protocol may use stem cells, transfect them with a vector or apply to them chemotherapy, and eventually place them back in the body of the same individual.

Pheromones: Various chemical substances secreted by animals and cells for the purpose of signaling and generating certain responses by members of the species, such as sex-attractants, stimulants, territorial markers, or other behavioral signals and cues. The male pheromone of Asian elephants, frontalin (exists in two enantiomorphs) is secreted during musth (annual period of increased sexual activity and aggression) by the temporal gland on the face. The proportion of the two forms and the extent of secretion of frontalin are sensed primarily by the ovulating females (Greenwood DR et al 2005 Nature [Lond] 438:1097). About 100 genes control the pheromones and their receptors in rodents and the signals are transmitted through G protein-associated signal transduction pathways. The mouse sex pheromones in the male urine includes several compounds, among them the strongest response is evoked by (methylthio) methanethiol for females. Apparently, only a small number of cells at the olfactory bulb responded to this compound, which for humans had a garlic-like odor (Lin DY et al 2005 Nature [Lond] 434:470). The lacrimal glands of adult male mice secrete a 7 kDa peptide to which the vomeronasal receptors of the sensory neurons of the female animals respond (Kimoto H et al. 2005 Nature [Lond] 437:898). The role of pheromones in humans may not be generally agreed upon. The steroid compounds 4,16-androstadien-3-one (AND) present in the sweat of human males and estra-1,3,5(10)-tetraen-3-ol (EST) present in the female urine appear to have pheromone-like properties. Their smelling causes sex-differentiated activation of the anterior hypothalmus of the brain. Male homosexuals respond to AND but not to EST in contrast to heterosexuals (Savic I et al 2005 Proc Natl Acad Sci USA 102:7356). Heterosexual men were found to respond to AND; lesbian women processed AND (unlike heterosexual women), not by the anterior pituitary but by the olfactory network (Berglund H et al 2006 Proc Natl Acad Sci USA 103:8269).

The pheromone receptor genes in rodents include *V1r* and *V2r*; apparently there are no human homologs. The sexually deceptive orchid plant *Chiloglottis* attracts the *Neozeleboria* insect pollinator males by secreting a volatile compound (2-ethytl-5-propylcyclohexan-1,3-dione), which is chemically identical with the insect female sex pheromone (Schiestl FP et al 2003 Science 302:437). RNA interference technique revealed that in silkworm, for sex pheromone production pheromone activating neuropeptide receptor (*PBANR*), pheromone gland-specific (PG) fatty acyl reductase (*pgFAR*), PGZ11/Δ10,12 desaturase (*Bmpgdesat1*), PG acyl CoA-binding protein (*pgACBP*) genes are essential (Ohnishi A et al 2006 Proc Natl Acad Sci USA 103:4398). In *Drosophila*, the male-specific pheromone 1-*cis*-vaccenyl acetate (cVA) acts through olfactory receptor Or67d. The *fruitless* (*fru*) gene controls three classes of olfactory receptors, one of which is Or67d. This single receptor controls both male and female mating behavior. Mutant males display homosexual tendencies whereas mutant females are less receptive to courting indicating that cVA has opposite effects for the two sexes, i.e., inhibiting males' mating behavior but stimulating that in females (Kurtovic A et al 2007 Nature [Lond] 446:542). Male flies show less interest in females, which have mated before, apparently by sensing cVA (Ejima A et al 2007 Curr Biol 17:599). The trichoid sensilla on the antennae has three olfactory receptors; receptor T1 responds primarily to male odor in the cuticular extracts whereas to the odor of virgin females receptors T2 and T3 respond (van der Goes van Naters W, Carlson JR 2007 Curr Biol 17:606). In male *Drosophila*, the synthesis of octopamine (a norepinephrine related substance) mediates aggressive behavior toward other males. In flies defective

for tyramine β-hydroxylase (the enzyme that converts octopamine from its precursor), courtship is observed (Cartel SJ et al 2007 Proc Natl Acad Sci USA 104:4706). Pheromone hydrocarbon chains are longer in females than in males. The transformer gene (tra) feminizes males and makes them produce longer (female type) hydrocarbon pheromones (Chertemps T et al 2007 Proc Natl Acad Sci USA 104:4273). ►mating type determination in yeast, ►sex determination, ►*fru*, ►olfactogenetics, ►vomeronasal organ, ►signal transduction, ►homosexual, ►RNAi, ►silkworm, ►kairomones, ►mimicry, ►Bruce effect; Kohl JV et al 2001 Neuroendocrinol Lett 22(5):309; Luo M et al 2003 Science 299:1196; Prestwich GD, Blomquist GJ 1987 Pheromone Biochemistry, Academic Press, Orlando, Florida; Wang Y, Dohlman HG 2004 Science 306:1508; Dulac C, Torello AT 2003 Nature Rev Neurosci 4:531; minireview: Stowers L, Marton TF 2005 Neuron 46:699; review of vertebrate pheromone communication: Brennanm PA, Zufall F 2006 Nature [Lond] 444:308; pheromone signaling circuits: Dulac C, Wagner S 2006 Annu Rev Genet 40:449; insect pheromones: http://www.pherobase.com.

Phialide: Fungal stem cells from which conidia are budded.

Philadelphia Chromosome: In the Philadelphia chromosome, the long arm (q34) of human chromosome 9, carrying the *c-abl* oncogene is translocated to the long arm (q11) of chromosome 22 carrying site *bcr* (breakpoint cluster region). The *bcr-abl* gene fusion is then responsible for 85% of myelogenous (Abelson) and acute leukemia as a consequence of the translocation and fusion. In the acute form, a 7.5 kb mRNA is translated into protein p190, and in the myelogenous form an 8.5 kb mRNA is translated into a chimeric protein p210. The fusion protein is a deregulated tyrosine kinase acting on hematopoietic cells and causes leukemia-like oncogenic transformation in mice. Synthetic antisense phosphorothioate oligonucleotides ([S]ODN) complementary to the 2nd exon of BCR or to the 3rd exon of the ABL of the fused genes block temporarily the proliferation of the chronic leukemic cells, without harming the normal cells, in a mouse model. The outcome of such a therapy could be improved by simultaneously targeting also the c-Myc oncogene with an antisense construct. Further effectiveness was observed by exposing the cells to a low concentration of mafosfamide, an antineoplastic drug that promotes apoptosis, or to cyclophosphamide. ►ABL, ►BCR, ►leukemia, ►hematopoiesis, ►cancer gene therapy, ►apoptosis, ►cyclophosphamide, ►antisense technologies, ►transresponder, ►Knudson's two mutation theory; Saglio G et al 2002 Proc Natl Acad Sci USA 99:9882; Goldman JM et al 2003 N Engl J Med 349:1451.

Phlebotomous: A blood-sucking (insect), or phlebotomy bloodletting surgical procedure.

Phloem: A plant tissue involved in the transport of nutrients; it contains sieve tubes and companion cells, phloem parenchyma, and fibers. ►sieve tube, ►parenchyma, ►xyleme, ►root, ►proteoglycan; Bonke M et al 2003 Nature [Lond] 426:181.

Phlorizin: A dichalcone in the bark of trees (*Rosaceae*); it blocks the reabsorption of glucose by the tubules of the kidney and causes glucosuria. ►disaccharide intolerance, ►chalcones

PHO81: A yeast CDK inhibitor homologous to $p16^{INK4}$. ►CDK, ►$p16^{INK4}$

PHO85: A cyclin-dependent kinase of *Saccharomyces cerevisiae*. ►CDK, ►KIN28, ►CDC28, ►PHO81

phoA: A gene for alkaline phosphatase.

Phobias: Phobias exist in different forms, all characterized by unreasonable avoidance of objects, events, or people. A phobia may amount to serious, morbid mental illness. Apparently, duplication in human chromosome 15q24-q26 is associated with one form and also with laxity of the joints. ►panic disorder, ►panic obsessive disorder, ►anxiety; Gratacós M et al 2001 Cell 106:367.

Phocomelia: The absence of some bones of the limbs proximal to the trunk. It may occur as a teratological effect of various recessive and dominant human genetic defects or as a consequence of teratogenic drugs, e.g., thalidomide use during human or primate pregnancy. ►limb defects in humans, ►Roberts syndrome, ►teratogen, ►thalidomide

PHOGE (pulsed homogeneous orthogonal field electrophoresis): A type of pulsed field gel electrophoresis, within the range of 50 kb to 1 Mb DNA, permitting straight tracks of large number of samples. ►pulsed field gel electrophoresis

PhoQ: *Salmonella* kinase, affecting regulator of virulence PhoP. ►virulence, ►*Salmonella*

PhoR: Phosphate assimilation regulated by PhoR kinase upon phosphorylation of regulator PhoB.

Phorbol Esters: Facilitators of tumorous growth that work by activating protein kinase C. ►TPA, ►protein kinases, ►procarcinogen, ►carcinogen, ►PMA, see formula at ►PMA

Phorbol 12-Myristate-13-Acetate (PMA): ►phorbol esters, ►PMA (see Fig. P62).

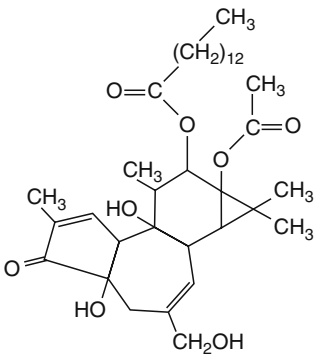

Figure P62. Myristoylphorbol acetate (ester)

Phosphatases: In animals, both acid and alkaline phosphatases are common, in plants acid phosphatases are found. Some of the phosphatases have high specificities and have indispensable role in energy release in the cells. A series of non-specific phosphatases carry out only digestive tasks. In humans, the erythrocyte and fibroblast expressed acid phosphatase (ACP1) isozymes are coded in chromosomes 2 and 4. It has been suggested that these enzymes split flavin mononucleotide phosphates. In megaloblastic anemia, ACP1 level is increased. The tartrate-resistant acid phosphatase type 5 (TR-AP) is an iron-glycoprotein of 34 kDa (human chromosome 15q22-q26), and it is increased in the spleen in case of Gaucher disease. Lysosomal acid phosphatase (ACP2) is located in human chromosome 11p12-p11. Alkaline phosphatase (ALPL) is present in the liver, bone, kidney, and fibroblasts, is often called the non-tissue-specific phosphatase (human chromosome 1p36-p34), and is deficient in hypophosphatasias. The alkaline phosphatase ALPP is located in the placenta (human chromosome 2q37) and several allelic forms have been identified. A similar alkaline phosphatase is present also in the testes and the thymus and the gene occurs at the same chromosomal location, but its expression is highly tissue-specific. Protein phosphatase 2A (PP2A) catalytic subunit, encoded at human chromosome 9q34, is involved in the control of many cellular processes, including the mitotic spindle (Sclaitz A-L et al 2007 Cell 128:115). The structure of the holoenzyme is known (Xu Y et al 2006 Cell 127:1239). ►serine/threonine and tyrosine protein phosphatases, ►hypophosphatasia, ►hypophosphatemia, ►dual-specificity phosphatase, ►megaloblastic anemia, ►Gaucher's disease

Phosphate Response of Plants: The inorganic phosphate level is frequently growth-limiting in plants. *Arabidopsis* is an extremely sensitive indicator of P is soils. The photograph illustrates *Arabidopsis* growth on a Missouri soil sample, without and with PO_4 addition (see Fig. P63) (Rédei GP 1966 unpublished).

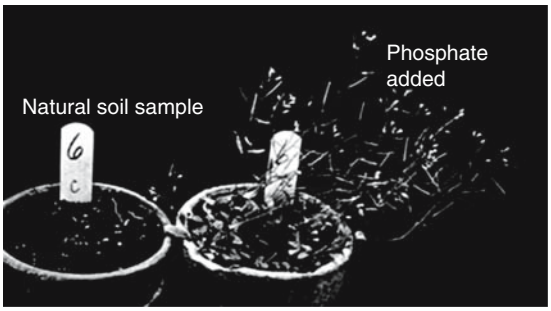

Figure P63. *Arabidopsis* growth with and without PO_4 addition

The physical contact of the *Arabidopsis thaliana* primary root tip with low-phosphate medium arrests root growth. Loss-of-function mutations in *Low Phosphate Root1* (*LPR1*) and its close paralog *LPR2* strongly (encoding multicopper oxidases) reduce this inhibition (Svistoonoff S et al 2007 Nature Genet 39:792). The non-protein coding gene *IPS1* (Induced by phosphate starvation1) contains a motif with sequence complementarity to the phosphate (Pi) starvation-induced miRNA miR-399. When the pairing is interrupted by a mismatched loop at the expected miRNA cleavage site, IPS1 RNA is not cleaved but instead sequesters miR-399. Thus, IPS1 overexpression results in increased accumulation of the miR-399 target PHO2 mRNA (phosphate-starvation) and, concommitantly, in reduced shoot Pi content (Franco-Zorilla JM et al 2007 Nature Genet 39:1033).

Microarray hybridization of transcript abundance among 22,810 *Arabidopsis* genes indicated that 612 were coordinately induced, whereas 254 genes were suppressed by inorganic phosphate. These genes are involved with metabolic pathways, ion transport, signal transduction, transcriptional regulation and other cellular processes (Misson J et al 2005 Proc Natl Acad Sci USA 102:11).

Phosphatidate: A precursor of diaglycerol (see Fig. P64). ►diaglycerol, formula at right.

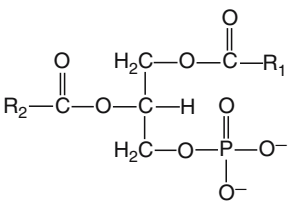

Figure P64. Phosphatidate

Phosphatidylinositol (1,2-diacyl-sn-glycero-3-phospho [1-o-myoinositol]): A cell membrane phospholipid. Phospha-tidylinositol-transfer protein is required for vesicle budding from the Golgi complex. Phospha-tidylinositol-3,4,5-trisphosphate activates protein kinase B. Phosphatidylinositol-kinase-3 mutations are oncogenic (Kang S et al 2005 Proc Natl Acad Sci USA 102:802). ►PIK, ►pleckstrin domain, ►PKB, ►Golgi apparatus, ►PTEN, ►phosphoinositides, ►wortmannin; Bourette RP et al 1997 EMBO J 16:5880; Abel K et al 2001 J Cell Sci 114:2207.

3´-Phosphoadenosine-5´-Phosphosulfate: ►PAPS

Phosphodegron: SCFβ-TRCP promotes Chk1-dependent Cdc25A ubiquitination, and this involves serine 76, a known Chk1 phosphorylation site, but other sites of phosphorylated amino acids may make a protein liable to degradation by ubiquitination. ►SCF, ►Chk-1, ►CDC25, ►ubiquitin

Phosphodiester Bond: A phosphodiester bond attaches the nucleotides into a chain by hooking up the incoming 5′-phosphate ends to the 3′-hydroxy tail of the preceding nucleotide: R^1 and R^2 represent nucleosides, O: oxygen, H: hydrogen, P: phosphorus (see Fig. P65). ►Watson-Crick model, formula.

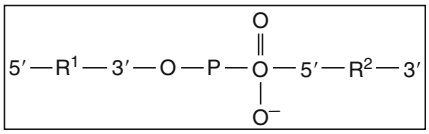

Figure P65. Phosphodiester bond

Phosphodiesterases: Exonucleases. The snake venom phosphodiesterase starts at the 3′-OH ends of a nucleotide chain and splits off the nucleoside-5′-phosphate. The 3′-phosphate terminus does not lend the nucleotide chain for its action. The spleen phosphodiesterase, on the other hand, generates nucleoside-3′-phosphate molecules by splitting on the other side of the nucleotides. Phosphodiesterase converts cyclic AMP into AMP or cGMP into GMP. Phosphodiesterase 5 inhibitors are therapeutics for erectile dysfunction and several other diseases. The sensitivity of RNA phosphodiesterases is affected by the secondary and tertiary structure of the RNA as well by the adjacent nucleotides. ►phosphodiester bond, ►nitric oxide, ►priapism, ►stroke; structure: Sung BJ et al 2003 Nature [Lond] 425:98; catalytic domains for different inhibitors: Card GL et al 2004 Structure12:2233.

Phosphoenolpyruvate: Phosphoenolpyruvate is efficient in transferring phosphate group to ADP to form ADP (see Fig. P66).

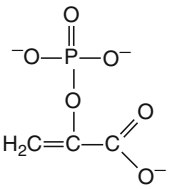

Figure P66. Phosphoenolpyruvate

Phosphofructokinase M (glycogen storage disease VII, 12q13.3): A phospho-fructokinase in the muscles (PFKM). It deficiency may cause muscle cramps and myoglobinuria. Lactate production is reduced and fatigue develops after exertion. ►glycogen storage diseases, ►myoglobin, ►fructose-2,6-bisphosphatase

Phosphofructokinase Platelet Type (PFKP, 10p15.3-p15.2): PFKP is expressed in the platelet but it displays 71% identity of amino acid sequence of the muscle type and 63% identity with the liver enzyme.

Phoshpofructokinase X (PFKX): A chromosome 2-encoded enzyme, which is expressed in the fibroblasts and the brain.

Phosphofructo-2-Kinase/Fructose-2,6-Bisphosphatase (PFKFB, PFRX, Xp11.21): A bifunctional enzyme encoded in the X chromosome of humans and rodents. The PFKFB3 locus is in 10p15-p14. The PFKFB4 enzyme is in 3p22-p21.

Phosphofructose Kinase 1 (PFK-1, PFKL, phospho-fructokinase): PFK-1 enzyme catalyzes the formation of fructose-1-6-bisphosphate from fructose-6-phosphate in the presence of ATP and Mg^{2+}. PFKL (liver enzyme) is encoded in human chromosome 21q22.3. The tetrameric enzyme may exist in five different forms due to the random association of the products of two different loci.

Phosphofructose Kinase 2 (PFK-2): PFK-2 mediates the formation of fructose-2,6-bisphosphate from fructose-6-phosphate. It enhances the activity of fructosephosphate 1 enzyme by binding to it, and also inhibits fructose-2,6-bisphosphatase and therefore enhances glycolysis. ►glycolysis

Phosphoglucomutase (PGM): The enzyme that catalyzes the reaction:

$$\text{GLUCOSE} - 1 - \text{PHOSPHATE} \rightleftarrows \text{GLUCOSE} - 6 - \text{PHOSPHATE}$$

Phosphoglucomutase proteins are homologous in structure through the animal kingdom. In humans, there are several PGM enzymes and some with multiple allelic forms with characteristic patterns and are reasonably stable. Therefore, PGM is used in forensic

genetics for personal identification on samples up to 6 months old. Their human chromosomal locations are: PGM1 (1p31, PGM2 (4p14-q12), PGM3 (6q12), and PGM5 (9p12-q12). ►forensic genetics

Phosphogluconate Oxidative Pathway: Same as pentose phosphate pathway.

3-Phoshoglycerate Dehydrogenase Deficiency (PHGDH, 1q12): PHGDH results in recessive serine biosynthetic defect, microcephaly, and neurological defects and seizures. ►serine

Phosphoglyceratemutase Deficiency: ►myopathy, ►glycerophospholipid

Phosphoglyceride: ►glycerophospholipid

Phosphohexose Isomerase (PHI): PHI catalyzes the glucose-6-phosphate⇔fructose-6-phosphate conversions. It is encoded in human chromosome 19cen-q12. Its defects result in dominant hemolytic anemia. ►anemia, ►hemolytic anemia

Phosphoinositide-3-Kinases: ►PIK, ►phosphoinositides

Phosphoinositides: Inositol-containing phospholipids. They play an important role as second messengers, and in phosphorylated/dephosphorylated forms they participate in the regulation of traffic through membranes, growth, differentiation, oncogenesis, neurotransmission, hormone action, cytoskeletal organization, platelet function, and sensory perception. The signals converge on phospholipase C (PLC, 20q12-q13.1). It hydrolyzes phosphatidylinositol-4,5-bisphosphate ($PtdInsP_2$) into inositol trisphosphate ($InsP_3$) and diacylglycerol (DAG). $PtdInsP_2$ segregation is mediated by PTEN, and CDC42 control apical morphogenesis (Martin-Belmonte F et al 2007 Cell 128:383). $InsP_3$ regulates Ca^{2+} household and DAG activates PLC. $InsP_3$ levels also regulate pronuclear migration, nuclear envelope breakdown, metaphase-anaphase transitions, and cytokinesis. Cytidine diphosphate-diacylglycerol synthase (CDS) is required for the regeneration of $PtdInsP_2$ from phosphatidic acid. CDS is a key regulator in the G-protein-coupled photo-transduction pathway. Pleckstrin homology domains selectively bind phosphoinositides. ►inositol, ►phospholipase, ►stoma, ►DAG, ►signal transduction, ►IP_2 [$InsP_2$ for formula], ►IP_3 [$InsP_3$ for formula], ►phosphatidylinositol, ►*myo*inositol, ►PIK, ►pleckstrin, ►PTEN, ►CDC42; Czech MP 2000 Cell 100:603; Vanhaesebroeck B et al 2001 Annu Rev Biochem 70:535; Sato TK et al 2001 Science 294:1881; De Matteis MA et al 2002 Curr Opin Cell Biol 14:434; review: Di Paolo G, Di Camilli P 2006 Nature [Lond] 443:651.

Phosphoinositide-Specific Phospholipase Cδ: Cδ signal transducers and generates the second messengers inositol-1,4,5-triphosphate and diaglycerol. ►signal transduction, ►second messenger

Phospholamban (phosphorylated pholamban, PLN, 6q22.1): A regulator of sarcoplasmic reticulum Ca^{2+}-ATPase (SERCA); it is a kinetic regulator of heart muscle function. Mutation in PLN leads to hereditary cardiomyopathy and premature death (Haghighi K et al 2006 Proc Natl Acad Sci USA 103:1388). ►cardiomyopathy

Phospholipase (PL) A, D, C: Each split specific bond in phospholipids. PLC-β generates diacylglycerol and phosphatidylinositol 2,4,5-triphosphate from phosphatidylinositol 4,5-bis-phosphate. These second messenger molecules play roles in signal transduction. PLC-γ is activated by receptor tyrosine kinases and one of its homologs is the SRC oncoprotein. PLC-γ1 with VEGF—through the FLT-1 receptor—controls the strength of the heartbeat by regulating calcium signaling in the myocytes (Rottbauer W et al 2005 Genes Dev 19:1624). PLA is present in mammalian inflammatory exudates. Form A2 is coded by human chromosome 12, the other PLA2B by chromosome 1. Phospholipase C is coded in human chromosomes at the following locations: PLCB3 (11q11), PLCB4 (20p12), and PLCG2 (16q24.1). ►serine/threonine phosphoprotein phosphatases, ►SRC, ►signal transduction, ►phosphoinositides, ►Ipk1, ►Ipk2, ►VEGF, ►stoma; Rhee SG 2001 Annu Rev Biochem 70:281; Wang X 2001 Annu Rev Plant Physiol Mol Biol 52:211.

Phospholipid: A lipid with phosphate group(s). ►liposome, ►lipids

Phosphomannomutase Deficiency: A rare defect of glycosylation displaying large differences in expressivity. It involves inverted nipples, fat pads, strabismus, hyporeflexia (sluggish responses), mental retardation, hypogonadism, and early death. (See Grünewald S et al 2001 Am J Hum Genet 68:347).

Phosphomannose Isomerase (MPI, 15q22-qter): The defects of MPI affect many glycosylation reactions in the cell. MPI is involved in the conversion of fructose-6-phosphate into mannose-6-phosphate. Clinically, it may cause diarrhea, enlarged liver, hypoglycemia with convulsions, coma, etc. The 5 kb gene includes 8 exons.

Phosphomonoesterase: A phosphatase digesting phosphomonoesters, such as nucleotide chains. ►phosphodiester bond

Phosphonitricin (Basta): ►herbicides

Phosphoramidates: Phosphoramidates are used in antisense technologies by the modification of the sugar-phosphate backbone of oligonucleotides (see Fig. P67). ►antisense technologies, ►trinucleotide-directed mutagenesis; Jin Y et al 2001 Bioorg Med Chem Lett 11:2057; Faria M et al 2001 Nature Biotechnol 19:40.

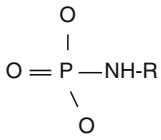

Figure P67. Phosphoramidate

Phosphoramide/Ink Jotting: A rapid method of DNA analysis. (See Cooley P et al 2001 Methods Mol Biol 170:117).

Phosphorelay: ►two-component regulatory system

Phosphorescence: ►fluorescence, ►luminescence

Phosphoribosylglycinamide Formyltransferase: Phosphoribosylglycinamide formyltransferase is human chromosome 21q22.1 dominant and it controls purine, pyrimidine biosynthesis, and folate metabolism.

Phosphoribosylpyrophosphate Synthetase (PRPS1, Xq22-q24): An enzyme of the purine/pyrimidine salvage pathway. Its deficiency may cause hyperuricemia (excessive amounts of uric acid in the urine), deafness, and neurological disorder.

Phosphorimaging: The detection of radioactive labels in tissues by phosphorescence.

Phosphorolysis: In phophorolysis, glycosidic linkage holding two sugars together is attacked by inorganic phosphate and the terminal glucose is removed (from glycogen) as α-D-glucose-1-phosphate.

Phosphorothioates: Analogs of oligodeoxynucleotides; they are used in antisense technology. Their attachment to the 3′-end inhibits the activity of nucleases that attacks RNA from that end. They can bind to proteins, but do not stimulate the activity of RNase H (phosphoro-dithioate modified heteroduplexes may stimulate RNase H), inhibit translation, and are relatively easily taken up by cells. Some of the truncated mRNAs can, however, be translated into truncated proteins (Hasselblatt P et al 2005 Nucleic Acids Res 33:114). Some of the effects of these molecules are not based on their anti-sense properties (e.g., binding to CD4, NF-κB, inhibition of cell adhesion, inhibition of receptors, etc.). Phosphorothioate-modified nucleotides (one of the oxygen attached to P is replaced by S) are used also in in vitro mutagenesis to protect the template strand from nucleases, while the strand to be modified is excised before re-synthesis in a mutant form. ►antisense technologies, ►antisense RNA, ►antisense DNA, ►OL(1)p53, ►ribonuclease H, ►CD4, ►NF-κB; Sazani P et al 2001 Nucleic Acids Res 29:3965; ►quenched autoligation probe

Phosphorylase b Kinase: An enzyme that phosphorylates two specific serine residues in *phosphorylase b*, thus converting it into *phosphorylase a* upon the action of cAMP-dependent protein kinase (synonym protein kinase A). Phosphorylase b kinase mediates glycogen breakdown. This enzyme is a tetramer and for activation the two regulatory subunits (R) must be separated from the two catalytic subunits to be able to function. The dissociation is mediated by cAMP through A-kinase. The δ subunit is calmodulin. ►epinephrine, ►cAMP-dependent protein kinase, ►cAMP, ►A-kinases, ►calmodulin; Brushia RJ, Walsh DA 1999 Front Biosci 4:D618.

Phosphorylases (kinases): ►serine/threonine kinases, ►tyrosine protein kinase, ►Jak kinase, ►phophorylase B, ►A-kinases, ►signal transduction, ►serine/threonine phosphoprotein phosphatases, ►phospholipase C, ►signal transduction, ►calmodulin, ►phosphorylase b kinase

Phosphorylation: Adding phosphate to a molecule. It may play an important role in signal transduction, and depending on which of the potentially several sites is phosphorylated, the function of some transcription factors may be altered. In the proteins serine and threonine, residues are frequently phosphorylated. If phosphoserine and phosphothreonine residues are replaced by the lysine analog aminoethylcyteine or β-methylaminoethylcysteine, the lysine-specific proteases cleave at these sites and thus these phosphorylation sites can be revealed (Knight ZA et al 2003 Nature Biotechnol 21:1047). Phosphorylation sites are detectable also by tandem mass spectrometry. The mouse genome contains more than 500 kinases. The nerve synapse system alone operates with 650 phosphorylation events involving 331 sites. Some proteins, like MAP1B, have 33 such sites. The bioinformatics information indicates that a small number of kinases phosphorylate many proteins and some substrates are phosphorylated by many kinases. These phosphorylations form elaborate interacting networks (Collins MO et al 2005 J Biol Chem 280:5972). ►oxidative phosphorylation, ►kinase, ►phosphorylases, ►tandem mass spectrometry, ►unstructured proteins; Whitmarsh AJ, Davis RJ 2000 Cell Mol Life Sci 57:1172; protein phosphorylation site prediction (DISPHOS): http://core.ist.temple.edu/pred/pred.html; PHOSIDA phosphorylation site database: http://www.phosida.com/; protein

three-dimensional phosphorylation sites: http://cbm.bio.uniroma2.it/phospho3d.

Phosphorylation Potential (Δg_p): The change in free energy within the cell after hydrolysis of ATP.

Phosphoserinephosphatase: Phosphoserinephosphatase hydrolyzes O-phosphoserine into serine; it is encoded in human chromosome 7p15.1-p15.1.

Photoactivated Localization Microscopy: Photoactivated localization microscopy can detect activable fluorescent proteins within cells and cellular organelles at nanometer resolution (Betzig E et al 2006 Science 313:1642). ►microscopy

Photoaffinity Tagging: In photoaffinity tagging, the labels may be radioactive or fluorescent and bind to certain compounds by non-covalent bonds upon illumination. (See Knorre DG et al 1998 FEBS Lett 433:9).

Photoaging: In photoaging, skin collagens and elastin are damaged by the ultraviolet light induced metalloproteinases and this results in wrinkling of the skin similar to what occurs during aging. These enzymes are upregulated by AP-1 and NF-κB transcription factors. ►aging, ►collagen, ►elastin, ►AP-1, ►NF-κB

Photoallergy: Immunological response to a substance activated by light.

Photoautotroph: An organism that can synthesize in light all its required organic substances and energy from inorganic compounds. The majority of green plants are photoautotrophic. By introducing a glucose transporter gene into obligate photoautotrophic alga, the organism could be converted to light-independent growth on glucose. (See Zaslavskaia LA et al 2001 Science 292:2073).

Photochemical Reaction Center: The site of photon absorption and initiation of electron transfer in the photosynthetic system. ►photosynthesis

Photodynamic Effect: Photosensitivation, photodestruction. A dye or pigment absorbs light and converts the energy to a higher state and exerts specific effects. Photodynamic effects may have various therapeutic applications. Phenothiazines, phthalocyanines, porphyrines, and other molecules with photoactive properties have been successfully tested as photoinactivating agents against Gram-positive and Gram-negative bacteria. After absorption of light, singlet oxygen ($^1O_2$) may be generated and the oxidative damage to proteins and lipids may kill the bacteria even if they are resistant to antibiotics. ►ROS, ►singlet oxygen; Langmack K et al 2001 J Photochem Photobiol B 60:37; Maisch T et al 2007 Proc Natl Acad Sci USA 104:7223.

Photoelectric Effect: The photoelectric effect has very wide applications of modern technology (television, computers and other electronic instruments). Atoms may emit electrons when light hits a suitable target. When X-rays hit a target, very high energy photoelectrons may be generated.

Photogenes: Chloroplast DNA-encoded proteins involved in photosynthesis. One of the most studied is *photogene* 32 (*psbA*), which codes for a 32 kDa thylakoid protein involved in electron transport in photosystem II. Also, it binds the herbicide atrazine and by removing or altering this binding site, one can obtain plants resistant to the weed killer through molecular genetic manipulations. ►photosynthesis, ►herbicides; Rodermel SR, Bogorad L 1985 J Cell Biol 100:463.

Photography: Photography, in the laboratory, has special requirements depending on the objects. Cell cultures in Petri plates can be best photographed through macrolenses (for extreme close ups, use extension rings or teleconverter) and through using highly sensitive color films, such as Kodak Gold 400. To eliminate reflection, the blue photoflood lamps should be adjusted at an angle of about 45°. Agarose gels can be photographed with a polaroid camera mounted on a copying stand and using high speed (ASA 3000) films. Ultraviolet light sources of the longer wavelength are less likely to damage the DNA. The contrast can be enhanced by the use of orange filters on the camera (such as Kodak Wratten 22A). Note that ultraviolet light is dangerous to the skin and particularly to the eyes. Use gloves, goggles, and wear a long-sleeved shirt. For photomicrography, built-in automatic exposure meters are very advantageous, if frequently used. Otherwise, numerous exposures, at the proper color temperature, are necessary. For photocopying and editing, halftone image computers with (color) scanners can be used. The resolution now provided by digital cameras is satisfactory for most biological applications; they are very convenient and the high pixel (up to 8–10 megapixel [picture elements]) units are very powerful.

Photolabeling: Adding photoactivatable groups to proteins, membranes, or other cellular constituents in order to detect their reaction path. The labels are generally small molecules, stable in the dark and highly susceptible to light. They work without causing photolytic damage to the target and are stable enough to permit analytical manipulations of the sample. Synthetic peptides containing substances, such as 4′-(trifluoromethyl-diazirinyl)-phenylalanine or 4′-benzoyl-phenylalanine, etc., have been used to analyze biological structures (membranes, proteins, etc.). ►green fluorescent protein, ►luciferase

P

Photolithography: A modification of a more-than-a-century-old printing process. A solid plate is coated with a light-sensitive emulsion, overlaid by a photographic film, and then, illuminated. An image is formed after the plate is exposed to light. A similar principle has been adapted now to visualize DNA sequences for the purpose of large scale mapping, fingerprinting, and diagnostics. The process is also used for the synthesis of nucleotide probes. ►DNA chips, ►microarray hybridization; Barone AD et al 2001 Nucleosides Nucleotides Nucleic Acids 20 (4–7):525; review of techniques: Truskett VN, Watts MP 2006 Trends Biotechnol 24:312.

Photolyase: A flavoprotein repair enzyme (M_r 54,000) that splits cyclobutane pyrimidine dimers (Pyr < > Pyr) into monomers upon absorption of blue light. A photolyase-like 42-nucleotide deoxyribozyme is also capable of repairing thymine dimers optimally at 300 nm light (Chinnapen DJ-F, Sen D 2004 Proc Natl Acad Sci USA 101:65). In *E. coli*, two chromophores assist the process of photolyase action; 5,10-methenyltetrahydrofolate absorbs the photoreactivating light and 8-hydroxy-5-deazariboflavin, and the energy is then transferred to $FADH_2$, although the latter too absorbs some energy. The excited $FADH_2$* then transfers the energy to the dimer and while $FADH_2$ is regenerated, the dimer splits up, the recipient member of the dimer breaks down, and monomeric pyrimidines are formed. A second cofactor, 5,10-methenyl-tetrahydrofolylpolyglutamate (MTHF), may be the light harvester. It is interesting that the blue light photoreceptor cryptochromes of plants bear substantial similarities to the bacterial photolyase and its cofactors are also the same, yet the exact role of photolyases in plant DNA repair is unclear. Cyclobutane photolyase does not split the pyrimidine-pyrimidinone (6-4) photoproducts. The 6-4 photolyases are under the control of two different genes. Topical application of photolyase and light to sunburnt human skin may alleviate the symptoms by repair of the DNA damage. ►DNA repair, ►direct repair, ►photoreactivation, ►pyrimidine dimer, ►cyclobutane ring, ►cryptochrome, ►base flipping, ►pyrimidinone; Tanaka M et al 2001 Mutagenesis 16:1; Komori H et al. 2001 Proc Natl Acad Sci USA 98:13560; crystal structure: Mees A et al 2004 Science 306:1789; repair process: Kao Y-T et al 2005 Proc Natl Acad Sci USA 102:16128.

Photolysis: Degradation of chemicals or cells by light.

Photomixotrophic: An organism that can synthesize some of its organic requirements with the aid of light energy, while for others it depends on supplied organic substances.

Photomorphogenesis: Light-dependent morphogenesis. Light affects the growth and differentiation of plant meristems (photoperiodism), plastid differentiation, and directly or indirectly many processes of plant metabolism. Certain stages in photomorphogenesis can be reached at low intensity (fluence) illumination (or even in darkness), such as the formation of proplastids and etioplasts. Other steps such as the full differentiation of the thylakoid system and photosynthesis-dependent processes require high fluence rate and critical spectral regimes (red and blue). Several genes involved in the control of plastid development have been identified in *Arabidopsis* and other plants. The *lu* mutation is normal green at low light intensity but it is entirely bleached and dies at high light levels. Wild type plants can make etioplasts in the dark but the *deetiolated* (*det1*), *constitutive photomorphogenesis* (*cop1* and *cop9*) mutants develop chloroplasts in darkness. The Cop9 complex includes eight subunits, forming a signalosome in plants and a homolog is found also in animals. The *gun* (*genome uncoupled*) mutants grow normally in the dark but do not allow the development of etioplasts into chloroplasts. Various pale *hy* (*high-hypocotyl*) mutants, deficient in phytochrome, make light green plastids indicating that phytochrome is not a requisite for plastid differentiation to an advanced stage. The *blu* (*blue light uninhibited*) class of mutants is inhibited in hypocotyl elongation by far red light. The *HY4* locus of *Arabidopsis* encodes a protein, homologous to photolyases, and the recessive mutations are insensitive to blue light for hypocotyl elongation. Mutants were identified, some of which showed no response to blue light and others displayed very high blue light requirement for curvature. Most of these light responses appear to be mediated by signal transduction pathways. The chlorophyll-b free, yellow green mutants (*ch*) display chloroplast structure appearing almost normal by electronmicroscopy. Several mutations defective in fatty acid biosynthesis and/or photosynthesis are rather normal in photomorphogenesis. Some mutants are resistant to high CO_2 atmosphere, and normal chloroplast differentiation requires high CO2. Other mutants can be protected from bleaching only at 2% CO_2 atmosphere. The *Arabidopsis* nuclear mutants of the *im* (*immutans*) type display variegation under average greenhouse illumination, but they are almost normal green under low light intensity and short daily light cycles whereas at high intensity continuous illumination they are almost entirely free of leaf pigments. Under the latter condition, by continuous feeding of an inhibitor or repressor of the de novo pyrimidine pathway, the leaf pigment content may increase twenty-fold. In these variegated plants, the green cells have entirely normal chloroplasts

whereas the white cells lack thylakoid structure. The azauracil-treated plants display fully functional, although morphologically altered thylakoids. An insertional mutation at the *ch-42 locus* (*cs*) identified a thylakoid protein, essential for normal greening of the plants without abolishing cell viability. The *PRF* (*pleiotropic regulatory factor*) locus, tagged by a T-DNA insertion, controls several loci involved in photomorphogenesis. The product of the gene is a subunit of the G-protein family. The *det2*, *cyp90*, *cop*, *fus*, *dim axr2*, and the *cbb* dwarf mutations develop their characteristic phenotypes because of defects in the brassinosteroid pathway. The nuclear gene *chm* (*chloroplast mutator*) induces a wide variety of plastid morphological changes, due to extranuclear mutation. ►photoperiodism, ►florigen, ►phototropism, ►phytochrome, ►circadian rhythm, ►signal transduction, ►brassinosteroids, ►COP, ►proteasome, ►dominance reversal; Wada M, Kadota A 1989 Annu Rev Plant Physiol Plant Mol Biol 40:169; von Arnim A, Deng X-W 1996 Annu Rev Plant Physiol Plant Mol Biol 47:215; Quail PH 2002 Nature Rev Mol Cell Biol 3:85.

Photon: A quantum of electromagnetic radiation, which has zero rest mass and an energy h times the frequency of the radiation. Photons are generated by collisions between atomic nuclei and electrons and other processes when electrically charged particles change momentum. ►measurement units

Photoperiodism: The response of some species of plants to the relative length of the daily light and dark periods.

Besides the length of these cycles, the spectral properties and the intensity of the light are also important. Responses of plants include, the onset of flowering, vegetative growth, elongation of the internodes, seed germination, leaf abscission, etc. *Short-day*, *long-day* and *day-neutral* plants are commonly distinguished on the basis of the critical daylength or, in the latter category, by the lack of it (see Fig. P68). The geographic distribution of plants is correlated with their photoperiodic response. In the near equatorial regions, short-day species predominate whereas in the regions extending toward the poles long-day plants are common. The onset of flowering of short-day plants is promoted by 15–16 h of dark periods whereas in long-day plants, the flowering is accelerated by continuous illumination or by longer light than dark daily cycles. The critical day-length is not an absolute term; it varies in different species. Usually, there is a minimum number of cycles to evoke the photoperiodic response. Mutants of *Arabidopsis* (*gi*, *co*, *ld*; Rédei GP 1962 Genetics 47:443) and others shed light on some of the basic mechanisms involved (Schultz TF, Kay SA

Figure P68. Henbane (*Hyoscyamus niger*) Long-day plants flower only under long daily light periods (after appropriate cold treatment). Courtesy of Professor G. Melchers

2003 Science 301:326). The most important photoreceptor chromoprotein is *phytochrome*. The effect of phytochrome is affected by different plant hormones. Typical long-day plants are henbane (*Hyoscyamus*), spinach, *Arabidopsis* [without a critical daylength], the majority of the grasses and cereal crops (wheat, barley, oats), lettuce, radish, etc. Typical short day plants are Biloxi soybean, cocklebur, aster, chrysanthemum, poinsettia, dahlia, etc. In the majority of species, the photoperiodic response is controlled by one or a few genes. Some processes in animals are also under photoperiodic control. In the Japanese quail, the gene encoding type 2 iodothyronine deiodinase, which catalyzes the conversion of the prohormone into the active 3,5,3′[-triiodothyronine is induced by light. The anatomical location of the response center is in the hypothalamus, while the target site is the differentiation of the gonads (Yoshimura T et al 2003 Nature [Lond] 426:178). ►phytochrome, ►florigen, ►cryptochromes, ►photomorphogenesis, ►circadian rhythm, ►phototropism, ►vernalization, ►flower evocation, ►floral induction, ►dominance reversal; Jackson SD, Prat S 1996 Plant Physiol 98:407; Amador V et al 2001 Cell 106:343; Quail PH 2002 Curr Opin Cell Biol 2002 14:180; Mockler T et al 2003 Proc Natl Acad Sci USA 100:2140S; Yanofsky MJ, Kay SA 2003 Nature Rev Mol Cell Biol 4:265; Chen M et al 2004 Annu Rev Genet 38:87.

Photophosphorylation: ATP formation from ADP in photosynthetic cells.

Photoreactivation: Elimination of the harmful effects of ultraviolet irradiation by subsequent exposure to visible light (that activates enzymes splitting up the pyrimidine dimers in the DNA). With a few exceptions, e.g., *Haemophilus influenzae*, most organisms

possess light-activated repair enzymes. The majority of mammals do not have efficient photoreactivation system, except the marsupials. ►light repair, ►photolyase dark repair, ►excision repair, ►glycosylases, ►error-prone repair, ►DNA repair; Kelner A 1949 J Bacteriol 48:5111; Tuteja N et al 2001 Crit Rev Biochem Mol Biol 36(4):337; Sancar GB 2000 Mutation Res 451:25.

Photoreceptors: Humans have, in the eye, the very sensitive rod cells, mediating black and white vision and the less sensitive cone cells for color vision. ►phytochrome, ►rhodopsin, ►CRX, ►metalloproteinases, ►phototropism, ►*sevenless*, ►S-cone disease; Calvert PD et al 2006 Trends Cell Biol 16:560.

Photoreduction: In photosynthetic cells, light induced reduction of an electron acceptor.

Photorespiration: Oxygen consumption in illuminated plants used primarily for the oxidation of the photosynthetic product phosphoglycolate; it also protects C3 plants from photooxidation. Step-wise nuclear transformation of *Arabidopsis* with five chloroplast-targeted bacterial genes encoding glycolate dehydrogenase, glyoxylate carboligase, and tartronic semialdehyde reductase converted chloroplast glycolate directly to glycerate. Transgenic plants grew faster, produced more shoot and root biomass, and contained more soluble sugars, reflecting reduced photorespiration and enhanced photosynthesis that correlated with an increased chloroplast CO_2 concentration (Kabeish R et al 2007 Nature Biotechnol 25:593). ►respiration, ►Calvin cycle, ►C3 plants; Wingler A et al 2000 Philos Trans R Soc Lond B Biol Sci 355:1517.

Photorhabdus luminescens: A gram-negative enterobacterium that maintains a mutualistic association with insect-feeding Heterorhabditis species of nematodes. When the nematodes invade the insects, the bacteria are released, kill the host with the help of the toxin, emit light, and make the cadaver luminescent. The toxins (tca and tcd) are potential insecticide, fungicide, and antibacterial agents, somewhat similarly to that of *Bacillus thüringiensis*. *Arabidopsis* plants, transgenic for the *TcdA* gene driven by the constitutive cassava vein mosaic virus promoter and equipped with the 5′ and 3′ untranslated sequences of the tobacco *osmotin* gene, were especially resistant to feeding insects (Liu D et al 2003 Nature Biotechnol 21:1038). The osmotin gene sequences increased the mRNA stability. The activity of the transgene was affected significantly by the position of the insertion site in the plant chromosome. Strain TT01 genome contains 5,688,987 bp and encodes presumably 4839 proteins (Duchaud E et al 2003 Nature Biotechnol 21:1307). ►*Bacillus thüringiensis*; Ehlers RU 2001 Appl Microbiol Biotechnol 56:623; Szállás E et al 1997 Int J Syst Bacteriol 47:402; Bowen D et al 1998 Science 280:2129.

Photosensitizers: Photosensitizers may increase the oxidative damage to DNA. Their action may involve initial electron or hydrogen transfer to the DNA by the excited photosensitizer, followed by the generation of free radicals. Alternatively, they generate singlet oxygen that interacts with the DNA and then produces peroxidic intermediates. Most commonly, guanine suffers lesions. ►oxidative DNA damages

Photosynthesis: Using light energy for the conversion of CO_2 into carbohydrates with the assistance of a reducing agent such as water. The photosynthetic system appears to have evolved from the core of the cyanobacterial genome (Mulkidjanian AY et al 2006 Proc Natl Acad Sci USA 103:13126). ►photosystems, ►Z scheme, ►chlorophyll binding proteins, ►thermotolerance, ►C3 plants, ►C4 plants, ►Calvin cycle; Matsuoka M et al 2001 Annu Rev Plant Physiol Mol Biol 52:297; Xiong J, Bauer CE 2002 Annu Rev Plant Biol 53:503.

Photosystems: In photosynthesis, photosystem I is excited by far red light (~700 nm) while photosystem II requires higher energy red light (~650–680 nm). In the thylakoids of the chloroplast of plants, the immunophilin FKB20-2, an FK-506 binding protein, is required for the assembly of the photosystem II complex (Lima A et al 2006 Proc Natl Acad Sci USA 103:12631). Photosynthesis in bacteria that does not evolve oxygen uses only photosystem I. Upon absorption of photons, photosystem I liberates electrons that are carried through a cascade of carriers to NADP+, which is reduced to NADPH. The departure of electrons generates a "void" in the P700 photoreaction center of photosystem I and that is filled then by electrons produced through splitting of water molecules in photosystem II. The overall reaction flow is:

$$2H_2O + 2\,NADP^+ + 8\,photons \rightarrow O_2 + 2NADPH + 2H^+$$

Mutants of *Chlamydomonas* alga lacking photosystem I survive as long as the actinic light (beyond violet) reaches 200 microeinsteins per m^2/second. The photosystem II of cyanobacteria (similar to that of plants and algae) is a complex of 20 proteins and 77 cofactors including 14 integrally bound lipids and their crystal structure has been determined at 3.0 Å resolution (Loll B et al 2005 Nature [Lond] 438:1040). Photosystem I has 17 protein subunits and the crystal structure of the supercomplex has been determined at 3.4 Å resolution (Amunts A et al 2007 Nature [Lond] 447:58). ►CAB, ►LHCP, ►antenna, ►chloroplast, ►thylakoid, ►Z scheme, ►immunophilins; Annu Rev

Genet 29:755, Guergova-Kuras M et al 2001 Proc Natl Acad Sci USA 98:4437; Jordan P et al 2001 Nature [Lond] 411:909; Chitnis PR 2001 Annu Rev Plant Physiol Plant Mol Biol 52:593; Szabó I et al 2001 J Biol Chem 276:13784; Rhe K-H 2001 Annu Rev Biophys Biomol Struct 30:307; Saenger W et al 2002 Curr Opin Struct Biol 12:244; Munekage Y et al 2004 Nature [Lond] 429:579; structure of photosystems: Nelson N, Yocum CE 2006 Annu Rev Plant Biol 57:521.

Phototaxis: A movement of organisms (plants, animals and microbes) in response to light.

Phototransduction: The transmission of light signals mediating gene expression. A scaffold protein (InaD in *Drosophila*) assembles the components of the light transduction pathway. ►signal transduction, ►rhodopsin, ►retinal dystrophy

Phototroph: An organism that uses light to generate energy and uses this energy to synthesize its nutrients from inorganic compounds.

Phototropin: Flavoprotein photoreceptors for plant phototropism. They have two flavin mononucleotide-binding domains (LOV1 and LOV2) and a serine-threonine kinase domain at the carboxyl end. Phototropins 1 and 2 are blue light-activated kinases for low and high intensity light. ►flavoprotein; Harper SM et al 2003 Science 301:1541.

Phototropism: The reaction of an organ or organism to light, involving apparently more than a single photoreceptor (see Fig. P69). In *Arabidopsis*, the phytochromes and two complementary cryptochrome mutations (*CRY1, CRY2*) have been identified. Inactivation of both is required to eliminate phototropic response. It was suggested that one of the receptors is a membrane protein with autophosphorylating ability. Additional genes (*NPH1, NPH2, NPH3, RPT, NPL1*) are required for processing the responses after perception of the signals. Phototropin (phot1) detects low fluence blue light. Phytochromes modulate phototropism by phytochrome A signaling components. Phytochrome kinase substrate proteins (Pks1, Pks2 and Pks4), in a complex with phot1 and NPH3 (non-phototropic hypocotyl), are involved in the signaling to phototropism (Lariguet P et al 2006 Proc Natl Acad Sci USA 103:10134). ►photoreceptors, ►gravitropism, ►phytochromes, ►cryptochromes, ►phototropin; Briggs WR, Liscum E 1997 Plant Cell Environ 20:768; Quail PH 2002 Curr Opin Cell Biol 2002 14:180; Chen M et al 2004 Annu Rev Genet 38:87.

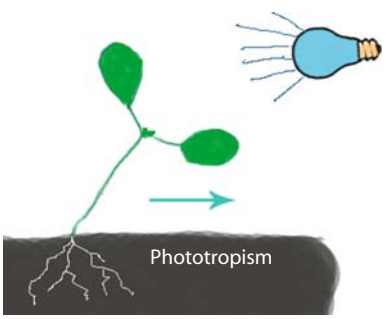

Figure P69. Phototropism

Phox: An oxidation subunit of proteins that is activated by phosphorylation. (Hoyal CR et al 2003 Proc Natl Acad Sci USA 100:5130).

Phragmoplast: A hollow-looking ring- or barrel-like structure formed near the end of mitosis in the middle plane of plant cells before the *cell plate* appears, separating the two daughter cells. ►mitosis; Gu X, Verma DP 1996 EMBO J 15:695; Zhang Z et al 2000 J Biol Chem 275:8779.

PHRAP: One of the frequently used DNA sequence alignment programs. A quality score of $10^{X/10} \approx 30$ corresponds to an accuracy of 99.9% regarding the base sequence. ►PHRED, ►CONSED, ►base-call; Harmsen D et al 2002 Nucleic Acids Res 30:416; http://www.phrap.org.

PHRED: An automated base-calling computer program. ►PHRAP, ►PolyPhred, ►base-call

Phycobilins: Highly fluorescent photoreceptor pigments in blue-green, red, and some other algae. They contain a linear tetrapyrrole prosthetic group for light harvesting. They also contain bile pigments and an apoprotein. This family of pigments includes the blue phycocyanins, the red phycoerythrins, and the pale blue allocyanins. These pigments may form phycobilisome, attached to the photosynthetic membrane. Phytochromes are also related pigments. ►light-harvesting protein, ►phytochrome; Wu SH et al 1997 J Biol Chem 272:25700.

Phycocyanin: The pigment of blue-green algae. ►phycobilins

Phycoerythrin: The red pigment of red algae. ►phycobilins, ►phycocyanin

Phycomycetes: Fungi with some algal characteristics. *Ph. blakesleeanus* is easy to grow with four-days-long asexual cycle and about two-months-long sexual cycle. It forms heterokaryons (n = 14) and can be subjected to formal genetic analyses, although the tetrads may be irregularly amplified. Transformation is feasible. It is well suited for physiological and developmental studies.

Phyletic Evolution: Gradual emergence of a species in a line of descent. The gaps in the fossil records are supposed to be due to accidents in the preservation of the intermediate forms.

Phyllody: Developmental anomaly of conversion of floral parts into leaves, generally after infection by pathogens.

Phylloquinone: Phylloquinone is composed of a p-naphthokinone and a phytol radical and it catalyzes oxydation-reduction reactions in plants. ►vitamin K

Phyllotaxy (phyllotaxis): In phyllotaxy, the consecutive leaves of plants do not occur above each other. Quite commonly, single leaves are at opposite positions (unless they occur in whorls) (see Fig. P70). This arrangement makes sense for the optimal utilization of light. In many plants, the leaves may not alternate in 180° but they may be arranged in any other determined pattern. This pattern is called phyllotaxy. If the leaves are opposite to each other, the phyllotaxy is 1/2. A common phyllotactic index is 2/5 (144°). This means that if the leaves are positioned by this index, leaf #1 will be followed by #2 at 144°, then #3 will take the place in a spiral at 288°, i.e., it will be above #1 (because 288:144 = 0.5 and 0.5 × 360 = 180), and so on. The arrangement of the fruits on the stem may also be caused by such an obliquity, following either clockwise or counterclockwise directions. The phyllotactic arrangement is determined by the flow of auxin, and it may be negatively regulated by cytokinins in the shoot meristem (Giulini A et al 2004 Nature [Lond] 430:1031). ►embryogenesis in plants, ►Fibonacci series, ►decussate; Hake S, Jackson D 1995 ASGSB Bull 8 (2):29; Kuhlemeier C, Reinhardt D 2001 Trends Plant Sci 6:187; Reinhardt D et al 2003 Nature [Lond] 426:255; Jönsson H et al 2006 Proc Natl Acad Sci USA 103:1633; Smith RS et al 2006 Proc Natl Acad Sci USA 103:1301.

Figure P70. Phyllotaxy

Phylogenetic Analysis: Phylogenetic analysis in forensic science uses pathogen strain DNA comparisons for identifying the source of infection, e.g., the retroviral DNA in case of HIV. ►acquired immunodeficiency, ►DNA finger printing, ►forensic genetics

Phylogenetic Depth: The total number of genetic changes, which separate an organism from its ancestors.

Phylogenetic Profile Method: The phylogenetic profile method studies the correlations of inheritance of pairs of proteins among various species. These proteins are not necessarily homologous but they appear to be linked functionally. ►rosetta stone sequences; http://dip.doe-mbi.ucla.edu.

Phylogenetic Tree: The phylogenetic tree graphically represents the phylogeny of organisms. Trees have been constructed in the past on the basis of morphology, the sequences of single genes, or sequences of entire genomes. Similarity between two organisms can also be determined by dividing their total number of genes by the number of genes they have in common. Phylogenetic analysis based on molecular information greatly increases the precision of map construction. Although insights into the various genomes greatly facilitate the elucidation of phylogenetic relationships, none of the molecular methods are completely free of problems because duplications, deletions, horizontal gene transfer, and the evolution of new genes from various sequences may create problems in interpretation. ►evolutionary tree, ►BAMBE; Madsen O et al 2001 Nature [Lond] 409:610; Murphy WJ et al. 2001 Nature [Lond] 409:614; Kristian H et al 2007 Bioinformatics 23:793; http://www.treefam.org/.

Phylogenetic Weighting: As per phylogenetic weighting, DNA sequence information from various taxa is included in the phylogenetic tree in decreasing order of relationship. Thus, alignment from distant relatives should not precede alignment of closer relatives. This procedure prevents confounding similarity and descent. ►evolutionary tree, ►maximum parsimony, ►homology, ►DNA sequence alignment, ►homology; Robinson M et al 1998 Mol Biol Evol 15:1091.

Phylogenomics: Phylogenomics uses evolutionary information to infer function of genes or the reconstruction of phylogenetic history on the basis of genomes. (See Delsuc F et al 2005 Nature Rev Genet 6:361; metabolic networks from protein structure: Caetano-Anollés G et al 2007 Proc Natl Acad Sci USA 104: 9358; phylogeny of protein domains: http://www.bioinformatics.nl/tools/treedom/; Berkeley phylogenomics: http://phylogenomics.berkeley.edu; search several gene families

simultaneously: http://www.cs.nuim.ie/distributed/multiphyl.php; distributed computing: http://distributed.cs.nuim.ie/multiphylOnlineManual.php; prokaryotic phylogenomics: http://genetrees.vbi.vt.edu).

Phylogeny: The evolutionary descent of a species or other taxonomic groups. ►evolution, ►ontogeny, ►speciation, ►genome conservation; Huelsenbeck JP et al 2001 Science 294:2310; information at the web site: http://beta.tolweb.org/tree/; http://mrbayes.csit.fsu.edu/.

Phylotype (phylogenetic type): A species representing a branch of a phylogenetic tree on the basis of shared similarity of nucleotide sequences. ►phylogenetic tree

Phylum: The first main category of the plant and animal, and other kingdoms.

Physarum polycephalum: A single-cell slime mold that displays physiological dioecy. The cell forms a plasmodium, i.e., the nuclei divide without cell division and thus, the cell becomes multinucleate. In the early embryos, only the S and M phases of the cell cycle are detectable.

Physcomitrella patens: A moss with a principal life phase as a haploid gametophyte. It can be used for the production of various mutants, for parasexual research, transformation, study of plant hormones on developmental processes, and various tropisms. Sequencing of the genome is nearly complete by 2005. The estimated genome size (n = 27) ~511 Mb (~0.53 pg). The chloroplast genome is 122890 bp encoding 83 proteins. (See Schaefer DG 2002 Annu Rev Plant Biol 53:477; Cove D 2005 Annu Rev Genet 39:339).

Physical Containment: ►containment

Physical Map: A map where the genome is ordered in DNA fragments or nucleotide sequences rather than in units of recombination. The first physical maps were constructed in bac-teriophages with small genomes. The DNA of phage P4 was cleaved completely by restriction endonuclease EcoRI into four fragments, which could be separated by electrophoresis according to size:

ν	ζ	ζ	ψ
A	C	B	D

After incomplete digestion for 5 min, larger fragments were also detected that contained fragments A + B + C, C + B, and the combined size of C + D appeared but no fragment appeared with the size B + D. The cause of the absence of B + D must have been that B and D were not adjacent in the circular DNA. Therefore, the sequence of the fragments in the chromosome could only have been: A − B − C − D.

The much larger polyoma genome was mapped by a different procedure. With a single EcoRI cut, the circular DNA was linearized and that cut was designated as the zero coordinate of the map. HinDIII cut the circle into two fragments: A = 55% and B = 45% (see Fig. P71). HpaII produced eight fragments: a = 27%, b = 21%, c = 17%, d = 13%, e = 8%, f = 7%, g = 5%, and h = 2% of the total genome. When EcoRI and HpaII cleaved the DNA, fragment b (21%) was not detected by electrophoresis, but instead, two new fragments of 1% and 20% were found. Obviously, the EcoRI cut was 1% from one end and 20% from the other end of fragment b. In the following step, the HindIII is shown to generate a fragment that was digested by HpaII. Fragments c, d, e, g, and h were found again (17 + 13 + 8 + 5 + 2 = 45) and two pieces of 3% and 7% were also obtained. When the HinDIII fragment of 45% length was exposed to HpaII fragment, f remained intact but two other fragments of 18% and 20% were recovered. Therefore, the fragments could be pieced together as follows:

HindIII A:	7%	-	45%	-	3%			
	part of a				part of b			
HindIII B:	18%	-	7%	-	20%			
	part of b		f		part of a			

Figure P71. Fitting the positions of hypothetical double digest fragments

Incomplete digestion of A by HpaII produced fragments: a + c, c + e, e + d, h + g, and g + b, therefore the polyoma DNA appeared as: b − f − a − c − e − d − h − g, with the zero coordinate in b and g near the 100 coordinate.

Larger genomes such as *E coli*, yeast, or those of higher eukaryotes are generally pieced together by a chromosome walking like procedure, using overlapping fragments generated by several restriction endonucleases, e.g.:

Fragments generated by enzyme A :

1	2	3
abcde	fghijklmn	oprstuvwz

Fragments generated by enzyme B :

4	5
cdefghi	jklmnoprst

will be tied into the order 1, 2, 3 on the basis of the hybridization of 4 with 1 and 2, and hybridization of 5 with 2 and 3, but not 5 with 1 or 4 with 3. In the initial steps, generally YAC clones are used because they cover large segments of the genomes. Cosmid clones usually follow this and eventually large

continuities (contigs) are established without gaps. By the employment of anchors, fragments with genetically or functionally known sites, the physical map can be correlated with the genetic map determined by recombination frequencies, and thus *integrated maps* are generated. The individual fragments can then be sequenced and thus maps of ultimate physical resolution can be obtained. ►RFLP, ►chromosome walking, ►FISH, ►SAGE, ►integrated map, ►dynamic molecular combing, ►anchoring, ►contigs, ►cosmids, ►restriction enzymes, ►EcoRI, ►HindIII, ►HpaII, ►genomic screening, ►electronic PCR, ►PCR; Bhandarkar SM et al 2001 Genetics 157:1021.

Physical Mutagens: The most widely used forms of physical mutagens are *electromagnetic*, ionizing radiations such as X rays and γ rays emitted by radioisotopes. The most commonly used radiation sources for the induction of mutation by γ rays are cobalt^{60} (Co^{60}) and cesium^{137} (Cs^{137}). *Particulate radiations* such as produced by atomic fission are also ionizing. Ionization is the dislodging of orbital electrons of the atoms. The particulate (corpuscular) radiation source is uranium^{235}, which releases neutrons, uncharged particles (slightly heavier than that the hydrogen atom) with very high penetrating power and the ability to release about 15 times as much energy along their path as the hard X rays (of short wave length and high energy). The *fast neutrons* have energies between 0.5 and 2.0 MeV (million electron volt). The *thermal neutrons* have much lower level of energy (about 0.025 eV) because they have been "moderated" by carbon and hydrogen atoms. Radioactive isotopes emit also *β particles* (electrons). Their level of energy and penetrating power depend a great deal on the source; H^3 (tritium) has very short path (about 0.5 μm) and P^{32} is much more energetic (2600 μm). Beta emitters are rarely used for mutation induction. They can, however, be incorporated directly into the genetic material by using radioactively labeled precursors or building blocks of nucleic acids, and thus are capable of inducing localized damage, the degree of localization depends on the effective path length. Uranium238 emits *α particles* (helium nuclei) releasing thousands of times more energy per unit track than X rays. Because of the very low penetrating power, it can be stopped by a couple of sheets of cells in contrast to X rays and gamma rays which require heavy concrete or lead shielding. Alpha radiation, because of its high energy per short path, can very effectively destroy chromosomes. The most common genetic effect of all ionizing radiations is chromosome breakage and particularly deletions.

Another physical mutagen is *ultraviolet* (*UV*) radiation. The latter causes excitation, rather than ionization, in the biological material. Excitation may raise the orbital electrons to a higher level of energy, from which they return to the ground state very shortly. UV radiation sources are commonly mercury or cadmium lamps (black light, germicidal, and sun lamps). Natural light also includes UV radiation, especially in the clean air of the higher mountains. Near ultraviolet light, UV-B (290–400 nm) may be present in the emission of fluorescent light tubes and in the presence of sensitizers it may be genetically effective on a few layers of cells. The most common genetic effect of UV light is the production of pyrimidine dimers.

The effect of radiation on cells and organisms may be *direct*, i.e., the radiation actually hits the target molecules or it may be *indirect*, i.e., the radiation produces reactive molecules in the intra- or extra-cellular environment, and these in turn cause the genetic and/or physiological damage. Exposure to high temperature may enhance mutability. If radiation is received during DNA replication, damage is more likely than in the dormant state. Generally, hydrated cells and tissues are more sensitive to ionizing radiation than dry or non-metabolizing cells. ►X-rays, ►radioisotopes, ►radiation effects, ►ultraviolet light, ►chemical mutagens, ►maximal permissive dose, ►carcinogens, ►LET, ►chromosomal mutation, ►DNA repair, ►genetic sterilization, ►cosmic radiation, ►genomic subtraction, ►nuclear reactors, ►atomic radiations, ►electromagnetic radiation, ►pyrimidine dimer, ►cycloputane ring; Hollaender A (ed) 1954–56 Radiation Biology, McGraw-Hill, New York.

Physiology: The discipline dealing with the functions of living cells and organisms.

Phytanic Acid: A 20-carbon, branched chain fatty acid is formed from the phytol alcohol ester of chlorophylls and it degraded by β-oxidation into propionyl-, acetyl-, and isobutyryl-CoA. Deficiency of this oxidation leads to Refsum disease in humans. ►Refsum diseases, ►peroxisome

Phytic Acid (inositol hexaphosphoric acid, IP^6): Phytic acid combined with Ca^{2+} and Mg^{2+} salts are called phytins and are commonly present in plant tissues. Phytate also ties up iron in the plant tissues and limits its availability for human nutrition, unless it is degraded by phytase. ►*myo*inositol, ►phosphoinositides; engineered phytate-free seeds: Stevenson-Paulik J et al 2005 Proc Natl Acad Sci USA 102:12612.

Phytoalexins: Generally relatively low molecular weight, yet diverse, compounds synthesized through the phenylpropanoid pathway. They were attributed to defense systems against various plant pathogens. Currenty, they are considered to be mainly consequences of infection rather than active defense

molecules. ►host-pathogen relation, ►phenolics; Hammerschmidt R 1999 Annu Rev Phytopath 37:285.

Phytochromes: Five regulatory proteins with alternating absorbance peaks in red and far-red light (see Fig. P72). Through their absorbance peaks (red [R] 660 nm and far-red [FR] 730), they control various photomorphogenic processes, such as short- and long-day onset of flowering, hypocotyl elongation, apical hooks, pigmentation, etc. These chromoproteins are homodimers of 124 kDa subunits and a tetrapyrrole complex, joined covalently through a cystein residue at about 1/3 distance from the NH_2 end. The molecule exists in two conformations corresponding to the R and FR absorption states. The interconversion between these states is mediated very rapidly by light of R and FR emission peaks. In etiolated plant tissue, the inactive P_r conformation may constitute up to 0.5% of the protein. The transition from the P_r conformation into the active P_{fr} form also entails the degradation of this receptor. The apoprotein, coded by different genes (*PHYA* and *PHYB*) in *Arabidopsis* may have only about 50% homology in amino acid sequences, although they bind the same chromophore. The specificity of PhyA (far-red) and PhyB (red) resides in the N-termini. The C-terminal domain of phytochrome B attenuates the transducing signals (Matsishita T et al 2003 Nature [Lond] 424:571). Phytochromes can induce and silence the expression of genes in a specific selective manner. The transcription of the phytochrome genes is also light regulated; R light reduces the transcription more effectively than FR. Phy-A perceives continuous FR, whereas phy-B responds to continuous red light.

Phytochrome B is also a photoreceptor in the circadian rhythm. Phytochrome A appears to be serine/threonine kinase. Phytochrome C is a light-stable molecule. SPA1 (suppressor of phy-A), a WD-protein with sequence similarity to protein kinases, mediates, among other factors, the photomorphogenic reactions. The phytochrome responses are under complex genetic regulatory systems involving light response elements, transcription factors, and components of the signal transduction circuits. PIF3 (phytochrome-inducing factor) is a basic helix-loop-helix protein that attaches to the non-photoactive C-terminus of phytochromes A and B and mediates their conversion into active forms. PIF3 also binds to a G-box in the promoter and thus regulates transcription. Nucleoside diphosphate kinase 2 (NDPK2) preferentially binds to the red light activated form of phytochrome and appears to play a role in eliciting light responses. In photomorphogenic responses, phytochromes interact with cryptochromes. Although phytochrome is known as a ubiquitous plant product, the yeast *Pichia* also synthesizes phytochromobilin (PΦB), a precursor of this plant chromophore. PΦB deficient plants can be complemented by the insertion of the algal phycocyanobilin gene (Kami C et al 2004 Proc Natl Acad Sci USA 101:1099). Also, a phytochrome-like protein (Ppr) has been identified in non-photosynthetic prokaryotes (*Deinococcus radiodurans, Pseudomonas aeruginosa*). In the *Rhodospirillum centenum*, a purple photosynthetic bacterium, a photoreactive yellow (PYP) pigment has been identified with a central domain resembling phytochromes.

In cyanobacteria, the circadian input kinase (CikA), a bacteriophytochrome, mediates the circadian oscillations. ►photoperiodism, ►photomorphogenesis, ►signal transduction, ►phycobilins, ►cryptochromes, ►brassinosteroids, ►WD-40, ►G box; Neff MM et al 2000 Genes Dev 14:257; Martinez-Garcia JF et al 2000 Science 288:859; Smith H 2000

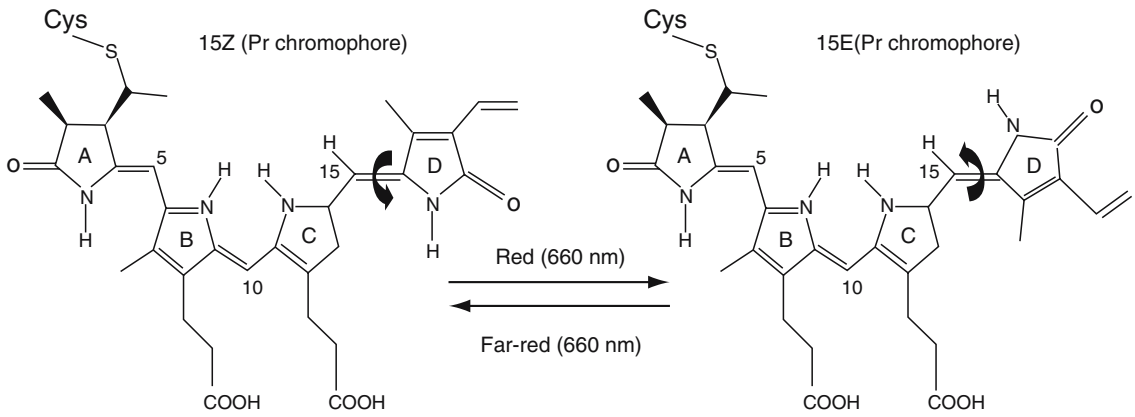

Figure P72. Phytochrome chromophores: The two isomers of phytochromobilin. (See Chen M et al 2004 Annu Rev Genet 38:87; courtesy of Dr. Meng Chen and Dr. Joanne Chory)

Nature [Lond] 407:585; Bhoo S-H. et al 2001 Nature [Lond] 414:776; Nagy F, Schäfer E 2002 Annu Rev Plant Biol 53:329.

Phytoestrogens: Estrogen-like plant products, such as the isoflavones (genistein, daidzein), and they can take advantage of the animal estrogen receptors and regulate gene expression similarly to other estrogens. Isoflavones can thus be used in hormone replacement therapies used to alleviate postmenopausal symptoms and for other purposes of selective modulation of estrogen receptors. ►estradiol, ►estrogen receptor, ►sterol, ►genistein; An J et al 2001 J Biol Chem 276:17808; Yellayi S et al 2002 Proc Natl Acad Sci USA 99:7616.

Phytoextraction: ►bioremediation

Phytohemagglutinin: ►PHA

Phytohormones: ►plant hormones

Phytophthora: A group of heterothallic plant pathogenic fungi. Each individual can produce both antheridia and oogonia. The fertilized oogonium develops oospores. The A1 mating type secretes α1 hormone (see Fig. P73), which induces oospore formation in A2 mating types, and A2 individuals secrete α2 hormone, which induces oospore formation in A1 types (See Qi J et al 2005 Science 309:1828). A draft of the genomes of *P. soyae* and *P. ramosa* is available, indicating 19,027 and 15,743 genes in the respective species and revealing evolutionary origin of related organisms (Tyler BM et al 2006 Science 313:1261). ►hormones, ►mating type, ►oöspore, ►oogonium, ►antheridium; genome: http://phytophthora.vbi.vt.edu/; functional genomics: http://www.pfgd.org/.

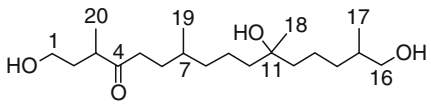

Figure P73. Alpha1 mating harmone

Phytoplankton: Aquatic, free-flowing plants. ►bacterioplankton

Phytoplasmas (Mollicutes, 530–1350 kbp circular DNA): Minute, round (200–800 µm or filamentous) bacteria without cell wall, infecting the phloem cells of plants and causing disease. The symptoms vary from yellowing to sterility, stunting, and heavy branching. Phytoplasmas resemble somewhat mycoplasmas of animals but cannot be cultured in cell-free media. They are propagated by sucking insects that cause economic loss in vegetables and trees. Phytoplasma infection may be exploited for gain by floriculture to obtain bushier Poinsettias (Lee I-M et al 1997 Nature Biotechnol 15:178). Phytoplasmas may be identified by DNA-DNA hybridization and serological means. ►mycoplasma, ►phyllody; Lee IM et al 2000 Annu Rev Microbiol 54:221.

Phytoremediation: ►bioremediation

Phytosulfokines (PSK): PSK-α, a sulfated pentapeptide, and PSK-β, a tetrapeptide, are cell proliferation promoting compounds of plants.

Phytotron: A plant growth chamber system with maximal physical regulation facilities.

Pi: Inorganic phosphate.

pI (pH_I): Isoelectric point. ►isoelectric focusing

PI 3 Kinase: ►phosphoinositide 3 kinase

PI Vector: The PI vector contains packaging site (*pac*) and allows about 115 kb to be packaged, and it infects *E. coli* at a pair of *lox P* recombination sites, at which the *Cre* recombinase circularizes DNA inside the host cell. ►vectors

Pibids: ►trichothiodystrophy

PIC (preinitiation complex): Proteins associated with RNA polymerase before transcription. During preinitiation, the carboxyterminal domain (CTD) is hypophosphorylated but during initiation, the movement four kinases in a step-wise manner phosphorylate the RNA polymerase. Phosphorylation regulates the attachment of additional proteins. ►transcription factors, ►open promoter complex, ►TBP, ►transcript elongation, ►chromatin remodeling, ►mediator complex; He S, Weintraub SJ 1998 Mol Cell Biol 18:2876; Tsai FT, Sigler PB 2000 EMBO J 19:25; Soutoglou E, Talianidis I 2002 Science 295:1901; Wilcox CB et al 2004 Genetics 167:93; Chen H-T, Hahn S 2004 Cell 119:169.

PIC: ►polymorphic information content

PIC (SUMO): A ubiquitin-like protein associated with RanGAP. ►ubiquitin, ►UBL, ►sentrin, ►RanGAP, ►SUMO

Pick Disease (FTDP-17, frontotemporal dementia and parkinsonism): A chromosome 17q21.11 dominant behavioral, cognitive, and motor disease involving variable loss and atrophy of the frontal and temporal part of the brain, caused by defects in the splicing of the Tau microtubule-associated protein. The mutations responsible for the conditions occur in exon 10 of Tau or in its 5′-splicing site, resulting in duplications in Tau mRNA (14q24.3). Frontotemporal dementia (FTD) may be tau-negative in case of mutation/loss of progranulin, a 68.5 kDa regulatory protein encoded at 17q21.31 (Baker M et al 2006 Nature [Lond] 442:916; Cruts M et al 2006 Nature

[Lond] 442:920). ►dementia, ►Parkinsonism, ►tau, ►RNAi

Picornaviruses: The single-stranded RNA genomes of picornaviruses, measuring about 7.2 to 8.4 kb (ca. 2.5 to 2.9 × 10^6 Da), are transcribed into four major polypeptides. Their RNA transcript lacks the 5′ cap in the mRNA, characteristic for other eukaryotic viruses. A functional picornavirus IRES in a dicistronic mRNA may support the activity, not only of the downstream, but also of the upstream reporter gene at high salt concentrations in *cis*. Analysis of different experimental parameters influencing this effect shows that the enhanced availability of the initiation factor eIF4F provided by a functional picornavirus IRES on the same RNA molecule in *cis* causes this translation enhancement effect (Jünemann C et al 2007 J Biol Chem 282:132). They include *enteroviruses* (a group of mostly unsymptomatic intestinal viruses. The paralytic *poliovirus* may also belong to this group). *Cardioviruses* (responsible for myocarditis [causing inflammation of the heart muscles] and encephalomyelitis [inflammation of the brain and heart]), *rhinoviruses* (in over 100 variants responsible for the common cold and other respiratory problems in humans and animals), and *aphtoviruses* (causing foot-and-mouth disease in cattle, sheep and pigs and occasionally infecting also people) are other types of picornaviruses. The *hepatitis virus* may also be classified among the picornaviruses. ►papovaviruses, ►animal viruses, ►coxsackie virus, ►polio virus, ►IRES, ►eIF-4F; Knipe DM et al (Eds.) 2001 Fundamentals of Virology, Lippincott Williams & Wilkins, Philadelphia, Pennsylvania.

P

PIDD: A p53-inducible death domain protein, which promotes apoptosis. ►death domain, ►apoptosis, ►p53

PIE: Polyadenylation inhibition element. ►polyadenylation signal

Piebaldism: Piebaldism in animals is the result of hypomelanosis (low melanin), it is generally restricted to spots on the body; white spots occur on a black background. It may be a mutation of the KIT oncogene (4q12), or may be due to other factors. ►albinism, ►nevus, ►vitilego, ►melanin, ►Himalayan rabbit, ►mouse, ►pigmentation in animals, ►KIT oncogene, ►spotting, ►Hirschsprung disease, see Fig. P74.

Figure P74. Piebald rat

Pierre-Robin Syndrome: An autosomal recessive defect, involving the tongue (glossoptosis), small jaws (micrognathia), and sometimes cleft palate and syndactyly of toes. In an autosomal dominant form, reduced digit number (oligodactyly) is also found. There is also an X-linked form involving clubfoot and heart defect. Another X-linked form shows and increase in the number of the bones in the digits (hyperphalangy). (See terms under separate entries).

Piezoelectric Mechanism: By piezoelectric mechanism, crystalline material, under pressure, may generate electricity. Also, expansion and contraction may take place in matter in response to alternative electric current mechanical stress. This latter property has been exploited for insertion of cell nuclei into eggs after the destruction of its original egg nucleus. This type of nuclear transplantation may help achieve cloning of higher animals. ►nuclear transplantation

PIF: Proteolysis inducing factor.

PIG (*Sus crofa*): 2n = 38. The domesticated breeds are the descendants of the crosses between the European wild boar and the Chinese pigs and they can still interbreed with the wild forms of similar chromosome number. The wild European pig is 2n = 36. The Caribbean pig-like peccaries (*Tayassuidae*) are 2n = 30. There are about 300 breeds of the domesticated pig. The various breeds of minipigs weigh generally less than 50 pounds as adults and are used for biomedical research. Sexual maturity sets in by about five to six months and the gestation period is about 114 days. It is a multiparous species with a litter size of 4–12. By adult somatic cell nuclear transplantation, live clones can be produced. ►animal genetics; Polejaeva IA et al 2000 Nature [Lond] 407:86; dispersal in Southeast Asia: Larson G et al 2007 Proc Natl Acad Sci USA 104: 4834; nuclear transplantation: http://www.toulouse.inra.fr/lgc/pig/hybrid.htm; http://www.animalgenome.org/QTLdb/; http://www.piggenome.org/; http://ascswine.rnet.missouri.edu/Description.html; http://www.piggis.org/; http://pig.genomics.org.cn/.

Pigeon: *Columbia livia*, 2n = 80. Great morphological variations among the various breeds of pigeons had already caught Darwin's attention, who made a few crosses between "pure races" and observed some "mendelian" patterns (see Fig. P75). Homing pigeons follow important landmarks such as railway tracks and highways as guided by their learned memory (Lipp H-P et al 2004 Curr Biol 14:1239). The "homing" ability, i.e., pigeons can return from great distances, is probably based on magnetoreception of the earth magnetic field facilitated by the upper beak

area and may be aided also by olfactory nerves (Mora CV et al 2004 Nature [Lond] 432:508).

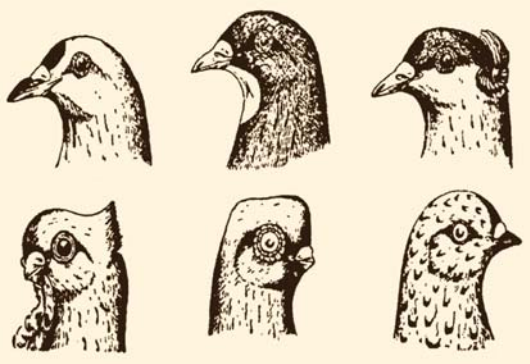

Figure P75. Variations in pigeons

PiggyBac: A cabbage moth (*Trichoplusia ni*) transposon-derived transformation vector of several different insect species. It is 2.5 kb with 13 bp inverted terminal repeats and contains a 2.1 kb open reading frame. Its specific target is TTAA. PiggyBac is particularly useful for large-scale and general disruption of *Drosophila* genes (Thibault S et al 2004 Nature Genet 36:283). PiggyBac efficiently transposes also in human and mouse cells (Ding S et al 2005 Cell 122:473). The high transposition activity of *piggyBac* and the flexibility for molecular modification of its transposase suggest the possibility of using it routinely for mammalian transgenesis (Wu SC-Y et al 2006 Proc Natl Acad Sci USA 103:15008). Frequently green fluorescent protein marker is used for its easy detection. ►transposon, ►open reading frame, ►transposon vector, ►sleeping beauty, ►GFP; Handler AM et al 1998 Proc Natl Acad Sci USA 95:7520; Horn C et al 2003 Genetics 163:647; inducible piggyBac: Cadiñanos J, Bradley A 2007 Nucleic Acids Res 35(12):e87.

Pigment Epithelium-Derived Factor (PEDF): A potent inhibitor of angiogenesis of the retina. Its defect leads to opacity of vision and blindness. ►angiostatin, ►endostatin, ►thrombospondin, ►angiogenesis

Pigmentation Defects: ►albinism, ►piebaldism, ►hypomelanosis, ►incontinentia pigmenti, ►pigmentation in animals, ►LEOPARD syndrome, ►Fanconi anemia, ►hematochromatosis, ►neurofibromatosis, ►tuberous sclerosis, ►Waardenburg syndrome, ►Hermansky-Pudlak syndrome, ►polyposis hamartomatous, ►Addison disease, ►focal dermal hypoplasia, ►erythermalgia, ►skin diseases

Pigmentation of Animals: In mammals, tyrosine is the primary precursor of the complex black pigment melanin. The enzyme tyrosinase (located in the melanosomes) hastens the oxidation of dihydroxyphenylalanine (DOPA) into dopaquinone, which is changed by non-enzymatic process into leukodopachrome. Leukodopachrome is an indole-derivative that is oxidized also by tyrosinase into an intermediate of 5,6-dihydroxyindole. After another step of oxidation, indole-5,6-quinone is formed. Coupling the latter to 5,6-dihydroxyindole is the first step in the addition of further dihydroxyindole units in the process of polymerization to melanin. When cysteine is combined with dopaquinone, through a series of steps, reddish pigments are formed in hair and feathers. The different pigments may have also other adducts at one or more positions to yield various colors. In the formation of the eye color of insects, tryptophan is a precursor to the formation of formylkynurenine → kynurenine → hydroxykynurenine → ommin, ommatin. The catabolic pathway of amino acids contributes to the formation of guanine and through the latter to pteridines that contribute to the coloration of insects, amphibians, and fishes, and serves also as a light receptor. The Xanthopterin and leucopterin account for the yellow and white pigmentation of butterflies, sepiapterin, is found in the eyes of *Drosophila* and biopterin is found in the urine and liver of mammals. The degradation of the heme group yields a linear tetrapyrrole from which the bile pigment biliverdin and ultimately bilirubin diglucuronide is synthesized. Bilirubin diglucuronide is secreted into the intestines and may accumulate in the eyes and other organs causing jaundice when the liver does not function normally. Oxidized derivatives of bilirubin, urobilin, and stercobilin color the urine. Mutations were detected already during the early years of genetics that block the biosynthetic paths of these pigments and thus contribute to understanding how genes affect the phenotype. The color of the skin in humans is determined by its melanin content. Phaeomelanin is a reddish pigment and eumelanin is black. The former is responsible for the light skin and red hair color and it also potentially generates free radicals and thus may make the individual susceptible to UV damage. Eumelanin provides protection against UV. The melanocyte-stimulating hormone (MSH) and its receptor (MC1R) regulate the relative proportion of these two melanins. A putative cation exchanger (SLC24A5, human chromosome 15q21) has modulatory effect on the formation of melanosomes and due to different single nucleotide polymorphisms has impact on the determination of pigmentation, depending also on the climatic regions and exposure to sunlight (Lamson RL et al 2005 Science 310:1782). In mice, about 100 genes are known that control pigmentation. Differences in the pigmentation of the

human skin in various geographic areas of the world seem to be correlated with the degree of exposure to ultraviolet radiation. ►chorismate, ►tryptophan, ►tyrosine, ►phenylalanine, ►albinism, ►melanin, ►eye color in humans, ►Himalayan rabbit, ►Siamese cat, ►pigmentation in plants, ►agouti, ►melanocyte-stimulating hormone, ►hair color, ►tanning, ►opiocortin; hair and skin color: Rees JL 2003 Annu Rev Genet 37:67; Price T Borntrager A 2001 Curr Biol 11:R405; evolution, genetics, physiology [folate, vitamin D, UV light exposure] and variation in human skin color: Jablonski NG 2004 Annu Rev Anthropol 33:585; Sturm RA 2006 Trends Genet 22:464; Lin JY, Fisher DE 2007 Nature [Lond] 445:843.

pIgR (polymeric immunoglobulin receptor): ►antibody polymers

P_{II}: P_{II} proteins (are involved in bacterial glutamine synthesis) accelerate hydrolysis of NtrC in the presence of NtrB and ATP in limited N supply and low levels of 2-ketoglutarate. P_{II} uridylylation permits the increase of NtrC-phosphate level and increases transcription from the glnAp2 promoter. In excess N supply, PII is not altered resulting in no NtrC build-up and glnA2 activation ceases. ►*NtrB*, ►*NtrC*, ►*glnAp*

PI3K (PI(3)K): ►PIK

PIK/PI(3)K (phosphatidylinositol kinases): PI(3)K preferentially phosphorylates the 3 and 4 positions on the inositol ring. PIK-catalyzed reaction products (PtdIns) are second messengers. They participate in meiotic recombination, immunoglobulin V(D)J switches, chromosome maintenance and repair, progression of the cell cycle, etc. The mouse Pik3r1 regulatory gene encodes proteins p85α, p55α, and p50α. p55/p50 are essential for viability. Their defect may lead to immunological disorders and cancer. In ovarian cancer, increase of PIK3CA and increased PIK activity were detected. In different types of human cancers, mutations in the catalytic subunit is high (Samuels Y et al 2004 Science 304:554). PIK inactivation of its γ-subunit may lead to invasive colorectal cancer in mice. PI3Kγ may signal to phosphokinase B or to MAPK. PI3K is negatively controlled by PTEN. PIK related kinases are TOR, FRAP, TEL, MEI, and DNA-PK. Their inhibitor is wortmannin. ATM, ATR, DNA-P-related protein kinases, ATRIP, and Ku80 share a terminal amino acid sequence motif (734 AKEESLADDLFRYNPYLKRRR) of the Nijmegen breakage syndrome (Nbs1) protein that recruits these kinases to the site of DNA damage and cell cycle checkpoint control and repair (Falck J et al 2005 Nature [Lond] 434:605). The nuclear GTPase PIKE enhances PIK activity and is regulated by protein 4.1N. ►phosphatidylinositol, ►second messenger, ►immunoglobulins, ►DNA repair, ►ATM, ►ATR, ►DNA-PK, ►Ku, ►ATRIP, ►Nijmegen breakage syndrome, ►cell cycle, ►wortmannin, ►MEC1, ►phosphoinositides, ►PTEN, ►protein 4.1N, ►colorectal cancer, ►chemotaxis, ►Langerhans islets; Kuruvilla FG, Schreiber SL 1999 Chem Biol 6:R129; Katso R et al 2001 Annu Rev Cell Dev Biol 17:615.

Pileus: The umbrella-shaped fleshy mushroom fruiting body. Also, it is a membrane that may be present on the head of newborns.

Pilin: The protein material of the pilus. ►pilus

Pilomatricoma: Usually benign, calcifying skin tumors, densely packed by basophilic cells and developing into hair follicle-like structures. Their origin is attributed to mutation in LEF/β-catenin. ►LEF, ►catenins, ►basophil, ►follicle

PILRα: Inhibitory receptor of myeloid cell encoded at human chromosome 7q22. ►ITIM

Pilus: A bacterial appendage, which may be converted into a conjugation tube through which the entire or part of the replicated chromosome is transferred from a donor to a recipient cell (see Fig. P76). It may also serve as protein conduit. In pathogenic enterobacteria (*Neisseria gonorrhoea*, *Vibrio cholerae*) and in some types of *E. coli*, the so-called pilus type IV may be formed. It facilitates bacterial aggregation (bundle-forming pilus, BFP, encoded by a 14-gene operon), and the expression of the LEE (enterocyte effacement) element enhances the association of the bacteria with the mucous intestinal membranes and triggers diarrhea. The pilin protein may undergo antigenic variation to escape host defenses. The pilus may also form an attachment to the invaded eukaryotic cell. ►conjugation, ►conjugation mapping, ►PapD, ►pilin, ►antigenic variation, ►mating bacterial, ►shoufflon, ►pseudopilus [ψ-pilus]; Jin Q, He S-Y 2001 Science 294:2556.

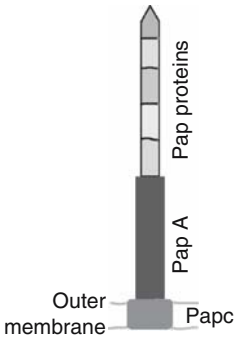

Figure P76. Pilus

PIM Oncogene: The PIM oncogene is located in human chromosome 6p21-p12 and in mouse chromosome 17. The gene is highly expressed in blood-forming (hematopoietic) cells and myeloid cells and overexpressed in myeloid malignancies and some leukemias. The human protein is a serine/threonine kinase. ►oncogenes, ►serine/threonine kinases

Pimento (*Pimento dioica*): Also called allspice. Tropical dioecious spice tree; 2n = 2x = 22.

PIN1: A peptidyl-prolyl cis/trans isomerase in human cells. It is important for protein folding assembly and/or transport. Its deficiency leads to mitotic arrest, while its overproduction may block the cell cycle in G2 phase. It interacts with NIMA kinase. PIN1 membrane protein of plants regulates auxin transport. ►cell cycle, ►NIMA, ►parvulin

PIN$^+$: The prion form of the yeast protein Rnq1. ►prion; Bradley ME, Liebman SW 2003 Genetics 165:1675.

pIN: The promoter of the transposase gene of a transposon. There are two GATC sites involved in *dam* methylation within pIN. ►RNA-IN, ►*dam*

Pinch: A group of proteins with LIM and additional domain(s). ►CRP, ►LMO, ►LIM domain

Pineal Gland: The site of melatonin synthesis and photoreception in the brain. ►melatonin, ►opsins, ►Rabson-Mendenhall syndrome, ►brain

Pineapple (*Ananas comosus*): A monocotyledonous tropical or subtropical plant (2n = 50, 75, 100). The flowers and bracts sit on a central axis and form fleshy fruits. The lack of seeds is caused by self-incompatibility of the commercial varieties but they develop seeds if allowed to cross-pollinate with other varieties. ►seedless fruits

Pines (*Pinus* spp): Trees, all 94 species are 2n = 2x = 24. ►spruce

Ping-Pong Kinetics: The property of some dimeric or multimeric enzymes catalyzing two "half reactions." First, they release the first product and form an enzyme intermediate before binding of the second substrate. After the second reaction and release of the product, the enzyme returns to the initial state. (See Frank RAW et al 2004 Science 306:872).

Pinna: The ear lobe, the lobe of a compound leaf or frond. ►hairy ear

Pinning: Pinning uses a floating replication tool with about 100 or more pinheads to test yeast colonies on different culture media. ►replica plating

Pinocytosis: The formation of ingestion vesicles for fluids and solutes by the invagination of membranes of eukaryotic cells. ►phagocytosis, ►endocytosis

Pinosome: A small cytoplasmic vesicle originating by invagination of the cell membrane. ►endocytosis

PinPoint Assay: The PinPoint assay identifies single nucleotide polymorphism (SNIP). The polymorphic DNA site is extended by a single nucleotide with the aid of a primer annealed immediately upstream to the site. The extension products are analyzed by MALDI-TOF mass spectrophotometry. ►SNIP, ►primer extension, ►MALDI-TOF; Haff LA, Smirnov IP 1997 Genome Res 4:378.

PIN*POINT (protein position identification with a nuclease tail): An in vivo method to ascertain the position of the critical promoter-binding proteins involved in the LCR. Fusion proteins with an unspecific nuclease tail are studied for how the cleavage position affects the expression of the gene (s). ►LCR; Lee J-S et al. 1998 Proc Natl Acad USA 95:969.

PIP: Phosphatidylinositol phosphate. ►phosphoinositides, ►PIP2[PIP_2], ►PIP3

PIP2: Phosphatidylinositol (4,5)-bisphosphate is involved (with PIP3) in mediating the inositol phospholipid signaling pathway and in the activation of phospholipase C (PLC). PIP_2 also controls the ATP-regulated potassium ion channel (K_{ATP}) by binding to the intracellular C-domain of the channel protein and interfering with the binding of ATP. Since K_{ATP} channels affect pancreatic β cells and vascular and cardiac muscle tone, they may have relevance for human diseases, e.g., diabetes. Pleckstrin homology domains selectively bind phosphoinositides. ►phosphoinositides, ►PITP, ►ion channels, ►diabetes, ►InsP, ►pleckstrin, ►TIRAP; Martin TF 2001 Curr Opin Cell Biol 13:493.

PIP3 (phosphoinositol-3,4,5-trisphosphate): An intracellular messenger and stimulator of insulin, epidermal growth factor, etc., that works by adding another phosphate to PIP2 and activating PKB. ►PKB, ►PTEN, ►chemotaxis, ►InsP; Hinchliffe KA 2001 Curr Biol 11:R371.

Pipecolic Acid (homoproline): An intermediate in lysine catabolism (see Fig. P77). Increase of pipecolic acid (hyperpipecolathemia/hyperpipcolicacidemia) in the blood plasma and urine leads to increase in the size of the liver (hepatomegaly), resulting in growth retardation, vision defects, and demyelination of the nervous system.

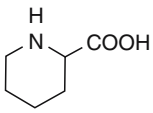

Figure P77. Pipecolic acid

Pipes (piperazine-*N,N′*-bis(2-ethanesulfonic acid): A buffer within the pH range of 6.2–7.3.

PIR (protein information resource): ►MIPS; http://pir.georgetown.edu/.

PIR-A, PIR-B: Immunoglobulin-like regulatory molecules (activator/inhibitor) on murine B cells, dendritic cells, and myeloid cells. A single gene encodes Pir-B whereas a multigene family encodes the six Pir-A proteins. ►ITIM; Dennis G Jr et al 1999 J Immunol 163:6371.

Piriformospora indica: Root endophytic fungus that may associate with both dicotyledonous and monocotyledonous plants and convey resistance to fungal disease, salt tolerance, improved nitrogen metabolism, and lead consequently to higher yield. ►symbiont, ►host–pathogen relationship, ►salt-tolerance; Waller F et al 2005 Proc Natl Acad Sci USA 102:13386.

piRNA (Piwi interacting RNA): 26-31-nucleotide-long RNA regulating germ and stem cell development when bound to Argonaute family proteins (Aubergine, Piwi, Ago3). In mouse, the MIWI/Piwi RNA associates with the polysomes and chromatoid body during spermatogenesis (Grivna ST et al 2006 Proc Natl Acad Sci USA 103: 13415). It is involved also in regulating transposons activity (Brennecke J et al 2007 Cell 128:1089). ►RNAi, ►Argonaute, ►chromatoid body, ►Slicer; Aravin A et al 2006 Nature [Lond] 442:203; Girard A et al 2006 Nature [Lond] 442:199; review: O'Donell KA, Boeke JD 2007 Cell 129:37.

PISA (protein in situ assay): In the PISA assay, PCR-generated DNA fragments are transcribed and translated in a cell-free protein expression system on a coated microtiter plate where the protein was immobilized. Single chain antibody fragments and luciferase have been successfully arrayed. ►PCR; He M, Taussig MJ 2001 Nucleic Acids Res 29(15):E73.

Pistil: A central structure of flowers (gynecium) consisting of the stigma, style, and ovary. ►gametophyte female, ►gametophyte male, ►flower differentiation

Pistillate: Flower or plants that carries the female sexual organs. A female parent in plants.

Pisum sativum (pea): A legume (2n = 14). It played an important role in establishing the Mendelian principles of heredity and contributed further information on genetics. Curiously, the famous "wrinkled" gene of Mendel turned out to be an insertional mutation. ►pea

Pit: An indentation. Also, the stony endocarp of some fruits, e.g., plums, apricot, cherry.

Pitalre (cdk9): ►acquired immunodeficiency, ►TEFb; Darbinian N et al 2001 J Neuroimmunol 121:3

Pitch: The length of a complete turn of a spiral (helix) and the translation per residue is the pitch divided by the number of the residues per turn. In a keratin alpha helix, it is 0.54 nm/3.6 = 0.15 nm. Also, a dark black residue after distillation. The auditory pitch is the physiological response of the ear to sound depending on the frequency of vibration of the air. Pitch-selective neurons are located in the auditory cortex of the brain in monkeys and humans (Bendor D, Wang X 2005 Nature [Lond] 436:1161). Perfect/absolute pitch is ability for recognizing musical notes by talented artists. ►musical talent, ►prosody

Pith: The parenchyma tissue in the core of plant stems, e.g., in elderberry (*Sambucus*).

Pithecia (saki monkey): ►Cebidae

PITP (phosphatidylinositol transfer proteins, 35 and 36 kDa): PITP is required by for the hydrolysis of PIP_2 (phosphatidyl-inositol bis-phosphate) by PLC (phospholipase C). In a GTP-dependent signal pathway, PITP is required also by epidermal growth factor (EGF) signaling. ►PIP, ►PIP_2, ►EGF, ►GTP, ►phosphoinositides; Cockcroft S 1999 Chem Phys Lipids 98:23.

PI-TR: Phosphatidylinositol transfer protein involved in transfer of lipids among organelles within cells.

PITSLRE: Members a cyclin-dependent protein kinase family involved in RNA transcription or processing. They are associated with ELL2, TFIIF, TFIIS, and FACT. ►ELL, ►transcription factors, ►TFIIS, ►protein 14-3-3; Trembley JH et al 2002 J Biol Chem 277:2589.

Pituitary (hypophysis): The hypophysis is located at the base of the brain and is connected also to the hypothalmus (a ventrical part of the brain). The anterior part secretes the pituitary hormones and the posterior part stores and releases them. ►brain human, ►gonads, ►septo-optic dysplasia; Fauquier T et al 2001 Proc Natl Acad Sci USA 98:8891; Scully KM, Rosenfeld MG 2002 Science 295:2231.

Pituitary Dwarfism: Pituitary dwarfism is due to recessive mutation, deletion, or unequal crossing over in the gene cluster containing somatotropin and homologs in human chromosome 17q22-q24. Administration of somatotropin may restore growth. The defect may also be in the hormone receptor (human chromosome 5p13.1-p12, mouse chromosome 15) and in these cases, the growth hormone

level may be high (Laron types of dwarfisms). The level of somatomedin (insulin-like growth factors) may also be low. Somatomedin is a peptide facilitating the binding of proteins and in addition shows insulin-like activity. In either case, dwarfism may result. Dominant-negative mutations in IGHD2 (isolated growth hormone deficiency) are also known. ►dwarfism, ►GH, ►insulin-like growth factor, ►hormone receptor, ►binding protein, ►stature in humans, ►pituitary gland, ►growth hormone pituitary; Machinis K et al 2001 Am J Hum Genet 69:961.

Pituitary Hormone Deficiency, Combined Familial: The pituitary hormone deficiency fails to produce normally one or more of these hormones—growth hormone (HGH), prolactin, and thyroid-stimulating hormone (TSH)—because of mutation in the POU1F1 gene (3p11). Mutation in the PROP1 gene (5q), however, cannot produce luteinizing hormone (LH) and follicular stimulating hormone (FSH). Corticotropin deficiency is caused by mutation in the LHX4 gene. LHX3 is a homeobox gene with LIM repeats. ►animal hormones

Pituitary Tumor (GNAS1, 20q13.2): Pituitary tumor is caused by autosomal dominant mutations in the α chain of a G-protein (G_s). This protein is also called gsp (growth hormone secreting protein) oncoprotein. The human securin, mediating sister chromatid cohesion, has substantial sequence homology with the pituitary tumor-transforming gene. Securin may block sister chromatid separation and thereby can be responsible for chromosome loss or gain, common characteristics of tumors. ►G-protein, ►McCune-Albright syndrome, ►sister chromatin cohesion

Piwi: ►piRNA

Pixel: A picture element in the computer that represents a bit on the monitor screen or in the video memory. ►bit, ►byte

pK_a: The negative logarithm of the dissociation constant K_a; stronger acids have higher pK_a whereas weaker acids have lower. The dissociation of weaker acids is higher and that of stronger acids is lower. (See http://www.jenner.ac.uk/PPD/).

PKA: Protein kinase A (activated by cAMP). There are two types, PKA-I and PKA-II; they share a common catalytic subunit (C) but distinct regulatory subunits, RI and RII. RI/PKA-I controls positively cell proliferation and neoplastic growth. RII/PKA-II controls growth inhibition, differentiation, and cell maturation. RI is detectable in many types of cancers. Antisense methylphosphonate RNA of the RI_α subunit has been known to arrest proliferation of cancer cells without toxicity to normal cells. ►protein kinases, ►antisense technologies, ►cocaine, ►export adaptors

PKB (protein kinase B): A serine/threonine kinase, the same as Rac or Akt. It is activated by phosphatidylinositol-3,4,5-trisphosphate by binding to its pleckstrin homology domain. ►CaM-KK, ►protein kinases, ►phosphoinositides, ►pleckstrin domain

PKC: Protein kinase C. ►protein kinases

PKD: ►polycystic kidney disease

PKI (protein kinase I): A small protein, which attaches to the catalytic subunits of the heterotetrameric PKA and, with the aid of its nuclear localization sequence (NES), sends the complex to the nucleus. ►export adaptors, ►PKA, ►nuclear localization sequence

PKR: A double-stranded RNA-dependent serine-threonine protein kinase, involved in NF-κB signaling. One of the most important targets of PKR is the eIF-2A translation factor and thus, protein synthesis. It may control cell division, apoptosis, and may serve as tumor suppressor. Translation is required for viral infection of mammalian cells. Viral infection may trigger the activation PKR as a defense against infection through shutting off protein synthesis. PKR inhibits protein synthesis by autophosphorylation and phosphorylation of the Ser51 residue of eIF2α. Mutation at the Thr446 site prevents autophosphorylation at the catalytic domain activation segment and impairs phosphorylation of eIF2α and viral binding (Dey M et al 2005 Cell 122:901). The PKR active cell may succumb to apoptosis but the animal may survive. Several viruses (adenovirus, vaccinia virus, HIV-1, hepatitis C, poliovirus, SV40, etc.) use various mechanisms to inhibit activation of PKR by interfering either with its dimerization or RNA binding, or regulation of eIF-2A, etc. PKR preferentially binds mutant huntingtin protein in Huntigton disease. ►NFκB, ►oncolytic virus, ►reovirus, ►eIF-2A, ►PERK, ►interferon, ►apoptosis, ►Huntington's chorea; Kaufman RJ 1999 Proc Natl Acad Sci USA 96:11693.

PKS Oncogenes: PKS oncogenes are located in human chromosomes Xp11.4 and 7p11-q11.2. These genes display very high homology to oncogene RAF1 and apparently encode protein serine/threonine kinases. ►*raf*, ►oncogenes

PKU: ►phenylketonuria

PLAC: Plant artificial chromosome. ►artificial chromosome, ►YAC

Place Cells: Place cells in the brain are the locations for the firing of specific nerve cells.

Placebo: A presumably inactive but similar substance used in parallel to different individuals in order to serve as a concurrent (unnamed) control for testing the effect of a drug. In some instances the placebo has positive effects not by physical or chemical properties but by expectation-caused dopamine release, e.g., in Parkinson disease. ►concurrent control, ►double-blind test; de la Fuente-Fernández R et al 2001 Science 293:1164; Ramsay DS, Woods SC 2001 Science 294:785.

Placenta: The maternal tissue that is in most intimate contact with the fetus through the umbilical chord, found within the uterus of animals. Most commonly, the placenta is located on the side of the uterus; the placenta praevia is situated at the lower part of the uterus. The latter situation may be correlated with the age of the mother. Also, placenta refers to the wall of the plant ovary to which the ovules are attached. During pregnancy, the placenta of eutherian mammals includes both maternal and zygotic tissues in close association (feto-maternal interface). The interaction between these two types of tissues is essential for normal embryo development and viability of the conceptus. In normal pregnancy, the uterus is invaded by the cytotrophoblasts (the nutritive cells of the conceptus) but defects in the cell adhesion system may adversely affect the pregnancy and may lead to ecclampsia. In embryonic tissues of mouse, after 10.5 day hematopoietic stem cells develop to an extent comparable to the aorta-gonad-mesonephros (AGM) region (Gekkas C et al 2005 Dev Cell 8:365). The mesonephros is part of the embryonic kidney tissue. ►ecclampsia, ►imprinting, ►incompatibility; Zhou Y et al 1993 J Clin Invest 91:950; Georgiades P et al 2001 Proc Natl Acad Sci USA 98:4522; placenta of animal species: http://medicine.ucsd.edu/cpa/.

Placode: A heavy embryonal plate of the ectoderm from what organs may develop. ►ecto-derm, ►AER, ►ZPA, ►organizer, ►neural crest, ►germ-layer

PLADs (pro-ligand-binding assembly domains): aggregate the (death) receptors before binding the ligands. ►death receptors

Plagiary: ►publication ethics, ►ethics

Plague: The term plague has been used to loosely define widespread, devastating diseases. Strictly, the term applies today to infection by the *Pasteurella pestis* (*Yersinia pestis*) bacterium. The disease may occur in three main forms: *bubonic* plague (most important diagnostic features of is swelling lymph nodes, particularly in the groin area), *pneumonic* plague (attacking the respiratory system) and *septicemic* plague (causing general blood poisoning). Many of its symptoms overlap with those of other infectious diseases. A 1°C increase in spring temperature and wetter summers may increase the carrier gerbil (rodent) population and can result in >50% increase of the prevalence of plague in Central Asia (Stenseth NC 13110). It used to be known also as the "black death" on account of the dark spots, appearing in largely symmetrical necrotic tissue with coagulated blood. The bacilli spreads to human populations from rodents by fleas, but infections occur also through cough drops of persons afflicted by pneumonic plague. Various animal diseases are also called plague (pestis) but, except those in rodents, are caused by other bacteria or viruses. Pasteurellosis can be effectively treated with antibiotics although some strains become resistant to a particular type of antibiotics (streptomycin, chloramphenicol). Eradication of rodent pests is the best measure of prevention. During the great epidemics in the 14th century, the disease claimed an estimated 25 million victims. Sporadic occurrence is known even today in the underdeveloped areas of the world. ►zoonosis, ►*Yersinia*, ►plant vaccines, ►biological weapons; Parkhill J et al. 2001 Nature [Lond] 413:523.

Plakin: >200 kDa dimeric, coiled coil, actin-binding proteins forming molecular bridges between the cytoskeleton and other subcellular structures. They also bind microtubules. ►cytoskeleton, ►filaments, ►microtubule; Jefferson JJ et al 2007 J Mol Biol 366:244.

Plakoglobin: 83 kDa protein localized to the cytoplasmic side of the desmosomes. ►desmosome, ►adhesion, ►desmoplakin

Planar Cell Polarity (PCP): PCP is determined by several genes involved in embryonal development, neural tubes, cochlear sensory hair cells of the ear, etc.

Planarians (flatworms): Relatively simple carnivorous organisms inhabiting fresh waters. There are about 15,000 species, all with bilateral symmetry and elaborate digestive tract and nervous system. They are well suited for studies of regeneration. The tapeworms and flukes are serious human parasites. ►flatworm, ►regeneration; http://planaria.neuro.utah.edu/.

Planck Constant (h): A constant of energy of a quantum of radiation and the frequency of the oscillator that emitted the radiation. $E = h\nu$ where E = energy, ν = its frequency; numerically 6.624×10^{-27} erg^{-s}.

Plankton: The collective name of many minute free-floating water plants, animals, and prokaryotes. ►phytoplankton, ►bacterioplankton; microbial oceanography: DeLong EF, Karl DM 2005 Nature [Lond] 437:336; Giovannoni SJ, Stingl U 2005 Nature [Lond] 437:343; Arrigo KR 2005 Nature

[Lond] 437:349; viruses in the sea: Suttle CA 2005 Nature [Lond] 437:356; genetic and metabolic survey of microbial plankton from 10 m to 4000 m oceanic depth: DeLong EF et al 2006 Science 311:496.

Plant Breeding: An applied science involved in the development of high-yielding food, feed, and fiber plants. It is concerned also with the production of lumber, renewable resources of fuel, and many types of industrial raw products (such as latex, drugs, cosmetics, etc.). A major goal of plant breeding is to improve the nutritional value, safety, disease resistance, and palatability of the crops. Plant breeding and technological improvements in agriculture have resulted in a near 10-fold increase in maize production and doubled wheat yields in the twentieth and twenty-first century. Plant breeding is based on population and quantitative genetics, and biotechnology. (Mazur B et al 1999 Science 285:372).

Plant Defense: Plant defense against herbivores is mediated by the signaling peptide *systemin* activating a lipid cascade. Membrane linolenic acid is released by the damage and converted into phytodienoic and jasmonic acids, structural analogs to the prostaglandins of animals. As a consequence, tomato plants produce several systemic *wound response proteins*, similar to those elicited by oligosaccharides upon pathogenic infections. Mutation in the octadecanoic (fatty acid) pathway blocks these defense responses. ►host-pathogen relations, ►insect resistance in plants, ►jasmonic acid, ►prosta-glandins, ►fatty acids, ►systemin, ►oleuropein

Plant Disease Resistance: ►host-pathogen relation, ►plant defense

Plant Genomes: Plant genomes generally differ in size and organization from those in animals and pose new problems and answer unique questions of analysis. (See Peterson AH 2006 Nature Rev Genet 7:174).

Plant Genomics Database: http://sputnik.btk.fi; plant molecular markers: http://markers.btk.fi; see also crop plants and individual plant species in the alphabetical order.

Plant Hormones: Auxins, gibberellins, cytokinins, abscisic acid, brassinosteroids, jasmonate, and ethylene. Polypeptide hormones play roles in the defense systems of plants (Ryan CA et al 2002 Plant Cell 14:251). The natural *auxin* in plants is indole-3-acetic acid (IAA) but a series of synthetic auxins are also known such as dichlorophenoxy acetic acid (2,4-D), naphthalene acetic acid (NAA), indole-butyric acid (IBA), etc. Auxins are involved in cell elongation, root development, apical dominance, gravi- and phototropism, respiration, maintenance of membrane potential, cell wall synthesis, regulation of transcription, etc. The bulk (≈95%) of IAA in plants is conjugated through its carboxyl end to amino acids, peptides, and carbohydrates. The conjugate regulates how much IAA is available for metabolic needs, although some conjugates may be directly active as hormones. Enzymes have been identified that hydrolyze the conjugates. Over the developing tissues, auxins show concentration gradients, indicating its role in positional signaling similarly to animal morphogens. The conjugates may transport IAA within the plant. *Gibberellic acid* and gibberellins control stem elongation, germination, and a variety of metabolic processes. *Cytokinins* also occur in a wide variety of forms such as kinetin, benzylamino- purine (BAP), isopentenyl adenine (IPA), zeatin, etc. Their role is primarily in cell division but they regulate the activity of a series of enzymes. Regeneration of plants from dedifferentiated cells requires a balance of auxins and cytokinins. *Abscisic acid* and terpenoids control abscission of leaves and fruits, dormancy and germination of seeds and a series of metabolic pathways. *Ethylene* was recognized as a *bona fide* plant hormone more recently. It is involved in the control of fruit ripening, senescence, elongation, sex determination, etc. The hormone type action of *brassinosteroids* in controlling elongation and light responses has been recognized by genetic evidence only in 1996. *Jasmonic acid* is also a hormone like substance with role in parasite defense. Generally, the various plant hormones signal to each other and their dynamic cooperative effects are essential for plant responses (Schmelz EA et al 2003 Proc Natl Acad Sci USA 100:10552). A survey indicated that hormones affected 4666 genes of *Arabidopsis* but most commonly different hormones regulated distinct members of protein families (Nemhauser JL et al 2006 Cell 126:467). ►hormones, ►signal transduction, ►abscisic acid, ►ethylene, ►indole acetic acid, ►jasmonic acid, ►gibberellic acid, ►kinetin, ►zeatin, ►brassinosteroids, ►seed germination; Kende H 2001 Plant Physiol 125:81; Mok DWS, Mok MC 2001 Annu Rev Plant Physiol Mol Biol 52:89; http://www.ualr.edu/botany/hormimages.html.

Plant Pathogenesis: Plant pathogens pose risks for agricultural, horticultural, and forest plants and may damage natural habitats of different organisms, plants as well as animals. Several plant pathogens and saprophytes may pose human health hazards, especially for immunologically compromised individuals. (See Vidaver AK, Tolin S 2000 In: Fleming DO, Hunt DL (Eds.) Biological Safety, ASM, Washington DC, pp 27–33; ►host–pathogen relation; http://www.pathoplant.de.

Plant Vaccines: Transgenic plants may express immunogenic proteins, which by consuming the plant tissues by humans or animals, may protect against bacterial or viral diarrhea. Also, plant synthesized immunoglobulins may protects against *Streptomyces mutans*, responsible for dental caries and gum disease. Hepatitis B surface antigen (HBsAg), Norwalk virus capsid protein (NVCP), *E. coli* heat-labile enterotoxin B subunit (LT-B), cholera toxin B subunit (CT-B), and mouse glutamate decarboxylase (GAD67) have been propagated in tobacco and potato tissues, respectively. Hepatitis B vaccine delivered by raw potatoes—when a sufficient quantity was consumed—increased the serum antiHB surface antigen titer in up to 62.5% of the volunteers (Thanavala Y et al 2005 Proc Natl Acad Sci USA 102:3378). So far, these edible vaccines have not shown clinical use. The S1 protein of the SARS corona virus propagated in tomato and tobacco plants displayed good immunogenicity in mice after both parenteral (injection) and oral administration. This result is similar to the early tests of gastroenteritis vaccine in swine and the infectious bronchitis virus vaccination of chickens by plant vaccines (Progrebnyak N et al 2005 Proc Natl Acad Sci USA 102:9062). Apparently, very effective vaccines can be produced by introducing into plants (tobacco) the F1 and V and the F1–V fusion antigens of *Yersinia*, the agent of plague (Santi L et al 2006 Proc Natl Acad Sci USA 103:861). Vaccinia virus antigenic domain B5 propagated in tobacco and collard plants when introduced orally in mice or the minipig (miniature pig) did not generate an anti-B5 immune response, but intranasal administration of soluble pB5 led to a rise of B5-specific immunoglobulins, and parenteral immunization led to a strong anti-B5 immune response in both mice and the minipig. Mice immunized i.m. (intramuscularly) with pB5 generated an antibody response that reduced smallpox virus spread in vitro and conferred protection from challenge with a lethal dose of vaccinia virus (Golovkin M et al 2007 Proc Natl Acad Sci USA 104:6864). ►vaccines, ►immunoglobulin, ►transformation genetic, ►plantibody, ►TMV, ►SARS, ►plague, ►*Yersinia*, ►bronchitis, ►gastroenteritis; Daniell H et al 2001 J Mol Biol 311:1001; Ruf S et al 2001 Nature Biotechnol 19:870; Sojikul P et al 2003 Proc Natl Acad Sci USA 100:2209.

Plant Viruses: Plant viruses vary a great deal in size, shape, genetic material, and host-specificity. The majority of them have single-stranded positive-strand RNA as genetic material and are either enveloped or not. The Reoviridae may have several double-stranded RNAs, and the Cryptovirus carries two double-stranded RNAs. The Cauliflower (Caulimo) virus has double-stranded DNA, whereas the Geminiviruses have single-stranded DNA genetic material. The size of their genome usually varies between 4 to 20 kb and their coding capacity is at least four proteins. The 5′-end may form methylguanine cap or it may have a small protein attached to it. The 3′-end may have a polyA tail or may resemble the OH end of the tRNA. Approximately, 600–700 plant viruses have been described. ►viruses, ►cap, ►polyA tail, ►tRNA, ►viroid, ►TMV, ►CaMV, ►geminivirus, ►viroid; Knipe DM et al (Eds.) 2001 Fundamental Virology, Lippincott Williams & Wilkins, Philadelphia, Pennsylvania; Harper G et al 2002 Annu Rev Phytopathol 40:119; Tepfer M 2002 Annu Rev Phytopathol 40:467; general virus database, including plant viruses: http://www.ncbi.nlm.nih.gov/ICTVdb/ictvdb.htm.

Plantibody (antibody synthesized by plants): A modified immunoglobulin produced in transgenic plants carrying the genetic sequences required for the recognition of the site of the viral coat or other proteins. The yield of the plantibody molecules is very high, up to 1% of the soluble plant proteins. The modification of the immunoglobulin involves usually the elimination of the constant region of the heavy chain while retaining the variable region. The plant antibodies are usually formed as single chains (ScFv). Other modifications for solubility and tissue-specific expression may be introduced. The plantibodies are modified also by intrinsic plant mechanisms (N-glycosylation) within the endoplasmic reticulum. Unfortunately, plant tissue lack β1,4-galactosyltransferase, which is required for the synthesis of mammalian-like glycans. By transformation, the gene of this enzyme has been transferred into tobacco plants and it functions normally. Retention and excretion of ScFv immunoglobulin molecules is increased if the KDEL amino acid sequence is present in the polypeptide chain. For some medical applications, the plantibodies may not be suitable because they may carry plant-specific β-1,2-xylose and α-1,3-fucose residues at the galactose-carrying N-glycans and cause allergic reactions in monoclonal antibodies. When, however, a hybrid enzyme called XylGalT that consists of the N-terminal domain of the *Arabidopsis* xylosyltransferase and the catalytic domain of human β-1,4- galactosyltransferases is used in tobacco plants, the core-bound xylose and fucose residues are sharply reduced. This type of monoclonal plantibody thus appears promising (Bakker H et al 2006 Proc Natl Acad Sci USA 103:7577). Single-chain variable fragment (scFv)-Fc (fragment crystalline) antibodies, with N-terminal

signal sequence and C-terminal KDEL tag, can accumulate to very high levels as bivalent IgG-like antibodies in *Arabidopsis thaliana* seeds and illustrate that a plant-produced anti-hepatitis A virus scFv-Fc has similar antigen-binding and in vitro neutralizing activities as the corresponding full-length IgG. As expected, most scFv-Fc produced in seeds contained only oligomannose-type *N*-glycans, but, unexpectedly, 35–40% was never glycosylated. A portion of the scFv-Fc was found in endoplasmic reticulum (ER)-derived compartments delimited by ribosome-associated membranes. Additionally, consistent with the glycosylation data, large amounts of the recombinant protein were deposited in the periplasmic space, implying a direct transport from the ER to the periplasmic space between the plasma membrane and the cell wall. Aberrant localization of the ER chaperones calreticulin and binding protein (BiP) and the endogenous seed storage protein cruciferin in the periplasmic space suggests that overproduction of recombinant scFv-Fc disturbs normal ER retention and protein-sorting mechanisms in the secretory pathway (Van Droogenbroeck B et al 2007 Proc Natl Acad Sci USA 104:1430).

Monoclonal antibody against the non-protein Lewis Y oligosaccharide antigen is over-expressed in breast, lung, ovary, and colon cancers. Monoclonal antibody (mAb BR55-2) specific for LeY was expressed (30 mg/kg fresh weight of leaves) in low-alkaloid content in transgenic tobacco plants and bound specifically to SK-BR3 breast cancer and SW948 colorectal cancer cells. Its binding to the FcγRI receptor was the same as that derived from mammalian cells. The plantibody was effective in cytotoxicity assays as well as in grafting onto nude mice; thus, indicating its potential suitability for immunotherapy (Brodzik R et al 2006 Proc Natl Acad Sci USA 103:8804).

Plant-produced antibodies may find biomedical application in humans and animals. Transgenic plants may produce large quantities of IgA and IgG-IgA at low cost. In *Nicotiana benthamina* leaves, high-level expression of functional full-size monoclonal antibody (mAb) of the IgG class in plants has been ascertained. The process relies on synchronous coinfection and coreplication of two viral vectors, each expressing a separate antibody chain. The two vectors are derived from two different plant viruses that were found to be noncompeting. Unlike vectors derived from the same virus, noncompeting vectors effectively coexpress the heavy and light chains in the same cell throughout the plant body, resulting in yields of up to 0.5 g of assembled mAbs per kg of fresh-leaf biomass (Giritch A et al 2006 Proc Natl Acad Sci USA 103: 4701).

Also, other components of the immunization system may thus be synthesized with single plants after combining the genes through classical crossing procedures. By eating IgA secreting plant tissues, protection is expected through mucosal immunity or may protect against dental caries. If the antibody is expressed in seed tissues, it can be stored at room temperature (perhaps for years) without a loss of the variable region of the antibody and its antigen-binding ability. ►antibody, ►host-pathogen relations, ►ScFv, ►KDEL, ►immunization, ►mucosal immunity, ►monoclonal antibody, ►monoclonal antibody therapies, ►plant vaccine, ►molecular pharming, ►Lewis blood group, ►breast cancer, ►colorectal cancer, ►cancer therapy, ►cancer gene therapy, ►nude mouse, ►tobacco, ►BiP, ►calreticulin, ►periplasma; Bakker H et al 2001 Proc Natl Acad Sci USA 98:2899; Mayfield SP et al 2003 Proc Natl Acad Sci USA 100:438; Ma JK-C et al 2003 Nature Rev Genet 4:794.

PLAP Vector: ►axon guidance

Plaque: The clear area formed on a bacterial culture plate (heavily seeded with cells) as a consequence of lysis of the cells by virus; turbid plaques indicate incomplete lysis (see Fig. P78). ►lysis

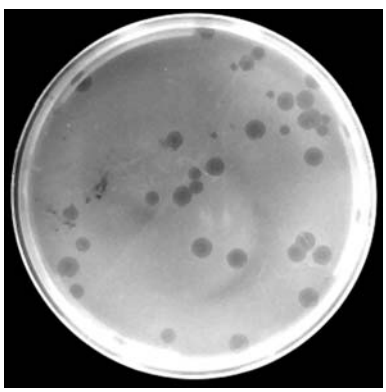

Figure P78. T3 bacteriophage plaques on petri plate heavily seeded by bacteria. (Courtesy of Dr. CS Gowans)

Plaque-Forming Unit: The number of plaques per mL bacterial culture.

Plaque Hybridization: ►Benton-Davis plaque hybridization

Plaque Lift: Plaque lifts on bacteriophage plates plaques are marked and overlaid by cellulose nitrate films. After denaturation and immobilization of the plaques on the filter, they are hybridized with probes to identify recombinants and return to the saved master

plate for obtaining plugs of interest from the original plate. The procedure generally requires repetition in order to isolate unique single recombinants. ►colony hybridization; Frolich MW 2000 Biotechniques 29:30.

Plasma: The fluid component of the blood in which the particulate material is suspended. The blood plasma is free of blood cells but clotting is not allowed during its isolation, and it contains the platelets, which harbor animal cell growth factors. ►PDGF, ►platelets, ►serum, ►cytoplasm, ►cytosol

Plasma Cell (plasmacyte): B lymphocytes can differentiate into either memory cells or plasma cells and the latter secrete immunoglobulins. ►lymphocytes, ►immunoglobulins, ►immune system

Plasma Membrane: The plasma membrane envelops all cells. ►cell membranes

Plasma Nucleic Acid: During pregnancy, a small number of fetal cells can escape into the plasma and some can also shed their chromosomal DNA (see Fig. P79). Such plasma nucleic acids can be exploited for prenatal diagnosis without many intrusive procedures (Lo YMD et al 2007 Nat Rev Genet 8:71). ►prenatal diagnosis, ►DNA circulating

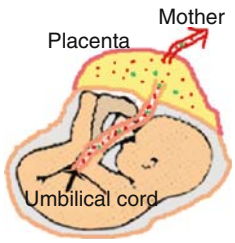

Figure P79. Contact is between fetus and mother through the umbilical cord and both normal (red) and different cells (green) are transferred to the maternal plasma

Plasma Proteins: Proteins in the blood plasma. The major components are serum albumin, globulins, fibrinogen, immunoglobulins, antihemophilic proteins, lipoproteins, α_1 antitrypsin, macroglobulin, haptoglobin, and transfer proteins, such as transferrin (iron), ceruloplasmin (copper), transcortin (steroid hormones), retinol-binding proteins (vitamin A), and cobalamin-binding proteins (vitamin B_{12}). The lipoproteins carry phospholipids, neutral lipids and cholesterol esters. In addition, there are a great variety of additional proteins present in the serum. In a small population of 96 healthy individuals, 76 structural variants were observed in 25 proteins by affinity-based mass spectrometric assays. This large variation predicts that analysis of plasma proteins may yield important biomarkers for medical purposes (Nedelkov D et al 2005 Proc Natl Acad Sci USA 102:10852)

Plasmablast: A precursor of plasmacyte or precursor cell of the lymphocytes.

Plasmacytoid Cell: Functionally, it is one type of dendritic cells with antigen-presenting properties (see Fig. P80). Plasmacytoid cells may not display dendritic morphology. They produce a large quantity of interferon α/β in response to bacterial or viral infection. They have roles in both innate and acquired immunity. ►dendritic cell, ►interferon, ►acquired immunity; McKenna K et al 2005 J Virology 79:17.

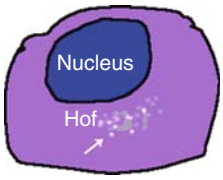

Figure P80. Plasmocytoid cell

Plasmacytoma: The cancer (myeloma) of antibody producing cells. Resistance against it is controlled mainly by different alleles of the complex FRAP. ►Fk506; Bliskovsky V et al 2003 Proc Natl Acad Sci USA 100:14982.

Plasmagene: Non-nuclear genes (mitochondrial, plastidic or plasmid). ►mitochondrial genetics, ►chloroplast genetics

Plasmalemma: The membrane around the cytoplasm or the envelope of the fertilized egg.

Plasmatocyte: Macrophage-like elements in the insect hemolymph. ►macrophage, ►hemolymph

Plasmid: The dispensable genetic element, which can propagate independently and can be maintained within the (bacterial) cell, and may be present in yeast and mitochondria of a number of organisms. The plasmids may be circular or linear double-stranded DNA. The conjugative plasmids possess mechanisms for transfer by conjugation from one cell to another. The non-conjugative plasmids lack this mechanism and are therefore preferred for genetic engineering because they can be easier confined to the laboratory. During evolution, some of the advantageous plasmid genes are assumed to have been incorporated into the chromosomes and the plasmids, lost. The persistence of the plasmids may be warranted by their ability to disperse genetic information

horizontally. Plasmids occur also in the organelles of higher eukaryotes and lower eukaryotes. ►vectors, ►curing of plasmids, ►pBR322, ►pUC, ►transposon conjugative, ►cryptic plasmids, ►Ty; Summers DK 1996 The biology of plasmids, Blackwell; Thomas CM (Ed.) 2000 The Horizontal Gene Pool: Bacterial Plasmids and Gene Spread, Harwood Press, Durham, UK; http://plasmid.hms.harvard.edu.

Plasmid Addiction: The loss of certain plasmids from the bacterial cells may lead to an apoptosis-like cell death, called post-segregational killing or plasmid addiction. ►apoptosis

Plasmid, Chimeric: An engineered plasmid carrying foreign DNA.

Plasmid Incompatibility: Plasmids are compatible if they can coexist and replicate within the same bacterial cell. If the plasmids contain repressors effective for inhibiting the replication of other plasmids, they are incompatible. Generally, closely related plasmids are incompatible, and they thus belong to a different incompatibility group. The plasmids of enterobacteria belong to about two-dozen incompatibility groups. Plasmids may be classified also according to the immunological relatedness of the pili they induce to form (such as F, F-like, I, etc.). The replication system of the plasmids defines both the pili and the incompatibility groups. Cells with F plasmids may form F sex pili; the R1 plasmids belong to FII pili group, etc. ►pilus, ►F^+, ►F plasmid, ►R plasmids, ►enterobacteria, ►incompatibility plasmids

Plasmid Instability: Plasmid instability indicates difficulties in maintenance caused by defect(s) in transmission, internal rearrangements, and loss (deletion) of the DNA. ►cointegration

Plasmid, 2 μm: A 6.3 kbp circular DNA plasmid of yeasts, present in 50–100 copies per haploid nucleus. It carries two 599 bp inverted repeats separating 2774 and 2346 bp tracts. Re-combination between the repeats results in A and B type plasmids. Its recombination is controlled by gene *FLP* and its maintenance requires the presence of the *REP* genes. ►yeast; Scott-Drew S, Murray JA 1998 J Cell Sci 111:1779.

Plasmid Maintenance: Plasmid maintenance in prokaryotes is secured either by the high number of copies, or in low copy number plasmids, by a mechanism reminiscient to some extent to that of the centromere is mitosis of eukaryotes. The proteic plasmid maintenance system operates by the coordination of a toxin and an unstable antidote. When the labile antidote decays, the toxin kills the cells that do not have the plasmid. The antidote may be a labile antisense RNA that keeps in check the toxin gene. A plasmid-encoded restriction-modification may also be involved. When the modification system recedes beyond an effective level in the plasmid-free cells, the genetic material falls victim to the endonuclease. One of such systems in *E. coli* is the *hok* (host killing)-*sok* (suppressor of killing)-*mok* (modulation of killing) system of linked genes. ►partition, ►antisense RNA, ►restriction-modification, ►killer plasmids; Gerdes K et al 1997 Annu Rev Genet 31:1; Møller-Jensen J et al 2001 J Biol Chem 276:35707; Hayes F 2003 Science 301:1496.

Plasmid Mobilization: Plasmid mobilization may take place by bacterial conjugation. Plasmid vectors use the gene *mob* (mobilization) if they do not have their own genes for conjugal transfer. Some plasmids may rely on *ColK* (colicin K, affecting cell membranes) that nicks plasmid pBR322 at the *nic* site, close to *bom* (basis of mobility). Mobilization proceeds from the nicked site (base 2254 in pBR322). Plasmids lacking the *nic/bom* system, e.g., pUC, cannot be mobilized. (See Chan PT et al 1985 J Biol Chem 260:8925).

Plasmid Rescue: The plasmid rescue procedure was designed originally for transformation with linearized plasmids of *Bacillus subtilis* that normally does not transform these bacteria. The linearized plasmid could be rescued for transformation in the presence of the *RecE* gene if recombination could take place.

The linearized monomeric plasmid then could carry also any in vitro ligated passenger DNA into cells. If the host cells carry a larger number of plasmids (multimeric), special selection is necessary to find the needed one. Plasmid rescue has also been used for re-isolation of inserts (plasmids) from the genome of transformed cells of plants.

The re-isolation requires appropriate probes for (the termini) of the inserts to permit recognition, after which, ithe DNA is re-circularized and cloned in *E. coli* and they have at least one selectable marker and an origin of replication compatible with the bacterium. The cloned DNA insert or its fragments are inserted into the M13 phage for nucleotide sequencing. This permits the identification of any changes that may have taken place in the original transforming DNA and permits an analysis of the flanking sequences of the target sites as well. A number of different variations of the procedure have been adopted in prokaryotes, microbes, animals, and plants. ►T-DNA, ►DNA sequencing, ►Rec; Perucho M et al 1980 Nature [Lond] 285:207, see Fig. P81.

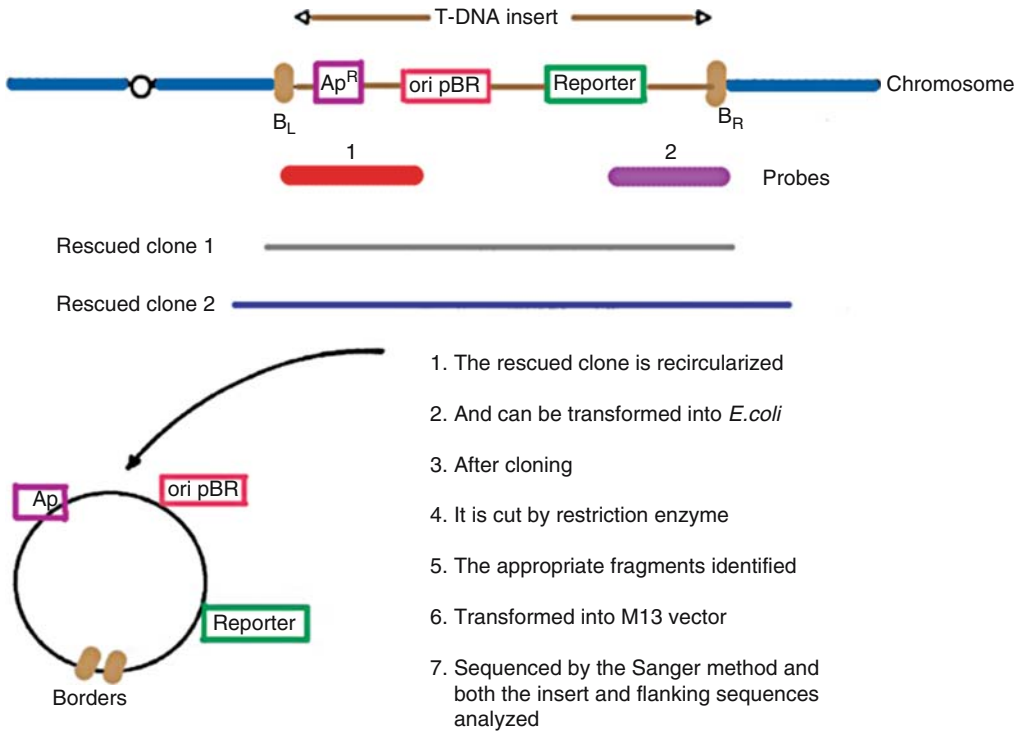

Figure P81. Outline of a plasmid rescue procedure exemplified by isolating T-DNA insert from *Arabidopsis*. Ap = ampicillin-resistance gene (Ap^R) of the pBR322, oripBR = origin of replication of the PBR322 plasmid present in the plant-transforming vector, reporter is hygromycin resistance, left (B_L) and | right (B_R) border sequence of the T-DNA. (After Koncz C, et al. 1989. Proc. Natl. Acad. Sci. USA 86:8467.)

Plasmid Segregation: In plasmid segregation, before cell division, plasmids are partitioned to ensure transmission to mother and daughter cells. The segregation is mediated by *par* (partitioning) loci of the plasmids. Type I pars encode Walker box ATPases and Type II *pars* encode actin-like ATPases. The actin-like filaments act in similarity to the microtubules in higher organisms. The *par* loci involve two proteins and a centromere-like cis-acting site. The presence of Type I par locus positions the plasmids in the center of the cell. Integration host factor (IHF) of the bacteria plays a role in plasmid segregation. The mechanisms of plasmid segregation vary among different plasmids. ►actin, ►ATPase, ►Walker box, ►IHF; Ebersbach G, Gerdes K 2005 Annu Rev Genet 39:453.

Plasmid Shuffling: The general procedure of plasmid shuffling in yeast first disrupts the particular gene in a diploid strain. After meiosis, the cells can be maintained only if the wild type allele is carried on a replicating plasmid (episome). Mutant copies of that particular gene are then introduced into the cell on a second episome and exchanged (shuffled) for the wild type allele. The phenotype of any of the mutant alleles can be studied in these cells that carry the disrupted (null) allele. (See Sikorski RS et al 1995 Gene 155:51; Zhao H, Arnold FH 1997 Nucleic Acids Res 25:1307).

Plasmid Telomere: Linear plasmids require exonuclease protection at the open ends. The problem may be resolved by capping with proteins or forming a lollipop type structure by fusing the ends of the single strands as shown in Figure P82. ►telomere

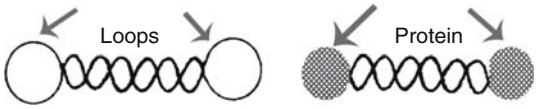

Figure P82. Plasmid telomeres

Plasmid Vehicle: A recombinant plasmid that can mediate the transfer of genes from one cell (organism) to another. ►vectors

Plasmids, Amplifiable: Amplifiable plasmids continue replication in the absence of protein synthesis (in the presence of protein synthesis inhibitor). ►amplification

Plasmids, Conjugative: Conjugative plasmids carry the *tra* gene, promoting bacterial conjugation and can be transferred to other cells by conjugation and can also mobilize the main genetic material of the bacterial cell. ►conjugation, ►F plasmid

Plasmids, Cryptic: Cryptic plasmids have no known phenotype.

Plasmids, Monomeric: Monomeric plasmids are present in a single copy per cell.

Plasmids, Multimeric: Multiple plasmids have multiple copies in a cell.

Plasmids, Non-Conjugative: Non-conjugative plasmids lack the *tra* gene required for conjugative transfer, but have the origin of replication and therefore when complemented by another plasmid for this function, they can be transferred. ►conjugation

Plasmids, Promiscuous: Promiscuous plasmids have conjugative transfer to more than one type of bacteria.

Plasmids, Recombinant: Recombinant plasmids are chimeric; they carry DNA sequences of more than one origin. (See Fig. P83).

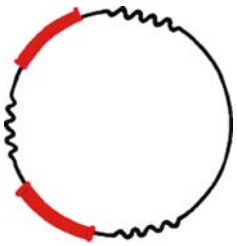

Figure P83. Recombinant plasmid

Plasdmids, Relaxed Replication: Relaxed replication plasmids may replicate to 1000 or more copies per cell.

Plasmids, Runaway Replication: In runaway replication plasmids, the replication is conditional, e.g., under permissive temperature regimes they may replicate almost out-of-control whereas under other conditions their number per cell may be quite limited.

Plasmids, Single Copy: Single copy plasmids may have single or very few copies per cell.

Plasmids, Stringent Multicopy: Stringent multicopy plasmids may grow to 10 to 20 copies in a cell.

Plasmin (fibrinolysin): Proteolytic protein (serine endopeptidase) with specificity of dissolving blood clots, fibrin, and other plasma proteins. For its activation, urokinases (tissue plasminogen activator) are required. Plasmin may be used for therapeutic purposes to remove obstructions in the blood vessels. ►urokinase, ►plasminogen, ►plasminogen activator, ►streptokinase, ►CAM; Lijnen HR 2001 Ann NY Acad Sci 936:226.

Plasmin Inhibitor Deficiency (PLI, AAP): Plasmin inhibitor deficiency is encoded in human chromosome 18p11-q11 as recessive gene, and is involved in the regulation of fibrinolysin. ►plasmin

Plasminogen: A precursor of plasmin. Human plasminogen markedly increases mortality of mice infected with streptococci due to bacterial expression of streptokinase. Streptokinase is highly specific for human plasminogen but not for other mammalian plasminogens (Hun H et al 2004 Science 305:1283). ►plasmin, ►plasminogen activator, ►angiostatin

Plasminogen Activator (PLAT): PLAT cleaves plasminogen into plasmin; it is encoded in human chromosome 8q11-p11. The plasmin activator inhibitor (PLANH1/PAI-1) is encoded in human chromosome 7q21-q22 and PLANH2 at 18q21.1-q22. The plasminogen activator receptor was localized to 19q13.1-q13.2. Tissue-specific plasminogen activator coupled to the surface of red blood cells can dissolve blood clots and prevent thrombosis (Murciano, J-C et al 2003 Nature Biotechnol 21:891). ►plasminogen, ►plasmin, ►urokinase, ►PN-1, ►streptokinase, ►thrombosis, ►MET oncogene

Plasmodesma (plural plasmodesmata): About 2µm or larger channels connecting neighboring plant cells, lined by extension of the endoplasmic reticulum. Functionally, they correspond to the gap junctions of animal cells. Various molecules, signals, including even viruses, may move through these intercellular communication channels. The plasmodesmata are subject to temporal and spatial regulation. ►gap junctions; Zambryski P, Crawford K 2000 Annu Rev Cell Dev Biol 16:393; Hake S 2001 Trends Genet 17:2; Haywood V et al 2002 Plant Cell 14:S303; Kim I et al 2005 Proc Natl Acad Sci USA 102:11945.

Plasmodium: A syncytium of the amoeboid stage of slime molds (such as in *Dictyostelium*).

Plasmodium: One of the several parasitic coccid protozoa causing malaria-like diseases in vertebrates, birds, and reptiles. A single *Plasmodium falciparum* (n = 14, ~23 Mb, ~5268 proteins) parasite transcribes simultaneously multiple *var* genes (at several chromosomal locations), encoding the erythrocyte-membrane protein (PfEMP-1) that binds to the vascular endothelium and red blood cells. Functionally related genes tend to be clustered in the subtelomeric regions of the chromosomes. A protein interaction network of *P. falciparum* expressed at the intra-erythrocyte-stage parasites involving >2000 fragments of 1295 genes

has been constructed on the basis of the two-hybrid system. These networks can reveal potential drug targets (LaCount DJ et al 2005 Nature [Lond] 438:103). These interaction networks are quite different from those known in other organisms (Suthram S et al 2005 Nature [Lond] 438:108). Alignment of these *var* genes in heterologous chromosomes at the nuclear periphery may facilitate gene conversion and promotes diversity of antigenic determinants and adhesive phenotypes. Such a mechanism aids the evasion of the host immune system. The parasite invades the erythrocytes and destroys the host cells through the formation of merozoites (mitotic products) and spreading thus to other cells (see Fig. P84). The merozoites may develop into gametocytes (gamete forming cells) that infect blood-sucking mosquitos where they are transformed into sporozoites (the sexual generation) that are transmitted through insect bites to the higher animal host. The invaders first move to the liver where merozoites are formed and then return to the erythrocytes; thus the cycle continues. *Plasmodium falciparum* causes falciparum malaria. *P. malariae* is responsible for the *quartan*, or fourth day recurring malaria. The protozoon contains two double-stranded extranuclear DNA molecules; that of circular DNA resembles mitochondria whereas the second bears similarities to ctDNA, and contains 68 genes. Mutation in a single gene (*pfmdr1/PfEMP1*) encoding the P-glycoprotein homolog, Pgh1, may result in resistance to several antimalarial drugs of which some may or may not be chemically related. Transformation of the gene encoding the SM1 peptides into the *Anopheles* vector may render the insect resistant to *Plasmodium* infection. The rodent parasite *Plasmodium yoellii yoellii* genome (~23.1 Mb) is similar to that of *P. falciparum*. ►malaria, ►sex determination, ►thalassemia, ►antigenic variation, ►mRNAP, ►mtDNA, ►chloroplast, ►PfEMP1, ►rifins, ►gene conversion, ►serpine, ►antigenic variation, ►epigenetic memory; Fidock DA et al 2000 Mol Cell 6:861; Ito J et al 2002 Nature [Lond] 417:452; the sequenced *P. falciparum* genome: *Nature* 419, issue 6906, Oct 30, 2002; *Anopheles* genome: Science 298, 4 Oct 2002; Joy DA et al 2003 Science 3000:318; *P. falciparum* linkage and gene association: Su X et al 2007 Nature Rev Genet 8:497; comparative genome analysis of *P. berghei* and *P. chabaudi*: Hall N et al 2005 Science 307:82; invasion of the blood: Cowman AF, Crabb BS 2006 Cell 124:755; http://www.plasmodb.org/plasmo/home.jsp; http://www.tigr.org/tdb/tgi/.

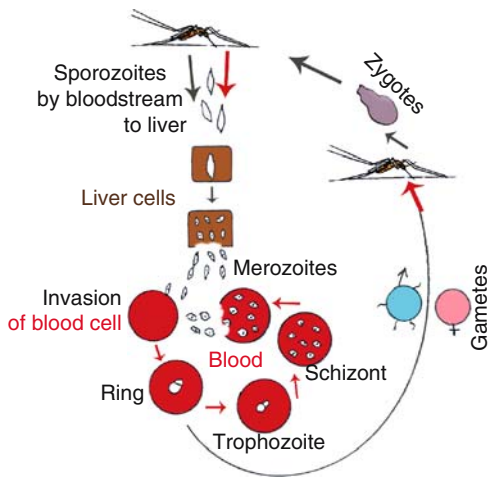

Figure P84. Life cycle of *Plasmodium* in humans and mosquitos

Plasmogamy: fusion of the cytoplasm of two cells without fusion the two nuclei and thus resulting in dikaryosis. Plasmogamy is common in fungi but may occur in fused cultured cells of plants and animals. ►fungal life cycle, ►cell genetics

Plasmolemma (plasmalemma): Plant cell membrane; the ectoplasm of the fertilized egg of animals.

Plasmolysis: The shrinkage of the plant cytoplasm caused by high concentration of solutes (salt) outside the cell resulting in loss of water. The cytoplasm separates from the cell wall.

Plasmon: The sum of non-nuclear hereditary units such as exists in mitochondrial and plastid DNA. ►mtDNA, ►chloroplasts, ►plastome

Plasmon-Sensitive Gene: ►nucleo-cytoplasmic interaction

Plasmophoresis: A procedure to filter blood to allow the plasma proteins of the patient to be removed. At the same time, new donor plasma is replaced into the patient's blood, which is located in the plasmaphoresis machine. Subsequently, the blood is sent back to the patient. ►hemolysis

Plasmotomy: The fragmentation of multinucleate cells into smaller cells without nuclear division.

Plasmovirus: The plasmovirus bears some similarity to phagemids but in this case a retrovirus is combined with an independent vector cassette containing various elements. The envelope gene of the Moloney provirus is replaced by a transgene to prevent infective retroviral ability and it would not regain it by chance recombination with another retrovirus. Such a construct can express transgene(s), can multiply within the target cells, and provide a tool for cancer therapy. ►vectors, ►retrovirus, ►transgene, ►cancer therapy, ►viral vectors, ►phagemid; Morozov VA et al 1997 Cancer Gene Ther 4(5):286.

Plasticity: In general, the ability of a cell or organism to display different expressions (phenotype) dependent on the environment. The ability of cells to change from what they normally are enables them to perform tasks not normally found in differentiated cells. ►stem cells, ►MAPCs, ►adaptation, ►noise, ►reaction norm

Plastid: The cellular organelle of plants, containing DNA. It may differentiate into chloroplasts, etioplasts, amyloplasts, leucoplasts, or chromoplasts. In *Arabidopsis*, mechanosensitive ion channel proteins (localized in the plastid envelope) seem to control plastid size and shape (Haswell ES, Meyerowitz E M 2006 Curr Biol 16:1). ►under separate names, ►plastid number per cell, ►plastid male transmission, ►ctDNA, ►chloroplast, ►chloroplast genetics, ►apicoplast

Plastid Male Transmission: Generally, the genetic material in the plastids is transmitted only through the egg cytoplasm but in a few species of higher plants (*Pelargonium*, *Oenothera*, *Solanum*, *Antirrhinum*, *Phaseolus*, *Secale*, etc.) a variable degree of male transmission takes place. Biparental transmission of plastid genes (about 1%) may occur also in the alga *Chlamydomonas reinhardi*. The male transmission of these nucleoids is controlled by one or two nuclear genes. The nucleoids of the plastid and mitochondria of the male are usually degraded or if they are included in the generative cells of the male, most commonly fail to enter the sperm or are not transmitted to the egg cytoplasm. In contrast to the angiosperms, in conifers (pines, spruces, firs) the plastid DNA is usually transmitted through the males. In some interspecific hybrids, exclusively paternal, exclusively maternal, and biparental transmission were also observed. In other conifer crosses, the mtDNA is transmitted maternally. In redwoods, the transfer is paternal. One scientific claim posits that the destruction of the paternal ctDNA in the females is carried out by a restriction enzyme while the maternal ctDNA is protected by methylation. Others implicate a special nuclease C. ►chloroplast, ►genetics, ►ctDNA, ►mtDNA, ►paternal leakage; Diers L 1967 Mol Gen Genet 100:56; Avni A, Edelman N 1991 Mol Gen Genet 225:273; Sears B 1980 Plasmid 4:233.

Plastid Number Per Cell: In the giant cells of *Acetabularia* algae, there may be one million chloroplasts but in the alga *Chlamydomonas* there is only one per cell. In higher plants, the number of plastids vary according to the size of the cells, about 30–40 in the spongy parenchyma to about twice as many in the palisade parenchyma. ►plastid, ►ctDNA

Plastochrone: The pattern of organ differentiation in time and space is genetically controlled. (See Miyoshi K et al 2004 Proc Natl Acad Sci USA 101:875).

Plastocyanin: an electron carrier in photosynthesis between cytochromes and photosystem I. ►Z scheme; Ruffle SV et al 2002 J Biol Chem 277:25692.

Plastome: The sum of hereditary information in the plastids. ►ctDNA, ►chloroplast genetics

Plastome Mutation: Mutation in the plastid (chloroplast) DNA. ►chloroplast genetics, ►mutation in cellular organelles

Plastoquinone: An isoprenoid electron carrier during photosynthesis. ►isoprene

Plate: A Petri dish containing a nutrient medium for culturing microbial or plant cells. Cell plate divides the two daughter cells after mitosis.

Plate Incorporation Test: The most commonly used procedure for the Ames test when the *Salmonella* suspension (or other bacterial cultures), the S9 activating enzymes, and the mutagen/carcinogen to be tested are poured over the bacterial nutrient plate in a 2 mL soft agar. After incubation for two days at 37°C, the number of revertant colonies is counted. ►Ames test, ►spot test

Platelet Abnormalities: ►Glanzmann's disease, ►thrombopathic purpura, ►thrombopathia, ►giant platelet syndrome, ►Hermansky-Pudlak syndrome, ►May-Hegglin anomaly, ►platelets

Platelet Activating Factor (PAF): An inflammatory phospholipid. PAF acetylhydrolase may be a factor in atopy. ►platelets, ►atopy

Platelet-Derived Growth Factor (PDGF): A mitogen, secreted by the platelets, the 2–3 μm size elements in the mammalian blood, originated from the megakaryocytes of the bone marrow, and concerned with blood coagulation. PDGF controls the growth of fibroblasts, smooth muscle cells, blood vessel formation, nerve cells, cell migration in the oocytes, etc. This protein bears substantial homologies to the oncogenic product of the simian sarcoma virus, the product of the KIT oncogene, and the CSF1R (it activates also other oncogenes, such as c-fos). The PDGF is required for the healing of vascular injuries and in these cases the expression induced Egr-1 (early growth response gene product) may bind to the PDGF β chain promoter after displacing Sp1. PFGF- and insulin-dependent S6 kinase ($pp70^{S6k}$) is activated by phosphatidylinositol-3-OH kinase. Its receptor (PDGFR) is a tyrosine kinase. The detection of PDGF is facilitated by the construction of aptamers labeled with pyrene monomers at both ends. When an excimer is produced, the fluorescence emission is increased from 400 nm to 485 of PDGF bound excimer. The principle may be applicable to other molecules for facilitating biomedical analyses (Yang CJ et al 2005 Proc Natl Acad Sci USA

102:17278). ►oncogenes, ►growth factors, ►signal transduction, ►platelets, ►Sp1, ►S6 kinase, ►phosphatidyl inositol, ►aptamer, ►excimer, ►heart diseases; Betsholtz C et al 2001 Bioessays 23(6):494; Duchek P et al 2001 Cell 107:17.

Platelets: Platelets originate as cell fragments or "minicells" (without DNA) from the megakaryocytes of the bone marrow. Their function is in blood clotting and in the repair of blood vessels; they also secrete mitogen(s). Platelet abnormalities may cause stroke, myocardial infarction (damage of the heart muscles), and unstable angina (sporadic, spasmic chest pain). A balance between Bc*l*-x and Bak determines the life span of platelets. Inactive Bcl-x may cause thrombocytopenia (Mason KD et al 2007 Cell 128:1173). ►blood, ►megakaryocyte, ►platelet derived growth factor, ►blood serum, ►BAK, ►BCL, ►thrombocytopenia; Prescott SM et al 2000 Annu Rev Biochem 69:419.

Plating Efficiency: The percentage of cells or protoplasts placed on a Petri plate that grows. The relative plating efficiency compares the fraction of growing cells in a treated series to that of an appropriate control.

Platyfish (*Xiphophorus/Platypoecilus*): Tropical fishes with complex sex determination. WX, WY, and XX are females and the males are XY and YY. The pseudoautosomal region seems to be long. Their melanocytes frequently turn into melanoma. ►pseudoautosomal, ►sex determination, ►melanocyte, ►melanoma

Platykurtic: ►kurtosis

Platypus: ►monotrene

Platysome: The nucleosome core (when it was thought of as a flat structure). ►nucleosome

Playback: The number of non-repetitive sequences in a DNA can be determined by the saturation of single-strand DNA with RNA of unique sequences. The kinetics of saturation, R_0t (by analogy to C_0t), is then determined. The annealed fraction is generally a small percent of the eukaryotic DNA, which is highly redundant. To be sure that the RNA is hybridized to only the unique DNA sequences, in the DNA-RNA hybrid molecules the RNA is degraded enzymatically and the remaining DNA is subjected to a reassociation test to determine its C_0t curve. This "play-back" then reveals whether all the DNA so isolated, includes only genic DNA and is not redundant. Such studies may assist in estimating the number of housekeeping genes plus the genes that were transcribed when the RNA was collected. ►c_0t, ►housekeeping genes, ►gene number

PLC: Phospholipase C. ►phospholipase

Pleated Sheets: Relaxed β-configuration polypeptide chains hydrogen-bonded in a flat layer. ►protein structure

Pleckstrin Domain: The pleckstrein domain is approximately 100-amino acids in length and occurs in many different proteins such as serine/threonine kinases, tyrosine kinases, and the substrates of these kinases, phospholipase C, small GTPase regulators, and cytoskeletal proteins. Pleckstrin domains may participate in various signaling functions; they bind phosphatidylinosotol 4,5-bisphosphate. Pleckstrin is a substrate of protein kinase C in activated platelets. separate entries, ►PH, ►SHC, ►SH2, ►SH3, ►WW, ►PTB, ►adaptor proteins, ►phosphatidylinositol, ►platelets, ►desensitisation, ►phosphoinositides; Lemmon MA, Ferguson KM 1998 Curr Top Microbiol Immunol 228:39; Rebecchi MJ Scarlata S 1998 Annu Rev Biophys Biomol Struct 27:503.

Plectin: A 500 kDa keratin of the cytoskeleton encoded in human chromosome 8q24. ►epidermolysis ►[bullosa simplex], ►keratin

Plectonemic Coils: The DNA double helix represents plectonemic coils (see Fig. P85). Here, the two coils are wound together, therefore they can be separated only by unwinding rather than simple pulling apart, like in paranemic coils. ►paranemic coils

Figure P85. Plectonemic coil

Pleiomorphic: A pleiomorphic organism displays variable expression (without a genetic basis for the special changes).

Pleiomorphic Adenoma: A salivary gland tumor caused by human chromosome breakage points, primarily at 8q12, 3p21, and 12q13-15. The translocation t(3;8)(p21;q12) results in swapping the promoters of PLAG1, a Zn-finger protein encoded in chromosome 8 and β-catenin (CTNNB1), and activation of the oncogene. ►Zinc finger, ►β-catenin

Pleiotrophin (PTN): A 18 kDa heparin-binding cytokine, inducible by the platelet derived growth factor (PDGF). It is 50% identical with retinoic acid-inducible midkine growth factor, which like PTN is also a growth and differentiation factor. PTN reduces cell colony formation, interacts with receptor protein tyrosine phosphatase, and leads to tumor growth, angiogenesis, and metastasis. PTN regulates phosphorylation of serine 713 and 726 of β-adducin by activating protein kinase C and mediates its translocation to the nucleus. This phosphorylation contributes to uncoupling of the adducin–actin–spectrin

complexes and stabilizes the cytoskeleton (Pariser H et al 2005 Proc Natl Acad Sci USA 102:12407). ►adducin, ►actin, ►protein kinase, ►spectrin, ►cytoskeleton; Meng K et al 2000 Proc Natl Acad Sci USA 97:2603; PTN in breast cancer: Chang Y et al 2007 Proc Natl Acad Sci USA 104:10888.

Pleiotropy: One gene affects more than one trait; mutation in various elements of the signal transduction pathways, in general transcription factors, or in ion channels may have pleiotropic effects. The existence of pleiotropy has been questioned with the emergence of the one gene–one enzyme theory. Earlier, it was inconceivable on the basis that one tract of DNA could code for more than a single function ("Pleiotropism non est… that is the dogma", p 161. In Genetics, 1959 Sutton EH (ed), Josiah Macey Found, New York). However, it has been since shown that mutation at different sites within single mitochondrial tRNA genes may lead to several different human diseases. Cytokines involved in signaling through different receptors in different pathways are pleiotropic molecules. The complete sequence of the *Drosophila* genome shows that ~13,601 genes encode ~14,113 transcripts indicating that a minimum of nearly 4% of the genes display pleiotropy. An analysis of 150,000 high-abundance human proteins derived from two-dimensional gels indicated an average of 10 isoforms per protein following the (MALDI-TOF) matrix-assisted laser desorption ionization/time of flight mass spectrometry (Humphery-Smith I 2004, p 2 In: Albala JS, Humphery-Smith I (Eds.) Protein Arrays, Biochips, and Proteomics, Marcel Dekker, New York). In yeast, pleiotropy is attributable to multiple consequences of single functions (He X, Zhang J 2006 Genetics 173:1885). *Antagonistic pleiotropy* claims that evolution does not work against variations, which adversely affect the individuals after the completion of the reproductive stage of life, and the alternative genotypes display opposite phenotypes. Actually, the genes displaying antagonistic pleiotropy can be silent in early life but are harmful later and contribute to aging; yet, they may have some selective advantage early and this assures their maintenance in populations.

The F1F0-ATP synthase is a ubiquitous mitochondrial enzyme that works as a rotary motor, harnessing the electrochemical proton gradients to carry out ATP synthesis from ADP and inorganic phosphate. It is composed of a membrane-embedded proton-translocating sector (F0), coupled to a soluble sector (F1) that contains catalytic sites for ATP synthesis/hydrolysis. Several of the most deleterious human mitochondrial diseases, such as the maternally inherited Leigh syndrome, neurogenic ataxia, retinitis pigmentosa, and some cases of Leber hereditary optic neuropathy are caused by point mutations in the mitochondrial *ATP6* gene that encodes subunit 6 of the ATP synthase F0 sector. The same single point mutation can produce either Leigh syndrome or retinitis pigmentosa, depending on the mtDNA mutation load. The mtDNA mutations most frequently associated with retinitis pigmentosa or Leigh syndrome are T8993G, T8993C, T9176G, and T9176C, which replace the conserved leucine residues at positions 156 or 217 of subunit 6 by arginine or proline, respectively. The primary molecular pathogenic mechanism of these deleterious human mitochondrial mutations is functional inhibition in a correctly assembled ATP synthase (Cortés-Hernández P et al 2007 J Biol Chem 282:1051). ►signal transduction, ►transcription factors, ►epistasis, ►two-hybrid method, ►mitochondrial diseases in humans, ►MALDI-TOF, see Fig. P86.

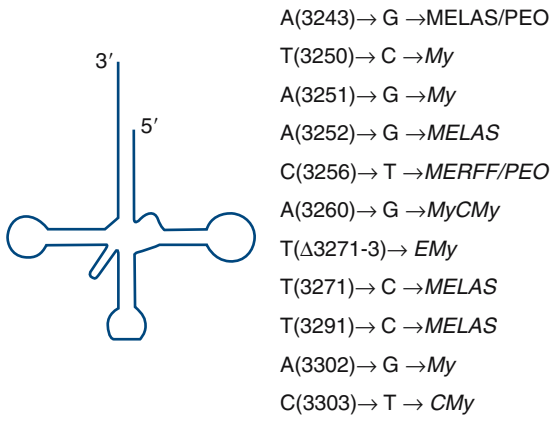

Figure P86. Pleiotropic mutations in the mtDNA Leu tRNA^{UUR} gene. The diagram displays the mutations in the human mitochondrial Leu tRNA^{UUR}. The first letter indicates the base that is changed, in parenthesis is the nucleotide number at the physical map, after the → the substituted base is given and after → the diseases described under mitochondrial diseases in humans are identified with abbreviations. Redrawn after Moraes CT 1998, p 167 In: Singh KK (Ed.) Mitochondrial DNA Mutations in Aging, Disease and Cancer, Springer, New York

Pleomorphism: Carl Wilhelm Nägeli's nineteenth century suggestion claiming lack of hard heredity in bacteria and that they simply exist in a variety of pliable forms. This idea held back the development of bacterial genetics, although physicians like Robert Koch and the taxonomist W. Migula sharply criticized it and stated that it ignored facts known by the 1880s. ►*Hieracium*

Plesiomorphic: A trait in its more primitive state among several evolutionarily related species. ►apomorphic, ►symplesiomorphic, ►synapomorphic

Pleura: Serous (moist) membrane lining the lung or insects' thoracic cavity.

Plexins: Receptors for semaphorins. Plexin-B1 is activates GTPase for RAS (Oinuma I et al 2004 Science 305:862). ►semaphorins, ►RAS, ►GTPase

PLGA: See Fig. P87, ►angiogenesis

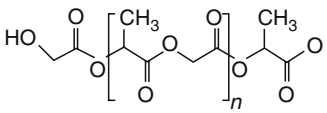

Figure P87. PLGA

Plk (polo-like kinase): Plk regulates the maturation of the centrosome, spindle assembly, the PICH checkpoint helicase, and the removal of cohesins, inactivates the anaphase promoting complex inhibitors, and controls mitotic exit and cytokinesis. ►polo, terms in alphabetical order; Baumann C et al 2007 Cell 118:101.

Ploidy: Ploidy represents the number of basic chromosome sets in a nucleus. The haploids have one set (x), the diploids two (xx), autotetraploids (xxxx), and so on. ►polyploidy

P-Loop: The ATP- and GTP-binding proteins have a phosphate-binding loop, the primary structure of which typically consists of a glycine-rich sequence followed by a conserved lysine and a serine or threonine. (See Saraste M et al 1990 Trends Biochem Sci 15:430).

P

PLTP (phospholipid transfer protein): The PLTP mediates the exchange of HDL cholesteryl esters with very low-density triglycerides and vice versa. ►HDL, ►cholesterol, ►CETP

Plug-In: A small circuit in a developmental function that can be present in several developmental networks.

Plum (*Prunus*): Basic chromosome number x = 7 but a variety of polyploid forms exist. (Bliss FA et al 2002 Genome 45:520).

Plumule: The embryonic plant shoot-initial.

Pluralism in Evolutionary Biology: Pluralism indicates sympatric speciation. ►sympatric

Pluripotency: A cell with pluripotency has the ability to develop into various, but not necessarily all types of tissues. Embryonic stem cells (from the inner mass of blastocysts), embryonic germ cells (primordial cells of the gonadal ridge), and the mesenchymal stem cells of the bone marrow possess pluripotency. Transcription factor Zfx controls the self-renewal of embryonic and hematopoietic stem cells (Galan-Caridad JM et al 2007 Cell 129:345). The good cultures may grow for more than 70 doublings ($2^{70} \geq 10^{20}$) and may be free of chromosomal defects. The ability of the embryonic stem cells to differentiate into many types of cells is regulated by MYC and Nanog proteins that regulate transcription factors, signal molecules, and suppress lineage specific cells. These two factors target a core set of 345 genes. The mouse and human MYC and Nanog target sites overlap in ~9 to 13% (Loh Y-H et al 2006 Nat Genet 38:431). Nanog proteins enable the reprogramming of somatic cells into pluripotent stem cells after fusion with embryonic stem cells of mouse (Silva J et al 2006 Nature [Lond] 441:997). Histone3 arginine26 methylation appears to be a crucial event in the formation of the pluripotent inner cell mass of the four-cell stage mouse embryos. CARM1 methyltransferase activity also upregulates Nanog and Sox2 proteins (Torres-Padilla A-E et al 2007 Nature [Lond] 445:214). ►totipotency, ►CARM1, ►MYC, ►Nanog, ►Sox, ►stem cells, ►ZFX; Donovan PJ, Gearhart J 2001 Nature [Lond] 414:92.

Plus and Minus Method (Sanger F et al 1975 J Mol Biol 94:441): The plus and minus method was an early version of DNA sequencing using dideoxy analogs of nucleosides (+ batch) during replication. After the analog was incorporated to a site, T4 exonuclease failed to continue degradation. In the minus (−) batch the synthesis stopped depending upon which single nucleotide was omitted (the precursor mixture containing only 3 deoxyribonucleotides). Thus nucleotide sequences of specific ends and length were generated and the fragments of different lengths were analyzed by electrophoresis. The Sanger et al (1977 Proc Natl Acad Sci USA 74:5463) method and its improvements replaced it. ►DNA sequencing

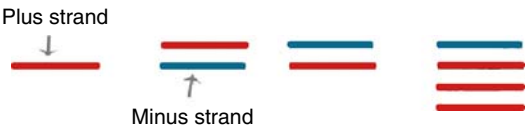

Figure P88. Plus and minus strands

Plus End: The preferential growing end of microtubules and actin filaments. ►minus end

Plus Strand: The plus strand of the single stranded DNA or RNA of a virus is represented in the mature virion whereas the minus strand serves as a template for the transcription (replication) of the plus strand and the mRNA (see Fig. P88). In most cases, the plus strands are synthesized far in excess to the minus strands. (►replicative form, ►RNA replication). The plus strand viral genomic RNA serves directly as mRNA.

Plutonium (Pu): A metallic fissile element (atomic number 94, atomic weight 242) produced by neutron bombardment of uranium (U^{238}) during the production of nuclear fuel and used for making nuclear weapons. Radioactive Pu powers some heart pacemakers. Thus, the wearers, as well as his/her family members and surgeons, will be exposed to some radiation, generally below 1.28 Sv per person per year, a little more than the average natural background (the doses are additive, however). If the highly toxic particles of Pu are inhaled (the most common type of ingestion), the element may affect the lung and may eventually be preferentially deposited in the skeletal system, causing bone cancer by the emission of X and γ rays. Pu^{238} has a half-life of 86.4 years. It propels some space vehicles. Pu^{239} has a half-life of 24.3×10^3 years and targets primarily the bone marrow. Other Pu isotopes have an even longer half-life. The level of Pu may be detected by radioactivity in the urine and by instruments placed on the body. Appropriate instruments can detect as low as 4 nCi (nanoCurie) values. ►atomic radiation, ►isotopes, ►radiation hazard assessment, ►Curie

Plx1: A kinase that phosphorylates the amino-terminal domain of Cdc25. ►Cdc25

Plymouth Rock: A recessive white-feathered breed of chickens with the genetic constitution of *iicc*. The dominant *I* gene is a color inhibitor and *C* symbolizes color. ►White Wyandotte, ►Leghorn White

PLZF: The zinc-finger protein encoded in human chromosome 11q23. It normally represses the promoter of cyclin A but a transposition of RARα (retinoic acid receptor) results in transactivation of the cyclin A gene, and may be involved in the initiation of cancer. ►cyclin A, ►RAR, ►transcriptional activator, ►transactivator, ►leukemia [acute promyelotic leukemia].

PMA: See ►phorbol 12-myristate-13-acetate (Fig. P89)

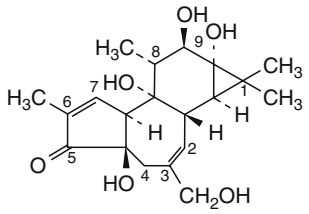

Figure P89. Phorbol

PMAGE (polony multiplex analysis of gene expression): PMAGE can detect single mRNA molecules in three cells (Kim JB et al 2007 Science 316:1481). ►polony

pMB1: ►ColE1

PMCA (protein misfolding cyclic amplification): ►prion

PMDS (persistence of Müllerian duct syndrome): ►Müllerian ducts

PME: Point mutation element where in the 3′-UTR regulatory proteins may bind and cause developmental switching.

PMF (peptide-mass fingerprinting): A method of rapid identification of proteins without sequencing but using mass spectrometry information. ►MALDI; Jonsson AP 2001 Cell Mol Life Sci 58:868.

PML (promyelotic leukemia): A putative Zinc finger protein, encoded in human chromosome 15q21. Formerly, this gene was called MYL. There are about 10–20 PML bodies of ~0.3–1 μm per mammalian nuclear matrix. In acute promyelotic leukemia, these bodies become disorganized as the PML-RARα oncogenic complex is formed. PML bodies are associated with caspase- and FAD-induced apoptosis. Casein kinase 2 (CK2) promotes PML ubiquitin-mediated degradation by phosphorylation at serine 517. In case of resistance to CK2, tumor-suppressor activity of PML is enhanced (Scaglioni PP et al 2006 Cell 126:269). Overexpressed PML also promotes apoptosis but without an enhanced caspase-3 activity. In the absence of PML ($PML^{-/-}$), the cells become resistant to ionizing radiation. ►leukemia, ►PLZF, ►nuclear matrix, ►RAR, ►apoptosis, ►POD, ►AKT; Lallemand-Breitenbach V et al 2001 J Exp Med 193:1361.

PML39: A yeast upstream effector regulating Mlp1/Mlp2 nucleopore-associated proteins suppressing nuclear export of un-spliced mRNA (Palancade B et al 2005 Mol Biol Cell 16:5258). ►nuclear pores

PMS1 (2q31-q33), **PMS2** (7q22) yeast homologs and colorectal cancer: Increased post-meiotic segregation in yeast and increased colorectal cancer (or Turcot syndrome) in humans due to mismatch repair deficiency. ►mismatch repair, ►colorectal cancer, ►Turcot syndrome

PN-1 (protease nexin): A 43 kDa inhibitor of serine proteases (thrombin, plasminogen activator). It is involved in the development of embryonic organs (cartilage, lung, skin, urogenital system, and nervous system). PN-1 is abundant in the seminal vesicle and its dysfunction leads to male infertility. ►thrombin, ►plasminogen activator, ►urokinase, ►nexin, ►infertility, ►claudin-11; Murer V et al 2001 Proc Natl Acad Sci USA 98:3029.

pN: ►Newton

PNA: ►peptide nucleic acid

Pneumococcus: ►*Diplococcus pneumoniae*

Pneumocystis carinii: A group of pathogenic ascomycetes with special susceptibility to immune-compromised individuals (e.g., AIDS patients) and rodents. It carries about 3740 genes in the about 8 Mb genome. It reproduces both asexually and sexually. ►acquired immunodeficiency, ►ascomycete; Kolls JK et al 1999 J Immunol 162:2890.

PNPase: ►polynucleotide phosphorylase

Pocket: The motif of the retinoblastoma (RB) tumor-suppressor protein family that binds to viral-DNA coded oncoproteins. Binding of RB to the E2F family of transcription factors blocks transcription, needed for the progression of the cell cycle. The pocket proteins share this retinoblastoma (RB) motif. ►E2F1, ►tumor suppressor, ►cell cycle, ►transcription factors, ►retinoblastoma, ►p107, ►p130; Botazzi ME et al 2001 Mol Cell Biol 21:7607.

POD (PML-oncogenic domain): ►PML

Podophyllotoxin (epipodophyllotoxin): Antimitotic plant product.

Podosomes (invadopodia): Actin-containing electron-dense adhesion structures on human primary macrophages, Src-transformed fibroblasts, and in some cancer cells, controlling cell motion migration and immune reactions. N-WASP WH2 nucleation promoting protein domains capture the barbed end (the protrusive attachment structure of actin) to the podosome (Co C et al 2007 Cell 128:901). ►Src, ►macrophage, ►actin, ►WASP, ►immune reaction; Linder S, Aepfelbacher M 2003 Trends Cell Biol 13:376.

Podospora anserina: n = 7, is a genetically well-studied ascomycete fungus.

Pof (Painting of fourth): *Drosophila* protein that binds only to the small 4th chromosome.

pogo: ►hybrid dysgenesis

Poikilocytosis: A hemolytic anemia with variable-shape red blood cells. The defect is due to the reduction of ankyrin binding sites or mutation in spectrin. ►ankyrin, ►spectrin, ►anemia

Poikiloderma Atrophicans (poikiloderma telangiectasia): ►Rothmund-Thompson syndrome

Poikiloploidy: In poikiloploidy, different cells of the body have different numbers of chromosomes.

Poikilothermy: In poikilothermy, the body temperature or the organism depends on the surrounding environmental conditions.

Point Mutation: Point mutations do not involve detectable structural alteration (loss or rearrangement of the chromosome), and are expected to involve base substitutions. The point mutation rate per locus in eukaryotes in about 10^{-5} and may vary from locus to locus and among various organisms. The rate per nucleotides of a locus is in the range of 10^{-8}. ►substitution mutation; Krawczak M et al 2000 Hum Mut 15:45.

Point-of-Care Technologies: Point-of-care technologies use small bench top analyzers (for example, saliva, blood gas, and electrolyte systems) and hand held, single use devices (such as urine albumin, blood glucose, and coagulation tests). Hand held devices have been developed using microfabrication techniques. They are outwardly simple but internally complex devices that perform several tasks for example, separate cells from plasma, add reagents, and read color or other end points (Price CP 2001 BMJ 322:1285). These are also called bedside technologies, because the samples do not have to be transferred for analysis to laboratories and therefore are much faster, especially when the newest microfluidic devices are used. ►microfluidics; Herr AE et al 2007 Proc Natl Acad Sci USA 104:5268.

Poise: ►viscosity, ►stoke

Poison Sequence: A poison sequence may be present in the genomes of some RNA viruses and thus even their cDNA cannot be cloned in full length in bacterial hosts. The problem may be overcome by propagating it in segments. (Brookes S et al 1986 Nucleic Acids Res 14:8231).

Poisson Distribution: Basically, an extreme form of the normal distribution, found when in large populations rare events occur at random, such as e.g., mutation. The general formula is e^{-m} (m^i/i!), and expanded e^{-m}(m^0/0!, m^1/m!, m^2/2!…m^i/i!), where e = base of natural logarithm (≅ 2.718), m = mean number of events, i = the number by which a particular m is represented at a given frequency, ! = factorial (e.g., 3! = 3 × 2 × 1, but 0! = 1). (See Fig. P90, ►negative binomial).

Pokemon: A repressor of the tumor suppressor ARF; thus, it represents a protooncogene. ►ARF, ►oncogenes; Maeda T et al 2005 Nature [Lond] 433:278.

poky (synonym: *mi-1*): A slow-growing and cyanide-sensitive respiration defective mitochondrial mutation in *Neurospora*. The basic defect appears to be a four-base deficiency of the 15 bp consensus at the 5′-end of the 19S rRNA of the mitochondria. Because of this defect, a further upstream promoter is used, making the transcript longer but during processing, shorter RNAs are made. It is analogous to the petite colony mutations of budding yeast. ►petite colony mutation, ►stoppers, ►mtDNA; Akins RA, Lambowitz AM 1984 Proc Natl Acad Sci USA 81:3791.

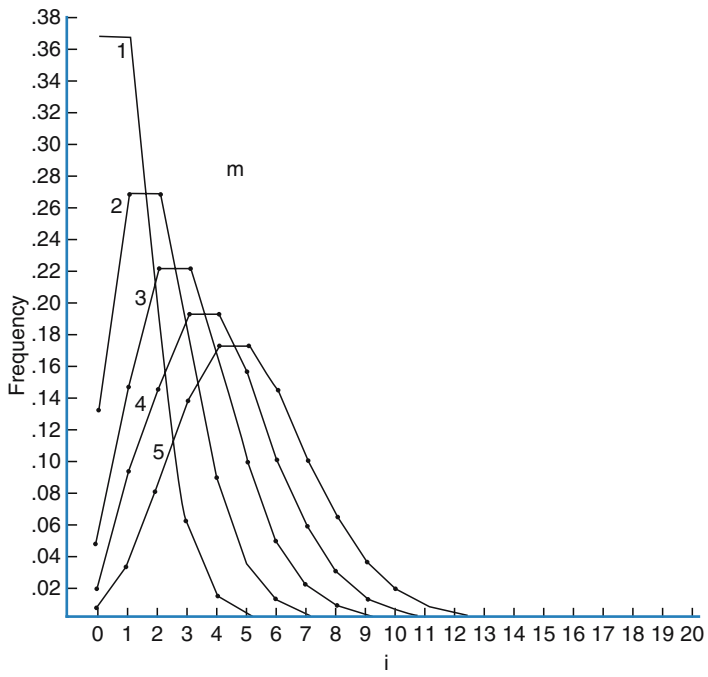

Figure P90. The Poisson distribution. Each curve corresponds to a numbered m value. The i classes represent the distribution of each mean value (m) with the ordinate indicating the frequencies

pol (bacterial RNA polymerase): pol synthesizes all the bacterial and viral RNAs in the bacterial cells. Its subunits are $\alpha\alpha\beta\beta'$ and σ. The σ subunit identifies the promoter sequences and is required for the initiation of transcription within the cell. After about a half dozen nucleotides are hooked up, it dissociates from the other subunits and further polymerization continues with the assistance of elongation protein factors. ►transcription, ►pol I, ►pol II, ►pol III eukaryotic RNA polymerases

pol I: Prokaryotic DNA polymerase, where the polymerase (Klenow fragment) and exonuclease functions are located about 30 Å distance apart in a subunit, and editing (removal of wrong bases) follows the melt and slide model. It plays a major role in prokaryotic repair and in the extension of the Okazaki fragments for joining them into a contiguous strand by ligase. It adds 10–20 nucleotides/second to the chain and so it is much slower than pol III. ►melt and slide model, ►DNA replication, ►replication fork, ►Klenow fragment, ►pol III, ►DNA ligase

pol I: RNA polymerase involved in the synthesis of ribosomal RNA (except 5S rRNA) in eukaryotes. By endonucleolytic cleavage, it generates the 3′ end of rRNA from longer transcripts. The upstream control regions for transcription initiation (binding proteins) vary from species to species. The human RNA pol I requires an activator UBF (upstream binding factor) and promoter selectivity factor SL1, including the TBF (TATA box binding protein) and associated subunits, TAF_I 110, TAF_I 63, and TAF_I 48. The former two keep contact with the promoter, whereas TAF_I 48 interacts with UBF and prevents RNA pol II from using this promoter site. ►ribosome; Reeder RH 1999 Progr Nucleic Acid Res Mol Biol 62:293; Grummt I 1999 Progr Nucleic Acid Res Mol Biol 62:109.

pol II: Prokaryotic DNA polymerase, the functions of which are not completely defined so far; it has known role in repair. ►DNA repair

pol II: The RNA polymerase transcribes messenger RNA and most of the snRNAs of eukaryotes with the assistance of different transcription factors. Nine or ten of its subunits are very similar to other polymerases; pol II has four to five smaller unique subunits. The two largest subunits are very similar in the three eukaryotic RNA polymerases and are similar also to prokaryotic subunits. It is most sensitive to α-amanitin inhibition (0.01 μg/mL). The site of sensitivity is in the largest 220 kDa polypeptide. This large subunit is activated by phosphorylation. At the carboxy terminal, there are 26 (yeast), 40 (*Drosophila*), or 52 (mouse) heptapeptide (Tyr-Ser-Pro-Thr-Ser-Pro-Ser) repeats. These repeats are essential for function. The Ser and Thr residues may be phosphorylated. Phosphorylation of the carboxy-terminal domain may affect the promoter-specificity of

the enzyme. The C-terminus of (CTD) of the large subunit is instrumental also in the processing of the 3′-end of the transcript and the termination of transcription downstream of the polyA signal. CTD does not seem to affect initiation of transcription but it also mediates the response to enhancers. This enzyme is different from RNA pol I and RNA pol III inasmuch that it requires a hydrolyzable source of ATP for the initiation of transcription. RNA pol II is different from the other polymerases in its requirement for a large array of special transcription factors that modulate the transcription of the thousands of proteins. ►transcription factors, ►regulation of gene activity, ►α-amanitin, ►transcription factories, ►RNA polymerase; Cramer P et al 2001 Science 292:1863.

pol III: Prokaryotic DNA polymerase, where the α subunit carries out the replication function and the ε-subunit is involved in editing (exonuclease) activity. It plays a major role in the replication of the leading and lagging strands. The replication has a speed of ≈1 kb/sec. There are only about 10–20 copies of the 10-subunit holoenzyme/cell. ►DNA replication, ►replication fork, ►core polymerase, ►replisome

pol III: RNA polymerase involved in the synthesis of transfer RNA, 5S rRNA, 7S rRNA and U6 snRNA in eukaryotes. Transcription of pol III is higher during S and G2 phases of the cell cycle than during G1. Many neoplastic cells display high pol III activity indicating that protein synthesis is demanded for tumorous growth. The RET protein appears to be a suppressor of increased pol III activity. ►tRNA, ►ribosomal RNA, ►ribosomes, ►La; Geiduschek EP, Tocchini-Valentini GP 1988 Annu Rev Biochem 57:873; Huang Y, Maraia RJ 2001 Nucleic Acids Res 29:2675.

pol IV: A low-fidelity lesion bypass DNA polymerase belonging to the Y family. ►Y-family DNAS polymerases, ►RNA polymerase

polα: DNA polymerase (encoded in fission yeast by gene *pol1/swi7*), replicating the nuclear DNA (lagging strand) in cooperation with the primase of eukaryotes. Its mutation may result in mutator activity (Gutiérrez PJA, Wang TS-F 2003 Genetics 165:65). ►lagging strand, ►replication fork, ►DNA polymerases, ►primase

pol β: A eukaryotic DNA repair polymerase. ►DNA polymerases

pol δ: A eukaryotic DNA polymerase (replicating the leading strand) of the nuclear chromosomes. ►replication fork, ►DNA polymerases

pol δ_2: Synonymous with pol ε. ►DNA polymerases

pol ε: A eukaryotic DNA polymerase (*cdc20*) with repair role. ►DNA polymerases

pol γ: A DNA polymerase replicating eukaryotic organelle DNA. ►θ type replication, ►DNA polymerases

pol ζ: A eukaryotic DNA polymerase without exonuclease activity. It is a repair enzyme inasmuch that it can bypass pyrimidine dimers more efficiently than polα. It is insensitive to 200 μM aphidi-colin (and in this respect it is similar to polβ and polγ) and also insensitive to dideoxynucleotide triphosphates (which inhibit polβ and polγ). It is moderately sensitive to 10 μM butylphenyl-guanosine triphosphates. It is relatively inactive with salmon sperm DNA or primed homo-polymers. ►DNA polymerases

Poland Syndrome: An autosomal dominant defect with low penetrance. the teratogenic effects of diverse exogenous factors complicate the inheritance pattern. It is characterized by fusion of fingers (syndactily), short fingers, and anomalies of chest and, sometimes, other muscles. ►limb defects, ►syndactily, ►penetrance, ►teratogenesis

Polar: Hydrophilic, i.e., soluble in water; molecules with polarized bonds.

Polar Body: ►gametogenesis in animals

Polar Body Diagnosis: In polar body diagnosis, the genetic constitution of the polar body is tested by molecular techniques prenatally. ►prenatal diagnosis

Polar Bond: A polar bond is covalent, yet the electrons are more firmly tied to one of the two molecules and therefore the electric charge is polarized.

Polar Coordinate Model: The polar coordinate model of regeneration states that when cells are in non-adjacent positions, the process of growth restores all intermediate positions by the shortest numerical routes. The shortest intercalation mandates that small fragments may undergo duplication and large fragments may require regeneration. The position of each cell on a collapsed cone (the idealized primordium) is specified by the radial distance from a central point at the tip of the cone and the circumferential position on the circle defined by the radius of the base. ►distalization; Held LI 1995 Bioessays 17:721.

Polar Cytoplasm: Polar cytoplasm is situated in the posterior (hind) portion of the fertilized egg cell. ►pole cells

Polar Ejection Force (PEF): Microtubule

Polar Granules: The polar granules are present in the posterior pole region of insect eggs and have maternal effect and germ cell specification roles during

embryogenesis. These granules are the mitochondrially coded 16S ribosomal RNA large subunits (mtRNA), exported from that organelle. ►animal pole, ►morphogenesis in *Drosophila*, ►RNA localization; Strom S, Lehmann R 2007 Science 316:392.

Polar Molecule: A polar molecule is generally soluble in water; the distribution of the positive and negative charges are not even, thus resulting in a polarized effect.

Polar Mutation: A polar mutation may be a base substitution (nonsense mutation), insertion, frame shift, or any chromosomal alteration that affects the expression of genes down-stream in the transcription–translation system. ►frame shift mutation; Jacob F, Monod J 1961 Cold Spring Harbor Symp Quant Biol 26:193.

Polar Nuclei: The polar nuclei occur in the embryosac of plants, and are formed at the third division of the megaspore. After they have fused (n + n) and have been fertilized by one sperm (n) they give rise to the triploid (3n) endosperm nucleus. ►megagametophyte, ►embryosac

Polar Overdominance: An unusual type of inheritance, i.e., mutants heterozygous for the dominant *callypige* gene of sheep (chromosome 18) display the (*CLPG*) allele only when inherited from the males but not from the females. The phenotype is a muscular hypertrophy resulting from the cis-regulation of four imprinted genes. ►imprinting, ►overdominance; Charlier C et al 2001 Nature Genet 27:367; Smit M et al 2003 Genetics 163:453.

Polar Transport: Certain metabolites move only in one direction in the plant body, e.g., the auxins under natural conditions are synthesized in the tissues over the ground and then move toward the roots.

Polarimeter: The polarimeter measures the rotation of the plane of polarized light.

Polarisome: A polarisome defines polarity within a cell with the aid of several proteins. (See Weiner OD 2002 Curr Opin Cell Biol 14:196).

Polarity, Embryonic: Embryonic polarity is required for differentiation and requires asymmetric cell divisions. In *Caenorhabditis*, the PAR proteins (serine/threonine kinase) control embryonic polarity and a non-muscle type myosin II heavy chain protein (NMY-2) is a cofactor of this polarity. Upon fertilization the Rho guanosine triphosphatase-activating protein CYK-4—enriched in the sperm—and the RhoA guanine exchange factor ECT-2-modulate myosin light chain activity and create an actomyosin gradient, which determines the anterior domain in the one-cell embryo in *Caenorhabditis* (Jenkins N et al 2006 Science 313:1298). In *Drosophila*, the major body axes, primarily the anterior-posterior polarity are controlled by the gurken-torpedo gene products, but other genes are also involved. Polarity may be achieved either by the asymmetric distribution of proteins or mRNA. ►morphogenesis in *Drosophila*, ►differentiation, ►polar cytoplasm, ►RNA localization, ►BUD, ►RHO, ►myosin, ►actomyosin; Drees BL et al 2001 J Cell Biol 154:549; Wodarz A 2002 Nature Cell Biol 4:E39; Frizzled pathway: Seifert JRK, Mlodzik M 2007 Nature Rev Genet 8:126.

Polarity of Hyphal Growth: See Fig. P91, Nelson WJ 2003 Nature [Lond] 422:766.

Figure P91. Polarity of hyphal growth

Polarity Mapping: ►mapping mitochondrial genes

Polarization: The distortion of the electron distribution in one molecule caused by another. ►bouquet of chromosomes

Polarized Differentiation: the basis of morphogenesis, chemotactic response, response to pheromones, etc. Polarized differentiation and growth is typical for neural and microtubule growth, for the pollen tubes, and for the roots of plants. Neuronal polarization requires the activity of SAD kinases in mammals (Kishi M et al 2005 Science 307:929). ►asymmetric cell division; Hepler PK et al 2001 Annu Rev Cell Dev Biol 17:159; Science [2002] 298:1941–1964.

Polarized Light: Polarized light exhibits different properties in different directions at right angles to the line of propagation. Specific rotation is the power of liquids to rotate the plane of polarization.

Polarized Recombination: ►polarized segregation

Polarized Segregation: Polarized segregation may be brought about by meiotic anomalies, e.g., in maize plants heterozygous for some knobbed chromosomes (and syntenic markers) are preferentially included into the basal megaspore. Polarized segregation has been observed as a result of gene conversion, e.g., in *Ascobolus immersus* alleles of the *pale* locus in the cross $\frac{188 w^+}{188^+ w}$ segregated in both cases, it is 6:2, but in the first case the results were (4*[188]* + 2 *[w^+]*): 2 (*w*) whereas in the cross $\frac{w137^+}{w^+137}$ the conversion asci were (4 *[w]* + 2 *[137]*): 2 (w^+). The genetic order of these alleles were *188 w 137*. Thus in the first cross *white*

P

was in the minority class whereas in the second cross it was part of the majority class. ►gene conversion, ►meiotic drive, ►map expansion; Whitehouse HLK, Hastings PJ 1965 Genet Res 6:27.

Polarizing Microscope: The polarizing microscope uses a *polarizer* (a polaroid screen) in front of the light beam and an *analyzer* (permitting rotation) over the eyepiece. The anisotropic specimens (having difference in transmission or reflection depending on the angle of light) will display optical contrast. ►microscopy

Polarography: Electrochemical measurement of reducible elements.

Polaroid Camera: The Polaroid camera was developed during the 1940s and has found many uses in biological laboratories because it can provide almost immediate negative or positive images for recording observations such as those of electrophoretic gels. The combined developing and fixing solution is contained in between the exposed negative film and the receiving film or paper and when the storage "pod" bursts under pressure of pulling, the processing is carried out within the camera. For the majority of tasks, the digital cameras are even better suited for fast imaging.

Polaron: The part of a locus within which gene conversion (or recombination) is polarized. ►gene conversion, ►polarized segregation; Whitehouse HLK, Hastings PJ 1965 Genet Res 6:27.

Pole Cells: Pole cells localized in the posterior-most part of the cellularized embryo and give rise eventually to the germline. ►germline

Polintons: Typically, 15–20 kb long transposable elements in a wide range of lower and higher eukaryotes. They require a unique set of proteins for transposition such as protein-primed DNA polymerase B, retroviral integrase, cysteine protease, and ATPase. They show a 6 bp target site duplication and long inverted terminal repeats with 5′-AG and 3′-TC termini (Kapitonov VV, Jurka J 2006 Proc Natl Acad Sci USA 103:4540). ►transposable elements

Polioviruses: Icosahedral single-stranded RNA viruses with about 6.1 kb RNA in a total particle mass of about 6.8×10^6 Da; Type 1 was responsible for about 85% of the polyomyelitis (infantile paralysis) cases before successful vaccination (live oral, Sabin or inactivated, Salk) began to be widely used in the developed countries (see Fig. P92). These small RNA viruses are highly mutable because their genetic material lacks repair systems. The three serotypes produce a cell-surface receptor (PVR) by alternative

Figure P92. Apparent polio-stricken leg on a more than 3000 year old Egyptian hieroglyph

splicing of its transcript. Infectious poliovirus has been sythetized *de novo* without a natural template (Cello J et al 2002 Science 297:1016). Susceptibility to poliovirus was located to human chromosome 19q12-q13. Mice are very resistant to this virus because they lack the membrane receptor for the infection. ►picornaviruses, ►IRES, ►synthetic genes

Polled: A dominant/recessive gene (PIS) in goats and cattle, responsible for lack of horns/inter-sexuality. The forkhead transcription factor (FOXL2)—responsible also for blepharophimosis—may be involved. In goats, an 11.7 kb deletion at 1q43 (homologous to human band 3q23) normally encodes two mRNAs. The FOXL2 transcript is homologous with the human blepharophimosis syndrome gene. ►blepharophimosis; Crisponi L et al 2001 Nature Genet 27:159; Pailhoux E et al 2001 Nature Genet 29:453.

Pollen: The male gametophyte of plants developing from the microspores by two postmeiotic divisions (see Fig. P93). The first division results in the formation of a vegetative and a generative cell. The round vegetative cell directs the elongation of the pollen tube growing through the pistil toward the ovule. Pollen tube growth is guided by sporophytic secretions (GABA, arabinogalactans and

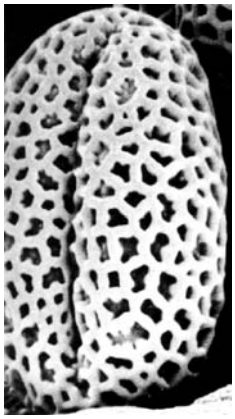

Figure P93. The sculptured surface of the mature pollen of *Arabidopsis*. (From Craig S, Chaudhury A 1994 In: Bowman JL (Ed.) *Arabidopsis*: An Atlas of Morphology and Development. Courtesy of Bowman JL By permission of Springer-Verlag, New York)

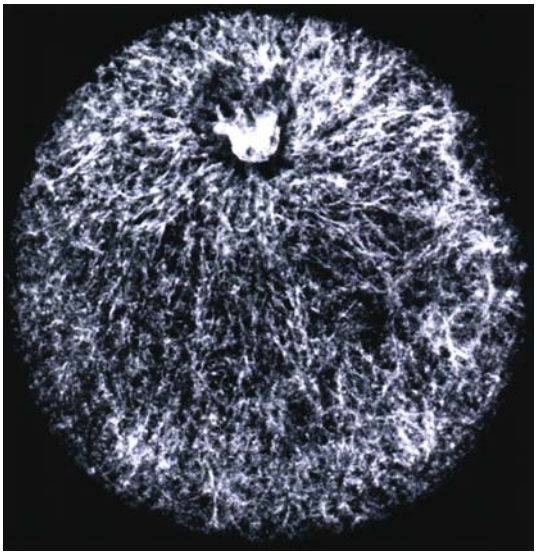

Figure P94. Fluorescent-phalloidin staining of the F-actin cytoskeleton in maize pollen. The bright spot on top is the pollen tube initial. (Courtesy of Dr. Chris Staiger. See Gibbon BC et al 1999 Plant Cell 11:2349)

proteins) (see Fig. P94). Synergids provide attraction by the 94-amino acid ZmEA1 protein in maize (Márton M et al 2005 Science 307:573).

The crescent-shaped generative cells may divide before or after the shedding of the pollen grains. One of them fertilizes the egg and thus, gives rise to the diploid embryo, the other fuses with the diploid polar cell in the embryosac and thus contributes to the formation of the endosperm. The pollen tube elongates quite rapidly; it may grow 15 cm in just 5 to 15 h. A protein that is glycosylated in that tissue regulates the pollen tube elongation. In allogamous species, a single individual may shed over 50,000,000 pollen grains whereas in autogamous species the number of pollen grains per anther may not exceed a couple of hundreds. Since the pollen grain is haploid and may be autonomous (gametophytic control), it may express its genetic constitution independently from the genotype of the anther tissues (e.g., waxy pollen, various color or sterility alleles), in some instances, however, the morphology of the pollen grain is under sporophytic control. Since the pollen is a more independent product than the megaspore, it is more likely to suffer from genetic defects for which the surrounding tissues cannot compensate, therefore pollen sterility is more common in plants than female sterility. However, pollen sterility may not necessarily affect the fertility of the individuals because of the abundance of functional pollen grains in case of heterozygosity for the defects. Under normal atmospheric conditions (high humidity) and high temperature, the viability of the pollen is maintained (depending on the species) for a few minutes or for several hours. In a refrigerator, at low humidity the viability of the pollen can be extended substantially. Freeze-dried and properly stored pollen of several species retains its ability to fertilize for years. Insects may carry viable pollen for long distances. According to a study, in rye populations cross-pollination (mediated by wind) may occur to 50% at 100 m distance and to 20% at about 400 m distance, but only to 3% at 600 to 700 m. Other studies reported in rye only 7% cross-pollination within a distance of 20 m. Creeping bentgrass (*Agrostis stolonifera*) pollen, transgenic for a resistance marker (5-enolpyruvylshikimate-3-phosphate synthase), was spread by the wind primarily within a distance of 2 km but some dispersal occurred up to 21 km (Watrud LS et al 2004 Proc Natl Acad Sci USA 101:14533). The prevailing environmental conditions (humidity, temperature, wind, etc.) and the quantity of the pollen influences the spread and viability. These problems gained new interest with the use of genetically engineered crops that are opposed by some environmentalists. The extracellular matrix of the pollen contains proteins, which recognize species-specificity and efficient pollination (Myfield JA et al 2001 Science 292:2482). These proteins are lipid-binding oleosins and lipases. ►microsporogenesis, ►gametogenesis, ►pollen tetrad, ►gametophyte, ►self-incompatibility, ►cross-pollination, ►GMO, ►autogamy, ►allogamy

Pollen Competition: ►certation

Pollen-Killer: Pollen-killer or spore-killer genes in wheat, tomato, and tobacco render the pollen incapable of functioning effectively in fertilization and may cause segregation distortion. ►segregation distorter, ►pollen tube competition, ►killer strains, ►killer plasmids, ►killer genes

Pollen Mother Cell: Microspore mother cell, microsporocyte. ►gametogenesis

Pollen Sterility: The inability of the pollen to function during fertilization. It can frequently be detected by the poor staining of the pollen grains with simple nuclear stains (acetocarmine, acetoorcein, etc.). Deletions, translocations, and inversion heterozygosity generally result in pollen sterility. Mitochondrial plasmids may also be responsible for some types of male sterility. ►pollen, ►certation, ►gametophyte, ►cytoplasmic male sterility, ►fertility restorer genes

Pollen Tetrad: The four products of a single male meiosis (see Fig. P95). The components of the pollen tetrad may not stick together and may shed in a scrambled state. In some instances (*Salpiglossis, Elodea*, some orchids), the tetrads remain together, however, in a way similar to the unordered tetrads of fungi. In *Arabidopsis*, induced mutations (*qrt1, qrt2, quartet*) cause the four pollen grains to stay together because of the alteration of the outer membrane of the pollen mother cell. Each tetrad may then fertilize four ovules. ►tetrad analysis

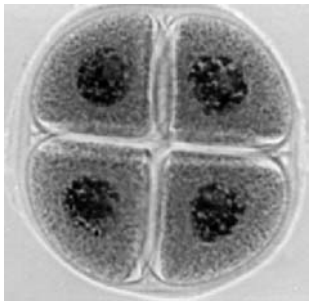

Figure P95. Pollen tetrad

Pollen Tube: In the majority of plants, the time between pollination and fertilization takes 24 to 48 h or less. In the alder tree (*Alnus*) the pollen tube travels slowly in the pistil (for about one month) because the ovary matures late and it arrives at fertilization in five successive steps. Also in some species, the ovaries may have multiple megaspore tetrads although, generally only one is fertilized (Sogo A, Tobe H 2005 Proc Natl Acad Sci USA 102:8770). ►pollen, elongating pollen tube in Figure P96, ►synergid, ►GABA, ►gametophyte, ►double fertilization; Palavinelu R, Preuss D 2000 Trends Cell Biol 10:517.

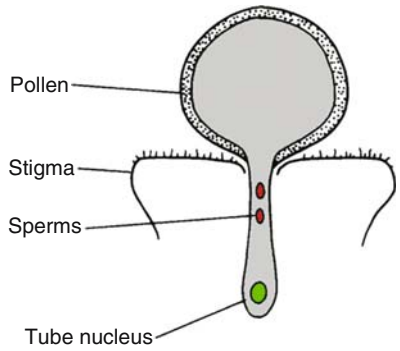

Figure P96. Pollen tube germination

Pollen-Tube Competition: ►certation

Pollination: The transfer of the male gametophyte to the stigmatic surface of the style (ovary). Obligate allogamous plant populations may suffer if the pollinator insect populations are reduced by adverse environmental conditions (Vamosi J C et al 2006 Proc Natl Acad Sci USA 103:956). ►gametophyte, ►autogamy, ►allogamy, ►fertilization, ►self-sterility

Pollinium: A mass of pollen sticking together and may be transported as such by the pollinator insects or birds.

Pollitt Syndrome: ►trichothiodystrophy

Pollution: Spoiling the environment by the release of unnatural, impure, toxic, mutagenic, carcinogenic, or any other undesirable and unaesthetic material, or to disturb nature by sound, odor, heat, and light. Pollution may cause mutation, cancer, and various other diseases. ►DNA-zyme; http://www.scorecard.org.

Polo: A 577-amino acid serine/threonine protein kinase of *Drosophila*, required for mitosis. It regulates centromeric cohesion protein MEI-S332 (Clarke AS et al 2005 Dev Cell 8:53). During interphase, it is predominantly cytoplasmic but at the end of prophase it associates with the chromosomes until telophase. Loss of polo kinase 4 allele(s) increases the probability of mitotic errors and cancer. In about 60% of the cells of mice, loss of heterozygosity takes place (Ko MA et al 2005 Nat Genet 37:883). ►CDC5, ►FEAR, ►cohesin; Llamazares S et al 1991 Genes Dev 5:2153; Alexandru G et al 2001 Cell 105:459.

Polony (polymerase colony): A small batch of DNA synthesized by PCR with the assistance of a primer to

be used for sequencing. The PCR colonies on the glass microscope slide are the "polonies." On a single slide in the polyacrylamide film, as many as 5 million clones can be amplified. The amplified products stay at the vicinity of the linear DNA. If acrydite modification is used, the DNA is covalently attached to the polyacrylamide matrix and thus further enzymatic modifications are possible on all clones. The technology is well suited for genotyping and localizing of SNPs. ►PCR, ►SNIPs; Mitra RD, Church GM 1999 Nucleic Acids Res 27(24):e34; Mitra RD et al 2003 Proc Natl Acad Sci USA 1000:5926.

Poly I-G: A DNA strand containing more cytosine is called heavy chain of a DNA double helix because it binds more of the polyI-G (inosine-guanosine) sequences. Ultracentrifugation in CsCl separates these DNA heavy strands. ►ultracentrifuge, ►density gradient centrifugation, ►DNA heavy chain, ►inosine

PolyA$^+$ Element: Transposons without long terminal repeats but poly-A sequences at the 3′-OH end. The RNA elements are usually mobilized via a DNA transcript with the aid of their encoded reverse transcriptase. Such elements are L1 (LINE) in mammals, the TART of *Drosophila*, the TRAS1 of silkworm, or the yeast Ty5 telomere-specific elements. Other polyA$^+$ elements (L1, I, and fungal and plant elements) can target a variety of other sites. ►TART, ►hybrid dysgenesis, ►transposable elements

polyA mRNA: Eukaryotic mRNAs post-transcriptionally polyadenylated at the 3′ tail before leaving the nucleus. Subsequently, in the cytoplasm, the tail may be reduced to 50–70 residues or further extended to hundreds. Polyadenylation improves the stability and efficiency of translation in cooperation with mRNA cap. The polyA tail and the mRNA cap seem to cooperate in the initiation of translation. PolyA tail is frequently added also to bacterial RNA. The addition of polyA tail accelerates the decay of RNA I of *E. coli*. All the data are consistent with polyadenylation being part of a quality control process targeting folded bacterial RNA fragments and nonfunctional RNA molecules to degradation. In *Escherichia coli*, polyadenylation may directly control the level of expression of a gene by modulating the stability of a functional transcript. Inactivation of poly(A)polymerase I causes overexpression of glucosamine-6-phosphate synthase (GlmS) and both the accumulation and stabilization of the *glmS* transcript (Joanny G et al 2007 Nucleic Acids Res 35:2494).

The majority of eukaryotic viruses (except areana- and reoviruses) also produce a poly A tail. In *Drosophila*, the length of the poly(A) tail may be correlated with the function in the differentiation of the mRNA. The regulatory mechanism of polyadenylation is interchangeable between mouse and *Xenopus*. Some genes use alternative polyadenylation sites (Edwalds-Gilbert G et al 1997 Nucleic Acids Res 25:2547). ►polyadenylation signal, ►mRNA tail, ►RNA I, ►PABP, ►mRNA degradation, ►capping enzymes, ►eIF; de Moor CH, Richter JD 2001 Int Rev Cytol 203:567; http://polya.umdnj.edu/.

polyA Polymerase (PAP): adds the polyA tail post-transcriptionally to the eukaryotic mRNA and antisense RNA transcripts (see Fig. P97). In yeast, at least two other genes *RNA14* and *RNA15* are involved in the processing of the 3′-end of the pre-mRNA.

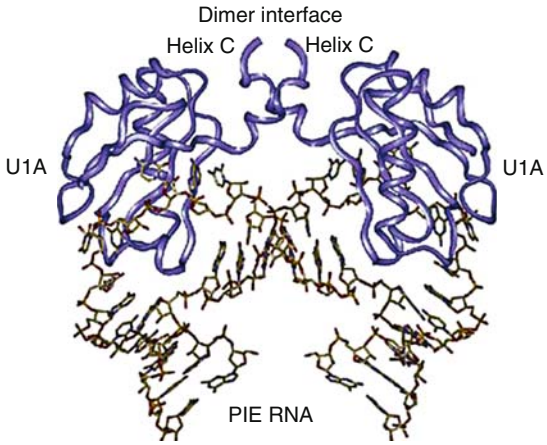

Figure P97. Poly(A) polymerase is regulated by inhibition (or stimulation) by the polyadenylation inhibition RNA element (PIE). PIE forms a trimolecular complex including the two U1A protein molecules. The U1A consists of a four-stranded β-sheet and two α-helices. The two C helices of the protein interface. The PIE RNA, which contains two asymmetric internal loops is separated by four Watson-Crick-paired nucleotides. (From Puglisi JD 2000 Nature Struct Biol 7:263)

E. coli also encodes at least two PAP enzymes. PolyA polymerase also facilitates the degradation of mRNA because it provides single-strand tails for polynucleotide phosphorylase. Bacterial PAP and tRNA nucleotidyl transferase are highly similar in structure but different in function inasmuch the latter catalyzes the addition of CCA to the 3′-end of tRNA. The C-terminal domain of nucleotidyl transferase restricts polymerization to these three nucleotides whereas a 27-aminoacid sequence determines whether the protein becomes a transferase or PAP. Both proteins have identical nucleotide recognition and incorporation domains (Betat H et al 2004 Mol Cell 15:389). ►mRNA tail, ►polyadenylation signal, ►polynucleotide phosphorylase; Dickson KS et al

2001 J Biol Chem 276:41810; Steinmetz EJ et al 2001 Nature [Lond] 413:327.

polyA Tail: ►polyadenylation signal, ►polyA mRNA

Polyacrylamide: See Fig. P98, ►electrophoresis, ►gel electrophoresis

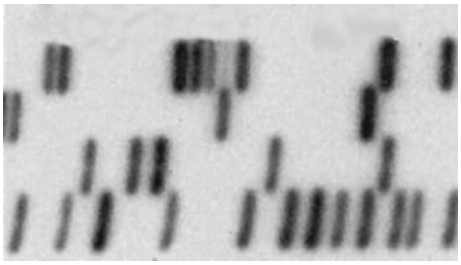

Figure P98. Polyacrylamide gel

Polyadenylation Signal: The endonucleolytic processing of the primary transcript of the majority of eukaryotic genes is followed by post-transcriptional addition of adenylic residues downstream of the structural gene. The consensus signal for the process is 5′-AAUAAA-3′ in animals and fungi, about half of the plants use the same signal, the rest rely on diverse signals. In humans, ~54%, and in mouse, ~32% of the genes have alternative polyadenylation sites and different cleavage sites resulting in heterogeneity of the transcripts, which may represent a type of regulation of gene expression (Tian B et al 2005 Nucleic Acids Res 33:201). In eukaryotes, the number of added A residues might vary from 50 to 250. The crystal structure of the 73 kDa subunit of the human polyadenylation-specificity endonuclease has been determined (Mandel CR et al 2006 Nature [Lond] 444:953).

Polyadenylation is under the control of several genes (see Fig. P99). The RNA transcript of eukaryotes besides the poly(A) signal contains a CA element (PyA in yeast) and a GU-rich downstream element.

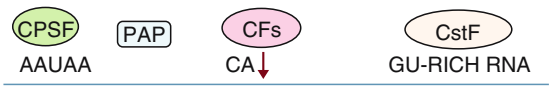

Figure P99. Some of the mechanisms in polyadenylation

To the AAUA AA *positioning element*, binds the *polyadenylation specificity factor* (CPSF) that is a tetrameric protein consisting of 160, 73, 100, and 33 kDa subunits. The *cleavage stimulating factor* (CstF), a trimeric protein of 64, 77, and 50 kDa subunits, binds to GU-rich element of the RNA. The *polyadenylation polymerase* protein (PAP) binds downstream of the CPSF binding sites. The *cleavage factors* (CFI) and (CFII) are positioned upstream of the GU-rich element and they terminate the mRNA. The polyadenylation complex of yeast is somewhat different. The PABP (poly-A-binding protein, 70 kDa) regulates mRNA stability, translation, and degradation. CPEB (cytoplasmic element binding protein), maskin, and cyclin B1 are regulators of polyadenylation and the transcription of some mRNAs. Poly(A)-specific ribonuclease (PARN) is a cap-interacting 3′ exonuclease. In cooperation with the cap, it mediates de-adenylation from cis position, or at low concentration it may be inhibitory to de-adenylation. From trans position, it inhibits de-adenylation if its concentration is high. The poly(A) tail, in synergy with the mRNA cap, stimulates the initiation of translation. The poly(A) binding protein (PABP) interacts with eIF4G of the eIF4F complex and eIF4E interacts with the cap and stabilizes mRNA. PABPs are located both in the nucleus and in the cytoplasm. In the human testes, a specific poly(A) binding protein occurs that is absent from other tissues (Féral C et al 2001 Nucleic Acids Res 29:1872). De-adenylation of the tail initiates mRNA decay and when less than ten A residue is left, an exonuclease attacks the RNA in 5′→3′ direction (Martînez J et al 2001 J Biol Chem 276:27923). In prokaryotes, rarely a few (14–60) adenine residues are also found at the mRNA 3′-terminus in 1 to 40% of the cases. In bacteria, *host factor q* (Hfq) plays a role similar to PABP. It stimulates the elongation of the polyA tail by poly(A) polymerase I (PAP) and protects against exoribonuclease attack. Some adenine sites are found in about 30% of both the early transcripts (transcribed by host polymerase) and late transcripts (transcribed by viral polymerase). Sometimes the poly-A sequence has interspersed other bases and may be located also within coding sequences. An interspersed long poly-(A) sequence was detected also in chloroplast RNA transcripts. In mitochondria, the poly-A tract (35–55 A residues) directly attaches to the termination codon without an untranslated sequence, after the endonucleolytic cleavage of the polycistronic transcript. In liver cancer, mitochondria tails of hundreds of As have been observed. In prokaryotes, two similar (36 and 35 kDa) poly-A polymerases with overlapping functions have been identified. With the exception of histone transcripts, all eukaryotic mRNAs appear polyadenylated, although some can be processed to become non-polyadenylated and the two types may coexist (bimorphic transcript). Polyadenylation of RNA in bacteria regulates plasmid replication and the degradation of RNAI. In yeast, the Trf4 complex recruits exosomes and the incorrectly folded polyadenylated RNA is degraded (Vañácová S et al 2005 PLoS Biol 3(6):e189). (In *Archaea* short poly-A tracts

exist). Cordycepin (3′-deoxyadenosine) is an inhibitor of polyadenylation.

In the *Drosophila melanogaster* genome, 17 polyadenylated sequences were detected without protein coding transcripts, yet many of these sequences were conserved in related species indicating some roles because of their conservation (Tupy JL et al 2005 Proc Natl Acad Sci USA 102:5495). Let-7 miRNPs, containing, Argonaute and GW182, dampen the synergistic enhancement of translation by the 5′-cap and 3′-poly(A) tail, resulting in translational repression (Wakyama M et al 2007 Genes Dev 21:1857). ►mRNA tail, ►U1 RNA, ►polyA polymerase, ►RNA I, ►cleavage stimulation factor, ►PABp, ►mRNA circularization, ►eIF4, ►TRAP, ►symplekin, ►microRNA, ►Argonaute, ►GW body; Hirose Y, Manley JL 1998 Nature [Lond] 395:93; Sarkar N 1997 Annu Rev Biochem 66:173; Beaudoing E et al 2000 Genome Res 10:1001; Mendez R Richter JD 2001 Nature Rev Mol Cell Biol 2:521; Wang L et al 2002 Nature [Lond] 419:312; http://polya.umdnj.edu/; http://polya.umdnj.edu/PolyA_DB2.

Poly(ADP-Ribose) Polymerase: A DNA-binding enzyme but it appears to have no indispensable function.

Polyamides: Polyamides containing *N*-methylimidazole and *N*-methylpyrrole amino acids have high affinity for specific DNA sequences and may regulate the transcription similarly to DNA binding proteins. ►binding proteins, ►inhibition of transcription, ►netropsin, ►lexitropsin; Maeshima K et al 2001 EMBO J 20:3218.

Polyamidoamine Dendrimers (PAMAM): Highly branched, soluble, non-toxic molecules with amino groups on their surface. They are suitable for attaching to this surface antibodies, various pharmaceuticals, and DNA. They are effective vehicles for transfection. (See Gebhart CL, Kabanov AV 2001 J Control Release 73:401).

Polyamines: Polyamines are various protein molecules derived in part from arginine and present in cells in millimolar concentrations, yet have important roles in RNA and DNA transactions, replication, supercoiling, bridging between strands, binding phosphate groups, biosynthesis, degradation, etc. Typical polyamines are spermine, spermidine, putrescine, etc. ►antizyme,►lexitropsins; Coffino P 2001 Nat Rev Mol Cell Biol 2:188; van Dam L et al 2002 Nucleic Acids Res 30:419.

Polyandry: A form of polygamy involving multiple males for one female. It may have the advantage of reducing the relatedness within colonies of social insects and thereby increasing fitness. In the live-bearing pseudoscorpions (*Cordylochernes scorpioides*), outbred embryos have beneficial effects on inbred half-siblings in mixed-paternity broods developing in the external, translucent brood sac and fed by nutrients of the maternal reproductive tract by an unclear mechanism (Zeh JA, Zeh DW 2006 Nature [Lond] 439:201). Honeybee queen matings with several drones enhances productivity and fitness of the colony (Mattila HR, Seeley TD 2007 Science 317:362). ►fitness; Tregenza T, Wedell N 2002 Nature [Lond] 415:71.

Polyaromatic Compounds: Polyaromatic compounds include various procarcinogens and promutagens, such as benzo(a)pyrene, dibenzanthracene, methylcholanthrene, etc. ►polycyclic hydrocarbons.

Polybrene (hexadimethrine bromide): A polycation used for introduction of plasmid DNA into animal cells; it is also an anti-heparin agent and an immobilizing agent in Edman degradation. Polybrene may have different toxicity to various cells. ►transformation genetic animal cells, ►heparin, ►Edman degradation

Polycentric Chromosome: ►neocentromeres

Polychlorinated Biphenyl (PCB): A highly carcinogenic compound and an inducer of the P-450 cytochrome group of monooxygenases. It had been used in electrical capacitors, transformers, fire retardants, hydraulic fluids, plasticizers, adhesives, pesticides, inks, copying papers, etc. *Pseudomonas* sp. KKS102 is capable of degrading PCB into tricarboxylic acid cycle intermediates and benzoic acid. ►microsomes, ►S-9, ►P-450, ►carcinogen; Ohtsubo Y et al 2001 J Biol Chem 276:36146.

Polychromatic: A polychromatic substance is stainable by different dyes or displays different shades when stained.

Polycistronic mRNA: A contiguous transcript of adjacent genes, such as exist in an operon but may also be formed in the short genes of eukaryotes, e.g., oxytocin. The *Trypanosomas* produce multicistronic transcripts. A gene (*mlpt*) of *Tribolium* involved in body segmentation also produces polycistronic mRNA. ►operon, ►oxytocin, ►*Trypanosoma*, ►*Caenorhabditis*, ►*Tribolium*

Polyclonal Antibodies: Polyclonal antibodies are produced by a population of lymphocytes in response to antigens. These are not homogeneous as are the monoclonal antibodies. ►monoclonal

Polycomb (*Pc*, chromosome 3-47.1): The *Drosophila* gene is a negative regulator of the *Bithorax* (*BXC*) and *Antennapedia* (*ANTC*) complexes (see Fig. P100). The homozygous mutants are lethal and the locus

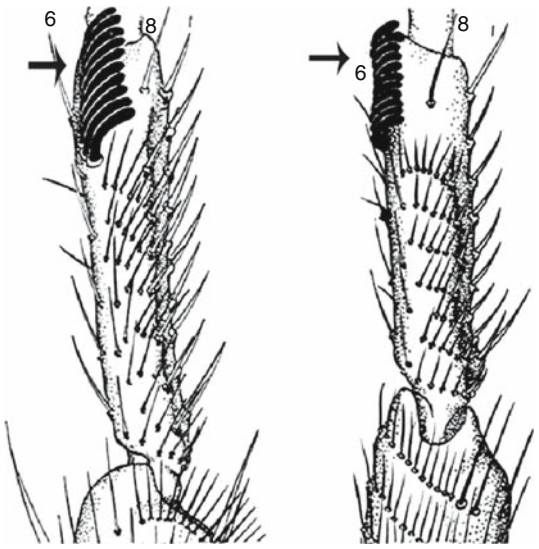

Figure P100. Sex combs on the second legs of male *Drosophila* in the *Sex comb extra* (*Scx*, 3.47, at left) and *Scx-Pc* (at right) homeotic mutants. Similar extra sex combs appear also on the third leg whereas sex combs in the wild type are limited to the first pair of legs. (After Hannah-Alava A 1958 Genetics 43:878)

(and its homologs in vertebrates [*M33* in mice]) is involved in the repression of homeotic genes, which control body segmentation. *Pc* is a member of a group (*Pc-G*) of repressors of homeotic genes (Cao R et al 2002 Science 298:1039). Although *Pc* is located in the euchromatin, it is involved in the silencing of genes by heterochromatin (Francis N et al 2004 Science 306:1574). Genes have been identified that are targeted for transcriptional repression in human embryonic stem (ES) cells by the Pc-G proteins suppressor of zeste 12 (*SUZ12*) and embryonic ectoderm development (*EED*), which form the Polycomb repressive complex 2 (*PRC2*) and which are associated with nucleosomes that are trimethylated at Lys27 of histone H3 (H3K27). Stem cell occupancy by *SUZ12* and *EED* and the trimethylation status of H3K27 for 77/177 genes showed evidence of cancer-associated DNA methylation when compared with matched normal colorectal mucosa. The observations suggest that the first predisposing steps towards malignancy may occur very early and are consistent with reports of field changes in histologically normal tissues adjacent to malignant tumors. These results provide a mechanistic basis for the predisposition of certain promoter CpG islands to cancer-associated DNA hypermethylation as an early epigenetic cancer marker (Widschwendter M et al 2007 Nat Genet 39:157).

Pc is involved in Histone2A ubiquitylation and the inactivation of mammalian X chromosome (de Napoles M et al 2004 Dev Cell 7:663). Insertion into the 5th exon of *M33* caused male→female sex-reversal. *Pc* is required for the activation of other silencing elements and its mutation may lead to derepression of these elements. The suppressive effect of *Pc* may be associated with chromatin remodeling and histone deacetylation. The Polycomb group of proteins forms a large complex and the TATA-box-binding proteins, Zeste and others, are associated with the general transcription machinery (Czermin B et al 2002 Cell 111:185). The SUZ12 subunit of the Polycomb Repressive Complex 2 (PRC2) extends over 200 genes encoding developmental regulators of human embryonic stem cells (such as Nanog, Oct4, Sox2, RNAp2 and SUZ12) (see Fig. P101). These genes are transcriptionally repressed because in the nucleosomes histone H3K27 is trimethylated. The PRC2 target genes are repressed in order to maintain pluripotency of these cells but they are activated during differentiation (Lee TI et al 2006 Cell 125:301). The PRC1 and PRC2 polycomb complexes co-occupy 512 genes and bind hundreds of others (►Venn diagram) coding for transcription factors during mouse embryonic development until differentiation (Boyer LA et al 2006 Nature [Lond] 441:349). ►morphogenesis in *Drosophila*, ►transdetermination, ►*SWI*, ►homeobox, ►homeotic genes, ►chromodomain, ►sex-reversal, ►*w* locus, ►*zeste*, ►*Antennapeadia*, ►*Bithorax*, ►*trithorax*, ►chromatin remodeling, ►nucleosomes, ►histone deacetylase, ►histones, ►TBP, ►transcription factors, ►Lyonization, ►ubiquitin, ►epigenesis, ►stem cells, ►genetic networks, ►pairing-sensitive repression; Breilling A et al 2001 Nature [Lond] 412:651; Simon JA, Tamkun JW 2002 Curr Opin Genet Dev 12:210; Polycomb repressor complex in epigenesis: Kuzmichev A et al 2005 Proc Natl Acad Sci USA 102:1859; review: Schwartz YB, Pirrotta V 2007 Nat Rev Genet 8:9; review: Schuttengruber B et al 2007 Cell 128:735.

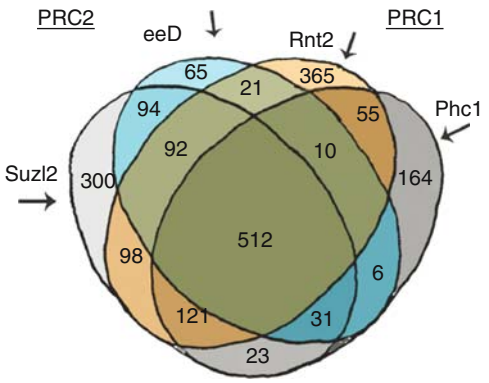

Figure P101. Polycomb group proteins overlap and repress many developmental regulators of mouse

Polycross: An intercross among several selected lines to produce a "synthetic variety" of a crop (See Tysdal HM et al 1942 Alfalfa Breeding, Nebr Agric Exp Sta Res Bull 124, Lincoln, Nebraska).

Polycyclic Aromatic Hydrocarbons (PAH): Generally, carcinogenic and mutagenic compounds. They become more active during the process of attempted detoxification by the microsomal enzyme complex. PAHs are the products of burning organic material (coal, charbroiling, smoking, etc.). Mice oocytes exposed to PAHs suffer apoptosis by activation of BAX. ►carcinogens, ►procarcinogens, ►mutagens, ►promutagens, ►benzo(a)pyrene, ►environmental mutagens, ►PAH, ►BAX, ►apoptosis; Matikainen T et al 2001 Nature Genet 28:355.

Polycystic Lipomembraneous Osteodysplasia with Sclerosing Leukoencephaly (PLOSL, Nasu-Hakola disease, 19q13.1): A recessive psychosis turning into presenile dementia and bone cysts limited to the wrists and ankles. Prevalence in Finland is 2×10^{-6}. The basic problem is a loss of function of the TYROBP/DAP12 tyrosine kinase binding transmembrane protein, an activator of killer lymphocytes. ►killer cells

Polycystic Kidney Disease (PKD): PKD occurs in two main forms, and within each several form variations exist (see Fig. P102). The short arm of human chromosome 16p13.31-p13.12 apparently controls the adult type dominant (ADPKD), which involves fragility of the blood vessel walls. In the autosomal recessive ARPKD, the basic defect is in the Ca^{2+}-permeable non-selective cation channel. About 15% of the APKD cases are due to mutation in the gene (PKD2) encoding polycystin. Another gene (PKD1) is involved in the proliferation of the epithelial cells lining the cyst cavity, the thickening of the basement membrane, fluid secretion, and protein sorting (Bukanov NO et al 2002 Hum Mol Genet 11:923). ARPKD generally has an early onset. Both forms occur at frequencies of 0.0025 to 0.001. Even the late onset type may be detectable early by tomography. The symptoms vary and involve kidney disease, cerebral vein aneurism (sac like dilatation), underdeveloped lungs, liver fibrosis, and growth retardation, etc. The dominant type can be identified with high accuracy using chromosome 16p13 DNA probes but less than 10% of the cases are due to genes not in chromosome 16. The autosomal recessive form is at an unknown location and it can be identified after the third trimester by ultrasonic methods because the kidneys are enlarged. The genetic transmission of the dominant and recessive diseases is very efficient. One polycystic kidney (PKD1, 4300-amino acid integral membrane glycoprotein) locus was assigned to 6q21-p12, and sequences were also found in 2p25-p23 and 7q22-q31; these are homologous to polycystic kidney disease of the mouse. There is a PKD2 locus in 4q21-q23 and this is similar in function to PKD1. PKD2 interacts with PKD1 and PKD2 interacts also with the Hax-1 protein binding F-actin, suggesting that the system affects the cytoskeleton. Thus defect in PKD2 may be one of the causes of cyst formation in the kidney, liver, and pancreas. The

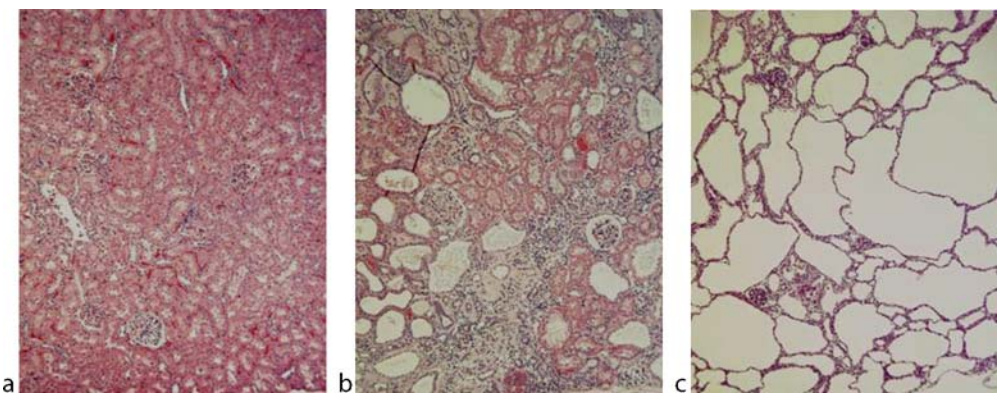

Figure P102. Polycystic kidney disease in RRRCHan:SPRD rat. a: wild type, b: heterozygote, and c: homozygous Pkdr1 mutant. The homozygous mutant rats die at age 3–4 weeks. Heterozygous males develop renal failures by about 6 months whereas the heterozygous females rarely progress to renal failure and death. Heterozygous males can be identified by blood urea nitrogen (BUN) level of the serum or plasma at age 9–10 weeks. PCR analysis and sequencing detected A for G substitution in exon 12 of the mutant gene. (The histological images are the courtesy of Professors Beth A. Bauer and Craig L. Franklin, Rat Resource and Research Center University of Missouri, Columbia, Missouri 6211; http://www.nrrrc.missouri.edu/Straininfo.asp?appn=46)

infantile type recessive PKD is also called Caroli disease. The ARPKD locus encodes a 968-amino acid protein, which forms six transmembrane spans with intracellular amino and carboxyl ends. It appears to be a voltage-activated Ca^{2+} (Na^{+}) channel protein. In a mouse model and in humans, TOR antagonist rapamycin protein may alleviate the dominant ADPKD disease (Schillingford JM et al 2006 Proc Natl Acad Sci USA 103:5466). The CDK inhibitor roscovitine ($C_{19}H_{26}N_6O$) appears to be an effective inhibitor of PKD in mouse (Bukanov NO et al 2006 Nature [Lond] 444:949). PKD1 may involve haploinsufficiency. The PKD1 homolog in *Caenorhabditis* (*LOV-1*) controls sensory neurons required for male mating behavioral steps. The traditional Chinese drug, a diterpene triptolide (Lei Gong Teng), induces PC2-dependent calcium release and attenuates cyst formation (see Fig. P103) (Leuenroth SJ et al 2007 Proc Natl Acad Sci USA 104:4389). ►cardiovascular disease, ►Caroli disease, ►hypertension, ►genetic screening, ►ion channels, ►haplo-insufficient, ►rapamycin, ►CDK; Pei Y et al 2001 Am J Hum Genet 68:355; Lin F et al 2003 Proc Natl Acad Sci USA 100:5286; autosomal dominant polycystic kidney disease: http://pkdb.mayo.edu/.

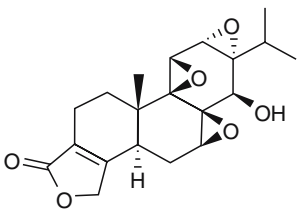

Figure P103. Triptolide

Polycystic Liver Disease; (PCLD, 19p13.2-p13.1): A dominant, often accompanying polycystic kidney disease. It involves fluid-filled cysts on the liver. The protein involved is hepatocystin. (See Drenth JPH et al 2003 Nat Genet 33:345).

Polycystic Ovarian Disease (Stein-Leventhal syndrome): Polycystic ovarian disease generally involves enlarged ovaries, hirsuteness, obesity, lack of or irregular menstruation, increased levels of testosterone high ratios of luteinizing hormone: follicle-stimulating hormone, and infertility. It appears to be due an autosomal factor, yet 96% and 82% of the daughters of affected mothers and carrier fathers, respectively, developed the symptoms indicating a meiotic drive-like phenomenon. Deficiency of 1-α-ketosteroid reductase/dehydrogenase (9q22) may cause polycystic ovarian disease as well as pseudohermaphroditism with gynecomastia in males. ►infertility, ►luteinization, ►Graafian follicle, ►meiotic drive, ►pseudohermaphroditism, ►gynecomastia

Polycystin: Polycystin proteins are supposed to regulate different functions, such as mating behavior, fertilization by the sperm, asymmetric gene expression, and mechanosensory transduction (Delmas P 2004 Cell 118:145).

Polycythemia (PFCP): An autosomal dominant proliferative disorder of the erythroid progenitor cells, resulting in an increase in the number of red blood cells and in vitro hypersensitivity to erythropoietin. Mutations in the von Hippel-Lindau protein are responsible for about half of the cases. Mutations of valine→phenylalanine at amino acid site 617 in Janus kinase 2 occurs in more than 80% of acquired polycytemic mice and leads to constitutive tyrosine phosphorylation and increased sensitivity to cytokinins (James C et al 2005 Nature [Lond] 434:1144) ►erythropoietin, ►Janus kinases, ►von Hippel-Lindau syndrome; Pastore Y et al 2003 Am J Hum Genet 73:412.

Polydactyly: The presence of extra fingers or toes. In *postaxial* polydactyly (the most common type), the extra finger is in the area of the "little finger" (see Fig. P104) and in *preaxial* cases, this malformation is on the opposite side of the axis (thumb) of the palm or foot. The various types of polydactyly may be determined by autosomal recessive or dominant gene(s) and their expression is usually part of other syndromes. Crossed polydactyly indicates coexistence of postaxial and preaxial types with discrepancy between hands and feet. Synpolydactyly is caused by an expansion of the normal 15 GCG trinucleotides to 22–29.

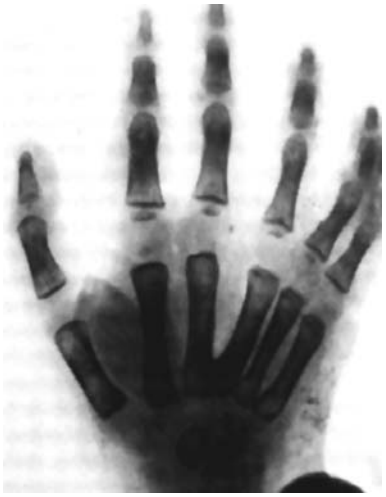

Figure P104. Polydactyly (From Bergsma D (ed) 1973 Birth Defects. Atlas and Compendium. By permission of the March of Dimes Foundation)

►Ellis-van Creveld syndrome, ►Opitz syndrome, ►Meckel syndrome, ►Majewski syndrome, ►orofacial-digital syndromes, ►Pätau's syndrome, ►diastrophic dysplasia, ►syndactyly, ►polysyndactyly, ►Greig's cephalopolysyndactyly syndrome, ►Rubinstein-Taybi syndrome, ►Pallister-Hall syndrome, ►focal dermal hypoplasia, ►ectrodactyly, ►adactyly, ►*hedgehog*

Polyelectrolytes: Polymers with attached anions and cations, respectively. Proteins and nucleic acids can be polyelectrolytes by carrying negatively and positively charged groups.

Polyembryony: In polyembrony, more than one cell of the embryo sac develops into an embryo in plants or in insects a single egg by clonal reproduction of hundreds of embryos. ►adventive embryos, ►embryo sac; Zhurov V et al 2004 Nature [Lond] 432:764.

Polydna Virus: ►parasitoid

Polyethylene Glycol (PEG): A viscous liquid or solid compound of low-toxicity, promoting fusion of all types of cells. PEG is widely used in textile, cosmetics, paint, and ceramics industry. ►PEG

Polyethyleneimine (PEI): A water-soluble polymer, which binds and precipitates DNA. It assists in the uptake of molecules including transforming DNA, especially in RGD-coated particles. Polyethyleneimine (25 kDa) contains N-acyl groups, which handicap its use for genetic transfection (see Fig. P105). Removal of these groups enhances its utility as an artificial vector. New linear PEIs synthesized by acid-catalyzed hydrolysis of poly(2-ethyl-2-oxazoline yielded products, which increased transfection efficiency up to 115-fold compared to deacetytlated commercial PEI. In addition, its efficiency for targeting lung cells increased 200-fold. Using this vector for RNAi delivery against the nucleocapsid protein gene of influenza virus dropped the virus titer in the lung of mice. A further advantage was the lower toxicity. Note: ethyleneimines are poisonous and mutagenic. ►RGD, ►vectors, ►gene therapy

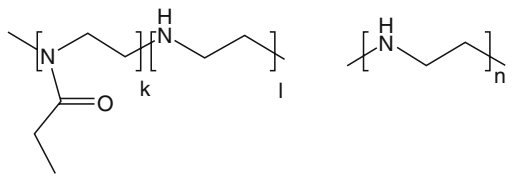

Figure P105. Left: PEI25 commercially available before hydrolysis. Right: Newly synthesized PEI after hydrolysis. After Thomas M et al. 2005 Proc. Natl. Acad. Sci. USA 102:5679

Polygalacturons: Complex carbohydrates in the plant cell wall.

Polygamy: Polygamy implies having more than one mating partner. In western human societies, it is illegal but in others, it is still acceptable for men to have more than one wife at the same time. Polyandry or polygyny is a common practice in animal breeding but it may be objectionable to humans on moral grounds. In the USA, polygamy laws are applied to all citizens, irrespective of religious affiliation or cultural tradition.

Polygenes: A number of genes involved in the control of quantitative traits. ►gene number in quantitative traits, ►QTL

Polygenic Inheritance: Polygenic inheritance is determined by a number of non-allelic genes, all involved in the expression of a single particular trait (such as height, weight, intelligence, etc.). Polygenic inheritance is characterized by counting and measurements and the segregating classes are not discrete but display continuous variation. ►quantitative genetics, ►QTL, ►complex inheritance, ►chaos, ►digenic diseases, ►selection long term, ►gain; Tanksley SD 1993 Annu Rev Genet 27:205; Klose J et al 2002 Nature Genet 30:385.

Polygenic Plasmids: are obtained when two plasmids carrying identical genes cointegrate. Such plasmids may have merit in genetic engineering if the genes show positive dosage effect for anthropocentrically useful traits. ►cointegration

Polygeny: In polygeny, one male has more than a single female mate. In *sororal polygeny*, the females are sisters. ►polygamy, ►effective population size

Polyglutamylase: The polyglutamylase enzyme adds several glutamic acids to the γ-carboxyl of a glutamate residue of proteins, such as tubulin and nucleosome assembly proteins (Janke C et al 2005 Science 308:1758).

Polyglutamine Diseases: ►trinucleotide repeats, ►resveratrol

Polygyne: Polygyne desribes social insect colonies with more than a single queen. ►monogyne

Polyhaploid: A polyhaploid has half the number of chromosomes of a polyploid. The gametes of polyploids are polyhaploid. ►polyploidy

Polyhedrosis Virus, Nuclear (BmNPV): An about 130 kbp DNA baculovirus of the silkworm (and other insects). It has been used (after size reduction) as a 30 kb cloning vector and it may propagate in a single silkworm larva about 50 µg DNA. ►baculoviruses,

►viral vectors, ►silkworm; Xia Q et al 2003 J Biol Chem 278:1094.

Polyhybrid: A polyhybrid is heterozygous for many gene loci.

Polyhydroxybutyrate (PHB): A bacterial polymer that can be manufactured by transgenic plants and is biodegradable.

Polyisoprenyl Phosphates: Intermediates in cholesterol biosynthesis; they play a role in signaling to the immune system. ►immune system, ►cholesterols

Polyketenes: Polymers of $CH_2 = C = O$ (ketene). Their biosynthesis is related to fatty acids. Several antibiotics (tetracycline, griseofulvin, etc.) contain ketenes. ►antibiotics

Polyketides: Various naturally occurring compounds, built from residues, which each usually contribute two carbon atoms to the assembly of a linear chain of which the β-carbon carries a keto group. These keto groups are frequently reduced to hydroxyls. The remaining keto groups at many of the alternate carbon atoms form the chains, which are called polyketides. Polyketide synthesis pathway resembles the fatty acid path. Flavonoids, mycotoxins, antibiotics, etc., occurring in plants from angiosperms to bacteria qualify for the polyketide collective name. Polyketide synthetases generate the precursors of erythromycin, rapamycin, and rifamycin antibiotics. ►lovastatin, ►epothilone; Khosla C et al 1999 Annu Rev Biochem 68:219; Walsh CT 2004 Science 303:1805.

Polykinetic Chromosome: A polykinetic chromosome has centromeric activity at multiple sites. ►neocentromeres

Polylinker: A DNA sequence with several restriction enzyme recognition sites (multiple cloning sites, MCS) used in construction of different cloning or transformation vehicles (plasmids). e.g., TTCTAGAATTCT sequence has an overlapping XbaI (TCTAGA) and an EcoRI recognition sites (GAATTC) and thus linking it to the DNA may generate both types of cloning sites. ►vectors, ►restriction enzymes, ►cloning sites, ►pUC

Poly(L-Lysine): A polycation that can form complex(es) with negatively charged DNA and mediate gene transfer using retroviral vector. In case the polycation has bound specific ligand(s), it can be targeted to special cell types. Without such a complex, the viral vector would have no target specificity. Some of the polycationic delivery systems are cytotoxic and/or may be subject to lysosomal degradation. ►transformation genetic; Putnam D et al 2001 Proc Natl Acad Sci USA 98:1200.

Poly-Marker Test: ►DNA fingerprinting

Polymer: A large molecule composed of a series of covalently linked subunits such as amino acids, nucleotides, fatty acids, carbohydrates, etc. ►DNA, ►protein; biopolymer motifs: http://bayesweb.wadsworth.org/gibbs/gibbs.html.

Polymerase: An enzyme that builds up large molecules from small units, such as the DNA and RNA polymerases generated from nucleotides DNA and RNA, respectively. ►pol

Polymerase Accessory Protein (RF-C): An essential part of the DNA replication unit in SV40. ►SV40

Polymerase Chain Reaction (PCR): A method of the rapid amplification of DNA fragments, employed when short flanking sequences of the fragments to be copied are known (see Fig. P106). The reaction begins by the denaturation of the target DNA, then primers are annealed to the complementary single strands. After adding a heat-stable DNA polymerase, such as Taq or Vent/Tli (originally the less thermostable Klenow fragment of polymerase I was used), chain elongation proceeds starting at the primers. The cycles are repeated 20–30 times, resulting in over a million fold (2^{20} = 1,048,576) replication of the target. The actual rate of replication may be less (80%) than that theoretically expected.

The DNA amplified can be subjected to molecular analysis such as preimplantation analysis, genetic

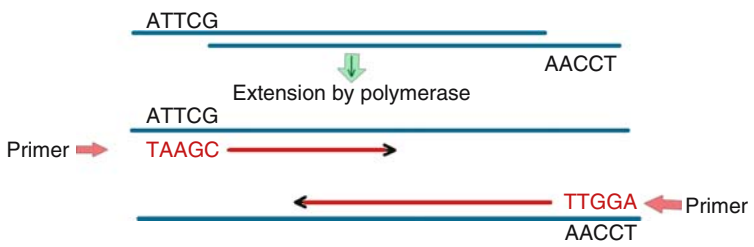

Figure P106. Polymerase chain reaction

screening, prenatal analysis, sperm typing, gene identification, etc. The error frequency for the Klenow fragment is about 8×10^{-5}, for Taq 10^{-5} to 10^{-4}, for Tli 2 to 3×10^{-5}. PCR amplification can be performed with a variety of mechanical devices, including chemical amplification on a microchip where the 20 cycles may be completed as fast as in 90 seconds. All types of technical information and references are available at http://apollo.co.uk/a/pcr. ►RAPDS, ►DNA fingerprinting, ►vectorette, ►sperm typing, ►genetic screening, ►prenatal analysis, ►preimplantation genetics, ►tissue typing, ►primer extension, ►ancient DNA, ►molecular evolution, ►RT-PCR, ►in situ PCR, ►recursive PCR, ►inverse PCR, ►capture PCR, ►PCR overlapping, ►tail-PCR, ►electronic PCR, ►PCR broad-base, ►PTPCR, ►methylation-specific PCR, ►AP-PCR, ►PCR asymmetric, ►PCR allele-specific, ►immuno-PCR, ►RNA-PCR, ►PCR-based mutagenesis, ►small-pool PCR, ►INTER-SS PCR, ►PRINS, ►reverse ligase-mediated polymerase chain reaction, ►thermal cycler, ►hot-start PCR, ►touch-down PCR, ►double PCR and digestion, ►PCR-LSA; Mullis KB, Faloona FA 1989, p 189 In: Wu R et al (Eds.) Recombinant DNA Methodology, Academic Press, San Diego, California; Innis M et al (Eds.) 1990 PCR Protocols: A Guide to Methods and Applications, Academic Press, San Diego, California; quantitative PCR primers: http://www.ncifcrf.gov/rtp/gel/primerdb/; http://medgen.ugent.be/rtprimerdb/; PCR primer design for mutation screening: http://bioinfo.bsd.uchicago.edu/MutScreener.html.

Polymerase Switching: In polymerase switching, DNA replication is initiated by the polymerase α/primase complex, but subsequently the chain elongation is continued by the eukaryotic polymerase δ. Polymerase ε may also have some role in the initiation and elongation. ►replication fork, ►DNA polymerases, ►primase, ►processivity

Polymery: In polymery, several genes cooperate in the expression of a trait. ►polygenes

Polymorphic: A trait that occurs in several forms within a population. The polymorphism may be balanced and genetically determined. ►polymorphism, ►balanced polymorphism, ►RFLP, ►SNP

Polymorphic Information Content (PIC): PIC is used to identify and locate a hard-to define marker locus. If the alleles of the marker locus are codominant, then PIC is the fraction of the progeny (the informative offspring) that cosegregates by phenotype with an index locus. The index locus (which is used for the detection of linkage with marker alleles) has two alternative alleles, a wild type and a dominant (mutant) allele. The marker locus is polymorphic for dominant (genetic or physical [nucleotide sequences]) alleles. Only those progenies are informative, where the index locus is homozygous in one of the parents and the other parent is heterozygous for the marker. The converse constitutions are not informative. In case both parents are heterozygous at the marker locus, only half of the offspring is informative.

$$\mathrm{PIC} = 1 - \sum_{i=1}^{n} p_i^2 - \left(\sum_{i=1}^{n} p_i^2\right)^2 + \sum_{i=1}^{n} p_i^4$$

where p_i = frequency of the index allele and *i* and *n* are the number of different alleles. The PIC values may vary theoretically from 0 to 1. A hypothetical example: four *A* alleles occur in a population with frequencies A^1: 0.2, A^2: 0.1, A^3= 0.15, and A^4 = 0.55. After substitution, $\mathrm{PIC} = 1 - (0.2^2 + 0.1^2 + 0.15^2 + 0.55^2) - (0.2^2 + 0.1^2 + 0.15^2 + 0.55^2)^2 + (0.2^4 + 0.1^4 + 0.15^4 + 0.55^4)$, thus $\mathrm{PIC} = 1 - 0.375 - 0.140625 + 0.0937125 \approx 0.578$, and in this case almost 58% of the progeny is informative. Usually, PIC values of 0.7 or larger are required for showing good linkage. The larger the number of the marker alleles, the more informative is the PIC. ►microsatellite typing; Da Y et al 1999 Anim Biotechnol 10:25.

Polymorphism: In polymorphism, morphologically different chromosomes, or different alleles at a gene occur, or variable length restriction fragments are found within a population. Polymorphism can now be also detected through automated molecular techniques. During PCR amplification of a gene, one or more fluorescent reporter probes are attached to the 5′ end, and a quencher substance(s) added slightly downstream or at the 3′-end. During amplification, the quencher may be cleaved by the Taq polymerase if it hybridizes to an amplified segment. The cleavage of the quencher enhances the fluorescence of the reporter fluorochrome. The samples placed in a 96-well plate can be scanned at three wavelengths in about 5 min. The procedure may be sensitive enough to detect a single base difference. In the human DNA sequences, there is ca. one variation/500 bp. About 15% of the polymorphism involves insertions or deletions. At least 100 chromosomes are usually examined for base substitution before the alteration is considered as a polymorphism. The average estimated nucleotide polymorphism in human populations is $\sim 8 \times 10^{-4}$. The diversity is variable at different loci and affected by several factors. Among normal human individuals, on the average, 11 deletions and duplications of the average length of 465 kb have been observed (Sebat J et al 2004 Science 305:525). ►balanced polymorphism, ►mutation, ►diversity, ►mutation detection, ►fluorochromes, ►PCR, ►clone validation, ►RLP, ►SNP,

►microsatellite, ►blood groups, ►linkage disequilibrium, ►haplomap; Reich DE et al 2002 Nature Genet 32:135; polymorphism detection tool for large datasets: http://pda.uab.es/pda/; http://pda.uab.es/pda2/; mammalian: http://mampol.uab.es/.

Polymorphonuclear Leukocyte (PMN): ►granulocytes, ►leukocyte

Polyomyositis: The inflammation of muscle tissues, which may lead to rheumatoid arthritis, lupus erythematosus, scleroderma, Sjögren syndrome, and neoplasia. Polymyositis is caused by two autoantigens PMSCL1 and PMSCL2. Dermatomyosities is a form affecting the connective tissues. Polymyosities as such are not under direct genetic control. conditions under separate entries, ►IVIG; Wang HB, Zhang Y 2001 Nucleic Acids Res 29:2517.

Polyneme: The linear structure includes more than one strands, e.g., polytenic chromosomes (salivary gland chromosomes) may have 1024 (2^{10}) parallel strands.

Polynucleotide: A nucleotide polymer hooked up through phosphodiester bonds.

Polynucleotide Kinase (PK): PK phosphorylates 5′ positions of nucleotides in the presence of ATP, such as $\mathrm{ATP} + \mathrm{XpYp} \xrightarrow{PK} \mathrm{p} - 5'\mathrm{XpYp} + \mathrm{ADP}$ (where X and Y are nucleotides), and can heal nucleic acid termini with ligase assistance. It functions in base excision repair and in non-homologous end-joining. ►ligase, ►DNA repair, ►non-homologous end-joining; crystal structure: Bernstein NK et al 2005 Mol Cell 17:657; Wang LK, Shuman S 2001 J Biol Chem 276:26868.

Polynucleotide Phosphorylase (PNPase): PNPase generates random RNA polymers [$(\mathrm{NMP})_n$]—without a template—from ribonucleoside diphosphates (NDP) and releases inorganic phosphate (P_i): $(\mathrm{NMP})_n$ + NDP →→→$(\mathrm{NMP})_{n+1}$ + P_i. It degrades mRNA from the 3′-end.

Polynucleotide Phosphotransferase: Polynucleotide phosphotransferase transfers nucleotides to the ends of DNA or RNA sequences, such as in the polyadenylation of mRNA or nucleotidyl transferase of DNA. ►polyA polymerase, ►terminal deoxynucleotidyl transferase

Polynucleotide Vaccination: Inoculation by subcutaneous, intravenous, or particle bombardment-mediated transfer of specific viral or other nucleotides/nucleoproteins to develop an immune response. The immune reaction is generally low. ►immunization genetic

Polyoma: Neoplasia induced by one of the polyomaviruses. The globoid (icosahedral) mouse polyoma viruses (a papova virus of 23.6×10^6 Da) contain double-stranded, circular DNA (4.5 kb). The BK and the JC viruses infect humans. ►Papova viruses; Cole CN, Conzen SD 2001, p 985 In: Knipe DM, Howley PM (Eds.) Fundamental Virology, Lippincott Williams & Wilkins, Philadelphia, Pennsylvania.

Polyp: An outgrowth on mucous membranes such as may occur in the intestines, stomach, or nose. They may be benign, precancerous, or cancerous. Nasal polyps may occur in aspirin sensitivity and can be treated surgically or with nasal steroid drugs. ►PAP, ►polyposis adenomatous, ►Gardner syndrome

Polypeptide: A chain of amino acids hooked together by peptide bonds. ►protein synthesis, ►amino acids, ►peptide bond

Polyphenols: Polyphenols are catechol-related plant products causing the formation of melanin-like brown color. The polyphenols in tea (theaflavin, catechins) have apparently antimutagenic and anticarcinogenic effects. ►thea

Polypheny: In polyphony, the same gene(s) can determine alternative phenotypes in response to internal or external cues, e.g., the queens and workers in social insects. Polyphenism in insect coloration may be the result of mutation of juvenile hormone-regulatory pathway and temperature effects may reveal hidden genetic variations. The mechanism that regulates developmental hormones can mask genetic variations and can act as an evolutionary capacitor for facilitating novel adaptive changes by genetic accommodation (Suzuki Y, Nijhout HF 2006 Science 311:650). Some older dictionaries and glossaries equate it with pleiotropy but this does not conform to current usage. ►genetic accommodation

Polyphosphates: Linear polymers of orthophosphates (*n* up to 100 or more) present in all types of cells with roles similar to ATP in metal chelation, bacterial competence for transformation, mRNA processing, growth regulation, etc. (see Fig. P107). Polyphosphates can buffer cellular phosphate levels in case of limited external supply and affect phosphate uptake (Thomas MR, O'Shea EK 2005 Proc Natl Acad Sci USA 102:9565). ►competence of bacteria, ►chelation; Kulaev I, Kulakovskaya T 2000 Annu Rev Microbiol 54:709.

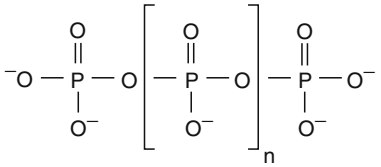

Figure P107. Polyphosphate

PolyPhred: A computer program that automatically detects heterozygotes for single nucleotide substitutions by fluorescence-based sequencing of PCR products at high efficiency. It is integrated by the Phred, Phrap, and Consed programs. ►SNIP, ►PCR, ►Phred, ►Phrap, ►Consed; Nickerson DA et al 1997 Nucleic Acid Res 25:2745.

Polyphyletic: An organism (cell) that originated during evolution from more then one line of descent. A polyphyletic group may contain species that are classified into this group because of convergent evolution. ►convergence, ►divergence

Polyplexes: Polyplexes are employed for delivery of DNA to cells. They include DNA-binding and condensing molecules, cell-specific ligands, and other molecules necessary for protection and uptake.

Polyploid Crop Plants: The most important polyploid crop plants include alfalfa (4x), apple (3x), banana (3x), birdsfoot trefoil (4x), white clover (4x), coffee (4x, 6x, 8x), upland cotton (4x), red fescue (6x, 8x, 10x), johnsongrass (8x), cultivated oats (6x), peanut (4x), Euro-pean plum (6x), cultivated potatoes (4x), sugarcane (*x), common tobacco (4x), bread wheat (6x), and macaroni wheat (4x). Most of these are apparently allopolyploids. ►allopolyploid

Polyploidy: Having more than two genomes per cell. Definitive identification of polyploidy requires cytological analysis (chromosome counts), although many of the polyploid plants display broader leaves, larger stomata, larger flowers, etc. Polyploidy regulates the expression of individual genes in + or − manner. A yeast study (using microarray hybridization) found that the level of expression of some genes remained the same in haploid and tetraploid cells, whereas the expression of some cyclin genes decreased with tetraploidy. Additionally, a gene associated with cell adhesion was greatly over-expressed with tetraploidy (see Fig. P108).

Figure P108. Autotetraploid (top) and diploid (bottom) flowers of *Cardaminopsis petraea* (G.P. Rédei, unpublished)

Polyploidy may permit separate evolutionary paths for the additional gene copies. ►autopolyploid, ►endopolyploidy, ►inbreeding autopolyploids, ►chromosome segregation, ►duplication, ►maximal equational segregation, ►alpha parameter, ►allopolyploid, ►tetrasomic, ►trisomy, ►microarray hybridization; Otto SP, Whitton J 2000 Annu Rev Genet 34:401.

Polyploidy in Animals: Polyploidy in animals is rare and limited mainly to parthenogenetically reproducing species (e.g., lizards). It occurs also in bees, silkworm, and other species. Some cells in special tissues of the diploid body may have increased chromosome number as a normal characteristic. Among mammals, tetraploidy was found in the red visacha rat, *Tympanoctomys barrarae* (2n = 112). The rarity of polyploidy in animals is attributed to its incompatibility with sex determination and dosage compensation of the X chromosome. ►parthenogenesis, ►honey bee, ►silk worm; Zimmet J, Ravid K 2000 Exp Hematol 28:3; Wolfe KH 2001 Nature Rev Genet 2:333.

Polyploidy in Evolution: Polyploidy in evolution is common in the plant kingdom but the majority of polyploid species are allopolyploid. Some of the single copy genes of invertebrates are, however, detectable up to four copies in vertebrates. A survey of plants indicated only 38% of polyploid species in the Sahara region, 51% in Europe, 82% in the Peary Islands, and thus show an increasing trend towards the North. In yeast, after polyploidization, different genes were lost leading to speciation (Scannell DR et al 2006 Nature [Lond] 440:341). In parasites, haploidy is advantageous because selection favors organisms that express a narrow array of antigens and elicitors. In contrast, in the host mounting a defense response, selection favors a broader array of recognition molecules and thus diploids or polyploids (Nuismer SL, Otto SP 2004 Proc Natl Acad Sci USA 101: 11036). Polyploids are also less vulnerable to mutation despite the fact that the mutational target numbers are larger. ►allopolyploid, ►duplications; Otto SP, Whitton J 2000 Annu Rev Genet 34:401; Wu R et al 2001 Genetics 159:869; function of the duplicated genes: Kellog EA 2003 Proc Natl Acad Sci USA 100:4369; Adams KL et al 2003 Proc Natl Acad Sci USA 100:4649.

Polyposis Adenomatous, Intestinal (APC): APC is controlled by autosomal dominant genes responsible for intestinal, stomach (Gardner syndrome), or other types (kidney, thyroid, liver, nerve tissue, etc.) of benign or vicious cancerous tumors. The various forms are apparently controlled by mutations or deletions in the 5q21-q22 region of the human chromosome and represent allelic variations. Retinal lesions (CHRPE)

are associated with truncations between codons 463–1387; truncations between codons 1403–1528 involve extra-codonic effects, etc. In addition, it is conceivable that this is a *contiguous gene* region where adjacent mutations affect the expression of the polyposis. By the use of single strand conformation polymorphism technique, DNA analysis may permit the identification of aberrant alleles prenatally or during the presymptomatic phase of the condition. The situation is further complicated, however, by the possibilities of somatic mutations. The *Min* gene of mouse appears to be homologous to the human APC, thus, lending an animal model for molecular, physiological, and clinical studies. The expression of *Min* is regulated also by the phospholipase-encoding gene *Mom1*, indicating the involvement of lipids in the diet. Polyposis may affect a very large portion of the aging human populations, especially high is the risk for females. Certain forms of polyposis may affect the young (juvenile polyposis). Regular monitoring by colorectal examination is necessary for those at risk. Bloody diarrhea and general weakness are symptoms usually too late for successful medical intervention. Molecular genetic information suggests that vertebrates use the same pathway of signal transduction as identified by *Drosophila* genes: *porcupine* (*porc*, 1.59)→*wingless* (*wg*, 2-30.0)→*dishevelled* (*dsh*, 1-34.5)→*zeste white3* (z^{w3}, 1.1.0)→*armadillo* (*arm*, 1-1.2)→cell nucleus. The normal human APC gene appears to be either a negative regulator (tumor suppressor) or an effector, acting between z^{w} and the nucleus. When it mutates, it can either no longer carry out suppression or it may become an effector. The product of *dsh* also appears to be a negative regulator of z^{w}. When the *zeste* product, glycogen synthase kinase (GSK3β) is inactive, the *arm* product (catenin) is associated with the APC product and a signal for tumorigenesis is generated. Alternatively, when no signal is received, GSK phosphorylates and activates a second binding site on APC for catenin but that causes the degradation of catenin and thus no tumor signal is generated. The APC protein may act as a tumor gene also by docking at its COOH end with a human homolog of the *dlg1* (*disc large*, 1-34.82) of *Drosophila*). The *Dlg* product belongs to the *membrane associated guanylate kinase* protein family that is analogous to proteins in vertebrates sealing adjacent cell membranes (tight junction). *Dlg* is also considered to be a tumor gene. Although, the molecular information reveals a number of mechanisms of action, it is not clear which one is being used or if multiple pathways are involved in polyposis. APC/FAP has a prevalence of about 1×10^{-4}. The EB1 protein binds the APC protein, is situated on the microtubules of the mitotic spindle, and serves as a checkpoint for cell division. ►Gardner syndrome, ►Turcot syndrome, ►cancer, ►single-strand conformation, ►GSK3β, ►polymorphism, ►hereditary non-polyposis colorectal cancer, ►contiguous gene syndrome, ►animal models, ►tight junction, ►catenin, ►effector, ►polyposis hamartomatous, ►polyposis juvenile, ►spindle, ►cyclooxygenase, ►microtubule, ►PTEN

Polyposis Hamartomatous (Peutz-Jeghers syndrome, PJS): A chromosome-19p13.3 rare dominant overgrowth of mucous membranes (polyp), especially in the small intestine (jeujunum), but also in the esophagus (the canal from mouth to stomach), bladder, kidney, nose, etc. Melanin spots may develop on lips, inside the mouth, and fingers. Ovarian and testicular cancers were also observed. The susceptibility to this cancer is due to deletion in a serine/threonine protein kinase gene (LKB). LKB1 mediates glucose homeostasis in the liver (Alessi DR et al 2006 Annu Rev Biochem 75:137). This gene signals to VEGF and it is a player in the anterior-posterior axis formation as well as in epithelial polarity. ►pigmentation of the skin, ►cancer, ►Gardner syndrome, ►colorectal cancer Muir-Torre syndrome, ►polyposis adenomatous intestinal, ►multiple hamartomas, ►VEGF; Hemminki A et al 1998 Nature [Lond] 391:184; Sapkota GP et al 2001 J Biol Chem 276:19469; Ilikorkala A et al 2001 Science 293:1323; Bardeesy N et al 2002 Nature [Lond] 419:162.

Polyposis, Juvenile: An early onset polyposis frequently turning malignant, caused by a defect at the carboxyl terminal of the SMAD4/DPC4 (552 amino acids) protein, encoded in human chromosome 18q21.1. SMAD4 in a trimeric association is involved in TGF-β signaling pathway. Although some of the symptoms are similar to other hamartomas, the Cowden disease gene (PTEN, phosphatase and tensin homolog) is encoded in chromosome 10 and the Peutz-Jeghers syndrome is coded for in chromosome 19. ►multiple hamartomas, ►TGF, ►polyposis hamartomatous, ►SMAD, ►DCC, ►PTEN; Howe JR et al 2002 Am J Hum Genet 70:1357.

Polyprotein: A contiguously translated long chain polypeptide that is processed subsequently into more than one protein.

Polypurine: A stretch of purine residues in nucleic acids.

Polypyrimidine: A sequence of multiple pyrimidines (mainly Us) in nucleic acids adjacent to the 3′ splicing site. Py-tract-binding proteins (PTB) recognize these such as the essential splicing factor $U2AF^{65}$, the splicing regulator sex-lethal (*Sxl*), etc. ►splicing, ►introns, ►sex determination; Le Guinier C et al 2001 J Biol Chem 276:43677.

Polyribosome: Same as polysome (see Fig. P109). ►protein synthesis

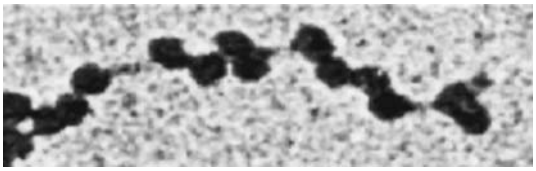

Figure P109. Polyribosome

Polysaccharide: Monosaccharides joined by glycosidic bonds (e.g., starch, glycogen, glycoprotein).

Polysome: In a polysome, the mRNA holds multiple ribosomes together. The ovalbumin polysomes comprise an average of 12 ribosomes and one peptide initiation takes place in every 6–7 s if all the required factors are functioning normally. The average polysome size for globin is ~5 ribosomes (1 ribosome/~90 nucleotides). Pactamycin may be an inhibitor of translation initiation and cycloheximide may interfere with peptide chain elongation. ►ribosome, ►mRNA, ►transcription, ►translation, ►pactamycin, ►cycloheximide

Polysome Display: In a polysome display, polysomes are isolated and screened by the affinity of the nascent peptides on an immobilized specific monoclonal antibody. The mRNA of the enriched pool of polysomes is reverse-transcribed into cDNA and amplified by PCR. The amplified template may be cloned and translated in vitro. The procedure is highly efficient for the screening of large, specific peptide pools. ►reverse transcription, ►cDNA, ►PCR, ►translation in vitro; Mattheakis LC et al 1994 Proc Natl Acad Sci USA 91:9022.

Polysomic Cell: In a polysomic cell, some chromosomes are present in more than the regular number of copies. The polyploids are polysomic for entire genomes. ►aneuploidy, ►polyploidy

Polysomy: In polysomy, some of the chromosomes in a cell are present in more than the normal numbers, examples of these cases in humans are 48,XXXX, 48, XXXY, 49,XXXXX or 49,XXXXY ►nondisjunction, ►polyploid, ►trisomy

Polyspeirism: In polyspeirism, one cell makes several types of related molecules, e.g., different chemokines. (See Montovani A 2000 Immunol Today 2(4):199).

Polyspermic Fertilization: In polyspermic fertilization, more than a single sperm enters the egg and, because each may provide a centriole, multipolar mitoses may take place resulting in aneuploidy and abnormal embryogenesis. ►fertilization

Polysyndactyly: Polysyndactyly is encoded by the HOXD13 gene at human chromosome 2q31-q32 (see Fig. P110). The amplification of the alanine codons (CCG, GCA, GCT, GGC) leads to an expanded (25 to 35) alanine residues in the protein. Some polysyndactyly is due to mutation in GLI3 gene at 7p13. ►trinucleotide repeats, ►syndactyly, ►Pallister-Hall syndrome

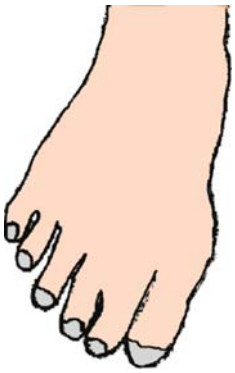

Figure P110. Polysyndactylic toes

Polytenic Chromosomes: Polytenic chromosomes are composed of many chromatids (e.g., in salivary-gland cell nuclei) because in such cases DNA replication was not followed by chromatid separation (see Fig. P111). The polytenic chromosomes in the salivary glands nuclei of diptera may have undergone ten cycles of replication ($2^{10} = 1024$) without division and may have over 1000 strands. Also, the polytenic chromosomes in the salivary glands are extremely long. A regular feature is the very close somatic pairing. Additionally, they all are attached at one point, at the chromocenter.

Polytenic chromosomes have been extensively exploited for analysis of deletions, duplications,

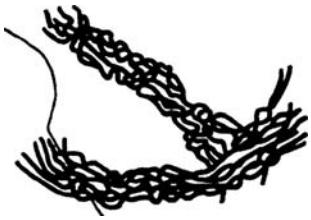

Figure P111. Polytenic chromosomes of *Allium ursinum*. Courtesy of G. Hasischka-Jenschke

inversions, and translocations. The characteristic banding pattern was used also as a cytological landmark for identification of the physical location of genes. Rarely, polyteny occurs in some specialized plant tissues (antipodals) too. ►salivary gland chromosomes, ►giant chromosomes, ►somatic pairing

Polytocous Species: Polytocous species produce multiple offspring by each gestation. ►monotocous

Polytomy: Multifurcating rather than bifurcating analysis of phylogenetic relations. ►evolutionary tree; Walsh HE et al 1999 Evolution 53:932.

Polytopic Protein (multispanning): A polytopic protein traverses the plasma membrane several times.

Polytropic Retrovirus: ►amphotropic retrovirus

Polytypic: A species that includes more than one variety or subtype.

POMC (pre-pro-opiomelanocortin): ►melanocortin, ►opiocortin, ►ACTH

Pomegranate (*Punica granatum*): A Mediterranean fruit tree, 2n = 2x = 16 or 18.

Pompe's Disease: ►glycogen storage diseases

Pongidae (anthropoid primates [hominoidea]): *Gorilla gorilla gorilla* 2n = 48 (see Fig. P112); *Hylobates con-color s* [gibbon] 2n = 52; *Hylobates lar* [gibbon] 2n = 44; *Pan paniscus* [pygmy chimpanzee] 2n = 48; *Pan troglodytes* [chimpanzee) 2n = 48; *Pongo pygmaeus* [orangoutan] 2n = 48; *Symphalangus brachytanites* 2n = 50. ►primates, ►chimpanzee

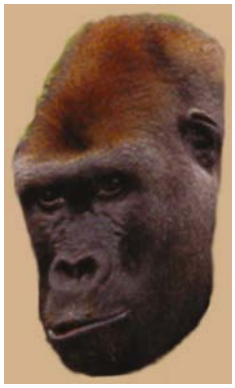

Figure P112. Gorilla

Pontin: ►chromatin remodeling

PO-PS Copolymers: Phosphorothioate-phosphodiester copolymers are used for antisense technologies. ►antisense RNA

POP′: POP′ symbolizes the ends of the temperate transducing phage genome integrating into the bacterial host chromosome. The corresponding bacterial integration sites are BOB′ and after integration (recombination) the sequence becomes: BOP′ and POB′, respectively ►attachment sites

Pop1p: A protein component of ribonuclease P and MRP. ►ribonuclease P, ►MRP

Poplar (*Populus* spp): 2n = 2x, 2n = 38 (see Fig. P113). Poplar includes cottonwood trees also. The genome of the black cottonwood (*Populus trichocarpa*, 485±10 Mb) has been sequenced and 45,000 putative protein-coding genes detected. Substantial portions of the nuclear and organellar (chloroplasts and mitochondria) genes the genome have been annotated in different tissues. About 8000 duplications were found (Tuskan GA et al 2006 Science 313:1596). (See Cervera M-T et al 2001 Genetics 158:787).

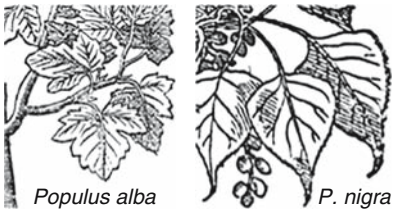

Figure P113. Poplars

Popliteal Pterygium Syndrome (PPS, 1q32-q41): PPS is allelic to the Van der Woude syndrome and it involves a defect in the interferon regulatory factor 6 (Ifr6). Clinical symptoms include cleft palate, harelip, and webbing of the skin. Pterygium is membrane or skin folding; popliteal indicates THE ligament behind the knee. ►Van der Woude syndrome, ►epithelial cell, ►Pterygium

Pop-Out, Chromosomal: Chromosomal pop-out originates due to the intrachromatid reciprocal exchange between direct repeats. It excises one of the repeats (the popout) but may retain the other member of the duplication. ►intrachromosomal recombination, ►sister chromatid exchange

Poppy (*Papaver somniferum*): The latex of poppy is a source of opium, codein, morphine, heroin, and other alkaloids. Their biosynthetic pathway, including a mutant blocked in the biosynthesis of the illicit drug (morphine and codeine) pathways (See Millgate AG et al 2004 Nature [Lond] 431:413). The plant is grown for its oil-rich seed as a food and also for pharmaceutical purposes (see Fig. P114). Basic chromosome number x = 11, diploid and tetraploid forms are known.

Figure P114. Poppy seed capsule

Population: A collection of individuals that may either interbreed and freely trade genes (Mendelian population, deme) or may be a closed population that is sexually isolated from other groups that share the same habitat. ►Hardy-Weinberg theorem, ►population equilibrium

Population Critical Size: ►critical population size

Population Density: The number of cells or individuals per unit volume or area.

Population Effective Size (N_e): The number of individuals in a group or within a defined area that actually transmit genes to the following reproductive cycles (offspring). Each breeding individual has 0.5 chance to contribute an allele to the next generation, and $0.5 \times 0.5 = 0.25$ is the probability to contribute two particular alleles. The probability that the same male contributes two alleles is $(1/N_m)$ 0.25 and for the same female it is $(1/N_f)$ 0.25 where N_m and N_f are the number of breeding males and females, respectively. The probability that any two alleles are derived from the same individual is $0.25N_m + 0.25N_f = 1/N_e$ and N_e is computed as $4N_mN_f /(N_m + N_f)$. ►founder principle, ►genetic drift, ►inbreeding and population size; Wright S 1931 Genetics 16:97.

Population Equilibrium: ►Hardy-Weinberg theorem

Population Genetics: Population genetics studies the factors involved in the fate of alleles in potentially interbreeding groups (see Fig. P115). The individuals within these groups (demes) may actually reproduce by random mating or selfing or by the combination of the two within this range. Population genetics can be entirely theoretical and developing mathematical formulas for predicting the allelic frequencies and the effect of various factors that affect these frequencies and the historical paths of the genes and factors as they emerge, become established or disappear, form equilibria or remain unstable during microevolutionary periods. Experimental population genetics conducts biological studies in the sense of the theoretical framework. Population genetics thus deals with the consequences of mutation, genetic drift, migration, selection and breeding systems and is also one of the most important approaches to experimental (micro) evolution. It provides also the theory for many human genetics, animal and plant breeding research efforts. The availability of molecular information greatly advanced the resolving power of population genetics. The availability of mitochondrial (maternally transmitted) and Y chromosomal (paternally transmitted) markers provide effective tools to study the dynamics and history of human populations. ►terms mentioned, and ►SNIPS, ►DNA chips, ►microsatellites, ►minisatellites, ►mtDNA, ►Y chromosome; population modeling software: http://www.trinitysoftware.com; population genetics tools and Internet resources: Excoffier L, Heckel G 2006 Nature Rev Genet 7:745; Arlequin, analysis of molecular genetic variations: Marjoram P, Tavaré S 2006 Nature Rev Genet 7:759.

Figure P115. Population genetics is concerned with the fate of genes in large collection of organism rather than in the descendants of single individuals

Population Growth, Human: $P_t = P_0(1 + r)^t$ where P_0 = the population at time 0, r = rate of growth and t = time. It can be calculated also by $P_t = P_0e^{rt}$ where e = the base of the natural logarithm. ►age-specific birth and death rates, ►human population growth, ►Malthusian parameter

Population Size, Ancestral: Ancestral population size can be estimated by different methods. The ancestral modern human population might have been about 10,000, whereas the common ancestral human and chimpanzee populations were of the order of 100,000. Newer estimate of the latter is only about 20,000 (Rannala B, Yang Z 2003 Genetics 164:1645).

Population Structure: Population structure is endemic by subpopulation groups. The dispersal of the subdivisions reflect adaptive genetic differences, gene

flow and natural selection pressure, inbreeding, overlapping generations, effective population size, and sometimes genetic drift. Sometimes there are too few differences in some population and therefore it is difficult to trace the origin of possible demographic changes. Parasites, e.g., viruses may evolve much faster and from their dispersal one may get good information on the demography/distribution of the host in a region (Bick R et al 2006 Science 311:538). ►population genetics, ►endemic, ►natural selection, ►genetic drift, ►population effective size, ►stratification; Marth G et al 2003 Proc Natl Acad Sci USA 100:376.

Population Subdivisions: Smaller relatively separated breeding groups with restricted gene flow among them. ►gene flow, ►migration

Population Tree: The population tree is constructed on the basis of genes frequencies among populations indicating their evolutionary relationship. ►evolutionary tree, ►gene tree

Population Wave: Periodic changes in the effective population size. ►population size effective, ►random drift, ►founder principle, ►gene flow

Porcupine Man (ichthyosis histrix): Ichthyosis is a dominant form of hyperkeratosis. ►keratosis, ►ichthyosis

Porencephaly: Porencephaly is a generally rare dominant (13qter region) brain disease with cerebrospinal fluid-filled cavities or cysts, affecting primarily infants and young children. Few survivors are plagued by many other debilitating symptoms. In a mouse mutant, single-nucleotide alteration in collagen Col4a1 was the primary cause of the disease. ►collagen; Gould DB et al 2005 Science 308:1167.

Porin: Porin is a voltage-dependent anion channel. It is opened by Bax and Bak pro-apoptotic proteins and closed by the anti-apototic Bcl-x_L. Bax and Bak permit the exit of cytochrome c from the mitochondria and thus facilitate apoptosis by the activation of caspases. In case of IL-7 deficiency and increase in pH over 7.8 the conformation of Bax is altered and the protein moves from the cytoplasm to the mitochondria and facilitates apoptosis. The anti-apoptotic, 24 amino acid-peptide prevents the translocation of Bax to the mitochondria (Guo B et al 2003 Nature [Lond] 423:456). The Bcl-2 protein, localized to the mitochondrial membrane, normally suppresses the release of cytochrome c. Bax deficiency extends the ovarian life span into advanced age of mice. Normally the ovarian follicles fade by menopause in women and at similar developmental stages also in mice. Degradation of Bax by the proteasomes may protect against the apoptosis over-protective effect of Bcl-2 and reduce cancer cell survival. For drug therapy of epithelial cancer the state of BAX vs. Bcl-2 may be significant. ►Bak, ►ion channels, ►cytochrome c, ►apoptosis, ►hypersensitive reaction; Suzuki M et al 2000 Cell 103:645; Gogvadze V et al 2001 J Biol Chem 276:19066; Scorrano L et al 2003 Science 300:135.

Porphyria: Porphyria is a collective name for a variety of genetic defects involved in heme biosynthesis resulting in under- and/or over-production of metabolites in the porphyrin-heme biosynthetic pathway. These diseases may be controled by recessive or dominant mutations. The affected individuals may be suffering from abdominal pain, psychological problems and photosensitivity. The autosomal dominant acute *intermittent porphyria* (human chromosome 11q23-ter) is caused by a periodic 40–60% reduction in porphobilinogen deaminase enzyme resulting in in-sufficient supplies of the tetrapyrrole hydroxymethyl bilane that is normally further processed by non-enzymatic way into uroporphyrinogen I. It was speculated that the famous Dutch painter van Gogh was a victim of this rare disease. Prevalence is in the range of 10^{-4} to 10^{-5}. Exogenous effects such as barbiturate, sulfonamide, alkylating and many other drugs, alcohol consumption, poor diet, various infections and hormonal changes, generally elicit the periodic attacks. An *adult type* of (hepatocutaneous) porphyria, controled by another human gene locus (1p34), involves light-sensitivity and liver damage by the accumulation of, porphyrins caused by uroporphyrinogen decarboxylase deficiency. The general effect may be less severe than in the intermittent porphyria. The rare congenital *erythropoietic porphyria* (CEP) is the result of a defect in the enzyme uroporphyrinogen III co-synthetase controled by a recessive mutation in human chromosome 10q25.2-q26.3. The laboratory identification is generally based on urine analysis for intermediates in the heme pathway. Porphyrias affect also various mammals. Defects in the porphyrin pathways are involved in several types of pigment deficiency mutations of plants. The *variegate porphyria* is caused by a defect of protoporphyrinogen oxidase (PPOX) with symptoms basically similar to that of intermittent porphyria. This dominant disease has low penetrance. Its prevalence is very high (about 3×10^{-3}) in South-African populations of Dutch descent; it apparently represents founder effect. The mental problems of King George III of England (reigned during the US War of Independence) were also attributed to variegate porphyria.

ALAD porphyria also known as "Doss porphyria," is a very rare porphyric disorder linked to a profound lack of porphobilinogen synthase PBGS, also known as δ-aminolevulinate dehydratase (ALAD), is encoded by the *ALAD* gene (9q34). Human (PBGS) exists as an

equilibrium of functionally distinct quaternary structure assemblies, known as morpheeins, in which one functional homo-oligomer can dissociate, change conformation, and reassociate into a different oligomer. In the case of human PBGS, the two assemblies are a high-activity octamer and a low-activity hexamer (Jaffe EK, Stith L 2007 Am J Hum Genet 80:329). ►porphyrin, ►heme, ►skin diseases, ►light-sensitivity diseases, ►founder effect, ►coproporphyria, ►aminolevulinic acid conformation

Porphyrin: Four special pyrroles joined into a ring; generally with a central metal, like iron in hemoglobin or in chlorophylls with magnesium (see Fig. P116). ►porphyria, ►coproporphyria, ►heme

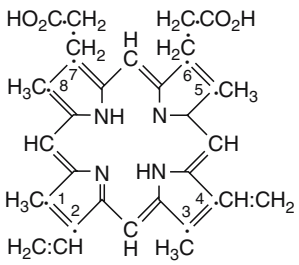

Figure P116. Protoporohyrin

Porphyrinuria: ►porphyria

Porpoise: *Lagenorhynchus obliquidens*, 2n = 44. ►dolphins

Portable Dictionary of the Mouse Genome: Data on ~12,000 genes and anonymous DNA loci of the mouse, homologs in other mammals, recombinant inbred strains, phenotypes, alleles, PCR primers, references, etc. The dictionary can be used on Macintosh, PC in FileMaker, Pro, Excel, and text formats, and is accessible through the Internet (WWW, Gopher, FTP), CD-ROM, or on floppy disk. Information: R.W. Williams, Center for Neuroscience, University of Tennessee, 875 Monroe Ave., Memphis, Tennessee 36163. Phone: 901-448-7018. Fax: 901-448-7266. e-mail: rwilliam@nb.utmem.edu.

Portable Promoter: An isolated DNA fragment, including a sufficient promoter that can be carried by transformation to other cells, and may function in promoting transcription. ►promoter, ►transformation, ►gene fusion

Portable Region of Homology: Insertion and transposon elements may represent homologous DNA sequences and can recombine. The recombination may then generate deletions, cointegrates or insertion, or inversions. These events can take place even in RecA$^-$ hosts. ►Tn*10*, ►cointegrate, ►deletion, ►inversion, ►targeting genes

Position Effect: change in gene expression by a change in the vicinity of the gene.

The new expression may be *stable* or variable (*variegation type position effect*) (see Fig. P117). Stable position effect is observed when promoterless structural genes are introduced by transformation and the transgene is expressed with the assistance of a "trapped" promoter that is regulated differently than the gene's natural (original) promoter. Variegated position effect (PEV) is more difficult to interpret by molecular models. When, however, centromeric heterochromatin was inserted at the *brown* locus of *Drosophila* during larval development the transposed hetero chromatin stochastically associated with the centromeric region and caused PEV (Dernburg AF et al 1996 Cell 85:745). The telomere-linked *ADE2* locus of yeast displayed alternative *ADE* and *ade* phenotypes (Gottschling DE et al 1990 Cell 63:751). It has been assumed that heterochromatin affects the intensity of somatic pairing and variations in somatic association and variations in cross-linking between the homologs by binding proteins bring about the silencing. The *trithorax-like* gene of *Drosophila* encodes a GAGA-homology transcription factor that enhances variegation type position effect (PEV) by decondensation of the chromatin. The mosaicism may also be the result of the spontaneous and random derepression of the promoter in the presence of an activator. The telomeric isochores have been also implicated in position effect (TPE). Position effect may be observed by altering the site or distance of the locus control region. In *Drosophila* over 100 genes were found that affect variegation type position effect (PEV). In *Drosophila* HP1, HP2 proteins of the heterochromatin and histone H3 lysine^9 methyltransferase play important role in gene silencing. It seems that RNAi also affects the heterochromatin and several genes encode the RNAi system and their mutations results in loss of silencing (Pal-Bhadra M et al 2004 Science 303:669). It has been hypothesized that these genes control the packaging of the DNA. Many of the cancers develop after translocations or transpositions, indicating the significance of position effect on the regulation of growth. Proteins affecting AT-rich heterochromatin can modify PEV. Transposable elements may also cause position effect (Kashkush K et al 2003 Nature Genet 33:102). Position effects may be exerted even from long distances (2 Mb) and may make difficult to distinguish the position effect causing gene from mutation within the target gene. Such cases may complicate positional cloning. Position effect occurs also in yeasts and other organisms. Some human genetic disorders are due to

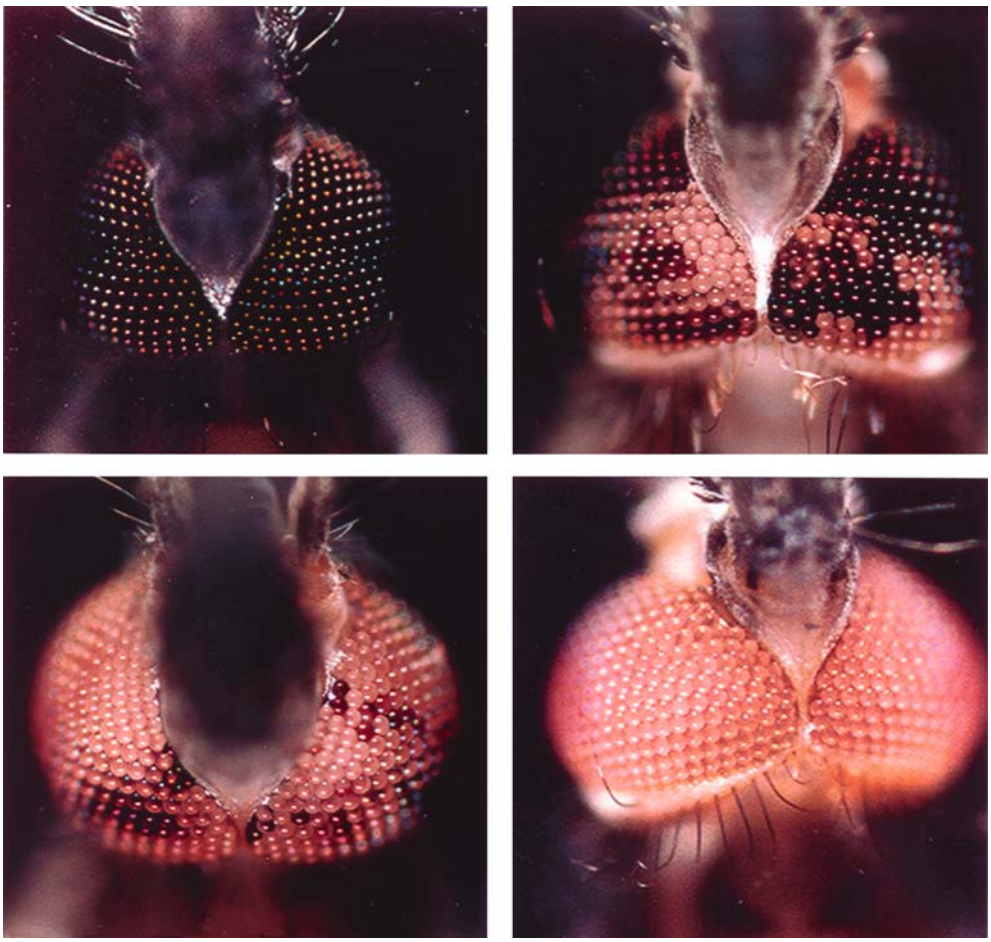

Figure P117. Duplication of the wildtype (*p*+) allele into heterochromatic DNA results in the (*p*) eyes variegated expression of *p*+ in the malaria mosquito *Anopheles gambiae*. (Courtesy of Dr. Mark Benedict, original photograph by James Gathany, CDC)

position effect. ►heterochromatin, ►histone methyltransferases, ►RdMD, ►LCR, ►Offermann hypothesis, ►regulation of gene activity, ►mating type determination in yeast, ►silencer, ►cancer, ►chromosomal rearrangements, ►chromosome breakage, ►locus control region, ►isochores, ►transposable elements, ►epigenesis, ►paramutation, ►positional cloning, ►RPD3, ►developmental-regulator effect variegation, ►RIGS, ►Dubinin effect; Kleinjahn DJ Heyningen V 1998 Hum Mol Genet 7:1611; Baur JA et al 2001 Science 292:2075; Ahmad K, Henikoff S 2001 Cell 104:839; Csink AK et al 2002 Genetics 160:257; suppressors: Ner SS et al 2002 Genetics 162:1763; Monod C et al 2002 EMBO Rep 3:747; Ebert A et al 2006 Chromosome Res 14:377; heterochromatin proteins: Greil F et al 2007 EMBO J 26:741.

Position-Specific Scoring Matrix (PSSM): PSSM represents amino acids at specific positions in a sequence alignment. It can be used for scanning proteins with matches to this tract. ►PWM; Gribskov M et al 1987 Proc Natl Acad Sci USA 84:4355.

Position Weight Matrix: ►PWM

Positional Cloning: ►chromosome walking, ►chromosome landing, ►map-based cloning

Positional Information: Positional information is provided to some cells by signal transducers in a multicellular organism and has an important influence on differentiation and development. ►morphogenesis, ►differentiation

Positional Sensing: Positional sensing provides information for specific differentiation functions. ►morphogenesis

Positive Control: In positive control, gene expression is enhanced by the presence of a regulatory protein (in contrast to negative control, where its action is

reduced). The arabinose operon of *E. coli* is a classic example. The regulator gene *araC* produces a repressor (P_1) in the absence of the substrate arabinose. If arabinose is available, P_1 is converted to P_2 (by a conformational change), which is an activator of transcription in the presence of cyclic adenosine monophosphate (cAMP). While the negative control (P_1) is correlated with a low demand for expression, the activator (P_2) appears in response to the demand for high level of expression. In general cases, the addition of an activator protein to the DNA makes possible normal transcription but adding a special ligand to the system removes the activator and the gene is turned off. ►*arabinose* operon, ►negative control, ►*lac* operon, ►autoregulation, ►catabolite activator protein, ►regulation of gene activity

Positive Cooperativity: Binding of a ligand to one of the subunits of a protein facilitates the binding of the same to other subunits.

Positive Interference: ►interference, ►coincidence

Positive/Negative Selection: Selection may be used to isolate cloned constructs containing the desired integrated sequence (positive selection). Negative selection is expected to eliminate integration sites containing the entire vector inserted at non-targeted sites and vector components that have no relevance to cloning. Negative selection is usually less efficient—if it takes place at all—than positive selection. For positive selection in case of hypoxanthine/guanine phosphoribosyl transferase marker, one may use hypoxanthine, aminopterin, and thymidine (HAT) chemicals, whereas in the same experiment for negative selection 6-thioguanine or 5-bromodeoxyuridine may be used.

Positive Selection: In general, it indicates the selection of a desirable type in a population rather than the elimination of the undesirable phenotype/genotypes. ►selection entries

Positive Selection of Lymphocytes: A process of maturation of lymphocytes into functional members of the immune system. In contrast, negative selection eliminates, by apoptosis, early lymphocytes with autoreactive receptors. ►immune system, ►lymphocytes

Positive Selection of Nucleic Acids: Positive selection of nucleic acids isolates and enriches desired types of nucleic acid sequences. The desired (tracer) sequences are digested by restriction endonucleases that generate cohesive ends. The rest of the nucleic acids (driver) are exposed to sonication (or the ends may be even dephosphorylated) and so much sticky ends are not expected. Thus, mainly the tracer-tracer sequences are annealed when the mixture is treated with a ligase enzyme. ►subtractive cloning, ►genomic subtraction, ►RFLP subtraction, ►ligase DNA, ►cohesive ends, ►sonicator

Positive-Strand Virus: The genome of a positive-strand virus is also a mRNA. Upon transcription, the virus may directly produce an infectious nucleic acid. This is a very large class of RNA viruses including the Brome Mosaic Virus, the Hepatitis C Virus, West Nile Virus, Corona Viruses, etc. Their replication is affected by at least 100 genes (Kushner DB et al 2003 Proc Natl Acad Sci USA 100:15764). ►replicase, ►plus strand, ►mRNA, ►negative strand virus

Positive Supercoiling: The overwinding follows the direction of the original coiling, i.e., it takes place rightward. ►supercoiling, ►negative supercoil

Positron Emission Tomography (PET): ►tomography

Post-Adaptive Mutation: Post-adaptive mutation is supposed to arise de novo in response to the conditions of selection. Actually, post-adaptive mutation may not be found if the data are well scrutinized. ►directed mutation, ►pre-adaptive mutation

Post Coitum (p.c.): During embryonal development, the days that follow mating.

Posterior: Pertaining to the hind part of the body or behind a structure toward the tail end.

Posterior Distribution: A summary of random variables collected after new empirical data became available. It is the product of likelihood and prior distribution. ►prior distribution

Posterior Probability: ►Bayes theorem

Post-Genome Analysis: The post-genome analysis studies the experimental results and the informatics of the sequential function (metabolic pathways) and interactions of genes and their products. ►annotation of the genome, ►genetic networks; Lin J et al 2002 Nucleic Acids Res 30:4574, http://www.genome.ad.jp; http://www.genome.ad.jp/kegg/comp/GFIT.html.

Postmeiotic Segregation: Postmeiotic segregation takes place when the DNA was a heteroduplex at the end of meiosis. Among the octad spores of ascomycetes, this may result in 5:3 and 3:5 or other types of aberrant ratios instead of the normal 1:1. Postmeiotic segregation may be an indication of failures in mismatch or excision repair. ►DNA repair, ►tetrad analysis, ►gene conversion

Postnatal: Postnatal refers to that which occurs after birth; generally one to 12 months after birth.

Postprandial: After consuming a meal, a process, e.g., protein anabolism modifies protein synthesis due the change in the amino acid pool or change in insulin supply after eating (postprandially).

Postreduction: As per postreduction, the segregation of the alleles takes place at the second meiotic division. ►tetrad analysis, ►meiosis, ►prereduction

Postreplicational Repair: ►unscheduled DNA synthesis, ►DNA repair

PostScript: A computer application to handle text and graphics the same time. The PostScript code determines what the graphics look like when printed, although may not be visible on the screen of the monitor.

Post-Segregational Killing: ►plasmid addiction

Post-Transcriptional Gene Silencing (PTGS): As per PTSG, the transcript of a transgene is degraded before translation takes place and thus, its expression is prevented. Also, it may be a defense mechanism against viruses in plants. The viral gene may be integrated into the chromosome and duly transcribed, yet it is not expressed. In addition, since the replication of the virus is mediated through a double-stranded RNA that has been found to be a potent inhibitor, it is conceivable that both the plant defense and the transgene silencing rely on similar mechanism(s). In some plant species, the potyviruses, tobacco etch virus, and cucumber mosaic virus may produce a *helper component protease* (HC-Pro) and may inactivate this plant defense by degradation. The HC-Pro may have another role. When a plant is infected simultaneously by two different viruses, one of them promotes the vigorous replication of the other, and the latter by its production of HC-Pro eventually facilitates the spread of the first type of the virus and thus enhances the symptoms of the viral disease. In some of the silenced plant cells, a 25-nucleotide long antisense RNA has been detected that seems to inactivate the normal transcript or infectious viral RNA. According to other studies, the ~25-nt RNA sequence apparently conveys specificity for a nuclease by homology to the substrate mRNA. Several types of hairpin structures of RNAs involving sense and antisense sequences and introns appeared to silence very effectively viral genes in plants. A calmodulin-related plant protein (rgs-CAM) may also suppress silencing. ►silencing, ►plant viruses, ►RNAi, ►RNA interference, ►co-suppression, ►homology-dependent gene silencing, ►methylation of DNA, ►host–pathogen relations; Bass BL 2000 Cell 101:235; Jones L et al 1999 Plant Cell 11:2291; Waterhouse PM et al 2001 Nature [Lond] 411:834; Mitsuhara I et al 2002 Genetics 160:343.

Post-Transcriptional Processing: The primary RNA transcript of a gene is cut and spliced before translation or before assembling into ribosomal subunits or functional tRNA; it includes removal of introns, modifying (methylating, etc.) bases, adding CCA to tRNA amino arm, polyadenylation of the 3′ tail, etc. ►opiotropin; McCarthy JEG 1998 Microbiol Mol Biol Revs 62:1492; Bentley D 1999 Curr Opin Cell Biol 11:347.

Post-Transcriptional Operons: A hypothesis according to which, functionally related genes may be regulated post-transcriptionally as groups by mRNA-binding proteins that recognize common sequence elements in the untranslated 5′ and 3′ subsets of the transcripts. This conclusion is based on findings that mRNA-binding proteins recognize unique subpopulations of mRNAs, the composition of these subsets may vary depending on conditions of growth and the same mRNA occurs in multiple complexes. These conserved *cis* elements were named USER (untranslated sequence elements for regulation) codes. These systems may permit plasticity during developmental processes or responses to drug treatment. ►operon, ►genetic networks; Keene JD, Tenenbaum SA 2002 Mol Cell 9:1161.

Posttranslational Modification: Enzymatic processing of the newly synthesized polypeptide chain, the product of translation. The modification may include proteolytic cleavage, glycosylation, phosphorylation, farnesylation, conformational changes, assembly into quaternary structure, etc. These modifications may alter function. Mass spectrophotometry is generally used for the identification the alterations. ►protein synthesis, ►protein structure, ►conformation, ►proteomics; Németh-Cawley JF et al 2001 J Mass Spectrom 36:1301; Mann M, Jensen ON 2003 Nature Biotechnol 21:255; http://dbptm.mbc.nctu.edu.tw/; tandem mass spectra interpretation server: http://modi.uos.ac.kr/modi/.

Post-Transplantational Lymphoproliferative Disease (PTDL): In PTDL, after engraftment, the Epstein-Barr virus-infected B cells may continue to proliferate because the immuno-suppressive therapy required to maintain the graft inhibits cytotoxic T lymphocytes. Bone marrow transplantation may alleviate the problems. ►Epstein-Barr virus, ►immuno-suppression, ►CTL

Postzygotic: ►prezygotic

Postzygotic Isolation: Postzygotic isolation arises when in allopatric evolution the taxa diverge from the common ancestor by accumulation of different non-deleterious mutations. Although the divergent forms are well adapted, their hybrids may be inviable or sterile because the negative effects of the alleles in a shared background. ►allopatric speciation; Orr HA, Turelli M 2001 Evolution 55:1085.

Potassium-Argon Dating: Potassium-Argon dating is based on the conversion of K^{40} into Ar^{40}, a stable gas.

It is used for dating rocks over 100,000 years old. ►argon dating, ►radiocarbon dating

Potassium Ion Channel: ►ion channel

Potato (*Solanum tuberosum*): The genus has 170 to 300 related species with basic chromosome number x = 12. In nature, species with diploid, tetraploid, and hexaploid chromosome numbers are found. The cultivated potatoes originated from the *S. brevicaulis* group in the Andes Mountains (Spooner DM et al 2005 Proc Natl Acad Sci USA 102:14694), and secondarily from *Solanum andigena* in Central America where they produce tubers under short-day conditions. The majority of the modern varieties is day-neutral and develops tubers under long-day conditions. The cultivated potatoes are usually cross-pollinating species but many set seeds also by selfing. Generally, the seed progeny is very heterogeneous genetically. Potatoes are rarely propagated by seed, as is a crop. The diploid relatives are usually self-incompatible whereas the polyploids may set seeds by themselves. Among the cultivated groups, the tuber color may vary from white to yellow to deep purple. Also the chemical composition of the tubers shows a wide range, depending on the purpose of the market. Potato, besides being a popular vegetable, is an important source of industrial starch. The related species carry genes of agronomic importance (disease, insect resistance, etc.) that have not yet been fully exploited for breeding improved varieties. The application of the molecular techniques of plant breeding seems promising. ►patatin; Isidore E et al 2003 Genetics 165:2107; http://www.tigr.org/tdb/tgi; https://gabi.rzpd.de/projects/Pomamo/; http://www.sgn.cornell.edu.

Potato Beetle: (*Leptinotarsa decemlineata*, n = 18): One of the most devastating pests of the agricultural production of potatoes (see Fig. P118). Plants transgenic for the δ endotoxin of *Bacillus thüringiensis* are commercially available ►potato, ►*Bacillus thüringiensis*

Figure P118. Potato beetle

Potato Leaf Roll Virus: The potato leaf roll virus has double-stranded DNA genetic material.

POTE: A family of genes encoding proteins with an amino-terminal cysteine-rich domain, a central domain with ankyrin repeats, and a carboxyl-terminal domain containing spectrin-like helices. In humans, the POTE gene family is composed of 13 closely related paralogs dispersed among eight chromosomes. These genes are found only in primates, and many paralogs have been identified in various primate genomes. The expression of POTE family is generally restricted to a few normal tissues (prostate, testis, ovary, and placenta but several family members are expressed in breast cancer and many other cancers (Lee Y et al 2006 Proc Natl Acad Sci USA 103:17885).

Potocki-Shaffer Syndrome: ►exostosis

Potocytosis: Moving ions and other molecules into cells by caveola vehicles. ►caveolae

POU: A region with several transcriptional activators of 150–160 amino acids (including a homeo-domain), involved with a large number of proteins controlling development. The acronym stands for a prolactin transcription factor (PIT), an ubiquitous and lymphoid-specific octamer binding protein (OTF), and the *Caenorhabditis* neuronal development factor (Unc-86). A POU domain may directly facilitate the recruitment of TBP and transcriptional activators and may stimulate transcription even when the enhancer is at a distance from the core promoter. POU domain proteins are involved in shuttling between nucleus and cytoplasm (Baranek C et al 2005 Nucleic Acids Res 33:6277). ►homeodomain, ►transcription factor, ►TBP, ►transcriptional activator, ►enhancer, ►core promoter, ►octa, ►unc, ►*Caenorhabditis*, ►deafness; Ryan AK, Rosenfeld MG 1997 Genes Dev 11:1207; Bertolino E, Singh H 2002 Mol Cell 10:397.

pOUT: A strong promoter opposing pIN and directing transcription to the outside end of an insertion element. ►RNA-OUT, ►pIN

Power of a Test: Algebraically, the power of a test is $1 - \beta$, where β = type II error. This test reveals the probability of rejecting a false null hypothesis and accepting a correct alternative. The experimenter needs as large a value of $1 - \beta$ as possible, by reducing β to a minimum. To improve the power, the size of the experiment (population) can be increased. In case the size cannot be increased, a more powerful test (statistics) should be chosen. ►error types, ►significance level

Pox Virus: A group of oblong double-stranded DNA viruses of 130–280 kbp (see Fig. P119). Some of these are parasites on insects, others in the family are the chicken pox, cowpox (vaccinia), and smallpox viruses (see Fig. P120).

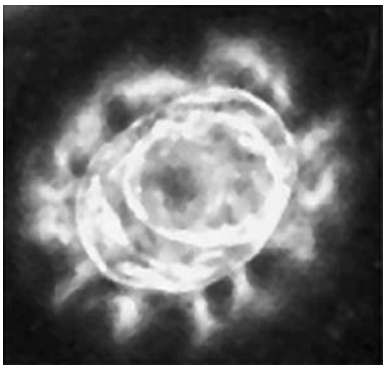

Figure P119. Pox virus

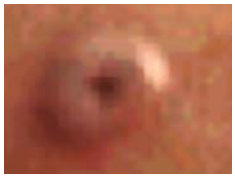

Figure P120. Pox virus lesion

Their transmission takes place through insect vectors or by dust or other particles. Engineered pox virus vectors that are not able to multiply in mammalian cells may have the ability to express passenger genes without the risk of disease. Due to the success of vaccination, smallpox as a disease has now been eradicated and vaccination against is no longer necessary except in case of terrorist attacks (Halloran ME et al 2002 Science 298:1428). The smallpox virus (VARV) linear DNA genome is about 186 kbp with inverted terminal repeats containing 196 to 207 open reading frames. Apparently, there is small variation among the various isolates. The genes of the smallpox virus overlapand its mRNA is not spliced (Esposito JJ et al 2006 Science 313:807).

Poxvirus based vectors are being used orally to protect wild life (red fox) from rabies, for the protection of chickens against the Newcastle virus. Recombinant canarypox virus is employed for the protection of dogs and cats against the distemper, feline leukemia, equine influenza, etc. Highly attenuated derivatives, expressing rabies virus glycoprotein, Japanese encephalitis virus polyprotein, or seven antigens of *Plasmodium falciparum* are used for safe and effective vaccination. Smallpox virus disease has been eradicated and at this time only the Center of Disease Control and Prevention in Atlanta, GA in the USA and the Russian State Research Center of Virology and Biotechnology in Kolsovo, Novosbirsk, Russia, maintain active samples. Limited-scale vaccinations have been performed as protection against terrorism. Large-scale use of the current vaccine may involve side effects such as heart disease in some individuals. A new vaccine developed and used in Japan does not pose serious side effects even at very high doses. It may revert to the wild type progenitor due to mutation of gene *B5R*. Fortunately, this gene can be eliminated without effect on protective immunity (Kidokoro M et al 2005 Proc Natl Acad Sci USA 102:4252). ►malaria, ►*Plasmodium falciparum*, ►variolation; Moss B, Shisler JL 2001 Semin Immunol 13:59; Takemura M 2001 J Mol Evol 52(5):419; Enserink M 2002 Science 296:1592; L1 protein: Su HP et al 2005 Proc Natl Acad Sci USA 102:4240; http://www.poxvirus.org.

POZ: Protein–protein interaction domain of Zinc finger-containing transcriptional regulatory proteins. ►Zinc finger, ►αβ T cells

PP-1, PP-2: Protein serine/threonine phosphatases that are inhibited by okadaic acid. PP-1 may be associated with chromatin through the nuclear inhibitor of PP-1 (NIPP-1). PP enzymes play key roles in many cellular processes. ►okadaic acid, ►DARPP

pp15: A protein factor required for nuclear import. ►membrane transport, ►RNA export

pp125^{FAK}: ►CAM

PP2A: The proline-directed heterotrimeric protein serine-threonine phosphatase dephosphorylates proteins in the MAP pathway of signal transduction and thus balances the effect of kinases. Its deregulation seems to be associated with several types of cancers, Alzheimer disease, and susceptibility to infections by pathogens. The crystal structure of the holoenzyme has been determined (Cho US, Xu W 2007 Nature [Lond] 445:53). PP2A subunit B56 regulates β-catenin signaling and several metabolic processes. PP2A is very sensitive to okadaic acid, a tumor-inducing agent. The non-catalytic α4 subunit of PP2A is a regulator of apoptosis by dephosphorylating c-Jun and p53 transcription factors, which upon phosphorylation promote apoptosis (Kong M et al 2004 Science 306:695). ►Sit, ►MAP, ►signal transduction, ►MAP kinase phosphatase, ►okadaic acid,►catenins, ►cyclin G, ►apoptosis, ►calcineurin, ►TGF

PPAR (peroxisome proliferator-activated receptor, 17q12): A transcription factor in the adipogenic (fat synthetic) pathways. The three types α, γ, and δ show different distribution in human tissues and associate with different ligands. PPARα is the target for the drugs and fibrates (amphipatic carboxylic acids) that reduce triglycerides. Type α also acts as a transcription

factor for several genes affecting lipoprotein and fatty acid metabolism. PPARγ is a (3p25) regulator of glucose, lipid, and cholesterol metabolism, may be sensitized by thiazolidinediones (TZD), and offers some hope to be used for the treatment of diabetes mellitus type2 (IDDM). PPARγ2 deficiency dramatically reduces adipogenesis in mouse fibroblasts whereas PPARγ1 affects obesity and diabetes (Zhang J et al 2004 Proc Natl Acad Sci USA 101:10703). The PPARγ 12Ala allele is associated with a small yet significant reduction in the risk for diabetes type II. PPARγ agonists have a controversial—promoting and suppressing—effect on polyposis of the colon and other cancers. In human thyroid carcinoma, PAX8–PPARγ1 has been observed. PPAR-α agonists are also successful for the treatment of some autoimmune diseases. PPARγ deficiency can also lead to hypertension. ►peroxisome, ►ROS, ►diabetes mellitus, ►polyposis, ►farnesoid X receptor, ►leukotrienes, ►leptin, ►obesity, ►Krox20, ►hypertension, ►PAX, ►thiazolidinedione, ►dizygotic twins, ►sirtuin, ►mesenchyma, ►retinoic acid; Lowell BB 1999 Cell 99:239; Kersten S et al 2000 Nature 405:421; Willson TM et al 2001 Annu Rev Biochem 70:341; Michalik L et al 2004 Nature Rev Cancer 4:61; review: Lehrke M, Lazar MA 2005 Cell 123:993.

pPCV: Plasmid plant cloning vector, designation (with additional identification numbers and/or letters) of agrobacterial transformation vectors constructed by Csaba Koncz.

ppGpp: ►discriminator region

PPI (peptidyl prolyl isomerase): An endoplasmic reticulum-bound protein assisting chaperone function. There are 3 PPI families: cyclophilins, FK506, and parvulins. ►chaperone, ►PDI; Dolinski K, Heitman J 1997, p 359 In: Gething MJ (Ed.) Guidebook to Molecular Chaperones and Protein Folding Catalysis, Oxford University Press, Oxford, UK.

ppm: Parts per million.

PP2R1B: PP2R1B at human chromosome 11q22-q24 encodes the β isoform of the PP2A serine/threonine protein phosphatase. The gene displays alterations (LOH) in a variable fraction of lung, colon, breast, cervix, head and neck, ovarian cancers and melanoma, and it is thus a suspected tumor suppressor gene. ►tumor suppressor gene, ►LOH; Mumby MC, Walter G 1993 Physiol Rev 73:673.

PPTs (palmitoyl-protein thioesterases): PPTs hydrolyze long chain fatty acyl CoA and PPT1 may cleave cysteine residues in the lysosomes. Its deficiency may lead to Batten disease. ►Batten disease

Prader-Willi Syndrome (Prader-Labhart-Willi syndrome): A very rare (prevalence 1/25,000) dominant defect involving poor muscle tension, hypogonadism, (hyperphagia [over-eating]) obesity, short stature, small hands and feet, mental retardation, compulsive behavior that sets in by the teens, caused by methylation of the paternal chromosome and by disomy for maternal chromosome 15 (see Fig. P121). The recurrence risk in affected families is about 1/1000. This and cytological evidence indicate that the condition is caused in about 60% of the cases by a chromosomal breakage in the so-called imprinting center (IC) in the long arm of human chromosome 15q11.2-q12. The same deletion (4–5 Mbp or sometimes shorter), when transmitted through the mother, results in the Angelman syndrome. At the breakpoints, the HERC2 gene (encoding a very large protein) may be repeated. The repeats may then recombine and generate the deletions. See two chromosomes shown in Figure P122, with different number of repeats, as detected by FISH. In some cases, there is no deletion but a mutation in an ubiquitin protein ligase gene (UBE3A). Mutations in the proximal part of IC lead to the Angelman syndrome and in the distal part to the Prader-Willi syndrome. Molecular studies indicated in many cases the missing (uniparental disomy) or silencing (imprinting) of a paternal DNA sequences in the patients.

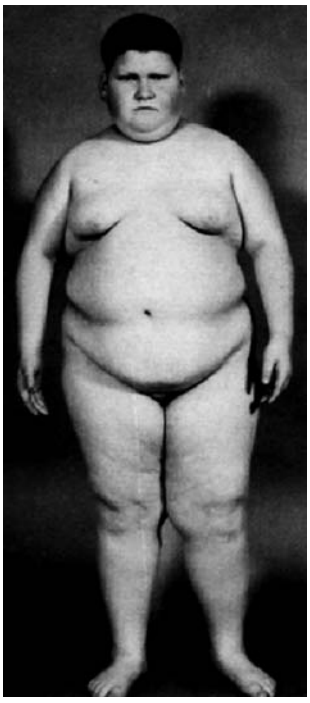

Figure P121. Prader-Willi syndrome at age 15. (From Bergsma, D., ed. 1973 Birth Defects. Atlas and Compendium. By permission of the March of Dimes Foundation)

Figure P122. Duplications in the Prader-Willi syndrome. (Redrawn from Amos-Landgraf JM et al 1999 Am J Hum Genet 65:370)

The deletions of this syndrome usually involve the promoter of an snRPN gene, resulting in the silencing (imprinting) of flanking genes (ZNF127 encoding a Zn-finger protein, NDN [necdin], IPW and PAR) on either side. Necdin and Magel2 also interact with Fez (fasciculation) protein and BBS4 (Bardet-Biedl protein) and they affect centrosome function (Lee S et al 2005 Hum Mol Genet 14:627). Lack of expression of snRNP is the most reliable clinical criterion for the syndrome, although snRPN alone does not appear to be the major pathogenic factor in the syndrome. The snoRNA appears to control alternative processing of the serotonin receptor 2C (Kishore S, Stamm S 2006 Science 311:230). Also, exon 1 (1920 bp) includes more than 100 5′-CG-3′ and 5′-GC-3′ dinucleotides liable to methylation. Among the 19 methyl-sensitive restriction enzyme sites within the telomeric region were completely methylated in this syndrome but none of these were methylated in case of the Angelman syndrome. A 2.2 kb spliced and polyadenylated RNA is transcribed 150 kb telomerically to snRPN in human chromosome 15q11.2-q12 and the homologous mouse chromosome 7 region. The transcript is not translated, however. This gene (IPW) is not expressed in individuals with the Prader-Willi syndrome and is therefore said to be imprinted in Prader-Willi syndrome. In the mouse gene *Ipw*, multiple copies of 147 bp repeats are found with retroviral transposons (IAP) insertions. ►obesity, ►imprinting, ►imprinting box, ►epigenesis, ►disomic, ►serotonin, ►alternative splicing, ►Angelman syndrome, ►head/face/brain defects, ►snPRN, ►IAP, ►Bardet-Biedl syndrome; Fulmer-Smentek SB, Francke U 2001 Hum Mol Genet 10:645.

Prairie Dog (ground squirrel, *Sciuridae*): Burrowing mammals with five different species. They are rodents, and not canidae, inhabiting arid areas (see Fig. P123).

Figure P123. *Cynomys ludovicianus Prairie dog*

pRB: Retinoblastoma protein. ►retinoblastoma

PRC1: A spindle midzone-associated kinase. ►midzone

PRD1: An icosahedral, double-stranded-DNA phage (*Tectiviridae*) of Gram-negative bacteria. It lacks the common phage tail and it acquires an injection device from the host membrane during phage assembly. The mature virion is 66 Mda, containing 20 protein species. It is evolutionarily related to adenovirus. ►phage, ►adenovirus; Abrescia NGA et al 2004 Nature [Lond] 432:68.

Pre-Adaptive: A pre-adaptive trait or mutation is that which occurs before selection would favor it but it becomes important when the conditions become favorable for this genotype. ►adaptation, ►post-adaptive mutation, ►fluctuation test

Prebiotic: Prebiotic refers to the period before life originated. ►evolution prebiotic

Precambrian: ►Proterozoic, ►Cambrian, ►geological time periods

Precise Excision: In precise excision, the genetic vector or transposon leaves the target site without structural alterations; the initially disrupted gene or sequence can return to the original (wild type) form.

Precursor Ion Scanning: A powerful technique in proteomics in connection with MS/MS and TOF. ►MS/MS, ►TOFMS; Steen H et al 2001 J Mass Spectrom 36:782; Hager JW 2002 Rapid Commun Mass Spectrom 16:512.

Predetermination: In predetermination, the phenotype of the embryo is influenced by the maternal genotypic constitution but the embryo itself does not carry the gene(s) that would be expressed in it at that particular stage. ►delayed inheritance, ►maternal effect genes

Predictive Value: The true estimate of the number of individuals afflicted by a condition on the basis of the tests performed in the population.

Predictivity: The predictivity of an assay system is, e.g., the percentage of carcinogens correctly identified

among carcinogens and non-carcinogens, by indirect carcinogenicity tests, based mainly on mutagenicity. ►accuracy, ►specificity, ►sensitivity, ►bioassays for environmental mutagens

Predictome: A database of protein links and networks. ►genetic networks

Predictor Gene: The expression of a predictor gene signals difference(s) among phenotypically similar but functionally different forms of malignancies. ►cancer classification

Predisposition: Susceptibility to disease. It may be based on a large number of alleles and environmental factors may also have a major role. A predispositional testing, based on the genetic constitution, may or may not indicate the probability of a disease.

Preeclampsia: ►ecclampsia

Preferential Repair: Transcriptionally active DNA is repaired preferentially. ►DNA repair

Preferential Segregation: Non-random distribution of homologous chromosomes toward the pole during anaphase I of meiosis. There are four loci in the Abnormal 10 chromosome (carrying a terminal large knob) in maize that affect neocentromere activity, increased recombination, and preferential segregation (Hiatt EN, Dawe RK 2003 Genetics 164:699). If harmful combination of genes (gene blocks) is preferentially included in the gametes, this may constitute a genetic load. ►meiotic drive, ►neocentromere, ►polarized segregation; Rhoades MM, Dempsey E 1966 Genetics 53:989; Buckler ES et al 1999 Genetics 153:415.

Prefoldins (PFDN): Molecular chaperones built as hexamers from the α and β subunits and four β-related subunits in eukaryotes. Prefoldin 1 was assigned to human chromosome 5, and prefoldin 4 to chromosome 7. Prefoldins may be required for gene amplification in tumors. ►chaperone; Siegert R et al 2000 Cell 103:621; prefoldin-like Skp structure: Walton TA, Sousa MC 2004 Mol Cell 15:367.

Preformation: An absurd historical idea supposing that an embryo preexists in the sperm (spermists) or in the egg (ovists) of animals and plants, rather than developing by epigenesis from the fertilized egg. ►epigenesis; Richmond ML 2001 Endeavour 25(2):55.

Pre-Genome RNA: The replication intermediate in retroid viruses. ►retroid virus

Pregnancy, Male: In seahorses (*Hippocampus*, Syngnathidae), the female lays unfertilized eggs in the ventral pouch of the male where he fertilizes them and the fetus develops.

Pregnancy Test: Pregnancy is the formation of a fetus in the womb; there are about 40 known pregnancy tests, based on chemical study of blood and urine or other criteria. The currently used tests rely on estrogen level. ►Aschheim-Zondek test

Pregnancy, Unwanted: The estimated frequency of unwanted pregnancy in the human population of the whole world was estimated between 35 to 53 million per year. ►pregnancy test, ►abortion medical

Pregnenolone: A precursor in the biosynthesis of several steroid hormones: CHOLESTEROL PREGNENOLONE→PROGESTERONE→ANDROSTENEDIONE→TESTOSTERONE→ESTRADIOL These steps are under the control mainly of several cytochrome P450 (CYP) enzymes and their deficiency or misregulation lead to pseudohermaphroditism, hermaphroditism, and various other anomalies of the reproductive system. ►steroid hormones

Preimmunity: ►host-pathogen relation

Preimplantation Genetics: Preimplantation genetics detects genetic anomalies either in the oocyte or in the zygote before implantation takes place. This can be done by molecular and biochemical analyses, and cytogenetic techniques. The status of the egg—in some cases of heterozygosity for a recessive gene—may be determined prior to fertilization by examining the polar bodies. Since the first polar bodies are haploid products of meiosis, if they show the defect, then presumably the egg is free of it. The purpose of this test is to prevent transmission of identifiable familial disorders. The technology permits selection for sex of the embryo but this is ethically controversial. ►gametogenesis, ►in vitro fertilization, ►ART, ►micromanipulation of the oocyte, ►polymerase chain reaction, ►sperm typing, ►PGD; Delhanty JD 2001 Am J Hum Genet 65:331; Wells D, Delhanty JD 2001 Trends Mol Med 7:23; Bickerstaff H et al 2001 Hum Fertil 4:24; Braude P et al 2002 Nature Rev Genet 3:941; ethical and legal considerations: Knoppers BM et al 2006 Annu Rev Genomics Hum Genet 7:201.

Preinitiation Complex: ►PIC, ►open promoter complex

Pre-mRNA (pre-messenger RNA): The primary transcript of the genomic DNA, containing exons and introns and other sequences. ►mRNA, ►RNA processing, ►introns, ►hnRNA, ►post-transcriptional processing, ►RNA editing, ►splicing enhancer exonic

Pre-Mutation: A genetic lesion, which potentially leads to mutation unless the DNA repair system remedies the defect before it is visually manifested. Pre-mutational lesions lead to delayed mutations. UV irradiation or chemical mutagens with indirect effects (that is the mutagen requires either activation or it induces the

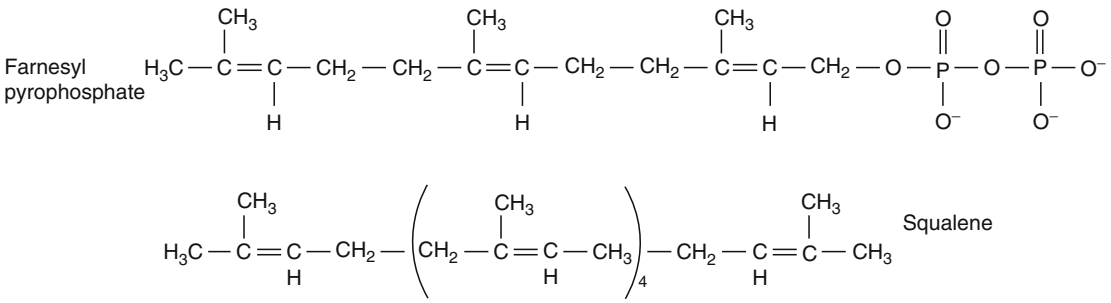

Figure P124. Two molecules of farnesyl pyrophosphate are converted into 30-C squalene in the presence of NADPH

formation of mutagenic radicals, peroxides) frequently cause pre-mutations. Incomplete expansion of trinucleotide repeats may also be considered pre-mutational, e.g., in the fragile X chromosome. ►chromosomal mutation, ►chromosome breakage, ►point-mutation, ►telomutation, ►trinucleotide repeats, ►fragile X, ►Sherman paradox under mental retardation; Auerbach C 1976 Mutation research. Chapman and Hall, London, UK.

Prenatal Diagnosis: Prenatal diagnosis determines the health status or distinguishes among the possible nature of causes of a problem with a fetus before birth. The results of cytological or biochemical analysis permit the parents to prepare psychologically and medically to the expectations. Although chromosomal abnormalities cannot be remedied, for metabolic disorders (e.g., galactosemia) advance preparations can be made. Similarly, fetal erythroblastosis may be prevented. In case of very severe hereditary diseases, abortion may be an option if it is morally acceptable to the parents and does not conflict with the existing laws. Prenatal diagnosis is now available for more than hundred anomalies. Until recently, prenatal diagnosis required mainly amniocentesis or sampling of chorionic villi, now in some instances the maternal blood can be scanned for fetal blood cells and by the use of the polymerase chain reaction, the DNA of the fetus can be examined. ►genetic testing, ►genetic screening, ►genetic counseling, ►amniocentesis, ►polymerase chain reaction, ►RFLP, ►DNA fingerprinting, ►DNA circulating, ►plasma nucleic acid, ►PUBS, ►MSAFP, ►sonography, ►fetoscopy, ►echocardiography, ►hydrocephalus, ►galactosemias, ►chorionic villi, ►pre-implantation genetics, ►ART; Weaver DD, Brandt IK 1999 Catalog of prenatally diagnosed conditions, Johns Hopkins University Press, Baltimore, Maryland; Fetal Evaluation: http://www.cpdx.com/.

Prenylation: The attachment of a farnesyl alcohol, in thioeter linkage, with a cystein residue located near the carboxyl terminus of the polypeptide chain. The donor is frequently farnesyl pyrophosphate. Cytosolic proteins are frequently associated with the lipid bilayer of the membrane by prenyl lipid chains or through other fatty acid chains. Prenyl biogenesis begins by enzymatic isomerization of isopentenyl pyrophosphate (CH_2=C[CH_3]CH_2CH_2OPP) into dimethylallyl pyrophosphate ([CH_3]$_2$C=$CHCH_2$OPP). These then react to form geranyl pyrophosphate ([CH_3]$_2$C= $CHCH_2CH_2$C[CH_3]=$CHCH_2$OPP). Geranyl pyrophosphate is then converted into farnesyl pyrophosphate as shown in Figure P124.

Members of the RAS family proteins, involved in signal transduction, cellular regulation, and differentiation are prenylated at cysteine residues of the COOH-terminus. Prenylation determines the cellular localization of these molecules. Cellular fusions are mediated by prenylated pheromones. The cytoskeletal lamins attaching to the cellular membranes are farnesylated. Prenylation of the C-termini of proteins is generally mediated by farnesyltransferase, a heterodimer of 48 kDa α and 46 kDa β subunit. Protein farnesylation is essential for early embryogenesis and for the maintenance of tumorigenesis (Mijimolle N et al 2005 Cancer Cell 7:313). Squalene is a precursor of cholesterol and other steroids (see Fig. P125). ►lipids, ►abscisic acid, ►lamin, ►RAS, ►cytoskeleton, ►pheromone

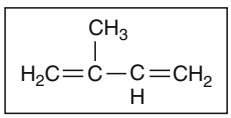

Figure P125. Isoprene units

Prepatent: The period before an effect (e.g., infection) becomes evident.

Prepattern Formation: The distribution of morphogens precedes the appearance of the visible pattern of particular structures. ►morphogen; Chiang C et al 2001 Dev Biol 236:421.

Prepriming Complex: A number of proteins at the replication fork of DNA involved in the initiation of DNA synthesis. ►DNA replication, ►replication fork

Preprotein: A preprotein is a protein molecule that has not completed yet its differentiation (trimming and processing).

Prereduction: In prereduction, the alleles of a locus separate during the first meiotic anaphase because there was no crossing over between the gene and the centromere. ►tetrad analysis, ►meiosis, ►post-reduction

Pre-rRNA: The unprocessed transcripts of ribosomal RNA genes; they are associated at this stage with ribosomal proteins and are methylated at specific sites. The cleavage of the cluster begins at the 5′ terminus of the 5.8S unit and proceeds to the 18S and 28S units. ►rRNA, ►rrn, ►ribosomal RNA, ►ribosome

Presence-Absence Hypothesis: The presence-absence hypothesis was advocated by William Bateson during the first few decades of the 20th century as an explanation for mutation. The recessive alleles were thought to be losses whereas the dominant alleles were supposed to indicate the presence of genetic determinants. Similar views, in a modified form, were maintained for decades later and were debated in connection with the nature of induced mutations. ►null mutation, ►genomic subtraction; Bateson W et al 1908 Rep Evol Comm R Soc IV, London, UK.

Presenilins (PS): Proteins associated with precocious senility, such the presenilin 1 (S182/AD3) encoded at human chromosome 14q24.3 (442 amino acids) and presenilin 2 (STM2/AD4, 467 amino acids encoded at 1q31-q34.2) proteins of the Alzheimer's disease. Mutations in presenilins account for about 40% of familial cases of the Alzheimer's disease. Presenilins are integral membrane proteases. Presenilin 1 and presenilin 2 increase the production of β-amyloid either directly or most likely by their effect on secretases. They may also promote apoptosis. Presenilins control calcium ion channels of the endoplasmic reticulum and the disruption of these channels can lead to Alzheimer's disease (Tu H et al 2006 Cell 126:981). Mutant PS1 strongly affects both the amplitude of evoked excitatory currents as well as the frequency of spontaneous excitatory synaptic currents by decreasing the number of functional synapses (Priller C et al 2007 J Biol Chem 282:1119). p53 and $p21^{WAF-1}$ promote inhibition of presenilin 1, and that may encourage apoptosis and tumor suppression as well. Presenilin 1 is associated with β-catenin and in the complex β-catenin is stabilized. Mutations in Presenilin 1 may destabilize β-catenin and the latter is usually degraded in Alzheimer's disease. Thus, mutation in Presenilin 1 may predispose to early onset Alzheimer's disease. Presenilin also controls pigmentation of the retinal epithelium and epidermal melanocytes, and mutation may lead to aberrant accumulation of tyrosinase (Wang R et al 2006 Proc Natl Acad Sci USA 103:353). Presenilin 2 contains a domain that is similar to that of ALG3 (apoptosis linked gene) and inhibits apoptosis. Presenilin 1 may also affect various (non-neurodegenerative) cancer-related pathways. The presenilins are involved in the processing of the transmembrane domain of amyloid precursor proteins (APP), and they are essential for normal embryonal development. Protein TMP21 is a component of presenilin complexes and modulates selectively γ-secretase but not ε-secretase (Chen F et al 2006 Nature [Lond] 440:1208). Presenilins also control the transduction of Notch signals. A presenilin locus exists in the third chromosome also (77A-D) of *Drosophila melanogaster*. ►Alzheimer disease, ►prion, ►apoptosis, ►p53, ►p21, ►calsenilin, ►catenins, ►ubiqulin, ►Notch, ►secretase, ►nicastrin; Sisodia SS et al 1999 Am J Hum Genet 65:7; Baki L et al 2001 Proc Natl Acad Sci USA 98:2381; Wolfe MS, Haass C 2001 J Biol Chem 276:5413; Marjaux E et al 2004 Neuron 42:189.

Present: The expressed open reading frames during particular times or conditions when analyzed by microarrays. ►open reading frame, ►microarray hybridization

Presenting: Behavioral signs shown by the female indicating receptivity to mating.

Presequence: A generic name for signal peptides and transit peptides.

Presetting: The penchant of a transposable element to undergo reversible alteration in a new genetic milieu. It may be caused by the methylation of the transposase gene. ►Spm, ►Ac-Ds

Presymptotic Diagnosis: The identification of the genetic constitution before the onset of the symptoms. ►prenatal diagnosis, ►genetic screening

Pre-tRNA: ►tRNA

Prevalence (K, λ): The proportion of a genetic or non-genetic anomaly or disease in a particular human population at a particular time. The percentage of hereditary diseases caused by presumably single nuclear genes in human populations: autosomal dominant 0.75, autosomal recessive 0.20, X-linked 0.05. Besides these, multifactorial abnormalities account for about 6% of the genetic anomalies. In case the general prevalence of the diseases in a population is x, the expected expression among sibs for autosomal

dominant is 1/2x, for autosomal recessives it is 1/4x, and for multifactorial control $1/\sqrt{x}$. ►incidence, ►mitochondrial diseases in humans

Prevention of Circularization of Plasmids: ►circularization

Preventive Medicine: Preventive medicine studies the genetic and physiological conditions of individuals and societies in order to take measures to avoid the onset of diseases. ►diseases in humans, ►genetic counseling, ►counseling genetic, ►genetic risk, ►recurrence risk, ►empirical risk, ►heritability

Prey: ►two-hybrid system

Prezygotic: The DNA molecule in the prokaryotic cell before recombination (transduction or transformation); after integration it becomes postzygotic.

Pri: ►cis-acting elements

PriA: Replication priming protein. ►replication fork, ►DNA replication, ►primase

Priapism: An uncommon prolonged engorgement of the penis or erection of the penis or the clitoris. Phosphodiesterase-5A dysregulation is one cause (Champion HC et al 2005 Proc Natl Acad Sci USA 102:1661). It is generally called idiopathic but is some families it occurs repeatedly. It may be evoked by alcoholism or by certain drugs. Chronic hemoglobinopathies and genital cancer may also cause it. ►idiopathic, ►hemoglobinopathies, ►nitric oxide, ►phosphodiesterase

Pribnow Box (TATA box): 5′-TATAATG-3′ (or similar) consensus preceding the prokaryotic transcription initiation sites by 5–7 nucleotides in the promoter region at about −10 position from the translation initiation site. Separated by 17 bp there is another conserved element (called extended promoter) in prokaryotes at −35 (TTGACA). The eukaryotic homolog of the Pribnow box is the Hogness box. ►Hogness box, ►open promoter complex, ►σ; Gold L et al 1981 Annu Rev Microbiol 35:365.

Pride: A living and mating community of animals under the domination of a particular male(s).

Primary Cells: Primary cells are taken directly from an organism rather than from a cell culture.

Primary Constriction: The centromeric region of the eukaryotic chromosome (see Fig. P126).

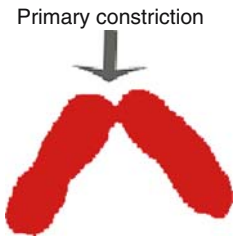

Figure P126. Primary constriction

Primary Nondisjunction: ►nonsdisjunction

Primary Response Genes: The induction of primary response genes occurs without the synthesis of new protein but requires only pre-existing transcriptional modifiers such as hormones. ►sign transduction, ►secondary response genes

Primary Sex Ratio: Ratio of males to females at conception. ►sex ratio

Primary Sexual Characters: The female and male gonad, respectively. ►secondary sexual characters

Primary Structure: The sequence of amino acid or nucleotide residues in a polymer.

Primary Transcript: The RNA transcript of the DNA before processing has been completed. ►processing, ►pre-mRNA, ►pre-rRNA

Primase: Polymerase-α/primase synthesizes an about 30-nucleotide RNA primer for the initiation of replication of the lagging strand of the DNA. In prokaryotes, the primosome protein complex fulfills the function. In bacteriophage M13, an imperfect hairpin is formed at the origin of replication, which is recognized by *E. coli* RNA polymerase σ^{70} holoenzyme and it synthesizes a 18–20 nucleotide primer suitable for synthesis by DNA polymerase III. The RNA polymerase leaves a protruding 3′-end of the RNA but maintains an RNA-DNA hybrid molecule of 8–9 bp. This 3-end of the RNA can then interact with DNA polymerase III. Filamentous phages and bacterial plasmids probably use the priming mechanisms (Zenkin N et al 2006 Nature [Lond] 439:617). The function of the primase is much slower than the processing of the DNA polymerase. Since the Okazaki fragments need priming several times while the leading strand is synthesized by the DNA polymerase, there must be a molecular brake there to assure that the two (leading and lagging) strands are synthesized in concert (Lee J-B et al 2006 Nature [Lond] 439:621). In *E. coli*, gene *DnaG* (66 min) encodes it and it is associated with the replicative helicase. In eukaryotes, the ∼60 and ∼50 kDa subunits of DNA polymerase α represent the primase.

The latter complex is associated with proteins and forms a mass of ~300 kDa. The primases prime any single-stranded DNA but they are far more effective at specific sequences. DnaG recognizes the 5′-CTG-3′ trinucleotide and synthesizes a 26–29 nucleotide RNA. The mouse primase works at ~17 sites that share either 5′-CCA-3′ or 5′-CCC-3′ at about 10 nucleotides downstream from the priming initiation site at the 3′-end. The active template is usually rich in pyrimidines. In eukaryotes, the primer is directly transferred to the DNA pol α without dissociating from the template. Primase inhibitors (cytosine or adenosine arabinoside, 2′-deoxy-2′-azidocytidine, etc.) have therapeutic potentials. Several binding proteins assist priming. ►replication fork, ►DNA replication, ►PriA, ►DNA polymerases, ►polymerase switching, ►Okazaki fragment, ►primosome, ►replication restart; Keck JL et al 2000 Science 287:2482; Arezi B, Kuchta RD 2000 Trends Biochem 25:572; Frick DN, Richardson CC 2001 Annu Rev Biochem 70:39; Augustin MA et al 2001 Nature Struct Biol 8:57.

Primates: The taxonomic group that includes humans, apes, monkeys, and lemur. To the higher primates, also called anthropoidea or simians, belong the old world monkeys (Cercopithecidae) such as the *Macaca*, *Cercopythecus*, etc., hominoidea (chimpanzee [*Pan*], gorilla [*Gorilla*], orangutan [*Pogo*], and humans, and also the now extinct early evolutionary forms. The anthropoidea includes also the new world monkeys (*Ceboidea*). The lower primates or prosimians mean the genera of the lemur, galago, etc. According to data of D.E. Kohne et al (1972 J Hum Evol. 1:627), on the basis of thermal denaturation of hybridized DNA the numbers in million years of divergence (and the % of nucleotide difference) of various primates from man was estimated to be: chimpanzee 15 (2.4), gibbon, 30 (5.3), green monkey 46 (9.5), capuchin 65 (15.8), galago 80 (42.0). Some of the DNA differences now need revisions (►chimpanzee). Humans have substantially lower variations in the DNA than the great apes, chimpanzees, and orangoutan (see Table P2) (Kaessmann H et al 2001 Nature Genet 27:155).

Table P2. The expressed genes indicate relations among three primate species as follows

	Chimpanzee	Orangutan	Rhesus macaque
Humans	110	128	176
Chimpanzee	-	150	141
Orangutan	-	-	129

(Data from Gilad, Y. *et al*. 2006 Nature [Lond) 440:242)

The taxonomic tree of primates can be outlined as:

PRIMATES: *I. Catarrhini*. IA1 Cercopithecidae (Old World Monkeys). IA1a Cercopithecinae, IA1b Colobinae. IA1c Cercopithecidae. IB. Hominidae (Gorilla, Homo, Pan, Pongo). IC. Hylobatidae (Gibbons). *II. Platyrrhini* (New World Monkeys): IIA. Callitrichidae (Marmoset and Tamarins). IIA1. Callimico. IIA2. Callithrix. IIA3. Cebuella. IIA4. Callicebinae. IIA5. Cebinae. IIA6. Pitheciinae. *III Strepsirhini* (Prosimians) IIIA Cheirogalidae. IIIA1 Cheirogaleus. IIIA2. Microcebus. IIIB. Daubentoniidae (Ayeayes). IIIB1. Daubentonia. IIIC Galagonidae (Galagos). IIIC1. Galago. IIIC2. Otolemur. IIID. Indridae. IIID1 Indri. IIID2. Propithecus (Sifakas). IIIE. Lemuridae (Lemurs). IIIE1. Eulemur. IIIE2. Hapalemur. IIIE3. Lemur. IIIE4. Varecia. IIIF. Loridae (Lorises). IIIF1. Loris. IIIF2. Nycticebus IIIF3. Perodicticus. IIIG Megalapidae. IIIG1. Lepilemur. *IV. Tarsii* (Tarsiers). IVA Tarsiidae (Tarpsiers). IVA1. Tarsius. ►human races, ►apes, ►prosimii, ►Cebidae, ►Callithricidae, ►Cercopithecideae, ►Colobidae, ►Pongidae, ►*Homo sapiens*, ►Hominidae, ►evolutionary tree; DeRousseau CJ (ed) 1990 Primate Life History and Evolution, Wiley-Liss, New York; Enard W et al 2002 Science 296:340; http://www.primate.wisc.edu/pin; phylogeny database: http://www.hvrbase.org/.

Primatized Antibody: A chimeric antibody constructed using the variable region of monkey antibody linked to the human constant region. ►antibody chimeric

Primer: A short sequence of nucleotides (RNA or DNA) that assists in extending the complementary strand by providing 3′-OH ends for the DNA polymerase to start transcription. In some viruses (hepadna viruses, adenoviruses), the replication of viral DNA, and in some cases viral RNA is primed by proteins. The 3′ OH group of a specific serine is linked to a dCMP and a viral enzyme drives the reaction. Replication may proceed from both ends of the linear molecules without being in the same replication fork. ►nested primers, ►primase, ►PCR, ►Vpg; http://www.genome.wi.mit.edu; primer identification: http://ihg.gsf.de/ihg/ExonPrimer.html; http://web.ncifcrf.gov/rtp/gel/primerdb/; primer design for promoters and exons: http://genepipe.ngc.sinica.edu.tw/primerz/; may better opens by: http://www.citeulike.org/user/sebastien_vigneau/article/1357047; Primer3 primer selection: http://www.bioinformatics.nl/cgi-bin/primer3plus/primer3plus.cgi.

Primer Extension: RNA (or single-strand DNA) is hybridized with a single strand DNA primer (30–40 bases), which is 5′-end-labeled. Generally, the primers are complementary to base sequences within 100 nucleotides from the 5′-end of mRNA to avoid

heterogeneous products of the reverse transcriptase which is prone to stop when it encounters tracts of secondary structure. After extension of the primer by reverse transcriptase, the length of the resulting cDNA (measured in denaturing polyacrylamide gel electrophoresis) indicates the length of the RNA from the label to its 5′-end. When DNA (rather than RNA) is used as template DNA-DNA hybridization must be prevented. The purpose of the primer extension analysis is to estimate the length of 5′ ends of RNA transcripts and identify precursors of mRNA and processing intermediates. The cDNA so obtained can be directly sequenced by the Maxam-Gilbert method or also by the chain termination methods of Sanger if dideoxyribonucleoside triphosphates are included in the reaction vessels. Primer extension preamplification (PEP) facilitates the preparation of multiple copies of the genome of a single sperm (Zhang L et al 1992 Proc Natl Acad Sci USA 89:5847). ►DNA sequencing, ►primary transcript, ►post-transcriptional processing, ►chimeric proteins, ►PCR-based mutagenesis, ►amplification; Reddy VB et al 1979 J Virol 30:279; Sambrook J et al 1989 Molecular cloning, Cold Spring Harbor Laboratory Press.

Primer Shift: The primer shift is used for confirmation that a PCR procedure indeed amplified the intended DNA sequence. For this purpose, a primer different from the one initially employed is chosen and attached to the template a couple of hundred bases away from the position of the first. After the completion of the PCR process, the amplified product is supposed to be as much longer as the difference between the position of the first and the second primer if the amplification involved the intended sequence. Such a procedure may be used when a DNA sequence corresponding to a deletion is amplified. ►PCR, ►primer

Primer Walking: A method in DNA sequencing whereby a single piece of DNA is inserted into a large-capacity vector. After a shorter stretch had been sequenced, a new primer is generated from the end of what has been already sequenced and the process is continued until the sequencing of the entire insert is completed. ►DNA sequencing; Zevin-Sonkin D et al 2000 DNA Seq 10(4–5):245; Kaczorowski T, Szybalski W 1998 Gene 223:83.

Primitive Streak: The earliest visible sign of axial development of the vertebrate embryo when a pale line appears caudally at the embryonic disc as a result of migration of mesodermal cells. ►organizer, ►differentiation, ►morphogenesis, ►Hensen's node, ►embryo node; Ciruna B, Rossant J 2001 Dev Cell 1:37.

Primordium: The embryonic cell group that gives rise to a determined structure.

Primosome: The complex of prepriming and priming proteins involved in replication of the Okazaki fragments (see Fig. P127). It moves along with the replication fork in the opposite direction to DNA synthesis. The primosome (containing helicase and primase) unwinds the double-stranded DNA and synthesizes RNA primers. ►DNA replication, ►replication fork, ►Okazaki fragment, ►primase; Marsin S et al 2001 J Biol Chem 276:45818; replication restart primosome PriB component structure: Lopper M et al 2004 Structure 12:1967; Zhang Z et al 2005 Proc Natl Acad Sci USA 102:3254; electron microscopic structure: Norcum MT et al 2005 Proc Natl Acad Sci USA 102:3623.

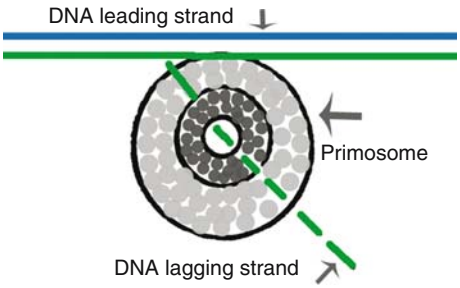

Figure P127. Primosome

Primula (Primrose): An ornamental plant. *P. kewensis* (2n = 36) is an amphidiploid of *P. floribunda* (2n = 18) and *P. verticillata* (2n = 18).

Principal Component Analysis: The aim of the principal competent analysis is to reduce the apparent complexity of the original variables and summarize the information in a simpler manner. The principal components are construed as linear functions of the original variables. ►factorial analysis, ►stratification; Joliffe IT 1986 Principal Component Analysis, Springer, New York.

PRINS (primed in situ synthesis): An in situ hybridization technique bearing some similarities to other methods of probing (e.g., FISH). The PRINS procedure uses small oligonucleotide (18–22 nucleotides) primers from the sequence of concern. After the primer is annealed to denatured DNA (chromosomal or other polynucleotides), a thermostable DNA polymerase is employed to incorporate biotin-dUTP or digoxygenin-dUTP. The procedure is very sensitive to mismatches (because the primer is short) and a mismatch at the 3′-end may prevent chain extension. The concentration of the primer (C) = $Ab_{260}/\varepsilon_{max}$ x L

where Ab_{260} = absorbance at 260 nm, ε_{max} = molar extinction coefficient (M^{-1}) and L = the path length of the cuvette of the spectrophotometer. The molar extinction coefficients are determined ε_{max} = (number of A × 15,200) + (number of T × 8400) + (number of G × 12,010) + (number of C × 7050) M^{-1}. (A = adenine, T= thymine, G = guanine, C = cytosine). PRINS are useful for many purposes, including determination of aneuploidy, DNA synthesis, viral infection, etc. ►PCR, ►FISH, ►in situ hybridization, ►LISA, ►biotinylation, ►extinction, ►non-radioactive label; Hindkjaer J et al 2001 Methods Cell Biol 64:55.

PrintAlign: A computer program for graphical interpretation of fragment alignments in physical mapping of DNA. ►physical map

PrintMap: A computer program that produces a restriction map in PostScript code. ►PostScript

PRINTS: A database for the analysis of the hierarchy of protein families on the basis of fingerprints. ►protein families; http://www.bioinf.man.ac.uk/dbbrowser/PRINTS/.

Prion (PrP^C, PrP^{Sc}, PrP*, PRPres): Infective, protease-resistant glycoprotein particles, responsible for the degenerative brain diseases such as scrapie in sheep, chronic wasting disease in deer and elk, BSE in cattle, kuru, Creutzfeldt-Jakob disease, Gerstmann-Sträussler syndrome, fatal familial insomnia of man and, possibly, also Alzheimer's disease. Protease-sensitive prions ($sPrP^{Sc}$) also exist. Prions are transmitted among various animal species although the expression may require a longer lag. Decreased transmission of the prion state between divergent proteins is termed "species barrier" and was thought to occur because of the inability of divergent prion proteins to co-aggregate. Species barrier can be overcome in cross-species infections, e.g., from "mad cows" to humans. The counterparts of yeast prion protein Sup35, originated from three different species of the *Saccharomyces sensu stricto* group exhibit the range of prion domain divergence that overlaps with the range of divergence observed among distant mammalian species. All three proteins were capable of forming a prion in *Saccharomyces cerevisiae*, although prions formed by heterologous proteins were usually less stable than the endogenous *S. cerevisiae* prion. Heterologous Sup35 proteins co-aggregated in the *S. cerevisiae* cells. However, in vivo cross-species prion conversion was decreased and in vitro polymerization was cross-inhibited in at least some heterologous combinations, thus demonstrating the existence of prion species barrier (Chen B et al 2007 Proc Natl Acad Sci USA 104:2791).

Mutations in the gene may result in prion potentiation. The non-familial Creutzfeldt-Jakob disease may be traced to infections by gonadotropins, human growth hormones extracted from cadavers, grafts, improperly-sterilized medical equipment contaminated by prions, or to eating the meat (primarily brain, lymphatic and nerve tissues) of infected animals. In case of chronic inflammation of the kidneys, scapie-infected mice excrete prions by the urine (Seeger H et al 2005 Science 310:324). Normal prion protein, PrPsen (PRP^C protease sensitive), is expressed as a membrane-bound glycophosphatidylinositol (GPI)-anchored protein (see Fig. P128). The GPI anchor may be the requisite for infectious transmission of this protein and the expression of typical scrapie (Chesebro B et al 2006 Science 308:1435). Other amyloidogenic proteins, which are involved in brain degeneration but lack GPI anchor, are not infectious. GPI-anchorless proteins can be secreted from the blood and can form deposits in the amyloid or non-amyloid forms in the brain and heart endothelia. In infected non-transgenic mice, it appears mainly in the non-amyloid form but in transgenic animals, mainly in the amyloid form. The protease-resistant prion causes heart disease (Trifilo MJ et al 2006 Science 313:94).

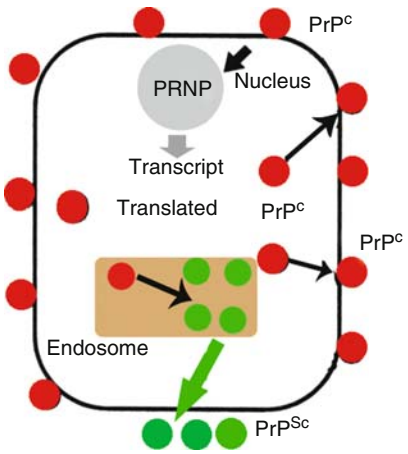

Figure P128. The normal PrP^C protein is encoded in the nucleus by the PRNP gene and after transcription the RNA transcript is translated in the cytoplasm. Some of the PrP^C molecules decorate the surface of the nerve cells and others may be sequestered into the endosomes or lysosomes. Within these compartments, a conformational alteration may take place and the infectious PrP* or PrP^{Sc} protein molecules are released. These altered molecules may then infect other, normal cells and initiate a process of degenerative protein accumulation. The conformational changes may be caused by mutations in PRNP and other genes located in several human chromosomes. (Modified after Weissmann C 1999 J Biol Chem 274:3)

On the basis of the degree and extent of glycosylation, about 400 prions have been distinguished. The N terminus of PrP contains a glycosaminoglycan (GAG)-binding motif. Binding of GAG is important in prion disease. Accordingly, all human mutant recombinant rPrPs bind more GAG, and GAG promotes the aggregation of rPrP more efficiently than wild-type recombinant normal cellular PrP (rPrPC). Furthermore, point mutations in *PRNP* gene also cause conformational changes in the region between residues 109 and 136, resulting in the exposure of a second, normally buried, GAG-binding motif. Importantly, brain-derived PrP from transgenic mice, which express a pathogenic mutant with nine extra octapeptide repeats also binds more strongly to GAG than wild-type PrPC (Yin S et al 2007 Proc Natl Acad Sci USA 104:7546).

Prions appear like virus particles but are free of nucleic acid. The 25 nm virus-like arrays in two cell lines with transmissible spongiform encephalitis (TSE) virions are structurally independent of pathological PrP in the intact cell (Manuelidis L et al 2007 Proc Natl Acad Sci USA 104:1965). It appears that a normal protein is structurally modified; the α helical structure is largely converted into β sheets, leading to the formation of these autonomous disease-causing proteins. Transmission of the disease in the absence of the protease-resistant prion is exceptional (Lasmézas CI 1997 Science 275:402). Although prions are infectious diseases of protein folding, some RNAs of mammals appear adjuvants of the pathogenic alterations in vitro whereas invertebrate RNA has no such effect (Deleault NR et al. 2003 Nature [Lond] 425:717). Experimental protein misfolding cyclic amplification (PMCA) reaction can yield in vitro generated prions that are indistinguishable from prions isolated from scrapie hamster brain in terms of proteinase K resistance, autocatalytic conversion activity, and, most notably, specific biological infectivity (Weber P et al 2006 Proc Natl Acad Sci USA 103:15818).

In order to develop prion disease in mice, the organism must have PrP^C, and if it is absent the animals become resistant to scrapie and show normal neuronal functions (Büeler H et al 1993 Cell 73:1339). PrPC-deficient cattle produced by a sequential gene-targeting system over 20 months of age are clinically, physiologically, histopathologically, immunologically and reproductively normal. Brain tissue homogenates are resistant to prion propagation in vitro (Richt JA et al 2007 Nature Biotechnol 25:132). Also, microglia (cells that surround the nerves and phagocytize the waste material of the nerv tissue) must be present to develop prion disease. Depletion of the endogenous neuronal PrP^C from mice by the Cre recombinase prevents the progression of the disease. The non-neural accumulation of PrP^{Sc} is not pathogenic but leads to an arrest of $PrP^C \rightarrow PrP^{Sc}$ conversion within neurons and prevents neurotoxicity (Malluci G et al 2003 Science 302:871). Depletion of endogenous neuronal prion protein (PrP^C) in mice with early prion infection reversed spongiform change and prevented clinical symptoms and neuronal loss. Thus, early functional impairments precede neuronal loss in prion disease and can be rescued. Further, they occur before extensive PrP^{Sc} deposits accumulate and recover rapidly after PrP^C depletion, supporting the concept that they are caused by a transient neurotoxic species, distinct from aggregated PrP^{Sc} (Malucci GR et al 2007 Neuron 53:325).

If microglia are destroyed by L-leucine-methylester, the neurotoxic PrP fragment, containing amino acids 106–126, does not harm the neurons. The transition from the normal $PrP^C \rightarrow PrP^{Sc}$ (the insoluble scrapie prion) conformation involves changes in amino acid residues 121–231, involved two antiparallel β-sheets and in three α-helices (see Fig. P129).

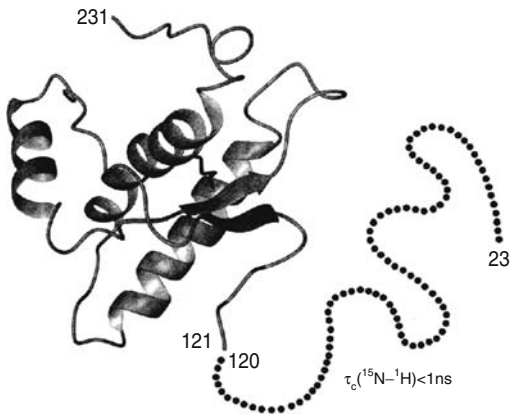

Figure P129. The nuclear magnetic resonance-revealed structure of the PrP^C protein. The amino end displays an about 100 residue flexible sequence that is modified when PRP^{Sc} is formed. (Modified after Riek R et al 1997 FEBS Lett 413:282. By Permission of Elsevier Science and Authors)

Monoclonal antibody 15B3 (Peretz D et al 2001 Nature [Lond] 412:739) and the anti-DNA antibody OCD4 as well the gene 5 protein (Zou W-Q et al 2004 Proc Natl Acad Sci USA 101:1380), both DNA-binding proteins, discriminate between the PrP^C and PrP^{Sc} and may help in the diagnosis of prion diseases or perhaps cure. Early diagnosis of prions (CJD) is possible because two peptides of PrP^C bind 3800 fold more effectively to PrP^{Sc} than to PrP^C (Lau AL et al 2007 Proc Natl Acad Sci USA 104:1151). The Tyr-Tyr-Arg monoclonal antibodies discriminate between PrP^C and PrP^{SC} and hold promise that immunoprophylaxis and/or immunotherapy may eventually

become available (Paramithiotis E et al 2003 Nat Med 9:893). Conformation-dependent immunoassay (CDI) can discriminate among different prion strains. This assay quantifies PrP isoforms by simultaneously following antibody binding to the denatured and native prion protein. When the denatured/native PrP is graphed as the function of PrP^{Sc} concentration, each strain occupies a different position indicating a unique conformation (Safar J et al 1998 Nature Med 4:1157). The CDI test is extremely reliable (Safar JG et al 2005 Proc Natl Acad Sci USA 102:3501).

It has been hypothesized—on the basis of experimental observations—that the toxicity of this protein is based on increased oxidative stress. The inactivation of the *PrP* gene in mice does not lead to an immediate deleterious condition, but by the age of 70 weeks, an extensive loss of the Purkinje cells (large neurons in the cerebellar cortex) takes place and the animals have problems with movement coordination (ataxia). In case the normal PrP protein accumulates in the cytosol, a self-perpetuating PrP^{Sc}-like transformation takes place and neurodegeneration results (Ma J et al 2002 Science 298:1781). The disrupted *PrP* genes make them resistant to prions. Susceptibility in mice is affected also by QTLs in chromosomes 4, 6, 8, and 17 (Moreno CR et al 2003 Genetics 165:2085). On the basis of some genetic tests, it was concluded that the period of incubation of the mouse scrapie is controlled by allelic forms of a separate gene (*Sinc/Prni*). Molecular evidence indicates, however, that codons 108 and/or 109 of the *Prp* gene control incubation. In the mouse, there is a second *PrP* locus 16 kb down-stream. This *Prnd* (d for Doppelgänger [alterego in German], downstream prion protein-like) is truncated at the amino end domain and encodes only 179 amino acids.

Although its amino acid sequence shows only 25% homology with PrP, the structure of Prnd is quite similar. Prnd originated probably as an ancient duplication. Mice homozygous knockouts for Prnd and PrC are sterile. Its expression is normally limited to the testes, but if it is expressed in the brain, it causes neurodegeneration.

In case the *PrP* (Prnp) exons are deleted, Doppelgänger exons can be spliced into the PrP mRNAs. In ataxic animals, this intergenic splicing is highly expressed. Apparently, the manifestation of ataxia, the loss of Purkinje cells, and the degeneration of cerebellar granule cells is correlated with the alteration of a ligand-binding site.

A mutant form of PrP, ^{Ctm}PrP, a trans-membrane protein, can also cause prion disease in the absence or presence of PrP^{Sc}. The latter may also modulate the synthesis of the transmembrane form. Actually "the ability of polypeptide chains to form amyloid structures is not restricted to the relatively small number of proteins associated with recognized clinical disorders, and it now seems to be a generic feature of polypeptide chains" (Dobson CM 2003 Nature [Lond] 426:884). PrP^{Sc} molecules could be formed *de novo* from defined components in the absence of preexisting prions. PrP^{Sc} can be formed from a minimal set of components including native PrP^{C} molecules, co-purified lipid molecules, and a synthetic polyanion. Inoculation of samples containing either prion-seeded or spontaneously generated PrP^{Sc} molecules into hamsters caused scrapie, which was transmissible on second passage (Deleault NR et al 2007 Proc Natl Acad Sci USA 104:9741).

PrP^{C} may be involved in signal transduction in nerve function. PrP^{Sc} apparently binds plasminogen that selectively imparts neurotoxicity to the prion protein.

In budding yeast, two non-nuclear elements [*URE3*] and [*PSI*] appear (among others) to be the infectious prion forms of the Ure2p protein that is also a regulator of nitrogen catabolism. When Urep was overexpressed in wild type strains, the frequency of occurrence of the [*URE3*] increased 20–200 fold. If the overexpression of Urep was limited only to the amino ends of this protein, the frequency of occurrence of [*URE3*] increased 6000 times. The carboxyl domain of Urep seemed to carry out nitrogen catabolism whereas the amino end induced the prion formation. Both [*URE3*] and [*PSI*] are the prion causing forms of nuclear genes *URE2* and *SUP35*, respectively. The *URE2* gene is involved in the control of utilization of ureidosuccinate as a nitrogen source, while the *SUP35* nuclear gene encodes a subunit (eRF3, eukaryotic release factor) of the yeast translation termination complex. Mutations in both the nuclear genes involve derepression of nitrogen catabolism that is normally repressed by nitrogen. The propagation of [*URE3*] and [*PSI*] depends on *URE2* and *SUP35* nuclear genes, respectively. Guanidine-HCl blocks the propagation of PSI^{+}. Gdn·HCl-induced loss of the [PSI^{+}] prion is due to a failure to segregate propagons from daughter cells and not because of degradation of the preexisting propagons (Byrne LJ et al 2007 Proc Natl Acad Sci USA 104:11688). In vitro, the Sup35 protein may show prion-like properties. Normally, translation terminates at a stop codon by an interaction between Sup35 and other proteins such as Sup45. If the Sup35 proteins aggregate, they may assume prion conformation and the translation continues beyond the stop codon and an additional protein sequence is formed (▶eRF). The conformation of the SUP35 prion motif varies among different fungal species and is important for its transmissibility. The amyloid fiber morphology and size may vary in different yeast prion strains (Diaz-Avalos R et al 2005 Proc Natl Acad Sci USA 102:10165). A certain conformation of SUP35 of *Saccharomyces cerevisiae* permits transmission to

Candida albicans and such *Candida* can then infect *Saccharomyces*. Thus strain conformation is critical for cross-species transmission (Tanaka M et al 2005 Cell 121:49; Tanaka M et al 2006 Nature [Lond] 442:585). A similar conclusion has been reached in mammals where a single or two residues determine critical requirement for amyloid transmission, yet preformed fibrils may overcome sequence-based structural preferences. For transmission, the amyloid protein conformation is the critical factor (Jones EM, Surewicz WK 2005 Cell 121:63). The cross-β spine structure explains the critical features of stability and self-perpetuation of the amyloid fibers (►cross-β spine). Heat shock protein Hsp104 catalyzes the formation and also the destruction of this yeast prion (Shorter J, Lindquist SW 2004 Science 304:1793). Deletion of Hsp104 eliminates Sup35 and Ure2 prions, whereas overexpression of Hsp104 purges cells of Sup35 prions, but not Ure2 prions. For both Sup35 and Ure2, Hsp104 catalyzes de novo prion nucleation from soluble, native proteins. Hsp104 fragments both prions to generate new prion-assembly surfaces. For Sup35, however, the fragmentation endpoint is an ensemble of noninfectious, amyloid-like aggregates and soluble proteins that cannot replicate conformation (Shorter J, Lindquist S 2006 Mol Cell 23:425). Five glutamine/asparagine-rich oligopeptide repeats at the N-terminus of Sup35 stabilize the aggregated form, and for replication, a chaperone-dependent element is also required (Osherovich LZ et al 2004 PLoS Biol 2(4): E86). In a somewhat different amyloid disease associated with transthyretin, only the highly destabilized molecules are degraded in the endoplasmic reticulum and only in certain tissues, indicating that endoplasmic reticulum-assisted folding depends on energetics, chaperone distribution, and metabolites (Sekijima Y et al 2005 Cell 121:78).

The human PrP repeat (PHGGGWGQ) can substitute for the yeast peptides (Parham SN et al 2001 EMBO J 202111). This feature of prions allows the development of diversity and may have evolutionary significance. Structurally, neither [*URE3*] nor [*PSI*] are similar to the mammalian PrP protein, indicating that there is more than one way for prions to arise. In the fungus *Podospora anserina*, the heterokaryosis incompatibility locus (*Het*) also makes prion-like proteins. The infectious forms of the normal Prp are also called PrP*, and the PrP^{Sc} is designated also PrP^{res} (protease-resistant prion). PrP^{C} and PrP^{Sc} appear to be conformational isomers. PrP* is the misfolded pathological core form. The yeast prion [PSI^{+}] can be reversibly removed, "cured" to [psi^{-}] 100% in seven to eight generations when exposed to guanine hydrochloride or methanol. Guanidin inactivates Hsp104 and Sup35 depolymerizes without a need for cell division (Wu Y-X et al 2005 Proc Natl Acad Sci USA 102:12789). The denaturants induce the expression of chaperones, giving further support to the notion that the prion functions are based on conformational changes. Recent evidence indicates that the $PrP^{C} \rightarrow PrP^{Sc}$ transition may involve the chemical thiol/disulphide exchange between the terminal thiolate of PrP^{Sc} and the disulfide bond of a PrP^{C} monomer and not only a conformational change (Welker E et al 2001 Proc Natl Acad Sci USA 98:4434). The protein chaperones HSP104, and to a lesser extent, HSP70, can affect the expression and transmission of [PSI^{+}] and its conversion to [psi^{-}]. In silico screening for compounds that fitted into a "pocket" created by residues undergoing the conformational rearrangements between the native and the sparsely populated high-energy states (PrP*) and that directly bind to those residues identified 2-pyrrolidin-1-yl-N-[4-[4-(2-pyrrolidin-1-yl-acetylamino)-benzyl]-phenyl]-acetamide (GN8), which efficiently reduced PrP^{Sc} and improved the survival of affected mice (Kuwata K et al 2007 Proc Natl Acad Sci USA 104:11921).

When the *URE2* and *SUP35* genes or the N-terminal domain of their products are deleted, the [*URE3*] and [PSI^{+}] elements permanently disappear. These yeast proteins are different from each other and from the prion proteins of higher eukaryotes, except the N-terminal region where homology exists. The NH_2 domain of SUP35, when fused to the rat glucorticoid receptor protein, can interact with the endogenous Sup35 protein and it undergoes a prion-like change of state. Self-replication requires a conformational conversion of initially unstructured Sup35 protein. Thus, the prion-like behavior is transmissible to another protein (Derkatch IL et al 2001 Cell 106:171). More recently, additional yeast proteins (RNQ1, NEW1) with prion-like properties have been identified (Tuite MF 2000 Cell 100:289; Derkatch IL 2000 EMBO J 19:1942). The *het-s* gene product of *Podospora anserina*, responsible for spore killer properties, also meets the criteria of being a prion (Perkins DD 2003 Proc Natl Acad Sci USA 100:6292). The so-called C hereditary units in *Podospora* have a nature similar to prions; they contain the MAPK cascade and trigger cell degeneration (Kicka S et al 2006 Proc Natl Acad Sci USA 103:13445).

The vCJD (variant of Creutzfeldt-Jakob disease) prions appear to have either single amino acid differences or differences in glycosylation which may also be the cause or consequence of conformational differences. The differences in electrophoretic mobility of the protease-digested prions are expected to shed light upon the problems of tracing the transmission of prions from cattle to man or among different animal species. The PrP gene in humans is in chromosome 20p12, and encodes 253 amino acids by a single exon.

The corresponding mouse gene is in chromosome 2. Other mammalian genes display very substantial homologies, although they may be transcribed by up to three exons. The NH^2-end of the protein displays an 8 amino acid repeat consensus (PHGGGW) in five to six copies, depending on the species. Deletions in these repeats do not involve disease symptoms. Short conserved amino acids downstream of the last repeats are important for $PrP^C \rightarrow PrP^{Sc}$ conversion. Another unique feature of PrP is an alanine-rich tract (AGAAAAGA). The transmission of prions among different species prolongs the incubation period. Mice lacking the gene for PrP^C cannot develop the disease even when inoculated (Büeler H et al 1993 Cell 73:1339). The PrR^C deficient mouse appears normal. Knocking out PrR^C from larger mammals would be an approach to avoid prion formation but because of technical difficulties, the use of shRNA is a viable alternative to block PrP expression and prevent encephalitis. Transgenic goats and cows produced by nuclear transplantation of the cognate shRNA gene resulted in more than 90% reduction in PrP expression (Golding MC et al 2006 Proc Natl Acad Sci USA 103:5285). The most infectious property was attributed to 300–600 kDa particles (14–28 PrP molecules) and less than five molecules, as well as very large aggregates, were much less effective in evoking neurodegenerative disease (Silveira JR et al 2005 Nature [Lond] 437:257). Also, immunodeficient mice, despite the fact that they may accumulate plaques upon scrapie infection, fail do develop the disease. It appears that human individuals who might have been exposed to the same BSE source may not all respond with the development of the disease.

$PrP^C \rightarrow PrP^{Sc}$ conversion by infection with a prion from another species (heterotypic conversion), especially when the inoculum is small or the inoculation occurs rarely, is less likely. The amino acid sequence in the 125–231 sequence displays differences among cow, sheep, dog, cat, pig, mouse, Syrian hamster, and human PrP^Cs and the structure varies as well (Lysek DA et al 2005 Proc Natl Acad Sci USA 102:640). Similarly, structural differences exist in elk compared to cow PrP^C (Gross AD et al 2005 Proc Natl Acad Sci USA 102:646). The chicken, turtle, and *Xenopus* PrP^Cs display only about 30% identity with the mammalian protein amino acid sequence, yet the molecular architectures are similar (Calzolai L et al 2005 Proc Natl Acad Sci USA 102:651).

Wild type mice brain infected with hamster prions did not develop scrapie, although a low level of maintenance of the hamster protein was detectable and reintroduced into hamsters; encephalitis followed. When the human prion is transferred to an animal, the PrP sequences in the new host are determined by the recipient and not by the donor, except when the animal is transgenic for the human PrP. Thus, the prion inoculum acts as a catalyst or as a chaperone. It is known that in Prp-deficient mice the immune system eliminates the PrP^C. It is also conceivable that in mice the hamster PrP^{Sc} is immunologically tolerated. The presence of the PrP gene is a requisite for the development of the PrP^{Sc} protein. PrP^{Sc} exists in multimeric rather than monomeric forms but PrP may become part of the interacting PrP^{Sc} molecular network. There are indications that prion and DNA interaction may modulate the harmful aggregation of the protein (Cordeiro Y et al 2001 J Biol Chem 276:49400). Hamster-adapted prion protein heated up to 600°C for 5 to 15 min (actually ashed) still retained some infectivity and points to the role of an inorganic template in the replication of scrapie. Heating to 1000°C abolished all activity. In case of relatedness between these two proteins, PrP^{Sc} may easily facilitate the conversion to prion. The expression of the PrP^{Sc} may require chaperones. One such protein was named X but its role is unclear. In vitro essay is available for fast and relatively inexpensive assaying of prions using mouse neuroblastoma cell line N2a (Klöhn P-C et al 2003 Proc Natl Acad Sci USA 100:11666).

According to some views, the "protein only" mechanism requires further proof, although all current evidence indicates a "protein only" basis. There is definite proof that the prions of yeast can be caused by the amino-terminal fragment of the Sup-35 protein without the help of any other substance (King C-Y, Diaz-Avalos R 2004 Nature [Lond] 428:319; Tanaka M et al 2004 ibid. 323). Additional recent evidence further supports this protein-only principle. A synthetic peptide (free of nucleic acids), containing mutation at site 102 leucine (see Fig. P130) folded into a β-conformation-rich form, was introduced into mice; and animals developed disease homologous to the Gerstmann-Sträussler syndrome in humans (Tremblay et al 2004 J Virol 78:2088). Furthermore, the peptide-induced disease was serially passaged into healthy mice, which developed symptoms indistinguishable from those appearing spontaneously in PrP^{Sc} leucine mutants. Similarly, recombinant protein consisting of the mouse prion sequence 89–231, rich in β-sheets, was cloned in *Escherichia coli* and then introduced into the brain of animals that over-expressed the normal PrP^C. Mice developed neuropathological symptoms characteristic of specific encephalopathy, and their protease-resistant extract evoked disease symptoms in other animals. There were two essential differences from the normal infection. The responding recipients produced excessive amounts of PrP^C before inoculation, and the period of incubation was substantially extended compared with the normal course of disease development (Legname et al 2004 Science 305:673).

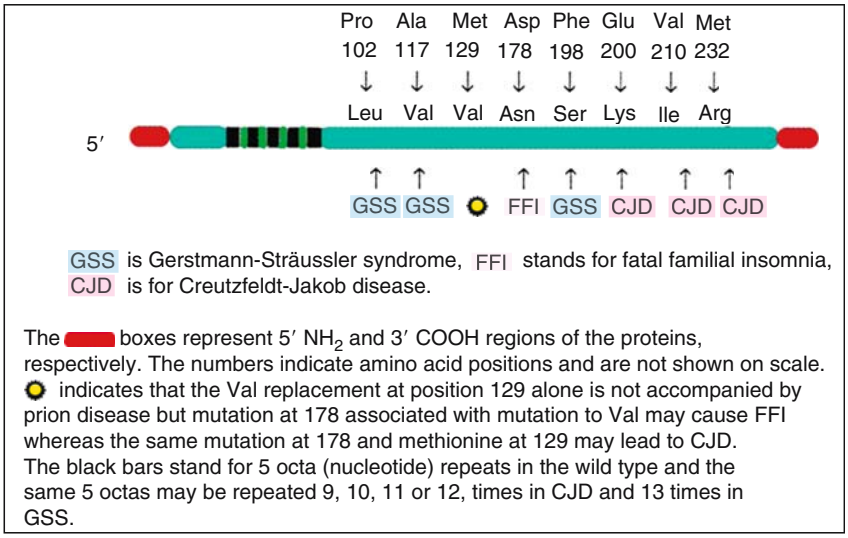

Figure P130. Prion mutations (Redrawn after Weissmann, C. 1999. J. Biol. Chem. 274:3.)

Cyclic amplification of protein misfolding (PMCA) in vitro produced protein identical to the protease resistant form in the brain of sick animals. Furthermore, this in vitro produced prion when introduced into healthy hamster caused the same type of disease as infection by PrP^{Sc} (Castilla J et al 2005 Cell 121:195). PMCA amplification technology can be automated and in 140 cycles leads to a 6600-fold increase in sensitivity compared to older techniques. Two successive rounds of PMCA increase the sensitivity of detection 10-million fold and can detect as few as 8000 molecules of PrP^{Sc} at 100% specificity (Castilla J et al 2005 Nature Med 11:982) and permit the detection of prions in the blood before the disease symptoms manifest (Saá P et al 2006 Science 313:92).

The existence of prions seems to be an exception to the "nucleic doctrine." Some evidence seemingly contradicts the infectious nature of the prions and points to accumulation of protein waste. The prion diseases may be familial, with an onset at about 50 years of age in humans. The sporadic forms are attributed to dominant somatic mutations. From cultured scrapie-infected mouse (but not of hamster) neuroblastoma cells, the branched polyamines (polyamidoamide dendrimers, polypropyleneimine, polyethyleneimine) purged PrP^{Sc} prions at non-toxic concentrations. Bis-acridines and a few other compounds appear inhibitory to prion replication in cell cultures (May BCH et al 2003 Proc Natl Acad Sci USA 100:3416). Kastellpaolitine, phenanthridines, 6-aminophenathridine, quinacrine, and chloropromazine appear effective in yeast against mammalian prions (see Fig. P131) (Bach S et al 2003 Nat Biotechnol 21:1075). By 2003, no real cure or preventive measures had emerged for prion diseases. There are some positive cues that proline-rich oligopeptides may restore the conformation of PrP^{Sc} to normal PrP. Preliminary results indicate that the lymphotoxin-β receptor may delay the onset of the symptoms temporarily in mice.

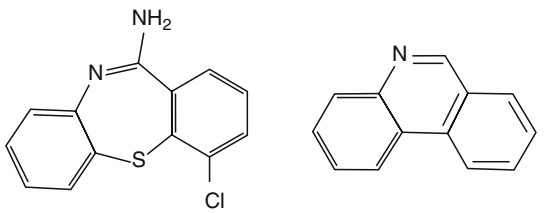

Figure P131. Kastellopaolitine 1 (left) is one of the other similar compounds, which have different substitutions at other positions at the right ring. Phenanthridine (right) basic structure

It seems that the complement component C3 is important for the prions to attach to the follicular dendritic cells, which mediate infection. Antibodies generated against the μ chain of PrP are a promising approach for the prevention of pathogenesis. ►Creutzfeldt-Jakob disease, ►Gerstmann-Sträussler disease, ►presenilin, ►kuru, ►encephalopathies, ►fatal familial insomnia, ►protein structure, ►Protein X, ►tau, ►curing plasmids, ►plasmin, ►chaperones, ►PSI^{+}, ►PIN^{+}, ►quinacrine mustard, ►*Cre/loxP*, ►virino hypothesis, ►conformation-dependent immunoassay, ►transthyretin, ►PMCA,

►MAPK, ►polyelectrolyte; Prusiner SB, Scott MR 1997 Annu Rev Genet 31:139; Cohen FE, Prusiner SB 1998 Annu Rev Biochem 67:793; Prusiner SB (ed) 2004 Prion Biology and Diseases, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York; Umland T C 2001 Proc Natl Acad Sci USA 98:1459; Heppner FL et al 2001 Science 294:178; Baskakov IV et al 2002 J Biol Chem 277:21140; Kanu N et al 2002 Curr Biol 12:523; Uptain SM, Lindquist S 2002 Annu Rev Microbiol 56:703; Chien P 2004 Annu Rev Biochem 73:617; Curr Mol Med 2004 June issue; valine at site 129 prevents CJD: Wadsworth JDF et al 2004 Science 306:1793; potential therapy: Cashman NR, Caughey B 2004 Nature Rev Drug Discovery 3:874; characterization review: Caughey B, Baron GS 2006 Nature [Lond] 443:803; characterization: Prusiner SB, McCarty M 2006 Annu Rev Genet 40:25.

Prior Distribution: A probability distribution of variables or parameters before empirical information was obtained. Generally, it is part of Bayesian inference. ►Bayes' theorem, ►posterior distribution

Prior Probability: The suspected incidence of a disease before a diagnostic test or change of environmental effects or other extrinsic factors before the onset of a condition are identified.

Prisoner's Dilemma: A game theory, applicable to the interpretation of pairwise competition between two types of organisms using conflicting strategies. The two may cooperate, or either may "defect" for selfish reasons(s) and exploit the other and consequently the fitness may decrease to $1 - s_1$. In case both of them defect (are uncooperative), the population has to pay a cost (c), and the fitness becomes $1 - c$. In case the defector gains a fitness advantage $(1 + s_2)$, it may invade the cooperators territory. If c is high ($[1 - c] < [1 - s_1]$, a stable polymorphism may result. This theory is applicable also to studies on economic activities and to other fields. ►snowdrift game, ►cooperation, ►tragedy of the common; Page KM, Nowak MA 2001 J Theor Biol 209:173; Neill 2001 J Theor Biol 211(2):159; Doebeli M et al 2004 Science 306:859; Imhof LA et al 2005 Proc Natl Acad Sci USA 102:10797.

Pristionchus pacificus: The *Pristionchus pacificus* nematode is somewhat similar to *Caenorhabditis elegans* http://www.pristionchus.org. ►Caenorhabditis

Privacy Rule: An individual's privacy is legally protected against unwanted disclosures, yet medical research has a legitimate need to use, access, and disclose protected health information with certain limitations. ►GWA; http://privacyrulesandresearch.nih.gov; http://privacyruleandresearch.nih.gov/pr_02.asp; European guidelines for human data: http://ec.europa.eu/justice_home/fsj/privacy/docs/wpdocs/2007/wp136_en.pdf; recommended confidentiality certificate of the US National Institutes of Health: http://grants.nih.gov/grants/policy/coc; human molecular genetic data: Lowrance WW, Collins FS 2007 Science 317:600.

Private Blood Groups: A collective name of various blood groups with low frequencies compared to *public blood* group systems that occur frequently.

Private Mutation: Private mutation occurs very rarely in a very limited number of families.

Privilege: ►immune privilege

PRL: ►prolactin

PRL-3 (PTP4A3, 8q24.3): A 22 kDa tyrosine protein phosphatase situated at the cytoplasmic membrane; its elevated expression is associated with metastasis of colorectal cancer. ►colorectal cancer, ►metastasis; Saha S et al 2001 Science 294:1343.

PRM (pattern recognition proteins): PRMs are involved in the regulation of transcription.

PRMT: Protein-arginine methyltransferase. (See Boisvert FM et al 2003 Mol Cell Proteomics 2:1319).

P_{RNP}: The human gene encoding the normal isoform of the prion protein; the same in mouse is P_{rnp}.

Proaccelerin: A labile blood factor (V); its deficiency may lead to parahemophilia and excessive bleeding during menstruation or after surgery or bruising. ►antihemophilic factors

Probabilistic Graphical Models of Cellular Networks: In biological modeling we may be interested in different attributes, e.g., in the random expression of the genes observed and the hidden attributes of the model, such as the cluster assignment of a gene. The model includes the joint probability distribution of all relevant random attributes. The probabilistic graphical model represents multivariate joint probability distributions by a product of terms, each involving only a few variables. In Bayesian Networks, the joint distribution is represented as a product of conditional probabilities of the genotype of each individual, given the genotypes of its two parents. In pedigree analysis, the joint distribution of genotypes is the product of conditional probabilities. In phylogenetic models, the probability, over all evolutionary sequences, is the product of the conditional probability of each sequence, given its latest ancestral sequence in the phylogeny. Another classes of models are Markov Networks representing joint distribution as product of potentials. Cellular networks are based upon gene expression data observed on thousands of genes over a large number of microarrays. Then $GeneCluster_g$ denotes the cluster assignment of gene g and

ArrayCluster$_a$ denotes the cluster assignment of array *a*. Co-expression of genes is assumed to be due to co-regulation. The regulation is mediated by the transcription factors attached to specific sequences of the promoter during transcription, and to interaction of protein products of the gene clusters. The interaction of the proteins may be dependent on modifications. The regulatory networks can be partitioned to expression modules rather than to the study of individual genes. Because of the large number of factors involved, appropriate statistics are necessary to evaluate the reality of the observations and the evaluations. Validation of the models against all biochemical information available is highly desirable. New experimental procedures, high-throughput systems, and bioinformatics are under continuous development. This field is impossible to summarize adequately in the frame of this work. A good overview of the status of the field in 2004 is provided by Nir Friedman in Science 303:799. ►joint probability, ►multivariate analysis, ►Bayes' theorem, ►Markov chain statistics, ►microarray hybridization, ►networks, ►genetic networks, ►model, ►small-world networks

Probability: The statistical measure of chance on a scale between 0 to 1, inclusive. 0 means the lack of chance for an event to occur, 1 indicates a certainty that it will occur, and any value expressed as a decimal or fraction indicate the intermediate chances. The probability function indicates the value of a frequency predicted from the observations related to the parameter. The *simple probability* reveals the chance of a single event; the *compound probability* is the chance of multiple events. When two events are independent, their *joint probability* is the product of their independent probabilities. *Alternate probability* exists in case of sex in dioecious species, when an individual is either female or male; no intermediates are considered. One must keep in mind that probability does not absolutely prove or disprove a point; it simply indicates the chance of its occurrence. ►binomial probability, ►conditional probability, ►likelihood, ►maximum likelihood

Proband: Person(s) through which a family study of the inheritance of a human trait is initiated (also called propositus if male, or proposita if female). Determining the pattern of inheritance on the basis of families chosen by probands may display an excess of affected individuals relative to Mendelian expectations because of the bias in sampling of the population. ►ascertainment test, ►pedigree analysis

Probasin: A secreted and nuclear protein abundant in the prostate epithelium. Its expression is regulated by androgens (two receptors at 5′ of the 17.5 kb gene) and zinc. Its promoter is extensively used with various modifications for the study of prostate function/cancer. ►androgen, ►prostate cancer; Logg CR et al 2002 J Virol 76:12783.

Probe: A labeled nucleic acid fragment used for identifying or locating another segment by hybridization. Similarly, immunoprobes using primarily monoclonal antibodies or enzyme probes or enzymes linked to antibodies can also be employed (see Fig. P132). The probe binds a reporter protein and another binding protein (binding p). For enzymatic detection of a probe, most commonly alkaline phosphatase or horseradish peroxidase are used. The tissue is incubated with the appropriate substrate of the enzyme and the colored precipitate formed through its action identifies its location. ►synthetic DNA probes, ►heterologous probe, ►recombinational probe, ►immunoprobe, ►labeling, ►nick translation, ►padlock probe, ►histochemistry

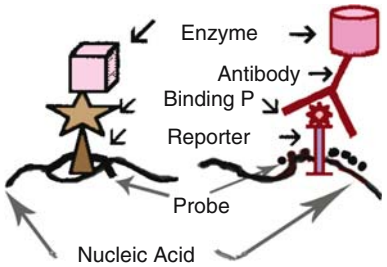

Figure P132. Protein-mediated detection of probe

Probe (primer oligo base extension, PO-BE): A diagnostic procedure for the identification of localized variation in DNA. It is a primer extension procedure using a polymerase, three different deoxyribonucleotide triphosphates, and a dideoxynucleotide triphosphate (ddNTP). The primer is extended until the variable SNP site is reached where the ddNTP is incorporated. The synthetic product is then analyzed by matrix-assisted laser desorption time of flight mass spectrometry. ►primer extension, ►MALDI-TOF, ►SNIP, ►dideoxyribonucleotide; Braun A et al 1997 Clin Chem 43:1151.

Probe Arrays: Oligonucleotides immobilized on silicon wafers in order to study simultaneously the functions of many genes. ►DNA chips, ►microarray

ProbeMaker: A computer program that converts DNA sequence files in FASTA format to digital restriction maps used for MapSearch Probes.

Probiotics: Beneficial bacteria in the body.

Probit: A cumulative normal frequency distribution is represented by an S curve. A cumulative curve can become a straight line by *probit transformation*. We

may represent the probability scale in units of standard deviations. Thus the 50% point is the 0 standard deviation, the 84.13 unit becomes +1, and the 2.27 point the −2 standard deviations. The cumulative percentages are also called *normal equivalent deviates* (NED). If the ordinates are in NED units and we plot the cumulative normal curve, a straight line results. Probits are thus the NEDs with 5.0 added and thus we do not get negative values for the majority of deviates. The probit value of 5.0 indicates a cumulative frequency of 50% and a probit value of 6.0 means a cumulative frequency of 84.13% whereas probit 3.0 indicates a cumulative frequency of 2.27%. Probit value tables are available (Fisher RA, Yates F 1963 Statistical Tables. Hafner, New York). Probit transformations are frequently used for dosage mortality responses to chemicals indicating the regression of cumulative mortalities on dosage. The graphs can be plotted on probit papers with abscissa on logarithmic scale. ►normal distribution, ►logit

Proboscis: Tubular snout (nose-like emergence) on the head such as the feeding apparatus of *Drosophila*, elephant trunk, snout of tapirs, shrews, etc. ►morphogenesis in *Drosophila*

Procaine Anesthetics: Benzoic acid derivatives with local numbing of nerves or nerve receptors.

Procambium: The primary meristem that gives rise to the cambium and the primary vascular tissue of plants. ►cambium, ►meristem, ►root

Procapsid: The empty capsid precursor of phage into which the DNA can be packaged. ►development, ►phage

Procarcinogen: A procarcinogen requires chemical modification to become carcinogenic. ►carcinogen, ►phorbol esters, ►activation of mutagens

Procaryote: ►prokaryote

Procentriole: An immature centriole that upon maturing becomes the anchoring site of the spindle fibers, cilia, and flagella. ►centriole, ►centromere, ►spindle fibers

Process, Genetic: Gene product(s) mediated changes to reach a certain goal in the cell.

Processed Genes: Processed genes are obtained by reverse transcriptase from mRNA and therefore are free of all elements (e.g., introns) removed during processing of the primary transcript. They are widely expressed, highly conserved, and short and low in GC. ►cDNA, ►intron, ►primary transcript

Processed Pseudogene (retropseudogene): A processed pseudogene is similar to mRNA, lacks introns, and may have a polyA tail, yet it is non-functional. The faulty reverse transcription of mRNA may have produced processed pseudogenes. Pseudogenes are widely expressed, generally short, highly conserved, and low in GCs. Many of the processed pseudogenes lack promoters and cannot be transcribed. About half of the human pseudogenes are the processed type. Some of processed pseudogenes are actually retroelements. Processed pseudogenes can be mapped in the genome and provide information on ancestral transcripts (Shemesh R et al 2006 Proc Natl Acad Sci USA 103:1364). ►reverse transcriptases, ►cDNA, ►processed genes, ►pseudogene, ►LINE; Gonçalves I et al 2000 Genome Res 10:672; http://pbil.univ-lyon1.fr/.

Processing: The trimming and modifying of the primary transcripts of the DNA into functional RNAs or cutting and modifying polypeptide chains prior to becoming enzymes or structural proteins. ►primary transcripts, ►protein synthesis, ►posttranslational modification

Processing Body: ►P body

Processivity: Processivity defines the number of nucleotides added to the nascent DNA chain before the polymerase is dissociated from the template. The processivity for *E. coli* DNA polymerase I, II, and III is 3–200, >10,000, >500,000, respectively. ►error in aminoacylation, ►clamp-loader, ►DNA polymerases, ►polymerase switching, ►replication fork

Processor: Data-processing hardware or a computer program (software) that compiles, assembles, and translates information in a specific programming language.

Prochiral Molecule: An enzyme substrate that after attaching to the active site undergoes a structural modification and becomes chiral. ►chirality, ►active site

Prochloron: ►evolution of organelles

Pro-Chromatin: A state of the chromatin that is conducive to transcription.

Prochromosome: Heterochromatic blocks detected during interphase. In this interphase nucleus of *Arabidopsis*, the centromeric heterochromatin was stained by fluorescent isothiocyanate and displayed yellow-green color (see Fig. P133). Courtesy of Drs. Maluszinszka J, Heslop-Harrison JH. ►heterochromatin, ►Barr body, ►mitosis

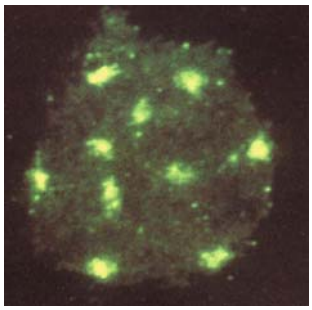

Figure P133. Prochromosomes

Procollagen: Precursor of collagen. ►collagen

Proconsul: A fossil ape that lived about 23–17 million years ago.

Proconvertin: Antihemophilic factor VII, and the deficiency of which may lead to excessive bleeding and hypoproconvertinemia. ►hypoproconvertinemia, ►antihemophilic factors

Proctodeum: An invagination of the embryonal ectoderm where the anus is formed later.

Procyclic: The stage at which *Trypanosoma* is in the gut of the intermediate host (tse-tse fly) and at is not infectious to higher animals. ►metacyclic *Trypanosoma*, ►*Trypanosoma*

Prodroma (prodrome): Ominous sign(s) of a looming disease before the actual onset.

Prodrug: A prodrug is processable to a biologically active compound. ►suicide vector, ►activation of mutagens, ►ADEPT

Producer Cell: An infected cell continuously produces recombinant retrovirus.

Product-Limit Estimator: The product-limit estimator is based on a number of conditional probabilities, e.g., the probability of survival after surviving for one day, then for the next day, and so on. Where $\hat{S}(t)$ the survival function at subsequent times, r_j = the number of individuals at risk at time $t_{(j)}$, d_j = the number of individuals involved in the event at risk time $t_{(j)}$.

$$\hat{S}(t) = \prod_{j|t_{(j)} \le t} \left(1 - \frac{d_j}{r_j}\right)$$

Product-Moment Correlation (Pearson's product-moment correlation coefficient): The correlation coefficient of a sample that is used as an estimator for the correlation coefficient of the population:

$$r_{XY} = \frac{\sum_i (X_i - M_X)(Y_i - M_Y)}{N S_X S_Y},\ s_X = \sqrt{\frac{\sum_i (X_i - M_X)^2}{N}},$$

$$s_Y = \sqrt{\frac{\sum_i (Y_i - M_Y)^2}{N}}$$

Where the N pairs of values (X_i, Y_i) represent the size of the sample and s_X and s_Y are the standard deviation of the respective variables as shown above. ►correlation

Product Ratio Method: ►F_2 linkage estimation

Product Rule: ►joint probability

Productive Infection: In productive infection, the virus is not inserted into the eukaryotic chromosome and can propagate independently from the host DNA and can destroy the cell while releasing progeny particles. ►lysis

Proembryo: The minimally differentiated fertilized egg.

Profile: A nucleotide or amino acid sequence probability motif. ►motif

Profilin: Profilin mediates actin polymerization. ►actin, ►Bni1, ►cytoskeleton, ►formin; Carlsson L et al 1977 J Mol Biol 115:465.

Proflavin: An acridine dye, capable of inducing frameshift mutations. ►acridine dye, ►frameshift mutation; Brenner S et al 1958 Nature [Lond] 182:933.

Progenitor: An ancestor or an ancestral cell of a lineage. Progenitor cells—unlike stem cells—may lose their ability of self-renewal yet they retain their mitotic ability and may generate one or different types of differentiated cells. ►stem cells, ►cancer stem cell; Reya T et al 2001 Nature [Lond] 414:105; Weissman IL et al 2001 Annu Rev Cell Dev Biol 17:387.

Progenote: The evolutionarily common, primitive ancestor of the eukaryotic cytoplasm and the bacterial cell (Woese CR, Fox GE 1977 J Mol Evol 10:1).

Progeny Test: A procedure for determining the pattern of inheritance. ►Mendelian segregation, ►Mendelian laws

Progeria (premature aging): ►aging, ►Hutchinson–Gilford syndrome

Progeroid Syndromes: ►aging

Progesterone: ►animal hormones, ►steroid hormones, ►testosterone, ►estradiol, ►progestin (see Fig. P134), formula

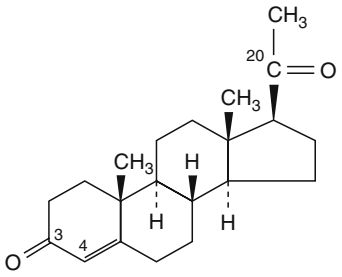

Figure P134. Progesterone (progestin)

Progesterone Receptors (PR): PRs are assembled with the cooperation of at least eight chaperones, including Hsp40, Hsp70, Hsp90, Hip, p60, p23, FKBPs, and cyclophilins. PRs are transcriptional regulators of progesterone-responsive genes. named proteins under separate entries; Hernández P et al 2002 J Biol Chem 277:11873.

Progestin: A steroid hormone, used as medication for the prevention of repeated spontaneous abortion. When added to estrogen, it reduces the risk of endometrial cancer. ►progesterone

Prognosis: The prediction of the course or outcome of a process, e.g., disease, cancer, etc.

Program: A set(s) of instructions in computer language (software) that permits the user to carry out specified tasks. In biology, program refers to the development proceeds according to a genetically determined pattern, realized by environmental effects.

Programmed Cell Death: ►apoptosis

Programming, Dyanamic: In dynamic programming, large groups of data are broken down to subsets to facilitate programming of the complex. ►genetic networks

Progression: A process involved in oncogenic transformation; after the initial mutation of a proto-oncogene progression changes it into an active oncogene. ►cancer, ►phorbol esters

Prohibitin: A 30 kDa tumor-suppressor protein localized mainly in the mitochondria, although it is encoded at human chromosome 17q21. The well-conserved protein is present in other mammals, *Drosophila*, the plant *Arabidopsis*, and several microbes (*Pneumocystis carinii*, the cyanobacterium *Synechocystis*).

Projectin: A myosin-activated protein kinase. ►myosin

Projection Formula: Modeling configurations of groups around chiral centers of molecules. ►chirality

Prokaryon: Same as prokaryote.

Prokaryote: An organism without membrane-enveloped (cell nucleus) genetic material (such as the case in bacteria). The majority of prokaryotic bacteria have circular double-stranded DNA chromosomes. However, *Borrelia*, *Streptomyces*, and *Agrobacterium tumefaciens* have a linear chromosome. The GC content varies between ~72% to ~27%. The genome size of prokaryotes varies 20-fold. The majority of bacteria carry their genes in the leading strand of the DNA. The pathogenic strain may have reduced genome size and/or increased number of pseudogenes. (http://www.cbs.dtu.dk/databases/DOGS/. ►cell comparisons, ►GC skew, ►*Borrelia*, ►*Streptomyces*, ►*Agrobacterium tumefaciens*; Bentley SD, Parkhill J 2004 Annu Rev Genet 38:771; regulation: http://regtransbase.lbl.gov.

Prolactin (PRL): A 23 kDa mitogen, stimulating lactation and the development of the mammary glands. Prolactin receptors are present on human lymphocytes and prolactin may form complexes with IgG subclasses. A prolactin releasing peptide was identified in the hypothalamus. ►lymphocytes, ►immunoglobulins, ►mitogen, ►brain, ►cathepsins; Mann PE, Bridges RS 2001 Progr Brain Res 133:251.

Prolamellar Body: The crystalline-like, lipid-rich structure in the immature plastids that upon illumination develops into the internal lamellae of the proplastids and into the thylakoids of the chloroplasts (see Fig. P135). ►chloroplast

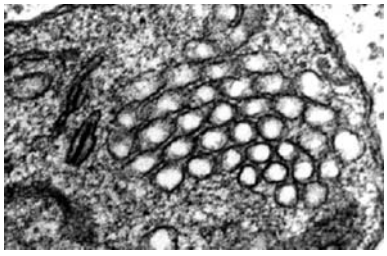

Figure P135. Prolamellar body

Prolamine: ►zein, ►high lysine corn

Proliferating Cell Nuclear Antigen: ►PCNA

Proliferation: The multiplication of cells or organisms. In cells, cytotoxic agents that may induce first cell death may cause proliferation and then regenerative growth, or it may be the result of the action of mitogens. ►mitogen, ►cancer

Proline Biosynthesis: Proline biosynthesis proceeds from glutamate through enzymatic steps involving glutamate kinase, glutamate dehydrogenase, and finally Δ′-pyrroline-5-carboxylate, which is converted to proline by pyrroline carboxylate reductase (see

Fig. P136). In some proteins, e.g., collagen, prolyl-4-hydroxylase generates 4-hydroxyproline from proline. The latter enzyme is coded in human chromosomes 10q21.3-q23.1 (α-subunit) and 17q15 (β-subunit). ►amino acid metabolism, ►hyperprolinemia

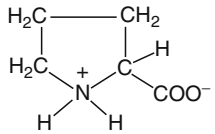

Figure P136. Proline

Prolog: A database management and query system in physical mapping of DNA. (See http://portal.acm.org/citation.cfm?id=711875&dl=ACM&coll=&CFID=15151515&CFTOKEN=6184618).

Prolyl Isomerase: ►PPI, ►immunophilin

Promastigote: ►*Trypanosoma*

Prometaphase: Early metaphase. ►mitosis

Prominin: ►CD133

Promiscuous DNA: Homologous nucleotide sequences occurring in the various cell organelles (nucleus, mitochondrion, plastid). They are assumed to owe their origin to ancestral insertions during evolution. ►insertion elements; Ayliffe MA et al 1998 Mol Biol Evol 15:738; Lin Y, Waldman AS 2001 Nucleic Acids Res 29:3975.

Promiscuous Plasmids: ►plasmids promiscuous

P

Promiscuous Protein: A promiscuous protein has affinity to more than one substrate. ►conformational diversity; Copley SD 2003, Curr Opin Chem Biol 7:265.

Promitochondria: Organelles in anaerobically grown (yeast) cells that can differentiate into mitochondria in the presence of oxygen. ►mitochondria

Promoter: The site of binding of the transcriptase enzyme (RNA polymerase), transcription factor complexes, and regulatory elements, including also the ribosome-binding untranslated sequences (see Fig. P137). Usually, the basal promoter is situated in front of the genes although pol III may rely on both upstream and downstream promoters.

The promoters of the 5S and tRNA genes are internal. Also, some *E. coli* genes have some weak promoters within open reading frames (Kawano M et al 2005 Nucleic Acids Res 33:6268). The arrangement of the promoter used by pol II is outlined.

The promoters used by RNA polymerase II may encompass several hundred nucleotides in yeast but in higher eukaryotes it may extend to several thousand bases. In yeast, UAS (upstream activating sequences) and URS (upstream repressing sequences) are regular binding sites. The transcription start site is usually within a stretch of 30 to 120 nucleotides downstream of the TATA box (see Fig. P138). The pol II enzyme frequently uses in mammals multiple promoters, within which there are multiple start sites, and alternative promoter usage generates diversity and complexity in the mammalian transcriptome and proteome (Sandelin A et al 2007 Nature Rev Genet 8:424). Some of the mammalian promoters are localized more than 100 kb upstream or located downstream, may be multiple, may overlap several genes, and are shared by other genes (Denoeud F et al 2007 Genome Res 17:746).

At the ends of the genes, insulators (boundary elements) separate the genes or the used promoters from the others. The DNase hypersensitive site(s) (also called locus control region) may permit the attachment of sequence-specific transcriptional activators, making the gene competent for transcription. The competence may involve histone acetylation.

Among 1031 human protein-coding genes, the Pol II-like enzymes commonly (~32%) use a TATA box both in prokaryotes and eukaryotes. The TATA box ca. 25 bp upstream from the initiation point of transcription is usually surrounded by GC-rich tracts (97%). Near the transcription initiation site (−3 to +5), there may be an initiator (Inr, 85%) with an ~average type of sequence: $(Pyrimidine)_2CA(Pyrimidine)_5$. Many eukaryotic genes do not have Inr but the TATA box directs the initiation. CAAT box is also a frequent (64%) element in the promoter. Some large eukaryotic genes utilize more than one promoter and the transcripts may vary. Some housekeeping and RAS genes do not use the TATA box. DNA-dependent RNA polymerase I synthesizes ribosomal RNAs; it has a core sequence adjacent to the transcription initiation site and upstream regulator binding sites (UCE). Pol III promoters facilitating the transcription of tRNA usually have split

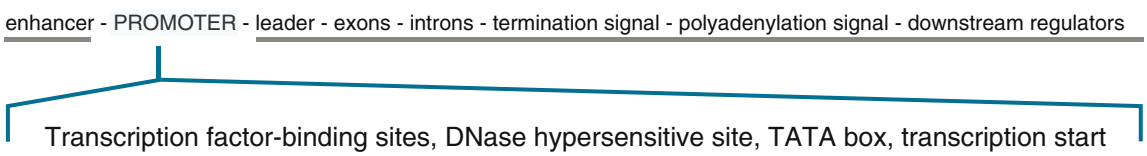

Figure P137. Organization of the promoter and other genic elements

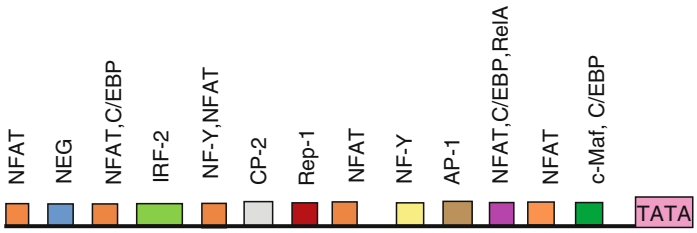

Figure P138. The promoter usually includes several regulatory boxes to which protein factors are recruited. (Modified after Guo, J. *et al.* 2001 J. Biol. Chem. 276:48871)

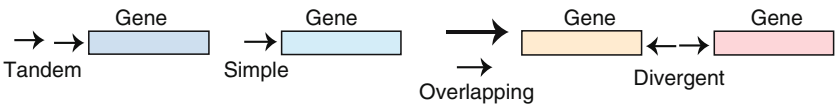

Figure P139. Arrows symbolize promoters; boxes represent structural genes

promoters with an A-box and a B-box about 40 bases apart, situated inside the transcription unit 20 and 60-base downstream from the transcription initiation site. The pol III promoter of some U RNAs has, however, a TATA box 30–60 bases upstream from the transcription initiation site and further upstream a proximal sequence element (PSE) near the TATA box. Synthetic promoters can be constructed with increased activity. The Promoter Scan II program identifies pol II promoters in genomic sequences and is available through Internet: http://www.cbs.umn.edu/software/software.html.

Promoters (→) may be of different types and some genes may rely on multiple promoters (see Fig. P139): TFD, TRANSFAC, or IMD databases can use the Signal Scan to find transcription factor binding sites. A high-resolution analysis revealed 10,567 promoters corresponding to 6763 genes in the human genome. Almost half of all mammalian genes have evolutionarily conserved alternative promoters (Baek D et al 2007 Genome Res 17:145). About 11% of the human promoters are bidirectional/divergent, are more active in transcription than other promoters, and are involved with RNA polymerase II and the modified histones H3K4me2, H3K4me3, and H3ac (Lin JM et al 2007 Genome Res 17:818). This information resulted by mapping the preinitiation complexes labeled by the attached TATA box associated protein and analysis by microarray hybridization of immunoprecipitated complexes (Kim TH et al 2005 Nature [Lond] 436:876). Libraries of engineered promoters can provide a fruitful approach for quantitative study of gene expression (Alper H et al 2005 Proc Natl Acad Sci USA 102:12678). The promoter of the *lac* operon of *E. coli* is controlled by cis elements that integrate signals coming from the cAMP receptor and the Lac repressor (Mayo AE et al 2006 PLoS Biol 4:e45).

Active promoters are marked by trimethylation of Lys4 of histone H3 (H3K4), whereas enhancers are marked by monomethylation, but not trimethylation, of H3K4. Computational algorithms, using these distinct chromatin signatures to identify new regulatory elements, predicted over 200 promoters and 400 enhancers within the 30 Mb region of the vertebrate genome (Heintzman N et al 2007 Nature Genet 39:311).

In vivo spatiotemporal analysis for approximately 900 predicted *C. elegans* promoters (~5% of the predicted protein-coding genes), each driving the expression of green fluorescent protein (GFP) using a flow-cytometer adapted for nematode profiling, generated "chronograms," two-dimensional representations of fluorescence intensity along the body axis and throughout development from early larvae to adults. Automated comparison and clustering of the obtained in vivo expression patterns show that genes coexpressed in space and time tend to belong to common functional categories (Dupuy D et al 2007 Nature Biotechnol 25:663).

►basal promoter, ►core promoter, ►DPE, ►minimal promoter, ►complex promoter, ►UAS, ►URS, ►portable promoter, ►cryptic promoter, ►divergent dual promoter, ►divergent transcription, ►transcription complex, ►transcription factors, ►open promoter complex, ►closed promoter complex *Lac* operon, ►*Tryptophan* operon, ►*Arabinose* operon, ►pol I, ►pol II, ►pol III, ►regulation of gene activity, ►promoter clearance, ►promoter trapping, ►TATA box, ►TBP, ►TAF, ►insulator, ►enhancer, ►LCR, ►chromatin remodeling, ►histone acetyl-transferase, ►promoter inducible, ►promoter tissue-specific, ►antisense DNA, ►microarray hybridization, ►preinitiation complex; analysis of ~900 putative human promoters: Cooper SJ et al 2006 Genome Res 16:1; Chalkley GE, Verrijzer CP 1999 EMBO J 18:4835; Suzuki Y et al 2001 Genome Res 11:677; Pilpel Y et al 2001 Nature Genet 29:153; Schuettengruber B et al 2003 J Biol Chem 278:1784; Ohler U et al 2002 Genome Biol 3:research0087.1;eukaryotic

promoters: http://www.epd.isb-sib.ch; eukaryotic promoters: http://cmgm.stanford.edu/help/manual/databases/epd.html; eukaryotic promoters: http://doop.abc.hu/; transcriptional start sites: http://dbtss.hgc.jp/; human promoter binding sites: http://genome.imim.es/datasets/abs2005/index.html; transcription factor binding sites: http://www.isrec.isb-sib.ch/htpse lex/; mammalian promoters/transcription factors/regulation: http://bioinformatics.med.ohio-state.edu/MPromDb/; mammalian regulatory promoters: http://bioinformatics.wustl.edu/webTools/portalModule/PromoterSearch.do; tissue specific promoters: http://tiprod.cbi.pku.edu.cn:8080/index.html; knowledge-based promoter search: http://bips.u-strasbg.fr/PromAn/; promoter motif search: http://melina2.hgc.jp/public/index.html.

Promoter Bubble: ►promoter clearance

Promoter Clearance (promoter escape): In promoter clearance, the RNA polymerase complex (promoter bubble) starts moving forward from the promoter as the first ribonucleotides are transcribed. The RNA polymerase can synthesize a few bases without leaving the promoter site, but after that tension develops, which discontinues the contact between the DNA and the RNA polymerase. Clearance is regulated by both positive and negative elongation factors. Negative elongation requires four polypeptides and two polypeptides sensitivity inducing factor (DSIF). Inhibition takes place when about 18 nucleotides were added to the growing transcript. The transcript length is regulated also by the inhibition of the transcript cleavage factor TFIIS; the latter can be active along the entire length of the transcript (Palangat M et al 2005 Proc Natl Acad Sci USA 102:15036).

The movement may be represented by an inchworm model or a moving domain model (the translocation involves the entire transcription box with minimal stretching) or the tilting model without a flexible polymerase, which is tilted along the axis of the DNA. ►bubble, ►replication bubble, ►inchworm model; Pal M et al 2001 Mol Cell Biol 21:5815; Liu C, Martin CT 2002 J Biol Chem 277:2725.

Promoter Conversion (Pro-Con): Promoter conversion changes the promoter to a heterologous one.

Promoter Escape: ►promoter clearance

Promoter, Extended: ►Pribnow box

Promoter, Inducible: Inducible promoters turn on genes in response to biological, chemical, or physical signals. ►metallothionein, ►*Lac*

Promoter Interference: Promoter interference may occur when within a single viral vector two genes are placed under separate controls, e.g., the strong promoter within the long terminal repeat (LTR) may suppress the function of an internal promoter irrespective of its orientation. This problem may be overcome by utilizing an IRES for the second gene in the common transcript:

LTR — 1st Gene — IRES — 2nd Gene —. ►IRES

Promoter Melting: In promoter melting, the double-stranded DNA unwinds (forms a promoter bubble) to allow access to the template strand for the RNA polymerase enzyme. In *E. coli*, the N-terminal 1–314 amino acids of the β′ subunit and the 94–507 amino acids of the σ subunit cooperate in the melting. ►RNA polymerase, ►promoter; Young BA et al 2004 Science 303:1382.

Promoter Occlusion: Promoter occlusion occurs when, in retroviral elements with direct LTR repeats, the promoters at the 3′-end are inactivated and prevented from binding enhancers or transcription factors because they cannot facilitate transcription due to their wrong orientation. ►LTR, ►enhancer, ►transcription factors

Promoter Swapping: An exchange of promoter by, e.g., reciprocal chromosome translocation. ►translocation, ►pleiomorphic adenoma

Promoter, Tissue-Specific: A tissue-specific promoter permits the transcription of genes only or mainly in specific tissue(s) (see Fig. P140). ►promoter, ►tissue specificity

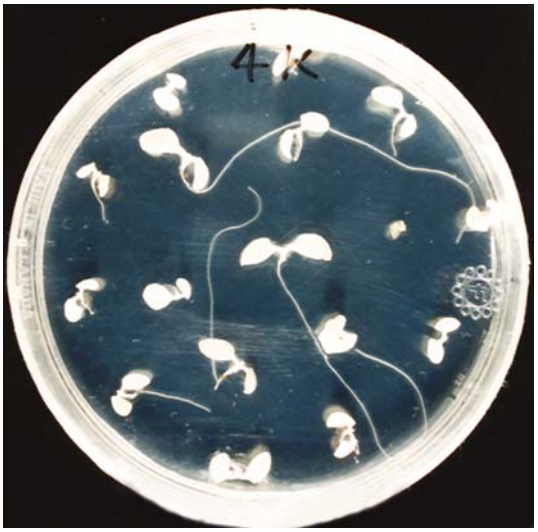

Figure P140. Tobacco seedlings segregating for kanamycin resistance on a root-tissue-specific promoter. Transformation was made by a promoter-less vector construct. The non-transgenic plants cannot grow roots on kanamycin medium. (From Y. Yao & G.P. Rédei)

Promoter Trapping: ►trapping promoters, ►transcriptional gene fusion vectors, ►translational gene fusion vectors, ►gene fusion, ►promoter; Medico E et al 2001 Nature Biotechnol 19:579.

Promoters of Tumorigenesis: Environmental substances or gene products that guide a group of precancerous cells toward malignant growth. The promoters themselves do not initiate cancer. ►carcinogenesis, ►phorbol esters, ►cancer, ►conversion

Promutagen: A promutagen requires chemical modification (activation) to become a mutagen. ►mutagen, ►activation of mutagens

Promyelocytic Body (PML): A nuclear product of the promyelocytic leukemia gene; it mediates the degradation of ubiquitinated proteins and is regulated by the nucleolus. PMLs contain also TRF1 and TRF2 telomeric proteins required for the maintenance of telomeres. PMLs may be targeted by viruses, may act as suppressors of growth and tumors, and mediate apoptosis. PML body may also occur in the cytoplasm and modulates TGF-β signaling. The PML protein also regulates centrosome duplication by the suppression of the Aurora protein. ►leukemia, ►ubiquitin, ►telomerase, ►apoptosis, ►transforming growth factor β, ►centrosome

Pronase: A powerful general (non-specific) proteolytic enzyme isolated from *Streptomyces*.

Pronucleus: The male and female gametic nucleus to be involved in the sexual union.

Proof-of-Concept (proof of principle): Experimental evidence that an idea works in practical application. ►validation

Proofreading: Bacterial DNA polymerase I (and analogous eukaryotic enzymes) can recognize replicational errors and remove the inappropriate bases by its editing 3′ - 5′ exo-nuclease function. In case the editing function is diminished by mutation, mutator activity is gained. In case of gain in editing, function antimutator attributes are observed. In bacteria, proofreading is performed also by the *dnaQ* gene encoding the ε subunit (an exonuclease) of the DNA polymerase III holoenzyme. The product of gene dnaE carries out the base selection. The enzymes MutH, MutL, and MutS and the corresponding homologs in higher organisms repair mismatches. The fidelity of replication due to the combined action of the sequentially acting bacterial genes was estimated to be in the range of 10^{-10} per base per replication. During the process of translation, the EF-Tu•GTP → EF-Tu•GDP change releases a molecule of inorganic phosphate (P_i) and allows a time window to dissociate the wrong tRNA from the ribosome. A similar correction is made also by the aminoacyl synthetase enzyme, by virtue of its active site specialized for this function. DNA polymerase η lacks exonuclease function required for proofreading, but correction is still accomplished by recruiting an extrinsic exonuclease to the error site. ►DNA polymerase I, ►DNA polymerase III, ►DNA polymerases, ►exonuclease, ►proofreading paradox, ►DNA repair, ►error in replication, ►error in aminoacylation, ►ambiguity in translation, ►protein synthesis, ►DNA repair; Friedberg EC et al 2000 Proc Natl Acad Sci USA 97:5681; Livneh Z 2001 J Biol Chem 276:25639; Shevelev IV, Hübscher U 2002 Nat Rev Mol Cell Biol 3:364.

Propagule: A part of an organism that can be used for propagation of an individual by asexual means.

Propeller Twist in DNA: The surface angle formed between individual base-planes viewed along the C^6–C^8 line of a base pair.

Properdin (Factor P): A serum protein of three to four subunits (each ca. 56 kDa, encoded in human chromosome 6p21.3). It is an activator of the complement of the natural immunity system that works by stabilizing the convertase. ►convertase, ►complement, ►complement, ►immune system; Perdikoulis MV et al 2001 Biochim Biophys Acta 1548:265.

Prophage: The proviral phage is in an integrated state in the host cellular DNA and it is replicated in synchrony with the host chromosomal DNA until it is induced and thus, becomes a vegetative virus (see Fig. P141). ►prophage induction, ►temperate phage, ►lysogeny, ►lambda phage

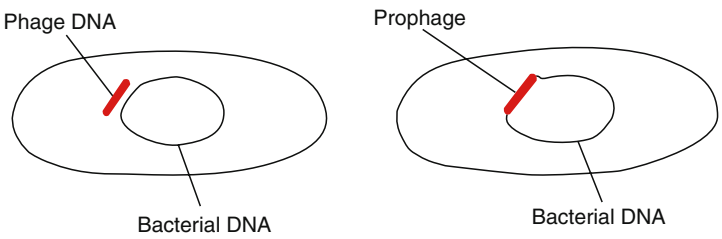

Figure P141. Phage DNA incorporated into bacterial DNA becomes prophage

Prophage Induction: Treating the bacterial cells by physical or chemical agents that cause the moving of the phage into a vegetative lifestyle resulting in asynchronous, independent replication from the host and eventually the lysis and liberation of the phage. ►prophage, ►lysogeny, ►zygotic induction

Prophage-Mediated Conversion: In prophage-mediated conversion, the integrated prophage causes genetic changes in the host bacterium, and it is expressed as an altered antigenic property, etc.

Prophase: ►meiosis, ►mitosis

Prophylaxis: Disease prevention.

Propionicacidemia: ►glycinemia ketotic, ►methylmalonicaciduria, ►isoleucine-valine biosynthetic pathway, ►tiglicacidemia; Chloupkova M et al 2002 Hum Mut 19:629.

Propionyl-CoA-Carboxylase Deficiency: ►glycinemia ketotic

Proplastid: The young colorless plastid without fully differentiated internal membrane structures; it may differentiate into a chloroplast (see Fig. P142). ►etioplast, ►chloroplasts

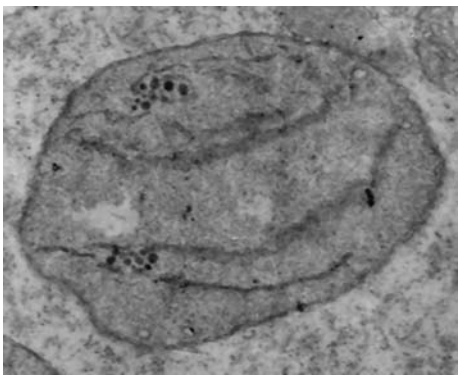

Figure P142. Proplastid

Proportional Counters: Proportional counters are used for measuring radiation-induced ionizations within a chamber. The voltage changes within are proportional to the energy released. It may be used for measuring neutron and α radiations with an efficiency of 35–50%. The equipment must be calibrated to the radiation source. ►radiation measurement, ►radiation hazard assessment

Propositus (Proposita): ►proband, ►pedigree analysis

Propyne (CH_3-C≡CH): An alkyne used as a modifier at the C-5 position of pyrimidines in antisense oligonucleotides, frequently in combination with other modifications such as phosphorothioate. ►antisense technologies

Prosimii (prosimians): A suborder of lower primates, including Galago, Lemur, Tarsius, and Tupaia. Lorisidae. ►primates, ►Lemur, ►Tupaia, ►Lorisidae

Prosite: A protein sequence database, searchable by PROSCAN (Bairoch A et al 1977 Nucleic Acid Res 25:217); http://pbil.univ-lyon1.fr/pbil.html; PROSITE for uncharacterized proteins: http://www.expasy.org/prosite/; improved PROSITE: http://www.expasy.org/tools/scanprosite/.

Prosody: The inability of sensing or expressing variations of the normal rhythm of speech. It seems to be independent of processing musical pitch. ►amusia, ►musical talent, ►pitch

Prosome: Small ribonucleoprotein body. It is identical with the ~20S multifunctional protease complex of the proteasome of eukaryotes and prokaryotes. ►proteasome

Prospective Study: Prospective study involves the epidemiological surveillance of a population after the occurrence of a disease or other harmful exposure. The exposed or involved individuals are compared with a concurrent control cohort. Prospective cohort studies improve on case control information. ►case control, ►concurrent control, ►cohort

PROST (pronuclear state embryo transfer): Basically, very similar to intrafallopian transfer of zygotes but the zygote here is at a very early stage. ►intrafallopian transfer, ►ART

Prostacyclins: Prostacyclins may be derived from arachidonic acid or prostaglandins, regulate blood platelets, cause vasodilation, and are antithrombotic. ►thrombosis, ►prostaglandins, ►COX

Prostaglandins: Long-chain fatty acids in different mammalian tissues with hormone-like muscle-regulating, inflammation-regulating, and reproductive functions; they exist in several forms. They occur in the majority of the cells and act as autocrine and paracrine mediators. Fever development is controlled by prostaglandin E_2 and EP_3 receptors. Prostaglandin synthesis is regulated by cyclooxygenases. Prostaglandin E (cyclopentenone prostaglandins) appears to be an inhibitor of IκB kinase. ►animal hormones, ►autocrine, ►paracrine, ►cyclooxygenases, ►IκB, ►leukotrienes, ►eicosanoids, ►pain-sensitivity, ►implantation, ►misoprosto, ►colorectal cancer; Rudnick DA et al 2001 Proc Natl Acad Sci USA 98:8885.

Prostanoids: Bioactive lipids such as the prostaglandins, prostacyclin, and thromboxane. Aspirin-like

drugs may inhibit prostanoid biosynthesis, reduce fever and inflammation, and interfere with female fertility. ►prostaglandins, ►prostacyclins

Prostate Cancer (HPC): About 9–10% of USA males eventually develop prostrate cancer. The autosomal dominant gene has a high penetrance: about 88% of the carriers become afflicted by the age of 85. Several other genes involved in prostate function may mutate and cause cancer. Recurrent fusion of the androgen-responsive promoter element of TMPRSS2 (a transmembrane protease serine 2, 21q22.3) with members of the ETS oncogene family ETV1 at 7p21.2) leads to prostate cancer (Tomlins SA et al 2005 Science 310:6744). Relative to low-grade prostate cancer (Gleason pattern 3) and high-grade cancer (Gleason pattern 4) shows an attenuated androgen signaling signature, similar to metastatic prostate cancer, which may reflect dedifferentiation and explain the clinical association of grade with prognosis (Tomlins SA et al 2007 Nature Genet 39:41). Androgen receptor and PTEN–AKT signaling may initiate and maintain prostate cancer. For therapeutic intervention, androgen receptor and AKT and/or growth factor receptor tyrosine kinases that activate AKT can be targeted (Xin L et al 2006 Proc Natl Acad Sci USA 103:7789). The high level of testosterone may increase the chances for this cancer. Reduced level of testosterone may not slow down advanced prostate cancer growth and metastasis. There is a possible therapeutic approach to prostate cancer in overexpressing an androgen receptor by ligand-independent activation of the N-terminal domain peptide to create decoy molecules that competitively bind the interacting proteins required for activation of the endogenous full-length receptor.

A genetic variant in the 8q24 region, identified by GWA, in conjunction with another variant, accounts for about 11–13% of prostate cancer cases in individuals of European descent and 31% of cases in African Americans (Gudmundsson J et al 2007 Nature Genet 39:631). Seven risk variants, five of them previously unreported, spanning 430 kb and each independently predicting risk for prostate cancer ($P = 7.9 \times 10^{-19}$ for the strongest association, and $P < 1.5 \times 10^{-4}$ for five of the variants, after controlling for each of the others). The variants define common genotypes that span a more than fivefold range of susceptibility to cancer in some populations. None of the prostate cancer risk variants aligns to a known gene or alters the coding sequence of an encoded protein (Haiman CA et al 2007 Nature Genet 39:638).

There is evidence that in vivo expression of the receptor decoys decreased tumor incidence and inhibited the growth of prostate cancer tumors (Quayle SN et al 2007 Proc Natl Acad Sci USA 104:1331). Growth hormone-releasing hormone (GHRH) antagonists increased the intracellular Ca^{2+} and activated tumoral GHRH receptors and induced apoptosis (Rékási Z et al. 2005 Proc Natl Acad Sci USA 102:3435). Metastatic prostate cancer cells may show high levels of caveolin-1 and reduced amount of testosterone. Caveolin-1 antisense RNA promoted apoptosis and increased testosterone. A metastasis suppressor gene, KAI1, in human chromosome 11p11.2, has been identified. The KaI1 protein appears to contain 267 amino acids with four transmembrane hydrophobic and one large hydrophilic domains. This glycoprotein is expressed in several human tissues and also in rats. A negative regulator of the MYC oncogene, MXI1 (encoded in human chromosome 10q24-q25), is frequently lost in prostate cancer. KaI1 is involved in chromatin remodeling by suppressing Tip60, β-catenin, and reptin, and in metastasis of prostate cancer cells (Kim JH et al 2005 Nature [Lond] 434:921). Cytokine-activated IKKα controls metastasis by repressing Maspin (Luo J-L et al 2007 Nature [Lond] 446:690). In the chromosome 10pter-q11 region, a prostate cancer suppressor gene, causing apoptosis of carcinoma, has been detected from loss of heterozygosity mutations (LOH). A major susceptibility locus was identified in human chromosome 1q24-q25 and at Xq27-q28. Candidate genes are expected in human chromosomes 3p, 4q, 5q, 7q32, 8p22-p23 and 8q, 9q, 10p15 (KLF6), 13q, 16q, 17p11, 18q, 19q12, 20q13, and 22q12.3. At 16q22 the transcription factor ATBF1 is transcribed, which negatively regulates AFP and MYB but transactivates CDKN1A and it may be reduced in about a third of the prostate cancer cells (Sun X et al 2005 Nature Genet 37:407). Insulin-like growth factor (IGF-1) levels may be predictors of prostate cancer risks before cancerous growth is observed but some other data are at variance with the claim. In prostate tumors, the prostate-specific cell-surface antigen (STEAP), in human chromosome 7p22.3, is highly expressed in different organs and tissues, except the bladder. A predisposing gene in 17p has been cloned. The various types of prostate cancers can be classified on the basis of DNA microarray and the result may assist treatment and prognostication (Lapointe J et al 2004 Proc Natl Acad Sci USA 101:811). In Northern Europe, about 42% of the cases were found to be hereditary and 58% were sporadic (Lichtenstein P et al 2000 N Engl J Med 343:78). The first-degree relative risk is 1.7–3.7 or more. American blacks have higher and Asians lower risks than Caucasians (Stanford JL, Ostrander EA 2001 Epidemiol Rev 23:19).

Prostate stem cell antigen (PSCA) may be the target for immunological therapy. About 11–12% of all prostate cancer patients harbored mitochondrial mutations in cytochrome oxidase I subunit; mutations

inhibiting oxidative phosphorylation can increase ROS and tumorigenicity (Petros JA et al 2005 Proc Natl Acad Sci USA 102: 719). Prostate cancer is the second most frequent cause of cancer mortality in the US but it is very rare in other animals, except dogs. ►PSA, ►cancer, ►tumor suppressor gene, ►IKK, ►Maspin, ►MYC, ►MYB, ►fetoprotein-α, ►CDKN1A, ►insulin-like growth factor, ►caveolin, ►antisense technology, ►automaton, ►testosterone, ►apoptosis, ►microarray hybridization, ►gene fusion, ►probasin, ►ROS, ►mitochondrial genetics, ►mitochondrial diseases in humans, ►Gleason score, ►automaton, ►chromatin remodeling, ►*erbB*, ►androgen, ►PTEN, ►AKT; Ostrander EA, Stanford JL 2000 Am J Hum Genet 67:1367; Xu J et al 2001 Am J Hum Genet 69:341; Stephan DA et al 2002 Genomics 79:41; Ostrander EA et al 2004 Annu Rev Genomics Hum Genet 5:151; susceptibility markers: http://cgems.cancer.gov/.

Prostates (prostata): Gland in the animal (human) male surrounding the base of the bladder and the urethra; upon ejaculation injects its content (acid phosphatase, citric acid, proteolytic enzymes, etc.) into the seminal fluid. ►PSA, ►prostate cancer; http://www.pedb.org.

Prosthesis: Any type of mechanical replacement of a body part, such as artificial limbs, false teeth, etc.

Prosthetic Group: A non-peptide group (iron or other inorganic or organic group) covalently bound (conjugated) to a protein to assure activity.

Prot: Na^+/Cl^--dependent proline transporter that also transports glycine, GABA, betaine, taurine, creatine, norepinephrine, dopamine, and serotonin in the brain. ►transporters

Protamine: The basic (arginine-rich) protein occurring in the sperm substituting for histones.

The protamine gene cluster is in human chromosome 16p13.2 and it includes genes PRM1, PRM2, and TNP2 (transition protein 2). They are transcribed at the postmeiotic round spermatid stage of spermatogenesis and translated in elongating spermatids (see Fig. P143). These messages are bound as cytoplasmic messenger ribonuclear protein particles until histone replacement is initiated with the transition proteins in late elongating spermatids. At this time the mRNAs are activated and then translated into the peptides that will repackage and compact the male genome in terminally differentiated spermatozoa. In humans and mice, the genes first acquire a DNase I-sensitive conformation in pachytene spermatocytes that is even maintained in human spermatozoa and transcription is facilitated (Martins RP, Krawetz SA 2007 Proc Natl Acad Sci USA 104:8340). Protamine 4 is a minor protein and it is different from PRM2 and PRM3 only by a short extension. The genes are potentiated at late pachytene before the haploid (n, 1C) spermatids are formed. In the mature spermatozoon, the histones are replaced by protamines. Protamine controls both condensation and decondensation of the DNA by anchoring to it at about each 11 bp. After fertilization it is removed. In *Drosophila*, the *Hira* gene is involved in the decondensation. The HIRA gene of mammals is essential for chromatin assembly in the male pronucleus and it uses histone variant H3.3 (Lappin B et al 2005 Nature [Lond] 437:1386). In the somatic cells, protamines constitute less than 5% of the nucleus. The majority of mammals have only a single protamine but mice and men have four. If protamines are deleted missing functional sperm is not produced because of haplo-insufficiency. ►histones, ►transition protein, ►haploinsufficiency, ►spermiogenesis, ►gametogenesis, ►C amount of DNA; Cho C et al 2001 Nature Genet 28:82.

Protandry: in monoecious plants the pollen is shed before the stigma is receptive. ►monoecious, ►stigma, ►protogyny, ►self-sterility

Protanope: ►color blindness

Protease (proteinase): Enzyme, which hydrolyzes proteins at specific peptide bonds; for *protease 3* see antimicrobial peptides. The human genome codes for at least 553 proteases. Proteases may either facilitate or reduce the expression of enzymes. ►proteasome, ►peptidase; Ehrmann M, Clausen T 2004 Annu Rev Genet 38:709; http://cutdb.burnham.org.

Protease Inhibitors: Protease inhibitors, such as leupeptin, antipain, and soybean trypsin inhibitors are credited with anticarcinogenic effects and potential cures for asthma, schistosomiasis. Proteases process the primary proteins into their functional role in viral/microbial or other systems. If this processing

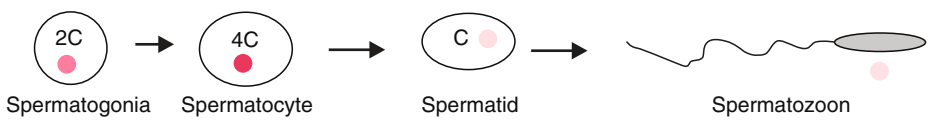

Figure P143. Development of the nuclear DNA in spermatozoa

is prevented, infectious or other agents may not or may have reduced adverse effect to the cells. ►carcinogen, ►cancer, ►AIDS, ►schistosomiasis, ►asthma

Proteasomes: Tools of degradation of intracellular proteins (see Fig. P144). Proteasomes have non-degradatory functions too, such as in transcription, DNA repair, and chromatin remodeling. ATP-dependent ubiquitinated proteins process intracellular antigens into short peptides that are then transported to the endoplasmic reticulum with the aid of TAP, and are responsible for MHC class I-restricted antigen presentation. Proteasomal polymorphism is determined, among others, by LMP2 and LMP7 genes encoded within the MHC class II region in the vicinity of TAPs that are upregulated by interferon γ. The 26S (~2500 kDa) proteasomes (~31 subunits) are hollow cylinders engulfing ubiquitinated proteins and degrade them with proteases. The lid and the base each are 19S (890 kDa). The ATP-dependent dissociation of the 19S subunits from the 26S complex leads to the protein degradation (Babbitt SE et al 2005 Cell 121:553). The ~20S (720 kDa) middle section barrel of the proteasomes contain multiple peptidases. Their active site is at the hydroxyl group of the N-terminal threonine in the β subunit. The PA proteins are proteasome activators. The 26S proteasome is associated with at least 18 ancillary and essential proteins (PSM proteins, including ATPase) and many of these are now genetically mapped to different human chromosomes. Chymostatin, calpain, and leupeptin, etc., are inhibitors. The proteases of the 20S proteasome are activated by the heptameric 11S regulators, which also control the opening of the barrel-shaped structure. The assembly of the 28 subunits of the 20S mammalian proteasomes is mediated by the heteromeric chaperones PAC1 and PAC2 (Hirano Y et al 2005 Nature [Lond] 437:13481). Proteasomes have also ubiquitin-independent function, such as the degradation of the excess amounts of ornithine decarboxylase, a key enzyme in polyamine biosynthesis. The proteasomes have important—although not fully understood—roles in differentiation and development by mediating protein turnover. Proteasomes control also apoptosis and carcinogenesis (Adams J 2004 Nat Rev Cancer 4:349). According to Princiotta MF et al 2003 (Immunity 18:343) each cell of the immune system contains 800,000 proteasomes (immunoproteasomes). The product peptides of the immunoproteasome are different from the regular proteasomes. They degrade 2.5 viral translation product substrates per minute and thus generate one MHC class I peptide complex for each 300 to 5000 viral translation product degraded. The misfolded proteins are removed from the endoplasmic reticulum and in the cytoplasm, after ubiquitination and de-glycosylation, they are degraded by the proteasome. On the average cellular proteins are degraded in about two days and about a third of the new proteins of mammals have less than 10 min half-life. The majority of these have a synthetic defect. In active mammalian cells, about 10 million polypeptides are formed per minute and within seconds these are degraded to amino acids by peptidases (Yewdell JW 2005 Proc Natl Acad Sci USA 102:9089). Membrane proteins US11 and Derlin-1 mediate MHC molecule dislocation from the endoplasmic reticulum (Lilley BN Ploegh HL 2004 Nature [Lond] 429:834; Ye Y et al 2004 *Ibid*. 841). In case the proteasome function is inhibited or lost, inhibitor resistant cells may grow out of the cultures that have a compensating mechanism for proteasome function. The Cop9 signalosome of *Arabidopsis* is functionally homologous to the lid element of the proteasome. It appears that the various elements of the proteasome complex are co-regulated by the RPM4 putative transcription factor. The yeast activators Gcn4, Gal4, and Ino2/4 are actually activated by exposure to the ubiquitin–proteasome system. It appears that after the transcription has started, the removal of the promoter-bound activators is beneficial for the continuation of transcription (Lipford JR et al 2005 Nature [Lond] 438:113). ►ubiquitin, ►LID, ►TAP, ►N-end rule, ►antigen presenting cell, ►MHC, ►antigen processing, ►JAMM, ►DRiP, ►immune system, ►polyamine, ►Skp1, ►tripeptidyl peptidase, ►Clp, ►photomorphogenesis, ►signalosome, ►lysosomes, ►unfolded protein response, ►immunoproteasomes, ►Gcn4, ►Gal4, ►exosome; Voges D et al 1999 Annu Rev Biochem 68:1015; Bochtler M et al 1999 Annu Rev Biophys Biomol Struct 28:295; Kloetzel P-M 2001 Nature Rev Mol Cell Biol 2:179; Ottosen S et al 2002 Science 296:479; Liu C-W et al 2003 Science 299:408; Puente XS et al 2003 Nature Rev Genet 4:544; Goldberg AL 2003 Nature [Lond] 426:895; lid structure: Sharon M et al 2006 PLoS Biol 4(8):e267; minireview: DeMartino GN, Gillette TG 2007 Cell 129:659.

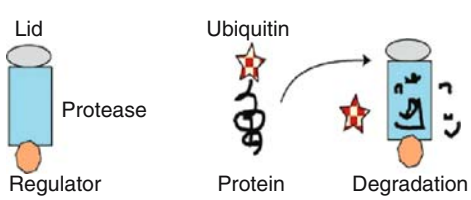

Figure P144. Proteasome and its function

Protectin (CD59): A protein component of the complement encoded at 11p13. ►complement, ►paroxysmal nocturnal hemoglobinuria; Kawano M 2000 Arch Immunol Ther Exp 48(5):367.

Protein: A large molecule (polymer) composed of one or more identical or different peptide chains. The distinction between protein and polypetide is somewhat uncertain; generally a protein has more amino acid residues (50–60) and therefore can fold. In animal cells, there are about 1×10^5 protein species. ►protein synthesis, ►protein structure, ►amino acid sequencing, ►subcellular localization; protein data Bank [PDB]: Westbrook J et al 2002 Nucleic Acids Res 30:245; http://www.rcsb.org/pdb/; http://pir.georgetown.edu/; http://www.ncbi.nlm.nih.gov/gquery/gquery.fcgi.

Protein 14-3-3: A family of 28–33 kDa acidic chaperone proteins named after their electrophoretic mobility. The proteins occur in many forms in different organisms and have roles in signal transduction (RAS-MAP), apoptosis, exocytosis, the regulation of the cell cycle (checkpoint), DNA repair, and oncogenes. They generally bind to phosphoserine/threonine domains. Protein 14-3-3σ isoform binds tumor suppressor p53, regulates translation through eukaryotic translation initiation factor 4B, and reduces the mitotic endogenous ribosomal entry site (IRES)-dependent cyclin Cdk1 (PITSLRE), among performing other functions. In the absence of this isoform, mitotic exit is impaired and causes aneuploidy and tumorigenesis (Wilker EW et al 2007 Nature [Lond] 446:329). ►Chk1, ►cell cycle, ►Cdc25, ►p53, ►CaM-KK, ►checkpoint, ►chaperone, ►longevity, ►PITSLRE, ►IRES, ►cdk, ►eIF-4B; Muslin AJ, Xing H 2000 Cell Signal 12(11–12):703; Masters SC, Fu H 2001 J Biol Chem 276:45193; Tzivion G, Avruch J 2002 J Biol Chem 277:3061; Sehnke PC et al 2002 Plant Cell 14:S339.

Protein A: Protein A is isolated from *Staphylococcus aureus*; it binds the Fc domain of immuno-globulins without interacting with the antigen-binding site. It is used both in soluble and insoluble forms for the purification of antibodies, antigens, and immune complexes. ►antibody, ►immunoglobulins

Protein Abundance: ►genome-wide location analysis

Protein Alignment: http://mozart.bio.neu.edu/topofit/index.php.

Protein Arrays: Protein arrays are used in a manner analogous to microarrays of DNA. On specially treated microscope slide or microtiter plates, samples of a protein or proteins are lined up and exposed to other proteins or to drug molecules or molecular fragments in order to assess their interaction. This new procedure is expected to be useful for analytical purposes and particularly for the development of new drugs. ►microarray hybridization, ►protein chips, ►reverse array; Avseenko NV et al 2001 Anal Chem 73:6047; Brody EN, Gold L 2000 J Biotechnol 74:5.

Protein Assays: ►Bradford method, ►Lowry test, ►Kjeldhal method; for analysis with single cell resolution: Zhang HT et al 2001 Proc Natl Acad Sci USA 98:5497; detection on magnetic nanoparticle-bio-barcode and antibody at 30 attomolar concentration: Nam J-M et al 2003 Science 301:1884.

Protein C (2q13-q14): A vitamin K-dependent serine protease, which selectively degrades antihemophilic factors Va and VIIIa, and it is thus, an anticoagulant. ►protein C deficiency, ►antihemophilic factors, ►thrombin, ►anticoagulation, ►thrombophilia

Protein C Deficiency (thrombotic disease): Protein C deficiency is human chromosome 2q13-q14 dominant and may be a life-threatening cause of thrombosis. ►thrombosis, ►protein C

Protein Chips: A protein mixture (e.g., serum) applied to an about 1 mm^2 surface containing a "bait" that is an antibody, a specific receptor, or other kind of specific molecule, which selectively binds a particular protein (tagged by fluorescent dye) and thus facilitates its isolation even when present only in minute amounts. Alternatively, recombinant proteins are immobilized on the chips and then putative interacting proteins (cell lysates) are applied to it. The unbound material is removed by washing and the bound one(s) are analyzed by mass spectrometry, or phage display or two-hybrid method may be used. These procedures can handle sppedily huge number of samples and bear similarity to DNA chips. ►microarray hybridization, ►ELISA, ►DNA chips, ►mass spectrum, ►MALDI, ►electrospray, ►phage display, ►two-hybrid method, ►gene product interaction, ►proteomics, ►protein microarray; Zhu H et al. 2001 Science 293:2101.

Protein Classification for Machine Learning: ►machine learning; http://hydra.icgeb.trieste.it/benchmark.

Protein Clock: ►evolutionary clock

Protein Complexes: Protein complexes usually play an important role in protein and cellular function. Their study requires enrichment of the complex either by chromatography, co-immunoprecipitation, co-precipitation by affinity-tagged proteins, and SDS-PAGE separation of the components before additional analytical techniques are employed. One study involving 1739 yeast genes, including 1143 human homologous, revealed 589 protein assemblies. Among these, 51% included up to five proteins, 6% more than 40 proteins, 4% 31–40, 6% 21–30, 15% of the complexes 11–20 proteins, and 18% displayed interactions among 6–10 proteins. The technology did not reveal interactions of very short durations.

Obviously, within the cells even more proteins interact. The modules of the interacting systems are better conserved during evolution than are random samples of other proteins. This indicates their importance in specific functions (Wuchty S et al 2003 Nature Genet 35:176). ►immunoprecipitation, ►immunolabeling, ►SDS-PAGE, ►LC-MS, ►mass spectrometry, ►TAP, ►two-hybrid method, ►genetic networks, ►SAGE, ►TAP; Gavin A-C et al 2002 Nature [Lond] 415:141; Ho Y et al 2002 Nature [Lond] 415:180; global surveys of budding yeast cell machineries: Gavin A-C et al Nature [Lond] 440:631; Krogan NJ et al 2006 Nature [Lond] 440:637; http://www.binddb.org/; protein–DNA complexes: http://gibk26.bse.kyutech.ac.jp/jouhou/readout/.

Protein Conducting Channel: Membrane passageways for proteins that interact with the membrane protein and lipid components. ►protein targeting, ►SRP, ►translocon, ►translocase, ►TRAM, ►ABC transporters, ►Sec61 complex; Spahn CM et al 2001 Cell 107:373.

Protein Conformation: ►conformation

Protein Data Bank (PDB): An archive of macromolecular structures. ►protein structure; http://www.pdb.org/; http://www.wwpdb.org/.

Protein Degradation: ►proteasome, ►ubiquitin, ►antizyme, ►lysosomes, ►endoplasmic reticulum, ►endocytosis, ►major histocompatibility complex, ►TAP, ►F-box, ►microRNA, ►RNAi, ►half-life

Protein Degradation within Cells: In protein degradation, endogenous proteins are digested primarily by the proteasomes and exogenous proteins are cleaved mainly by the lysosomal system, although the compartmentalization is not rigid. ►proteasome, ►lysosome, ►N-end rule

Protein Design: Computer programs exist now to design new proteins for physico-chemical potential function and stereochemical arrangements using combinatorial libraries of amino acids. The *designability of a protein* is determined by the amino acids that permit alterations without loss of structure or function. (See Dahiat BI, Mayo SL 1997 Science 278:82).

Protein, Disordered: A disordered protein contains at least one experimentally determined disordered region and lacks fixed structure. Such proteins and regions can carry out important biological functions and may be involved in regulation, signaling, and control. (See http://www.disprot.org).

Protein Domains: Protein domains are generally formed by the folding of 50–350 amino acid sequences for carrying out particular function(s). Small proteins may have only a single domain but larger complexes may have multiple modular units. The alternations of α helices and β sheets constitute a characteristic *motif*. The two β-sheet motifs are shown in Figure P145 in black and red, respectively. The compact motifs are generally covered by polypeptide loops. Domain similarities among proteins from different organisms indicate possible functional relationship (homology) of those proteins. ►protein structure-β sheets, ►α helices, ►helix-turn-helix, ►helix-loop-helix, ►zinc finger, ►binding proteins, ►motif; Ponting CP, Russell RR 2002 Annu Rev Biophys Biomol Struct 31:45; Pearl FM et al 2003 Nucleic Acids Res 31:452; http://smart.embl heidelberg.de/help/smart_about.shtml; http://www.ebi.acuk/interpro; http://smart.embl.de/; domain homology: http://genespeed.uchsc.edu/; conserved domains: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=cdd; conserved domains in new sequences: http://www.ncbi.nlm.nih.gov/Structure/cdd/wrpsb.cgi; three-dimensional structures: http://www.toulouse.inra.fr/prodom.html; domain search on the basis of sequence: http://www.icgeb.trieste.it/sbase; Superfamily domains: http://supfam.org; protein domain prediction: http://www.bioinfotool.org/domac.html.

Figure P145. Protein domains

Protein Engineering: Constructing proteins with amino acid replacements at particular domains and positions (e.g., substrate-binding cleft, catalytic and ligand-binding sites, etc.) or adding a label or another molecule, etc., to explore their effect on function. Incorporation of unnatural amino acids into particular proteins is a common way to accomplish it (Nowak MW et al 1998 Methods Enzymol 293:504). ►directed mutation, ►semisynthesis of proteins, ►DNA shuffling, ►iterative truncation, ►nonsense suppression, ►suppressor tRNA, ►expressed protein ligation, ►proteomics, ►enzyme design; Tao H, Cornish VW 2002 Curr Opin Chem Biol 6:858; Brennigan JA, Wilkinson AJ 2002 Nature Rev Mol Cell Biol 3:964; Wang L et al 2003 Proc Natl Acad Sci USA 100:56.

Protein, Essential: Essential for the viability of the organism in an environment.

Protein Families: Protein families share structural and functional similarities; generally share more than 30% sequence identity. The number of different families in vertebrates is about 750, in invertebrates and plants ~670, in yeast and larger bacteria ~550, and in small parasitic bacteria ~220 (Chotia C et al

2003 Science 300:1701). The average family size in higher organisms is about 20 whereas in lower forms it is 8 to 2. *Superfamilies*: (i) catalyze the same chemical reaction or (ii) different overall reactions that share common mechanistic properties (partial reaction, intermediate or transition state) and share 20 to 50% sequence identity. *Suprafamilies*: homologous enzymes but catalyze different reactions. Mutations affecting amino acid sequences in three different evolutionary groups (mammals, chickens, bacteria) are strikingly similar. For categories with the same divergence, common accepted mutations have similar frequencies and rank orders in the three groups. With increasing divergence, mutations increase at different rates in the buried, intermediate, and exposed regions of protein structures in a manner that explains the exponential relationship between the divergence of structure and sequence. This work implies that commonly allowed mutations are selected by a set of general constraints that are well defined and whose nature varies with divergence (Sasidharan R, Chothia C 2007 Proc Natl Acad Sci USA 104:10080). ►gene family, ►PRINTS; Enright AJ et al 2002 Nucleic Acids Res 30:1575; Aravind L et al 2002 Curr Opin Struct Biol 12:392; http://pfam.wustl.edu/; http://www.ebi.ac.uk/interpro; http://www.biochem.ucl.ac.uk/bsm/cath; http://mia.sdsc.edu/mia/html/bioDBs.html; http://systers.molgen.mpg.de; shifts in subfamilies: http://funshift.cgb.ki.se/; families in evolution: http://www.pantherdb.org/.

Protein Folding: The majority of proteins fold to acquire functionality, although some (mainly) surface proteins do not require folding. The pattern of hydrophobic and polar residues of a relatively small number may be required for folding. The native conformation is reached through intermediate stage(s) (see Fig. P146) (Sadqi M et al 2006 Nature [Lond] 442:317). Even at high (88%) amino acid identity, two proteins may have different structures and functions (Alexander PA et al 2007 Proc Natl Acad Sci USA 104:11963).

The native structure is stabilized primarily by hydrogen bonding between amide and carbonyl groups of the main chain. Glycosylation in the endoplasmic reticulum may affect the conformation of proteins.

The folding is determined by the amino acid sequence, however other factors (chaperones) may be needed to facilitate the process. the energetics of backbone hydrogen bonds dominate the folding process, with preorganization in

Besides the primary structure of amino acids, the energetics of backbone hydrogen bonds can dominate the folding process, with pre-organization in the unfolded state. Then, under folding conditions, the resultant fold is selected from a limited repertoire of structural possibilities, each corresponding to a distinct hydrogen-bonded arrangement of α-helices and/or strands of β-sheets (Rose GD et al 2006 Proc Natl Acad Sci USA 103:16623).

The classical diffusion–collision and nucleation–condensation models may represent two extreme manifestations of an underlying common mechanism for the folding of small globular proteins. Characterization of the folding process of the PDZ domain, a protein that recapitulates three canonical steps, is involved in a unifying mechanism, namely: (1) the early formation of a weak nucleus that determines the native-like topology of a large portion of the structure, (2) a global collapse of the entire polypeptide chain, and (3) the consolidation of the remaining partially structured regions to achieve the native state conformation. Classical kinetic analysis identified two activation barriers along the reaction coordinate, corresponding to a more unfolded transition state *TS1* and a more native-like transition state *TS2*. The PDZ2 (PDZ repeat from Protein Tyrosine Phosphatase-Bas Like folding process; Bas for basophil) provides evidence that its folding mechanism is distinct from the pure diffusion–collision as well as from the nucleation–condensation mechanism, but displays characteristic features of both models (Gianni S et al 2007 Proc Natl Acad Sci USA 104:128).

Prokaryotic proteins (which are generally smaller, two to three hundred amino acid residues) fold correctly only after the completion of the entire length of the amino acid chain. Eukaryotic proteins (usually on the average over four to five hundred residues) may

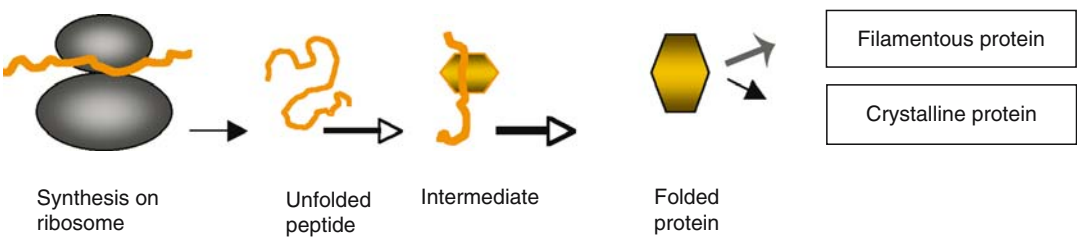

Figure P146. Protein folding

fold the separate domains in a sequential manner during their translation. Both prokaryotic and eukaryotic proteins may start folding before their translation is completed, i.e., co-translationally. Because of this, fusion proteins can also fold and this might have been of an evolutionary advantage. There is evidence that α helices fold faster than β sheets. Local interactions may facilitate speedier folding.

The global pattern of co-evolutionary interactions of amino acids is relatively sparse and a small set of positions in the proteins mutually co-evolves. The co-evolving residues are spatially organized into physically connected networks linking distant functional sites through packing interactions. By the method of statistical coupling analysis (SCA), it was revealed that the amino acid interactions specifying the atomic structure are conserved among the members of protein families. The conservation is not site independent and it occurs due to energetic interactions. The statistical energy functions can be appropriately estimated by the SCA method (Socolich M et al 2005 Nature [Lond] 437:512; Russ WP et al 2005 Nature [Lond] 437:579). Certainly many factors may affect the rate of folding and the rate among different proteins may be nine orders of magnitude. Besides folding, intrinsic plasticity of the enzyme proteins is a characteristic feature of catalysis. The motion is not limited to the active site but a more dynamic network is also involved (Eisenmesser EZ et al 2005 Nature [Lond] 438:117). Diseases may occur due to the misfolding of protein(s) such as in cystic fibrosis, Parkinsonism, prion, Alzheimer's disease, sickle cell anemia, etc. Some of the misfolding problems can be alleviated by inhibitors of the enzyme or by aiding its degradation by small molecules or by stabilizing the conformation (Cohen FE, Kelly JW 2003 Nature [Lond] 426:905). ►chaperones, ►chaperonins, ►conformation, ►calnexin, ►calreticulin, ►protein structure, ►amyloidosis, ►prion, ►encephalopathies, ►GroEL, ►trigger factor, ►endoplasmic reticulum, ►Sec61 complex, ►protein synthesis, ►folding, ►SCA; Bukau B et al 2000 Cell 101:119; Baker D 2000 Nature [Lond] 405:39; Parodi AJ 2000 Annu Rev Biochem 69:69; Klein-Seetharaman J et al 2002 Science 295:1719; Hartl FU, Hayer-Hartl M 2002 Science 295:1852; Myers JK, Oas TG 2002 Annu Rev Biochem 71:783; Gianni S et al 2003 Proc Natl Acad Sci USA 100:13286; Dobson CM 2003 Nature [Lond] 426:884; Selkoe DJ 2003 Nature [Lond] 426:900; evolutionary implications: DePristo MA et al 2005 Nat Rev Genet 6:678; protein misfolding and amyloid disease: Chiti F, Dobson CM 2006 Annu Rev Biochem 75:333; protein misfolding-human disease: Gregersen N et al 2006 Annu Rev Genomics Hum Genet 7:103; http://bioresearch.ac.uk/browse/mesh/D017510.html; protein refolding: http://refold.med.monash.edu.au/; protein folding potential software: http://flexweb.asu.edu/software/; predicting protein folding on the basis of amino acid sequence: http://psfs.cbrc.jp/fold-rate/; folding database: http://www.foldeomics.org/pfd/public_html/index.php.

Protein Function: Protein function is generally determined by biochemical and genetic analyses such as enzyme assays, two-hybrid system, etc. Many proteins are involved in complex functions and interact with several other proteins. These complex functions can be inferred from the known role of proteins in evolutionarily different organisms, from amino acid sequence information, by the rosetta stone sequences, the correlation of mRNA expression, and gene fusion information from sequence data. During evolution, some structural and functional properties of the diverging proteins are retained in the protein families but some groups have acquired new function such as substrate-specificity. These shifts can be analyzed by: http://FunShift.cgb.ki.se. ►rosetta stone sequences, ►microarray hybridization, ►two-hybrid system; http://biozon.org; functional sites, ligands: http://firedb.bioinfo.cnio.es.

Protein G: An immunoglobulin-binding (IgG) streptococcal extracellular cell surface protein.

Protein Grafting: The transfer of a binding epitope in biologically active conformation unto the surface of another protein. Such a procedure may produce an effective antiviral protein or may be used for other biological purposes. ►epitope; Sia SK, Kim PS 2003 Proc Natl Acad Sci USA 100:9756.

Protein H: Streptococcal IgG-binding protein. ►immunoglobulins

Protein Index: Guides to the main databases on proteomes such as Swiss-Prot, RefSeq, Ensembl, etc. ►protein classification; http://kinemage.biochem.duke.edu/~jsr/html/anatax.3a4.html.

Protein Information Resource: ►PIR; http://pir.georgetown.edu; the largest and most comprehensive source is the Swiss-Prot: http://www.expasy.ch/; ►databases

Protein Interactions: Interaction density (PID) is calculated as observed protein interaction/total number of possible pair-wise combinations. Conformational switches detectable by nuclear magnetic resonance relaxation experiments at the microsecond to millisecond time scale may modulate protein interactions (Koglin A et al 2006 Science 312:273). The various proteins may interact in many different ways and the ~6000 proteins of yeast may display about 100,000 relations. In a preliminary attempt to develop a human genome-wide interaction network,

~8100 Gateway-cloned ORFs allowed the detection of 2800 interactions (Rual J-F et al 2005 Nature [Lond] 437:1173). A new method permits prediction of interactions on the basis of protein sequence (Shen J et al 2007 Proc Natl Acad Sci USA 104:4337). Bioinformatic technology is required to separate the genuine from the spurious interactions (Jansen R et al 2003 Science 302:449). In *Drosophila* a draft of 7048 proteins and 20,405 interactions were detected and at a high confidence level 4679 proteins and 4780 interactions were verified by the two-hybrid method and mapped (Giot L et al 2003 Science 302:1727).

Photo-cross-linking permits detection of protein–protein interactions in living cells. Photoreactivable amino acids (e.g., photomethionine, as shown in Figure P147, the critical change is circled by dashed line) are very similar to natural counterparts and can be incorporated into the protein by the translation machinery. Activation by ultraviolet light results in cross-linking of the interacting proteins and it can be detected by western blotting (Suchanek M et al 2005 Nature Methods 2:261).

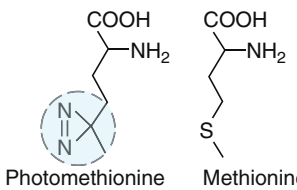

Figure P147. Photomethionine (left); methionine (right). (After Suchanek, M. et al. 2005 Nature Methods 2:261)

The bimolecular fluorescence complementation (BiFC) method permits the visualization of interaction *in situ* within living cells using yellow fluorescent protein variants (Hu C-D, Kerppola TK 2003 Nature Biotechnol 21:539). Protein interaction networks are largely preserved during evolution from prokaryotes to eukaryotes, although some specialization is also evident (Kelley BP et al 2003 Proc Natl Acad Sci USA 100:11394). A recent analysis of more than 70,000 binary interactions in humans, yeast, *Caenorhabditis*, and *Drosophila* showed only 42 were common to human, worm, and fly and only 16 were common to all. An additional 36 were common between fly and worm but not to humans, although by co-immunoprecipitation 9 were present in humans. Proteins known to be involved in similar disorders in humans showed interaction (Gandhi TKB et al 2006 Nat Genet 38:285). ►gene product interaction, ►two-hybrid method, ►protein-DNA interaction, ►affinity tagging, ►protein chips, ►networks, ►genetic networks, ►GRID, ►BIND, ►DIP, ►ORF, ►Gateway cloning, ►interactome; Bock JR, Gough DA 2001 Bioinformatics 17:455; Fernández A, Scheraga HA 2003 Proc Natl Acad Sci USA 100:113; MIPS database: Mewes HW et al 2002 Nucleic Acids Res 30:31; Jansen R et al 2002 Genome Res 12:37; http://bind.ca; http://string.embl.de; human protein reference/interaction database: http://www.hprd.org/; domain–domain interactions: http://3did.embl.de; http://mimi.ncibi.org; interactions from PubMed abstracts: http://cbioc.eas.asu.edu; protein interfaces: http://scoppi.org/; http://pre-s.protein.osaka-u.ac.jp/~prebi; protein domain interaction database: http://mint.bio.uniroma2.it/domino/; http://mint.bio.uniroma2.it/mint/Welcome.do; http://www.hsls.pitt.edu/guides/genetics/tools/protein/interaction/URL1138211431/info; Apid interaction analyzer: http://bioinfow.dep.usal.es/apid/index.htm; protein docking server: http://vakser.bioinformatics.ku.edu/resources/gramm/grammx; interaction software: http://www.ebi.ac.uk/intact/site/index.jsf; molecular ancestry network MANET: http://www.manet.uiuc.edu/.

Protein Intron: ►intein

Protein Isoforms: Closely related polypeptide chain family, encoded by a set of exons, which share structurally identical or almost identical subset of exons. ►family of genes

Protein Kinase: A protein kinase phosphorylates one or more amino acids (frequently threonine, serine, tyrosine) at certain positions in a protein, and thus two negative charges are conveyed to these sites, altering the conformation of the protein. This alteration then involves a change in the ligand-binding properties. The catalytic domain of this large family of enzymes is usually 250 amino acids. The amino acids outside the catalytic domains may vary substantially and specify the recognition abilities of the different kinases and serve in responding to regulatory signals. During the last three to four decades, hundreds of protein kinases have been discovered that can be classified into serine/threonine (TGF-β [transforming growth factor]), tyrosine (EGF [epidermal growth factor receptor], PDGF [platelet-derived growth factor receptor] protein kinases, SRC [Rous sarcoma oncogene product], Raf [product of the Moloney and MYC oncogenes]), MAP kinase, cell cyclin-dependent kinase (Cdk), cell division cycle (Cdc), cyclic-AMP- and cyclic-GMP-dependent kinases, myosin light chain kinase, Ca^{2+}/calmodulin dependent kinases, etc. Protein kinase R (PKR, dsRNA-dependent protein kinase) down-regulates protein synthesis in virus-infected cells. In the N-terminal region, two double-stranded RNA binding domains activate PKR by binding to dsRNA

and recruit it to the ribosome where it phosphorylates the eukaryotic elongation factor eIF2α. The consensus sequences for a few protein kinases are shown below:

Protein kinase A
(?)-Arg- (Arg/Lys)-(?)-(**Ser/Thr**)-(?)
Protein kinase G
(?)-{[Arg/Lys] 2x or 3x}-(?)-(**Ser/Thr**)-(?)
Protein kinase C
(?)-([Arg/Lys] 1-3x)-([?] 0-2x)-(**Ser/Thr**)-([?]0-2x)-(Se/[Thr]1-3x)-(?)
Ca^{++}/calmodulin kinase II
(?)-arg-(?)-(?)-(?)-(**Ser-Thr**)-(?)
Insulin receptor kinase
Thr-Arg-Asp-Ile-**Tyr**-Glu-Thr-Asp-**Tyr**-**Tyr**-Arg-Thr
EGF receptor kinase
Thr-Ala-Glu-Asn-Ala-Glu-**Tyr**-Leu-Arg-Val-Arg-Pro

(?) indicates any amino acid, the numbers after the amino acid with an "x" indicate how many times it may occur.

The majority of protein kinases require phosphylation in their activation loop to perform their function. The human genome apparently includes 518 protein kinase genes. Protein kinases play an important role in signal transduction as well in the development of diseases (cancer), behavior and memory. Protein kinase inhibitors have therapeutic potentials. The inhibitors must pass the gatekeeper function of selectivity filters at the site of one or more amino acids (Cohen MS et al 2005 Science 308:1318). ►cAMP-dependent protein kinase, ►epinephrine, ►phosphorylase b kinase, ►signal transduction, ►obesity, ►PKB, ►kinase, ►TGF, ►EGF, ►PDGF, ►RAF, ►MYC, ►MAP, ►tyrosine kinase, ►selectivity filter; Plowman GD et al 1999 Proc Natl Acad Sci USA 96:13603; Ung TL et al 2001 EMBO J 20:3728; Cohen P 2002 Nature Cell Biol 4:E127; Huse M, Kuryan J 2002 Cell 109:275; Manning G et al 2002 Science 298:1912; Noble MEM et al 2004 Science 303:1800; regulation: Nolen B et al 2004 Mol Cell 15:661; drug targets: Sebolt-Leopolt JS, English JM 2006 Nature [Lond] 441:457; protein kinase locking server: http://abcis.cbs.cnrs.fr/LIGBASE_SERV_ WEB/PHP/kindock.php.

Protein Binding: Protein binding involves binding protein to protein, to RNA, and to DNA. Induced fit, van der Waals interactions, electrostatic interactions, hydrogen bonds, and aromatic stacking (involving mainly tyrosine and phenylalanine) have been implied. Organic chemistry also uses pi–pi (π–π) stacking. terms mentioned; Mignon P et al 2005 Nucleic Acids Res 33:1779; Hunter CA 2004 Angew Chem Int Ed Engl 43:5310; protein ligands: http://www.bindingdb.org.

Protein Knots: Structural sites for ligand binding and enzyme activity.

Protein L: *Peptostreptococcus* bacterial protein binding to the framework of immunoglobulin κ chains. ►immunoglobulins, ►framework amino acids

Protein Length: Protein length shows great differences among individual molecules by the number of amino acids. There is a statistically significant increase along the advancement in the evolutionary rank, e.g., in Archaebacteria 270 ± 9, in bacteria 330 ± 5, and in eukaryotes (budding yeast and Caenorhabditis) 449 ± 25. Some of the mammalian proteins are huge, e.g., dystrophin.

Protein Likelihood Method: The protein likelihood method is used to determine evolutionary distance when the organisms are not closely related and when the non-synonymous base substitutions are higher than the synonymous ones. In such cases, the protein method may provide more reliable information. ►evolutionary distance, ►evolutionary tree, ►least square methods, ►four-cluster analysis, ►un-rooted evolutionary trees, ►transformed distance, ►Fitch-Margoliash test, ►DNA likelihood method; Whelan S Goldman N 2001 Mol Biol Evol 18:691.

Protein Machines: Multimolecular interacting systems such as metabolic circuits, intracellular signal transduction, or cell-to-cell communication. These systems are operated under process control strategies involving integrated feedback control. The input and output of the circuits or modules are coordinated to assure the normal or adaptive function of the cell or organism. ►feedback control, ►microarray hybridization; Baines AJ et al 2001 Cell Mol Biol Lett 6:691; Tobaben S et al 2001 Neuron 31:987.

Protein Mapping: Protein mapping localizes the pattern of expression of genes by identifying the sites of proteins within cells. An automated, multidimensional fluorescence microscopy technology permits mapping and interaction of hundreds of different proteins in a single cell (Schubert W et al 2006 Nat Biotechnol 24:1270). ►gene expression map; Huh W-K et al 2003 Nature [Lond] 425:686; Ghaemmaghami S et al 2003 Nature [Lond] 425:737.

Protein Microarray: Microspots of proteins immobilized on solid support and exposed to samples of binding molecules. In such a system, enzyme–substrate and protein–ligand relations can be visualized by the use of fluorescence, chemiluminescence, mass spectrometry, radioactivity, or electrochemistry. ►protein chips, ►protein profiling, ►antibody microarray, ►chemiluminescence, ►fluorescence,

►mass spectrum; Templin MF et al 2002 Trends Biotechnol 20:160.

Protein Network: The protein network detects functional organization of genomes. Two proteins may be related to other in the cell in case the presence of one seems to affect the presence or absence of another. Such a relation exists if both are required to form a structural complex or if they carry out sequential steps in an unbranched pathway. Under natural, biological conditions the presence or absence of multiple proteins exists. Another simple situation is where three proteins are followed. These may display eight different relations, such as C being present only if both A and B are present or A being present if only either B or A are present and so on. The various probabilities or uncertainties of the clusters can then be calculated in a single genome and in phylogenetic relatives to obtain information of the protein network organization (Bowers PM et al 2004 Science 306:2246). ►genetic networks; http://www.cellcircuits.org.

Protein 4.1N: 4.1 N binds to the nuclear mitotic apparatus protein NuMA, a non-histone protein that is associated with the mitotic spindle. It regulates the antimitotic function of the nerve growth factor NGF. ►NGF, ►PIK; Kontragianni-Konstatonopoulos A et al 2001 J Biol Chem 276:20679; Scott C et al 2001 Eur J Biochem 268:1084.

Protein-Nucleic Acid Interaction: ►transcription factors, ►two-hybrid method; thermodynamics of interactions: http://gibk26.bse.kyutech.ac.jp/jouhou/pronit/pronit.html.

P

Proteins, Number of in a human cell: may exceed that of the number of genes by a factor 5 or more but at this stage it is not known.

Protein Phosphatases: Protein phosphatases remove phosphates from proteins. They include enzymes that reverse the action of protein kinases and have an important role, together with the kinases, in signal transduction. ►protein kinases, ►membrane fusion, ►FK506; Barford D et al 1998 Annu Rev Biophys Biomol Struct 27:133; Terrak M et al 2004 Nature [Lond] 429:780.

Protein pI: isoelectric point of proteins varies between <3 to >12. ►isoelectric point

Protein Profiling: The characterization or identification of proteins on the basis of sequence, structure, mass spectrum, MALDI, MS/MS, high-performance liquid chromatography, protein microarrays, two-dimensional gel electrophoresis, etc. ►proteomics, ►protein chips, ►antibody microarray

Protein Purification: To purify proteins, disrupt cells→separate subcellular organelles by differential centrifugation→wash by buffer the separated bodies→treat the fraction(s) needed by denaturing agents→dialyze to remove the denaturing agent→use reducing agents for protection→concentrate→remove the unneeded or improperly folded protein fractions by ion-exchange chromatography, gel filtration, immunoaffinity, isoelectric focusing, high performance liquid chromatography or other steps→the wanted pure protein. Quantitate the amount or yield of the protein obtained by UV absorption or by the Lowry or Bradford methods. Each of these steps may need detailed operations. ►UV spectrophotometry of proteins, ►Lowry test, ►Bradford method

Protein Quality Control: ►unfolded protein response, ►endoplasmic reticulum-associated degradation

Protein Repair: Protein repair can be managed with assistance of chaperones. If the refolding is not feasible, proteolytic enzymes destroy proteins either directly or by the mediation of ubiquitins. Nascent polypetides, transcribed from truncated mRNAs without a stop codon, acquire a C-terminal oligopeptide (Ala, Ala, Asn, Asp, Glu, Asn, Tyr, Ala, Leu, Ala, Ala or a variant), encoded by an *ssrA* transcript. The ssrA is a 362-nucleotide tRNA-like molecule that can be charged with alanine. The addition of the peptide tag takes place on the ribosome by cotranslational switching from the truncated mRNA to the ssrA RNA. The polypeptide chain so tagged is degraded in the *E. coli* cytoplasm or periplasm by carboxyl-terminal-specific proteases. The Clp chaperone recognizes the peptides by the ssRA tag of AANDENYALAA and targets the proteins to the ClpX and ClpA ATPases. ►amino acids, ►chaperone, ►ubiquitin, ►periplasm, ►protease, ►DNA repair, ►tmRNA, ►Clp, ►ssRA; Wawrzynow A et al 1996 Mol Microbiol 21:895.

Protein S (PROS): The human chromosome 3p11 vitamin K-dependent plasma proteins preventing blood coagulation and a cofactor for Protein C. Their deficiency and dysfibrinogenemia are genetically determined causes of thrombosis. ►protein C, ►antithrombin, ►dysfibrinogenemia, ►thrombosis, ►APC, ►anticoagulation, ►thrombophilia, ►tissue factor

Protein Sequencing: ►amino acid sequencing

Protein Shuttling: The flow of protein within cells or cellular organelles. (See Ando R et al 2004 Science 306:1370).

Protein Similarity Matrix: http://mips.gsf.de/simap/.

Protein Sorting (protein traffic): The mechanism by which the polypeptides synthesized on the ribosomes in the endoplasmic reticulum reach their destination in the cell through secretory pathways by transport, with the aid of endocytotic vesicles. ►endocytosis, ►clathrin, ►Golgi apparatus, ►COP transport vesicle, ►RAFT, ►Sec, ►Fts; Tormakangas K et al 2001 Plant Cell

13:2021; Wickner W, Schekman R 2005 Science 310:1452.

Protein Splicing: ▶intein

Protein Structure: The *primary structure* means the sequence of the amino acids. The *secondary structure* is formed by the three-dimensional arrangement of the polypeptide chain. The polypeptides may form α helix or β conformation when hydrogen bonds are formed between pleated sequences of the same chain. The latter type of conformation is frequently found in internal regions of enzyme proteins and in structural protein elements such as silk fibers and collagen. The α helixes are commonly represented by cylinders, whereas the β sheets by ribbons frequently with arrows at their end. The *tertiary structure* involves a folding to either a globular or various types of rope kind of structure of the polypeptide chain that has already secondary structure. Mature proteins may be formed from multiple identical or different polypeptide subunits and this type of association is the *quaternary structure* (PQS) (see Fig. P148): http://pqs.ebi.ac.uk/pqs-doc.shtml. The quaternary structure frequently includes some other molecule(s). For special biological functions, more than one protein may be joined in *supramolecular complexes* such as the myosin and actin in the muscles, and histones and various non-histone proteins in chromatin. The primary structure is genetically determined and all additional structural changes flow from this primary structure although trimming, processing, and association with prosthetic groups may be involved. The information on protein structure is highly relevant for understanding its function (Pal D, Eisenberg D 2005 Structure 13:121). Proteins with greater than 30% sequence homology assume generally the same basic structures. Although the primary structure is relevant for inferences on function and homology, remote homologies are based on folding that indicates their accommodation into particular space required for performance even when the sequence has relatively low homology (see Fig. P149) (Hou J et al 2005 Proc Natl Acad Sci USA 102:3651). Protein structure information can be obtained through several Web sites: http://astral.berkeley.edu/; http://www.pdbj.org; or http://www.ncbi.nlm.nih.gov/entrez/query.

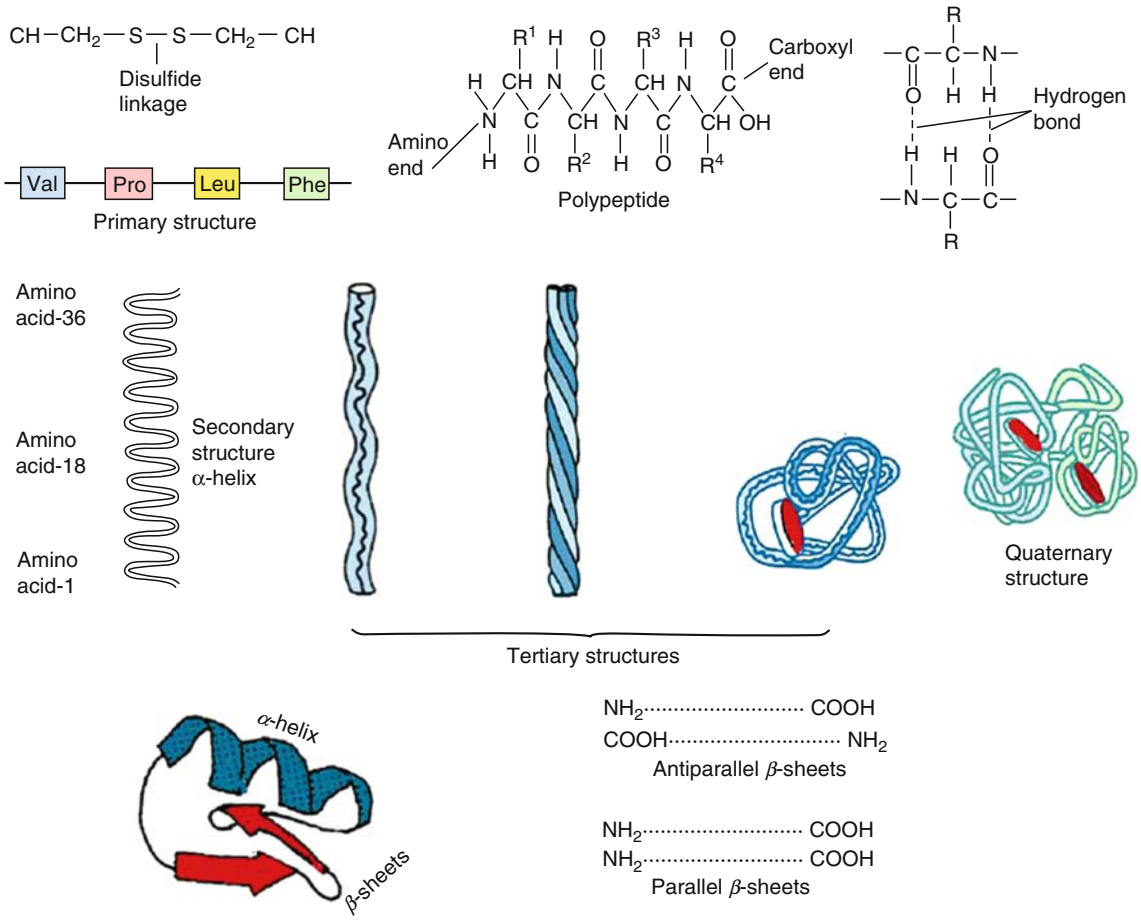

Figure P148. Protein structure

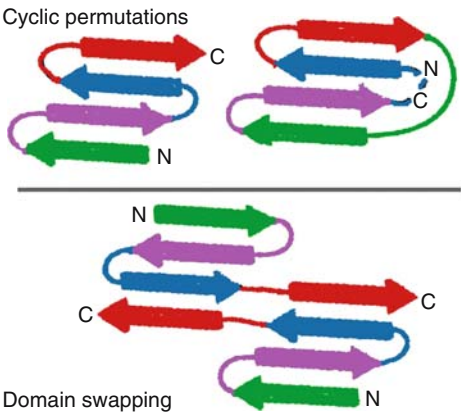

Figure P149. Cyclic permutations of the secondary structure or domain swapping of the α and β strands is tolerated in many proteins. The essential feature of a protein fold is the complementary packing of the secondary structural elements and not the precise manner of connection of the elements. Some of these changes retain stability of the protein and binding ability and can be used in protein engineering. (Diagram is modified after Tabtiang RK et al 2005 Proc Natl Acad Sci USA 102:2305)

fcgi?db=Structure; http://astral.stanford.edu/; http://www.imb-jena.de/IMAGE.html; http://scop.mrc-lmb.cam.ac.uk/scop/; ►protein synthesis, ►protein domains, ►molecular modeling, ►conformation, ►databases, ►CATH, ►SCOP, ►FEMME, ►electron density map of proteins, ►x-ray diffraction analysis, ►MANET, ►MOLSCRIPT, ►block; Goodsell DS, Olsen AJ 2000 Annu Rev Biophys Biomol Struct 29:105; Martí-Renom MA et al 2000 Annu Rev Biophys Biomol Struct 29:291; Koonin EV et al 2002 Nature [Lond] 420:218; Ouzounis CA et al 2003 Nature Rev Genet 4:508; review on structure predictions and biological significance: Petrey D, Honig B 2005 Mol Cell 20:811; tertiary structure matching of proteins: http://proteindbs.rnet.missouri.edu/index.php; molecular structure database tool: http://bip.weizmann.ac.il/oca-bin/ocamain; structural neighbors: http://fatcat.burnham.org/fatcat-cgi/cgi/struct_neibor/fatcatStructNeibor.pl; structural and functional annotation of protein families: http://cathwww.biochem.ucl.ac.uk:8080/Gene3D/; functional site prediction: http://sage.csb.yale.edu/sitefinder3d/; functional sites from sequence alignment: http://zeus.cs.vu.nl/programs/seqharmwww/; interacting protein motifs: http://caps.ncbs.res.in/imotdb/; comparative structure models: http://modbase.compbio.ucsf.edu/modbase-cgi-new/index.cgi; protein modeling: http://a.caspur.it/PMDB/; 3D structures: http://molprobity.biochem.duke.edu/; 3D conserved residues: http://3dlogo.uniroma2.it/; annotated three-dimensional structures: http://swissmodel.expasy.org/repository/; automated prediction: http://pcons.net/; tertiary structure: http://prokware.mbc.nctu.edu.tw/; protein short sequence motif search: http://past.in.tum.de/; computing physicochemical properties on the basis of amino acid sequence: http://jing.cz3.nus.edu.sg/cgi-bin/prof/prof.cgi; stability of mutant proteins: http://cupsat.uni-koeln.de/; http://www.ces.clemson.edu/compbio/protcom; interactive structures: http://www.compbio.dundee.ac.uk/SNAPPI/downloads.jsp; solvability and interfacing: http://pipe.scs.fsu.edu/; protein structure modeling: http://manaslu.aecom.yu.edu/M4T/; unstable (disorder) regions: http://prdos.hgc.jp/cgi-bin/top.cgi; http://biominer.cse.yzu.edu.tw/ipda/; structure animation (movie): http://bioserv.rpbs.jussieu.fr/~autin/help/PMGtuto.html.

Protein Synthesis: Has many basic requisites and a large number of essential regulatory elements. It intertwines with all cellular functions. The blueprint for protein synthesis in the vast majority of organisms (DNA viruses, prokaryotes and eukaryotes) is in the nucleotide sequences of the DNA code. In RNA viruses the genetic code is in RNA. However, the viruses do not have their own machinery for the actual synthesis of protein, rather they exploit the host cell for this task. The genetic code specifies individual amino acids by nucleotide triplets, using one or several synonyms for each of the 20 natural amino acids. The triplet codons are in a linear sequence of the nucleic acid genes. In the organisms with DNA as the genetic material, the process of transcription produces a complementary RNA sequence from one or both strands of the antiparallel strands of the DNA. The double-strands unwind and the RNA polymerase(s) synthesize(s) a complementary RNA copy of the sequence in the DNA. In the single stranded DNA and RNA viruses, the DNA or RNA may serve both purposes of being the genetic material and the transcript for protein synthesis. In cellular organisms three main classes of RNAs are made, messenger RNA (mRNA), transfer RNA (tRNA) and ribosomal RNA (rRNA), and all three are indispensable for protein synthesis. In addition to these RNAs, a large number of proteins are required for the transcription process (transcription factors), for the organization of the ribosomes (50–80 ribosomal proteins), for the termination of transcription, for the activation of the tRNAs, etc. A broad overview (without details) is shown in Figure P150. Some of the details of the transcriptional process are different in prokaryotes from that in eukaryotes. In the latter group, one DNA-dependent RNA polymerase is responsible for the synthesis of all RNAs. In eukaryotes, pol I synthesizes rRNAs with the exception of the 5S and 7S rRNA, pol II transcribes mRNA and the small nuclear RNAs (snRNA) and pol III synthesizes tRNAs and 5S and 7S rRNA.

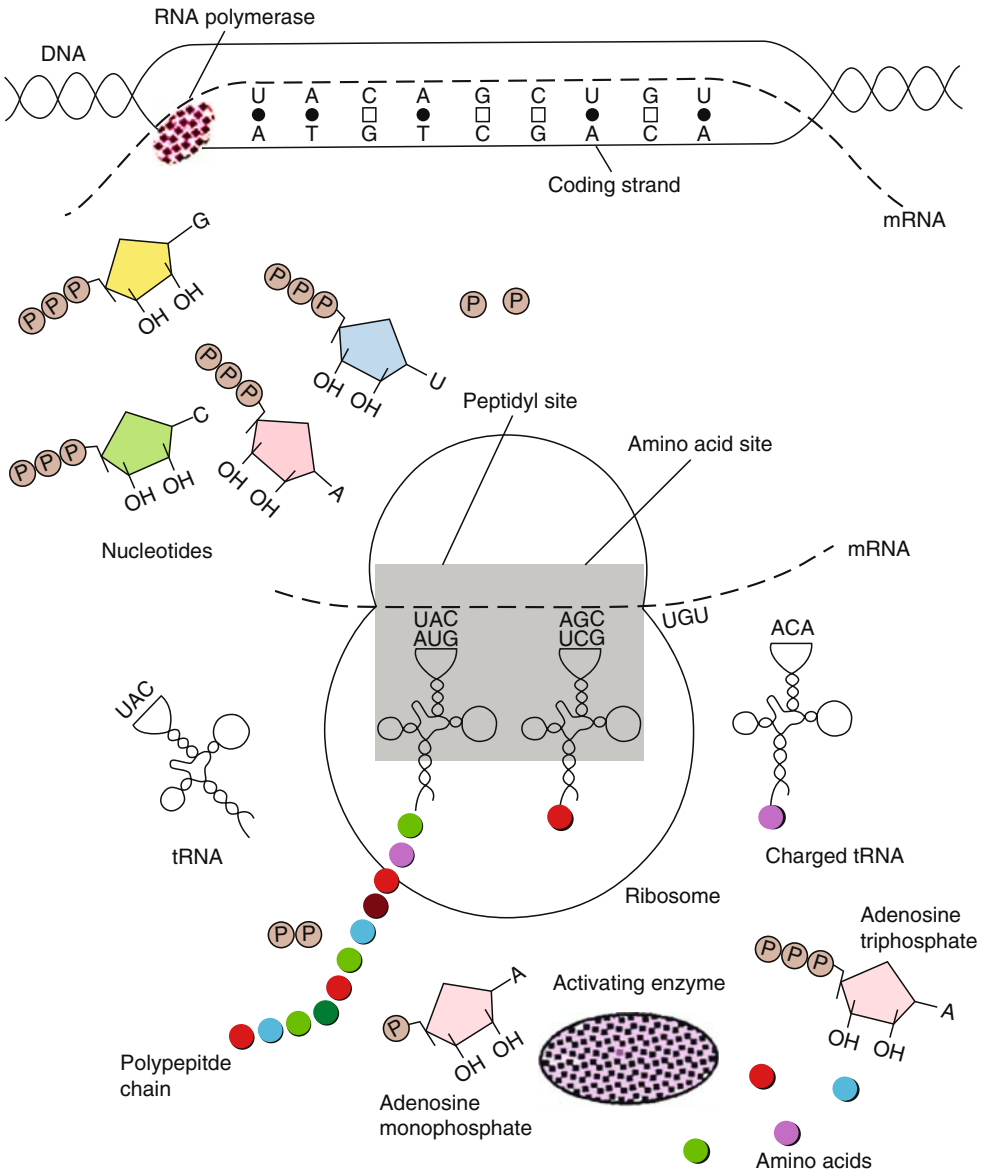

Figure P150. An over-simplified view of the protein synthesizing machinery

In prokaryotes, the process of transcription and translation are *coupled*, i.e., as soon as the chain of mRNA unwinds from the DNA it is associated with the ribosomes and protein synthesis begins. The primary RNA transcripts must be processed to functional size molecules in all categories that may require splicing and other post-transcriptional modifications (capping, formylation, etc.).

In eukaryotes when the mRNA is released from its DNA template it moves into the cytosol where protein synthesis takes place. A small fraction of polypeptides may be synthesized also in the nucleus of eukaryotes (Iborra FJ et al 2001 Science 293:1058). There is evidence for the association of ribosomal components into ribonucleoprotein complexes at the transcription sites of salivary gland chromosomes (Brogna S et al 2002 Mol Cell 10:93). The fate of the mRNA can be monitored by electronmicroscopy in both groups and these pictures show the elongation of RNA and protein strands (see Fig. P151). The first products of both display long strands and the short ones indicate the stage and place where they were started. The ribosomes are captured by the mRNA and form an association of multiple units in the form called *polysomes* (see Fig. P152).

The prokaryotic mRNA is directed to the proper position in the 30S ribosomal subunit by the Shine-Dalgarno nucleotide sequence within 8 to 13-base

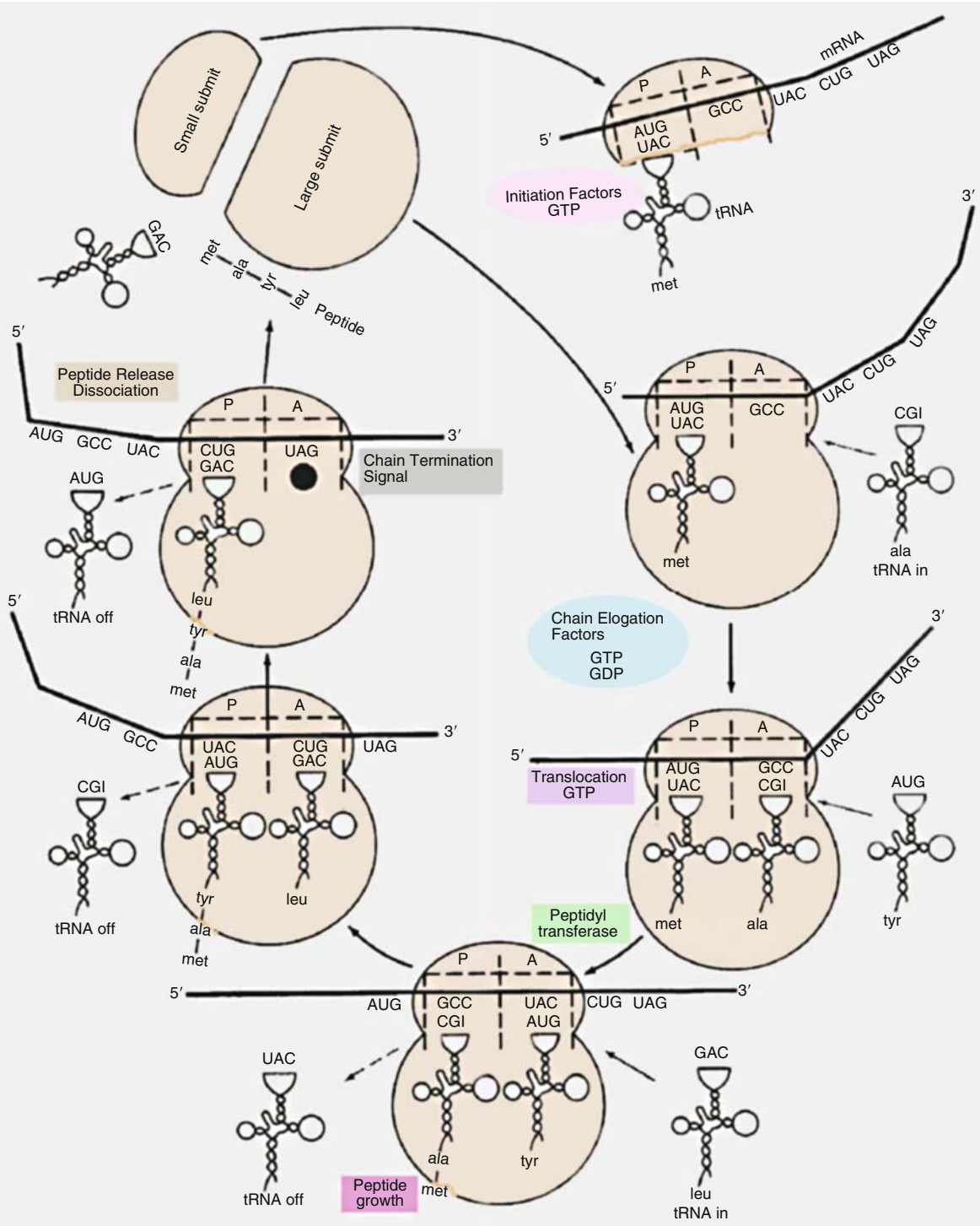

Figure P151. Classical model of translation on ribosomes

area upstream from the initiation codon. In eukaryotes, such a sequence does not exist and the mRNA is simply scanned by the ribosome until the first methionine codon is found.

The ribosomal units then slide from the 5′-end of the mRNA toward the 3′-end and thus, the amino end of the polypeptide chain corresponds to the 5′-end of the mRNA. The ribosomes in both prokaryotes and

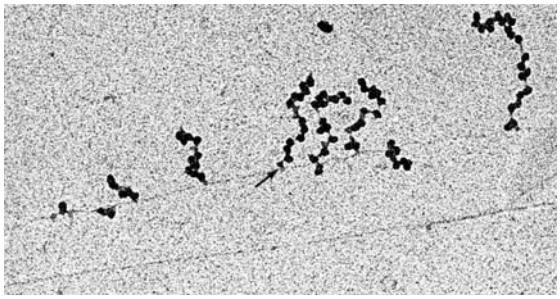

Figure P152. Transcription and translation coupled in *E. coli*. The thin thread is the DNA, the dark round structures are polysomes. The transcriptase attachment → is indicated. (From Hamkalo BA et al 1974 Stadler Symp 6:91)

eukaryotes are composed of a small and a large subunit. The size of these units is somewhat different in the two major taxonomic categories. The small and large subunits of the ribosomes jointly form two compartments, the so-called P (peptidyl-tRNA binding site) and the A (aminoacyl-tRNA binding site). A newer *hybrid-states model* of the translational process is described under the entry "ribosomes." The ribosomes actually do not look like as shown in these diagrams, because they are three-dimensional and have a more elaborate structure. Before protein synthesis (translation) begins and the primary structure of the mRNA is translated from the nucleotide triplet codon words into the singular amino acid word language of the protein, the tRNA molecules must be charged with amino acids. This process is also called activation of tRNA. (►aminoacyl-tRNA synthetase).

The amino-acid-charged methionine-tRNA ($tRNA^{Met}$) in eukaryotes and the formylated $tRNA^{fMet}$ in prokaryotes seek out the cognate codon in the mRNA at the P site of the ribosome through the complementary anticodon. This event requires the presence of protein initiation factor(s) and GTP as energy source. The GTP is cleaved to GDP + inorganic phosphate (Pi) and thus liberates some of the needed energy. The elongation factor proteins and GTP and GDP complexes also police the system to prevent the wrong charged tRNA to go to an A site (proofreading function). Actually a similar correction mechanism is carried out earlier in the process by one of the active sites of the aminoacyl synthetase (activating) enzyme that usually dissociates the amino acid—tRNA link in case of a misalliance. With the double checks available, misincorporation of amino acids is approximately in the 10^{-4} range. Protein synthesis in the mitochondria and chloroplasts is essentially patterned after the prokaryotic systems.

The 5′-base of the anticodon triplet may not be the exact and conventional base, yet it may function normally (►wobble). The two subunits of the ribosomes are combined and the second charged tRNA can now land at the A ribosomal site. The carboxyl end of the methionine forms a peptide bond with the amino terminus of the next incoming amino acid at the A site. This process is mediated by the enzyme peptidyl transferase. For this transferase function a 23S rRNA in the large subunit (a ribozyme) is responsible and not a protein. Again energy donors and elongation protein factors are cooperating in the process of peptide chain growth (►initiation and elongation factors IF, ►eIF, ►EF, ►EF-T, ►EF-Tu). When each peptide bond is completed the tRNA is released and recycled for another tour of duty. The *open reading frame* of the gene is terminated by a nonsense or chain-termination codon. When the ribosome slides to this point the mRNA is released from the ribosomes with the assistance of release factors (►transcription termination in eukaryotes, ►transcription termination in prokaryotes). Protein synthesis proceeds at a rather rapid rate; it has been estimated that in *E. coli* 50–200 amino acids may be incorporated into peptides in 5–10 s. The process is slower in eukaryotes (3–8 s) (see Fig. P153). According to Princiotta MF et al 2003 (Immunity 18:343), the cells of the immune system produce 40 million proteins/min on the 6 million ribosomes.

The ribosomes have an important role in the regulation of protein synthesis. It appears that the availability of active ribosomes is controlled at the level of the transcription of the rRNA genes. In most of the cases, the number of ribosomes is not a limiting factor of translation. Some of the bacterial ribosome proteins have dual roles and participate in transcription and translation (Squires CL, Zaporojets D 2000 Annu Rev Microbiol 54:775). When the supply of ATP and GTP is adequate, rRNA genes are activated for transcription. In case the level of these nucleotide triphosphates is low, rRNA transcription is reduced or halted. Abundance of free ribosomal proteins may feedback-inhibit ribosomal production. The ribosome-associated Rel-A protein may mediate the formation of ppGpp from GTP (and possibly from other nucleotides). Then ppGpp may shut off rRNA and tRNA synthesis by binding to the promoter of RNA polymerase or to its antitermination signal.

Some of the nascent peptides are segregated into the endoplasmic reticulum through the Sec61 conductance opening of the large subunit of the ribosomes. Within the endoplasmic reticulum, the translation continues and the protein is folded by the appropriate chaperones. In prokaryotes, only the completed polypeptide chains are folded whereas in eukaryotes, the separate domains of the large polypeptides are folded as the chain grows.

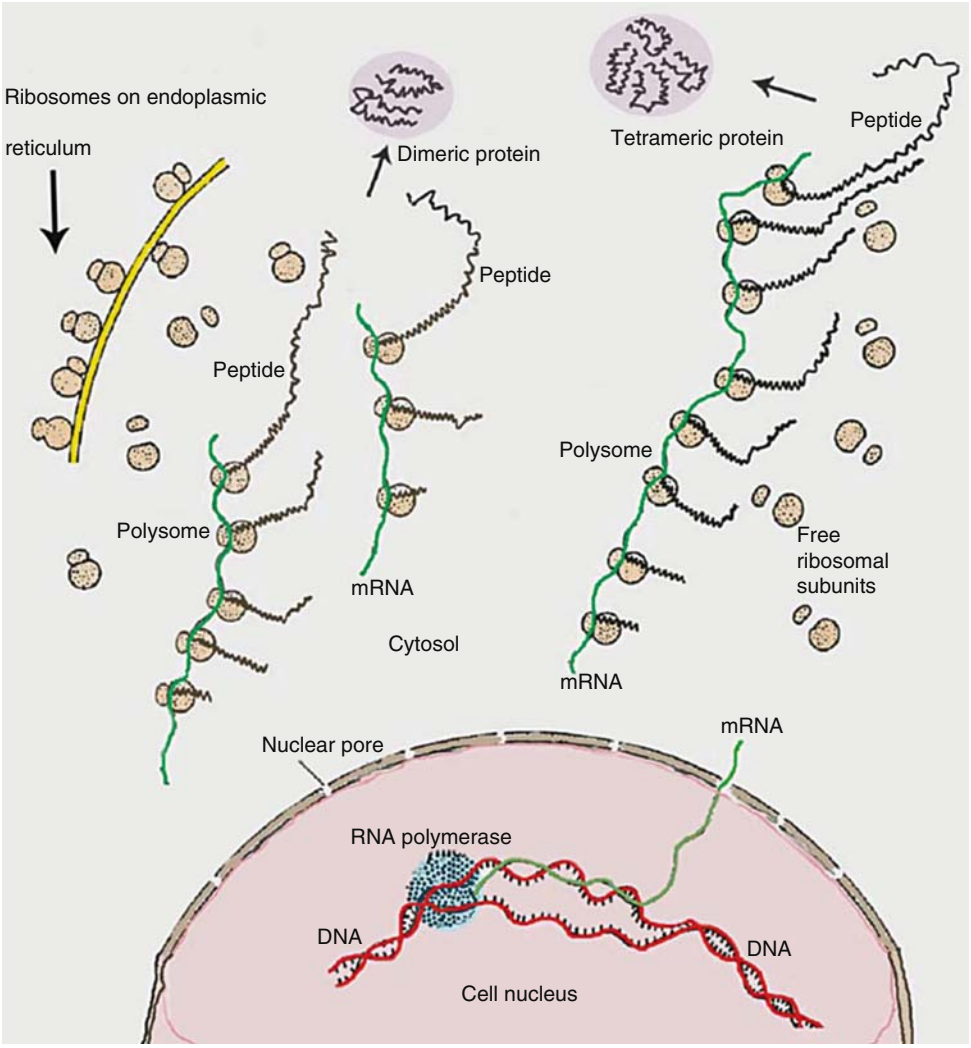

Figure P153. An overview of eukaryotic translation

The dimeric NAC (nascent-polypetide associated complex) interacts with the emerging polypeptide chains before 30 or fewer residue long chain is formed, and protects the nascent chain from becoming associated with other cytosolic proteins until the signal peptide fully emerges and then the signal recognition particle (SRP) crosslinks to the polypeptide. The purpose of the NAC is to assure that the polypeptide would be oriented to the proper SRP and the endoplasmic reticulum. Alternatively, if the protein does not carry a signal peptide, the nascent chain may be folded by chaperones such as heatshock proteins Hsp40 Hsp70 and TRiC. The completed amino acid sequences, the polypeptides, must be then converted to biologically active forms. This post-translational process may involve trimming (removal of some amino acids), proteolytic cleavage, folding to a tertiary structure, aggregation of different polypetide chains to form the quaternary structure, addition of prosthetic groups (such as heme, lipids, metals), and other non-amino-acid residues such as acyl, phosphate, methyl, isoprenyl and sugar groups.

Some proteins are expressed at very low level and by the classical methods of biochemistry or molecular biology the synthesis may not be detectable. A microfluidic device can, however, detect protein expression at the level of a single molecule (Cai L et al 2006 Nature [Lond] 440:358).

►code genetic, ►mRNA, ►tRNA, ►rRNA, ►ribosomes, ►aminoacyl-tRNA synthetase, ►wobble, ►cap, ►Shine-Dalgarno sequence, ►ribosome recycling, ►RNA polymerases, ►transcription factor, ►transcription initiation, ►elongation initiation factors, ►eIF, ►transcription termination, ►rho factor, ►transcription complex, ►signal sequences, ►transit peptide, ►signal peptides, ►regulation of

gene activity, ►antibiotics, ►toxins, ►ambiguity in translation, ►chaperone, ►SRP, ►signaling to translation, ►translation initiation, ►initiation complex, ►polysome, ►introns, ►prenylation, ►TRiC, ►heatshock, ►E site, ►EF-TU•GTP, ►discriminator region, ►protein folding, ►Sec61 complex, ►non-ribosomal peptides, ►tmRNA, ►translation in vitro, ►translation nuclear, ►subcellular localization, ►microfluidics; Sonenberg N et al (Eds.) 2000 Translational Control of Gene Expression, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, New York; Fredrick K, Noller HK 2002 Mol Cell 9:1125.

Protein Synthesis, Chemical: Building proteins from peptide domains by non-biological means. The peptides may be synthesized by the methods or organic chemistry and then ligated, spliced and folded in order to assure some specific function. Changing individual amino acids in the sequence may lead to new proteins. This procedure may become cumbersome because aggregation may create problems for proper folding. In contrast, solid phase synthesis is practical and any type of non-natural protein can now be produced using synthetic amino acids and peptides. Chemical synthesis of peptides requires stepwise addition of amino acids on solid support. Unfortunately, with the current technology (2005), routinely the synthetic proteins can be made only of about 40 residues although, e.g., 238-residue precursor of the green fluorescent protein has been made years ago (Nishiuchi Y et al 1998 Proc Natl Acad Sci USA 95:13549. [Bradley L et al. 2005 reviewed the principles of the various available peptide ligation techniques in Annu Rev Biophys Biomol Struct 34:91]. See Dawson PE, Kent SBH 2000 Annu Rev Biochem 69:923; Wei Y et al 2003 Proc Natl Acad Sci USA 100:13270).

Protein Synthesis Inhibitors: ►antibiotics, ►toxins, ►interferons

Protein Targeting: Can be co-translational, i.e., newly synthesized proteins are delivered to specific sites (endoplasmic reticulum) in the cell before the chain is completed or post-translational when the transport takes place after the polypeptide is completed. ►signal hypothesis, ►signal sequence recognition particle, ►translocon, ►TRAM, ►protein conducting channel, ►mitosome; Bachert C et al 2001 Mol Biol Cell 12:3152; Zaidi SK et al 2001 J Cell Sci 114:3093; Takayama S, Reed JC 2001 Nature Cell Biol 3:E237.

Protein Trafficking: ►protein sorting

Protein Transduction: The introduction of protein into the blood stream or organs for experimental or therapeutic purposes. This procedure is usually limited to small size (<600 Da) molecules. When, however, the 120 kDa β-galactosidase was fused to an 11-amino acid NH_2 domain of the Tat protein of HIV and introduced into the intraperitonial cavity of the mouse, the protein was detected in a biologically active form in several organs including the brain. ►AIDS, ►BBB, ►galactosidase, ►protein targeting; Embury J et al 2001 Diabetes 50:1706.

Protein Transport: ►protein sorting

Protein Truncation Test: The test may be used to detect the effects of several mutations that do not permit the completion of a polypeptide chain. The gene is transcribed by using polymerase chain reaction and the RNA is translated in vitro and the polypetide is analyzed in SDS minigels. ►PCR, ►SDS-polyacrylamide gel, ►rabbit reticulocyte in vitro translation; Lutz S et al 2001 Nucleic Acids Res 29:E16.

Protein Tyrosine Kinases (PTK): The phosphorylate tyrosine residues in some proteins. This function is frequently coded for by v-oncogenes of retroviruses but cellular oncogenes and other proteins may be involved and are controlling signal transduction and other cellular processes such as cell proliferation and differentiation. Cytosolic tyrosine kinases preferentially phosphorylate their own SH2 domains or related SH2 domains with hydrophobic amino acids at key positions, e.g., Ile or Val at −1 and Glu, Gly or Ala at the +1 position. Receptor tyrosine kinases prefer Glu at −1 position. These preferences specify their signaling role. The RET oncogene's receptor tyrosine kinase product can shift substrate specificity and thereby cause multiple endocrine neoplasia. Quercetin, genistein, lavendustin A, erbstatin and herbimycin are all natural plant products and inhibitors of these enzymes. ►tyrosine kinase, ►receptor tyrosine kinase, ►protein kinases, ►SH2, ►endocrine neoplasia multiple, ►signal transduction; Hubbard SR, Till JH 2000 Annu Rev Biochem 69:373; Blume-Jensen P, Hunter T 2001 Nature [Lond] 411:355.

Protein Tyrosine Phosphatase: ►tyrosine phosphatases

Protein X: A hypothetical chaperone facilitator of the $PrP^{C} \rightarrow PrP^{Sc}$ conversion in prion diseases. ►prion

Protein Zero: A major part of the nerve cell myelin sheath of vertebrates. Its defect may lead to neurological anomalies.

Proteinase A: An endopeptidase involved in protein folding. ►endopeptidase, ►protein folding

Proteinase K: A proteolytic enzyme, frequently used to remove nucleases during the extraction of DNA and

RNA. With appropriate heat treatment any DNase associated with it can be safely removed. ►protease

Proteinoid: A polymerized mixture of amino acids formed during prebiotic stage of evolution (or simulated conditions in the laboratory). They may resemble primitive cells and display fission like phenomena (see Fig. P154). ►prebiotic

Figure P154. Proteinoid (From S. W. Fox., 1964 BioScience 14(12):13, © Am Inst Biol Sci)

Proteinosis: Anomalous accumulation of protein at particular structures of the body.

Protein-DNA Interaction: Takes place between transcription factors and the DNA template of the RNA. These interactions have been mapped in vivo over the entire mammalian genome (Johnson DS et al 2007 Science 316:1497). ►transcription factors, ►regulation of gene activity

Protein-Protein Interaction: Mediates structural and functional organization of the cells. The knowledge of these processes reveals the essential nature of the biology of organisms. The two-hybrid method may reveal the pair-wise interactions, and by sequential and systematic analysis the interacting systems, the metabolic modules can be identified. ►two-hybrid method, ►microarray hybridization, ►networks, ►gene product interaction, ►networks

Protein-RNA Recognition: Almost all RNA functions involve RNA-protein interactions such as regulation of transcription, translation, processing, turnover, viral transactivation and gene regulatory proteins in general, tRNA aminoacylation, ribosomal proteins, transcription complexes, etc.

Proteobacteria: Gram-negative purple bacteria, putative ancestors of mitochondria. ►NUMTs

Proteoglycan: Heteropolysaccharides with a peptide chain attached through O-glycosidic linkage to a serine or threonine residue. Such molecules are enzymes, animal hormones, structural proteins, basement membranes, cellular lubricants (such as mucin), extracellular matrix proteins and the "antifreeze proteins" of Antarctic fishes. They control plant and animal growth, differentiation, development and signal transduction. The proteoglycan-like xylogen accumulates in the meristem of plants and directs continuous vascular development (Motose H et al 2004 Nature [Lond] 429:873). ►antifreeze proteins, ►amyloids, ►glypican, ►syndecan, ►glycosaminoglycan, ►glycoprotein, ►phloeme, ►xyleme; Selleck SB 2000 Trends Genet 16:206.

Proteolipid Protein: A major part of myelin in the brain. ►myelin

Proteolysis: The hydrolyzing peptide bonds of proteins. The tobacco etch virus (TEV) NIa protease recognizes a seven-residue consensus (Glu-X-X-Tyr-X-Gln/Ser) sequence and does not affect proteins not containing it. The protease attached to the ribosomal exit site is most efficient and permits selective cleavage special target proteins (Heinrichs T et al 2005 Proc Natl Acad Sci USA 102:4246). ►proteasome, ►ubiquitin; Ciechanover A 2005 Nature Rev Mol Cell Biol 6:79.

Proteolytic: Enzymes hydrolyze peptide bonds in proteins. ►proteolysis, ►peptide bond, ►peptidase

Proteome: All the cellular proteins encoded by the cellular DNA; it is the protein complement of the genome. In bacteria 10% of the genes encode 50% of the bulk of the protein in eukaryotes ~90% of the proteome is contributed by 10% of the cellular proteins (Humphery-Smith I 2004, p 5 In: Albala JS, Humphery-Smith I (Eds.) Protein Arrays, Biochips, and Proteomics, Marcel Dekker, New York). The genome is very stable (except rare mutations) and it is the same in practically all cells of an organism. The proteome displays variations according to the developmental stage, organs, metabolic rate and health of the organism, etc. Since the proteins are organized and expressed in interacting systems, their study may be very complicated. While the genome does not reveal the detail of the function of a cell(s), proteomics has exactly this goal. The immediate products of the genome, the RNA is frequently processed in more than one way (alternative splicing and combinatorial assembly) to be translated into more than a single type of polypeptide. The translated product can be further modified by trimming, docking, forming multimeric associations, recruitment of ligand, phosphorylation and/or dephosphorylation, acetylation, glycosylation and various other epigenetic mechanisms. Because of alternatives in transcription (using different promoters and processing of the transcripts) there are in general substantially more proteins than genes in the cells. The proteins have also various regulatory roles at the levels of replication, transcription, translation, etc. The amount and kind of RNAs are correlated with the amount of polypeptides yet this correlation is variable. Proteins may undergo substantial post-translational modifications. Although the genome is essentially constant,

the encoded proteins may display great variations during differentiation and development. There are no well-established procedures "fit for all" proteins such as DNA sequencing after cloning, PCR or microarray hybridization. Two-dimensional gel electrophoresis is powerful for the separation of thousands of proteins and monoclonal antibody techniques can be used for the localization of proteins. Although definitive information on the proteome may not come easily it should permit an insight into the function of cells, organisms, evolution and disease that cannot be matched by other means. The size of the human proteome much exceeds that of the number of genes determined by sequencing the genome. The size of the human proteome has been estimated by the formula $N_{CDS} = f_1.f_2.N_{genes}$ where f_1 is the proportion of non-pseudogenic genes and f_2 is the ratio of the total number of protein-coding transcripts to the total number of genes, including those that are spliced alternatively. The estimates so obtained also vary within a wide range (see Harrison PM et al 2002 Nucleic Acids Res 30:1083). ►genome, ►genomics, ►metabolic pathway, ►transcriptome, ►monoclonal antibody, ►two-dimensional gel electrophoresis, ►two-hybrid method, ►protein chips, ►MALDI/TOF/MS, ►electrospray, ►ICAT, ►ACESIMS, ►MS/MS, ►microarray hybridization, ►networks, ►genetic network, ►TOGA, ►core proteome; protein–protein interaction: HUPO: http://www.hupo.org; ►Uniporter; http://www.expasy.ch; https://www.proteome.com/proteome/; http://us.expasy.org; human proteome: http://www.hprd.org/; mass spectrometric characterization of peptide fragments: http://nwsr.bms.umist.ac.uk/cgi-bin/pepseeker/pepseek.pl?Peptide=1; mass spectrum of body proteome: http://www.mapuproteome.com; ►protein, ►genomic sequences, ►exon structure, ►polarity, ►hydrophobicity; Ito T et al 2001 Proc Natl Acad Sci USA 98:4569; Walhaut AJM, Vidal M 2001 Nature Rev Mol Cell Biol 2:55; Harrison PM et al 2002 Nucleic Acids Res 30:1083; Auerbach D et al 2002 Proteomics 2:611; Burley SK, Bonnano JB 2002 Annu Rev Genomics Hum Genet 3:243; Rost B 2002 Curr Opin Struct Biol 12:409.

Proteomic Profiling: Uses chemical labels for the identification of active groups of enzymes in complex mixtures and attempts the identification of the functional role of these groups of proteins. The procedure may reveal the role of protein arrays in the development of disease and may suggest targets for intervention. (See Adam GC et al 2002 Nature Biotechnol 20:805).

Proteomics: The study of the system of the proteome, the modules of metabolism as they carry out cellular functions of the organisms. The new technologies detect the composition/structure of proteins, isoforms, conformational changes, modulatory alterations during development, post-transcriptional and post-translational modifications (phosphorylation, glycosylation), interactions with other proteins or drugs, etc. With low mass tolerance, e.g., 10 ppm single proteins can be identified in a mixture among thousands of molecules. Proteomics has modified the basic approach to investigating biological function. Earlier the experimental design was based on hypotheses. With the aid of the proteomics technologies more direct approaches are possible based on the simultaneous expression patterns of interacting genetic networks. *Expression Proteomics* analyses proteins of the cells by two-dimensional gel electrophoresis (Wagner K et al 2002 Anal Chem 74:809). *Cell-Map Proteomics* is interested in the interaction between/among proteins at various phases of the cell function (Blackstock WP, Weir MP 1999 Trends Biotechnol 17(3):121). *Functional Proteomics* targets specific functions rather than the entire proteome (Graves PR, Haystead TA 2002 Microbiol Mol Biol Rev 66:39). *Structural Proteomics* seeks understanding of protein function on the basis of three-dimensional analysis and modeling (Norin M, Sundstrom M 2002 Trends Biotechnol 20:79; Sali A et al 2003 Nature [Lond] 422:216). *Reverse Proteomics* starts with the genes and proceeds to proteins. Liquid chromatography, two-dimensional polyacrylamide gel electrophoresis and tandem mass spectrometry are important tools of proteomics at large scale. Proteomics is concerned not only with the variability and interactions of proteins but may assist in modifying proteins for new types of interactions. The α-carboxyl group and preceding residues at the C-end of polypetides may offer a useful target for modifications. The PDZ and TPR domains are well qualified for interactions with the C-termini and may facilitate temporal and spatial interactions, degradation, neuronal signaling and other functions (Chung JJ et al 2002 Trends Cell Biol 12:146). The proteome data are expected to be much more complex than that of the genome sequences. The number of proteins and their isoforms far exceeds that of the number of genes. There is a need to develop computer programs that can properly assist in interpreting the "mountain" of information. One of the most complete sources of information on the *E. coli* metabolic system is at: http://ecocyc.org/. The increasing amount of information is fast becoming impossible to integrate for a single human mind and advanced computer models are indispensable. Now proteomic information has important impact of applied biology such as medicine, drug development and agriculture. In painted artwork protein (egg white) has been used since the fourteenth century and before then as

binding material. These old paintings now need restoration and for doing the best work, it is necessary to determine in a minimally invasive way the material the artists used. Modern proteomics technology can reveal the nature of the binder used in Renaissance paintings in ~10 µg samples (Tokarski C et al 2006 Anal Chem 78:1494). ►proteome, ►PFAM, ►Atlas human cDNA, ►genomics, ►annotation, ►MALDI, ►HMS-PCI, ►TAP, ►PDZ domain, ►TPR, ►peptide mass fingerprints, ►NMR, ►post-translational modification, ►quadrupole, ►LC-MS, ►FTMS, ►MS/MS, ►ion trap mass analyzer, ►linear ion trap analyzer, ►two-dimensional gel electrophoresis, ►two-hybrid system, ►protein chips, ►protein microarray, ►X-ray crystallography, ►genetic networks, ►networks, ►gene product interaction, ►nucleolomics, ►laser-capture microdissection, ►MCA, ►mass-coded abundance tagging, ►display technologies, ►MudPIT, ►PEDRO, ►protein engineering, ►semisynthesis of proteins, ►bioinformatics, ►International Protein Index; Washburn MP et al 2001 Nature Biotechnol 19:242; Mann M et al 2001 Annu Rev Biochem 70:437; MOWSE 2001 Trends Biotechnol 19(10):Suppl; Fraunfelder H 2002 Proc Natl Acad Sci USA 99(Suppl 1):2479; Altman RB, Klein TE 2002 Annu Rev Pharmacol Toxicol 42:113; Regnier FE et al 2002 J Mass Spectrom 37:133; Laurell T, Mako-Varga G 2002 Proteomics 2:345; Auerbach D et al 2002 Proteomics 2:611; Petricoin EF et al 2002 Nature Rev Drug Discov 1:683; Huber LA 2003 Nature Rev Mol Cell Biol 4:74; Patterson SD, Aebersold RH 2003 Nature Genet 33 (Suppl):311; analytical methods: Phizicky E et al 2003 Nature [Lond] 422:208; Zhu H et al 2003 Annu Rev Biochem 72:783; de Hoog CL, Mann M 2004 Annu Rev Genomics Hum Genet 5:267; mass spectrometry methods: Domon B, Aebersold R 2006 Science 312:212; http://www.ebi.ac.uk/interpro; http://dip.doe-mbi.ucla.edu/; Proteomics Identification Database: www.ebi.ac.uk/pride/.

Proterozoic (precambrian): The geological period five billion to 570 million years ago. Aquatic forms of living systems appeared during this era. ►geological time periods

ProtEST: A bioinformatics program tool for protein alignments. ►UniGene; Wasmuth JD, Blaxter ML 2004 BMC Bioinformatics 5:187.

Proteus Syndrome: Involves gigantism of parts of the body probably caused by lipomatosis (abnormally large local fat accumulation). The genetic control is unclear. ►PTEN; Cohen MM Jr 1993 Am J Med Genet 47:645.

Prothallium: The haploid gametophyte generation of ferns.

Prothrombin Deficiency: Caused by autosomal recessive, semidominant defects in the formation of anticoagulation factor VII, Stuart factor, Christmas factor and prothrombin. The human gene for prothrombin was assigned to chromosome sites 11p11-q12. Prothrombin is normally generated in sequential reactions by prothrombinase (Bianchini EP et al 2005 Proc Natl Acad Sci USA 102:10099). These proteins have similar proteolytic properties and the synthesis of all four depends on the presence of vitamin K. The patients have a tendency of bleeding similarly to hemophiliacs. Hereditary deficiency of factor VII itself is rare but it may be fatal if bleeding affects the central nervous system. Stuart factor deficiency has symptoms similar to those in deficiency of factor VII. All of these conditions can be treated by transfusion with blood plasma. ►antihemophilia factors, ►hemophilia, ►vitamin K dependence, ►coumarin-like drug resistance

Protist: A general term for single-cell eukaryotic organisms. The *Monera* including bacteria, blue green algae, viruses are also sometimes called protists although these are prokaryotes.

Protocell: Abiotic ancestor of living cells under prebiotic conditions. ►origin of life

Protochlorophyll: The precursor of chlorophyll ($C_{55}H_{70}O_5N_4Mg$); if the magnesium is removed protophaeophytin results. The NADPH:protochlorophyllide oxidoreductases in the prolamellar body of the etioplast are required for the establishment of the photosynthetic apparatus (deetiolation) and for photoprotection in plants. ►chloroplast, ►etioplast, ►NADP, ►photomorphogenesis, ►photosynthesis; Reinbothe S et al 2003 J Biol Chem 278:800.

Protogyny: In monoecious plants, the stigma is receptive before the pollen is shed. ►protandry, ►monoecious, ►stigma, ►self-incompatibility

Protomer: A polypeptide subunit of an oligomeric protein encoded by a cistron of a gene. ►cistron, ►oligomer

Proton: The positive nucleus of the hydrogen atom. The proton carries a positive charge equal to the negative charge of an electron but its mass is 1837 times larger.

Proton Acceptor: An anion capable of accepting protons. ►anion, ►proton

Proton Donor: An acid

Proton Pump: Mediates transport or exchange of protons across cellular membranes; energy is supplied usually by ATP or light. ►proton, ►ion pumps; Ferreira T et al 2001 J Biol Chem 276:29613.

Protonema: A filamentous stage in the formation of the gametophyte of mosses.

Protonoma: A red-color insensitive color blindness; an X-chromosomal anomaly. ►color blindness

Proto-Oncogenes: These are cellular c-oncogenes, which after genetic alteration(s) may initiate or predispose to cancerous transformation. They generally have their counterparts in oncogenic viruses (v-oncogenes). Also, they may be involved in processes of signal transduction in a variety of organisms in fungi, plants and animals. ►oncogenes, ►signal transduction, ►carcinogenesis, ►tumor suppressors, ►cell cycle

Protoperithecium: ►ascogonia, ►perithecium

Protoplasia: Formation of a new tissue.

Protoplasm: The viscous "live" content of the eukaryotic cell. ►cytoplasm

Protoplast: A cell surrounded by the cell membrane but stripped of the cell wall, generally by a combination of pectin and cellulose digesting enzymes. Protoplasts under appropriate conditions may be regenerated into normal cells and intact plants (see Fig. P155). The bacterial protoplasts are generally called spheroplasts and may have some parts of the cell wall still attached. ►cellulase, ►macerozyme, ►pectinase

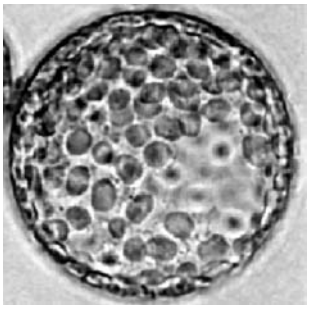

Figure P155. Plant protoplast (Durand J et al 1973 Z. Pflanzenphys. 69:26)

Protoplast Fusion: Protoplasts may fuse in the presence of polyethylene glycol (and some other agents). The fusion may take place within sister cells or with the cells (protoplasts) of any taxonomically distant organisms such as mammalian and plant cells (see Fig. P156). These somatic hybrids, unlike the zygotes derived from the fusion of eggs and sperm, contain all the contents of the two cells, nuclei and cytoplasm, although some cytoplasmic organelles may be lost eventually.

In certain rodent-human cell hybrids even the human chromosomes may be eliminated; similar observations are available for carrot and parsley cell hybrids. When the genetic differences between the fused protoplasts is large, the fused cells may not divide or may not divide continuously. Somatic hybrids between related species may, however, behave like allopolyploids and form fertile or sterile hybrids after regeneration. Fusion of animal cells with bacterial spheroplasts is shown in Figure P157. ►cell fusion, ►polyethylene glycol

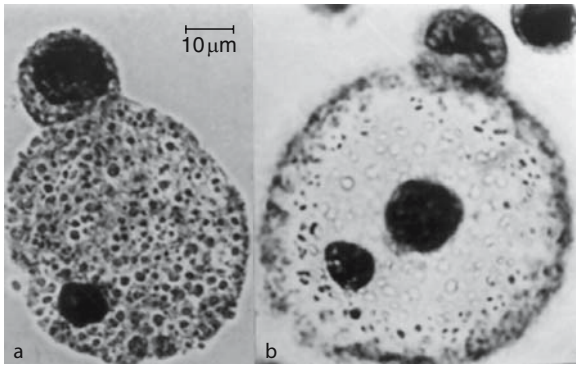

Figure P156. Human HeLa cells attached to tobacco protoplast (a), the HeLa nucleus (larger) inside the tobacco cell (b). (From Jones CW et al Science 193:401)

Protoporphyria, Erythropoietic: An autosomal (human chromosome 18q21.3) dominant (or recessive) disease involving light-sensitive itching, inflammation of the skin. The porphyrin level of the blood may increase by over 16-fold, to 1 g/100 mL. The excess protoporphyrin is deposited in the liver, causing potentially serious damage. The basic defect probably involves a deficiency (10 to 25%) of the mitochondrially located ferrochelatase (FECH). ►light-sensitivity defects, ►mitochondrial disease in humans, ►porphyria; Todd DJ 1994 Brit J Derm 131:751.

Protoporphyrin: The organic part of heme consisting of four pyrroles joined by methylene bridges. ►heme

Protosilencer: On its own, it is incapable of silencing gene(s) or its silencing effect is minimal but it can reinforce and maintain the function of silencers. ►silencers

Protosplice Site: Evolutionarily, the original splice site which is frequently AAG/CAG|GT where | is the insertion site. ►splicing

Protostome: Organisms that develop the mouth from the blastopore such as annelids, molluscs, arthropods. ►blastopore

Prototroph: A genotype that has wild type nutritional requirement. ►autotroph, ►auxotroph

Protozoa: Unicellular animals, mainly free-living (such as the *Paramecia*) some are, however, parasitic

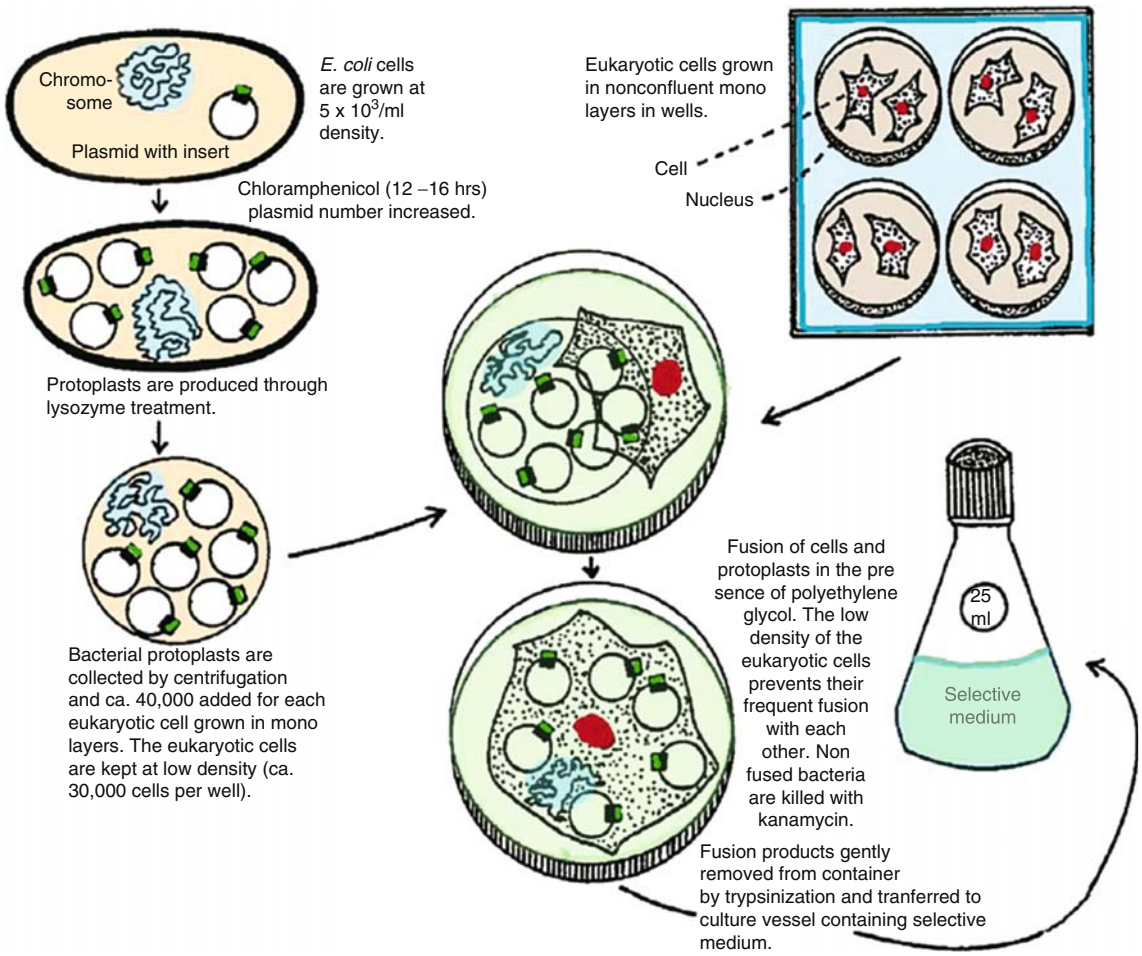

Figure P157. Transformation of mammalian cells by fusion to bacterial spheroplasts. (Modified after Sandri-Goldin, RM et al 1983 Methods Enzymol 101:402)

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(such as the *Giardias* which frequently contaminate drinking water sources), the *Trypanosomas* and *Leishmanias* which cause potentially lethal infections in animals and humans. ►*Trypanosoma*, ►*Leischmania*; for the genetic nomenclature of *Tetrahymena* and *Paramecia* see Genetics 149:459; micro- and macronuclear genes: http://oxytricha.princeton.edu/dimorphism/database.htm.

Provenance/Provenience: The origin of a genetic stock. ►accession

Provirus: A DNA sequence in the eukaryotic chromosomal DNA that is a reverse transcriptase product of a retroviral RNA. ►retroviruses, ►reverse transcription, ►prophage

Proximal: Situated in the vicinity of a reference point; e.g., a gene near the centromere is proximal, versus another that is in the direction of the telomere, and thus called distal. In conjugational transfer of bacteria the marker that is transferred before another is the proximal. ►centromere, ►telomere, ►conjugation mapping

Proximal Mutagen: A chemical that has been activated into a mutagenic substance; it may not have reached yet its most reactive state. ►promutagen, ►activation of mutagens, ►ultimate mutagen, ►chemical mutagens, ►activation of mutagens

Proximity Ligation: A protein analysis technique using specific DNA sequences, which bind specific proteins. Sensitivity is much enhanced when polyclonal or monoclonal antibodies are used in connection with oligonucleotide extensions brought in the proximity of the target. ►antibody; Gullberg M et al 2004 Proc Natl Acad Sci USA 101:8420.

PRP: An RNA-splicing factor component of the U snRNP complex. ►splicing

PrP (protease resistant protein): ►prion

Prp73: A mammalian chaperon binding to the first 20 residues (S peptide) of ribonuclease A and stimulates the uptake of polypeptides by lysosomes. ►ribonuclease A, ►Hsp70, ►lysosome

Prp20p: The yeast homolog of RCC1. ►RCC

PrPres (PrP*): A partially protease resistant aggregate of PrP^{C} and PrP^{SC}. ►prion

PrP-SEN: The general name of the protease-sensitive prion protein. ►prion

PRR: Post-replication repair. ►DNA repair

PRR: Positive regulatory region. ►negative regulation, ►*Arabinose* operon

PRR: Pathogen recognition receptor.

PRTF: Pheromone receptor transcription factors, cooperating with GRM (general regulator mating factor) in the determination of mating type. ►pheromone, ►mating type determination in yeast, ►*Schizosaccharomyces pombe*; Tan S, Richmond TJ 1990 Cell 62:367.

Przewalsky Horse: The Mongolian wild horse but can be found (~1200) only in captivity, although its reintroduction into the wild in Mongolia and China is underway. All existing individuals have descended from the 13 animals captured about a century ago. Its chromosome number is 2n = 66 yet it makes viable hybrids with the domesticated species. ►horse

PSA (prostate-specific antigen): A M_r 33,000 kallikrein type protease glycoprotein (APS) encoded at human chromosome 19q13. High levels of this protein in the serum may be an indication of prostatic carcinoma. The level of PSA varies a great deal and it is high after ejaculation and may provide false positive indication of cancer. It may serve as a target for cancer gene therapy. The six-transmembrane epithelial antigen of the prostate (STEAP, 7p22.3) is also elevated in prostate cancer. Hepsin (transmembrane serine protease) and pim-1 (serine/threonine kinase) levels are strongly correlated with prostate cancer as detected by tissue microarray analysis. The prostate-specific membrane antigen (PSMA) is highly expressed in prostate cancer cells and in other solid tumors. It is a glutamate carboxypeptidase and cuts methotrexate and the neuropeptide *N*-acteyl-L-aspartyl-L-glutamate; its crystal structure may facilitate drug development (Davis MI et al 2005 Proc Natl Acad Sci USA 102:5981). ►prostate cancer, ►cancer gene therapy, ►tissue microarray; Berry MJ 2001 N Engl J Med 344:1373; Dhanasekara S et al 2001 Nature [Lond] 412:822.

PSD-95: A family of membrane associated guanyl kinases; they also anchor K^+ channels by their PDZ domains. ►ion channels, ►GTP

PSE: Proximal sequence element. ►Hogness box

PSE: Pale soft exudative meat is controlled in pigs by the *Halothane* gene.

Pseudoachondroplasia: A dominant human-chromosome 19p12-p13.1 gene mutation controlling the cartilage oligomeric matrix protein (COMP), and it is responsible for short stature (see Fig. P158). ►achondroplasia, ►multiple epiphyseal dysplasia, ►COMP; Hecht JT et al 1995 Nature Genet 10:325; Briggs MD, Chapman KL 2002 Hum Mut 19:465.

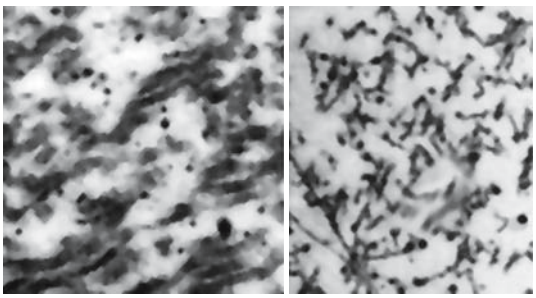

Figure P158. Left: Pseudoachondroplasiac, Right: Normal extracellular cartilage matrix

Pseudoaldostertonism (Liddle syndrome): A human chromosome 4 hypertension associated with hypoaldosteronism, hypokalemia, reduced renin and angiotensin. ►aldosteronism, ►hypokalemia, ►renin, ►angiotensin

Pseudoalleles: A cluster of not fully complementing genes, separable by recombination. Pseudoalleles, e.g., a^1 and a^2 when heterozygous in trans position $a^1\ a^+ //a^+\ a^2$ show mutant phenotype whereas in cis position $a^1\ a^2//a^+\ a^+$ are complementary (wild type), except when dominant alleles are involved. Since these alleles are closely linked, in order to be able to prove that recombination takes place (rather then mutation), the pseudoalleles must be genetically marked by flanking genes within preferably less than 10 m.u. apart of the locus. ►complex locus, ►step allelomorphism, ►morphogenesis in *Drosophila*, ►cis-trans test, ►SSNC; Carlson EA 1959 Quart Rev Biol 34:33.

Pseudoaneuploid: The chromosome number appears aneuploid but it is not truly the case only, centromere fusion or misdivision of the centromeres have caused the changes in numbers. ►Robertsonian translocation, ►misdivision, ►B chromosomes

Pseudoautosomal (PAR): Genes located in both telomeric regions of the X and Y chromosomes (~2.6 Mbp at the short arm [PAR1] and a similar PAR2 site in the long arm in the human genome) where recombination can take place and consequently, despite the sex-chromosomal location, sex-linkage is not obvious. A gene for schizophrenia was suggested to be pseudoautosomal. *SYBL1*, encoding a synaptobrevin-like protein is present in both X and Y chromosomal PAR regions and it displays lyonization in the X-chromosome and inactivation in the Y. The pseudoautosomal boundary is apparently spanned by one or another (depending on the species) 5′- or 3′-truncated gene. The short stature gene (SHOX1/SHOXY), the Leri-Weill dyschondrosteosis and a Hodgkin disease gene are all located in the PAR at Xpter-p22.32. The SHOX2 gene is at 3q25-q26.

All human and chicken homologues of the snake Z-linked genes were located on autosomes, suggesting that the sex chromosomes of snakes, mammals, and birds were all derived from different autosomal pairs of the common ancestor (Matsubara K et al 2006 Proc Natl Acad Sci USA 103:18190). ►autosome, ►sex determinations, ►differential segment, ►holandric genes, ►syntagmin, ►lyonization, ►IL-9, ►Hodgkin disease, ►short syndrome; Ciccodicola A et al 2000 Hum Mol Genet 9:395; Cormier-Daire V et al 1999 Acta Paediatr 88 (Suppl):55.

Pseudobivalent: The chromosomes associated are not homologous. ►synapsis, ►ille-gitimate pairing

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Pseudoborder: DNA sequences in certain agrobacterial vectors or within the cloned foreign DNA and may cause deletions and rearrangements within the T-DNA inserts in the transgenic plants. ►T-DNA, ►transformation genetic

Pseudocentromeric: ►supernumerary marker chromosome

Pseudocholinesterase Deficiency (CH1, BCHE): A dominant (human chromosome 3q26.1-q26.2) breathing difficulty (apnea) after treated with the muscle relaxant suxa-methonium (succinylcholine chloride), a drug used for intubation, endoscopy, cesarean section, etc., as an adjuvant to anesthesia. Several allelic forms respond differently to drugs. Individuals with a defective enzyme may be particularly sensitive to cholinesterase inhibitor insecticides (parathion). The frequency of the gene varies a great deal in different populations. In Eskimos, the frequency of the gene controlling the deficiency may be higher than 0.1; in other populations it may be less than 0.0002. The BCHE2 form was assigned to 2q33-35 and the same enzyme was suggested to 16p11-q23.

Pseudodiploidy: Retroviral particles because after infection only a single provirus is detected in the host. Normally retroviruses carry two RNA genomes associated by base pairing at several sites, particularly at the 5′end. It is assumed that the two copies are maintained for the purpose of assured survival and possible repair by recombination. They also contain tRNAs that prime replication. Other RNAs (5S, 7S and cellular mRNA fragments) may also be included. ►retroviruses

Pseudodominance: When a heterozygote loses the dominant allele, the recessive allele is uncovered (expressed) because of the lack of the dominant allele. Treating heterozygotes with mutagens (e.g., ionizing radiation) that cause deletions can readily induce pseudodominance. Before such experiments are conducted, it is advisable to place flanking genetic markers to the chromosome carrying the recessive markers to be able to rule out recombination and reversions. Segregation after somatic recombination may be a common cause of pseudo-dominance. Loss of heterozygosity is a frequent cause of oncogenic transformation. Pseudodominance-like phenomenon occurs in a population when the mating is between some cryptic heterozygotes. ►deletion, ►LOH, ►segregation, ►oncogenic transformation, ►mitotic crossing over

Pseudoextinction: The disappearance of a species by evolution into another form.

Pseudogamy: Apomictic or parthenogenetic reproduction. ►apomixia, ►parthenogenesis

Pseudogene: Has substantial homology with (clustered) functional genes of eukaryotes but it is inactive because of numerous mutations that prevent its full expression and may no longer available for transcription. Some pseudogenes are transcribed but the transcript is degraded by nonsense-mediated mRNA decay (Mitrovich QM, Anderson P 2005 Current Biol 15:963). Of the 201 pseudogenes identified by the 2007 ENCODE project, 20% were found to be transcribed (Zheng D et al 2007 Genome Res 17:839). Although pseudogenes may not have a protein product they may regulate the expression of their normal homolog either by stabilizing the normal transcript by blocking an RNase or by competitively inhibiting a transcriptional repressor (Hirotsune S et al 2003 Nature [Lond] 423:91). The number of pseudogenes is variable in different species. The human genome may contain 20,000 pseudogenes. Organisms with small genomes (e.g., *Drosophila*) have very few and it appears that some organisms eliminated from their genome the DNA sequences that are no longer functional. Pseudogenes may make difficult the estimation of the number of

genes on the basis of incomplete sequences and lack of functional information. Pseudogenes originated either from duplication or in case of processed pseudogenes (without intron) by reverse transcription. Their nucleotide sequence is rather well conserved indicating functional significance. Paired-end diTAG (PET) analysis may permit their detection (Ruan Y et al 2007 Genome Res 17:828). ►C-value paradox, ►gene relic, ►processed pseudogene, ►duplications, ►mRNA surveillance, ►paired-end diTAG; Harrison PM et al 2001 Nucleic Acids Res 29:818; Avise JC 2001 Science 294:86; Echols N et al 2002 Nucleic Acids Res 30:2515; Balakirev ES, Ayala FJ 2003 Annu Rev Genet 37:123; human pseudogenes-gene conversion targets: http://genome.uiowa.edu/pseudogenes/.

Pseudohairpin: The overall structure is folded back yet there is not full complementarity along the strands (see Fig. P159).

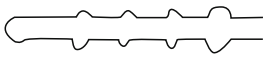


Figure P159. Pseudohairpin

Pseudohemophilia: A bleeding disease, distinct from hemophilia; it is caused by some abnormalities of the platelets. ►hemophilia, ►platelet anomalies, ►hemostasis

Pseudohermaphroditism: ►hermaphrodite

Pseudohermaphroditism, Male: It is determined by a gene in human chromosome 17q12-q21. It is responsible for the deficiency of 17-ketosteroid reductase/17-β-hydroxysteroid dehydrogenase and consequently for feminization in prepubertal males and gynecomastia and virilization after puberty when usually the enzyme is expressed. The affected individuals may be surgically assisted to develop into sterile female phenotype (by removal of the hidden testes) or into male phenotype by reconfiguration of the external male genitalia. Infertility, however, cannot be corrected,. Recessive mutations in the luteinizig hormone receptor gene (LHB, 19q13.32) may also be responsible. The condition may be due to deficiency of steroid 5-α-reductase (SRD5A2, 2p23). The SRDA1 isozyme encoded at 5p15 does not appear to be involved in this disorder. The afflicted XY individuals may have blind vagina and a rudimentary hypospadiac penis but no gynecomastia. They may produce viable sperm although they may sire offspring only by intrauterine insemination because of underdeveloped prostate and seminal vesicles. Several defects in steroid biosynthesis may cause male pseudohermaphroditism. The 17,20 desmolase deficiency is most likely X-chromosome linked. Lipoid adrenal hyperplasia (8p11.2) responsible for complex defects in cortisol or aldosterone may cause even life-threatening conditions. Luteinizing hormone/choriogonadotropin receptor (LHCCGR, 2p21) may cause abnormalities of the Leydig cell differentiation in XY and possibly in XX individuals. Methemoglobinemia and deficiency of cytochrome b5 (18q23) may also cause pseudohermaphroditism. ►gynecomastia, ►polycystic ovarian cancer, ►hermaphroditism, ►infertility, ►testicular feminization, ►luteinization, ►Müllerian ducts, ►anti-Müllerian hormone, ►Reifenstein syndrome, ►hypospadias, ►Wilms tumor, ►adrenal hyperplasia, ►adrenal hypoplasia, ►androgen-insensivity, ►methemoglobin, ►cytochromes

Pseudohitchhiking: Adaptive mutations near neutral loci may simulate genetic drift. ►hitchhiking

Pseudohomothallism: In the fungus (e.g., *Podospora anserina*) binucleate ascospores are formed and each spore contains both mating types and is thus self-fertile. ►homothallism, ►heterothallism

Pseudo-Hurler Syndrome: ►mucolipidosis

Pseudohypha (in *Saccharomyces cerevisiae*): The formation occurs by deficiency of nutrient (N) and may cause polarized growth on the surface of the agar medium favoring delay in mitosis and precocious entry into meiosis. The pseudohyphal growth is symmetric and synchronous in comparison to the regular budding that is asymmetric and asynchronous. Cyclins 1 and 2 promote pseudohyphal growth whereas cyclin 3 is inhibitory in yeast. Alternative controls exist. Protein Ste12, the MAP kinase signal transduction pathways also regulate hyphal growth. Filamentous growth is a requisite for pathogenicity of *Ustilago maydis* and *Candida albicans*. ►cyclin, ►CDK, ►*Ustilago maydis*, ►candidiasis, ►MAP, ►Ste

Pseudohypoaldosteronism (PHA; 1q31-q42, 17p11-q21, 12p13, 16p13-p12): hyperkalemic, hyperchloremic acidosis and hypertension. The genes at chromosomes 17 and 1 encode a threonine/serine kinase, WNK4, localized in the tight junctions. The disease in this protein is due to missense mutations. Mutations in WNK4 in mice cause higher blood pressure, hyperkalemia, hypercalciuria and marked hyperplasia of the distal convoluted tubule (DCT). WNT4 (chromosome 17) regulates the balance between NaCl reabsorption and K^+ secretion (Lalioti MD et al 2006 Nature Genet 38:1124) by altering the mass and function of the DCT through its effect on NCC (Na/Cl co-transporter). In chromosome 12 the cytoplasmic WNK1 is encoded and the defect is due to large intronic deletions that boost the expression of the protein. Both of these proteins are in the distal

nephron (a basic morphological and functional unit of the kidney) that is responsible for potassium and pH homeostasis. These two anomalies are dominant. The recessive PHA in chromosome 16 encodes subunits of an epithelial Na^+ ion channel. ►aldosteronism, ►Gordon syndrome, ►hypoaldosteronism, ►hyperkalemic, ►hypertension, ►intron, ►ion channels; Wilson FH et al 2001 Science 293:1107.

Pseudohypoparathyroidism: ►Albright hereditary osteodystrophy

Pseudoknot: Formed when a stem-and-loop RNA structure is bound at the base of the loop by hydrogen bonds or by a ligand resulting in a two-stem two-loop stacking (see Fig. P160). The actual configurations of the pseudoknots may vary. Pseudo-half-knots form only a single loop. Such structures may modulate RNA functions and can be exploited also in designing highly selective drugs. Some insect RNA viruses, which use CAA (glutamine) rather than AUG (methionine) for translation initiation do not require an initiator tRNA but apparently rely on a pseudoknot formed between a 15–43 nucleotide upstream loop and the sequence immediately preceding the CAA codon. Pseudoknot structure is highly conserved in telomerases. Mutations that disrupt the pseudoknot helix abolished telomerase activity whereas intraloop hairpin base-pairing did not reduce telomerase activity (Chen J-L, Greider CW 2005 Proc Natl Acad Sci USA 102:8080). Pseudoknots initiate translational frameshifting in overlapping genes. The Pseudoknot Local Motif Model and Dynamic Partner Sequence Stacking (PLMM_DPSS) algorithm, which predicts all PLM model pseudoknots within an RNA sequence in a neighboring-region-interference-free fashion. The PLM model is derived from the existing Pseudobase (collection of pseudoknots) entries and it is most sensitive. The innovative DPSS approach calculates the optimally lowest stacking energy between two partner sequences (Huang X, Ali H 2007 Nucleic Acids Res 35:656). ►repeat inverted, ►antisense RNA, ►overlapping genes, ►TFO, ►telomerase, ►frameshifting ribosomal; Kim Y-G et al 1999 Proc Natl Acad Sci USA 96:14234; Xayaphoummine A et al 2003 Proc Natl Acad Sci USA 100:15310; pseudoknot folding: http://bibiserv.techfak.uni-bielefeld.de/pknotsrg/.

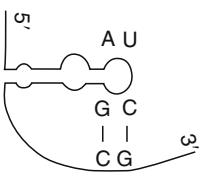


Figure P160. Pseudoknot

Pseudolinkage: The linkage due to translocation between non-homologous chromosomes. ►affinity

Pseudolysogen: Lyses the bacterial cells so slowly as if it would be lysogenic. ►lysogeny

Pseudomonas: *Pseudomonas* bacteria include several species that degrade oil spills, polycyclic hydrocarbons, benzene and other pollutants. ►oil spills, ►biodegradation; Coates JD et al 2001 Nature [Lond] 411:1039.

Pseudomonas aeruginosa: A 6.3 million-bp bacterium and an opportunistic human parasite. It is the most common cause of death in cystic fibrosis but it is involved in some pneumonias and other infections (urinary tract, burn victims, etc.). It grows also on soil and plant and animal tissues. This Gram-negative bacterium is highly resistant to antibiotics and disinfectants. Close to 10% of its genes is regulatory and the large number of its putative pump proteins explains its resistance to drugs. ►cystic fibrosis; Stover CK 2000 Nature [Lond] 407:959; genome, annotations: http://www.pseudomonas.com; http://www.systomonas.de.

Pseudomonas Exotoxin: Kills by irreversible ribosylation of ADP and subsequent inactivation of translation elongation factor, EF-2. Its applied significance is the potential for cancer therapy. ►toxins

Pseudomonas syringae: A plant pathogenic relative of *P. aeruginosa*. The 6.5 megabase sequenced genome includes a circular chromosome plus two plasmids including 5763 open reading frames of which 298 are putative virulence genes. This bacterium may promote secondary infection by the same pathogen rather than display a hypersensitive response in the host by a jasmonic acid structural mimic (coronatine). It can increase susceptibility also to herbivorous insects without relying on coronatine (Cui J et al 2005 Proc Natl Acad Sci USA 102:1791). Related *Pseudomonas* subspecies, distinguished by host-specificity, display differences in genes of antibiotic resistance, DNA repair and ectoin ([4S]-2-methyl-1,4,5,6-tetrahydropyrimidine-4-carboxylacid), a natural protective agent against external harmful effects (Feil H et al 2005 Proc Natl Acad Sci USA 102: 11064). ►ORF, ►host–pathogen relation; Buell CR et al 2003 Proc Nat Acad Sci USA 100:10181.

Pseudomonas tabaci: A bacteria causing "wildfire" disease (necrotic spots) on tobacco leaves (see Fig. P161). The symptoms may be mimicked by methionine sulfoximine, a methionine analog.

Figure P161. Wildfire disease spots (Courtesy of Dr. Peter. Carlson)

Pseudomosaic: May occur in a sample of amniocentesis caused by the conditions of culture rather than the genetic/chromosomal condition of the fetus.

Pseudo-Overdominance: Certain phenotype(s) may appear in excess of expectation in a population because of the close linkage of the responsible gene to advantageous alleles. Also QTL loci may appear overdominant if they are relatively closely linked and display heterosis because the QTL mapping techniques cannot determine the map positions with great accuracy, and the molecular function of the genes involved is not known. ►overdominance, ►fitness, ►QTL, ►interval mapping, ►hitchhiking

Pseudopilus (Ψ-pilus): A bacterial appendage (~55 nm) that may extend beyond the cell surface into the periplasm and may be a conduit for macromolecular transport in bacteria. ►pilus, ►DNA uptake

Pseudoplasmodium: A migrating slug of cellular slime molds. ►*Dictyostelium*

Pseudopodium: ►amoeba

Pseudopregnant: Female (mice) mated with vasectomized males and then implanted with blastocyst stage embryos derived from other matings. ►vasectomy, ►allopheny

Pseudoqueen: In social insects (bees, ants, termites) one worker (XX) may become fertile pseudoqueen after the loss of the queen of the colony. This type of development is promoted by special feeding (royal treatment) of the originally worker caste insects. ►honey bee

Pseudorecombinant: Reassortement of two viral genome components from different viruses, transmitted by the same insect vector.

Pseudoreplication: The samples are not independent replicates and the conclusion based on them may not be statistically reliable.

Pseudoreversion: An apparent back mutation caused by an extra-site suppressor mutation. ►reversion

Pseudorheumatoid Dysplasia: A rare recessive cartilage defect due to mutation in the cysteine-rich secreted protein gene family (see Fig. P162). ►arthritis, ►rheumatic fever

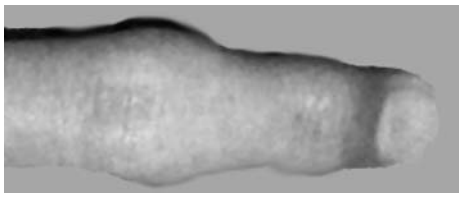


Figure P162. Swollen joints of a finger in pseudorheumatoid dysplasia

Pseudosubstrate: A molecule with similarity to an enzyme substrate but it is actually an inhibitor, and special regulators are required for its removal so the enzyme is permitted to access its true substrate. ►substrate, ►intrasteric regulation

Pseudotemperate Phage: It has a lysogenic cycle yet does not have a stable prophage state, e.g., the PBS1 transducing phage of *Bacillus subtilis*. ►lysogeny, ►prophage

Pseudotransduction: The virus is not integrated into the chromosome and the passenger DNA can be expressed only from the cytoplasm when the appropriate promoter is present in the vector.

Pseudo-Trisomic: It is actually disomic but one of the chromosomes is represented by two telocentric chromosomes, each represent one and the other arm of the same chromosome, thus two telocentrics + one normal chromosome occurs. ►trisomy, ►telocentric chromosome

Pseudotype: The virus carrying foreign protein on his envelope and may expand the normal host range.

Pseudotyping: If two types of viruses invade the same cell, genetic material of one may slip into the capsid of the other and this type of packaging permits the introduction of the viral genome into a host, which otherwise would be incompatible with the virion. This phenomenon may be taken advantage of also during the construction of viral vectors and helper viruses. The ability of a virus to infect a certain type of cell depends on the interaction between the viral glycoprotein and the nature of the cell surface receptors. The vesicular stomatitis virus viral envelope glycoprotein (VSV-G) is highly fusigenic for a wide range of cell types and organisms. Thus, it can be employed for pseudotyped viral vectors to expand their effective host range. The hemagglutinating

paromyxovirus of Japan (HVJ) and other viruses can also be used similarly. ►pseudovirus [pseudovirion], ►amphotropic, ►ecotropic, ►packaging cell lines, ►retroviral vectors; Mazarakis ND et al 2001 Hum Mol Genet 10:2109; Peng KV et al 2001 Gene Ther 8:1456.

Pseudouridine (ψ): A pyrimidine nucleoside (5-β-ribofuranosyluracil) occurs in the T arm of tRNA by post-transcriptional modification of a uracil residue. Pseudouridine has been also found in ribosomal RNAs and snRNAs. The modification is mediated by the nucleolar ψ synthase with the assistance of other proteins. A requisite for the process is that a small nucleolar RNA (snoRNA) carrying a single stranded H box (ANANNA) and a ACA-3′ Box would pair with the target RNA at about 12 or less region of complementarity. After the enzyme gained access to the U site, the N1—C1′ bond in a uracil is severed and after a 180° rotation the C5 position becomes available for the formation of a new bond. Thus the N1 and N3 sites may become readily available for hydrogen pairing and pseudouridine can bind easier in inter- or intramolecular reactions. Pseudouridine deficiency is not lethal in yeast yet it adversely affects growth. The crystal structure and function of the H/ACA ribonucleoprotein, a member of pseudouridine synthases, has been determined (Li L, Ye K 2006 Nature [Lond] 443:302). ►ψ for formula, ►tRNA, ►snoRNA; Bortolin M-L et al 1999 EMBO J 18:457; Hoang C, Ferré-D'Amaré AR 2001 Cell 107:929.

Pseudovirion (pseudovirus): Contains non-viral DNA within the viral capsid and can thus be used to unload foreign DNA into a cell if a helper virus is provided. ►virion, ►capsid; Liu Y et al 2001 Appl Microbiol Biotechnol 56:150; Ou WC et al 2001 J Med Virol 64:366.

Pseudowild Type: Displays wild phenotype because a mutation at a site different from the mutant locus that it masks, but most commonly a duplicated segment, compensates for the original and still present recessive mutation. In *Neurospora* it occurs at much higher frequency than expected by back mutation. It may also be due to a suppressor mutation. (See Mitchell MB et al 1952 Proc Natl Acad Sci USA 38:569).

Pseudoxanthoma Elasticum (PXE, 16p13.1): Autosomal recessive or dominant disorders of an ABCC6 (multiple drug resistance) transporter causing by degenerative changes in the skin (peau d'orange = orange rind), veins, eyes, intestines, etc., resulting in heart disease and hypertension. The defect involves dysplasia of elastin fibers and it affects the skin, retina, arteries, teeth, etc. ►coronary heart disease, ►hypertension, ►skin diseases, ►ABC transporters; Le Saux O et al 2001 Am J Hum Genet 69:749; problems of translation and advocacy of research models: Terry SF et al 2007 Nature Rev Genet 8:157.

Pseudo-Zellweger Syndrome: ►peroxisomal 3-oxoacyl-coenzyme A thiolase deficiency, ►Zellweger syndrome

PSI (ψ): Pseudouridine, and also the packaging signal in retrovirions. ►tRNA pseudouridine loop, ►retrovirus, ►retroviral vectors, pseudouridine formula on page at ►ψ

PSI$^+$: A yeast prion, an extrachromosomal protein suppressing nonsense codons. It functions in collaboration with the nuclear genes *SUP*35. Overexpression of this gene induces the formation of PSI$^+$ probably by a conformational change in the protein. Cells deleted in the amino-terminal region of Sup35 are resistant to PSI$^+$. Expansion of imperfect oligopeptide repeats in Sup35 (PQGGYQQYN) and in PrP (PHGGWGQ) seems to be responsible for the abnormality. Overexpression of Hsp104 heat shock protein cures the cells from PSI$^+$. ►prion, ►Hsp; Masison DC et al 2000 Curr Issues Mol Biol 2:51; Jensen MA et al 2001 Genetics 159:527.

Psi Vector: ►E vector

PSI-Blast: ►Blast

PsnDNA: 150–300 bp pachytene DNA sequences flanking 800–3000 bp internal chromosomal segments in eukaryotes, and the two short and the central DNA sequences are called PDNA (pachytene DNA). The PsnDNAs are supposed to be nicked by an endonuclease after homologous small nuclear RNA (snRNA) and a non-histone protein (PsnProtein) have opened the sequences to the action of the enzyme. These molecules appear only during late leptotene to pachytene and are assumed to be mediating recombination. ►crossing over, ►meiosis, ►snRNA, ►ZygDNA; Stern H, Hotta Y 1984 Symp Soc Exp Biol 38:161.

Psoralen Dye: Can combine with the DNA connecting nucleosomal core particles. After irradiation with near-ultraviolet light, cross-link between the two DNA strands occurs. Psoralen-conjugated triple helix forming oligonucleotides have been used to induce site-specific mutations in COS cells at very high frequency (see Fig. P163). Targeting psoralen cross-links with triple helix forming oligonucleotides can induce in base substitution and deletion mutations in mammalian cells. Deficiencies in non-homologous

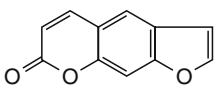


Figure P163. Psoralen

end-joining and mismatch repair did not influence the mutation pattern. In contrast, the frequency of base substitutions depended on ERCC1 and DNA polymerase ζ but it was independent of nucleotide excision repair and transcription-coupled repair genes (Richards S et al 2005 Nucleic Acids Res 33:5382). Some celery stocks may contain higher than normal amounts of psoralen. ►triple helix formation, ►site-specific mutation, ►COS cell, ►DNMA repair, ►DNA polymerases; Cimino GD et al 1985 Annu Rev Biochem 54:1151; Luo Z et al 1997 Proc Natl Acad Sci USA 97:9003; Oh DH et al 2001 Proc Natl Acad Sci USA 98:11271.

Psoriasis (PSOR): A scaly proliferation of keratinocytes, a type of autoimmune skin defect determined either by dominant gene(s) of reduced penetrance or polygenic inheritance involving relatively few genes. Its incidence is common in Caucasian populations (1–3%) but it is much less frequent in Orientals (Eskimos, American Indians and Japanese) and it was almost absent in Africa. Recurrence rate may vary (8–23% among first-degree relatives), depending on the type involved. If both parents are affected the recurrence among children may reach up to 75%. Concordance among monozygotic twins is 35% to 72% and only 12% to 23% in fraternal twins (Duffy DL et al 1993 J Am Acad Dermatol 29:428. The psoriasis haplotype appears to include HLA-BW 17, HLA-C and HLA-A 13 genes. Some observations indicate that bacterial superantigens may trigger psoriasis. Psoriasis-like skin disease and arthritis may be caused by epidermal deletion of Jun proteins in mice (Zenz R et al 2005 Nature [Lond] 437:369). Psoriasis susceptibility genes have been assigned to 16q, 10q, 19p13.3, 3q21, 1q21, 17q25, 4qter, 14q31-q32, 6p21 and 20p. Runx transcription factors may stimulate it. AP1/4/08 and AIRE may cause loss of self-tolerance (Nature Genet 17:399 [1997]). Linkage with other chromosomes is less certain. Psoriasis increases the risk of basal cell carcinoma. Microarray analysis revealed upregulation of transcription of at least 161 genes in psoriasis. Some the transcripts are modulated also in other skin diseases. ►HLA, ►keratosis, ►ichthyosis, ►skin diseases, ►nevoid basal cell carcinoma, ►Hirschsprung disease, ►dermatitis atopic, ►IL-20, ►APEBEC, ►AIRE, ►Runx, ►autoimmune disease, ►Jun; Bhalerao J, Bowcock AM 1998 Hum Mol Gen 7:1537; Bowcock AM et al 2001 Hum Mol Genet 10:1793; Int Psoriasis Genet Consortium 2003 Am J Hum Genet 73:430; review: Schön MP et al 2005 N Engl J Med 352:1899; Bowcock AM 2005 Annu Rev Hum Genet 6:93; review: Lowes MA et al 2007 Nature [Lond] 445:866.

P{Switch}: ►Gene-Switch, ►hybrid dysgenesis

Psychiatric Disorder: ►psychoses

Psychomimetic: Drugs affect the state of mind in a manner similar to psychoses. ►psychoses, ►psychotropic drugs, ►ergot

Psychoses: A group of mental-nervous disorders with variable genetic and environmental components. ►autism, ►manic depression, ►schizophrenia, ►paranoia, ►affective disorders, ►attention deficit hyperactivity, ►Tourette's syndrome, ►IQ, ►dyslexia, ►panic disorder, ►bipolar mood disorder

Psychopathology: The manifestation of a neuronal disease involved in mental and behavioral illness.

Psychotherapy: The treatment/support provided for transient or lasting emotional and behavioral disorders. It may involve verbal support or chemical medication. Genetic counselors need familiarity with the verbal support option. ►counseling genetic

Psychotropic Drugs: These affect the state of mind. They are used as medicine in various types of psychoses and may be very beneficial (e.g., lithium, valium, etc.) if applied under medical monitoring. Possible adverse side effects vary by the chemical nature of the drug and may include heart disease, birth defects, addiction, etc. ►psychoses, ►psychomimetic

Psychrophiles: Organisms that grow under low temperatures. ►antifreeze proteins

PTA Deficiency Disease: Controlled by incompletely dominant (4q35) genes. Plasma thromboplastic antecedent protein deficiency is involved that results in unexpected bleeding after tooth extraction or various surgeries. Nose bleeding (epistaxis) is common but uterine bleeding (menorrhagia) or blood in the urine (hematuria) is rare. The carrier frequency in Ashkenazy Jewish populations is about 8.1%. ►antihemophilia factors, ►pseudohemophilia

PTB (phosphotyrosine-binding domain): PTB is present in proteins involved in signaling. ►SH2, ►SH3, ►WW, ►SCK, ►pleckstrin, ►signal transduction

PTB (polypyrimidine tract binding protein, 58 kDa): Involved in regulation of eukaryotic mRNA metabolism, regulation of splicing, IRES-mediated translation initiation and mRNA stability. ►splicing, ►IRES, ►translation; Oberstrass FC et al 2005 Science 309:2054.

PTC: ►phenylthiocarbamide; also papillary thyroid carcinoma; a variant of the RET oncogene caused neoplasia. ►RET

PtdInsP$_2$: ►phosphoinositides

PTEN (phosphatase and tensin homolog; deleted in chromosome 10 [10ter-q11, 10q24-q26, 10q22-q23],

syn. MMAC1 [mutated in multiple advanced cancer]): A tumor suppressor involved in brain, prostate, breast, multiple hamartomas (Lhermitte-Duclos disease/Cowden syndrome), Bannayan-Zonona syndrome and other cancers. It inhibits cell migration and cell adhesion and dephosphorylates FAK, serine, threonine and tyrosine residues in proteins. The primary target of PTEN appears to be phosphatidylinositol-3,4,5 trisphosphate (PIP3) and acts as tumor suppressor by promoting apoptosis. PTEN and p53 mutually promote each other in tumor suppression (Chen Z et al 2005 Nature [Lond] 436:725). In vivo, PTEN may act as a lipid phosphatase and this function may be essential for tumor suppression. PTEN appears to guard centromere-kinetochore integrity and chromosomal stability (Shen WH et al 2007 Cell 128:157). The protein (tyrosine, serine/threonine) phosphatase activity may not be important for tumor suppression. Some cancer cells (glioma, prostate, breast cancer) may be reverted to normalcy by the addition of PTEN. The PTEN-Akt pathway probably governs stem cell activation by helping control nuclear localization of the Wnt pathway effector β-catenin. Akt phosphorylates β-catenin at Ser552, resulting in a nuclear-localized form in intestinal stem cells (ISC). Our observations show that intestinal polyposis is initiated by PTEN-deficient ISCs that undergo excessive proliferation driven by Akt activation and nuclear localization of β-catenin (He XC et al 2007 Nature Genet 39:189).

The catalytic domain identity motif is HCXXGXXRS/T. The two α-helix domains flanking the catalytic domain are encoded in its exon 5, and must be intact for proper function. The tensin-homology domain enables the recognition of the cell adhesion system (actin, integrin, FAK, Src). In mouse the *Pten*$^{+/-}$ heterozygotes are subject to autoimmune disease and FAS-mediated apoptosis. The normal FAS function can be restored by the administration of phosphatidyl inositol 3 kinase. PTEN has an influence on cyclin D1 and signal transduction. Mutations in PTEN may be found in Proteus syndrome or Proteus-like syndrome. Experimental deletion of *Pten* (by using seven doses of polyinosine-polycytidine in *Mx-1 Cre* mice) initiated leukemia cancer stem cell as well as hematopoietic stem cell proliferation. Without *Pten*, the hematopoietic stem cells were depleted by time in a cell autonomous manner. In contrast, the leukemia stem cells became transplantable and progressed to leukemia within 4–6 weeks. Rapamycin, which targets TOR, however, depletes leukemia stem cells and rescues *Pten*-deficient hematopoietic stem cells. Thus the two types of stem cells can be distinguished (Yilmaz ÖH et al 2006 Nature [Lond] 441:475; Zhang J et al 2006 Nature [Lond] 441:518). ►tumor suppressor, ►tensin, ►FAK, ►multiple hamartomas syndrome, ►Bannayan-Zonona syndrome, ►polyposis juvenile, ►AKT, ►catenins, ►*Wingless*, ►phosphat-idylinositol, ►prostate cancer, ►PIP2, ►PIP3, ►PIK, ►TOR, ►rapamycin, ►hematopoiesis, ►stem cell, ►chemotaxis, ►apoptosis, ►wound healing, ►Parkinson disease, ►Proteus syndrome, ►NEDD; Di Cristofano A, Pandolfi PP 2000 Cell 100:387; Wen S et al 2001 Proc Natl Acad Sci USA 98:4622; Maehama T et al 2001 Annu Rev Biochem 70:247; Waite KA, Eng C 2002 Am J Hum Genet 70:829; Zhou X-P et al 2003 Am J Hum Genet 73:404.

Pteridines: Purine derivatives, involved in coloring of insect eyes, wings, amphibian skin, etc. Pteridines may be light receptors. Reduction in tetrahydrobiopterin and related amines may be responsible for nervous disorders (see Fig. P164). ►photoreceptors, ►rhodopsin, ►ommochromes, ►GTP cyclohydrolase deficiency; Blau N et al 1998 J Inherit Metab Dis 21:433.

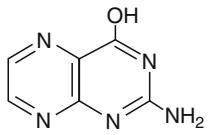


Figure P164. Pterine

Pterygium, Multiple, Syndrome (Escobar syndrome, 2q33-q34): The webbing of the neck and depressed areas (fossae) under the elbow, and other joints and hypogonadism in males, small labia and clitoris in females and other anomalies. ►hypogonadism, ►clitoris, ►Popliteal pterygium

PTG (protein targeting glycogen): Forms complexes of phosphatases, kinases and glycogen synthase with glycogen. ►glycogen, ►kinase

PTGS: Post-transcriptional gene silencing presumably by degradation of the mRNA or inactivation of infectious (viral) RNA. Recent evidence indicates the presence of a 25-nucleotide long antisense RNA in the silenced cells. ►RNAi, ►RIGS, ►methylation of DNA, ►epigenesis, ►post-transcriptional gene silencing, ►RNA surveillance

Ptilinum: An inflatable head of the larva emerging from the puparium that cyclically is inflated/deflated to pry open the puparium by a wedging type of operation.

PTIP (PAX transactivation interacting domain protein): Contains tandem BRCA1 carboxy terminal domains (BRCT) and it is responsible for phosphorylation-dependent protein binding a condition required for DNA repair. The Met^{1775} →Arg mutation in the BRCA1 (breast cancer) gene product fails to bind phosphopeptides and increases the susceptibility to

cancer. ►PAX, ►breast cancer; Manke IA et al 2003 Science 3002:636.

PTK: Protein-tyrosine kinase involved in regulation of signal transduction and in growth and differentiation of cells. ►protein kinases

Ptosis: Drooping eyelid(s). ►epicanthus, ►blepharophimosis

PTP: ►tyrosine phosphatase, ►protein-tyrosine phosphatase non-receptor

PTPCR (PicoTiterPlate PCR): A DNA amplification procedure on an extremely small platform in pL quantities. Subsequently the products can be transferred to solid support and transcription, translation or sequencing can be carried out (Leamon JH et al 2004 Electrophoresis 25:1176). ►amplification, ►polymerase chain reaction, ►measurement units

PTPN (protein tyrosine phosphatase non-receptor type, PTPN22, 1p13): Associated with autoimmune diseases (diabetes I, rheumatoid arthritis, lupus, Graves thyroiditis, Addison disease, etc.). In case of a gain-of-function mutation the T cell produce lower amounts of interleukin-2 when stimulated the T cell receptors (TCR) and the phosphatase negatively regulates activation of T lymphocytes. (See Vang T et al 2005 Nature Genet 37:1317).

PTPRC: Protein tyrosine phosphatase receptor type C.

pu (particle units): Used for quantifying the number of potentially infectious virus particles per volume. It is a newer alternative for the *pfu* units but it is supposed to be employed for highly purified preparations. The particle count is determined from the absorbance at 260 nm according to the formula that 1 unit at $A_{260} = 1.25 \times 10^{12}$ particles/mL. Generally, it corresponds to 10–100 times of the *pfu* titer. ►pfu

PU.1 (PU1): A transcription factor in blood-forming cells regulating the differentiation of macrophages, B lymphocytes and monocytes; it belongs to the ETS family of oncogenes. Deletion of an upstream regulatory element (URE) leads to acute myeloid leukemia (Rosenbauer F et al 2006 Nat Genet 38:27). ►ETS, ►monocytes, ►macrophages, ►lymphocytes, ►leukemia, ►transcriptional priming; Dekoter RP, Singh H 2000 Science 288:1439; Lewis RT et al 2001 J Biol Chem 276:9550.

PubChem: Biological activities of small molecules database: http://pubchem.ncbi.nlm.nih.gov/.

Puberty: The time of sexual maturation, accompanied by the appearance of secondary sexual characteristics such as facial hair in males, enlargement of the breast in females, etc. Puberty is initiated by the secretion of gonadotropin releasing hormone by the brain that activates the release of the pituitary hormones required for gonadal functions. It is facilitated by the KiSS-1 peptide and its receptor, GPR54 (Kaiser UB, Kuohung W 2005 Endocrine 26:277). ►gonadotropin, ►pituitary, ►gonads

Puberty Precocious: Autosomal dominant disorders occur in two forms: isosexual, when sexual maturation in both males and females takes place before age 10 and 8.5, respectively but may be even much earlier, especially in females. Another form is male-limited. Testosterone production seems to be independent from gonadotropin releasing hormone production. The disorder is associated with a defect in the luteinizing hormone receptor. ►luteinizing hormone-releasing factor, ►animal hormones, ►hormonal effects on sex expression, ►G-proteins

PubGene: A human gene-to-gene co-citation index involving 13,712 named human genes. (See Jenssen T-K et al 2001 Nature Genet 28:21).

Public Blood Systems: ►private blood groups

Public Opinion: In the underdeveloped world with inadequate educational systems, superstitions greatly affect people's view on all aspects of life and society. In the culturally and technically advanced nations the newspapers, television and Internet resources may influence public opinion to a great degree. Application of scientific principles is commonly decided by plebiscites or by legislative action. In a democratic society the citizens' view must necessarily be considered. The dilemma of how well informed is the general public or the legislative/governmental system regarding the implications of scientific principles is an important problem. In a survey in England the public indicated that automobiles are safer than trains. The actual statistics indicated, however, that the safety of trains is about 100 times better. People generally believe that atomic power plants expose the public to unnecessary health and genetic risks. The hazards burning fossil fuels or using wood fireplaces are much less frequently considered although they generate carcinogenic and mutagenic emissions. Very often even the scientists are unable to predict the future consequences of the scientific achievements they brought about as it was apparent by the consensus reached on recombinant DNA by the historical Asilomar Conference. The problems of using genetically modified organisms, cloning, stem cell applications cannot be resolved by political approaches. The problems created by technology and science can be resolved only by better scientific research. ►gene therapy, ►stem cells, ►GMO, ►recombinant DNA and biohazards, ►atomic radiations, ►informed consent, ►criticism on genetics

Publication Ethics: Subject to the same common sense rules as any other principle of ethics. The detailed guidelines in Human Reproduction 2001, vol 16:1783–1788 contain specific, valid points. Fabricated data in publications have serious effect on scientific research conducted in other laboratories unaware of the misconduct but faked reports are even more critical and dangerous when they influence clinical practice and may endanger life of patients (Unger K, Couzin J 2006 Science 312:38). ►ethics, ►misconduct scientific

PubMed Central: A digital archive of peer-reviewed journals containing >300,000 full text articles. Can be entered through Entrez. ►Entrez

PUBS: Percutaneous (through the skin) umbilical blood sampling, a method of prenatal biopsy for the identification of hereditary blood, cytological and other anomalies. ►amniocentesis, ►prenatal diagnosis

pUC Vectors: Small (*pUC12/13* 1680 bp, *pUC18/19* 2686 bp) plasmids containing the replicational origin (*ori*) and the Amp^r gene of pBR322, and they carry the *LacZ′* fragment of the bacterial β-galactosidase (see Fig. P165). The *Z′* indicates that within this region there is multiple cloning site (MCS) for recognition by 13 restriction enzymes. The orientation of the MCS is in reverse in pUC18 relative to pUC19. Genes inserted into *Lac* may be expressed under the control of the *Lac* promoter as a fusion protein. Most commonly, the insertion inactivates the *Lac* gene and white colonies are formed in Xgal medium rather than blue when the gene is active. The pUC vectors can be used with JM105 and NM522 *E. coli* strains. ►vectors, ►*Xgal*, ►*Lac*, ►filamentous phages; Messing J 1996 Mol Biotechnol 5:39.

Puccinia graminis: ►stem rust

PUF Proteins: They control mRNA stability by binding to the 3′-untranslated end. (Wickens M et al 2002 Trends Genet 18:150).

Puff: The swollen area of polytenic chromosomes active in transcription. Puffing is induced by expression of transcription factor genes regulated by steroid hormones (ecdysone).

Ecdysone formation comes in sequential pulses and thereby sequential activation of genes involved in metamorphosis of insects can be visualized at the level of the giant chromosomes. The puffs represent active transcription at particular genes, and the pattern of puffing shifts along the salivary gland chromosomes during development (see Fig. P166) and/or activation and the RNA extracted from the puffs reflect the differences in the base sequences of the genic DNA. Puffing has been described also in the rare polytenic chromosomes of some plant species, e.g., *Allium ursinum* or *Aconitum ranunculifolium*. These have been observed in specialized tissues of the chalaza or in the antipodal cells. ►giant chromosomes, ►ecdysone, ►PARP; Beermann W 1961 Verh Dtsch Zool Ges 1961:44; Mok EH et al 2001 Chromosoma 110:186.

Pufferfish, Japanese (*Fugu rubripes, Tetraodontidae*): A small vertebrate with about 365 Mbp DNA, i.e., only somewhat more than 1/10 of that of most mammals, and therefore it is suitable for structural and functional studies at the molecular level (see

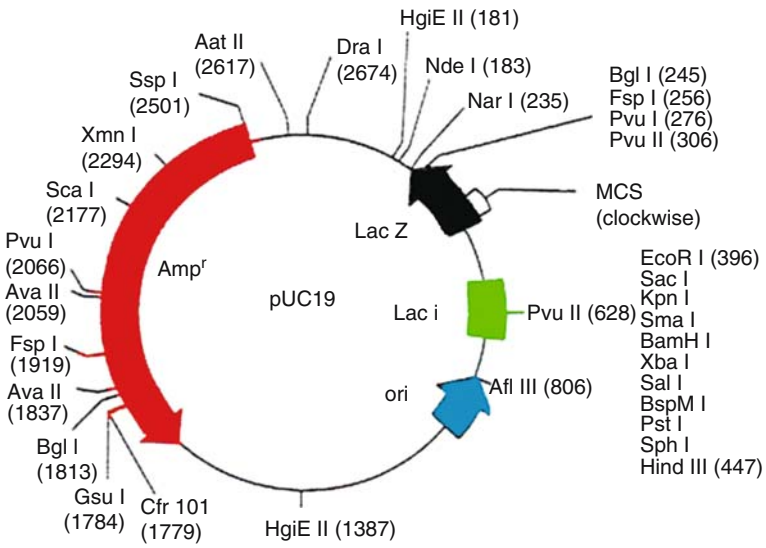


Figure P165. pUC_{19} (The diagram is the courtesy of CLONTECH Laboratories Inc., Palo Alto, CA.)

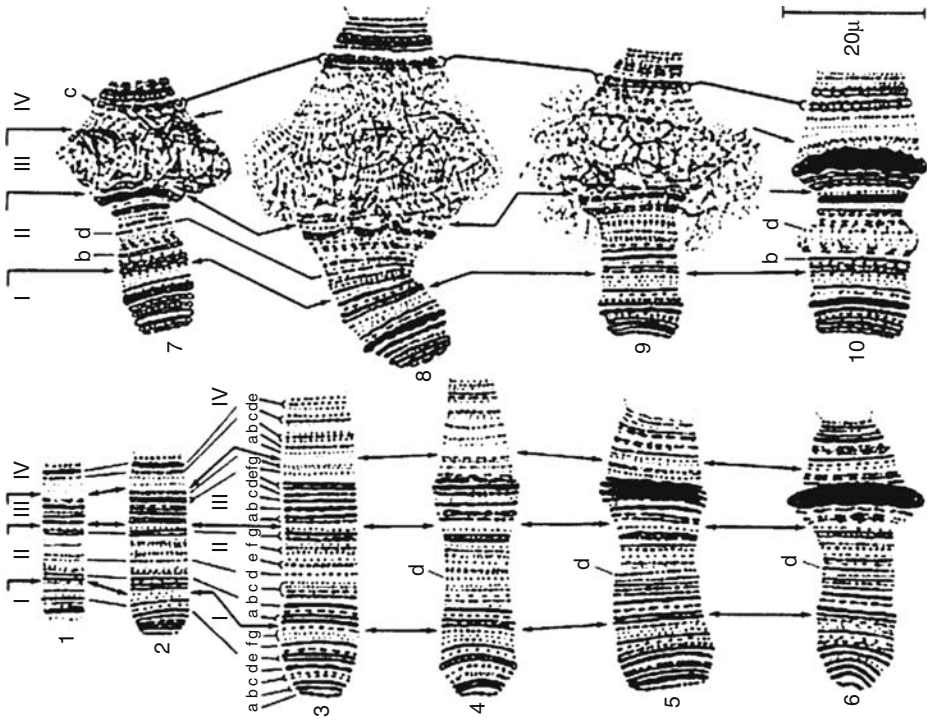


Figure P166. Selective activity of genes during development of the Dipteran fly *Rhynchosciara angelae* is reflected in the puffing pattern of the salivary gland chromosomes. Lower case letters designate bands. Roman numerals indicate regions of the chromosomes. (After Breuer M E, Pavan C 1954. By permission from Kühn A 1971 Lectures on Developmental Physiology, Springer-Verlag, New York)

Figure P167. Takifugu rubripes (courtesy of Wikipedia; author Chris 73)

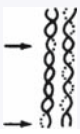
Fig. P167). More than 95% of the genome has been sequenced by 2002. About one-third of the genome is genic and repetitive sequences occupy less than one-sixth. The species, *Spheroides nephelus* is also used for studies of control of gene expression. *Tetraodon nigroviridis* (n = 21) DNA (27,918 genes) sequences have been used for the determination of human gene number. About 14,500 human ecores are conserved also in this pufferfish species ►ecores; Crollius HR et al 2000 Genome Res 10:939; Aparicio S et al 2002 Science 297:1301; Jaillon O et al 2004 Nature [Lond] 431:946.

Pull-Down Assay: Expected to reveal interacting proteins. One of the proteins is attached to agarose beads and so immobilized. Then the test protein is added and the mixture is incubated to allow time for forming some links. Subsequently the mix is centrifuged. If there is a binding between them both proteins are found in the pellet and interaction is assumed. ►immunoprecipitation, ►genetic networks; Brymora A et al 2001 Anal Biochem 295:119.

Pullulanase: A secreted Klebsiella enzyme (~117 kDa) which cleaves starch into dextrin. It occurs also in the endosperm of cereals and other plant tissues and it is regulated by thioredoxin. ►thioredoxin; Schindler I et al 2001 Biochim Biophys Acta 1548:175.

Pulmonary Adenoma: Lung cancer controlled by QTL. Dense SNP map of mouse identified the pulmonary susceptibility locus (*Pas1*) including within a 0.5 Mb region *Kras2* (Kirsten rat sarcoma oncogene 2) and *Casc1/Las1* susceptibility genes in chromosome 6. The *Glu102* allele of *Casc1* preferentially promotes susceptibility to tumorigenesis by chemicals (Liu P et al 2006 Nat Genet 38:888). Change from in the balance of expression of *Kras2* and *Pas1* entails susceptibility to resistance (To MD et al 2006 Nature

Table P3. Pulse-chase method. Autoradiographic analysis of the replication of the DNA in chromosomes by the pulse-chase procedure. (Drawn after Taylor JH et al 1957 Proc Natl Acad USA 43:122)

Grown without label	Replication in ^{3}H	Labeled chromosomes replicated in ^{3}H-free medium		
		no exchange	sister chromatids exchanged	
				Cytological observation
				Interpretative drawing of the distribution of the radioactive label ■
				Interpretation of the replication of the DNA helices in the two chromatids ^{3}H. . . . .

Genet 38:926). LKB1 hemizygosity or homozygous loss substantially accelerated pulmonary adenoma (Hongbin J et al 2007 Nature [Lond] 448:807). ►QTL, ►RAS, ►small cell lung carcinoma, ►non-small-cell lung carcinoma, ►LKB

Pulmonary Emphysema: The increase in size of the air space of the lung by dilation of the alveoli (small sac-like structures) or by destruction of their walls. Smoking may be a cause.

Pulmonary Hypertension (PPH, FPPH): Characterized by shortness of breath, hypoxemia and arterial hypertension caused by the proliferation of endothelial smooth muscles and vascular remodeling. It is a 2q33 dominant disorder with reduced penetrance. Various drugs (such as the banned anti-obesity drug fen-phen) may trigger it. The basic defect is in gene BMPR2 (bone morphogenetic protein receptor II). Haplo-insufficiency may cause it. The consequence is inappropriate regulation by the serine/threonine kinases of the phosphorylated Smad proteins leading to inadequate maintenance of blood vessel integrity. ►bone morphogenetic protein, ►Smad, ►hypertension, ►haplo-insufficient, ►bone morphogenetic protein, ►Smad; Machado RD et al 2001 Am J Hum Genet 68:92.

Pulmonary Surfectant Proteins: ►respiratory distress

Pulmonary Stenosis: ►stenosis

Pulse-Chase Analysis: Expose cells, for a period of time, to a radioactive compound such as ^{3}H-thymidine (pulse) and examine the labeling of chromosomes in some cells. The culture is then transferred to non-radioactive thymidine and allowed to complete a division (chased to another stage) and study again the distribution of the label and determine its fate in the cells. The experiment permitted the first time the valid conclusion that DNA replication is semi-conservative. ►radioactive tracer, ►radioactive label, see Table P3.

Pulsed Field Gel Electrophoresis (PFGE): A procedure combining static electricity and alternating electric fields with gel electrophoresis for the separation of DNA of entire chromosomes of lower eukaryotes, such as of yeast and *Tetrahymena* or large DNA fragments cloned in YAC vectors of any genome cut by rare-cutting restriction enzymes. ►CHEF, ►FIGE, ►OFAGE, ►YAC, ►PHOGE, ►TAFE, ►RGE; Mulvey MR et al 2001 J Clin Microbiol 39:3481.

Puma Cat (*Felis concolor*, *Puma concolor*): 2n = 38. (see Fig. P168).

Figure P168. Puma

PUMA (p53 upregulated modulator of apoptosis): ►p53, ►apoptosis, ►BAX, ►SLUG

PUMA2: The evolutionary analysis of metabolism, http://compbio.mcs.anl.gov/puma2/.

Pump: The various transmembrane proteins mediating active transport of ions and molecules through biological membranes. ►sodium pump

Punctuated Equilibrium: ►punctuated evolution

Punctuated Evolution: A theory that evolution would follow alternating periods of rapid changes and relatively stable intervals (punctuations). Natural selection of beneficial mutations appears after some intervals and spread over the population. At the DNA level about 22% of the substitutional changes represent punctuated evolution. Punctuational changes are more common in plants and fungi than in animals (Pagel M et al 2006 Science 314:119). ►speciation, ►beneficial mutation, ►neutral mutation, ►hopeful monster, ►shifting balance theory, ►gradualism; Gould SJ, Eldredge N 1993 Nature [Lond] 366:223; Elena SF et al 1996 Science 272:1797; Voigt C et al 2000 Adv Protein Chem 55:79.

Punctuation Codons (UAA, UGA, UAG): Terminate translation of the mRNA.

Punnett Square: Permits simple prediction of the expected pheno- and genotypic proportions. It is a checkerboard where on top and at the left column the male and female gametic output is represented and in the body of the table the genotypes are found (see Figure P169). If, e.g., the heterozygote has the genetic constitution of *Aa, Bb*, the gametes and genotypes will be AB, Ab aB and ab. In case of linkage and recombination the actual frequency of each type of gamete must be used to obtain the correct genotypic proportions in the body of the checkerboard. ►modified Mendelian ratios, ►Mendelian segregation

Male gametes		AB	Ab	aB	ab
Female gametes	AB	AB AB	AB Ab	AB aB	AB ab
	Ab	Ab AB	Ab Ab	Ab aB	Ab ab
	aB	aB AB	aB Ab	aB aB	aB ab
	ab	ab AB	ab Ab	ab aB	ab ab

Figure P169. Punnett square

Pupa: A stage in insect development between the larval stage and the emergence of the adult (imago) (see Fig. P170). ►*Drosophila*, ►juvenile hormone

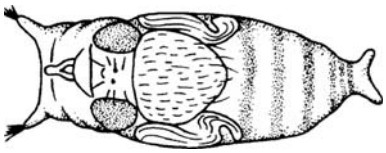


Figure P170. *Drosophila* pupa

Puparium: The case in which the *Drosophila* (and other insect) pupa develops for about four days after hatching of the egg, and in another four days the imago emerges. ►*Drosophila*

Pure Culture: Involves only a single organism. ►axenic culture

Pure Line: Genetically homogeneous (homozygous), and its progeny is expected to be identical with the parental line unless mutation occurs. (See Johannsen W 1909 Elemente der exakten Erblichkeitslehre, Fischer, Jena, Germany).

Pure-Breeding: Homozygous for the genes considered.

Purine: A nitrogenous base composed of a fused pyrimidine and imidazole ring; the principal purines in the cells are adenine, guanine, xanthine, hypoxanthine (but theobromine, caffeine and uric acid are also purines).

5′,8-Purine Cyclodeoxynucleosides: Formed in two diastereoisomers by exposure of DNA to reactive oxygen species. The cyclopurines may cross-link the C-8 adenine or guanine and the 5′ position of 2-deoxyribose (see Fig. P171). These diastereoisomers may block DNA replication and are cytotoxic.

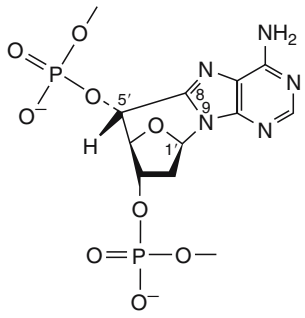


Figure P171. 5′,8-cyclo-2′-deoxyadenosine phosphate

Commonly excision repair may not correct the damage although the xeroderma pigmentosum A protein may cut at both flanks and excises them. These types of damaged nucleosides may accumulate by time and result in progressive neurodegeneration in xeroderma pigmentosum patients. ►cyclobutane, ►excision repair, ►xeroderma pigmentosum; Kuraoka I et al 2000 Proc Natl Acad USA 97:3837.

Purine Repressor (PurR): A member of the *Lac* repressor family of proteins regulating 10 operons involved in the biosynthesis of purine and affecting to some extent 4 genes controling de novo pyrimidine synthesis and salvage. Its ca. 60 amino acids, the NH_2 domain binds to DNA and its ca. 280 residue COOH domain binds effectors and it functions in oligomerization. ►*Lac* repressor, ►salvage pathway; Moraitis MI et al 2001 Biochemistry 40:8109.

Purity of the Gametes: One of the most important discoveries of Mendel. At anaphase I of meiosis of diploids the bivalent chromosomes segregate and at anaphase II, the chromatids separate. Therefore, in the gametes of diploids only a single allelic form of the parents is present with rare exceptions, e.g., nondisjunction and polyploids. ►meiosis, ►nondisjunction, ►gene conversion, ►Mendelian laws

Purkinje Cells: Large pear-shaped cells in the cerebellum, these are connected to multi-branched nerve cells traversing the cerebellar cortex. In the heart they are tightly appositioned cells transmitting impulses. ►cerebellum, ►motor proteins

Puromycin: An antibiotic, it inhibits protein synthesis by binding to the large subunit of ribosomes; its structure resembles the 3′-end of a charged tRNA. Therefore it can attach to the A site of the ribosome and forms a peptide bond but it cannot move to the P site and thus causes premature peptide chain termination. ►antibiotics, ►signaling to translation, (see Fig. P172) formula

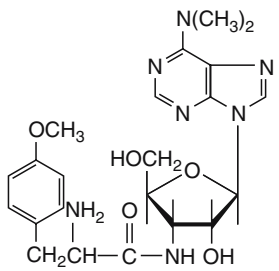


Figure P172. Puromycin

PUS: ►pyogenic

Pushme-Pullyou (pushmi-pullyu) Selection: A positive-negative selection system to isolate engineered chromosomes in somatic cell hybrids, which have retained the segment positively selected for, and lost the regions selected against. (See Higgins AW et al 1999 Chromosoma 108:256; Trimarchi JM, Lees JA 2002 Nature Rev Mol Cell Biol 3:11).

PV16/18E6: A human papilloma virus oncoprotein. (►oncoprotein) Burkitt lymphoma and murine lymphocytomas and may have activating role for MYC that is in the same chromosome. ►MYC, ►oncogenes, ►Burkitt lymphoma

πVX: A microplasmid (902 bp) containing a polylinker and an amber suppressor for tyrosine tRNA. It can be used for cloning eukaryotic genes. ►recombinational probe

PWM (position weight matrix): Used for identification of and search for functional nucleotide sequences, which are highly degenerate, e.g., the TATA boxes in the promoters. The PWM reflects the frequency of the four nucleotides (A, T, G, C) in an aligned set of different sequences sharing common function. After it had been determined in well-characterized core promoter regions, the PWM can be used to scan for TATA boxes in anonymous nucleotide sequences. The similarities between PWM and specific sequences and the matching value (within an accepted range) is determined and called a signal. Bucher (J Mol Biol 212:563) used a PWM for TATA box: GTATAAAGGCGGGG, and when the best fit was designated as 0, the majority of "unknown" TATA boxes scored within 0 to −8.16. Some of these might be, however, false positives. ►TATA box, ►core promoter, ►anonymous DNA segment, ►position-specific scoring matrix; Audic S, Claverie J-M 1998 Trends Genet 14:10.

PX (phox): A 125-amino acid module present in a variety of proteins involved in binding phosphoinositides.

$P2X_1$: A receptor for ATP in the in ligand-gated membrane cation channels. P2X is a component of the contractile mechanism of the vas deferens muscles, which propel the sperm into the ejaculate during copulation. Its defect entails ∼90% sterility although without apparent harm to the male or the female mice. It has also several other signaling functions. ►vas deferens, ►ion channels, c►ongenital aplasia of the vas deferens; Khakh BS, North RA 2006 Nature [Lond] 442:527.

PX DNA: A four-stranded molecule where the parallel helices are held together by reciprocal recombination at every site of juxtaposition. Its topoisomer is JX_2 and it also contains adjacent helices but there is no reciprocal exchange at the contact points. (See Yan H et al 2002 Nature [Lond] 415:62).

Pxr: ►SXR

Pycnidium: A hollow spherical or pear-shaped fruiting structure of fungi producing the pycnidiospores, which are released through the top opening, the ostiole. ►stem rust

Pycnodysostosis: A rare autosomal recessive (1q21) human malady characterized by defects in ossification (bone development) resulting in short stature, deformed skull with large fontanelles (soft, incompletely ossified spots of the skull common in fetuses and infants) and general fragility of the bones. The primary defects appears to be in cathepsin K, a major bone protease although interleukin-6 receptor has also been implicated. (see Fig. P173) ►Toulouse-Lautrec, ►cleidocranial dysostosis, ►cathepsins

Figure P173. The famous French artist Henri Toulouse-Lautrec (1864–1901) might have suffered from this malady and his self-portrait reveals some of the characteristics of the malformations. The exact nature of his condition cannot be diagnosed but it is known that his parents were close relatives. (By permission of the St. Martin Press, New York)

Pycnosis (pyknosis): A physiological effect of ionizing radiation on chromosomes expressed as clumping or stickiness. It is dose-dependent and the late prophase stage irradiation is most effective in causing it. Anaphase proceeds but the chromosomes have difficulties in separation, display chromatin bridges and may break up into fragments. ►bridge, ►karyorrhexis, ►heteropycnosis, ►acinus

Pygmy: The Central African human tribe of about 100,000 has an average height of 142 cm. In comparison, the average height of Swiss and Californian is 167–169 and 170–172 cm, respectively. The Pygmies do not respond to exogenous stomatotropin but the concentration of serum somatomedins in the adolescent Pygmies is about a third below that in non-Pygmies of comparable age. Although the shortness of Pygmies appears recessive, intermarriages indicate polygenic determination of height. ►dwarfism, ►stature in humans, ►nanism, ►somatomedin, ►somatotropin

PYK2: Protein tyrosine kinase links Src with G_i and G_q-coupled receptors with Grb2 and Sos proteins in the MAP kinase pathway of signal transduction. Lysophosphatidic acid (LPA) and bradykinin stimulate its phosphorylation by Src. Over-expressing mutants of Pyk or the protein tyrosine kinase Csk reduces the stimulation by LPA, bradykinin or over-expressed Grb2 and Sos. ►CAM, ►MAP, ►Src, ►G_i, ►G_q, ►lysophosphatidic acid, ►kininogen, ►Csk, ►Grb2, ►Sos, ►signal transduction; Felsch JS et al 1998 Proc Natl Acad Sci USA 95:5051; Sorokin A et al 2001 J Biol Chem 276:21521.

Pyknons: Short RNA motifs shared by genic and non-genic transcript regions of the human genome and are presumably mediating post-transcriptional gene silencing and RNA interference. Pyknons are most frequent in the 3′-nontranslated areas of genes (Rigoutsos I et al 2006 Proc Natl Acad Sci USA 103:6605).

Pyknosis: ►pycnosis

Pyloric Stenosis: A smaller than normal opening of the pylorus, the lower gate of the stomach that separates it from the small intestine (duodenum). It does not appear to have independent genetic control but it is part of some syndromes. It affects males five times as frequently as females; the overall incidence for both sexes is about 3/1000 birth. About 20% of the sons of affected females display this anomaly but only about 4% of the sons if the father has the malady. It may be caused by a deficiency of neuronal nitric acid synthase. ►sex-influenced, ►nitric oxide, ►imprinting

PYO: Personal years of observations; a term used in medical and clinical genetics

Pyocin: A bacteriotoxic protein produced by some strains *Pseudomonas aeruginosa* bacteria. ►bacteriocins

Pyogenic: Producing pus (DNA and protein-rich) excretum upon inflammation containing leukocytes in a yellowish fluid. It is produced abundantly by the body also after *Streptococcus* and *Staphylococcus* and other bacterial infections. ►IRAK, ►leukocyte, ►*Streptococcus*, ►*Staphylococcus*

Pyramidal Cells: Excitatory neurons in cerebral cortex. ►brain, ►neuron

Pyramiding: To build up on a larger base; to accumulate in plant protection introduction of more than one gene

and different transgenes into a plant variety conveying resistance to the same agent, in order to slow down or prevent development of resistance in the pathogen or pest.

Pyrene: A fluorochrome, frequently used as a bimolecular excimer (see Fig. P174). Pyrene incorporation into the sugar position of DNA by one carbon linker results in very weak monomer fluorescing because of quenching. Similar was the observation with RNA or RNA–DNA hybridization. Pyrene-modified RNA displayed drastically increased fluorescence however when paired with complementary RNA and is a useful tool for monitoring RNA hybridization (Nakamura M et al 2005 Nucleic Acids Res 33:5887). ►FRET, ►excimer

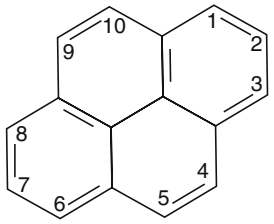


Figure P174. Pyrene

Pyrenoid: A dense, refringent protein structure in the chloroplast of algae and liverworts associated with starch deposition. ►chloroplast

Pyrethrin (pyrethroids, permethrin): Insecticides are natural products of *Pyrethrum* (*Chryanthemum cineraiaefolium*) plants (Compositae). They affect the voltage-gated Na^+ ion channels and humans may have severe allergic reactions to pyrethrins. ►ion channels, ►insecticide resistance

Pyrethrum (*Chrysanthemum* spp): A plant source of the natural insecticide, pyrethrin, with basic chromosome number x = 9 (see Fig. P175). Some species are diploid or tetraploids or hexaploids. ►pyrethrin

Figure P175. Pyrethrum

Pyridine Nucleotide: A coenzyme containing a nicotinamide derivative, NAD, NADP.

Pyridoxine (pyridoxal): Vitamin B_6 is part of the pyridoxal phosphate coenzyme, instrumental in transamination reactions (see Fig. P176). In *E. coli* bacteria vitamin B_6 is synthesized through deoxyxylulose 5-phosphate and phosphohydroxy-L-threonine. In plants (*Arabidopsis*) the synthetic pathway differs in as much as it is biosynthesized from ribose 5-phosphate or ribulose 5-phosphate and from dihydroxyacetone phosphate or glyceraldehyde 3-phosphate in the cytosol rather than in the chloroplasts (Tambasco-Studart M et al 2005 Proc Natl Acad Sci USA 102:13687).

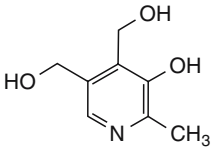


Figure P176. Pyridoxine

An apparently autosomal recessive disorder in humans involving seizures is caused by pyridoxin deficiency because of a deficit in glutamic acid decarboxylase (GAD) activity and consequently insufficiency of GABA, required for normal function of neurotransmitters. Administration of pyridoxin caused cessation of the seizures. The GAD gene was located in the long arm of human chromosome 2. An autosomal dominant regulatory pyridoxine kinase function has also been identified in humans. ►epilepsy

Pyridoxine Dependency: It may manifest as autosomal recessive seizures with perinatal onset (around birth).

Pyrimidine: A heterocyclic nitrogenous base such as cytosine, thymine, uracil in nucleic acids but also the sedative and hypnotic analogs of uracil, barbiturate and derivatives (see Fig. P177). Pyrimidine biosynthesis may follow either a de novo or a salvage pathway. Some of the pyrimidine moieties, e.g., of thiamin are biosynthesized through a route different from that of nucleic acid pyrimidines. ►J base, ►thiouracil, ►pseudouracil, ►*de novo* synthesis, ►salvage pathway, ►formulas; Fox BA, Bzik DJ 2002 Nature [Lond] 415:926.

Pyrimidine Dimer: Cross-linked adjacent pyrimidines (thymidine or cytidine) in DNA causing a distortion in the strand involved and thus interfering with proper functions (see Fig. P178). It is induced by short-wavelength UV irradiation. The thymidine dimers may be split by visible light-inducible enzymatic repair (light repair) or by excision repair (dark repair). ►cyclobutane ring, ►physical mutagens, ►genetic repair, ►DNA repair, ►photolyase, ►CPD, ►glycosylases, ►pyrimidine-pyrimidinone photoproduct,

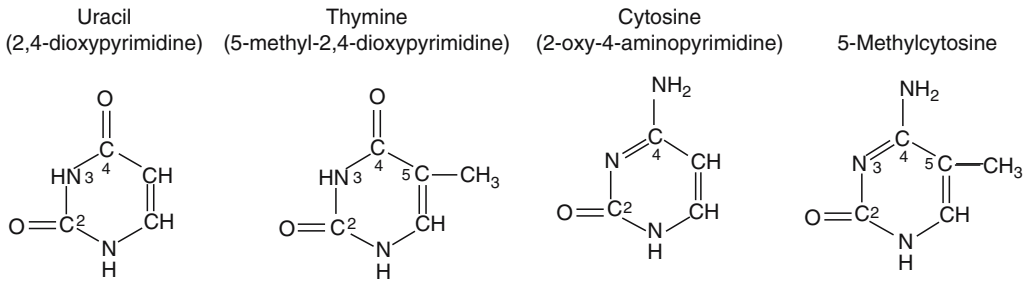


Figure P177. The major cellular pyrimidines

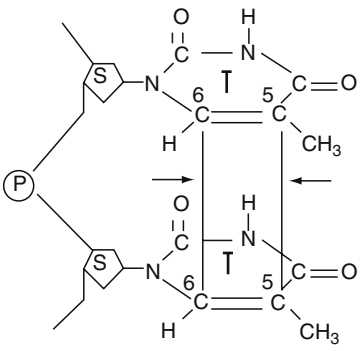


Figure P178. Cross-linked neighboring thymines in the DNA

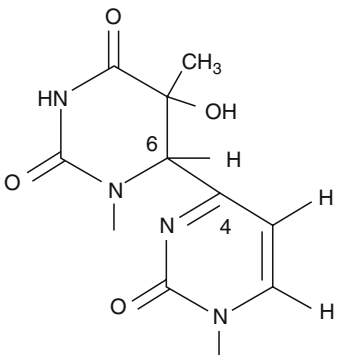


Figure P179. Thymine–Cytosine photoproduct

►photoreactivation; Otoshi E et al 2000 Cancer Res 60:1729.

Pyrimidine Dimer *N*-Glycosylase: A DNA repair enzyme that creates an apyrimidinic site. Then the phosphodiester bond is severed and a 3′-OH group is formed on the terminal deoxyribose. Exonuclease 3′→5′ activity of the DNA polymerase splits off the new 3′-OH end of the apyrimidinic site. After this, the replacement-replication—ligation process repairs the former thymine dimer defect. ►glycosylase, ►DNA repair, ►pyrimidine dimer; Piersen CE et al 1995 J Biol Chem 270:23475.

Pyrimidine 5′-Nucleotidase Deficiency (P5N): May cause hereditary hemolytic anemia as the pyrimidines inhibit the hexose monophosphate shunt in young erythrocytes. There are two isozymes of which P5NI is most commonly the cause of the anemia. ►pentose phosphate pathway, ►anemia; Marinaki AM et al 2001 Blood 97:3327.

Pyrimidine-Pyrimidinone Photoproduct: A pyrimidine dimer involving a 6—4 linkage between thymine and cytosine (see Fig. P179). ►cyclobutane, ►Dewar product, ►cis-syn dimer, ►translesion pathway, ►photolyase; Vreeswijk MP et al 1994 J Biol Chem 269:31858.

Pyrimidone: Hydroxypyrimidine (see Fig. P180).

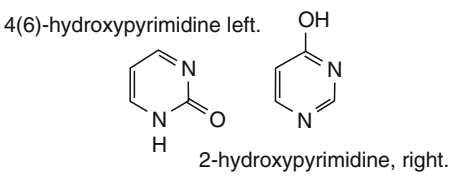


Figure P180. 4(6)-hydroxyprimidine (left); 2-hydroxypyrimidine (right)

Pyrimidopurinones: A malondialdehyde-DNA adduct derived from deoxyguanosine. ►adduct

Pyronin: A histochemical red stain used for the identification of RNA.

Pyrosequencing: Used for the analysis of the nucleotide sequence of less than 200 base long DNA strands for the detection of mutational alteration(s). Pyrosequencing has been applied to the analysis of the genome of Neanderthals. It uses the enzymes DNA polymerase, sulfurylase, firefly luciferase and apyrase. The incorporation of the nucleotides (which are not labeled) in the growing end is monitored by light flashes in a single tube. Electrophoresis is not used. Nucleotide triphosphates added to the reaction in sequence. Visible light is generated and detected when pyrophosphate is released during incorporation

from the nucleotide triphosphates with the cooperative effects of the sulfurylase and the luciferase. This is a very fast procedure and may be automated.

Another fast and convenient method of sequencing by synthesis involves four chemically cleavable fluorescent nucleotide analogues as reversible terminators. Each of the nucleotide analogues contains a 3′-*O*-allyl group and a unique fluorophore with a distinct fluorescence emission at the base through a cleavable allyl linker. These nucleotide analogues are good substrates for DNA polymerase in a solution-phase DNA extension reaction and that the fluorophore and the 3′-*O*-allyl group can be removed with high efficiency in aqueous solution. By this procedure 20 continuous bases of a homopolymeric DNA template immobilized on a chip were accurately sequenced. Such a methods can be extended eventually to longer sequences (Ju J et al 2006 Proc Natl Acad Sci USA 103:19635).

►DNA sequencing, ►sulfurylase, ►luciferase, ►apyrase, ►Neanderthal; Ronaghi M 2001 Genome Res 11:3; Marziali A, Akeson M 2001 Annu Rev Biomed Engr 3:195; Fakhrai-Rad H et al 2002 Hum Mut 19:479; Goldberg SMD et al 2006 Proc Natl Acad Sci USA 103:11240; Margulies M et al 2005 Nature [Lond] 437:376; note corrigendum Nature [Lond] 441:120.

Pyrrole: A saturated five-membered heterocyclic ring such as found in protoporphyrin. Pyrrole-imidazole polyamides may bind to specific DNA of the transcription factor TFIIIA and regulate the transcription of the 5S RNA. *N*-methylimidazole (Im)—*N*-methylpyrrole (Py) may target G≡C and Py—Im the C≡G base pairs, respectively. The Py—Py combination is specific for T= A and A= T. ►porphyrin, ►porphyria, ►heme

Pyrrolizidine Alkaloids (petasitenine, senkirkine): Occur in several plant species (*Tussilago, Heliotropium*, etc.) and some of which are used as food or medicinal plants but they are mutagenic/carcinogenic. They occur also in some moths and convey protection against predators. ►*Echinacea*; Ober D, Hartmann T 1999 Proc Natl Acad Sci USA 96:14777.

PZD: ►micromanipulation of the oocyte

Historical vignette

"…alle essentiellen Merkmale…epigenetisch sind, und da die Determinierung ihrer Specificität durch den Kern erhalten."

"*… all characters are epigenetic and their specificity depends on the cell nucleus*."

Pyrrolysine: The 22nd amino acid encoded in Archaea and Eubacteria by the stop codon UAG. Pyrrolysine is charged to $tRNA^{CUA}$ (encoded by *pylT*) by PylS aminoacyl-tRNA synthetase and thus can be incorporated into *E. coli* proteins (Blight SK et al 2004 Nature (Lond) 431:333). ►amino acids, ►genetic code, ►aminoacyl tRNA synthetase, ►unnatural amino acids, ►selenocysteine; Hao B et al 2002 Science 296:1462; Srinivasan G et al 2002 Science 296:1459; pyrrolysyl-tRNA synthetase crystal structure: Kavran JM et al 2007 Proc Natl Acad Sci USA 104:11268.

Pyruvate Dehydrogenase Complex: Contains three enzymes, pyruvate dehydrogenase, dihydrolipoyl transacetylase and dihydrolipoyl dehydrogenase and the function of the complex requires the coenzymes: thiamin pyrophosphate (TPP), flavine adenine dinucleotide (FAD), coenzyme A (CoA), nicotinamide adenine dinucleotide (NAD), and lipoate. The result of the reactions is oxidative decarboxylation whereby CO_2 and acetyl CoA are formed. ►oxidative decarboxylation; Zhou ZH et al 2001 J Biol Chem 276:21704.

Pyruvate Kinase Deficiency: A recessive (human chromosome 1q21-q22, PK1) hemolytic anemia actually caused by two enzymes that are the products either of differential processing of the same transcript or chromosomal rearrangement. In the presence of some tumor promoters hepatic pyruvate kinase activity decreases. ►anemia, ►hemolytic anemia, ►glycolysis

Pyruvic Acid: A ketoacid ($CH_3COCOOH$) formed from glycogen, starch and glucose under aerobic conditions (under anaerobiosis is reduced to lactate and NAD^+ is formed). Hyperpolarization technology permits imaging of pyruvate metabolic path in real time without invasive procedures (Golman K et al 2006 Proc Natl Acad Sci USA 103:11270). ►Embden-Meyerhof pathway, ►pentose phosphate shunt

PyV: Polyoma virus.

$PYY_{3–36}$: A neuropeptide Y (NPY)-like, but it is a gastrointestinal hormone that inhibits food uptake. ►obesity, ►leptin, ►neuropeptide Y; Batterham RL et al 2002 Nature [Lond] 418:650.