G

G: ►guanine. G also denotes generations after mutagenic treatment of mice, G_0, G_1, G_2, etc. This designation is somewhat confusing with the preempted cell cycle symbols. ►cell cycle

g: General intelligence. ►intelligence quotient, ►human intelligence

γ: ►gamma

g^2: ►genetic determination

G418 ($C_{20}H_{40}N_4O_{10}$. $2H_2SO_4$): An aminoglycoside antibiotic. ►geneticin

G3139: An 18-mer full-phosphorothioate deoxyoligonucleotide (5′-TCTCCCAGCGTGCGCCAT-3′ *Genta*, San Diego, California) with sequence antisense to the first six codons of the open reading of gene BCL-2, and it is used for therapy of lymphomas. ►Bcl-1, ►lymphoma, ►antisense technologies, ►phosphorothioate

G3854: A 20-mer full-phosphorothioate deoxyoligonucleotide with sequence antisense to open reading frame of gene BCL-2, and it is used for therapy of lymphomas. It is similar to G3139 but two nucleotides longer. ►Bcl-1, ►lymphoma, ►antisense technologies, ►phosphorothioate

G Banding: A chromosome staining method using Giemsa stain (a complex basic dyes, containing azures, eosin, glycerol and methanol), after pretreatment with the proteolytic enzyme, trypsin, it permits the identification of dark cross-bands that vary among the individual eukaryotic chromosomes and usually facilitates their identification even when their length and arm ratio is similar (see Fig. G1). The darkly stained bands represent (AT-rich) heterochromatin. ►chromosome banding, ►stains, ►rye

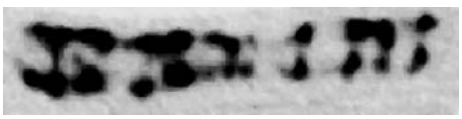

Figure G1. G-Banded human chromosome

G Box: A guanine-rich upstream cis element regulating transcription tion. Commonly it has the structure GA CAACGTC GC. The G- box activator protein binds to the framed core sequence. It is commonly found in environmentally sensitive genes. ►Simian virus 40, ►CAAT box, ►regulation of gene activity, ►phytochromes

Gbuilder: A nucleotide sequence visualization tool based on Java application of DNA clusters in EST data. ►Java, ►EST; Muilu J et al 2001 Genome Res 11:179.

***G* Element**: ►non-viral retrotransposable element, ►retrotransposons, ►retroposons

***g* Factor**: ►human intelligence

g Force: ►centrifuge

G_0 Phase: The state of a pause for the cell before it enters the G1 phase and until divisional activities start again after mitosis. ►cell cycle

G_1 Phase: The first phase of the cell cycle following mitosis (C value = 2). ►cell cycle

G_2 Phase: The phase following DNA replication during the cell cycle (C value = 4). ►cell cycle; O'Connell MJ et al 2000 Trends Cell Biol 10[7]:296.

G4 Phage: A single-stranded DNA phage (5507 bases), ~67% related to φX174. ►bacteriophages, φX174; Godson GN et al 1978 Nature [Lond] 276:236.

G Proteins: They are guanine nucleotide binding proteins that serve as intermediaries in biological signaling pathways. The signal is received by *receptors* and the *G-proteins* forward it by mediation of different number of intermediaries to the *effectors* that regulate genes in response to the signals. G-proteins are activated by aluminum fluoride and the α subunit can be ADP-ribosylated by mediation with the aid of bacterial toxins (cholera, pertussis).

The large G-proteins are heterotrimeric (α, β, γ) and control the opening and closing of the signal transduction pathways by changing the attached GDP ⇆ GTP. In the GTP-associated form, they have key role in signal transduction from receptors to effectors. The proteolysis of the large G proteins is regulated by RGS protein signaling and subject to N-end rule (Lee MJ et al 2005 Proc Natl Acad Sci USA 102:15030). There are also low molecular weight small G-proteins with a single (α) subunit. G-protein (G_s) is involved in the regulation of the level of the enzyme adenylyl cyclase and thus cAMP and cAMP-dependent protein kinase. The G_i form is involved in the inhibition of adenylate cyclase; G_{iia2} is required for insulin function. The light-activated GTPase activity is mediated by the G_t-protein, also called transducin. G-proteins stimulate the hydrolysis of phosphoinositides with the aid of phospholipase C. Ca^{2+} also mediates by G-proteins and cAMP degradation by cyclic nucleotide phosphodiesterase indirectly. G-proteins also regulate ion channels.

When a proper ligand binds to a transmembrane receptor, the trimeric G-protein dissociates into a βγ and an α subunit. The α subunit stimulates adenylyl cyclase, the first the transition of GDP to GTP, and later the transition of GTP to GDP through the mild GTPase activity. In the G-GDP state reassociation of the three subunits follows. G-proteins regulate also Ca^{2+} metabolism and indirectly control allosteric effector proteins. Several human diseases are associated with defects in the G proteins (pituitary tumors, McCune-Albright syndrome, Albright hereditary osteodystrophy, puberty precocious) or with defects in the G protein receptors (hypercalcemia, hypercalciuria, hyperparathyroidism, diabetes insipidus, retinitis pigmentosa, color blindness, glucocorticoid deficiency, opiate addiction, hypertension, myocardial ischemia, chronic heart disease). The human genome seems to include 800 to 1,000 G protein receptors. The most common among them (~89%) are rhodopsin-like molecules, the secretin-like molecules (~7$) and the metabotropic-glutamate-receptor-like proteins (~4%). These proteins, because of their key role in the regulation of metabolic pathways and disease development are important targets of existing and future drugs. Dozens of genes are involved with coding and regulation of G protein subunits, scattered among several human chromosomes. Many of the G protein-coupled receptors are without introns suggesting that retrogenes code for them. Mutations in exons may alter splicing sites remote from the mutation and thus create new variants. G proteins have important roles in both animal and plant cells, however, plants have much fewer genes encoding the trimeric G protein subunits. Several human diseases implicate G protein malfunctions. ►G region, ►G' region, ►G" region, ►G_α-, ►G_i-, ►G_q-, ►G_s-, ►G_o-, ►G_t- protein, ►GTPase, ►cAMP, ►adenylate cyclase, ►rhodopsin, ►signal transduction, ►N-end rule, ►calmoduline, ►receptor, ►effector, ►cholera toxin, ►pertussis toxin, ►GTP, ►phosphodiesterase, ►ion channel, ►adenylate cyclase, ►cell cycle, ►retrogene, see also the mentioned diseases under separate entries; Sp SR 1997 Annu Rev Biochem 66:639; Bockaert J, Pin JP 1999 EMBO J 18:1723; Farfel Z et al 1999 New England J Med 340:1012; Dohlman HG, Thorner J 2002 Annu Rev Biochem 70:703; Knoblich JA 2001 Cell 107:183; Peterson YK et al 2002 J Biol Chem 277:6767; Assmann SM 2002 Plant Cell 14:S355; Chalmers DT, Behan DP 2002 Nature Rev Drug Discover 1:599; G proteins in plants: Assmann SM 2005 Science 310:71; G protein signaling in yeast: Slessareva JE, Dohlman HG 2006 Science 314:1412; GEF and GAP regulation of G proteins: Bos JL et al 2007 Cell 129:865; http://www.hsls.pitt.edu/guides/genetics/tools/protein/information/URL1118091522/info?print_format=false; G protein ligands: http://gdds.pharm.kyoto-u.ac.jp/services/glida/.

G Quartet (guanine quartet): Guanine-rich nucleotide sequences may form four-stranded complexes, stabilized in Hogsteen structures. The G quartets may be formed in phosphorothioate octamers such as *S*-$T_2G_4T_2$ or from other sequences like GTG_2TG_3-TG_3TG_3T (see Fig. G2). These quartets or double quartets may be potent viral inhibitors. The latter may block HIV1 integrase. Guanine-rich sequences are common in the telomeres, transcription regulatory regions, and immunoglobulin switching areas, etc. Antisense RNAs containing G quartets seem to suppress to various degrees MYC and MYB cellular oncogenes, HIV integrase, etc. G quartets may regulate the translation of the mRNA transcript of Fragile X gene and thus, control synaptic activity of neurons in the brain. Despite the presence of well-defined non-guanine base quartets in a number of NMR and X-ray structures, the data suggests that most non-guanine quartets do not participate favorably in structural stability, and that these quartets are formed only by virtue of the docking platform provided by neighboring G-quartets (Gros G et al 2007 Nucleic Acids Res 35:30:64). ►antisense technologies, ►Hogsteen pairs, ►oncogenes, ►HIV, ►immunoglobulins, ►Fragile X chromosome, ►NMR; Horvath MP, Schultz SC 2001 J Mol Biol 310:367; G-quartet-rich sequences: http://bioinformatics.ramapo.edu/grsdb/index.php.

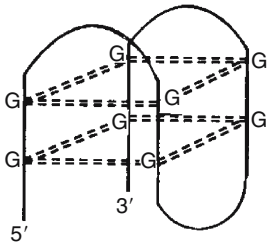

Figure G2. Quartet

G Region: Consensus N-K-X-D (see Amino Acid Symbols) in GTP-binding proteins that interacts with guanine in GTP. ►G-proteins

G´ Region of GTP Binding Proteins: With highly conserved consensus D-X-X-G-Q (see Amino Acid Symbols) it involves GTP-ase function and may affect oncogenicity. ►signal transduction, ►G-proteins

G´´Region: G″ region in RAS interacts with GTP through the E-T-S-A-K (see Amino Acid Symbols) consensus. In some G-proteins H-(F/M)-T-C-A

(T/V)-D-T may be the corresponding functional area. ►G-proteins

G8 RNA: ►thermal tolerance

γ Satellite: The repetitive heterochromatin in the pericentromeric area.

G Test: It is a goodness of fit test but instead of calculating the chi^2 in the common way the probability of p is divided by $\hat{p}$ = L (likelihood), and G = 2 *ln*(L) = 2(*ln*10)logL and the distribution is approximated by the χ^2 distribution in large samples. Instead of G sometimes the symbol I (information) is used. ►chi square, ►information; Sokal RR, Rohlf FJ 1969 Biometry, Freeman, San Francisco, California.

GA: ►gibberellic acid, ►plant hormones (see Fig. G3).

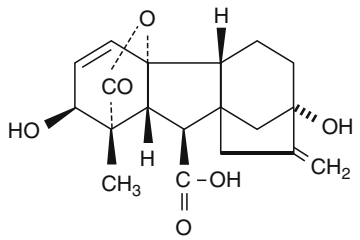

Figure G3. Gibberellic acid

G_α: The G-protein involved in hormonal stimulation of adenylate cyclase and may regulate ion channels or phospholipase C. The human G_s 1α gene contains 13 exons and 12 introns in a total size of 20 kbp. Gα types: $G_i\alpha$, $G_o\alpha$, $G_x\alpha$, $G_t\alpha$, $G\alpha_{12}$ and $G\alpha_{13}$ are subunits, which are stimulated by the p115 RhoGEF. The latter bound to p115RhoGEF catalyzes G nucleotide exchange on RHO but this may be inhibited by activated by $G\alpha_{13}$. These are very highly conserved proteins across phylogenetic ranges. In $G_s\alpha$ only 1/394 amino acid difference was found between man and rat, and the protein is entirely identical between humans and bovines. ►G-proteins, ►RGS, ►p115

GABA ($_\gamma$-aminobutyric acid): It plays an important role in neurotransmission of vertebrates and invertebrates. In the nematode *Caenorhabditis* a series of *unc* (uncoordinated movement) genes respond to GABAergic neuronal effects. $GABA_A$ receptors mediate synaptic inhibition but upon intense activation, they may excite rather than inhibit neurons. GABA controls Cl^- ion channels by efflux (depolarization and excitation of the nerve cell) and by influx (hyperpolarization and reduced excitability). By an increase of the level of $GABA_A$ receptor α4 premenstrual anxiety and susceptibility to seizures decrease. Progesteron also acts as a sedative by enhancing GABA function. Heteromeric GABA receptors ($GABA_BR1a/b$—$GABA_BR2$), in cooperation with G proteins, regulate potassium and calcium ion channels. The nineteenth century alcoholic beverage, absinthe, containing wormwood oil (thujone) is antagonistic to the $GABA_A$ receptor channels and that explains its convulsant and other neurological effects. GABA transaminase (16p13.3) is responsible for the catabolism of GABA and its deficiency leads to neuronal disorders. There are at least 13 GABA receptors encoded in different human chromosomes. It seems that GABA has a role also in the guidance of pollen tube to the plant ovule. ►glutamate decarboxylase deficiency disease, ►epilepsy, ►*Caenorhabditis*, ►neuron, ►cleft palate, ►neurotransmitter, ►ion channels; Ganguly K et al 2001 Cell 105:521.

Gαβγ: Heterotrimeric G-proteins and the three subunits are of 39–52, 35–36 and 7–10 kDa size, respectively. In mammalian cells, several genes are known for each subunit and their cDNAs may generate additional variations by alternative splicing. ►G proteins, ►splicing

GABA Transaminase: (16p13.3): ►GABA aminobutyrate transaminase

GABP: These are GAA sequence- (or their extension) binding heterotetrameric DNA-binding proteins (GABPα/β), members of ETS domain protein families (about 40) regulating gene transcription in a combinatorial manner with other proteins. The α subunit actually binds DNA whereas the ankyrin repeats in β recruit other protein domains. ►transcription factors, ►ETS oncogenes, ►ankyrin, ►combinatorial gene control

GABRIEL: A computer program designed to apply domain-specific and procedural knowledge for the analysis of DNA microarray data (Pan K-H et al 2005 Proc Natl Acad Sci USA 99:2118).

GAD: (Genetic Association Database, http://geneticassociationdb.nih.gov, http://hpcio.cit.nih.gov/gad.html): GAD contains information on association of genes with human diseases, primarily for medical professionals and also for the public. Anyone can submit information that will be reviewed before inclusion.

GADD45: It is a p53-inducible protein. It also binds PCNA. Deficiency of Gadd45a in mice leads to chromosomal instability, increased radiation sensitivity (cancer), and exencephaly. The GADD genes are induced by stress, inflammatory cytokines, tumor necrosis factor, transforming growth factor, and several cytokines. ►PCNA, ►p53, ►exencephaly; Takahashi S et al 2001 Cancer Res 61:1187; Kovalsky O et al 2001 J Biol Chem 276:39330.

GADD153 (growth arrest and DNA damage): A cellular enhancer-binding protein mediating stress of growth and differentiation. Under stress, it may be activated by phosphorylation of Ser^{78} and Ser^{81} residues and consequently enhanced transcription and inhibited adipose cell differentiation. It is the same as CHOP. GADD is activated under varied stress conditions. It may act also as an oncoprotein by suppressing differentiation, especially in various gene fusions brought about by chromosomal translocations. ►enhancer, ►DNA repair, ►chromosome breakage, ►cancer; O'Reilly et al 2000 Am J Physiol Lung Cell Mol Physiol 278:L552; Jousse C et al 2001 Nucleic Acids Res 29:4341; Lu B et al 2004 Nature Immunol 5:38.

GADS: A CD3 signaling adaptor that links SLP-76 to LAT. ►CD3, ►SLP-76, ►LAT

GAF: A DNA satellite-binding regulatory protein.

GAG: ►glycosaminoglycan

gag: Group-specific antigen, a viral coat protein. ►retroviruses

GAGA: A multipurpose transcriptional activator binding to the GA/CT sites in the promoter. Its major function may be to rearrange the chromatin to facilitate transcription. GAGA activates chaperones and binds to the promoter of the *Ultrabithorax* and other *Drosophila* genes. ►position effect, ►morphogenesis in *Drosophila*, ►heat-shock proteins, ►heterochromatin; Basturia A et al 2001 Development 128:2163.

GAIA Theory: Organisms contribute to a self-regulating feedback that keeps the environment stable and suitable for life. The global environment (living and non-living) determines, however, the outcome of natural selection through interacting feedback processes. (See Downing K, Zvirinsky P 1999 Artif Life 5[4]:291).

Gain: A practical measure of heritability, frequently used by animal breeders. By this criterion heritability, h^2 = (gain)/(selection differential). See graphical representation (After Lerner IM, Libby WJ 1976 Heredity, Evolution and Society, Freeman, San Francisco). The selection differential is the difference between the mean of the parental population and the mean of a portion of the parents selected for further reproduction to improve the herd. The gain/selection differential is often called *realized heritability*. The breeder may improve the gain either by increased heritability or by enhanced intensity of selection. Heritability estimates improve if environmental variation is kept at a low level by proper feeding and health care of the animals or appropriate tillage, fertilization, weed and pest control in plants. The intensity of selection is increased if the proportion of the individuals selected for parents is reduced. Although this may appear to be an easy approach to improve selection gains, the small populations may increase inbreeding and becomes counterproductive. In large mammals, the males generally have more offspring than the females. By the use of artificial insemination, the breeding value of the males can be determined even more precisely than that of the dams (see Fig. G4). Generally, the estimates improve with the age of the animals because larger number of offspring is available for evaluation. In practice, the selection is aimed simultaneously at several traits. Often these traits are negatively cor-related because high performance may make the animals (plants) more susceptible to disease. Thus, the gain in one trait may mean a loss in the others. Therefore, breeders frequently use a *selection index* that weighs each trait by a score and the total of the scores becomes the basis of the selection value. There are statistical methods for predicting the quantitative performance in a selective breeding program: $Yo = \bar{Y} + Hn(Yp - \bar{Y})$ where Yo is the predicted average performance of the progeny, Yp is the average of the two parental families selected $\bar{Y}$ = the average of the original population, Hn is heritability in the narrow sense. Example: the average number of eggs laid per year in a flock of chickens is 250, the heritability is 0.25, the average of the selected family of parents is 274, then the expectation for the offspring $Y_0 = 250 + 0.25(274 - 250) = 256$. The genetic gain from mass selection is computed from the covariance: (XY) = w = (1/2) 2σA. For determining the covariance see correlation; σ2A = additive variance (see genetic variances); the plot-to-plot environmental variance is σe2 and the plant-to-plant environmental variance = σ2we = σ2wf+σ2me and the genotype environmental variance, $\sigma^2_{G\times E} = \sigma^2_{A\times E} + \sigma^2_{D\times E}$.

If we consider the within-family variance = 0, then the gain for mass selection,

$$\Delta G_m = \frac{\frac{1}{2} i \sigma^2 A}{\sqrt{\sigma^2_A + \sigma^2_D + \sigma^2_{A\times E} + \sigma^2_{D\times E} + \sigma^2_e + \sigma^2_{me}}}$$

and i = selection intensity, σ^2_D = the dominance, $\sigma^2_{A\times E}$ = additive x environment, and $\sigma^2_{D\times E}$ = dominance x environment variances. This procedure is applicable to large populations at relative ease. In case of phenotypic recurrent selection, the equation for gain in mass selection above for cycle needs to be multiplied by 2 because the selection is applied to both parents. Additional formulas for other types of selection are to be found in Moreno-González J, Cubero, J *Plant Breeding*, pp. 281–313; Hayward MD et al eds 1993, Chapman & Hall, London, New York. ►polygenes, ►breeding value, ►selection index,

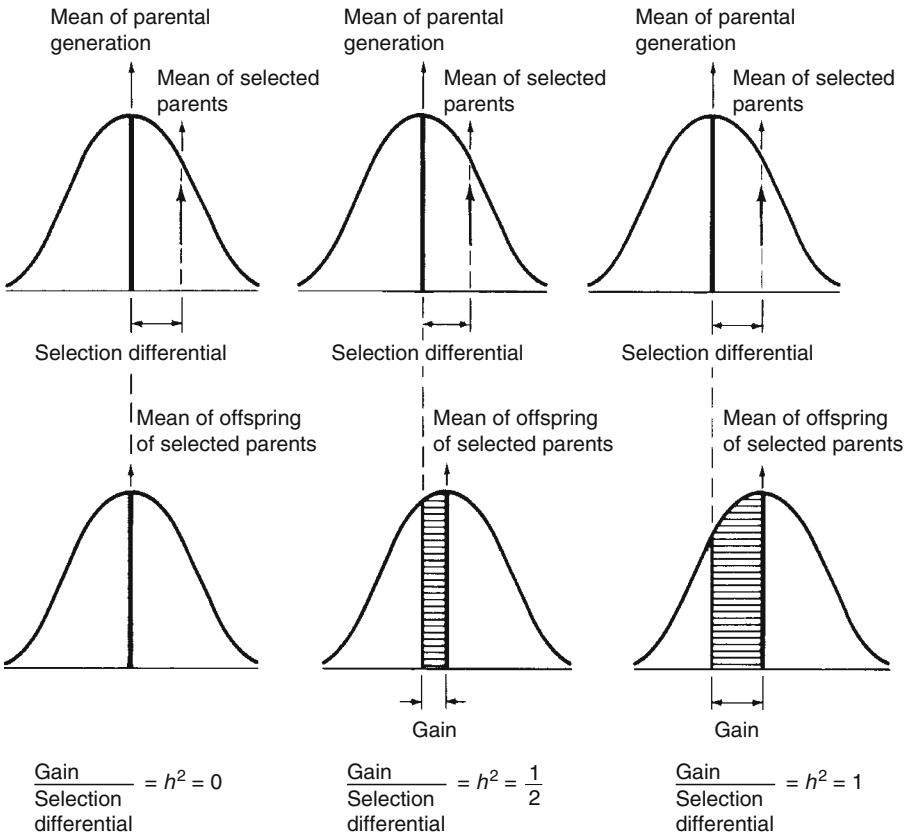

Figure G4. Gain

►quantitative genes, ►heritability, ►intraclass correlation, ►correlation

GAIN (Genetic Association Information Network): It involves private companies (Pfizer, Perlegen, Affymetrix, etc.) in a collaborative effort with the NIH to carry out genome-wide association studies for several common diseases. ►genetic association, ►genome-wide functional analysis, ►genome-wide location; http://www.fnih.org/GAIN/GAIN_home.shtml.

Gain-of-Function Mutations: Generally, mutations lead to loss of structures (for e.g., hairs or bristles) or certain function (e.g., auxotrophy). However, some of the homeotic mutants gain additional structures such as extra petals or stamens in flowers or legs on the head in *Drosophila.* These "gains" are the result of homeotic transdetermination regulated by altered transcription and/or transcript processing. ►transdetermination, ►transcription, ►processing, ►Huntington chorea, ►muscular dystrophy, ►homeotic genes, ►flower differentiation, ►loss-of-function mutation, ►dominant negative

GAL: ►galactose utilization

GAL4: A positive regulatory protein of the yeast galactose genes, it binds to a specific upstream regulatory DNA sequence. *GAL4* is activated by the interaction of Gal80p and Gal3p in the cytoplasm. In various constructs, introduced by transformation into other organisms, its activator domain is frequently utilized to boost the expression of selected reporter genes. Ubiquitylation of Gal4 seems to be required for elongation of mRNA. The F-box protein, Dsg1/Mdm30 mediates this turnover (Muratani M et al 2005 Cell 120:887). ►galactose utilization, ►activator proteins, ►reporter gene, ►transcriptional activator, ►Gene-Switch, ►p65, ►two-hybrid method, ►F-box; Hartley KO et al 2002 Proc Natl Acad Sci USA 99:1377; Peng G, Hopper JE 2002 Proc Natl Acad Sci USA 99: 8548; GAL3 and GAL80 regulatory functions: Ramsey SA et al 2006 Nature Genet 38:1082.

Galα1-3Gal: The terminal antigens present on the endothelial lining of blood vessels of majority of mammals, except humans and most primates because the latter higher animals do not have a functional 1,3-galactosyl transferase (GT). These antigens have the major role in organ graft rejection. In order to reduce

rejection, antisense technology may be used to block the synthesis of GT mRNA. Alternatively, an inhibitory ligand (aptamer) or an enzyme (H transferase) is used to add fucose (rather than galactose) to the molecule to compete in the reaction. The use of α-galactosidase may destroy the antigenic galactose terminals. ►immunity, ►xenotransplantation, ►grafting in medicine

Galactans: These are polymers of galactose. ►galactose, ►hyperacute reaction

Galactokinase Deficiency: Can be due to autosomal recessive defects at GALK1 (human chromosome 17q24) or GALK2 (chr. 15). Cataracts at infancy and hypergalactosemia occur due to this deficiency. Galactokinase converts galactose into galactose-1-phoshate. ►galactosemias, ►galactose

Galactose: One of the most common six-carbon monosaccharides differing from glucose only sterically at carbon-4 chiral centers (an epimer of glucose). It can be converted to glucose by an epimerase enzyme (UDP-Gal → UDP-Glucose) (see Fig. G5). Galactosyl groups are present in some anthocyanin, collagens, and immunoglobulins. Lactose (the milk sugar) is a disaccharide of galactose + glucose, split by the enzyme lactase. ►galactosemias, ►galactose utilization, ►chirality, ►epimers, ►galactosidase, ►galactose [see formula], ►galactose utilization, ►epilepsy, ►eye diseases, ►genetic screening

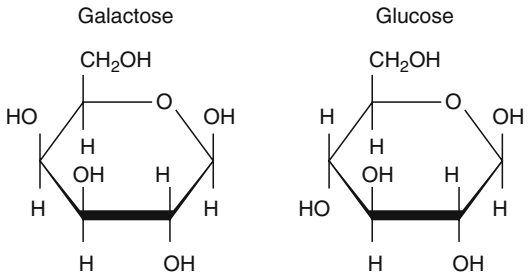

Figure G5. Galactose and glucose

Galactose Operon: ►galactose utilization

Galactose Utilization: Coordinately regulated in prokaryotes and eukaryotes. The galactose genes of *E. coli* are either clustered (*galE* [UDP-galactose-4-epimerase, *galEo* [operator], *galElp* [promoter], *galE2p* [promoter of gal*E*K], *galK* [galactokinase], *galT* [galactose-1-phosphate uridyltransferase]) all at map position 17 or gal*R* [galactose regulator] at map position 61, *galP* [galactose permease] at map position 63, and *galU* [glucose-1-phosphate uridyltransferase] at map position 27. In yeast, the uptake of galactose is mediated by galactose permease (gene *GAL2*). In the presence of ATP, galactose is phosphorylated (Gal-1-P) by galactokinase (gene *GAL*). Galactose-1-phosphate (Gal-1-P) + uridine-diphosphoglucose (UDP-glucose) generate UDP-galactose + glucose-1-phosphate by the action of galactose-1-phosphate uridyltransferase (gene *GAL7*) while the UDP-galactose-4-epimerase (gene *GAL10*) mediates the formation of UDP-glucose from UDP-galactose. Genes *GAL1, GAL7* and *GAL10* form a cluster in yeast chromosome 2 and *GAL2* is in chromosome 12. These yeast genes are coordinately inducible up to a 1000 fold by the presence of galactose although they are transcribed from separate promoters. Gene *GAL4* (linkage group 16) and gene *GAL80* (linkage group 13) regulate the GAL enzymes. *GAL4* is apparently a positive regulator of genes *1, 2, 7,* and *10* whereas some *GAL80* mutations abolish the need for induction of the same genes and convert them either to constitutive forms or make them non-inducible. It is assumed that the normal role of the product of gene *GAL80* is to prevent the transcriptional activation by *GAL4 but* the combination of the GAL1 protein with GAL80 protein inactivates the latter and then GAL1 activates GAL4, the activator of the system. This GAL1 protein is an enzyme as well as a regulator of transcription. The activation by *GAL4* depends on *upstream activating sequences* (UAS) located 200 to 400 base pair upstream of the genes, *1, 2, 7, 10* and *GAL80.* The presence of two UAS is sufficient for full expression (see Fig. G6). The consensus within the 17 bp palindromic (↔) UAS is:

Figure G6. Galactose UAS palindrome

The protein product of gene *GAL4* is about 100-kDA and it contains three essential domains. Amino acids from 1–65 are involved in DNA binding, residues 65–94 are concerned with dimerization. Amino acids 148–196 and 768–881 mediate activation of transcription (activation domain) and at the C-terminus, the sequence 851–881 also binds the *GAL80* gene. At the N-terminus, amino acid residues 10–32 display a Zinc-finger motif, common to binding proteins. At the C-terminus, there is a high density of acidic amino acids, a characteristics of regulatory proteins. The presence of inactivation by insertion elements in bacterial genomes was first recognized by a study of the *gal* operon in *E. coli*. ►galactose, ►operon, ►coordinated regulation, ►UAS, ►palindrome, ►IS elements, ►regulation of gene activity, ►Zinc fingers, ►binding proteins,

►two-hybrid method, ►galactosemia; Weickert MJ, Adhya S 1993 Mol Microbiol 10:245; Frey PA 1996 FASEB J 10:461.

Galactosemias: Autosomal hereditary diseases in humans caused by the deficiency of either the enzyme galactokinase (GALK, human chromosome 17q24) or more commonly galactose-1-phosphate uridyltransferase (GALT, 9p1, 4q263). Consequently, galactose cannot be transformed into glucose. Since the milk sugar is a disaccharide of galactose and glucose, galactose accumulates in the blood and is excreted in the urine. The accumulating galactose causes severe intestinal problems and the accumulating galactose-1-phosphate may damage the liver, brain, eye lens (cataracts) and other organs. Unless this anomaly is detected right after birth, infant death may result. By a diet free of any source of galactose, damage may be prevented. This condition is quite common, about 4×10^{-4}. A human galactokinase gene GALK is responsible also for cataracts. Deficiency of the enzyme that converts UDP- galactose ⇆ UDP-glucose, galactose epimerase (GALE, chromosome 1p35-p36) also leads to galactosemia. GALT deficiency may cause neurological dysfunctions because the reduction of galactose available for galactosyl ceramides and glycosphingolipids and the accumulation of their precursors such as glucosyl ceramides. Deficiency of UDP-galactose:ceramide galactosyltransferase (CGT, 4q26) results in thinner myelin sheets and mild ataxias, low IQ, memory deficit, reduced visuo-motor coordination, etc. Galactosemia (GALT) may cause ovary dysfunction because of the higher than normal levels of the follicle stimulating (FSH) and luteinizing hormones. ►ceramides, ►myelin, ►ataxia, ►human intelligence, ►animal hormones, ►ceramides, ►sphingolipids, ►sphingolipidoses, ►lipid; Riehman K et al 2001 J Biol Chem 276:10634.

Galactosidase-β: Probably the best studied bacterial gene, *lac* involves the determination and control of the enzyme β-galactosidase (see ►*lac* operon). The enzyme *α-galactosidase* an α-galactosyl hydrolase (melibiase, *α-galactoside galactohydrolase, ceramide trihexosidase)* is deficient in patients suffering from Fabry's disease (Xq22). In the plasma and in most of the tissues the trihexosyl ceramides Gal-Gal-Glc-Cer or Gal-Gal-Cer (Gal = galactose, Glc = glucose, Cer = ceramide) accumulate in the tissues. In various organs, extensive deposition of lipids occur and the patients suffer skin lesions, pain, paresthesia (burning, prickling sensation). In the extremities, ectasia (dilation, distention) in the skin vessels, edema (accumulation of fluids) in the legs, hypohidrosis (diminished sweating), albuminuria (protein accumulation in the urine), hyposthenuria (lowered amounts of solids in the urine) occurs. Death may result from renal failure. The disease is X-chromosome linked (q22). Heterozygous females have the same symptoms as hemizygous males but at reduced level. β-Galactosidase (a group of enzymes splitting galactosides, galactose linkages) activity is greatly reduced in patients affected by a group of human diseases called *gangliosidoses.* β-Galactosidase is a biological marker for cellular senescence. The general symptoms involve deterioration of psychomotor (brain and movement) activities, severe bony deformities and generally death by the age of two. These diseases occur in all ethnic groups as incurable autosomal recessive defects. Heterozygotes may be detected by β-galactosidase assays and the diseases can be identified by amniocentesis. ►galactose utilization, ►Fabry's disease sphingolipidoses, ►gangliosidosis general, ►Krabbe's leukodystrophy, ►lactosyl ceramidosis, ►*Lac* operon, ►Xgal; Pshezhetsky AV, Ashmarina M 2001 Progr Nucleic Acid Res Mol Biol 69:81)

Galactosyl Ceramide Lipidosis: ►Krabbe's leukodystrophy

1,3-Galactosyltransferase, α: Synthesizes α1-3-galactose epitopes, which are the major antigens causing rejection of pig to human xenotransplants. Knocking out or mutation in the gene responsible for the enzyme may render the organs more suitable for xenotransplantation. The majority of mammals—with the exception of humans, apes and Old World monkeys—carry a gene for this enzyme. ►xenotransplantation; Phelps CJ et al 2003 Science 299:411.

Galago: ►Lorisidae

Galanin: A bioreactive peptide (in humans Gly-Trp-Thr-Leu-Asn-Ser-Ala-Gly-Tyr-Leu-Leu-Gly-Pro-His-Ala-Val-Gly-Asn-His-Arg-Ser-Asp-Lys-Asn-Gly-Leu-Thr-Ser). Its composition is somewhat different in pigs or rats. In humans, it inhibits acetylcholine and glutamic acid release. It also reduces excitability of spinal neurons and blocks voltage-activated Ca^{2+}-channels. It may be involved in behavioral and cognitive deficits in Alzheimer disease. Its effects in other mammals are similar. ►ion channels, ►Alzheimer disease, ►acetylcholine, ►glutamica; Steiner RA et al 2001 Proc Natl Acad Sci USA 98:4184.

Galectin: A β-galatoside binding protein regulating growth and immunological responses. It may induce apoptosis in activated human T cells. Galectin-1 and -3 are part of the spliceosome where they interact with the Gemin4 protein. ►apoptosis, ►T cell; Park JW et al 2001 Nucleic Acids Res 29:3595; Wang JL et al 2004 Biochim Biophys Acta 1673:75.

Gall: A generally undifferentiated tissue growth in plants, caused by infection. ►crown gall

Gallstone: ►cholelithiasis

GALT (gut-associated lymphoid tissue): ►Peyer's patches

Galtonian Inheritance: Francis Galton (1822–1911), father of quantitative genetics formulated the rules for Galtonian Inheritance in different ways. He recognized that his ideas on "ancestral heredity" were partly inconsistent with the observed facts. His application of the concept of regression to the inheritance of multifactorial traits remained essentially correct and contributed to the modern concepts of heritability. By rejecting Darwins's pangenesis and suggesting the concept of "stirpes", he essentially laid the path to the concepts of hard heredity and particulate inheritance. His idea may still be applicable to the inheritance of organelle-coded functions: "We appear, to be severally built up out of a host of minute particles, of whose nature we know nothing, any one of which may be derived from any one progenitor, but which usually transmitted in aggregates, considerable groups being derived from the same progenitor. It would seem that while the embryo is developing itself, the particles, more or less qualified for each post, as it were in competition to obtain it. Also, the particle that succeeds must owe its success partly to accident of position and partly of being better qualified than any equally well-placed competitor to gain lodgment." (Galton F 1889 Natural Inheritance, New York). ►polygenic inheritance, ►correlation, ►heritability, ►hard heredity, ►sorting out, ►pangenesis; Roberts HF 1965 Plant Hybridization Before Mendel. Hafner, New York; Kevles DJ 1995 In the Name of Eugenics: Genetics and the Uses of Human Heredity, Harvard University Press, Cambridge, Massachusetts.

gam: ►lambda phage, ►Charon vectors

GAMBIT (genomic analysis and mapping by in vitro transposition): By knowing the sequence of the genome and specificity of the target of a transposon, using transposons all the essential genes containing the target sequence can be inactivated and thus their function revealed. ►targeting genes, ►insertional mutation, ►saturation mutagenesis; Kamichhane G et al 2003 Proc Natl Acad Sci USA 100:7213.

Gamborg Medium (B5): Developed for plant tissue culture, it is suitable for growing callus and different plant organs. Composition mg/L: KNO_3 2500, $CaCl_2.2H_2O$ 150, $MgSO_4.7H_2O$ 250, $(NH_4)_2SO_4$ 134, $NaH_2PO_4.H_2O$ 150, KI 0.75, H_3BO_3 3.0, $MnSO_4.H_2O$ 10, $ZnSO_4.7H_2O$ 2.0, $Na_2MoO_4.2H2O$ 0.25, CuSO4.5H2O 0.025, CoCl2.6H2O 0.025, Ferric-EDTA 43, sucrose 2%, pH 5.5, inositol 100, nicotinic acid 1.0, pyridoxine.HCl 1.0, thiamine. HCl 10, kinetin 0.1, 2,4-D 0.1 - 1.0. The microelements, vitamins and hormones may be prepared in a stock solution and added before use. For kinetin other cytokinins may be substituted such as 6-benzylamino purine (BA) or isopentenyl adenine (or its nucleoside), for 2,4-D (dichloro-phenoxy acetic acid), naphthalene acetic acid (NAA) or indole acetic acid (IAA) may be substituted or a combination of the hormones may used in concentrations that is best suited for the plant and the purpose of the culture. For solid media use agar or gellan gum. Heat labile components are sterilized by filtering through 0.45 µm syringe filters. This medium may be purchased from commercial suppliers in a dry mix ready to dissolve. ►Murashige & Skoog medium, ►embryo culture, ►cell culture, ►cell fusion, ►agar, ►gellan gum, ►plant hormones; Wetter LR, Constabel F (Eds) 1982 Plant Tissue Culture Methods Prairie Res Lab Saskatchewan, Canada.

Game Theory: Deals with decision-making under uncertainty. Before a decision is made, the probabilities of a set of actions, e.g., p(1) and p(2) must be assessed, generally by a subjective manner. An essential feature is a strategy that assures the maximal rewards for the good decisions. Such a procedure is most widely used in the business world (marketing) under competitive conditions. It may be applied also to natural sciences and evolution where exact statistical methods are not practical due to the variability and uncertainty of the conditions.

Decision-making involves computational tasks of the human brain and the Bayesian theorem provides statistical tools for the assessment of the roles of various kinds of uncertainties. In the neocortex and hippocampus of the brain, acetylcholine and norepinephrine have synergistic and permissive roles in assessing the *expected uncertainty* of environmental cues whereas norepinephrine is involved in the *uncertainty of the unexpected* based on a priory experience. Michel I. Posner, neurobiologist posited that a cue predicts a certain target by some degree of probability, called *cue validity*. Correctly cued target stimuli are processed more rapidly than incorrect ones. Acetylcholine level inversely varies with cue validity and thus indicates expected uncertainty. Physiological experiments with rodents and primates support this conclusion. Norepinephrine, in contrast, does not consistently interact with the probabilistic cuing task after the initial acquisition (Yu AJ, Dayan P 2005 Neuron 46:681). This model combines the physiological effects of neuromodulators and sensory cues for decision-making. ►prisoner's dilemma, ►winner's curse, ►Bayes' theorem, ►acetylcholine, ►animal hormones; Binmore K, Samuelson L 2001

J Theor Biol 210(1):1; Sigmund K 2001 Theor Popul Biol 59:3; Stearns SC 2000 Naturwiss 87(11):476; Demetrius L, Grundlach VM 2000 Math Biosci 168(1):9.

Gamergate: Exceptional worker (reproductive female) in social insects that mates and can lay eggs. ►social insects

Gametangia: Sex organs of fungi; oogonium in the "female" and antheridium in the "male."

Gamete: Haploid male or female generative cell (egg, sperm). Gametic fusion (formation of the zygote) takes place during sexual reproduction. The zygote (2n) has twice the number of chromosomes of the haploid (n) gametes. ►gametogenesis, ►fertilization, ►germ cell

Gamete Competition: If multiple gametes are available, their success in fertilization may be determined by genetically controlled viability or vigor. It occurs commonly among sperms of animals and plants, pollen tubes (certation) and also among eggs in multiparous animals or in plants where more than one megaspore of the tetrad may produce the egg. ►certation, ►meiotic drive, ►selective fertilization, ►preferential segregation, ►segregation distorter

Gametic Array: Gametic array of diploids, in case of independent segregation, can be determined by different procedures:

In a dihybrid: (A + a)×(B + b) = AB, Ab, aB, ab in a trihybrid: (A + a) × (B + b) × (C + c) = ABC, ABc, AbC, Abc, aBC, aBc, abC, abc or using any type of gene symbols such as I/i, R/r A/a the combinations can be read from left to right by following the paths of the arrows and at right we obtain the gametic arrays (see Fig. G7). In general, in diploids, in case of independent segregation, the gametic output can be determined by 2n where n corresponds to the number of allelic pairs, e.g., in a trihybrid cross $2n = 2^3 = 8$ as derived above. For gametic array in autopolyploids and trisomics see autopolyploidy and trisomy, respectively. ►Mendelian segregation

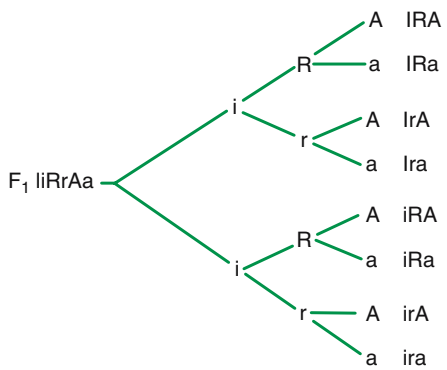

Figure G7. Derivation of gametic combinations

Gametic Lethal: Death at the egg or sperm stage. ►zygotic lethal

Gametocide: Any chemical that causes male sterility. They may be used in plant breeding to sparse the efforts of emasculation in large-scale hybridization or may be used as birth-control agents when applied shortly before copulation. Some gametocidal genes induce chromosome breakage during interphase. ►male sterility

Gametocyte: A cell that produces gametes. ►*Plasmodium*

Gametogenesis: The animal egg is formed by differentiation without further cell division from a haploid product of meiosis and so do the spermatozoa from the spermatids. (See Fig. G8 for development of the female and male gametes of higher animals and plants) Basically, gametogenesis in animals and plants shows substantial similarities because in both cases it is based on meiosis. The processes of gametogenesis are regulated in a complex manner by various hormones. In animals, the primordial germ cells colonize the gonads (spermatocytes and oocytes) through the mediation of chemokines such the stromal cell-derived factor-1 and its receptor CXCR4 (Ara T et al 2003 Proc Natl Acad Sci USA 10:5319). These chemokines control diverse other developmental processes too. More than 2,300 genes produce germ cell-specific transcripts (Schultz N et al 2003 Proc Natl Acad Sci USA 1000:12201). In *Caenorhabditis*, according to one study, 132 proteins are enriched during spermatogenesis and 444 during oogenesis whereas 370 are enriched during the formation of both types of gametes (Chu DS et al 2006 Nature [Lond] 443:101). Sparmatogonial stem cells transplanted into immature testes produce viable sperm cells even when the donor is rat and the recipient is mouse. Through such a procedure the xenogeneically produced spermatozoa yielded viable rat offspring when microinjected into rat oocytes (Shinohara T et al 2006 Proc Natl Acad Sci USA 103:13624). In mice in addition to "actual stem cells", which are normally self-renewing, a second population ("potential stem cells") also exists, which is capable of self-renewing but do not self-renew in the normal situation. Potential stem cells rapidly turn over in normal testes, suggesting that they belong to the transit-amplifying, rather than the dormant, population. During the long natural course, actual stem cells are occasionally lost and compensated for by progeny of their neighbors (Nakagawa T et al 2007 Dev Cell 12:195). ►spermiogenesis, ►gametophyte, ►germ cells, ►histone variants, ►protamines, ►animal hormones, ►GDNF, ►Wolffian ducts, ►Müllerian ducts, ►hedgehog, ►azoospermia, ►atresia, ►synergid, ►CXCR, ►SDF, ►stem cells

G

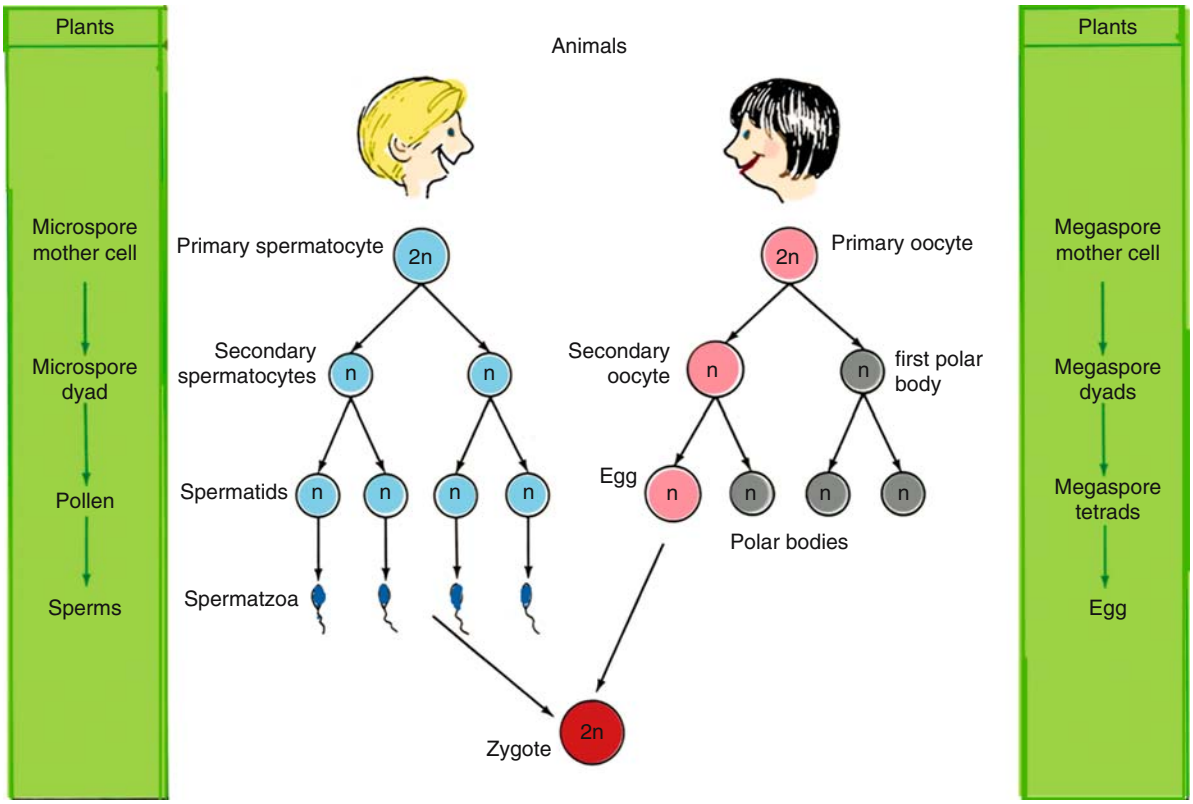

Figure G8. Comparative view of animal and plant gametogenesis

Gametophore: Leafy shoots of mosses bearing gametangia. ►gametangia

Gametophyte: The cells resulting from the meiosis of plants that have half the chromosome number of the zygotes. The gametophytes (megaspores, microspores) will form the gametes (egg and sperm). Selection at the gametophyte level is much more effective than in the sporophytic generation when the intended target of the selection is expressed at this developmental stage. The effectiveness of selection is particularly needed when the frequency of the gene selected for is low. Selection at the haploid level was apparently successful for tolerance to herbicides, toxins secreted by pathogens, alcohol dehydrogenase mutations, and possibly against certain stress effects. There are evolutionary variations in gametophyte structures (Friedman WE 2006 Nature [Lond] 441:337).

CHR11 chromatin remodeling factor is essential for the development of the female gametophyte in *Arabidopsis* (Huanca-Mamani W et al 2005 Proc Natl Acad Sci USA 102:17231). The effectiveness of selection is particularly needed when the frequency of the gene selected for is low. Selection at the haploid level.

In the somatic cells of flowering plants a germline-restrictive silencing factor (GRSF) suppresses the expression of genes required for the function of the sperms by binding to the promoter of silencing sequences in lily and *Arabidopsis* (Haerizadeh F et al 2006 Science 313:496). Mutant *cdka1* pollen has only a single nucleus, which results in lack of fertilization of the diploid endosperm and consequently in seed sterility in *Arabidopsis* (Nowack MK et al 2006 Nature Genet 38:63). In the absence of the *FIS*-class genes the *cdka1* plants can produce reduced size maternal endosperm, which is smaller yet weakly functional (Nowack MK et al 2007 Nature [Lond] 447:312). See Figs. G9 and G10; ►sporophyte, ►cytoplasmic male sterility, ►male sterility, ►pollen competition, ►certation, ►gametophyte factor, ►incompatibility alleles

Gametophyte Factor: Affects the haploid gametophyte and may be responsible for reduced transmission of the chromosome (gamete) that carries it in a heterozygote. Gametophyte factors generally have more detrimental effect on the male but in rare cases the female is also influenced to various degrees. ►certation, ►gametophyte, ►meiotic drive, ►preferential segregation, ►selective fertilization, ►zygotic lethal, ►pollen-pistil interactions; Swanson R et al 2004 Annu Rev Genet 38:793.

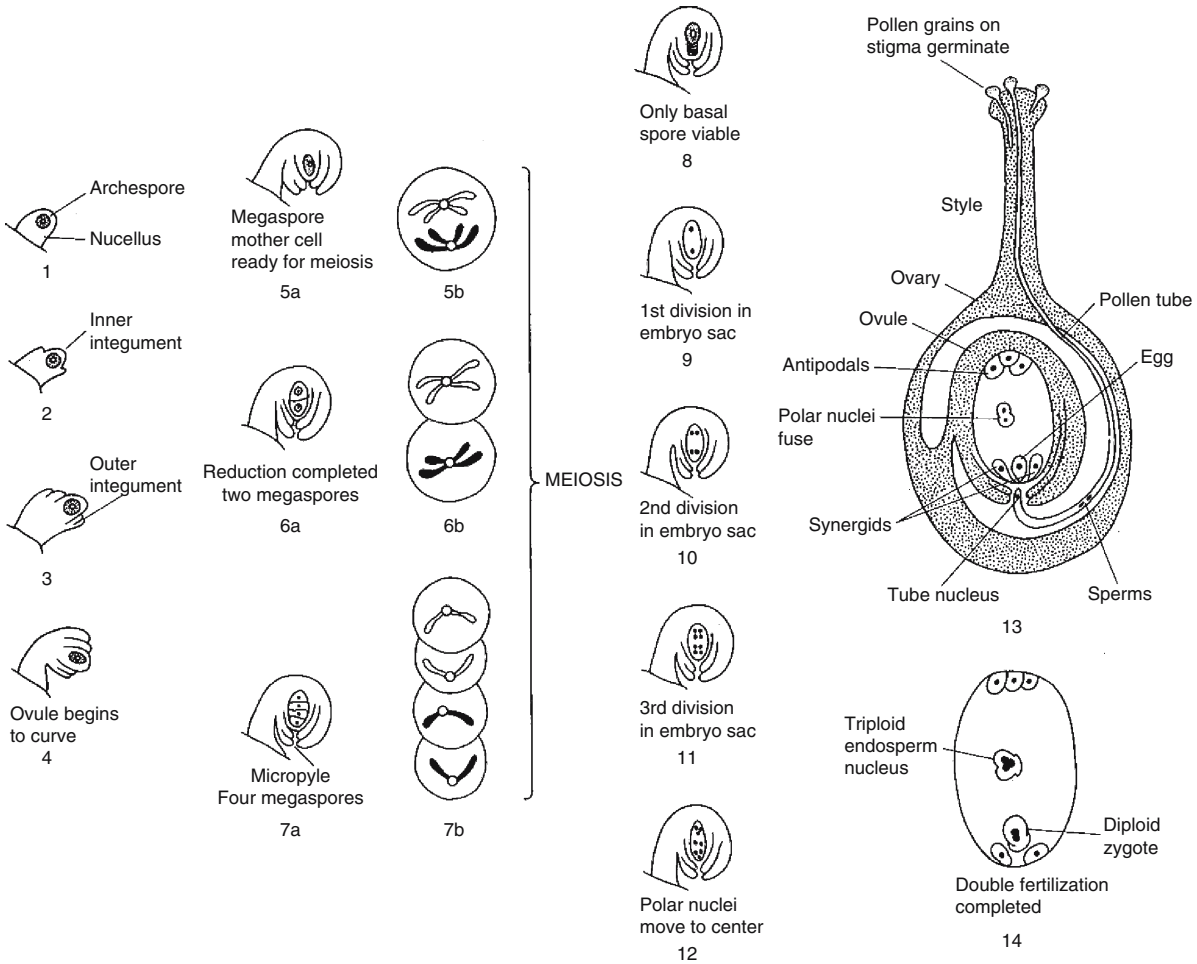

Figure G9. Development of the female gametophyte of higher plants. (The meiotic stages show only one bivalent)

Gamma (γ): The risk for a disease or other attribute associated with a particular genotype. ►risk

Gamma Distribution: Distribution of the amount of time until the x^{th} occurrence of an event by the Poisson distribution. It has been used to fit the evolutionary rate variation among protein sites. The gamma distribution and similar statistical concepts serve for the theoretical

$$f(x) = \frac{1}{\Gamma(n)} e^{-x} x^{n-1}, \text{ the } \Gamma(n) = \int_0^\infty e^{-x} x^{n-1} dx,$$

$$\text{when n is an integer } \Gamma(n) = (n-1)!$$

foundations for the t-distribution, F-test and chi square frequently used in genetic analyses. ►Poisson distribution, ►t-test, ►F-test

Gamma Field: An area or space where chronic exposure is usually provided from a source of electromagnetic radiation (e.g., ^{60}Co). Such a field may help in studies assessing the effects of long-term exposures on various biological materials (mutation, chromosome breakage, physiological changes) in case of nuclear accidents. ►electromagnetic radiation, ►radiation effects, ►radiation hazard assessment, ►radiation protection, ►gamma rays

Gamma Interferon Activation Site (GAS): TTNCNNNAAA. ►signal transduction, ►Jak-STAT, ►ISRE, ►STAT, ►interferon

Gamma Rays: These are ionizing radiations (photons, electromagnetic radiation) emitted by isotopes (such as ^{137}Cs, ^{60}Co, and others). They are similar to X-rays but have much higher energy and have an ability to traverse even several centimeters of lead. Gamma rays from ^{60}Co (1.2 - 1.3 MeV) have a linear energy transfer 0.3 LET compared to hard X-rays (250 keV). [LET measures ionizing radiation in keV/nm path]. ►physical mutagens, ►electromagnetic radiations, ►Volt, ►eV

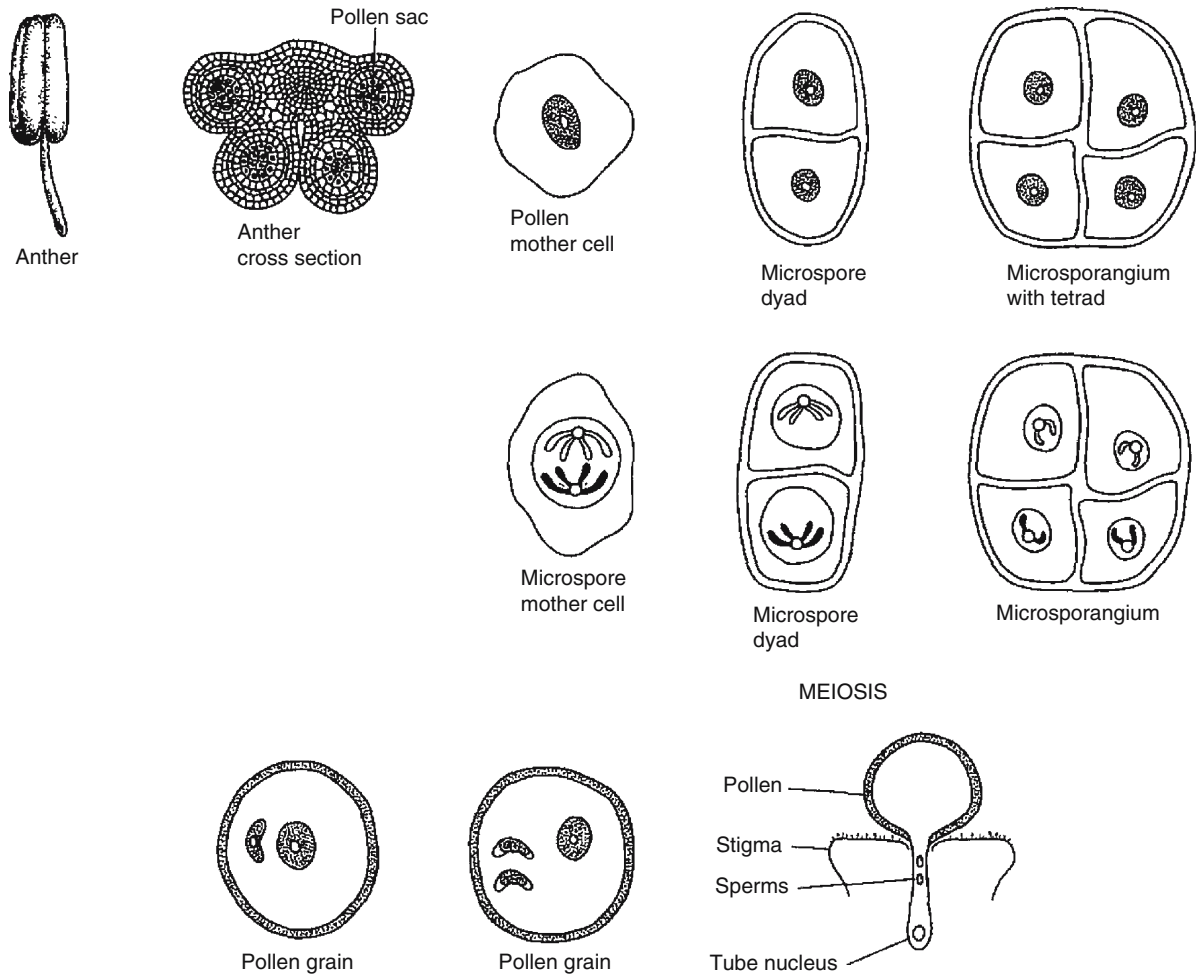

Figure G10. Development of the male gametophyte of higher plants. The meiotic stages (showing only one bivalent)

Gamma Selection Parameter: $\gamma = 2N_e s$ where N_e is the effective population size and s is the selection coefficient. ►effective population size, ►selection coefficient

Gammaglobulin: An immunoglobulin (IgG) consisting of either the light chains κ or γ and the heavy chains have one of the $C_{\gamma 3}$, $C_{\gamma 1}$, $C_{\gamma 2}$, $C_{\gamma 4}$ coded constant regions. ►antibody, ►immunoglobulins, ►agammaglobulinemia, ►immunodeficiency

Gammopathy: A condition of defective immunoglobulin (gammaglobulin) synthesis.

Gamodeme ►deme

Gancyclovir: (GCV): A guanine analog, 9-[1,3-dihydroxy]-2-propoxymethylguanine) and a derivative of gancyclovir (2-amino-1,9-dihydro-9-[{2-hydroxyethoxy} methyl]-6-H-purine-6-one, DCV). Both are antiviral (herpes) and anticancer drugs when incorporated into DNA because the analogs will prevent further replication of the genetic material (see Fig. G11). GCV requires activation, usually by herpes virus thymidine kinase (HSV-TK) that converts it to a monophosphate form and subsequently cellular kinases mediate the production of the toxic triphosphate. ►suicide vector, ►adoptive cell therapy, ►see shingles for acyclovir structure

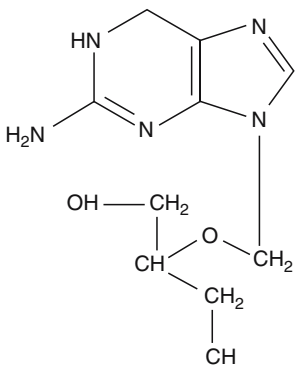

Figure G11. Gancyclovir.

Ganglion: A group of nerve cells outside the central nervous system.

Ganglioneuromatosis: ►MEN, ►tyrosine receptor kinase

Gangliosides: These are sphingolipids containing several units of acidic sugars attached to the fatty acid chain; they are common in nerve tissues. Their synthetic pathway is:

Uridine-diphosphate[UDP]-glucose + ceramide → glucosyl ceramide + UDP-galactose → galactosyl-glucosyl ceramide. Galactosyl-glucosyl ceramide + cytidine monophosphate-N-acetyl-neuraminic acid (CMP-NANA) → ganglioside G_{M3}. Ganglioside G_{M3} + UDP-N acetyl-galactosamine → ganglioside G_{M2} + UDP. Ganglioside G_{M2} + UDP galactose → ganglioside G_{M1} + UDP. Ganglioside G_{M1} + nCMP-NANA → higher gangliosides. If the sialic acid group (acetyl neuraminic acid, glucosyl neuraminic acid) is removed, asialogangliosides are generated. Several diseases, sphingolipidoses, are involved in their accumulation and breakdown. Ganglioside synthesis is indispensable for the normal development of the central nervous system and its absence leads to neurodegeneration and death. ►sphingolipids, ►sphingolipidoses, ►gangliosidoses, ►unfolded protein response, ►cancer gene therapy, ►Tay-Sachs disease; Kolter T et al 2002 J Biol Chem 277:25859.

Gangliosidoses: It includes a variety of forms. The general gangliosidosis Type I is β-galactosidase deficiency (3p21.33) disease leading to severe, progressive degeneration of the brain and death by the age of two. The overall symptoms resemble the Tay-Sachs disease caused by hexoseaminidase A deficiency and the Niemann-Pick disease brought about by sphingomyelinase deficiency. The newborns already show abnormally low activity accompanied by facial and other edemas (fluid accumulation). The distance between the upper lip and nose is enlarged, the ears are set low, there is light hairiness on the front and neck, the spinal column is deformed, the fingers are short, poor appetite and lethargy and general weakness. The liver and spleen become enlarged. Type II juvenile gangliosidosis has a later onset, and death is delayed to age four to five. This form has also very low β-galactosidase levels yet another enzyme seems to be involved. In contrast to Type I disease, in Type II liver and spleen enlargement as well as bone deformities are absent. The heterozygotes can be identified by β-galactosidase assay and the recurrence may be avoided by genetic counseling. Type III is an adult form and it is controlled by a locus different from that of type I. Besides the autosomal Type III, there is an X-linked GM3-gangliosidosis and the latter affects young children. The classification of gangliosidoses is quite complicated. ►GM-gangliosidoses, ►galactosidase, ►sphingolipidoses, ►sphingolipids, ►Tay-Sachs disease, ►Sandhoff's disease, ►spleen

Gap: An unknown sequence in between contigs, gapped genome. Before a first-draft sequence is produced filling must close the gaps in the sequences that may exist between contigs. ►contig, ►first-draft sequence, ►genome projects; Frohme M et al 2001 Genome, Res 11:901.

GAP: GTPase activating protein is encoded in the long arm of human chromosome 5. Tyrosine-phosphorylated GAP is in the cell membrane whereas the unphosphorylated is mainly in the cytosol. RHO and RAS-related GTPases are abundant in the cells and they regulate signal transduction and the cytoskeleton. ►RAS, ►RHO, ►GTP, ►signal transduction, ►GED, ►von Recklinghousen disease, ►RanGTPase; Ross EM, Wilkie TM 2000 Annu Rev Biochem 69:795.

GAP Genes: Gap genes in *Drosophila* have some segments missing or have fused segments (see Fig. G12). The body pattern is along the longitudinal axis (posterior→ anterior) of the wild type *Drosophila* embryo. Some of the gap mutations delete and/or modify the segments. ►morphogenesis, ►morphogenesis in *Drosophila*, ►*knirps*, ►*Krüppel*

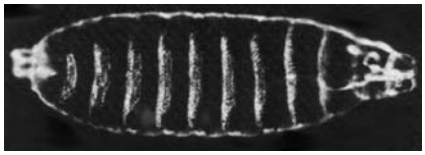

Figure G12. Body segments

Gap Junctions: The connecting channels (made of connexins) between apposed cells that permit the transfer of molecules and electric signals between cells. Peptides, such as the class I MHC molecules, up to 1,800 molecular weight may be transmitted between neighboring cells unless the three-dimensional structure interferes (Neijssen J et al 2005 Nature [Lond] 434:83). The same task in plants is assigned to plasmodesmata. Carcinogenic agents may block gap junctions. The function of gap junction can be monitored through transfer of fluorescent dyes or by complementation of nutrients. ►connexin, ►hemichannel, ►innexins, ►plasmodesma, ►CAM, ►MHC, ►Charcot-Marie-Tooth disease, ►oculodentodigital dysplasia; Kumar NM, Gilula NB 1996 Cell 84:381; connection formation: Shaw RM et al 2007 Cell 128:547.

Gap Penalty: When similarities are sought in nucleotide alignments for the sake of construction of evolutionary trees (or determine relatedness) and gaps are encountered, these are subtracted from the matches to avoid unwarranted conclusions regarding homologies.

GAPO Syndrome: Autosomal recessive defect characterized by retarded growth, reduced hair development (alopecia) toothlessness (pseudoanodontia) and progressive wasting of the optical nerves. It bears similarity to progeria. ►progeria, ►growth retardation, ►Gombo syndrome

G

Garden of Eden: The evolutionary theory supposes that the human population originated from single group and about 100,000 years ago, after passing through several bottlenecks, they differentiated into several subpopulations and dispersed from Africa. ►out-of-Africa hypothesis, ►multi-regional origin; Ambrose SH 1998 J Hum Evol 34:623.

Gardner Syndrome (APC, adenomatous polyposis of the colon; mutation in FAP): An autosomal dominant (human chromosome 5q21-q22, 8535 bp) familial polyposis of the colon (FPC). Mutation or deletion occurring at a frequency of about $2–3 \times 10^{-5}$ (in Ashkenazim populations the carrier frequency may exceed 7%), and it may cause adenomatous intestinal polyposis (a cancer) and breast cancer. Penetrance is very high and the prevalence in the general population is ~1/8,000. The syndrome includes several symptoms, especially if the genetic lesion extends to a larger segment in the region of several genes nearby. Congenital hypertrophy of the retinal pigment epithelium (CHRPE) may be an early diagnostic sign. In some cases, the polyps are limited only to the colon but there are cases where other parts of the intestinal tract, the stomach, the forehead, soft bony tissues, epidermal cysts may also become tumorous. Some forms were associated with increased ornithine decarboxylase activity. Pre-symptomatic diagnosis may detect deletions by the use of appropriate DNA markers. Gene targeting experiments revealed the deletion of exon 14 of APC leads to rapid development of adenomas in mice. In the absence of the WNT morphogenetic signal, APC interacts with glycogen synthase kinase (GSK) and β-catenin. In this case, the Tcf (T cell transcription factor) and Lef (lymphoid enhancer factor) are blocked and the complex leads to tumor suppression. If APC is inactivated monomeric β-catenin appears in the cytoplasm and tumors are formed. Catenin seems to be a transcriptional co-activator of Tcf and Lef. The APC tumor suppressor has apparently a nuclear export function. The c-MYC oncogene is repressed by the wild type APC protein but activated by β-catenin through Tcf-4 binding sites in the MYC promoter. APC appears to link microtubules (spindle fibers) to the kinetochore, more specifically the Bub protein, a mitotic checkpoint control kinase. This large gene locus includes 15 exons with phenotypic difference among the different allelic mutations/deletions and this causes some ambiguity in the nomenclature. APC is generally associated with chromosomal instabilities because mutation in the APC protein no longer controls the regular function of the kinetochore and its association with the spindle fibers. ►colorectal cancer, ►FAP, ►skin diseases, ►cancer, ►polyposis, ►Turcot syndrome, ►Muir-Torre syndrome, ►targeting gene, ►Cre/LoxP, ►exon, ►adenoma, ►WNT, ►catenins, ►conductin, ►kinetochore, ►spindle fibers, ►GSK, ►MYC, ►hereditary non-polyposis colorectal cancer, ►desmoid disease hereditary, ►mismatch repair; Bienz M, Clevers H 2000 Cell 103:311; Su L-K et al 2000 Am J Hum Genet 67:582; Livingston DM 2002 Nature [Lond] 410:536; Fearnhead NS et al 2001 Hum Mol Genet 10:721; Haigis KM, Dove WF 2003 Nature Genet 33:33.

Gargoylism: A defect in L-iduronidase such as in the Hurler and Hunter syndromes. ►mucupolysaccharidosis

Garlic (*Allium sativum*): A spice, 2n = 16. Its alliin (allicin) component inhibits cystein proteinases and thereby may exert antibiotic effects on some parasitic microorganisms (see Fig. G13). Its ajoene (sulfur-rich) extract may be antimitotic, microtubule-regulatory, anti-hypertension and anticarcinogenic. ►onion; Li M et al 2002 Carcinogenesis 23:523; Ledezma E et al 2004 Cancer Lett 206:35, Macpherson LJ et al 2005 Current Biol 15:929.

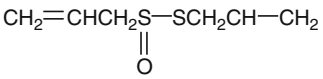

Figure G13. Allicin

GAS: ►gamma interferon activation site, ►interferons, ►signal transduction

Gas Chromatography: ►chromatography, ►gas-liquid chromatography

Gas-Liquid Chromatography (GLC): GLC is suited for the separation of volatile compounds according to their ability to be dissolved in the material of the column bed. An inert gas (helium) driven through the column carries the volatile compounds, and they are sequentially eluted and collected. Some material must be converted to more volatile derivatives before applied to the columns. This method has been

extensively used to separate and isolate fatty acids and other compounds. ►chromatography

Gastric Cancer (hereditary diffuse gastric cancer, HDGC, 16q22.1, 5q31.1): As the chromosomal locations indicate two forms of gastric cancer are known. One of them involves a methylation of 6–18 CpG nucleotides in the cadherin1 (CDH1, 16q22) promoter leading to inactivation. Predisposing genes: non-polyposis colon cancer, familial adenomatous polyposis, Peutz-Jeghers syndrome and the Cowden disease. ►cadherins, ►hereditary nonpolyposis colon cancer, ►Gardner syndrome, ►polyposis hamartomatous, ►multiple hamartoma syndrome

Gastrin: Hormones of 14 to 34 amino acid residues, released in the stomach and regulate stomach acid secretion, other enzymes and esophagal and gall bladder contraction.

Gastroenteritis: Inflammation of the lining of the stomach and intestines.

Gastrointestinal Stromal Tumor, Familial: ►KIT oncogene

Gastroschisis: A fissure of the abdominal cavity and some of the intestines are protruded through failure of the wall of the abdomen. The pattern of inheritance is unclear. ►omphalocele

Gastrula: An early stage of embryonic development following the blastula. Gastrulation patterns vary in different animal taxa. The general pattern is an invagination of the epithelial layer into the blastocoel (at the so-called vegetal pole) forming the endoderm that gives rise later to the gut. The outer layer, the epithelium, becomes the ectoderm that will form the epidermis and the nervous system. The cells in-between these two layers develop into a mesoderm that will differentiate into the notochord (a vertebral column or its substitute), into the connective tissues, bones, cartilages, fibers, muscles, the urogenital system and the vascular system, including the heart and blood vessels. Gastrulation of the human embryo takes place during the third week of embryonal development (in mice 6–7 days post coitum). In arthropods, gastrulation is followed by anterior-posterior segmentation and dorsal-ventral, medial-lateral identification of embryonal regions. ►blastula, ►morphogenesis, ►coitus, ►organizer, ►embryo node, ►p38

GATA: Mammalian transcription factors mediating the formation of erythrocytes. GATA-1 (Xp11.23) recognizes the $\frac{\text{TGATAG}}{\text{ACTATC}}$ or very similar upstream DNA sequences. Several other GATA factors have been identified also in other vertebrates. GATA-3 (10p15) is a human hematopoietic factor responsible also for the differentiation of T cells of the immune system. Loss of GATA3 results in noradrenaline deficiency and embryonic lethality in mice. GATA factors may include 4 Zinc finger domains. Mutation in GATA1 results in dyserythropoietic anemia and thrombocytopenia. GATA-2 and GATA-3 regulate adipocyte differentiation and their deficiency may lead to obesity. GATA-4 (8p22-p23), GATA-5 and GATA-6 are expressed on the developing heart. ►transcription factors, ►hematopoiesis, ►T cell, ►T-bet, ►DNA-binding protein domains, ►erythropoietin, ►dyserythropoietic anemia, ►thrombocytopenia, ►obesity, ►transcriptional priming, ►DiGeorge syndrome, ►noradrenaline; Charron F, Nemer M 1999 Semin Cell Dev Biol 120:85; Molkentin JD 2000 J Biol Chem 275:38949; Patient RK, McGhee JD 2002 Current Opin Genet Dev 12:416.

Gatekeeper: ►selectivity filter

Gatekeeper Gene: It acts in the pathway of carcinogenesis by representing a certain threshold that must be passed before mutation of the tumor suppressor or activator gene(s) can mediate the development of the recognizable oncogenic transformation. Genes preventing other cellular processes are also called gatekeepers. ►oncogenic transformation, ►oncogenes, ►transformation oncogenic, ►progression, ►cancer, ►phorbol esters, ►caretaker gene; Kinzler KW, Vogelstein B 1997 Nature [Lond] 386:761; Gomis-Ruth FX, Coll M2001 Int J Biochem Cell Biol 33 (9):939.

Gating in Cytometry: Used for typing different cells (e.g., $CD4^+$, $CD8^+$ lymphocytes) in cytometers. The gates permit the selective identification and counting of specific type on the basis of fluorochromes or antibody, etc. labels. The procedure may facilitate the clinical evaluation of the status of, e.g., AIDS patients. ►acquired immunodeficiency; Bergeron M et al 2002 Cytometry 50:53.

Gateway Cloning: A procedure for large-scale identification of open reading frames (ORFeome) in order to annotate the genome and determine the protein-coding open reading frames. The outline of the protocol: 1. Collect a large set of open reading frames from databases. 2. Establish a large number of appropriate primers. 3. Carry out PCR on the cDNA library. 4. Clone recombinant sequences into *E. coli* plasmid vector. 5. Isolate the cloned plasmids. 6. Sequence tagged ORFs (OSTs) and obtain Phred score. 7. Align the ORFs on genomic sequences. 8. Identify thus the location of ORFs and can enter them into a database (Reboul J et al 2003 Nature Genet 34:35). ►ORF, ►ORFeome, ►OST, ►polymerase chain reaction, ►Phred

Gaucher Disease: A chromosome 1q21 recessive complex of glucosyl ceramide lipidoses. There are six genes and two pseudogenes within a 75 kb region and ten different crossing over sites and shared CACCA recombinational hot spots were detected (Tayebi N et al 2003 Am J Hum Genet 72:519). Glucosyl ceramide sphingolipids accumulate in the reticuloendothelial "Gaucher cells" because of deficiency of a β-glucosidase (glucosylceramidase). These Gaucher cells occur in the lymphoid tissues, spleen, bone marrow, inside the veins, lung alveoli and other tissues. The Type I disease occurs in various age groups and the most characteristic symptoms are enlargement of the spleen and bone anomalies. The neuronopathic or malignant Type II form appears before age of six months and results in death by the age of two. The cranial nerves and the brain stem are attacked although there is not much lipid accumulation in these tissues. The less severe juvenile form (Type III) may permit survival to the age of thirty years. Gaucher's disease is of relatively common occurrence. Cure can be provided by enzyme replacement therapy. A mouse model indicates that transplantation of bone marrow or gene therapy through retroviral transduction either prevented or corrected the disease (Berglin Enquist I et al 2006 Proc Natl Acad Sci USA 103:13819). Prenatal diagnosis is feasible by the use of RFLP and enzyme assays. ►sphingolipid, ►sphingolipidoses, ►glucosidase, ►RFLP, ►prenatal diagnosis, ►lysosomal storage disease Jews and genetic diseases, ►enzyme replacement therapy, Lewy body; Koprivica V et al 2000 Am J Hum Genet 66:1777.

Gaudens: *Oenothera lamarckiana* contains a ring of 12 translocation chromosomes and one bivalent (see Fig. G14). The translocations contain two complexes, *gaudens* (happy) conveys green color and *velans* (concealing) determines narrow leaves, pale color and disease susceptibility. The (complex) heterozygotes appear normal. Because of the translocations and the recessive lethal genes they carry, half of the progeny is inviable (*gaudens/gaudens* and *velans/velans* homozygotes) and the other half (the balanced lethal translocation heterozygotes) breeds true and is of normal phenotype. ►multiple translocations, ►complex heterozygote, ►*Oenothera*

Gaussian Distribution: ►normal distribution

Gazella: In the Dorcas gazella (*Gazella dorcas*) and the Grant's gazella (*Gazella granti*) the male has 31 chromosomes the female 30. In the *Gazella leptoceros* the males are 2n = 33, the females 2n = 32. The Thomson's gazella (*Gazella thomsoni*) is 2n = 58.

G_β: ►$G_{\alpha\beta\gamma}$

G-BASE: Genomic database of mouse, for access see Mouse Genome Database, Encyclopedia of the Mouse Genome. ►mouse, ►databases

G-Box Element: An upstream binding site (GACAACGTGGC) in plants of which the critical part is the CAACGTG core sequence that binds the G-box protein, a transcriptional activator.

GBP: GSK binding protein. ►GSK

GC Box: GC BOX in eukaryotic promoters generally contain the 5′-GGGCGG-3′ motif, a binding site for transcriptional regulator proteins.

GC (guanine-cytosine) Content: GC content of DNA contributes to the higher buoyant density of the molecules. In the DNA of the majority of eukaryotes, the GC content is about 40%. Higher organisms seem to display higher GC content yet genome size among eukaryotes does not involve higher GC content. It has been suggested that higher GC content affects the expression of genes but it could not be confirmed by more extensive analysis (Sémon M et al 2005 Hum Mol Genet.14:421). ►buoyant density, ►density gradient centrifugation, ►ultracentrifugation,

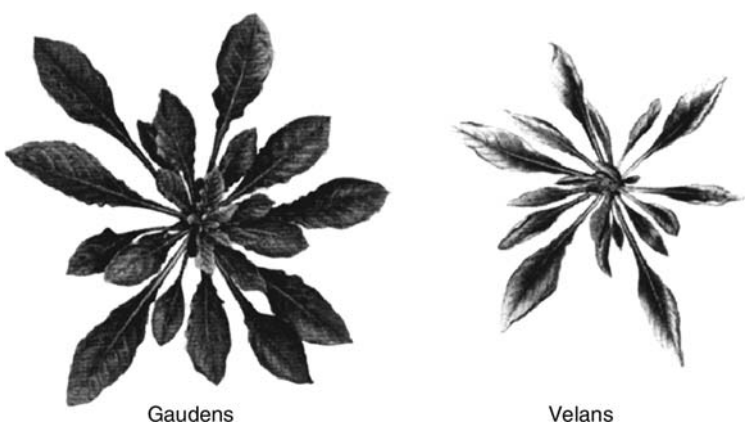

Figure G14. *Oenothera* pictures from deVries H 1913 Gruppenweise Artbildung, Borntraeger, Berlin

►DNA, ►base composition; GC identification tool: http://tubic.tju.edu.cn/GC-Profile/.

GC Skew: (G − C)/(G + C) indicating the not entirely random distribution of G and C on the two DNA strands. In *E. coli* there is 26.22% G in the leading strand whereas in the lagging strand it is 24.58%. ►DNA replication prokaryotes

GC-MS: Gas-liquid chromatography combined with mass spectrometry is an analytical procedure. ►gas-liquid chromatography, ►mass spectrum

GCN1/GCN20: A ribosome-binding complex bound by the N domain of GCN2 and it required for activation of the latter in starved yeast cells. (See Kubota H et al 2001 J Biol Chem 276:17591).

GCN2: It is dimeric and is required for the activation of GCN4. It has ribosome-binding, tRNA-binding, protein kinase and GCN2/GCN20-binding domains. Heatshock protein 90 assists its maturation folding. Its sequence is conserved across fungi, insects and mammals. (See Marbach I et al 2001 J Biol Chem 276:16944).

GCN4: The yeast transcription factor of a leucine zipper structure controlling the transcription of several genes. Its transcription is triggered by amino acid starvation when eukaryotic peptide elongation factor GCN2•eIF-2a becomes phosphorylated. The DNA binding site consensus for GCN4 is: ATGACTCAT / TACTGAGTA (See ►leucine zipper, ►eIF-2a, ►HRI, ►PEK; Yu L et al 2001 J Biol Chem 276:33257; Natarajan K et al 2001 Mol Cell Biol 21:4347).

GCN5: A yeast transcriptional co-activator with a histone acetyl transferase domain including amino acids 99–262 of the 439-amino acid protein (see Fig. G15). It consists of four antiparallel β-strands, an α-helix and a fifth β-strand. This domain is shared by other histone acetyltransferases as well as by other acetyltransferases such as an aminoglycoside 3-*N*-acetyltransferase and serotonin *N*-acetyltransferase belonging to the GNAT superfamily. It consists of four antiparallel β-strands, an α-helix and a fifth β-strand. This domain is shared by other histone acetyltransferases as well as by other acetyltransferases such as an aminoglycoside 3-*N*-acetyltransferase and serotonin *N*-acetyltransferase belonging to the GNAT superfamily. These enzymes transfer an acetyl group from Acetyl-CoA to a primary but different amino group. ►histone acetyl transferase, ►p300, ►aminoglycosides, ►acetyl CoA, ►TAF_{II}, ►transcriptional activators, ►enhanceosome; Kuo MH et al 2000 Mol Cell 6:1309.

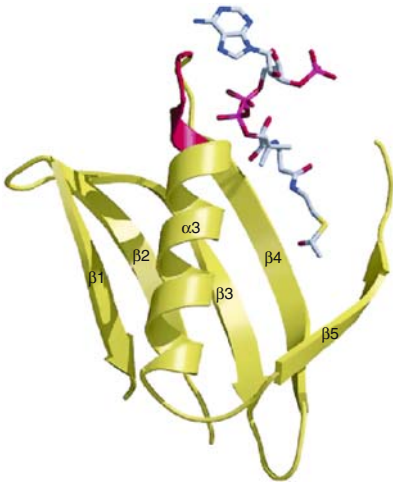

Figure G15. Crystal structure of GCN5 showing the four acetyl transferases. Courtesy of Drs. Sternglanz R and Shindelin H 1999 Proc. Natl. Arcad. Sci. USA 96: 8807

GCR: G protein coupled receptor. ►G proteins

G-CSF (granulocyte-colony stimulating growth factor): A lymphokine, modulating the effect of growth factors, fetal and post-natal development. ►GM-SCF, ►M-CSF

GCSF (G-CSF): ►granulocyte colony stimulating factor, ►lymphokine

GD: ►hybrid dysgenesis

γδ Element (Tn*1000*): An insertion element (IE) of the bacterial F plasmid that may produce various Hfr bacterial strains either by co-integration or recombination. The pDUAL/pDelta vector series of the γδ family vectors have been successfully used for generating (nested) deletions in both strands of a cloned insertion sequence. The plasmid replication origin and γsome selectable marker(s) are located in both strands in such a way that none of the essential information would be outside the transposon. ►co-integration, ►Hfr, ►F factor, ►F plasmid, ►Tn3 family, ►nested; Broom J et al 1995 DNA Seq 5 [3]:185; Kumar P et al 2004 Biochemistry 43:247.

γδ T Cells: Express any of the Vγ and Vδ immunoglobulin genes, recognize non-peptidic antigens and the antigen. The γδ T cells do not need professional antigen presenting cells and do not require processing by MHC class I or class II molecules and their ligands in order to be recognized by them in contrast to the αβ T cells (Brandes M et al 2005 Science 309:264). The γδ T cells (~2–10% of all T cells) are very different from the most prevalent αβ T cells and they can be stimulated also by non-peptide antigens such as

phosphocarbohydrates, X-uridine and X-thymidine-5′-triphosphates (TUBBag3 and TUBbag4, respectively) and isopentenyl pyrophosphate. The γδT cell differentiation is promoted by the Sox13 transcription factor of the thymocytes whereas the same transcription factor opposes the development of the αβ T cells (Melichar HJ et al 2007 Science 315:230). The molecules may be the product of nucleic acid salvage pathways and intermediates of the lipid metabolism. The γδ T cells mount primarily an innate immune response but because they stimulate chemokines and secrete cytokines they promote also the acquired immune system (αβ T cells). In the absence of γδ T cells IgE and IgG1, IL-5 and eosinophils are reduced and mice in this condition does not show allergic asthma of the airways in response to peptidic allergens. The γδ T cell receptor is different from that of the αβ T cell receptor (Adams EJ et al 2005 Science 308:227). ►immunoglobulins, ►T cells, ►αβ T cells, ►T cell receptor, ►salvage pathway, ►HLA, ►immune system, ►eosinophil, ►IL-5, ►allergen, ►asthma; Silva-Santos B et al 2004 Science 307:925; Allison TJ et al 2001 Nature [Lond] 411:820.

GDB: Genome database, the official depository of information of the human genome project. It can be accessed by Internet http://gdbwww.gdb.org/. (See also http://www.ncbi.nlm.nih.gov/Entrez/).

GDF (growth and differentiation factor): A member of the bone morphogenetic protein family. GDF5 mutations cause chondrodysplasia. ►BMP

GDEPT: Gene delivered enzyme-prodrug therapy. ►prodrug

GDI (guanine nucleotide dissociation inhibitor): GDI inhibits the dissociation of GDP from certain G proteins. ►G protein, ►signal transduction, ►GEF

GDLD (gelatinous drop-like corneal dystrophy): A rare hereditary amyloidosis. ►amyloidosis

gDNA: ►genomic DNA

GDNF (glial-cell-line-derived neurotrophic factor): Assists in the maintenance of central dopaminergic, noradrenergic and motor neurons and peripheral and sympathetic neurons. It is a family with several functional members neurturin, perefin and artemin. This protein is structurally related to the transforming growth factor (TGF-β) family and GDNF is a receptor tyrosine kinase. GDNF function requires a glycosylphosphatidyinositol-linked protein (GDNFR-α) and RET. It has been considered as a potential drug for Parkinson's disease, amyotrophic lateral sclerosis and Alzheimer's disease. GDNF also regulates spermatogenesis. ►dopamine, ►neuron, ►receptor tyrosine kinase, ►Parkinson's disease, ►amyotrophic lateral sclerosis, ►Alzheimer's disease, ►kinase, ►TGF, ►RET oncogene, ►MEN; Hashino E et al 2001 Development 128:3773; Bahuau M et al 2001 J Med Genet 38:638; Lee CS et al 2005 Exp Neurol 191:65.

GDRDA: ►genetically directed representational difference analysis

GDP: Guanosine 5′-diphosphate

GE81112: An antibiotic consisting of four amino acids (3-hydroxypipecolic acid, 2-amino-5-[(aminocarbonyl)oxy]-4hydroxypentanoic acid, histidine and 5-chloro-2-imidazolylserine). It inhibits specifically peptide initiation on the 30S prokaryotic ribosomal subunit by interfering with the binding of the fMet-tRNA (Brandi L et al 2006 Proc Natl Acad Sci USA 103:39). ►antibiotics

GECN (genetically effective cell number): ►genetically effective cells

GED: GTPase effector domain located at the C-end of dynamin. ►dynamin, ►GTPase, ►GAP

GEF: Translation factor similar in function to eIF-2B. ►eI factors, ►TU

GEF (guanine nucleotide exchange [release] factor): It facilitates the dissociation of GDP from G proteins. It is similar to ►Cdc25. ►GDI, ►GAP, ►Cdc25, ►G protein, ►signal transduction, ►SOS, ►ARF, ►faciogenital dysplasia, ►cytohesins, ►SOS; Vetter IR, Wittinghofer A 2001 Science 294:1299; Brugnera E et al 2002 Nature Cell Biol 4:574; Vazquez-Prado J et al 2004 Methods Enzymol 390:259.

GEFITINIB: ►Iressa

Geiger Counter (Geiger–Müller counter): Registers the rate of disintegration of radioactive isotopes. They are necessary in all isotope laboratories, also for monitoring contamination and spillage (see Fig. G16). The counter also detects environmental pollution of radioactivity in case of fallout. It measures β radiation with efficiency of 30–45% and for γ radiation (shield closed) 5,000 counts per minute per milliröntgen (mR). A typical full-scale reading is 0.2 to 20 mR/hr. It is very useful equipment for surveying because of good sensitivity and within seconds response. Its shortcomings are energy dependence, saturation at high rates and interference by ultraviolet and microwave radiations. A special adaptation of the Geiger counter is the strip counter that detects radiation in chromatograms, membrane filters, blots, etc. ►scintillation counters, ►ionization chambers, ►radiation hazard assessment

Figure G16. Geiger counter

Geitonogamy: Pollination by neighboring plants of basically the same genetic constitution.

Gel Electrophoresis: Nucleic acid fragments are electrophoresed in agarose and polyacrylamide gels, depending on the size of the fragment. In agarose larger, in polyacrylamide smaller fragments can be separated, e. g., in 0.3% agarose 5–60 kb, in 0.7% 0.8–10-kb fragments can be analyzed. In 5% polyacrylamide 0.5–0.8-kb, in 2% 0.04–0.1-kb fragments can be resolved (see DNA fingerprinting). Proteins can be electrophoresed in various media (paper, starch, polyacrylamide) by charge or by size in polyacrylamide-sodium dodecylsulfate (SDS) gels. ►electrophoresis, ►two-dimensional gel electrophoresis

Gel Filtration: Porous polymers such as Sephadex, Bio-Gel (commercially available in various pore sizes) can be used to separate high molecular weight DNA or proteins from smaller molecules (unincorporated dNTPs, linkers, etc.) The large molecule is excluded while the smaller fragments are retained on the gel during chromatography. For rapid purification it can be used in syringes. ►Sephadex, ►linker

Gel Mobility Assay: ►gel retardation assay

Gel Retardation Assay: Compared to DNA alone, DNA-bound protein retards the movement of the complex in the electrophoretic field (band shifting), and this way DNA-bind-ing proteins can be isolated and analyzed. To the protein bound to DNA, other protein(s) may also bind making the complex increasingly slow moving from the start site. This process is called *supershift*. A more specific test uses DNA affinity chromatography. ►DNA-binding domains, ►DNA binding proteins, ►affinity chromatography, ►electrophoresis

Gelatinase: ►metalloproteinases

Gelding: Castrated male horse. ►castration

Geleophysic Dysplasia: A mucopolysaccharidosis with happy face, dysotosis and heart problems. ►mucopolysaccharidosis; Wraith et al 1990 Am J Med Genet 35:153.

Gellan Gum: A synthetic polysaccharide, used for solidifying plant tissue and bacterial culture media (instead of agar). ►agar, ►embryo culture

Gelsolin: An actin-binding protein that regulates the cytoskeleton. ►actin, ►cytoskeleton, ►amyloidosis, ►fodrin

Gem: A GTP-binding protein, induced by mitogens; it is related to RAS. ►GTP, ►mitogen, ►RAS

GEM91: A 25-mer antisense phosphorothioate. ►antisense technologies, ►phosphorothioates

Gemini of Coiled Bodies: These consist of heterogeneous nuclear ribosomal proteins (hnRNP), coiled bodies, and "survival-of-motor-neuron" proteins (SMN). SMN forms are tightly associated with protein SIP1 (SMN interacting protein). SMN1 is located in human chromosome 5q13 and SMN2 is almost identical to SMN1 but lacks an exon-7 domain. SMN1 is frequently replaced by SMN2 in spinal muscular atrophy. ►coiled bodies, ►hnRNP, ►spinal muscular atrophy; Matera AG, Frey MR 1998 Am J Hum Genet 63:317.

Geminin: A ~25-kDa protein preventing aberrant replication of the chromosomes after the S phase of mitosis. It keeps in check Cdc6/18 and Cdt1. It accumulates during mitosis but it is degraded at the transition from metaphase to anaphase. After it is degraded, Cdc6/18 and Cdt1 rebuild and associate with the chromatin in preparation for the S phase. ►mitosis, ►cell cycle, ►Cdc6, ►Cdc18, ►Cdt, ►MCM, ►ORC, ►replication licensing factor; Wohlschelegel JA et al 2000 Science 290:2309; Luo L 2004 Nature [Lond] 427:749.

Geminiviruses: These contain single-stranded small DNA genomes (~2.7 kb). Some can infect monocots others infect dicots (see Fig. G17). Their capsules may be geminate (doubled) or their DNA may exist in two partially-identical (200 bases) rings. They may be used for plant vector construction. ►agroinfection; Lazarowitz SG 1992 Crit Rev Plant Sci 11:327.

Figure G17. Geminiviruses particles

Gemmules: An ancient term for hereditary units.

GenBank: Data bank for information on nucleic acid and protein sequences, Los Alamos Natl. Laboratory, Group T-10, Mail Stop K710, Los Alamos, NM 87545, USA, Tel: (505) 665–2177, e-mail: general inquiries genbank%life@lanl.gov, sequence submission and forms: gb-sub%life@lanl.gov. ►EMBL,

►DDBJ, ►ENTREZ, ►Sequin, ►sperm bank, ►databases; Dennis A et al 2005 Nucleic Acid Res 33:DB34; http://www.ncbi.nlm.nih.gov/, complete genomes: http://www.ncbi.nlm.nih.gov/Genomes/index.html, updating: update@ncbi.nlm.nih.gov/projects/collab/FT/inex.html, feature table: http://www.ncbi.nlm.nih.gov, description of features: http://www.ncbi.nlm.nih.gov/collab/FT/index.html), unfinished large scale genomic high-throughput products: http://www.ncbi.nlm.nih.gov/HTGS/.

Genboree: Human Genome Sequencing Consortium sequencing and annotation programs. (See http://www.genboree.org/java-bin/login.jsp).

Gencode: An integrated annotation of existing cDNA and protein resources to define transcripts with both manual review and experimental testing procedures.

Gender: The sexual type, e.g., female or male in societal or lexicographic context; in physiology or genetics the word sex is more appropriate.

Gender Dimorphism: Separate individuals represent the two sexes.

Gender Discrimination: The difference between males and females is a biological fact yet that does not justify the ethical and moral principle that equal contribution must be equally rewarded. It is unfair, however, to evaluate men and women by identical criteria because the majority of the social criteria are male-oriented and disadvantageous for women. In general, males and females carry the same chromosomes except the gene-poor Y chromosome and the dosage of the X chromosomes, which are in duplicate in a normal female but the X is present only in a single dose in the normal males and dosage compensation may not be perfect. Both male and female attributes have special advantages. Maleness, in general, have been associated with more aggressiveness, less empathy compared with femaleness. There is no evidence, however, for differences in originality of thinking or creativeness, therefore for the frequently found lower appreciation for women in leadership or scientific contribution is not justified. In certain positions, males (e.g., when great physical strength is an advantage) and in others female characteristics (e.g.,dealing with young children) are more desirable. The social differences between the sexes are frequently called gender gap. The gender gap was historically larger than it is today and it is steadily diminishing in business and academics. During the last 30 years among 4,227 life-scientists, patenting by women was only 40% of that by men (Ding WW et al 2006 Science 313:665). ►discrimination genetic, ►dosage compensation; Lawrence PA 2006 PLoS Biol 4[1]:e19.

Gender Preselection: Separation of X- and Y-bearing sperms before fertilization. Success in such a procedure may prevent the transmission of X-chromosome linked genetic defects. It may become an alternative to ethically or morally objectionable procedures of negative eugenenics (Anyhow, it should be called sex preselection.) ►eugenics, ►abortion; Fertility & Sterility 75:861–864 [2001].

Gender Trading: In hermaphroditic animals the individuals may donate sperm or oocyte or both.

Gene: A specific functional unit of the DNA (or RNA) potentially transcribed into RNA or coding for protein. A group of co-transcribed exons but due to alternative splicing, or exon shuffling, or overlapping, or using more than one promoter or termination signal, the same nucleic acid sequence may encode more than a single protein. A common structural organization of protein encoding genes in eukaryotes: ►enhancer, ►promoter, ►leader, ►exons, ►introns, ►termination signal, ►polyadenylation signal, ►downstream regulators

The vast majority of human genes are 'mosaics' containing 7–9 exons of 120–150 bps, each. In some genes the exon number and size can be much larger. In between exons there are 1000 to 3,500 bp long introns. The size of the introns may also be several times larger. The number of coding nucleotides varies between 1,100 to 1,300 but the larger genes may have much larger coding sequences. The exons + introns + 5′ and 3′ untranslated sequences combined, the genomic genes, in general, extend to 14–27 kb DNA. A large fraction of the human genes is alternatively spliced and thus the same "gene" may be translated into three or more kinds of proteins. In human chromosome 10, the average known gene has 4.76 transcripts but the *adducin 3* gene has 22 variants. The organization of other eukaryotic genes may vary quantitatively. Genic sequences are richer in GC nucleotides than the non-coding tracts. In prokaryotes, introns are rare and the size of the genes is smaller. Computational procedures might assist the identification of promoters and first exons in the human (and other) genomes. Genes generally originate by duplication that is followed by mutational alterations to gain a new function. Alternatively, new functions may arise by reorganization of exons or modules or by emergence of functional sequences from non-coding DNA tracts. Lateral transfer delivers genes from one organism to another. Although the gene is a rather stable complex molecule, its function is mediated, modulated and controlled by several proteins. The potential role of epigenesis in gene expression and development is steadily increasing. The concept of the gene is undergoing now further complications since it became known that most of

the DNA (rather than a small "genic" fraction) is transcribed into RNA and these RNAs seem to have hitherto not completely understood function in controlling the expression of genes (Kapranov P et al 2007 Science 316:1484). A new definition of the classical 'beads on a string' concept of gene has now emerged: "A gene is a union of genomic sequences encoding a coherent set of potentially overlapping functional products" (Gerstein MB et al 2007 Genome Res 17:699). The idea of "number of genes" is becoming difficult to define not because of problems of sequences and annotation. The final product of gene expression can be somewhat elusive because transcripts of exons and introns are overlapping in different contexts. In addition, some components of an expressed gene may be situated away from the core and can be in a different chromosome. Thus, the number of genes may greatly increase if we do not count the components of these systems but the variety of intertwined products. Paradoxically, if the genes are counted according to the number of these expression modules, the number of genes becomes much fewer (Gerstein MB et al 2007 Genome Res 17:669). It is now understandable why the prescience of Richard Goldschmidt (1958) questioned whether corpuscular genes may actually exist and rather we have to accept that complex position effects and interacting systems determine the function of the genes. ►reaction norm, ►one gene–one enzyme, ►splicing, ►dystrophin, ►titin, ►gene number, ►ORF, ►pseudogene, ►lateral transfer, ►mosaic genes, ►epigenetics, ►microRNA, ►RNAi, ►overlapping genes, ►operon, ►regulon, ►gene-associated region, ►non-Mendelian inheritance, ►ENCODE; Snyder M, Gerstein M 2003 Science 300:248; Wolfe KH, Li W-H 2003 Nature Gen 33 (Suppl):255; Rédei GP et al 2006; Advances Genet 56:53; gene location–function: http://www.cmbi.ru.nl/GeneSeeker/, gene records of more than 3,500 taxa: http://www.ncbi.nlm.nih.gov/projects/Gene/gentrez_stats.cgi.

Gene Action: The type and mechanism of expression of genes.

Gene Activation: Turning genes on; initiates expression of genes.

Gene Activator Proteins: ►transcriptional activators

Gene Alignment: Arranging the nucleotide sequences of functionally or by evolution-related genes, in such a manner that the homologous and non-homologous stretches of nucleotides can be assessed. ►homology, ►dot matrix

Gene Amplification: ►amplification

Gene and Protein Names: See http://www.ba.cnr.it/keynet.html.

Gene Assignment: Locating genes to chromosomes.

Gene-Associated Regions: Regions not part of the classical gene, yet retain an important role in gene function. Furthermore, they can contribute to the expression of several genes. Examples for such long-range elements are the Locus Control Regions (LCR) of beta-globin that contributes to the expression of several genes, and will likely be the case for many other enhancers as their true gene targets are mapped. It can also be applied to untranslated regions that contribute to multiple gene loci, such as the long spliced transcripts observed in the ENCODE region and *trans*-spliced exons (Gerstein MB et al 2007 Genome Res 17:669).

Gene Bank: ►GenBank, ►DDBJ, ►EMBL, ►sperm bank, ►databases

Gene Block: A group of syntenic genes. Gene blocks can be preserved in their original linkage phase if they are within inversions because the single recombinants are generally inviable and the double recombinants are very rare within short regions. Paracentric inversion testers have been used to locate advantageous gene blocks for utilization in plant breeding projects. Inversion homozygotes are backcrossed with inbred stocks, and the F_1 is backcrossed with the inversion-homozygote tester. This progeny is half homozygous for the inversion and half is heterozygous for it. The two groups can be easily distinguished by genetic markers or by semisterility of the heterozygotes (if any crossing over takes place). If the heterozygotes surpass the parental forms in quantitative traits, the good performance is attributed to the inverted segment tested. Favorable gene blocks (quantitative gene loci, QTL) may also be identified by linkage to RFLP markers. During evolution, some gene blocks were rather well preserved. In chicken after > 300 million years of separation from the human lineages 13 segments still represent 72% of human chromosome 12. About 87% of chimpanzee and rhesus macaque sequences can be aligned with human chromosome 12 (Scherer SE et al 2006 Nature [Lond] 440:346). ►inversions, ►QTL, ►operon, ►gene cluster, ►RFLP

Gene Cassette: A special type mobile genetic element, which carries, most commonly, only a single gene (e.g., antibiotic resistance) and a recombination sequence. For mobility, it depends on another element, the integron. ►integron; Recchia GD , Hall RM 1997 Trends Microbiol 5:389.

Gene Center: The geographical area where the greatest genetic diversity within a species is found, and

therefore it is considered as the evolutionary cradle of that species. ►evolution; Vavilov NI 1928 Verhandl V Internat Kongr Vererbungswiss Berlin, 1:342.

Gene-Centromere Distance: ►centromere mapping, ►tetrad analysis, ►alpha parameter

Gene Chips: ►DNA chips, ►microarray hybridization

Gene Circuits: A collection of genetically encoded proteins with regulated expression. In the *elementary gene circuit,* only a single specific transcription factor operates the gene under the influence of a signal. In a biological system the number of players may extend to numerous (hundreds) of proteins. ►Gene-Switch cassette, ►networks, ►oscillator, ►genetic network, ►synthetic biology; Sprinzak D, Elowitz MB 2005 Nature [Lond] 438:443.

Gene Cloning: The propagation of a piece of DNA, in identical copies, in a bacterial, viral or yeast (or other) vectors in order to increase its quantity. It is the same as molecular cloning.

Gene Cluster: Juxtapositioned genes sometimes with related function. ►operon, ►regulon, ►transcripton, ►immunoglobulin genes

Gene Conversion: A biological event that results in the change of one allele to another present in the homologous chromosome. It is a specific type of non-reciprocal recombination. As a consequence, the meiotic output is changing from 2:2 to 3:1 or if the conversion takes place in the opposite direction, to 1:3. In case an additional mitotic division following meiosis forms octads, other types of conversion asci can be identified (see Fig. G18: the left-most octad is normal; the other five indicate gene conversions). Gene conversion within a locus proceeds in a polarized fashion, following the direction of DNA replication. Gene conversion may involve *map expansion* because within very short distances the neighboring sites may be co-converted and thus reducing the chance of their separation. This is in contrast to classical recombination when the presence of multiple markers permits the detection of higher number of recombinational events. The conversion is characterized by *fidelity,* i.e., the converter and the converted alleles are identical. The 3:1 and 1:3 spore ratios in the tetrads generally occur with equal frequency, and this was named *parity.* Mitotic gene conversion may produce somatic sector(s). Although gene conversion is not a classical recombinational event itself, it is accompanied by exchange of markers at the flanking region in about half of the cases. It has been assumed that gene conversion not associated with recombination of flanking markers, the donor of genetic information may be a cDNA. In yeast genes *RAD51, RAD55*, and *RAD57* activity is involved in mitotic recombination and gene conversion between two DNA molecules. In RNA-mediated gene conversion these are dispensable but gene *RAD1* (encoding an endonuclease) is required.

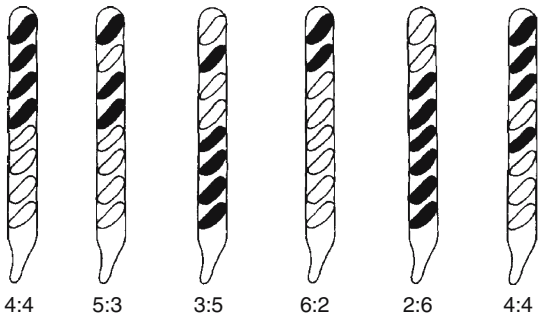

Figure G18. Gene conversion asci

Originally, gene conversion was discovered in ascomycetes, now it is believed to occur in other eukaryotes too but the identification of gene conversion is still the easiest on the basis of tetrad data (or half tetrads in *Drosophila* with attached X-chromosomes). The frequency of gene conversion may be highly variable from gene to gene ranging from less than 0.5% to a few percent in yeast. The average size of the converted segment may extend to 1000 bp. Not all aberrant spore output can be attributed to gene conversion. Polysomy, polyploidy, nondisjunction, premeiotic mitotic recombination, suppressor mutations, etc. may all produce aberrant asci similar to the results of gene conversion. The different types of gene conversions are best identified in the asci where meiosis is followed by an additional mitosis. The detection of gene conversion is relatively simple in organisms where the (pollen) tetrads are preserved (*Salpiglossis* or *Arabidopsis* mutants).

In some instances in human c4lls, the frequency of gene conversion much exceeded that of homologous reciprocal recombination, verified by molecular analysis. Actually, at special hot spots within short chromosomal regions (HLA-DBP1 and the PAR pseudoautosomal region of the human Y chromosome] the frequency of recombination by crossing over was lower than that by gene conversion ($0.9–1.2 \times 10^{-3}$ versus $1.3–3.4 \times 10^{-3}$, respectively). At some other regions, the frequency of conversion was in the range of 5×10^{-5}. The conversion tract observed was minimum 300 bp to a maximum of 1,091 bp. The conversion appeared limited to sperm (meiosis) and was not observed in blood (mitosis). Other investigations detected gene conversion in somatic cells of animals. The conversion rate declined very rapidly

with increased distance. Sperm typing by PCR was used for the studies. The use of PCR technology may permit the detection of converted sequences within any eukaryotic gene even in the absence of tetrad analysis. The center of conversion events overlapped with the crossing over peaks. The results suggest similarities in the mechanism of gene conversion and crossing over (Jeffreys AJ, May CA 2004 Nature Genet 36:151). The mismatch repair of double-strand breaks may involve gene conversion. ►conversion asci, ►half conversion, ►recombination mechanisms, ►recombination models, ►sex circle model, ►PCR, ►mismatch repair, ►sperm typing; Fogel S et al 1971 Stadler Symp 1–2:89; Quintana PJE et al 2001 Genetics 158:757.

Gene Conversion, Ectopic: The interpretation for the variations in the non-recombining regions of the X and Y chromosomes in feline species. Since chromosome pairing is a requisite for the classical gene conversion, it is hypothesized that accidental pairing may occur. (See Slattery JP et al 2000 Proc Natl Acad Sci USA 97:5307).

Gene Copy Numbers: In lower organisms, the majority of the genes occur in single copies per genome yet, even in bacteria, ribosomal genes may be present in seven copies. In the amphibian oocytes, during the great need for protein synthesis ribosomal genes may be amplified 1,000 to 1,500 fold and form more than a thousand nucleoli. After meiosis this excessive amount of rRNA genes are discarded. In maize plants, there may be 10,000 to 20,000 copies of ribosomal genes per diploid cells. *Xenopus* may have 24,000 copies of the rRNA genes and 200 copies of each of the tRNA genes. *Drosophila* has about 500 copies of 5S RNA genes in the right arm of chromosome 2. Some particular sequences (SINE and LINE) occur in all eukaryotes in high numbers. In many higher eukaryotes, repetitive sequences may exceed 80% of the genome. Decreased copy number of the *Fcgr3* gene of rodents or the human homolog FCGR3B predisposes to glomerulonephritis in systemic lupus erythematosus (Aitman TJ et al 2006 Nature [Lond] 439:851). ►amplification, ►glomerulonephritis, ►lupus erythematosus, ►SINE, ►LINE, ►gene number; Romero D, Palacios R 1997 Annu Rev Genet 31:91.

Gene Delivery: The system of introduction of foreign gene(s) into a cell(s). ►transformation genetic, ►transfection, ►microinjection, ►biolistic transformation, ►electroporation, ►vectors, ►receptor-mediated gene transfer, ►cytofectin, ►liposomes, ►endocytosis

Gene Density: In *Drosophila* 1/13.4 kb was reported but it is variable (1/5.6 to 1/78 kb); in the plant *Arabidopsis* 1/4.5 kb. It appears that in the human nucleus, the chromosomes with large gene density (e.g., 19/Mb) are more centrally located whereas the chromosomes with lower gene density (e.g., 18) are situated more at the periphery. The size of the chromosomes does not affect their position. The average human gene density is about 10/Mb, in chromosome 13 being 6.5 and in chromosome 22 being 26. In human chromosome 12 the size of the gene clusters vary; there 9 natural killer cell genes at 12p13.2-p12.3 and 14 keratin II genes at 12q13.3 whereas there are 3 aquaporin genes at 12q13.1 (Scherer SE et al 2006 Nature [Lond] 440:346). The marine chordate, *Oikopleura dioica*, has a minimum genome size of 51 Mb, about 15,000 genes and a very short life cycle (two to four days, depending on the temperature). Its gene density appeared only 1/5 kb, the lowest among chordates. Persistently open chromatin domains have more essential genes that enable reduced noise by avoiding transcriptional fluctuation associated with chromatin remodeling. Essential genes are rare in subtelomeric regions (Batada NN, Hurst LD 2007 Nature Genet 39:945). (See Boyle S et al 2001 Hum Mol Genet10:211; Seo H-C et al 2001 Science 294:2506).

Gene Discovery: The completion of genome sequencing still does not reveal the function of all open reading frames. Functional genomics seeks the identification of what the individual or clusters of genes do within the cell. Because genes are expressed in complex networks new functions will be discovered for times to come. ►EST, ►UniGene, ►normalization, ►subtraction, ►genetic networks; Giallourakis; C et al 2005 Annu Rev Genomics Hum Genet 6:381; http://www.geneatlas.org.

Gene Disruption: ►insertional mutation, ►targeting genes, ►insertion elements, ►transposons

Gene Distribution: Gene distribution in prokaryotes (*E. coli, Bacillus subtilis*) is unequal between the leading and lagging strands. The majority of the essential, genes are expressed in the leading strand and the essentiality of function, and not the expression level, determines this strand bias. Some chromosomes and chromosomal regions display higher or lower gene density than the average. ►leading strand, ►lagging strand; Rocha EPC, Danchin A 2003 Nature Genet 34:377.

Gene Diversity: Estimated on the basis of allelic frequencies in a population. H = gene diversity at a locus, n = number of individuals, m = number of alleles at the locus, x_i = the frequency of the i*th* allele. For self-fertilizing species n/(n−1) replaces 2n/2n−1.

►evolutionary distance, ►diversity; Nei M Roychoudhury AK 1974 Genetics 76:379; Nei M 1987 Molecular Evolutionary Genetics. Columbia University Press, New York.

$$H = \frac{2n}{(2n-1)}\left(1 - \sum_{i=1}^{m} xi^2\right)$$

Gene Dosage: The number of identical and repeated genes in the genome. ►polyploidy

Gene Duplication: ►duplication

Gene Editing: Parts of natural genes are replaced or completed by synthetic DNA chains or a natural repair process eliminates gaps or mismatches in the DNA (called also proofreading). ►editing, ►DNA polymerases, ►mtDNA, ►RNA editing

Gene Evolution: The process by which once similar genes diverged or different genes assumed similar structure and function. The starting material is usually the duplication of gene or a chromosomal segment. During evolution, some genes are lost because their function is no longer needed in the altered environment. Parasites may exploit host functions and let some of their own functions and genes lapse. In some instances, host proteins are either hijacked for use by mobile elements or recruited to defend against them. Some yeast genes (e.g., those involved in DNA repair) may be subject to selective pressures imposed by mobile elements and could favor alleles that might be otherwise deleterious for their normal roles related to genome stability. NHEJ genes could have profound consequences for genome integrity in many organisms, making mutations that are subtly deleterious for NHEJ function nonetheless selectively favored because of their ability to combat mobile element insertions (Sawyer SL, Malik HS 2006 Proc Natl Acad Sci USA 103:17614). ►divergence, ►convergence of genes, ►duplication, ►NHEJ

Gene Expression: The realization of the genetic blueprint encoded in the nucleic acids. Gene expression may be modified, enhanced, silenced, and timed by the regulatory mechanism of the cell responding to internal and external factors. The *expression capacity* is the ratio of the maximal to minimal level of expression in response to signals. Usually it is the transcription of DNA into RNA. The number of genes expressed in one or more copies in human cell lines was estimated by 'massively parallel signature sequencing' to be 10,000 to 15,000. About 1/3 to ½ of the genes displayed cell specificity whereas half or more were generally expressed (Jongeneel CV et al 2003 Proc Natl Acad Sci USA 100:4702). Using RNAi technology, the 19,075 genes of *Caenorhabditis* were targeted. The data indicate that about 40% of the genes are expressed at the early embryonic stage, 36% in the late embryos, 16% in the larvae, and 8% in the adults (Sönnnichsen B et al 2005 Nature [Lond] 434:462). Interestingly, in *Arabidopsis* plants only 12% of the ethylmethane sulfonate induced mutations expressed at adult plant stages when 89.2% of the total estimated genes displayed mutant phenotype (Rédei GP et al 1984, p. 285, Mutation, Cancer, and Malformations; Chu HY, Generoso WM eds Plenum, New York).

Analysis of the sequence of regulatory elements 800 bp upstream of genes provides high probability for the prediction of their level of expression (Beer MA, Tavazoie S 2004 Cell 117:185). Regulation of gene expression differentiates evolutionary categories more distinctly than the base sequences of the DNA (Rifkin SA et al 2003 Nature Genet, 33:138). By the use of the *lac* bacterial gene or the aequorin (*GFP*) gene, gene activitiy can be visualized in living cells and the dynamics of transcription, RNA processing and DNA repair can be optically traced (Tsukamoto T et al 2000 Nature Cell Biol 2:871). Large scale co-expression of genes can be detected by regression analysis of microarray hybridization data (Persson S et al 2005 Proc Natl Acad Sci USA 102:8633). ►regulation of gene activity, ►protein synthesis, ►SAGE, ►FANTOM, ►microarray hybridization, ►massively parallel signature sequencing; Whitfield ML et al 2002 Mol Biol Cell 13:1977; Levsky JM et al 2002 Science 297:836; Bar-Joseph Z et al 2003 Proc Natl Acad Sci USA 100:10146; Gene Resource Locator; GEO [Gene Expression Omnibus]: http://www.ncbi.nlm.nih.gov/geo; http://www.HugeIndex.org; http://www.biotechnologycenter.org/hio/; http://expression.gnf.org/cgi-bin/index.cgi; mouse: http://www.Informatics.jax.org/menus/expression_menu.shtml; mouse gene expression pattern database: www.genepaint.org/; complexity of gene expression: http://www.bioinf.med.uni-goettingen.de/services/deep/.

Gene Expression Maps: They combine topological information on expression, co-expression and correlation of gene expression with all possible intrinsic (e.g., developmental) and extrinsic (e,g., heat shock) factors. These maps then allow predictions on biological processes, functions and phenotypes. ►protein mapping; Kim SK et al 2001 Science 293:2087; Ihmel J et al 2002 Nature Genet 31:370.

Gene Expression Omnibus: The gene expression/molecular abundance repository supporting MIAME compliant data submissions, and a curated, online resource for gene expression data browsing, query and retrieval. ►MIAME, http://www.ncbi.nlm.nih.gov/projects/geo/; http://www.ncbi.nlm.nih.gov/geo.

Gene Family: The number of genes (paralogous loci) closely related by structure and generally also by function. They probably originated through duplications, domain shuffling, splicing and fusion (and some divergence) during evolution. The members of these gene families are frequently (closely) linked but may also be dispersed in the genome. The complete genome sequences can now reveal the relationships impossible to detect by earlier methods. Amino acid sequence comparison for 25, 193 human proteins indicate that on average that the vast majority of them involve relationship to ~26 other proteins. The average number of related amino acids is 36.5 for the majority that are related (Britten RJ 2005 Proc Natl Acad Sci USA 102:5466). ►orthologous loci, ►paralogous loci, ►duplication, ►deletion, ►exon shuffling, ►paranome, ►lateral transmission, ►homoeologous chromosomes, ►homoelogous alleles, ►evolution of proteins, ►protein families, ►immunoglobulins, ►protein isomorphs; Thornston JW, De Salle R 2000 Annu Rev Hum Genet 1:41.

Gene Farming: Cloning, transformation and propagation of genes in another species.

Gene Fission: May occur during evolution by splitting one gene into two parts. This process has taken place most frequently in thermophilic archaea. ►gene fusion

Gene Flow: The spread of genes in a population by migration of individuals and cross-fertilization. Gene flow, depending on its intensity, may rapidly alter gene frequencies in a population. Gene flow may be hindered or prevented by geographic isolation, physiological factors (differences in sexual maturity and breeding seasons), genetically (by chromosomal rearrangements causing hybrid sterility, incompatibility alleles and differences in chromosome number [polyploidy]). In neighboring populations, at the overlapping borders, repeated backcrosses may occur resulting in *introgressive hybridization* and permanent inclusion of new alleles into the gene pool in one or more populations. The availability of transformation techniques may overcome the natural gene flow and transfect genes among taxonomic groups that were earlier unable to exchange genetic information because of complete sexual isolation. The wave of advance of an advantageous gene was calculated by RA Fisher: $r = \sqrt{2gm}$ where g = the initial growth rate and m = the migration rate per time and space. Molecular markers greatly facilitate tracing of the path of genes in human and other populations. Analysis of the mitochondrial DNA, X and Y chromosomes are the most useful tools for this purpose. ►migration, ►introgressive hybridization, ►Wahlund's principle, ►transformation, ►Y chromosome, ►X chromosome, ►Eve mitochondrial foremother, ►out-of Africa; Wells RS et al 2001 Proc Natl Acad Sci USA 98:10244; Oota H et al 2001 Nature Genet 29:20; Weale ME et al 2002 Mol Biol Evol 19:1008; Goldstein DB, Chikhi L 2002 Annu Rev Genomics Hum Genet 3:129; Cavalli-Sforza LL et al 1994 The History and Geography of Human Genes, Princeton University Press, Princeton, New Jersey.

Gene-For-Gene: The relationship between host and pathogen. ►Flor's model, ►host-pathogen relation, ►co-evolution

Gene Frequency: The frequency of a certain allele relative to all alleles at a locus within a particular population ►allelic frequencies, ►Hardy-Weinberg theorem, ►selection, ►drift, ►genetic equilibrium, ►forensic genetics, ►DNA fingerprinting, ►ceiling principle

Gene Function: The typical action of the product of the gene. Relying on the sequenced genomes and the proteomic technology, the correlation between the transcriptome and the metabolome can be experimentally studied. ►transcriptome, ►metabolome; Hirai MK et al 2004 Proc Natl Acad Sci USA 101:10205; gene function network tool: http://whipple.cs.vt.edu:8080/virgo, analysis of genes against any set of function: http://genetrail.bioinf.uni-sb.de/.

Gene Fusion: Attaching to a structural gene by in vitro genetic engineering, a selected promoter or other element(s), or a promoterless structural gene is transformed into a host cell and expressed only if it can trap in vivo an appropriate host promoter (enhancer). The procedure permits a study of the nature of the fused heterologous genetic element. If gene fusion occurs between coding regions of two genes, the translation product becomes a *fusion protein* that contains amino acid sequences from two structural genes. This process may modify the function of the fusion protein. During evolution, the fused chimeric genes develop amino acid substitutions that are rare or missing from the ancestral mutants (Jones CD, Begun DJ 2005 Proc Natl Acad Sci USA 102:11373). Fusing ablation factors, such as ricin or diphteria toxin to site- or tissue-specific promoters may facilitate the study of differentiation and development because certain cell types can be eliminated during critical periods. Gene fusion may occur during evolution. Fused genes are frequently scattered in the evolutionary ranks, indicating that they did not evolve by vertical common descent (Yanai I et al 2002 Genome Biol 3(5):res0024.1). Metabolic enzymes of *E. coli* fuse three-fold more commonly than other proteins. Gene fusion may have pathological consequences; the fusion of the breakpoint cluster genes with that of Abelson murine

leukemia viral oncogene leads to leukemia (CML). Recurrent fusion of the androgen-responsive promoter element of TMPRSS2 (a transmembrane protease serine 2) with members of the ETS oncogene family leads to prostate cancer (Tomlins SA et al 2005 Science 310:6744). Several cases of cancers are caused by chromosomal rearrangement (translocations) and fusion of different genic elements. ►transcriptional gene fusion vectors, ►translational gene fusion vectors, ►trapping promoters, ►fusion protein, ►read-through proteins, ►intergenic transcript, ►ablation, ►diphteria toxin, ►gene fission, ►leukemia, ►prostate cancer, ►chromosomal rearrangement; Casadaban MJ 1976 J Mol Biol 104:541; Silhavy TJ et al 1984 Experiments with Gene Fusions, Cold Spring Harbor Lab., Cold Spring Harbor, NY, USA; Lavasani LS, Hiasa H 2001 Biochemistry 40:8438; gene fusion and translocation breakpoints: http://genome.ewha.ac.kr/ChimerDB/.

Gene Gun: ►biolistic transformation

Gene Identification: This may be required after a particular DNA tract has been sequenced but its function is unknown. The simplest approach is checking the DNA databases for homologous sequences among genes with known function. Extensive amounts of redundant sequences may make the comparisons difficult but computer programs are available to identify repeats in human genes (pythia@anl.gov or ftp:ncbi.nlm.nih.gov) or BASTX for other organisms: http://www.cshl.org/genomere/supplement/harris.htm. BLAST, FASTA can search databases. ►databases, ►Blast, ►Fasta, ►BLOCKS; Fickett JW 1996 Trends Genet 12:316.

Gene Indexing: Organizing information on groups of genes according to sequences/ functions/EST using Unigene, STACK and HGI. ►Unigene, ►STACK, ►HGI, ►expressed-sequence tag; Haas SA et al 2000 Trends Genet 16:521; http://genenest.molgen.mpg.de/; http://www.tigr.org/tdb/tgi.

Gene Interaction: A common misnomer; in most cases the products of the genes interact—with a few exceptions such as gene insertion, gene fusion, etc. ►gene product interaction, ►epistasis, ►modified Mendelian ratios, ►morphogenesis in *Drosophila*, ►networks

Gene Isolation: The first gene isolation was reported in 1969. The *Lac* gene of *E. coli* was inserted in reverse orientation in bacteriophages λ and φ80 by a modification of specialized transduction. The DNA of these phages was extracted, denatured and the heavy chain of λ was combined with the heavy chain of φ80. Since the base sequences of the two phage strands were not complementary, only the *Lac* sequences annealed, and the phage DNA sequences remained single-stranded. S_1 nuclease degraded the single strands but the double-stranded *Lac* gene was preserved in pure form. Somewhat similarly, genes from F' plasmids could also be isolated. These ingenious methods did not have general applicability. A more general procedure was developed by isolation cDNA from mRNA. The problem was that a eukaryotic cell might contain over 40,000 mRNA molecules at a time. To be reasonably certain (say at 99% probability) that the desired molecule is included, a very large number of molecules had to be isolated in order that the desired one be included:

$$[1 - (1/40,000)]^n = 1 - P = 1 - 0.99 = 0.01$$

hence

$$n = \frac{\log 0.01}{\log[1 - (1/40,000)]} \cong 184,213$$

where n is the number of molecules to be screened to find at least 1 at P (=0.99) probability.

The desired mRNA may be enriched by "cascade hybridization." The mRNAs can be extracted from cells at different developmental stages. Also, substrate induction, heat shock, drug, hormone or pathogen caused induction can be used for enrichment of the mRNA. If a *DNA library* is available and the gene can be probed by colony hybridization, the fragments containing the gene or parts of it can be identified by the use of DNA probes. The simplest method of isolation of genes uses *heterologous probes*. Such a probe contains a homologous sequence of the gene to be isolated. The probe is labeled by *nick translation* using either radioactive nucleotides or biotinylation or any other non-radioactive fluorochromes or immunoprobes. The probe permits the selective isolation of the DNA fragment annealed with the probe. If the amino acid sequence of at least part of the gene product is known, synthetic probes can also be generated.

Genes can be labeled also by transposon mutagenesis or by insertional inactivation using transformation (transfection). In case close genetic or physical mapping information is available, the gene may be isolated by the use of overlapping YAC clones and "chromosome walking" (*map-based gene isolation*). Linker scanning can identify essential regulatory elements of the gene. The identity of the gene generally requires confirmation by in vitro translation and testing the function of the protein so obtained. ►biotinylation, ►chromosome walking, ►cloning, ►colony hybridization, ►cosmids, ►DNA library, ►DNA probes, ►fluorochromes, ►heterologous probes, ►immunoprobes, ►insertional mutation, ►linker scanning, ►nick translation, ►plasmid rescue, ►radioactive labeling,

►synthetic probes, ►transfection, ►transformation, ►transposon mutagenesis, ►YAC vectors, ►functional cloning, ►positional cloning, ►candidate gene, ►EST; Nieuwlandt D 2000 Curr Issues Mol Biol 2:9; Birnstiel ML. 2002 Gene 300:3.

Gene Knockout: ►knockout, ►gene disruption, ►targeting genes, ►excision vector, ►*Cre/loxP*

Gene Library: A collection of cloned genes. ►cloning

Gene Locus: ►locus

Gene Manipulation: ►genetic engineering

Gene Mapping: ►mapping genetic, ►mapping function, ►physical mapping

Gene Marking: The insertion of a stable retroviral vector into some stem cells, blood cells or other tissue and detect its functional state or contamination with neoplastic cells or immunological reaction, etc. It may serve—besides diagnostic purposes—therapeutic goals for hereditary disorders, viral infections. It can be employed for the introduction of drug-resistance genes and test the therapeutic index (maximal, optimal or toxic dose of pharmaceuticals). ►retroviral vectors

Gene Mutation: Molecular alteration within a gene (base substitution or frameshift, point mutation, substitution mutation). ►mutation

Gene Neighbor Method: This method infers functional linkage of genes from the information of genetic linkage. It is applicable primarily to prokaryotes where operons are relatively common.

Gene Nomenclature: See http://www.gene.ucl.ac.uk/nomenclature/ for human genes/ or http://www.gene.ucl.ac.uk/cgi-bin/nomenclature/gdlw.pl; ►gene symbols, ►databases

Gene Number: The number of genes per genome of an organism can be estimated on the basis of mRNA complexity, or by total sequencing of the genome. The estimates based on mRNA can be best determined when the entire genome is sequenced. By this method the single-stranded RNA phage, MS2 was found to have 4 genes. The gene number has been estimated also from mutation frequencies. If the overall induced mutation rate, for e.g., is 0.5 and the average mutation rate at selected loci is 1×10^{-5} then the number of genes is $0.5/(1 \times 10^{-5}) = 50{,}000$. Although this method has some errors, the estimates so obtained appear reasonable. On the basis of mutation frequency in *Arabidopsis* the total number of genes was estimated to be about 28,750 (Rédei GP et al 1984 in Mutation, Cancer, and Malformation, p. 306; Chu EHY & Generoso WM, (eds), Plenum). The number of protein-coding gene number of *Arabidopsis* was estimated as 25,498 after sequencing the entire genome. The estimate after annotation has grown to 30,700 by June 2004 (TIGRE Annotation Database). By the late 1920s, John Belling counted 2,193 chromomeres in the pachytene chromosomes of *Lilium pardalinum* and assumed that this number corresponded to that of the genes.

In *Drosophila* ~17,000 genes were claimed on the basis of mRNA complexity. Based on the sequenced genome, the estimate was ~13,600. During the 1930s CB Bridges counted ~5,000 bands in the *Drosophila* salivary chromosomes and for many years it was assumed that each band represented a gene. Nucleotide sequencing of 69 salivary bands in the long arm of chromosome 2 of *Drosophila* pointed to the presence of 218 protein-coding genes, 11 tRNAs and 17 transposable element sequences within that ~2.9 Mb region. The shotgun sequencing of the *Drosophila* genome identified ~13,600 genes, encoding 14,113 transcripts because of alternate splicing. The number of protein-coding *Drosophila* genes was estimated to be ~14,000 (Yandell M et al 2005 Proc Natl Acad Sci USA 102:1566). In humans, 75,000–100,000 genes were expected on the basis of EST; of these about 4,000 may involve hereditary illness or cancer. The human gene number estimates in 2003 still varied from ~24,500 to ~45,00 (Pennisi E 2003 Science 301:1040). After the 'completion' of the sequencing the number was estimated between 28,000 to 35,000 yet the number of transcriptional units in humans appeared to be 65,000 to 75,000 (Wright FA et al 2001 Genome Biol 2(7):Research 0025). However, by 2004 the best estimate was 25,000–30,000. The finished euchromatic human genome seems to contain only about 20,000 to 25,000 genes (Nature [Lond] 431:931, 2004). Human chromosome 18 has the lowest gene density of 337 plus 171 pseudogenes (Nusbaum C et al 2005 Nature [Lond] 437:551). The ways of alternative splicing, the use of more than a single promoter (initiation codon) by the same DNA tract complicates the difficulties in estimation of functional units

In *Saccharomyces,* in the 5,885 open reading frames 140 genes encode rRNA, 40 snRNA and 270 tRNA (see also for revisions *Saccharomyces cerevisiae*). About 11% of the total protein produced by the yeast cells (proteome) has metabolic function, 3% each is involved in DNA replication and energy production, respectively; 7% is dedicated to transcription, 6% to translation and 3% (200) are different transcription factors. About 7% are concerned with transporting molecules and about 4% are structural proteins. Many proteins are involved with membranes.

In *Caenorhabditis* 19,099 protein-coding genes are predicted on the basis of sequencing of the genome.

The minimal essential gene number has also been estimated by comparing presumably identical genes in the smallest free-living cells *Mycoplasma genitalium* (482) and *Haemophilus influenzae* (1,749), both completely sequenced. In *Mycoplasma* 382 + 5 protein-coding genes are essential but 28% of the protein-coding genes have no known function (Glass JI et al 2006 Proc Natl Acad Sci USA 103:425). The minimal gene number among the ~4,000 in *Bacillus subtilis* appears to be 192 but another 79 are predicted to be essential (Kobayashi K et al 2003 Proc Natl Acad Sci USA 100:4678). Insertional inactivation mutagenesis indicated the minimal number to be ~265 to 300. Gene knockout indicates that some of the apparently minimally required genes of *Mycoplasma* are dispensable. Furthermore, only about 200 of the *Mycoplasma* genes are represented by orthologous genes in other organisms.

In *Caenorhabditis elegans* about 20 times more genes are indispensable for survival. In higher organisms, the number of open reading frames may be larger than the number of essential genes.

The gene number may not accurately reflect the functional complexity of a genome or organism because the combinatorial arrangement of proteins may generate great diversity and specificity. Many plants have about twice the number of genes of humans. ►gene, ►gene number in quantitative traits, ►transcriptome, ►genetic network, ►proteome, ►duplications, ►knockout, ►mtDNA; Cell 86:521 [1996]; Science 276:1962 [1997]; Adams MD et al 2000 Science 287:2185; Rubin GM et al 2000 Science 287:2204; Aparicio SAJR. 2000 Nature Genetics 25:129; Koonin EV 2000 Annu Rev Genomics Hum Genet 1:199; Akerley BJ et al 2002 Proc Natl Acad Sci USA 99:966; Moran NA 2002 Cell 108:583.

Gene Number in Quantitative Traits: It has been estimated by various complex statistical procedures (Mather, Jinks 1971 Biometrical Genetics, Chapman & Hall, London, UK) but none of the estimates are entirely reliable because the number of genes with minor contribution or greatly influenced by environmental effects, genetic linkage, etc. confound the picture. Perhaps the number of polygenes controlling one quantitative trait may not be more than five or six major genes rather than hundreds, postulated by some authors. Sewall Wright provided a very simple formula in 1913:

$$n = \frac{R^2}{8\left(s_1^2 - s_2^2\right)}$$

gene number (n) = where R is the difference between parental means, $[s_1]^2$ is the variance of the F_1 and $[s_2]^2$ is the variance of the F_2 generations.

An improved model of Zeng, considered linkage and variation in their effect where $\bar{c}$ is the average recombination rate between loci and C is the coefficient of variation for the distribution. ►polygenes, ►QTL, ►gene number; Jones CD 2001 J Hered 92:274; Schliekelman P, Slatkin M 2002 Am J Hum Genet 71:1369.

$$\hat{n} = \frac{2\bar{c}\hat{n} + C2(\hat{n} - 1)}{1 - \hat{n}(1 - 2\bar{c})}$$

Gene Number Paradox: Although viruses and bacteria have fewer genes than eukaryotes, at first glance it appears unusual that the very simple nematode, *Caenorhabditis* has more (37%) genes than the much more complex *Drosophila*. The rice plant seems to show substantially more genes than humans, currently 37,544 seem to code for proteins. The cause appears to be in the difference of regulation, alternative splicing, and in a more elaborate array of transcription factor and transcriptional cofactors. The average human gene may be transcribed in three to four different ways. *Drosophila* seems to have about 1,000 transcription factors, whereas humans have more than 3,000. Ape's genomes are more than 99% identical to humans, although great deal of difference exists in the function of the nervous system, and in morphology. ►C value paradox; Levine M, Tjian R 2003 Nature [Lond] 424:147.

Gene Ontology (GO): A set of gene classification rules regarding their molecular function, biological role and cellular location. The same set of criteria is employed for the genomes of *Saccharomyces cerevisiae*, mouse, *Drosophila melanogaster, Arabidopsis,* etc. GOs include categories (and additional groups within the main entry) such as Nucleic Acid Binding Proteins, Cell Cycle Regulators, Chaperones, Motor Proteins, Actin Binding, Defense Proteins, Enzymes, Enzyme Activators, Enzyme Inhibitors, Apoptosis Proteins, Signal Transducers, Storage Proteins, Structural Proteins, Transporters, Ligands, Ubiquitin, Tumor Suppressors, Metabolism, Organelle Control, Developmental Regulators, Sensory Perception, Behavior, etc. ►genome projects, ►ontology; Ashburner M et al 2000 Nature Genet 25:215; Anonymous 2001 Genome Res 11:1425; WGS; http://www.geneontology.org; sequence ontology: http://song.sourceforge.net/; gene ontology annotation: http://wego.genomics.org.cn/cgi-bin/wego/index.pl; human and ten other organisms′ gene partition: http://bcl.med.harvard.edu/proteomics/proj/gopart/menu.php; combination of information from 31 different species; converting between different database identifiers; finding orthologous genes from other species and searching a large body of public gene

expression data for co-expression: http://biit.cs.ut.ee/gprofiler/; functional profiling on the basis of several tools: http://vortex.cs.wayne.edu/projects.htm.

Gene Order in the Chromosome: It can be determined by three-point or multipoint testcrosses in eukaryotes or by similar principles in prokaryotes. Conservation of the order permits evolutionary inferences among species. ▶mapping genetic, ▶bacterial recombination, ▶chromosome walking, ▶physical map

Gene Pool: The sum of alleles that can be shared by members of an interbreeding population. ▶population genetics

Gene Prediction: Computer analysis of DNA sequences for matching known genes. ▶Genie, ▶GENSCAN, ▶FGENE, ▶GRAIL, ▶Mzef, ▶GenomeScan, ▶TWINSCANM, ▶SGP-1, ▶SLAM, ▶GeneWise, ▶Gnotator, ▶HMMgene, ▶Ace.mbly, ▶EST_GENOME, ▶annotation of the genome; Mathé C et al 2002 Nucleic Acids Res 30:4103; Guigó R et al 2003 Proc Natl Acad Sci USA 100:1140.

Gene Product: The transcript(s) of a gene and by extension the processed transcripts and even the translated polypetides or RNAs. ▶processing, ▶transcript, ▶polypeptide, ▶RNA

Gene Product Interaction: It is responsible for epistasis, additive, complementary and suppressor type of modifications of Mendelian segregation ratios. These are frequently called gene interactions but actually, the gene products interact. Interaction among gene products is quite extensive in yeast 250 sequence-specific regulators were found to affect the expression of ~6,000 genes. It appears that genes are co-regulated at the level of transcription. ▶modified Mendelian ratios, see examples under ▶morphogenesis in *Drosophila*, ▶protein-protein-interaction, ▶microarray hybridization, ▶two-hybrid method, ▶networks, ▶genetic networks, ▶phage display, ▶proteomics, ▶interactome, ▶epistasis, ▶protein complexes; Adamkewicz JI et al 2001 J Biol Chem 276:11883; Ito T et al 2001 Proc Natl Acad Sci USA 98:4569; Minton AP 2001 J Biol Chem 276:10577; von Mering C et al 2002 Nature [Lond] 417:399; http://www.genome.ad.jp/brite/; http://dip.doe-mbi.ucla.edu.

Gene Rearrangement: ▶immunoglobulins, ▶phase variation, ▶sex determination in yeast, ▶transposons, ▶chromosomal rearrangements, ▶gene replacement, ▶targeting genes

Gene Regulation: ▶regulation of, ▶gene activity

Gene Relic: Usually a member of a multigene family that does not have all the elements necessary for function; it is actually a pseudogene. Their existence is explained by losses during evolution. ▶pseudogene, ▶processed pseudogene

Gene Replacement: Accomplished with the aid of genetic vectors that carry a different allele and the flanking sequences of a chromosomal locus (see Fig. G19). This constitution permits intimate homologous pairing in the area. If double crossing over or gene conversion takes place, the allele in the vector may replace the one in the chromosome. Because the frequency of such an event is very low, selectable markers (*URA3* in the diagram in this integrating vector) must be used to screen out the replacement in a large population. For the selection, one may use an antibiotic resistance gene with a defect in the upstream area and in the vector the same but with a defect downstream may restore antibiotic resistance and that can selectively be isolated on media containing the antibiotic. By the use of the LoxP-Cre system, larger than 100 kb mouse chromosomal segment can be replaced by homologous human DNA tracts and the procedure called recombinase-mediated genomic replacement (RMGR) can be used to model human genetic diseases in mouse (Wallace HAC et al. 2007 Cell 128:197). ▶targeting genes, ▶localized mutagenesis, ▶site-specific mutation, ▶transformation, ▶Cre/LoxP, ▶FLP/FRT, ▶knockout, ▶homologous recombination, ▶site-specific recombination, ▶RMCE; Richardson PD et al 2001 Curr Opin Mol Ther 3(4):327.

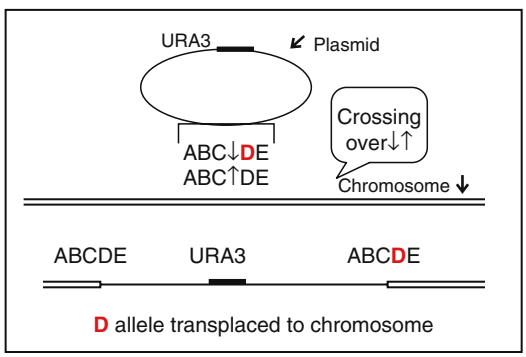

Figure G19. Gene replacement

Gene Rescue: ▶plasmid rescue, ▶marker rescue

Gene Resource Locator (GRL): A database on gene expression pattern, regulation, alternatively spliced transcripts. ▶gene expression, ▶regulation of gene activity; http://grl.gi.k.u-tokyo.ac.jp.

Gene Scanning: ▶linker scanning

Gene Sharing: An evolutionary process; a gene may acquire a new function without losing the original one, e.g., the crystalline protein gene δ2 in chickens

and ducks my have argininosuccinate lyase function as well as structural role in the eye lens (Piatigorsky J, Wistow G 1991 Science 252:1078).

Gene Silencing: ►silencer

Gene Size: It can be measured in different ways. If only the translated number of codons is considered, the smallest genes appear to be the 21 bp *mccA* coding for the antibiotic heptapeptide, microcin C7 (MW 1,177 Da) of *Enterobacteria* (Tenson T et al 1997 J Biol Chem 272:17425). Another is the pentapeptide encoded within the 23S ribosomal subunit by only 15 nucleotide pairs (González-Pastor JE et al 1994 Nature [Lond] 369:281). The largest mammalian genes, including introns and upstream and downstream regulatory sequences, may be in the range of hundreds of kbp. The human dystrophin gene with 2.34 x 10^6 bp includes 79 exons and it is probably the longest gene known (Tennnyson CN et al 1995 Nature Genet 9:184). Processed genes, reverse-transcribed from mRNA, are free of introns and other non-coding sequences are naturally shorter (Hollis et al 1982 Nature [Lond] 296:321). In human chromosome 7, the average gene length is 69,877 bp and it contains 10.1 exons with an average size of 261 bp. In human chromosome 10, the gene sizes vary from 1,776,209 bp (CTNNA3, CATENIN α3) to 859 bp (CLML5, CALMADULIN-LIKE 5). The longest exon is 9,763 bp (SH3MD1, SH3 multiple domain 1), the shortest is 3 bp (CDH23, CADHERIN 23). The "average" gene may have 400 codons and thus encode 46 to 48-kDa proteins. The 26,564 annotated human genes show an average of 8.8 exons and 7.8 introns. About 80% of the human exons are less than 200 bp. Less than 0.01% of the introns are less than 20 bp, and fewer than 10% are longer than 11,000 bp (Sakharkar MK et al 2004 In Silico Biol 4(2): 0032). The human genome of about 3 x 10^9 bp contains an estimated 25,000–30,000 genes. *Haemophilus influenzae* bacterium has 1,749 sequenced genes whereas budding yeast in its 1.8 x 10^7 genome encodes ~5,885 genes by 12,068-kb DNA; thus, its "average" gene is about 2,050 nucleotides long. By sequencing the genome of *Caenorhabditis* 1 gene was found per ~5-kb; the average intron number was found to be 5. In *Drosophila* upon completion of the sequencing of the "entire" genome, the average transcript size appeared to be ~3,058 bp with an average of ~4 exons. The intron sizes varied between 40 bp to > 70. The largest *Drosophila* protein, the cytoskeletal linker, Kakapo contains 5201 amino acids and the smallest is the 21-amino acid L38 ribosomal protein. The smallest gene numbers, four, are found in some viruses. ►introns, ►exons, ►genomic DNA, ►*Enterobacteria*, ►Mbp, ►dystrophin, ►ribosomal RNA, ►*Haemophilus influenzae*, ►*Saccharomyces cerevisiae*, ►*Aspergillus*, ►exon, ►intron, ►gene

Gene Space: Regions of high gene density in the genome; generally it is rich in GC content. ►FANTOM, ►desert, ►jungle

Gene Substitution: The replacing of an old allele by a new one in a population, and chromosome substitution.

Gene Switching: It uses various ligands (tetracycline, rapamycin, estrogen analogs) that may down or regulate gene expression without turning it off. ►gene switch, ►tetracycline, ►rapamycin, ►estrogen

Gene Symbols: The abbreviated representation of the function of the genes or it designates it in a unique manner using a single or more letters. Very frequently, the allele that fails to carry out the normal function provides the name for the locus, e.g., the white eye locus in *Drosophila* is symbolized as *w* although the normal color of the eye is red. The symbols used vary in different organisms. Generally, the symbols begin with the first letter of the name and it is usually italicized. The recessive alleles in eukaryotes are symbolized with lower case letters whereas the wild type alleles either begin with a capital letter or all the letters are capitalized. Symbols of genes in the same chromosome strand are usually separated by a space in between them. Genes in the homologous strands customarily have a slash in between them (*a/b*). A semi-colon separates genes in non-homologous chromosomes and one space (*a; d*). Multiple alleles in *Drosophila* are designated by the same letter(s) representing the locus and further identified by superscripts, e.g., w^a, w^{a2}, w^{aM}, w^{a79i} or other additional distinctive signs. Recessive or dominant alleles in a series of mutant alleles are frequently symbolized as a^R or a^D, respectively. The common dominant allele may be designated also as a^+ or A^+. Absence of a gene or lack of its function may be symbolized by a lower case letter such as a^-.

Isoenzyme determining alleles may be designated as Adh^F, Adh^S, and the superscript indicating fast or slow run in the electrophoretic field. A^n means null allele, a^l may be used for a lethal allele, if necessary with additional specifications. Non-allelic loci with similar phenotypes may be symbolized with the same letter(s) and subscripts: a_1 and a_2. Also, non-allelic loci with similar phenotypes (mimics) may be symbolized as *tu-1a, tu-1b, tu-2*. Different loci encoding similar proteins may be designated with the same letters but attaching to the letters different numbers or by the addition of an abbreviated form of the molecular weight of the protein (*Hsp68, Hsp83*). Transpositions are symbolized with the designation of the original symbol followed in parenthesis the

new location: [ry^+](*sd*), indicating that the *rosy* gene was moved from chromosome 3–52 location to the *scalloped* locus in chromosome 1-51.5. The designation of transformants follows that of transpositions. Modifier genes, such as suppressors may be designated as the symbol of the modifier, followed in parenthesis the gene modified: *su*(lz^{34}). Some symbols may carry also the name of the discoverer or the location of discovery of the mutation or the mutagenic agent used. Rv may indicate reversion in superscript. Capital letters and additional specifications designate chromosomal aberrations. Translocations (reciprocal interchanges between/among non-homologous chromosomes) are represented as *T(1;Y;3)* indicating that chromosomes 1 (X-chromosome), Y and 3 are involved. Each chromosome may be further specified using a capital letter superscript indicating the approximate position of the break point as P (proximal to the centromere), D (distal), or M (median). An X-chromosomal ring (of *Drosophila*) may be symbolized as *R(1)1*. Paracentric inversions are represented as *In*(*2L*) or *In*(*2R*), depending whether the left or right arm of chromosome 2 is involved. *In*(*2L,R*) indicates pericentric inversion of chromosome 2. To this symbol, genes closest to the break points may be attached. For transposition (non-reciprocal transfer of chromosomal segments) the symbol is *Tn* and in parenthesis first the donor, followed by the recipient chromosome, e.g., *Tn*(*2;3*). Again, the gene(s) involved may be included in the symbols. Deficiencies are symbolized by *Df* followed by the indication of the chromosome (arm) and locus involved: *Def*(*2R*)*vg*. Duplications are symbolized with *Dp* such as *Dp*(*3;1*) indicating that duplicated segment of chromosome 3 is located in the X-chromosome. When the duplicated segment has a centromere and it is a free element, it is symbolized with a letter *f*, e.g., *Dp*(*1;f*). In case there are multiple repeats: *Dp*(*1;1;1*). When a combination of multiple chromosomal rearrangements occur, they are indicated one after the other with a "+" sign between them. The location of break points may be designated by the euchromatic (1 to 102) or heterochromatic (h1 to h61) segment numbers. The older symbols in plants followed the customs in *Drosophila*. Recently, largely for convenience of typing or printing, the subscripts are substituted with a number written together with the gene symbol and the allelic number is attached hyphenated: *a2-5* the second *a* locus and allele 5 (rather than superscript 5). Mouse geneticists identify loci with three or four italicized letters, the first is capitalized. Human geneticists also use three or four (commonly not italicized) all-capital letter symbols with additional numbers. In Yeast and *Arabidopsis,* the new gene symbols use three italicized capital letters for the wild type and three italicized lower case letters for the recessive alleles. In the majority of fungi the wild type alleles are designated with a superscript *" + "*. Allelic designation frequently follows the locus designation in parenthesis: *ilv*(*STL6*) or *pyr-3* (*KS43*). Suppressor mutation symbols may include also the gene they modify: *su*(*met-7*)*-1*. The symbol *ssp* means supersuppressors. Mitochondrial mutations are designated as *mi*, and additional numbers. RFLP fragments are identified with an italicized three-letter symbol of the laboratory and a serial number. Transposable elements are symbolized similarly to the genes. In human genetics only capital letter symbols (no more than 4–5 letters) are used without sub- or superscripts. Hyphens or punctuations in the symbols are exceptional. Different loci by the same symbol are numbered, e.g., BPAG1, BPAG2. Alleles may be indicated by an asterisk after the symbol and followed by other designation e.g., ACY1*2. A slash between two symbols stands for the diploid genotype, hetero- or homozygous. Lack of synteny is indicated by semicolons(s) between the symbols. If linkage is unknown comma is used. Gene order is usually started from the short arm down.

Bacterial geneticists designate the loci with italicized three lower case letters followed by a capital letter: *lacI, lacZo, lacZ* indicating the lactose utilization operon regulatory (inhibitor), operator and the β-galactosidase genes, respectively. The letters *p, o, a,* stand for promoter, operator and attenuator, respectively.

Protein products of the genes are generally symbolized with the abbreviations of the genes but they are all in capitals or in yeast, the first letter is capital and the rest are lower case and not italicized.

Arabic numerals and chromosomes generally designate linkage groups by Roman numerals. In some publications, the linkage groups may not be correctly identified with particular chromosomes.

Gene symbols have been periodically revised in some organisms and this may make reading the older literature difficult. Creating new symbols is a cheap attempt to gain citations. If new symbolism is warranted that should not be used retroactively to published and used symbols. It is quite unfortunate that many genes have multiple synonyms and symbols. ►*Drosophila*, ►databases [plants–Mendel], gene nomenclature assistance; for *Caenorhabditis*, Horvitz HR et al 1979 Mol Gen Genet 175:129; mouse, Maltais LJ et al 2002 Genomics 79:471; humans, Wain HM et al 2002 Genomics 79:64; http://www.gene.ucl.ac.uk/nomenclature; www.flynome.com.

Gene Synthesis: The generation of nucleotide sequences by the methods of organic chemistry. These sequences—and their variations—can then be tested

for function after transformation into suitable host cells (see Fig. G20). The first entirely synthetic genes coded for tRNAs. Gene may be carried out also in a different and much simpler way. Sometimes an investigator wishes to remove or add a restriction enzyme recognition site or alter the coding properties so a different amino acid would be inserted into the protein. The desired sequence can be synthesized by using pairs of 10–15mer oligonucleotides and anneal them at the 3′-ends of long oligonucleotides as templates and primers. At the same time, several sequences can be generated each up to 400 nucleotides and then ligated before transforming them into a vector. The simplest diagrammatic representation is as follows:

Figure G20. Gene synthesis. Annealed, then use T7 DNA Polymerase and proceed with synthesis

On programmable microchips, multiple genes (21) can be synthesized (Tian J et al 2004 Nature [Lond] 432:1050). ►genes synthetic, ►synthetic genes, ►DNA chips, ►microfluidic; Uhlmann E 1988 Gene 71:29.

Gene Tagging: Gene tagging places an insertion or transposable element or any other DNA sequence into a gene with the aid of genetic transformation (transfection). When the inserted sequence is known and can be probed by molecular hybridization and/or genetical inactivation or altering the function (insertional mutation), it can identify the target gene. Some insertions going into intergenic or untranslated (intron) regions may not affect the expression of the gene involved. ►labeling, ►probe, ►insertional mutation, ►targeting genes, ►biolistic transformation, ►transformation genetic, ►transposons; Johnson GC et al 2001 Nature Genet 29:233.

Gene Targeting: A method of transformation using cell-specific promoter attached to the prospective transgene in the vector. The goal is to localize the transgene expression to only one type of cells. ►promoter, ►transformation genetic, ►gene replacement, ►targeting genes, ►targeted gene transfers, ►knockout, ►localized mutagenesis, ►excision vector, ►*Cre/loxP*, ►*FLP/FRT*; Reynolds PN et al 2001 Nature Biotechnol 19:838.

Gene Therapy: The insertion of a functional gene into an organism for the purpose of correcting or compensating for genetic defect or combat or prevent infection. In contrast to biochemical compensation for a genetic defect (e.g., use of insulin), gene therapy may provide a dynamic supply of the missing or deficient metabolite rather than in discrete shots. The vector RetroTet-Art was designed to modulate the expression of the transgene by employing the tetracycline inducible system as well as the p16 growth arrest protein (Rossi FM et al 1998 Nature Genet 20:389). The most important requisite of gene therapy is the correct identification of the genotype responsible for the phenotype determined by clinical means. It can be carried out either in somatic cells or in the germline (gametes, zygotes). Germline gene therapy may be risky because of various chromosomal rearrangements may be caused in the transgenic cells. There is, however, a possibility to achieve some of the goals of introducing into the gametes or zygotes genetically engineered DNA. In vitro fertilization followed by screening of the 8-cell stage embryos for some of the defects present in the heterozygous families may permit the transfer into the uterus only those embryos, which are free from the genetic defect. This procedure avoids most of the risks of directly manipulating the genome, and it is the technology used by natural selection during evolution. The methods potentially available are microinjection of (foreign) DNA or transformation with retroviral or adenovirus vectors, liposomes (see transformation of animals; human gene transfer) and gene replacement by homologous recombination. Another possibility is “knockout” when the function of a deleterious gene is eliminated by insertional inactivation or deletion. The technology is available for transformation or in vitro mutation that can be followed by injecting embryonic stem cells into blastocytes that are introduced into the uterus of a female to develop genetically modified embryos and eventually viable offspring. Recently introduction of —into mice with induced tyrosinemia—hepatic cells that could proliferate in the defective liver was successful in the laboratory with a model organism. The transformation technology needs refinements before it can be widely applied to humans. Polyelectrolyte films such as poly(L-glutamic acid/PLG) and poly(L-lysine/PLL) in the presence of charged cyclodextrin seem to be effective delivery vehicles for DNA. Such construct may be maintained at elevated level in the specific target environment and facilitate internalization of the DNA into the nucleus (Jessel N et al 2006 Proc Natl Acad Sci USA 103:8618).

The current gene therapy protocols (several hundreds available) involve altering the somatic cells. The techniques of embryo implantation are widely used to overcome female inability of conceive without surgical assistance. Before implantation, these fertilized embryos may be then tested for

expression of transferred remedial genes. These procedures may become potentially useful for preventing the expression of genetic diseases under the control of single genes such as the Lesch-Nyhan syndrome, Tay-Sachs disease, cystic fibrosis, muscular dystrophy, Gaucher's disease, β-thalassemia, ADA, melanoma, neuroblastoma, multiple myeloma, lymphoma, breast cancer, colorectal cancer and several others. An ADA patient treated by gene therapy appeared relatively well and survived more than ten years after the use of retroviral transformation although her immune system was below normal. Autologous $CD34^+$ and functional ADA gene transplantation by umbilical cord blood resulted in low frequency (1–10%) of ADA expressing T lymphocytes, too low to be effective for a cure. Polyethylene-glycol-conjugated ADA enzyme treatment was much more effective yet not without undesirable effects. Liposomal vectors carrying the human leukocyte antigen (HLA)-B7 and the β_2 microglobulin cDNA to tumors can express these genes (see Fig. G21). One lentiviral vector contains an antibody for special cell recognition and a mutant viral glycoprotein, which is inactivated in binding ability to its receptor but retains its ability to trigger pH-dependent membrane fusion. Such a vector recognizes the target cell membrane and attaches to it. The antibody induces endocytosis. There the fusogenic molecule of the vector responds to the low pH and triggers membrane fusion and virus can enter the cytosol. After reverse transcription and migration to the nucleus the vector can integrate into the host genome and the transgene can be inherited (Yang L et al 2006 Proc Natl Acad Sci USA 103:11479).

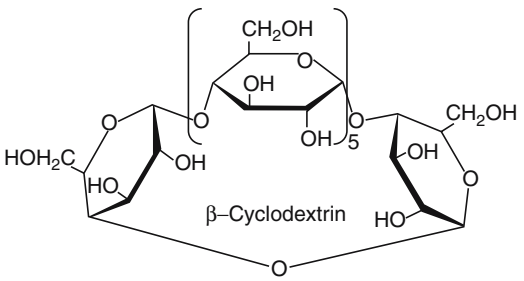

Figure G21. β Cyclodextrin

SCID-X1 patients were transfused by hematopoietic stem cells, expressing the CD34 surface marker and transfected by a defective Moloney retroviral vector carrying the γc cDNA of the SCID-X1 human gene (Cavazzana-Calvo M et al 2000 Science 299:669). The CD34 cells are capable of differentiating into all types of blood cells. The SCID-X1 gene is a cytokine receptor. The patients so treated displayed normal lymphocytes and immune reactions ten months after the treatment. Actually, in three months they were able to leave the complete isolation of the hospital. The apparent success of this treatment—compared to the earlier attempts described above—was due to improvements in the cell culture techniques (using Flt3 protein). Flt3 is a natural embryo cell growth factor. The new method avoided the administration of polyethylene glycol-conjugated ADA enzyme that exerted earlier a toxic effect by deoxyadenosine. Another important technical improvement was the use of transfected stem cells rather than mature transgenic T cells. More recently, highly efficient endogenous human gene correction (SCID) has been reported by the use zinc finger nucleases. Library of zinc finger proteins have been engineered for the recognition of unique chromosomal sites and fused to a nuclease domain. Such a construct can bring about double-strand breaks in the DNA required for homologous recombination. A plasmid-carried corrective DNA can thus replace the defective gene. Actually, 7% of IL2Rγ genes, responsible for SCID, were corrected in both X chromosomes and expressed the right mRNA and protein (Urnov FD et al 2005 Nature [Lond] 435:646).

In 2002, acute lymphoblastic leukemia was observed in some of the children so treated (Science 298:34). The leukemia was caused in two cases by insertional mutation affecting the Lmo12 oncogene and in two instances into the IL-2rg gene. In one case, integration took place at both of these sites. It seems these cytokine receptors enhance leukemia (leukemogenesis). Davé UP et al 2004 (Science 303:333) are optimistic regarding the use of this type of therapy because the frequency of harmful insertions is relatively low. Clinical trials in the USA continue with careful consideration given to each case. In several European countries, temporary bans have been lifted or new rulings were suggested in 2004. Unfortunately, since then additional leukemia cases have been reported. Adverse effect of the gamma c gene subunit of the T cell antigen receptor (7p15-p14)—contained by the vaccine—has been suspected in the leukemogenic effects in some case. These adverse experiences cause a halt in this type of gene therapy and limit its application to cases where other approaches failed.

Using adenovirus vector with the human cystic fibrosis transmembrane conductance regulator (CFTR) resulted in expression of the gene for nine days in the nasal or bronchial membranes. With retroviral vector the low-density lipoprotein (LDL) receptor, important for familial hypercholesterolemia, has been successfully transformed and functioned. Promising initiatives were made by treatment of patients with retroviral vectors carrying interleukin-4 (IL-4) to fibroblasts resulting in infiltration

of the tumor with $CD3^+$ and $CD4^+$ T cells and cell adhesion molecules. The treatment resulted in some trials in the increase of $CD8^+$ tumor-specific cytotoxic T lymphocytes (CTL) and eosinophils as well as $CD16^+$ killer cells. Another approach is using intrabodies. As a treatment of the HIV-1 virus infection, intrabodies are directed to the lumen of the endoplasmic reticulum of the cells where they prevent the secretion of the gp160 glucoprotein precursor (a viral envelope protein) and its transport to the cell surface. Using anti-gp120 intrabodies the gp120-gp160 envelope proteins of the virus may be neutralized. Anti-tat antibody fragments introduced into the cells may prevent the activation of transcription by the viral TAT and the cellular NF-κB proteins. Intrabodies against the Rev splicing element may also reduce the replication of the virus. Intrabodies against fusin may hinder HIV entry into the cells. The somatic cell genetic therapy may target cancer cells with interleukins, tumor necrosis factor, granulocyte macrophage colony stimulating factor to reinforce the immune system or use monoclonal antibodies against cancer cells equipped with toxins or sources of radiation (see lymphocytes; magic bullet). Some of the genes that are suitable for germline modification may be targeted to specific organs for alleviating or to overcome the symptoms of the disease. In some cases, e.g., neurological disorders, *ex vivo* methods have been sought of for the restoration of the normal function (in Alzheimer disease) of nerve growth factor (NGF) or transplanting dopamine-producing tissue (in Parkinson disease). Bone marrow transplantation may alleviate or reverse the course of lysosomal storage diseases. In the future, targeting the medication to specific cells, tissue or organs may gain increased significance because it will permit greater effectiveness and higher dosage without side effects. Purified genetically engineered myoblasts and myofibers can be propagated *ex vivo* and re-injected into the body. The multinucleate muscle cells may make possible the delivery of two or more different small vectors (e.g., AAV), which may be simultaneously expressed within the same cell and their product(s) released into the circulatory system to treat not only muscle but also other problems (Ozawa CR et al 2004 J Clin Invest 113:516).

One problem of gene therapy is that the cell defense mechanism may inactivate the introduced gene by methylating their promoters or immunologically neutralize the foreign proteins. Integration of the vector into tumor suppressor genes results very rarely in cancerous transformation. Other problems arise by unexpected restitution of the retroviral pathogenicity through recombination of the vector and endogenous human viruses. These latter problems are reduced by the use of DNA (rather than retroviral) vectors. Some of the adenoviral vectors contain a much-truncated DNA to prevent viral replication and reduced immunological response against the vector but other adenoviral proteins are actually immunosuppressors and their deletion may cause the elimination of the vector by the host cells. Currently the adeno-associated and the lentiviral vectors may be most promising.

Somatic gene therapy involves apparently smaller risks. The possible harmful consequences of germline alterations are much more difficult to assess. Some gene therapy protocols combine the procedure with chemical treatment. Introduced into a cancerous brain, by a viral vector, working only with dividing cells, the herpes simplex virus thymidine kinase (HSTK) gene, it is assured that the vector lands only in the tumor cells because the normal cells do not divide. After the establishment of the transgene the patients are treated with ganciclovir. This drug after phosphorylation by HSTK can be incorporated into the DNA but it prevents then DNA replication resulting in the selective death of the cancer cells. Recombinant proteins may be used to remedy diverse metabolic defects. Ideally, the protein supply should be as under natural conditions, i.e., the amount would be variable in response to the need. For success of such treatments it is usually important that the protein would be rapidly secreted in response to orally administered drugs and the secretion would be rapidly stopped after discontinuation of the drug. Moreover, the protein must not incite an immunologically adverse reaction. Enzyme replacement or enhancement may be effective for lysosomal storage diseases (Desnick RG, Schuman EH 2002 Nature Rev Genet 3:954).

Recently, in utero treatments of fetuses afflicted by α-thalassemia or severe combined immuno deficiency (SCID), which may harm the developing embryo before or immediately after birth, respectively, have been considered. Such treatments may have still unknown side effects both on the fetus and mother. Some defects involving differentiation of limbs or brain (e.g., Greig's syndrome) occur early during pregnancy and may not be obvious until it is too late to apply any treatment. The α-Antitrypsin deficiency is manifested in adult stage and then oral administration of 4-phenylbutyric acid facilitates the release of antitrypsin from the endoplasmic reticulum and as a "chemical chaperone" may prevent the injuries resulting from AAT deficiency.

Human neural progenitor cells can be modified to release glial cell derived neutrotrophic factor (GDNF) under an inducible promoter. After partial lesion of the dopamine system of rats, the engineered cells were transplanted into the brain of rats. Two weeks after implantation the engineered cells migrated within the striatum and released physiologically

relevant level of GDNF and facilitated survival of the neurons, and after eight weeks it even migrated to the substantia nigra. Loss of dopaminergic neurons in the substantia nigra is usually associated with Parkinson disease. The same type of cells survived for three months in the brain of aged monkeys and released GDNF. This technology shows promise to eventual cure of Parkinson disease currently largely incurable (Behrstock S et al 2006 Gene Therapy 13:379).

Some people oppose gene therapy on biological and/or ethical grounds. The arguments against gene therapy stem from the fears of unforeseable damage to the human gene pool and the possibility of using these procedures for "genetic enhancement". Genetic enhancement would have similar goals as eugenics and eventually may be exploited to create "super-soldiers" or other antisocial individuals with "uniform" genetic makeup. These fears are frequently fanned by political agenda or by unfounded speculations. The argument in favor of gene therapy is that it provides means to prevent the perpetuation of "disease genes" by specifically targeting the single defects. It may result not only in elimination of suffering but may also reduce health maintenance cost on the long run. In case of somatic gene therapy, unintended insertions into the germline may happen rarely. The US Federal Drug Administration proposed that such insertion should be limited to less than 50 per µg of DNA employed and genetically this may mean less than 1 insertion/6,000 sperm. It is true that not all possible consequences of gene therapy have been seen in an evolutionary history. The same criticism may also apply to several drugs that are part of current medical practice. Many of the medicines have physiological and genetic side effects (e.g., diagnostic and therapeutic X-rays, several antibiotics, anticancer drugs, etc.) yet the benefits are supposed to outweigh their risks. In human gene transfer, there are some potential risks of new constructs to develop by recombination with the viral vector. In some cases, the decision is very difficult, e.g., human dwarfism can be cured by the application of growth hormones or by functional growth hormone genes. Dwarfism is not an acute life-threatening anomaly yet it interferes in many ways with the normal fulfillment of life. The question arises then how far social philosophy should be permitted to affect the life of an individual. Animal models can be successfully applied for the testing of the physiological and biochemical consequences of gene therapy but it may not detect all the consequences for human behavior and mental abilities. One possibility appears the repair of disease genes at the site of the defect. Single-stranded DNAS, double-stranded DNA, DNA-RNA hybrid constructs, artificial chromosomes have been designed that may repair the defective nucleotides through site-specific recombination. Although the numerous repair attempts are promising and some initial successes have been reported, the efficiency of the system is not sufficient for clinical applications (Liu L et al 2003 Nature Rev Genet 4:679). Thus, gene therapy still has to face not just biological, technical problems but ethical ones as well. The public often mistrusts new technologies, especially when the application suffers initial mishaps. The freedom of scientific inquiry and the innate human striving for knowledge should not be prevented, however, for any reason. Although the same caution may be necessary as it was applied with the techniques of "recombinant DNA". Some of the problems to be solved include the development of more effective vectors and extrapolating successfully from animal models to humans. Sporadic tragic misfortunes (Teichler Zallen D 2000 Trends Genet 16:272) with the application of this technology cannot be a rational cause for opposing these innovative and promising medical research efforts. By July 2002, there were no US Government-approved gene therapy product on the market (Cimons M 2002 Nature Med 8:646), and none by 2008. The approximate share of the various genetic vectors in gene therapy experiments: retroviruses 40%, adenovirus 26%, liposomes 14%, plasmids 9%, vaccinia virus 5%, adeno-associated virus 2%, fowlpox virus 2%, canarypox virus 1%, RNA 1%, herpes simplex virus 0.3%. Gene therapy has potential applicability not only to hereditary diseases but also for a wide variety of acquired illnesses. (See diseases and terms under specific entries; ►hemophilia, ►thalassemia, ►rheumatoid fever, ►hypertension, ►Niemann-Pick disease, ►Tay-Sachs disease, ►transformation genetic, ►human gene transfer, ►transfection, ►receptor-mediated gene transfer, ►ultrasonics, ►immunostimulatory DNA, ►*ex vivo*, ►viral vectors, ►non-viral vectors, ►adeno-associated, ►virus, ►retroviral vectors, ►onco-retroviral vectors, ►MoMuLV, ►lentivirus vectors, ►liposome, ►T cells, ►molecular breeding, ►hysteresis, ►immune system, ►adoptive cell therapy, ►cell, ►sickle cell anemia, ►mosaic, ►epitope, ►cancer gene therapy, ►biomarker, ►intrabody, ►ribozyme, ►HIV, ►NF-κB, ►Rev, ►phenotypic knockout, ►ganciclovir, ►immunization genetic, ►antivector cellular immunity, ►targeting genes, ►targeting vector, ►polyethyleneimine, ►nanoparticles, ►thalassemia, ►SCID, ►adenosine deaminase deficiency [►ADA], ►disaccharide intolerance, ►mitochondrial gene therapy, ►ornithine transcarbamylase, ►muscular dystrophy, ►IUGT, ►ART, ►informed consent, ►public opinion, ►enzyme replacement therapy, ►antisense technologies, ►RNAi, ►locked nucleic acids, ►SCID, ►zinc finger nuclease, ►stem cell, ►mitochondrial diseases in humans; Anderson WF 2000 Science 288:627; Am J Hum Genet 2000 87:272;

Romano G et al 2000 Stem Cells 18:19; Hanazano Y et al 2001 Stem Cells 19:12; Factor PH ed 2001 Gene Therapy for Acute and Acquired Diseases, Kluwer, Boston; Pfeifer A, Verma IM 2001 Annu Rev Genomics Hum Genet 2:177; Opalinska JB, Gewirtz AM 2002 Nature Rev Drug Discovery 1:503; neuronal gene therapy: Sapolsky RM 2003 Nature Rev Neurosci 4:61; viral vectors: Thomas CE et al 2003 Nature Rev Genet 4:346; advances on vectors and therapeutic applications; Smyth Templeton N ed 2004 Gene and Cell Therapy, Marcel Dekker, New York; Verma IM, Weitzman MD 2005 Annu Rev Biochem 74:711; OBA; CBER; genetic medicine; O'Connor TP, Crystal RG 2006 Nature Rev Genet 7:261; Criggler-Najjar syndrome; RAC; http://www4.od.nih.gov/oba/rac/clinicaltrial.htm; http://www.advisorybodies.doh.gov.uk/genetics/gtac/index.htm.

Gene Therapy for Infectious Diseases: Gene therapy is most commonly directed against hereditary diseases or other acquired conditions for what drugs are not sufficiently effective. Gene therapy may be designed against pathogenic microorganisms too. The available or potentially working approaches to be considered are: transformation by resistance genes, DNA vaccination, suicide genes, use of lytic phage, antibody genes, increase the production of metabolites that interfere with the development of the disease, use of antisense technology, RNAi, transgenesis for antimicrobial peptides, ribozyme-mediated cleavage of RNA, activation of antimicrobial defense genes, increase the dosage of antimicrobial genes, inactivate receptors required fort infection, recruit antagonists of parasites, etc. A great variety of possible strategies may be developed. (See terms listed in separate entries in this book; Kaslow DC 2004 Trans R Soc Trop Med Hyg 98:593).

Gene Titration: Determining the quantitive expression of gene(s) as a function of dosage. ►dosage effect, ►titration; Yinduo J et al 2001 Science 293:2266; Shiau AL et al 2005 J Virol 79:193.

Gene Transfer: ►transformation, ►human gene transfer, ►gene transfer lateral

Gene Transfer by Microinjection: It was the principal means of transformation of animals in the 1980s. Today gene targeting and other procedures are preferred (see Fig. G22). (See diagram, ►transformation genetic [animals], ►gene replacement, ►targeting genes

Gene Transfer, Lateral: The transmission of genes and genetic elements by infection, plasmids, transposable elements and the acquisition of mitochondria and chloroplasts during evolution. ►infectious heredity, ►plasmids, ►organelle sequence transfer, ►evolution

Gene Trap Vectors (entrapment vector): These are equipped with a reporter gene that can insert at a splice acceptor site. The resulting gene fusion may facilitate the transcription of the reporter gene. It may be used with (mouse) embryonic stem cells to detect genes expressed during early development (Hansen J et al 2003 Proc Natl Acad Sci USA 100:9918). Actually, this procedure can tag any gene even if it is not expressed. ►ES, ►gene fusion, ►insertional mutation, ►reporter gene, ►OMNIBANK; Medico E et al 2001 Nature Biotechnol.19:579; Stanford WL et al 2001 Nature Rev. Genet 2:756; Lai Z et al 2002 Proc Natl Acad Sci USA 99:3651.

Gene Trapping: A vector cassette consisting of a promoterless reporter gene and/or a selectable marker

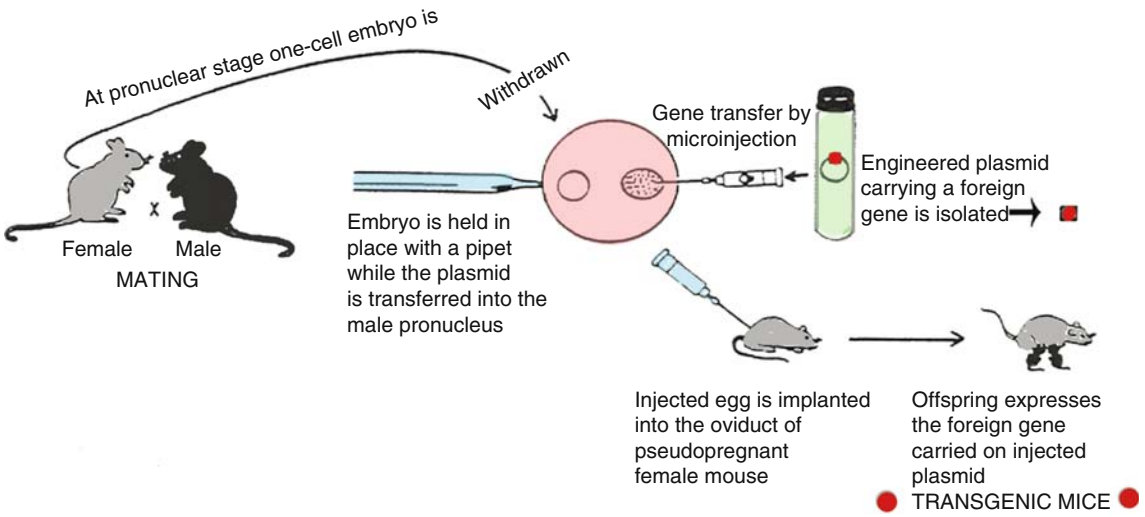

Figure G22. Gene transfer by microinjection

flanked by an upstream splice acceptor site and a downstream transcriptional termination sequence is used. When inserted into an intron of a target gene, the cassette is expressed from the host promoter fused to and easily recognized by the expression of the reporter. Since it contains a termination signal (such as for polyadenylation), the protein product is truncated. The insertion represents a tag on the disrupted target gene. Such a system permits tagging of a large number of genes across the entire genome of an organism. In plants, any somatic cell can be regenerated into intact seedlings. In animals, the targeting may use site-specific recombination system limited to somatic cells to avoid germline mutations. In self-fertilizing plants, the transferred gene or the knockout can become homozygous in the following generation of selfing. In mice, it is commonly used for knocking out genes. In bisexual animals, homozygosity can be achieved by mating of individuals that are heterozygous for the mutation. In mouse, embryonic stem cells can be genetically manipulated in vitro and offspring can be obtained by injecting the stem cells into early embryos. ►splicing, ►promoter, ►trapping promoters, ►targeting genes, ►knock-out; Schnütgen F et al 2005 Proc Natl Acad Sci USA 102:7221.

Gene Tree: It reveals when a population was divided into two subgroups on the basis that one of the subgroups has a particular mutation(s) and the other does not. Such an analysis can be continued for any number of genes. ►evolutionary tree, ►population tree

Genealogy: The list and description of successive ancestors in a family. An extensive study of Icelandic populations of the last 300 years indicates a faster evolutionary rate for the matrilinear than the patrilinear descendants based on mtDNA and Y chromosome haplotype data. ►pedigree, ►coalescent; Helgason A et al 2003 Am J Hum Genet 72:1370.

GeneCards: ►GeneNote, ►EST, http://genecards.weizmann.ac.il/genetide-bin/tide.cgi.

GeneChip: ►microarray hybridization

GeneDB: The sequences and annotations by the Sanger Institute Pathogen Sequencing Unit (PSU). (http://www.genedb.org/).

GeneEMAC: A computerized method for the monitoring of gene expression during development by external marker-based automatic congruencing (EMAC). (See Streicher J et al 2000 Nature Genet 25:147).

Genefinder: A computer program for finding genes within DNA sequences on the basis of identifying likely splicing sites, translation starts, coding potential, intron sizes, etc., by statistical criteria based on log likelihood ratios. The prokaryotic gene finder GISMO combines searches for protein family domains with composition-based classification based on a support vector machine. GISMO is highly accurate and highly sensitivity and specific. It performs well for complete prokaryotic chromosomes, irrespective of their GC content, and also for plasmids as short as 10 kb, short genes and for genes with atypical sequence composition (Krause L et al 2007 Nucleic Acids Res 35:540). ►lod score, ►support vector machine; Rogic S et al 2001 Genome Res.11:817.

Genelet: ►SVD

Geneology: The recorded or inferred steps of descent from ancestors, a family history ►pedigree analysis, ►evolutionary tree

GeneNote: A database of human gene expression in normal tissues. ►GeneCard, ►Recon; http://bioinfo.weizmann.ac.il/genecards.

General Acid-Base Catalysis: The proton transfer from and to a molecule, water excepted.

General Recombination: The recombination between homologous sequences. ►illegitimate recombination, ►recombination genetic, ►gene conversion

General Transcription Factors: ►transcription factors

Generalized Transduction: It can be mediated by either temperate or virulent bacteriophages. The phage infects a donor bacterium (step 1) carrying the wild type allele (a^+) and then lyses it (step 2). Some phage shells scoop up *at random* only or almost only *any* bacterial DNA fragment rather than phage DNA (see Fig. G23). When these unusual phages infect a recipient cell, they can transfer the donor bacterial gene into the recipient (step 3). The transduced DNA and the indigent DNA can synaps (step 4) if they are homologous and by a double exchange replace the recipient's gene with that of the donor. This step then completes the generalized transduction. In case the donor DNA carries alleles $\underline{a}^{\pm}\underline{b}^{\pm}$ and the constitution of the recipient is $\underline{a}\ \underline{b}$ recombination frequencies can be calculated as shown by the formula:

$$\frac{(a+b)(ab^+)}{(a^+b)+(ab^+)+(a^+b^+)}$$

With generalized transduction recombination can be estimated only within very short intervals, e.g., within genes. ►marker effect, ►*pac* sites, also ►specialized transduction, ►abortive transduction, ►bacterial, ►recombination frequency; Lederberg J et al 1952 Cold Spring Harbor Symp Quant Biol 16:413; Burke J et al 2001 Proc Natl Acad Sci USA 98:6289.

Generation Time: The time required for a cell division in continuous culture or the period from birth of an

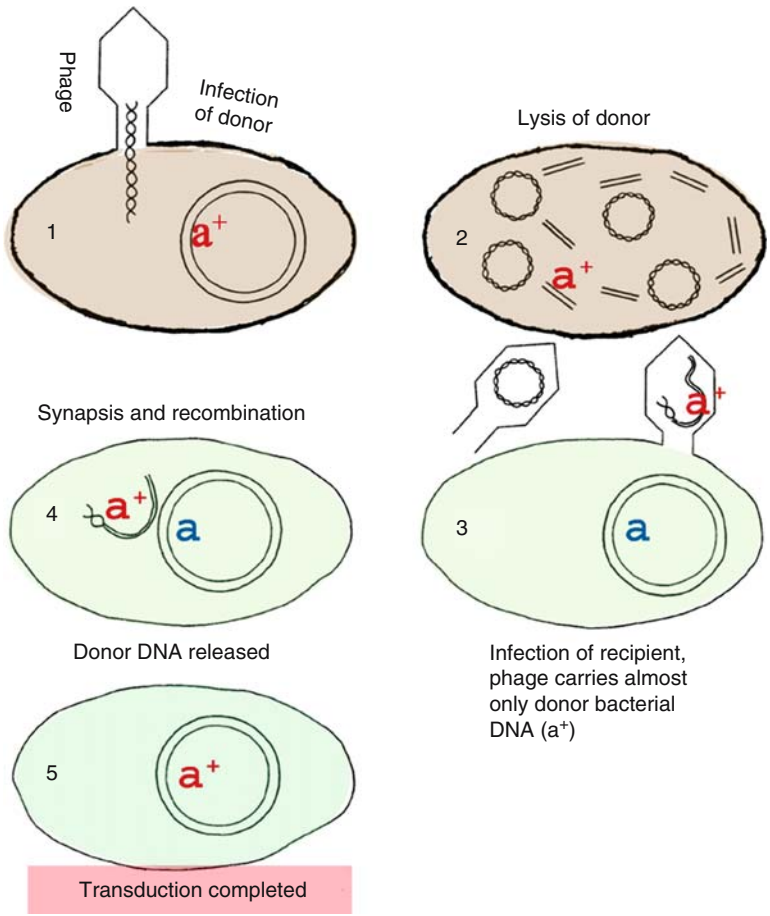

Figure G23. Generalized transduction

individual to the birth of its offspring (reproductive cycle).

GeneReviews: ►genetic testing

Genes, Good: They do not affect health adversely. Also, genes, which are transmitted and expressed in simple Mendelian fashion are called "good." ►expressivity, ►penetrance, ►polygenic inheritance, ►QTL

Genes, Split: They contain introns; the vast majority of eukaryotic genes are therefore split into segments of exons. ►introns, ►exon

Genes, Synthetic: These have been produced since the 1970s. In 1976, Khorana synthesized the tyrosine suppressor tRNA genes of *E. coli* by classical methods or organic chemistry. In vitro synthesis of 26 oligonucleotide tracts were ligated into a 207 bp DNA containing the 86 nucleotide sequence of the gene plus leader, promoter and the terminator sequence. This gene turned out to be biologically active and suppressed an amber mutation when transformed into bacterial cells. ►tRNA, ►suppressor tRNA, ►synthetic genes [for a diagram]; Ryan MJ et al 1979 J Biol Chem 254: 10803.

GENESCAN: A computer program for the detection of gene structure, transcriptional and translational splicing signals, exons, introns and intergenic regions of the mammalian genome on probabilistic basis. Multiple sequences are identified (Burge C, Karlin S 1997 J Mol Biol 268:78).

GeneScape: A computer program that seeks out miniset clones, DNA sequences, gene alignments to restriction maps and allows zooming from a display to the entire map of *E. coli.*

Gene-Scribe: A commercial transcriptional kit with a T7 phage RNA polymerase. It can be used to transcribe cloned genes without subcloning. ►EMBL3, ►λDASH, ►λFIX

Genesis: Used with several meanings such as inception, origin, the process of differentiation and development; also in composite words such as embryogenesis, morphogenesis, neurogenesis, etc.

Gene-Specific Repair Assay: Detects the presence of functional repair enzymes acting at a specific gene. The procedure: (i) expose cells (DNA) to mutagen/carcinogen, (ii) withdraw DNA after specific time periods, (iii) separate replicated and unreplicated DNAs on cesium chloride gradient ultracentrifugation, (iv) restriction enzyme digestion, (v) employ repair enzymes (uvrABC, T4 endonuclease, Fpg, endonuclease III), (vi) electrophorese DNA and on Southern blots probe the gene of interest, (vii) on the autoradiographed gel compare band intensities after allowed for repair as in (v). In the absence of repair, the intensity of the critical band in the gel is independent from the time allowed for repair whereas if repair is working the intensity of the band increases by the length of the period of incubation. ►DNA repair, ►uvrABC, ►endonuclease, ►Fpy, ►density gradient centrifugation, ►autoradiography; Anson RM, Bohr VA 1999 Methods Mol Biol 113:257; Ayala-Torres S et al 2000 Methods 22:135.

Gene-Switch Cassette: A construct facilitating turning genes on and off in a controllable manner. It encodes the DNA-biding domain of GALA4, the human progesterone receptor-ligand-binding domain and the activation domain of the human p65 protein gene. In the presence of the antiprogestin mifepristone (RU486) the chimeric molecule binds to the upstream activating domain (UAS) and in a ligand-dependent manner transactivates the appropriate downstream genes. The construct can be inserted into *Drosophila* by adenoviral or P vectors. A toggle switch system has been constructed in bacteria by the use of two repressible promoters arranged in a mutually inhibitory network. By chemical or temperature treatment, the system can be flipped between two stable states. Such system has potential application in biotechnology, gene therapy and biocomputing (Gardner TS et al 2000 Nature [Lond] 403:339). ►GALA4, ►progesterone, ►RU486, ►UAS, ►p65, ►transactivator, ►tetracycline, ►hybrid dysgenesis, ►gene circuit; Roman G et al 2001 Proc Natl Acad Sci USA 98:12602; Osterwalder T et al 2001 Proc Natl Acad Sci USA 98:12596; Galimi F et al 2005 Mol Ther 11:142.

Genet: Genetically identical ramets that are clonal progeny of a single individual. ►ramet

GeneTest: A publicly funded medical genetics information resource developed for physicians, other healthcare providers, and researchers, available at no cost to all interested persons. According to GeneTest, in 2007 there have been 1,054 clinical tests and 297 research tests for 1,351diseases. (See: http://www.genetests.org/; http://www.fnih.org/GAIN/GAIN_home.shtml).

Genethics: ►ethics

Genetic Accommodation: Mutation or environmental effects cause the appearance of a novel adaptive phenotype through quantitative genetic changes. It is similar to genetic assimilation but unlike genetic assimilation, genetic accommodation results in increased environmental sensitivity of a plastic phenotype (Suzuki Y, Nijhout HF 2006 Science 311:650). ►genetic assimilation, ►polypheny

Genetic Assimilation: An adaptive mechanism in a population to fix genes as permanent parts of the genome by selection. An initially epigenetic (acquired-phenotypic) modification becomes fixed by heredity. ►adaptation, ►genetic accommodation, ►assimilation, ►fixation, ►fixation index, ►canalization, ►epigenetic, ►reaction norm, ►plasticity, ►fitness, ►Baldwin effect; Palmer AR 2004 Science 306:828; Waddington CH 1953 Evolution 7:118.

Genetic Association: The correlation between the presence of a genetic marker and a certain type of multifactorial disease. For the trustworthiness of the conclusions large populations and high statistical probability are required (Dahlman I et al 2002 Nature Genet 30:149; Xiong M et al 2002 Am J Hum Genet 70:1257). ►GAIN

Genetic Association Information Network (GAIN): GAIN is a public-private partnership of the Foundation for the National Institutes of Health, Inc., which includes corporations, private foundations, advocacy groups, concerned individuals, and the National Institutes of Health. This initiative will take the next step in the search to understand the genetic factors influencing risk for complex diseases. Through a series of whole genome association studies, using samples from existing case-control studies of patients with common diseases, the project will contribute to the identification of genetic pathways that make us more susceptible to these diseases and thus facilitate discovery of new molecular targets for prevention, diagnosis, and treatment. (See: http://www.fnih.org/GAIN/GAIN_home.shtml).

Genetic Background: All residual genes, besides the one(s) of special interest. It may be critical for

analysis because the background may affect (+/−) the expression of particular genes. Therefore, failure of identifying the background may make confirmation of the results impossible. It is improper in a scientific paper to state only that the material was purchased in a certain store.

Genetic Balance: ►balance of alleles, ►balanced lethals, ►balanced polymorphism

Genetic Bar-Code: ►DNA chip, ►bar code

Genetic Block: Mutation in a gene may prevent or slow down the flow of a metabolic pathway. ►null allele, ►leaky mutant

G

Genetic Burden: Same as genetic load.

Genetic Cascade: Genes of a developmental pathway are activated in successive waves; the expression of "earlier" genes activates the next ones.

Genetic Circuits: ►gene circuits

Genetic Circularity: A consequence of circular DNA genetic material, i.e., the genetic map has no ends although one point is generally designated as origin. ►DNA circular

Genetic Code: It consists of 64 contiguous nucleotide triplets; 61 specify 20 amino acids and three serves as signals for termination of translation on the ribosomes (see Table G1). The number of triplet codons for a particular amino acid varies from one to six. In animals, the 21st encoded (UGA) amino acid is selenocysteine and in Archaea and Eubacteria UAG may encode the 22nd amino acid, pyrrolysine. In addition, programmable ribozymes may attach non-natural amino acid to RNAs and incorporate them into engineered proteins (Bessho Y et al 2002 Nature Biotechnol 20:723). In an engineered *E. coli* bacterium the amber codon my direct the incorporation of the non-natural amino acid p-aminophenylalanine into protein at high efficiency (Mehl RA et al 2003 J Am Chem Soc 125:935). More than a dozen unnatural amino acids can be incorporated into proteins. The number of triplet codons for a particular amino acid varies from1 to 6. It is of theoretical and of practical importance to amplify the genetic code beyond the "magic number". Chemically modified, unnatural amino acids may alter protein function if

Table G1 The genetic code in RNA triplets

5′ Nucleotide	Second nucleotide				3′ Nucleotide
	U	C	A	G	
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	ochre	opal	A
	Leu	Ser	amber	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

Ala = alanine (4)
Arg = arginine (6)
Asp = aspartic acid (2)
Asn = asparagine (2)
Cys = cysteine (2)
Glu = glutamic acid (2)
Gln = glutamine (2)
Gly = glycine (4)
His = histidine (2)
Ile = isoleucine (3)
Leu = leucine (6)
Lys = lysine (2)
Met = methionine (1)
Phe = phenylalanine (2)
Pro = proline (4)
Ser = serine (6)
Thr = threonine (4)
Trp = tryptophan (1)
Tyr = tyrosine (2)
Val = valine (4)

RNA codons represent the universal genetic code for amino acids. The table shows the three nonsense codons (chain-termination codon, boxed) and 61 sense codons coding for amino acids.
The numbers after the amino acids (right-most column) indicates the number of synonymous codons for each amino acid.
methionine and tryptophan each have only..... 1
asparagine, aspartic acid, cysteine, glutamic acid,
glutamine, histidine, lysine, phenylalanine, tyrosine, each has.....2
isoleucine has..... 3
alanine, proline, threonine, and valine have..... 4
arginine, leucine, serine all have..... 6 codons.
The codon usage is not random; it varies among organisms and genes

Table G2. Exceptional codon meanings

Mycoplasma capricolum	*Tetrahymena thermophila*	*Euplotes octacarinatus*	*Mitochondria*			
			Mammal	*Drosophila*	*Yeast*	*Neurospora*
UGA: Trp	UAA: Gln	UGA: Cys	AUA: Met	AUA: Met	AUA: Met	CUN: Thr
	CAG: Gln	UAA: stop	AUU: Met	AUU: Met	CUA: Thr	
	UAG: Gln	UAG: absent	AUG: Met	AUG: Met	CUC: Met	
			AUC: Met	.....	CUU: Met	
			UGA: Trp	UGA: Trp	CUG: Met	
			AGA: stop	AGA: Ser		
			AGG: stop			

The UGA "universal" stop codon means Trp in the mitochondria of vertebrates, insects, molluscs, echinoderms, nematodes, platyhelminthes, fungi and ciliates. Selenocysteine is also coded by UGA in *E. coli* and mammals.

incorporated in vivo in place of the natural ones. Modified special tRNAs and mutant aminoacyl tRNA synthetases may achieve incorporation. Mutations at the editing sites of *E. coli* $tRNA^{Val}$ synthetase incorporated in higher than 29% aminobutyrate, a steric analog of cysteine into the site of cysteine (see Table G2).

Besides providing information for the primary sequence of amino acids in proteins, the genetic code includes parallel information for binding sequences for regulatory and structural proteins, signals for splicing, and RNA secondary structure. The universal genetic code can efficiently carry arbitrary parallel codes much better than the vast majority of other possible genetic codes. The ability to support parallel codes is strongly tied to the identity of the stop codons and to the minimization of the effects of frame-shift translation errors. Whereas many of the known regulatory codes reside in nontranslated regions of the genome, it seems that the protein-coding regions can readily carry abundant additional information (Itzkovitz S, Alani U 2007 Genome Res 17:405).

►code genetic, ►amino acid symbols in proteins sequences, ►genetic code second, ►xDNA, ►evolution of the genetic code, ►initiation codon, ►magic number, ►tRNA, ►codon, ►aminoacyl-tRNA synthetase, ►unnatural amino acids, ►decoding; Knight RD et al 2001 Nature Rev Genet 2:49; Wang L et al 2001 Science 292:498; Döring V et al Science 292:501; Wang L, Schultz PG 2004 Angew Chem Int Ed Engl 44:34; Yanofsky C 2007 Cell 128:815; For additional special differences and exceptions in the coding dictionary see http://www.ncbi.nlm.nih.gov/Taxonomy/taxonomyhome.html; and http://www.ncbi.nlm.nih.gov/Taxonomy/Utils/wprintgc.cgi; mitochondrial codons: http://darwin.uvigo.es/software/gendecoder.html; ►microbial culture collections, sperm banks, ►code genetic, ►histone code

Genetic Code, Combinatorial: The transcription factor binding sites are assembled to form tissue-specific enhancer elements. ►enhancer, ►tissue-specificity, ►transcription factors

Genetic Code, Second: Determines the binding specificities of the transcription factors. ►aminoacyl-tRNA synthetase

Genetic Colonization: An infection of plants by Agrobacteria results in the expression of bacterial genes in the plant cells and the gene products, such as opines, and is utilized only by the bacteria. In population genetics, colonization means also the establishment of a breeding population in new habitat. ►*Agrobacterium*, ►transformation, ►opines; Harding RM, McVean G 2004 Curr Opin Genet Dev 14:667.

Genetic Complementation: ►complementary alleles, ►complementation groups, ►allelic complementation, ►complementation maps

Genetic Conflict Theory: The evolutionary conflict between maternal and paternal genes such as exists in imprinting. ►imprinting; Wilkins GF, Hasig D 2003 Nature Rev Genet 4:359.

Genetic Conservation: The preservation of species and subspecific genetic variations in protected areas, national parks, game reserves, botanical gardens,

zoos, seed depositories, culture corrections, sperm banks (Ryder OA 2005 Cytogenet Genome Res 108:6).

Genetic Correlation: Linked genes are expected to segregate together depending on the frequency of recombination. Members of the same family display correlation, and even assortative mating shows correlations although the latter may not be genetic. From the correlation between certain phenotypes the chromosomal location of genes can be predicted. The term genetic correlation in animal breeding is defined as a measure of the ratios of additive variances: Cov (X,Y)/$\sqrt{Var(X)xVar(Y)}$. ►correlation

Genetic Counseling: Provides information, medical diagnosis on hereditary bases, recurrence risk, family history, and possible management of genetic anomalies for the benefit of the family. It has no eugenic purpose and it does not make recommendations for decision; it merely informs the concerned individual(s). ►counseling genetic, ►risk, ►recurrence risk, ►utility index for genetic counseling; Mahowald MB et al 1998 Annu Rev Genet 32:547; Thornburn DR, Dahl HH 2001 Am J Med Genet 106:102; GENETests: http://www.ornl.gov/sci/techresources/Human_Genome/medicine/genecounseling.shtml; http://www.nlm.nih.gov/medlineplus/geneticcounseling.html; http://www.genetest.org/.

Genetic Death: Genetic death occurs if an organism leaves no offspring or a gene is not transmitted to subsequent generations. ►mutation beneficial, ►mutation neutral, ►fitness, ►selection coefficient, ►selection conditions, ►transmission, ►apoptosis; Hay BA et al 2004 Nature Rev Genet 5:911.

Genetic Determination (g^2): Similar to heritability in the broad sense (measured by intraclass correlation) where MS_b and MS_w stand for between and within strain mean squares, respectively. The 2n –1 in the denominator is used in testing inbred strains to compensate for the increase of additive genetic variances during inbreeding. ►intraclass correlation, ►heritability, ►variance

$$\frac{MS_b - MS_w}{MS_b + (2n-1)MS_w} = g^2$$

Genetic Discrimination: Prejudicial treatment on the basis of phenotypic or genotypic constitution by employers, insurance companies or any other person or institution. ►genetics and privacy, ►bioethics; Nowlan W 2002 Science 297:195; Rothenberg KH, Terry SF 2002 Science 297:196; Wright Clayton E 2003 New Engl J Med 349:562). Genetic discrimination is also for the detection of differences in the genetic material of cells, e.g., normal and cancer cells (Huang J et al 2004 Human Genomics 1:287.

Genetic Diseases: An estimated 4,000 human genes are directly or indirectly involved in the determination of human malformations and physical and mental disabilities. According to some estimates 15 to 20% of newborns are afflicted by some hereditary problems and a large fraction of the abortions are caused by chromosomal anomalies and/or recessive or dominant lethal genes. Approximately 25% of the hospitalizations are due to maladies with a genetic component. One study found that ~71% of the 4,224 children admitted to a hospital a significant genetic component of the illness they were treated for (McCandless SE et al 2004 Am J Hum Genet 74:121). After birth, defective enzymes have the largest share in the disorders. Anomalous genetic regulation accounts for the majority of the developmental defects. Amino acid replacement mutations (based on six human diseases) indicate that evolutionarily conserved sites are most common in human disease. From the degree of physicochemical alterations in the protein caused by missense mutation the grade of the disease or the likelihood of developing cancer can be predicted (Stone EA, Sidow A 2005 Genome Res 15:978). Polymorphic replacement mutations and silent mutations appear, however, randomly distributed. In several countries, population databases are being established with purpose to gain information on the interplay among genes and environmental factors and eventually to facilitate individualized medical treatment. Epidemiological observations indicate adulthood diseases are affected not only by genetic causes but also by early environmental factors such as conditions at the time of conception, fetal and infant environment as well as by adult life style (Gluckman PD, Hanson MA 2004 Science 305:1733). Very often genes are not the absolute cause of the disease because many of them can be prevented by proper life-style and preventive medication if disposition exists. The occurrence of genetic disease sometimes can be avoided or the risks reduced by proper education, premarital genetic counseling. During gestation, transcription factor and enzyme defects are the most prevalent fraction of diseases of the fetus. ►eugenics, ►gene therapy, ►readthrough, ►selection coefficient, ►inbreeding, ►consanguinity, ►risk, ►recurrence risk, ►DALY, ►prevalence, ►genetics and privacy, ►OMIM, ►genetic screening; Miller MP, Kumar S 2001 Hum Mol Genet 10:2319; Perez-Iratxeta C et al 2002 Nature Genet 312:316; Dean M et al 2002 Annu Rev Genomics Hum Genet 3:203; Homophila; statistical tests for genome-wide identification

of disease genes: Marchini J et al 2005 Nature Genet 37:41; frequencies: http://archive.uwcm.ac.uk/uwcm/mg/fidd/; candidate disease genes: dhttp:// disease.bork.embl-heidelberg.de/g2d/; disease genes: http://dgcst.ceinge.unina.it/.

Genetic Disorder: In the manifestation of the anomaly (disease) hereditary factors play major role. Single genes determine primarily some of the diseases; others are under the control of several genes. In either case, environmental factors can modify the expression of the disorder. ►monofactorial inheritance, ►polygenic inheritance, ►QTL, ►mitochondrial diseases in humans

Genetic Dissection: Analyzes the mechanism(s) of genetic determination and control of biological traits, morphogenesis and/or other function(s) by the techniques of mutation, recombination and pattern of inheritance in pedigrees or populations. ►one gene—one enzyme theorem, ►morphogenesis in *Drosophila*, ►metabolic pathways

Genetic Distance: Genetic distance (d) can be measured by different procedures. One simplesolution is based on a geometric model is $d^2 = 1 - \sqrt{p_1 p_2} - \sqrt{q_1 q_2}$ where p and q represent the frequencies of the two alleles of a locus in populations 1 and 2, respectively. For actual determination of the distance between two populations more than one allelic pair must be considered. Genetic distance, F_{ST} is calculated also as $V_p/\bar{p}(1-p)$ where V_p is the variance between gene frequencies in a set of n populations and $\bar{p}$ = their average gene frequencies. ►evolutionary distance, ►evolutionary tree; Nei M 1972 Am Nat 106:283; molecular distances among some animals: http://warta.bio.psu.edu/DED.

Genetic Divergence: ►divergence

Genetic Diversity: The variations in the gene pool of a population or the genetic variations in the populations. ►gene pool, ►genetic variation, ►genetic conservation, ►diversity

Genetic Drift: A change in gene frequencies by sampling error(s) of the gametic array so the genes are not maintained on the basis of their fitness or selective advantage they may convey but the selection is the outcome of chance. In case of two alleles, selection by chance alone is determined by the frequency of the alleles, the binomial distribution and population size. Thus, if the frequency of allele *A* is p and that of *a* is q the frequency of alleles by chance alone will follow the binomial distribution of $(p + q)^n$ where n = the number of individuals that leave offspring surviving to the reproductive age; e.g., in case the allelic frequencies are equal and four individuals survive, the probability that all 4 will be homozygous recessives is 0.0625. ►effective population size, ►founder principle, ►binomial distribution, ►Pascal triangle, ►Eve foremother; Cavalli-Sforza LL, Bodmer WF 1971 The Genetics of Human Populations, Freeman, San Francisco, California.

Genetic Endpoint: Classification of the types of genetic lesions such as mutation, chromosomal aberration, unscheduled DNA synthesis, etc. that are detected in mutagen testing. ►bioassays in genetic toxicology

Genetic Engineering: Construction of special chromosomes by cytogenetic manipulations, somatic cell fusions, or introduction of organelles into cells by mechanical means (genetic microsurgery). Isolation and propagation of DNA molecules in suitable hosts, molecular modification of genes and regulatory elements for special purposes, and transfer genes among diverse organism by bypassing the constraints of sexual reproduction and manipulate them for medical, industrial and agricultural use. ►transformation, ►cloning vectors, ►homologous recombination, ►chromosome substitution, ►alien addition, ►alien substitution, ►alien transfer lines, ►metabolite engineering, ►protein engineering, ►pathogen identification, ►intercellular immunization, ►intracellular immunization, ►input trait, ►gene therapy, ►cancer gene therapy, ►transgenic, ►genomics, ►biotechnology, ►monoclonal antibody, ►intein, ►monoclonal antibody therapies, ►targeting genes, ►nuclear transplantation, ►terminator technology, ►scaffold, ►GMO, ►stem cells, ►tissue engineering, ►stem cells, ►RAC, ►synthetic biology

Genetic Enhancement: ►gene therapy, ►plant breeding, ►animal breeding, ►eugenics

Genetic Equilibrium: Exists when gene frequencies are stable for generations. (See also ►mutations and genetic equilibrium). In a panmictic diploid equilibrium population, the frequency of heterozygotes is twice the square root of the product of the frequencies of the two homozygous classes: $2 = H/\sqrt{D \times R}$ where H, D, R and stand for heterozygotes, homozygous dominants, and homozygous recessives, respectively (see Table G3). This is derived from the middle term of the Hardy-Weinberg formula, $2pq = h = 2\sqrt{p^2 q^2} = 2 \times \sqrt{DxR}$ and hence $2 = H/\sqrt{DxR}$.

This principle can graphically be represented (see Fig. G24). In an equilibrium population the frequency of heterozygotes is represented by a parabola as the proportion of the alleles vary from 0 to 1 to 0 as long the as three genotypes have equal fitness. With respect to an individual locus, equilibrium is attained

Table G3. Genotypic frequencies

The four populations represented in the body of the table below all have identical gene frequencies, p = 0.8, q = 0.2 yet the genotypic proportions are quite different. According to the definition in the text only population 4 is in equilibrium.			
Populations	**Genotypic Frequencies**		
	AA	**Aa**	**aa**
1	0.80	0.00	0.20
2	0.70	0.20	0.10
3	0.60	0.45	0.00
4	0.64	0.32	0.04

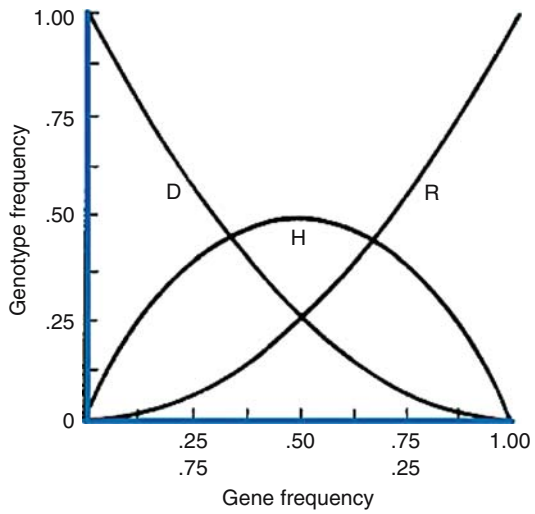

Figure G24. Genetic equilibria.

within one generation of random mating. As long as random mating prevails and there is no selection; gene and genotypic frequencies do not change and the Hardy-Weinberg principle prevails. Multiple loci require more generations to attain equilibrium. Also, equilibrium depends on the intensity of linkage among the loci. Progress toward equilibrium is delayed if the genes are sex-linked. If in the original mating the homogametic sex is homozygous for a recessive allele (X^aX^a) and the heterogametic sex carries the other allele (X^AY), the allelic frequencies in the two sexes will follow an oscillatory path during the generations because of the zigzag pattern of inheritance of the X chromosome. In equilibrium, the allelic proportions in the two sexes will be represented by the proportions of the X chromosomes.

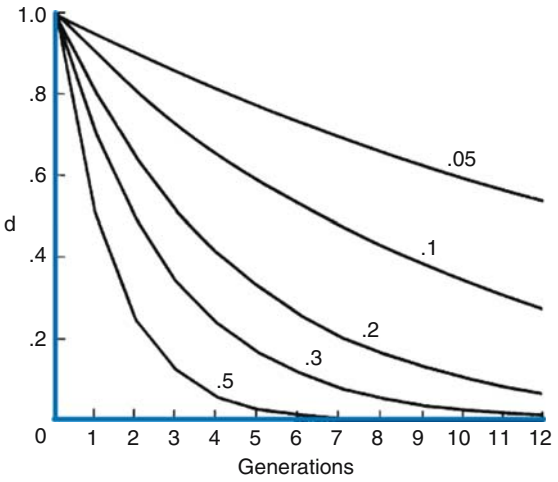

Figure G25. Progress toward genetic equilibrium in case two genes are linked in repulsion at zero generation time. At equilibrium the repulsion and the coupling phases are equal. Four of the curves (0.05 to 0.3) represent the courses to equilibria at various intensities of recombination; 0.5 indicates independent segregation. (Modified after Falconer, D.S. Introduction to Quantitative Genetics. Longman, London, UK)

Somewhat similar situation exists in hermaphrodites carrying self-sterility alleles (*S*) (see Fig. G25). The mating of plants self-incompatibility alleles (*S*) produce the offspring shown in the table (See Table G4) below.

Table G4. Self-sterility progenies

Female	Male	Offspring
S_1S_2	Either S_1S_3 or S_2S_3	$\frac{1}{2}\ S_1S_3 + \frac{1}{2}\ S_2S_3$
S_1S_3	Either S_1S_2 or S_2S_3	$\frac{1}{2}\ S_1S_2 + \frac{1}{2}\ S_2S_3$
S_2S_3	Either S_1S_2 or S_1S_3	$\frac{1}{2}\ S_1S_2 + \frac{1}{2}\ S_1S_3$

Half of the progeny is the same as the male whereas the other half has a different constitution. The genetic constitution of the females does not reappear in the immediate progeny because of the self-sterility. Therefore, if the frequencies of the alleles are not identical, the genotypes most common among the parents will be the least frequent among their offspring although will reappear in advanced generations. Equilibrium is reached however if the frequencies of the alleles are equal.

In polyploids the progress toward equilibrium is quite complicated and can be determined according to

CC Li (First Course in Population Genetics, Boxwood Press, California). If the gametic output of an autotetraploid population is $G_0 \equiv x(AA) + 2y\,(Aa) + z(aa) = 1$, the frequency (p) of A = x + y and the frequency (q) of a = y + z. The gametic proportions in the course of generations (n) is expressed as $d = (y^2 - xz) = y^2 - (p - y)(q - y) = y - pq$, and *d* is the index of divergence from the equilibrium condition. This index is reduced by 2/3 during each generation of random mating. The gametic proportions and gene frequencies can thus be obtained as:

$$yn = pq + dn = pq + \left(\frac{1}{3}\right)nd \rightarrow pq,$$

$$xn = p - yn = p2, - \left(\frac{1}{3}\right)nd \rightarrow p2,$$

$$zn = q - yn = q2 - \left(\frac{1}{3}\right)nd \rightarrow q2$$

►Hardy-Weinberg, ►linkage disequilibrium, ►autopolyploidy, ►sex-linkage, ►self-sterility, ►Wahlund's principle

Genetic Essentialism: A criticism of modern genetics for "equating" human (and other) beings with a molecular entity (DNA), including social, historical and moral complexities and responsibilities. In contrast, some physicians and ethicists emphasize the holistic approaches, which integrate also human consciousness. ►vitalism

Genetic Fine Structure: Analysis involves recombination within the boundaries of individual genes.

Genetic Fingerprinting: ►DNA fingerprinting

Genetic Hazards: ►risk, ►genetic risk, ►λ_S, ►recurrence risk, ►empirical risk, ►genotypic risk ratio, ►radiation hazard assessment, ►radiation effects, ►environmental mutagens, ►Kaplan-Meier estimator of survival, ►GMO

Genetic Homeostasis: The property of a population to maintain its genetic composition and resist changes in gene frequencies by phenotypic regulation under variable environmental conditions. ►homeostasis, ►canalization, ►artificial selection; Lerner IM 1954 Genetic Homeostasis, Wiley, New York.

Genetic Homology: The degree of similarity in the base sequences of DNA and RNA or the amino acid sequences in the proteins. ►DNA sequencing, ►RNA sequencing, ►protein structure, ►amino acid sequencing, ►homology, ►databases

Genetic Information: Instructions in the nucleic acids for the cellular machinery.

Genetic Instability: ►instability genetic

Genetic Interaction: Genetic interaction is becoming increasingly interesting in modern biology and needs new (bioinformatics) approaches for its genome-wide use. The global performance of four existing classes of inference algorithms using 445 *Escherichia coli* Affymetrix arrays and 3,216 known *E. coli* regulatory interactions from RegulonDB have been tested. The context likelihood of relatedness (CLR) algorithm can also be applied as a novel extension of the relevance networks class of algorithms. CLR demonstrates an average precision gain of 36% relative to the next-best performing algorithm. At a 60% true positive rate, CLR identified 1,079 regulatory interactions, of which 338 were in the previously known network and 741 were novel predictions (Faith JJ et al 2007 PloS Biol 5(1)e8). ►epistasis, ►gene product interaction, ►QTL, ►genetic networks, ►systems biology

Genetic Isolation: The lack of ability to interbreed (incompatibility) and/or hybrid inviability or sterility between/among different taxonomic groups. ►isolation genetic, ►speciation

Genetic Load: Sum of deleterious genes in the genome. Recessive alleles cannot generally be detected in the heterozygotes. These heterozygotes may continuously contribute homozygotes to the population and if the recessives are deleterious, they may adversely affect the fitness of the population; thus constituting a genetic load. The amount of hidden genetic variation is revealed by the coefficient of inbreeding. In F_1, 100% of the population is heterozygous. In successive generations of selfing, the heterozygosity decreases by $(0.5)^n$ where n = the number of selfed generations (e.g., by F_5 there are four selfings). Thus, the sum of the heterozygotes = $1 - (0.5)^n$. The coefficient of inbreeding F, in the offspring of first cousins, is 0.0625 whereas among unrelated individuals it is presumed to be 0. Thus, if the mortality range in a certain age group is, say, 11% in the general population, and 16% among the children of first cousins, the difference is 5%. Therefore, $16 \times 0.05 = 0.80$, and 80% would be the average mortality if the coefficient of inbreeding would reach 100%. Recessive zygotic lethality requires homozygosity at the same locus (present in both parental gametes). According to the Hardy–Weinberg theorem, the frequency of the double recessive genotypes is expected to be q^2, and the frequency of at least one lethal equivalent gene is then $\sqrt{0.80} \approx 0.89$. This indicates that almost 90% of the gametes carried a lethal gene or a combination of genes that cause lethality at homozygosity. On this basis, the genetic load of this population is close to one lethal equivalent factor per gamete. Other investigations estimated the genetic load to be twice as high in some

The frequency of deleterious alleles is proportional to the mutation rate and selection coefficient: $\hat{q}^2 = u/s$. By rewriting the formula, the mutational load of recessive alleles becomes $u = s\hat{q}^2$, and $\hat{q} = \sqrt{u/s}$.

The mutational load of dominant genes is $2u$. In the absence of dominance in a random-mating population, the mutational load is $L = 2u/(1 + u)$. The mutational load in the most common cases is proportional to the rate of mutation and not to the severity of the affliction.

populations. The amount of the genetic load may vary. It is affected by exposure to environmental mutagens, drugs, exposure to chemicals in the food chain (natural toxins or insecticides, pesticides) or in industrial pollutants, occupational hazards, presence of mutator genes (transposable elements), and natural or other types of radiations (X-rays, UV, etc.). Completely dominant lethal mutations do not contribute to the genetic load because they may eliminate the carriers of the genetic defect and thus no load is passed on to successive generations. Of course, some mutations may show intermediate types or conditional expression and may or may not contribute to the load. Some deleterious genes are closely linked to advantageous genes and thus transmitted beyond their merit by this "hitchhiking" effect. In such a situation, a recombinational load may exist. Environmental load is generated in highly variable environments where under certain conditions genes are selected that normally convey inferior fitness. Incompatibility load arises in cases of deleterious maternal—fetal interactions, such as those that may arise if the mother is Rh negative for this blood antigen and the fetus is positive or if the mother expresses phenylketonuria but the fetus is heterozygous (maternal epistasis). ►allelic frequencies, ►Hardy–Weinberg theorem, ►mutation neutral, ►mutation beneficial, ►recombinational load, ►selection coefficient, ►fitness, ►coefficient of inbreeding, ►consanguinity, ►incest, ►genetic risk, ►lethal equivalent, ►Muller's ratchet, ►incompatibility, ►epistasis, ►mutation in human populations, ►death, ►truncation; Cavalli-Sforza LL, Bodmer WF 1971 The genetics of human populations, Freeman, San Francisco; Muller HJ 1950 Am J Hum Genet 2:111; Drake JW et al 1998 Genetics 148:1667; Szafraniec K et al 2001 Proc Natl Acad Sci USA 98:1107; Kondrashov AS et al 2002 Proc Natl Acad Sci USA 99:14878.

Genetic Lottery: (Journalistic) chance of individuals to inherit certain genes in a population.

Genetic Manipulation: Application of genetic, cytological, or molecular techniques for constructing altered organisms. ►genetic engineering, ►chromosome engineering

Genetic Map: The relative position of genes or other chromosomal markers represented in a linear manner on the basis of recombination frequencies. ►mapping genetic, ►physical map, ►mapping function, ►deletion maps, ►linkage group

Genetic Markers: Genetic markers help identify nuclear chromosomes, cytoplasmic organelles, and isolated cells on the basis of their inherited behavior and facilitate the identification of the genetic mechanisms involved in special phenomena, such as recombination, gene conversion, mutation, chromosomal rearrangements, genetic transformation, cell fusion, selection, etc.

Genetic Material: Either DNA (in eukaryotes and the majority of prokaryotes) or RNA (in some viruses). These nucleic acids can occur in either double or single-stranded forms. ►RNA, ►mtDNA, ►ctDNA, ►prion, ►Watson and Crick model

Genetic Medicine: Genetic medicine aims to correct diseases by the use of DNA, RNA, or proteins. Inborn errors of metabolism were recognized since the beginning of the twentieth century and metabolic corrections or alleviations of the defect has been used by modified defect. Phenylketonuric patients were placed on phenylalanine-restricted diet, or in case of fructose intolerance, fructose-rich food was proscribed. Low-cholesterol diet and the use hydroxymethylglutaryl co-enzyme A (HMG CoA) inhibitor statins alleviate hypercholesterolemia. To avoid iron overload caused by the frequent blood transfusions in thalassemia, the iron chelating desferrioxamine proved useful. In several diseases, *protein augmentation* therapy corrected for the low level of a protein in the extracellular compartment; purified proteins were introduced into the body in case of endocrine disorders, immunoglobulin deficiencies, lysosomal storage diseases, and others. This approach was successful only when the administration was effective and simple, allergic or immunological reactions were not prohibitive, and the supply was adequate at reasonable cost. This type of therapy is applicable (at least in principle) to the approximately 1,800 human diseases involving a single major gene. The complex, multigenic quantitative diseases and chromosomal aberrations are generally not amenable to this type of corrections. Some of the disease sites are difficult to reach directly (e.g., in the brain in utero). Others, e.g., α-antitrypsin (ATT) deficiency is manifested in adult stage and then, oral administration of 4-phenylbutyric acid facilitates the release of antitrypsin from the endoplasmic

reticulum. Antitrypsin, as a "chemical chaperone", may prevent the injuries resulting from AAT deficiency. Some injuries of the brain or spinal cord, or tissue degeneration (e.g., prion diseases, Parkinson disease, cardiac muscle defects, hematological anomalies, etc.) can eventually be remedied in humans, also by the use of embryonic or somatic stem cells. Gene therapy and stem cell mediated cures are generally expected to be effective for all variations within a specific monogenic disease. MicroRNA or RNAi technology must target specific sites (corresponding to that RNA) to be effective. ►antisense technology, ►microRNA, ►RNAi, ►gene therapy, ►readthrough, ►cancer gene therapy, ►stem cell, ►biomarker, ►drug development, ►SADR; O'Connor TP, Crystal RG 2006 Nature Rev Genet 7:261.

Genetic Milieu: ►genetic background

Genetic Module: ►module, ►genetic network

Genetic Mosaic: An individual with cell patches of different genetic constitutions. It may come about by somatic mutation, movement of insertion- or transposable elements, somatic recombination, nondisjunction, deletion, etc. ►individual entries, ►chimera, ►codominance

Genetic Network: The connections between DNA, RNA, protein, cis- and transacting regulators, operons, epistasis, signals and the signal transducing systems, and feedback, involving a large number of genetic and environmental inputs (see Fig. G26). M.

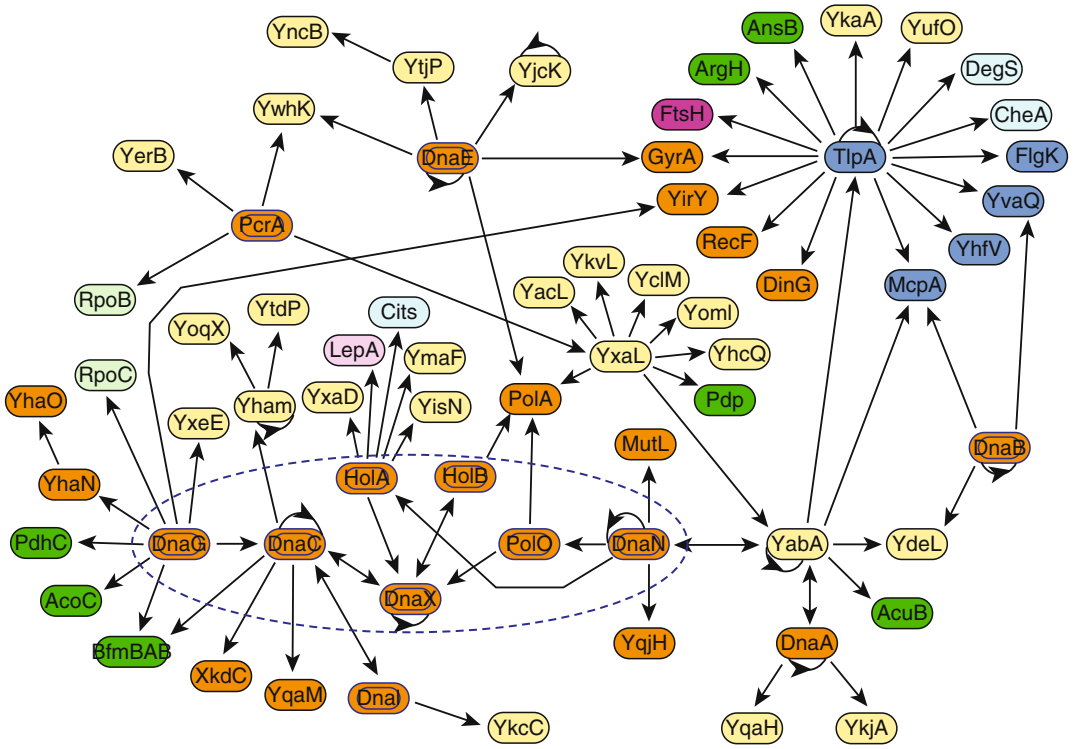

Figure G26. A network of 69 proteins involved in 91 specific interactions centered on the replication machinery of *Bacillus subtilis*. It shows the relations of DNA replication with recombination and repair, membrane-bound protein complexes, and signal transduction. The names, basic function, and location in the physical map of most of the specific proteins can be found in Kunst F et al 1997 Nature [Lond] 390:249, reporting the complete genome sequence of this prokaryotic genome. Two-hybrid tests were used to determine the interacting components. The arrows are oriented from bait to prey. Double blue lines designate the primary baits (with the exception of PriA and DnaD). The dashed black oval outlines the replisome. The number of the interacting components varies from 17 to 1. Details can be accessed by http://www-mig.versailles.inra.fr/bdsi/SpiD. The color code identifies functional categories. Orange: DNA replication/ recombination/ repair. Dark blue: mobility and chemotaxis. Light blue: signal transduction. Light green: transcription. Pink: protein synthesis. Dark green: metabolism of carbohydrates and amino acids. Purple: cell division. Yellow: unidentified functions. (From Marie-Françoise Noirot-Gros,.Etienne Dervyn, Ling Juan Wu, Peggy Mervelet, Jeffery Errington, S. Dusko Ehrlich and Philippe Noirot 2002 Proc Natl Acad Sci USA 99:8342–8347. Courtesy of Dr. M.-F. Noirot-Gros, I.N.R.A., France. Copyright 1992 National Academy of Sciences, U.S.A.).

Demerec in 1933 said (J. Hered. 24: 369) "We know today, however, that no single gene has the sole responsibility for the appearance of any one character. The final effect is produced through the interaction of the whole complement of genes, although certain genes may have greater influence on the expression of certain characteristics than some other genes have."

Genes involved in common processes tend to be expressed in detectable hierarchical waves. Exposure of yeast cells to Cd^{2+} induced 54 proteins, the majority of the sulfur assimilated by the cells was utilized for the formation of glutathion, and this reduced the production of other sulfur-rich proteins. The regulation takes place at the mRNA level. Glutathione is required for detoxification (Fauchon M et al 2002 Mol Cell 9:713). Interacting proteins may be identified experimentally by the two-hybrid system, TAP, three-dimensional structures, or by mass spectrometry.

Computational methods exist that reveal the co-inheritance of functional linkages across phylogenetic boundaries. By such procedures in yeast 3,875 linkages of 804 proteins have been revealed (Date AV, Marcotte EM. 2003 Nature Biotechnol 21:1055). In yeast, 4681 genes, i.e., ~81% of the genome, displayed ~34,000 probabilistic linkages (Lee I et al 2004 Science 306:1555). In *E. coli*, 74% of the known metabolic enzymes seem to be clustered in modules with an average pathway specificity of 84% (von Mering C et al 2003 Proc Natl Acad Sci USA 100:15428). On the basis of experimental data available or perturbation of the systems as the result of the recent molecular techniques, mathematics-aided models can be developed that may be applied to medical and biotechnological problems (Tegnér J et al 2003 Proc Natl Acad Sci USA 100:5944). Highly connected topological modules are combined into larger, less cohesive units and display similarities across different organisms. During development, multigenic feedback loops and spatial repressive control systems operate both periodically and constitutively in a dynamic manner (de Lichtenberg U et al 2005 Science 307:724). Behavioral traits of *Drosophila* displayed dramatically different interactions depending on the genetic background (van Swinderen B, Greenspan RJ 2005 Genetics 169:2151). The protein interaction networks are conserved in even unrelated species (Sharan R et al 2005 Proc Natl Acad Sci USA 102:1974). In 17 fungal genomes, cis-regulatory elements are conserved for several interacting modules. However in the ribosomal modules for dozens of promoters, new cis elements have emerged and switched on while retaining the functionality of the modules and shedding light on the evolution of regulatory networks (Tanay A et al 2005 Proc Natl Acad Sci USA 102:7203). In some fungal species, the transcriptional network is altered by the loss of cis-regulatory functions (Ihmels J et al 2005 Science 309:938). A model of oscillatory signals may offer greater quantitative precision (Lipan O, Wong WH 2005 Proc Natl Acad Sci USA 102:7063). Herpes virus (Kaposi sarcoma-associated herpesvirus and varicella-zooster virus) proteins interact within their proteomes and with the human proteome (Uetz P et al 2006 Science 311:239).

Some network designs may require revisions when additional knockout(s) indicate no significant downstream consequence of the gene loss. In yeast, however, in some cases 4,000 double knockouts lead only to synthetic lethality (see Fig. G27) (Yeang C-H et al 2005 Genome Biol 6:R62).

The protein–protein interaction networks can facilitate understanding the pathogenic mechanisms involved in disease. In hereditary human ataxias and neural degenerations, Purkinje cell defects are

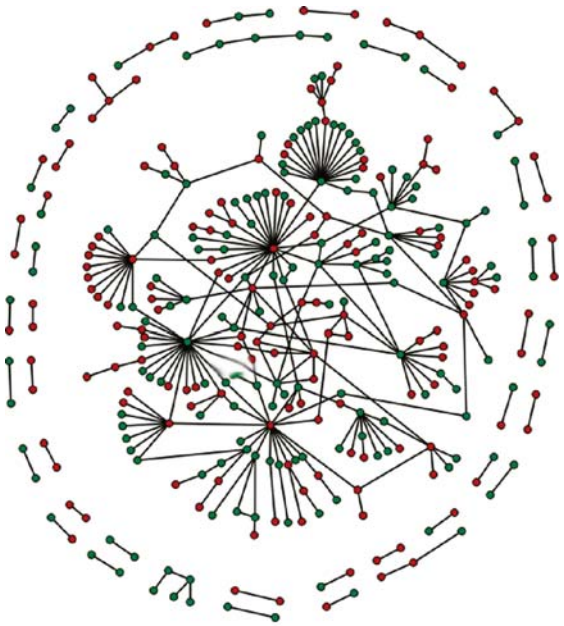

Figure G27. Genetic network of yeast nuclear proteins displaying 318 interactions of 329 proteins. Note the reduced links between highly connected proteins and the preference between highly connected and low-connected pairs of proteins. Green nodes correspond to viable null-mutations. Red nodes represent indispensable functions and their mutation is lethal. The map was constructed on the basis of two-hybrid data and the statistical properties of the interactions are discussed by Maslov S, Sneppen K 2002 Science 296:910. (Courtesy of Dr. Sergei Maslov)

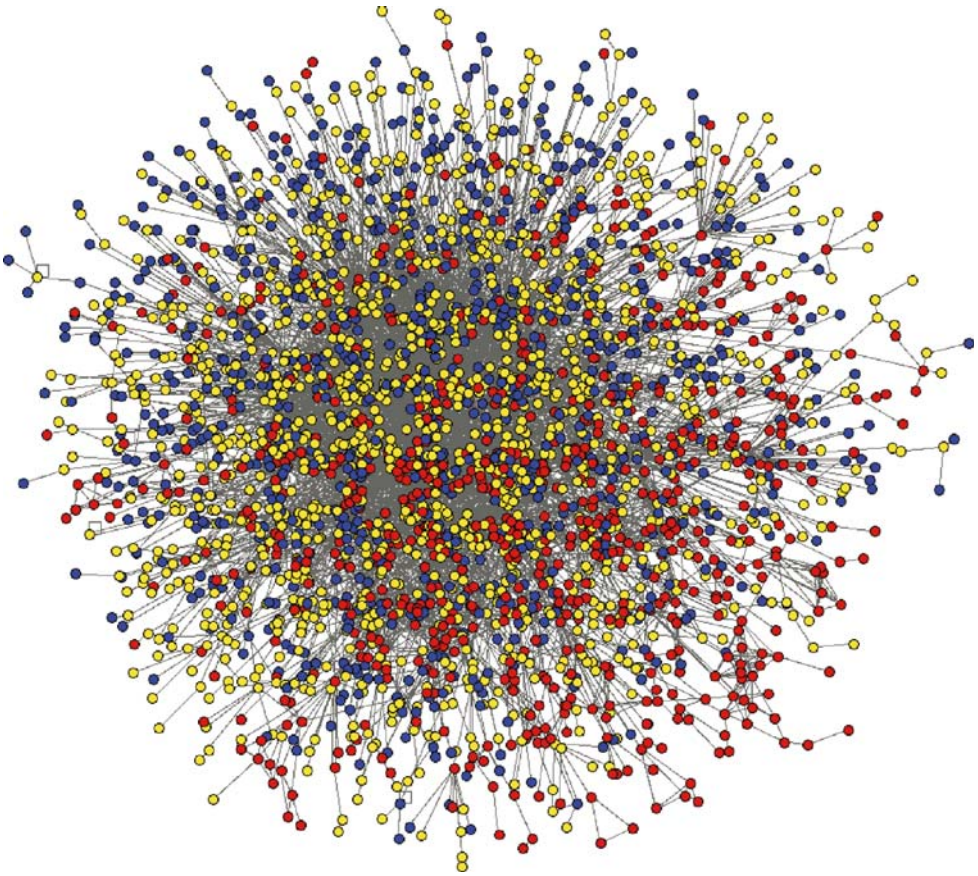

Figure G28. *Caenorhabditis elegans* interactive network (interactome) displaying approximately 5,500 interactions. The experiment involved the use of yeast two-hybrid method. The nodes (circles) of proteins are colored according to phylogenetic class. Red: ancient, yellow: multicellular and blue: worm specific sets. See for details Li, S. *et al*. 2004 Science 303:540; the illustration is the courtesy of Drs. Marc Vidal and Nicolas Bertin

involved. A study of 54 proteins of 23 genetically determined ataxias revealed 770 protein–protein interactions by stringent yeast two-hybrid system; 83% of the interaction could be verified also in mammalian cells (Lim J et al 2006 Cell 125:801 (see Fig. G28)). In *Caenorhabditis*, using RNAi interference of gene expression by simply feeding RNAi containing bacteria revealed that a few "hub" genes affected several others, including homologs of genes involved in hereditary diseases. The data indicated that these genes modify the state of the chromatin and can affect the expression of many functionally unrelated genes and provide new information on the complexity of human disease (Lehner B et al 2006 Nature Genet 328:896).

Regulatory interactions affect the evolution of proteins that can be different in coding properties (see Fig. G29).

Evolution of genetic networks may be based either on the *link dynamics* or on *node dynamics.* Comparison of genetic networks may be relatively simple if the species are closely related, and it can be measured by sequence comparisons (see Fig. G30). In case the species are less closely related, unrelated sequences may assume similar function within the network. These problems of evolutionary analyses can be resolved by a Bayesian parameter inference. Correlation coefficients of gene expression measured on RNA microarrays can be used to assess quantitatively the divergence between humans and mice, even when there is loss or gain of genes (Berg J, Lässig M 2006 Proc Natl Acad Sci USA 103:10967).

A probabilistic method, called Geronemo, aims to identify the mechanism by which genetic changes perturb the regulatory network. Geronemo automatically constructs a set of coregulated genes (modules), whose regulation can involve both sequence variations and expression of regulators. By exploiting the modularity of genetic regulatory systems, it reveals regulatory relationships that are indiscernible when

genes are considered in isolation, allowing the recovery of intricate combinatorial regulation. By incorporating both expression and genotype of regulators, Geronemo captures cases where the effect of sequence variation on its targets is indirect. The results suggest that a significant part of individual variation of expression in yeast arises from the evolution of a small number of chromatin structure modifiers (Lee S-I et al 2006 Proc Natl Acad Sci USA 103:14062).

Time-series microarray expression experiments can provide dynamic information about the expression of thousands of genes that are activated or repressed in response to stimuli such as environmental stress. Transcriptional modules, subsets of transcription factors (TF) and genes, such that genes in the same module tend to be similarly expressed and regulated by the same TFs across a number of experimental conditions. Integrated chromatin immunoprecipitation (ChIP-chip) data with expression data can identify active motifs and combinations of motifs and target genes under certain conditions. A computational method integrates the time-series expression data and ChIP-chip or motif information to infer an annotated *global* temporal map. This map describes the main transcriptional regulatory events leading to the observed time-series expression patterns and the factors controlling these events during a cell's response to stimuli (Ernst J et al 2007 Mol Systems Biol 3:74).

Mechanisms exist for signaling pathways that share components to respond specifically to any one stimulus. One of these mechanisms is insulation, i.e., the shared component(s) are relegated into distinct and specific macromolecular complexes or to different subcellular complexes. Another mechanism can be mutual inhibition to eliminate unwanted interactions between the pathways. These mechanisms can maintain the identity and specificity of different signaling pathways despite shared components (McClean MN et al 2007 Nature Genet 39:409).

(See separate entries mentioned, ►small-world networks, ►networks, ►cell model, ►hub, ►microarray, ►protein complexes, ►protein interactions,

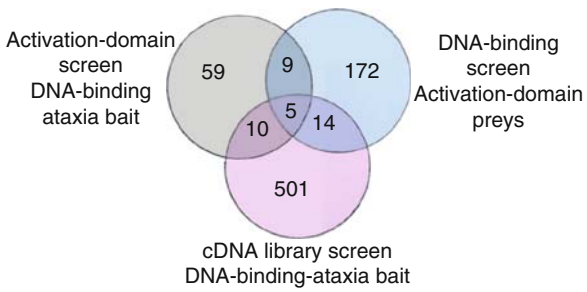

Figure G29. Yeast two-hybrid interactions for 54 ataxia-associated proteins

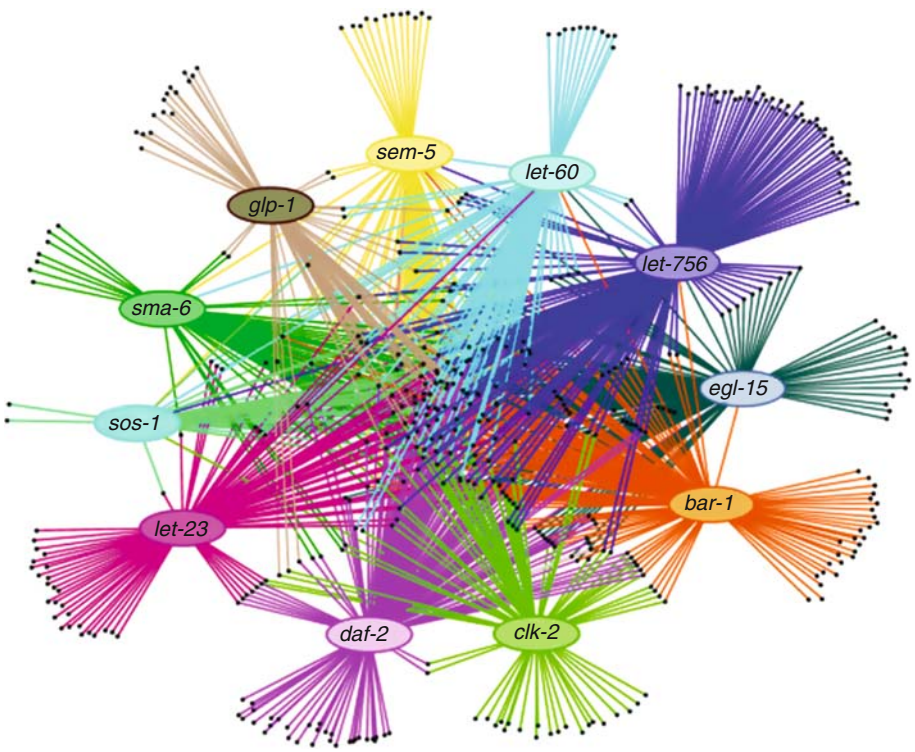

Figure G30. The SGI network. (From Byme AB et al 2007 J. Biol. 6(3): 8)

►protein network, ►two-hybrid system, ►entropy, ►regulon, ►epistasis, ►interlogs, ►synthetic genetic arrays, ►probabilistic graphical models of cellular networks, ►autoregulation, ►proteome, ►transcriptome, ►überoperon, ►genome-wide location analysis, ►signal transduction, ►metagene, ►one gene-one enzyme theorem, ►HUPO, ►reactome, ►cooperative stability, ►knockout, ►synthetic lethal, ►synthetic genetic array, ►ataxia, ►ChIP, ►signal transduction; Kalir S et al 2001 Science 292:2080; Becskei A et al 2001 EMBO J 20:2528; Hasty J et al 2001 Nature Rev Genet 2:268; Davidson EH et al 2002 Science 295:1669; Gavin A-C et al 2002 Nature [Lond] 415:141; Saito R et al 2002 Nucleic Acids Res 30:1163; Guet CC et al 2002 Science 296:1466; Shen-Orr SS et al 2002 Nature Genet 31:64; Wyrick JJ, Young RA 2002 Current Opin Genet Dev 12:130; Dietmann S et al 2002 Current Opin Struct Biol 12:362; Valencia A, Pazos F 2002 Current Opin Struct Biol 12:368; Rison SC, Thornton JM 2002 Current Opin Struct Biol 12:374; Ravasz E et al 2002 Science 297:1551; Gilman A, Arkin AP 2002 Annu Rev Genomics Hum Genet 3:341; Hasty J et al 2002 Nature [Lond] 420:224; Pawson T, Nash P 2003 Science 300:445; Davidson EH et al 2003 Proc Natl Acad Sci USA 100:1475; regulatory module networks: Segal E et al 2003 Nature Genet 34:166; molecular networks in yeast: Galitski T 2004 Annu Rev Genomics Hum Genet 5:177; interaction network in *E. coli*: Butland G et al 2005 Nature [Lond] 433:531; yeast networks based of synthetic lethality: Boone C et al 2007 Nature Rev Genet 8:437; statistical evaluation of transcription regulatory signals: Garten Y et al 2005 Nucleic Acids Res 33:605, 18,183 interactions of *Caenorhabditis* genes computed from intergrated interactome of yeast worm and fly information: Zhong W, Sternberg PW 2006 Science 311:1481; evolution of interactions: Weitz JS et al PloS Biol 5(1)e11; molecular interaction database: http://www.ebi.ac.uk/intact; http://dip.doe-mbi.ucla.edu; http://visant.bu.edu/; www.genepath.org; http://string.embl.de/; http://wwwmgs.bionet.nsc.ru/mgs/gnw/genenet/; commercial supplies: http://www.biocarta.com/; structural genomics: http://sg.pdb.org/; protein network: http://www.cellcircuits.org.

Genetic Nomenclature: ►gene symbols, ►databases, ►Genew; http://www.mblogic.net/point_of_view/1/.

Genetic Polymorphism: Gene loci (or chromosomal arrangements, organelles) in a population are represented by more than one (allelic) form. ►allele

Genetic Predisposition: Genetic predisposition implies that the genetic constitution is favorable for the development of a disease or anomaly.

Genetic Privacy: The right of an individual to keep his/her genetic record closed to the public. There are two aspects of this right: protection from discrimination by employers, insurance companies, etc.; and its possible hinderance of research on genetic disorders and development of new drugs. In the USA, law now recognizes "protected medical information." ►genetic testing, ►wrongful life, ►ethics, ►privacy rules; Hall MA, Rich SS 2000 Am J Hum Genet 66:293; Skene L 2002 Trends Mol Med 8:48; Roche PA, Annas GJ 2001 Nature Rev Genet 2:392.

Genetic Profile: Electrophoretic pattern of microsatellites, restriction fragments, PCR products, etc. The purpose of the procedures is to detect potential health risks. It requires consent by the individuals or parents unless state law mandates screening. It should not violate privacy and should not be used for any kind of discrimination. ►electrophoresis, ►RFLP, ►PCR, ►genetic screening; Almond B 2006 Nature Rev Genet 7:67.

Genetic Recombination: ►recombination, ►recombination frequency, ►crossing over, ►bacterial recombination frequency, ►intragenic recombination, ►mapping genetic, ►illegitimate recombination, ►unequal crossing over, ►site-specific recombination, ►sister chromatid exchange, ►recombination variations of, ►recombination molecular mechanism prokaryotes, ►mtDNA, ►mitochondrial genetics, ►chloroplast genetics, ►recombination mechanisms eukaryotes, ►recombination models, ►gene conversion, ►targeting genes, ►homologous recombination, ►bacterial recombination frequency

Genetic Repair: ►DNA repair

Genetic Risk: The chance that an offspring will be affected by a hereditary defect. The risk can be inferred from the heritability of a particular gene or gene complex in a population. In case of simple Mendelian inheritance, for example in cystic fibrosis, in some Caucasian populations in genetic equilibrium, the frequency of this anomaly is ≈1/2,000 = 0.0005. Thus, the frequency of the recessive allele is $\sqrt{0.0005} \approx 0.022 = q$. At genetic equilibrium, the frequency of carriers (heterozygotes) is $H = 2pq = 2 \times (1 - q) \times q$ 0.043 1/23. If a person heterozygous for such a deleterious gene (q = 0.5) marries a spouse by random choice (q = 0.022), the chance that they will have an afflicted offspring is 0.5 × 0.022 = 0.011, i.e., approximately 1/91. If the same heterozygous person marries a first cousin who may have a 0.25 chance carrying the same allele, the probability that they will have an afflicted child may be as high as 0.5 × 0.25 = 0.125, i.e., 1/8. If, however, an average Caucasian will have an offspring with an average Japanese spouse (q = 0.004) the probability that their child

would be afflicted by cystic fibrosis is only 0.022 × 0.004 = 0.000088 or 1/11,363. The genetic risk will slowly rise with the application of medical care that compensates for the hereditary defects, e.g., administration of insulin to diabetics or by the use of gene therapy without replacing the defective gene(s). The remedial treatments will not much affect the incidence of rare diseases in the shorter term. If the incidence of a dominant human anomaly is 1×10^{-5} at the present, it may take 3,000 years (100 generations) to increase its prevalence to 1×10^{-3}. The incidence of recessive anomalies will rise at a much slower rate because the alleles are already sheltered from selection in the heterozygotes. The genetic risk can now be estimated with good precision if molecular information is available on the nucleotide sequences of a gene. E.g., in familial hypercholesterolemia in the gene encoding cardiac β-myosin, a substitution of Glu for Gly at position 256 involves only 0.56 chance for the penetrance of the disease, whereas a Gln→Arg change at position 403 predicts a 100% penetrance and thus sudden death. ►genetic load, ►genetic counseling, ►empirical risk, ►risk, ►genotypic risk ratio, ►Hardy-Weinberg theorem, ►allelic frequencies, ►amniocentesis, ►clinical tests for heterozygosity, ►mutation rate, ►genetic screening, ►prenatal tests, ►transgenic, ►selection–medical care; Falconer DS 1965 Ann Hum Genet 29:51; Coulson AS et al 2001 Methods Inf Med 40(4):315.

Genetic Scanning: ►genotyping

Genetic Screening: This type of screening is applied to an asymptomatic population as (i) *prenatal tests* during pregnancy such as for mucopolysaccharidosis, muscular dystrophy, cytological tests for Down syndrome and fragile X conditions, ultrasound test for developmental anomalies, blood groups (Rh), and infections (syphilis, toxoplasmosis, cytomegalovirus). These tests may be mandated or voluntary. Screening of (ii) *newborns* aims to reveal whether they are afflicted by autosomal recessive disorders that require immediate medical attention to prevent severe later consequences. Most frequently the tests include biotidinase deficiency, congenital hypothyroidism, galactosemia, hereditary tyrosinemia, homocystinuria, maple syrup urine disease, phenylketonuria, and sickle-cell anemia. Law in the USA mandates some of these tests. Congenital adrenal hyperplasia, cystic fibrosis, hyperphenylaninemia, arginosuccinase deficiency, galactokinase deficiency, phosphoglucomutase deficiency, homocystinuria, glucose-6-phosphate dehydrogenase deficiency and others (altogether more than 1000 diseases) may also be involved. The frequency of the genetic defects may vary in different ethnic groups and some of the tests are limited to families where history provides clues to potential risk. The tests may be performed on blood withdrawn from the neonates by specialized laboratories using standard and reliable procedures such as ELISA, enzyme assays, immuno essays, Guthrie test and DNA tests, radioimmune assays, high-performance liquid chromatography, tandem mass spectrometry, cytological tests, etc. (iii) *Carrier testing* detects heterozygotes for "recessive" disorders in order to facilitate informed decisions by prospective parents regarding risks, especially in populations where the frequency of the deleterious genes is expected to be high, as in the cases of Tay-Sachs disease among Ashkenazi Jews (0.02), thalassemia in people of Mediterranean ethnicity occuring at frequencies exceeding 0.1 in high malaria areas, and cystic fibrosis with variable (generally about 0.02) frequency but much higher in ethnic populations with high degree of consanguinity. About 70% of those afflicted by cystic fibrosis had a CTT (Phe) deletion of codon 508 in exon 10 (ΔF508). This assay is not yet used widely. (iv) *Presymptomatic* and susceptibility screening may be applied to younger individuals with liability to late onset genetic anomalies such as autosomal polycystic kidney disease, Charcot-Marie-Tooth disease, Huntington chorea, familial hypercholesterolemia, retinitis pigmentosa. Some tests predict susceptibility to diabetes mellitus, coronary heart disease, breast cancer, etc. In some countries, predictive premarital testing is mandated for some diseases. Some tests, e.g., Factor V Leiden (parahemophilia, 1q23, heterozygosity for the deficiency is in the range of 10^{-3}, homozygosity 10^{-6}) may involve venous thrombosis for women taking oral contraceptives and the test is not recommended (Grody WW et al 2001 Genet Med 3:139).

Testing for predispositions must require confidentiality because of the obvious relevance to finding jobs or health insurance. Genetic screening of individuals who do not have a family history of disorder may involve psychosocial and ethical issues. It is important that screening be conducted only for essential diseases or pre-disposition, for conditions that are medically treatable and for which, informed choices are available in case the test proves positive. Appropriate and safe procedure should be available, the test should not be objectionable to the population in general, and should be acceptable by the subjects. Genetic screening raises several ethical question regarding the right or advisability of withholding information, disclosure of the information to members of the family, what is the right to know or not to know by whom, and storage, safe-keep, and release of the information. (See terms used under specific entries, ►prenatal diagnosis, ►GMS, ►RDA, ►polymerase chain reaction, ►tandem mass

spectrometry, ►sperm typing, ►pre-implantation genetics, ►ART, ►false positive, ►false negative, ►cascade testing, ►eugenics, ►abortion medical, ►selective abortion, ►genetic counseling, ►genetic testing, ►Guthrie test, ►Guthrie card; Levy HL, Albers S 2000 Annu Rev Genomics Hum Genet 1:139; Pastinen T et al 2000 Genome Res 10:1031; Chace DH 2001 Chem Rev 101:445; McCabe LL, McCabe ERB 2004 Annu Rev Genomics Hum Genet 5:57; http://mchb.hrsa.gov/screening/; screening resources: http://genes-r-us.uthscsa.edu/).

Genetic Segregation: ►Mendelian segregation, ►modified segregation ratios, ►meiosis, ►preferential segregation, ►somatic segregation

Genetic Sexing Lines: Mechanical separation of insects by sex is often very difficult or nearly impossible at larger scale although this may be required for control by genetic sterilization. By genetic engineering, strains can be developed where under defined conditions, either the female or the male individuals can be selectively eliminated upon induction. ►sexing, ►autosexing, ►genetic sterilization; Robinson AS, Franz G 2000 In: Handler AM, James AJ (eds) Insect Transgenesis: Methods and Applications, CRC Press, Boca Raton, FL, p 307.

Genetic Similarity Index: The genetic similarity index expresses the similarities between different strains on the basis of the number of shared restriction fragments, identified by probes such as DNA minisatellite sequences, etc. ►minisatellite, ►microsatellite, ►probe, ►genetic distance

Genetic Stability: Genetic stability is good if the gene and chromosomal mutabilities are relatively rare, transposable elements are absent, and the population is in genetic equilibrium. ►mutability, ►genetic equilibrium, ►transposable elements, ►genetic homeostasis; Li SL, Rédei GP 1969 Theor Appl Genet 39:68.

Genetic Sterilization (sterile insect technique, SIT): In genetic sterilization, heavy doses of ionizing radiation (X-rays) break the chromosomes but do not necessarily kill the irradiated animals that are even capable of mating. However, because of the chromosomal rearrangements that follow, sterility or lethality may occur in their progeny, or, although the irradiated males may copulate, they cannot fertilize the eggs of the females and leave no offspring. This basic genetic knowledge was successfully applied to insect eradication. The screwworm (*Cochliomya hominivorax*), a tropical and subtropical parasite of warm-blooded animals, produces larvae that hatch in the wounds of livestock and cause great damage to the hide, making it inferior for the leather industry. Additional damage results to agriculture by weight loss in cattle, sheep, and game; further, the fly may pose hazards even to people. The chemical control of this insect is difficult to achieve in live animals and not without danger of causing pollution and damaging health. Therefore, pupae were reared in a large laboratory and treated with about 7,500 R X-radiation, and every week two million irradiated males were released in the heavily-infested areas. The monogamous females so mated either failed to produce offspring, or more sophisticated chromosomal constructs were used to generate "genetic time bombs" (recurring genetic defects) that kept on killing the offspring due to chromosomal or genic defects (temperature-sensitive alleles).

In some areas and some years, this pest control was so effective that the screwworm population was reduced to 1% of that before the initiation of the program. A similar procedure was successfully applied for mosquito control as well. Particularly good results were observed in the control of lepidopteran insects with holocentric chromosomes where the delayed and sustained lethal effects could be best exploited.

Constructing a conditional lethal dominant genetic system may cause death without irradiation. The insect becomes lethal when specific conditions are met. In one construct designed in a *Drosophila* model, a tetracycline-repressible transactivator (tTa) protein was placed under the control of the Yp3 fat-body gene promoter. In the absence of tetracycline, any gene controlled by a tetracycline-responsive element (tRe) is normally expressed in the females. On a culture medium containing as low as 0.1 µg/mL tetracycline, females produced no progeny because the tTa prevented the synthesis of fat body (a yolk protein) that is required for storage of nutrients and for the insect immune system. The progeny of the males was not affected because they do not produce eggs and do not need fat body for fertility. In a similar manner, a mutant allele of the *male-specific lethal 2* gene ($msl\text{-}2^{NOPU}$), selectively killed the females by activating the dosage compensation mechanism in both males and females. By the same principles, insect-mediated (insect vector) human viral (Dengue fever, West Nile fever, Yellow fever), bacterial (Plague, Typhus, Lyme disease), protozoan (Malaria, Leishmaniasis, Sleeping sickness, Chagas disease), and worms-inflicted diseases (River blindness, Filariasis) may be controlled. With the increased knowledge of genetic transformation and the availability of various transposable elements, new approaches may open up in insect control. ►holocentric chromosomes, ►translocations, ►radiation effects, ►GSM, ►SIT, ►tetracycline, ►TetR, ►tTA, ►rtTA, ►sex determination, ►*msl*, ►high-dose/refuge strategy, ►refractory genes; Thomas DD et al 2000 Science 287:2474; Robinson AS 2002

Rev Mut Res 511:113; Horn C, Wimmer EA 2003 Nature Biotechnol 21:64; female-specific alternative splicing: Fu G et al 2007 Nature Biotechn 25:353; Dyck, V., Hendrichs J, Robinson A (eds.) 2005 Sterile Insect Technique: Principles and Practice in Area-Wide Integrated Pest Management, Springer, Dordrecht, H.

Genetic Surgery: Genetic surgery replaces single or a few (defective) genes of an organism with the aid of (plasmid) vectors or introducing into cells foreign genetic material (organelles, chromosomes) with microsyringes or microcapillaries controlled by micromanipulators under microscopes. ►gene replacement, ►gene therapy, ►genetic engineering, ►gene transfer by microinjection, ►targeting genes, ►transformation genetic

Genetic Switch: Mechanisms to turn genes on and off, based on interaction between specific DNA and protein sequences. ►regulation of gene activity, ►DNA binding proteins, ►DNA-binding protein domains, ►immunoglobulins, ►transposition, ►mating type determination in yeast, ►phase variation, ►*Trypanosomas*, ►*Borrelia*, ►serotype

Genetic Systems: Primarily the prevalent mode of reproduction (selfing, inbreeding, random mating, assortative mating, etc.). Generally, the mechanisms affecting variability (recombination, mutational mechanisms, etc.) are also included in this term. ►mating systems

Genetic Testing: Genetic testing may reveal the liabilities of an individual to certain diseases and genetic anomalies. The purpose of the tests can be diagnosis and/or risk assessment for symptomatic and asymptomatic cases, population screening, and reproductive decision-making. The test may consider family histories and environmental factors. Identification of carriers may be of particular importance for reproductive counseling. The results may aid prevention an/or treatment. Genetic information may facilitate the proper selection of drugs; e.g., mercaptopurine must be avoided for leukemia patients, and those deficient in thiopurinemethyl transferase. Cytogenetic, biochemical/pharmacogenetics and molecular tests can be used. DNA sequencing identifies alterations within genes, although heterozygotes may not necessarily bear a direct burden or risk. Microarray hybridization may also reveal genetic defects, although the tests are more expensive and the results may be ambiguous in case of heterozygosity of the diploid cells. Single strand conformation polymorphism and denaturing gradient gel electrophoresis are also applicable techniques. An individual may benefit from it because glucose-6-phosphate dehydrogenase deficiency may make a person more susceptible to environmental oxidants (ozone, nitrogen dioxide). Thalassemias may increase the dangers of exposure to lead and benzene, porphyrias to chloroquine and barbiturates, pseudocholinesterase deficiency to organophosphate and insecticides, and so on. Molecular tests may reveal non-symptomatic heterozygosity for genetic diseases and may predict the risk for various disorders in the offspring. On the other hand, employers and health insurance companies may discriminate against individuals on the basis of genetic records. Genetic testing may not be applicable for the identification of certain anomalies or diseases, and the results of the tests for some conditions may not accurately predict the onset of a disease. With the approval of the Genetics and Insurance Committee of the United Kingdom, private health insurance companies in the UK already use seven tests for mutant alleles for the early onset Alzheimer disease, breast cancer, familial adenomatous polyposis coli, Huntington disease, and three other monogenic diseases. Those who are positive are obligated to pay higher premiums to obtain life insurance over £100,000 and have mortgage insurance. An extensive public welfare and healthcare system is available in the UK. Nevertheless, the ethical aspects of such a policy of insurance have been questioned. It must be recognized that genetic tests may not yet provide the wished answers to all health problems (Khoury MJ et al 2000 Genet Med 2:198), although 1,100 genetic tests had become available by 2007. Non-communication to patients of genetic risks may have legal liability to the physician or to the counselor (J. Clin. Oncology 21:2397 [2003]). Direct genetic testing of consumers (DTC) requires caution, and must not be considered without adequate context or counseling because some tests from laboratories of dubious quality mislead through unproven claims of benefit. In the USA, only about half of the states permit it (Hudson K et al 2007 Am J Hum Genet 81:635). ►genetic privacy, ►genetic screening, ►prenatal diagnosis, ►compliant mutation, ►refractory mutation, ►DNA sequencing, ►microarray hybridization, ►conversion, Yan H et al 2000 Science 289:1890; Cutler DJ et al 2001 Genome Res 11:1913; regulatory problems in genetic tests: Burke W, Zimmern RL 2004 Nature Rev Genet 5:955, http://www4.od.nih.gov/oba/, www.genetests.org, http://www.geneclinics.org.

Genetic Toxicology: ►gene-tox

Genetic Transfer: A genetic transfer may be mediated by the gametes during sexual reproduction, by cytoplasmic organelles, plasmids, episomes, infectious heredity, bacteriophages (transduction) or plasmids, fusion of somatic cells, transfer of isolated organelles,

transformation, vectors, viruses, retroviruses, prions, microinjection, electroporesis, and targeting genes.

Genetic Transformation: ►transformation genetic, ►transformation oncogenic, ►transfection

Genetic Transfusion: Transfer of organelles and cellular inclusions by protoplast fusion.

Genetic Translation: ►protein synthesis, ►regulation of gene activity

Genetic Tumors: More than two dozens tumor genes have been assigned to *Drosophila melanogaster chromosomes* 1, 2, and 3. The majority of these are not malignant and occur freely or attached to internal organs in the thorax and in the abdomen.

They are distinguished already at the third instar larva stage and persist through the life of the individuals. Most of the tumors become melanotic. The melanotic tumors determined by genes *mbn* and *Tum* have malignant characteristics. In several inbred mice strains, ovary tumors, testis tumors, B cell lymphoma, kidney adenocarcinoma, leukemia, and pulmonary tumors are under polygenic control. *Bilateral retinoblastoma* (tumor of the eyes) of humans is controlled by a dominant gene. Deficiencies involving the long arm of chromosome 13 may also induce retinoblastoma. Genes involved in the skin disease, *xeroderma pigmentosum*, is based on deficiency in the genetic repair mechanism. Initially the disease involves excessive freckle formation and may become tumorous. Exposure to ultraviolet light (sunlight) enhances the formation of skin tumors, particularly in fair skinned and albino individuals.

About 5–10% of human cancers (hereditary or sporadic) show definite genetic components. Cancer cells commonly display hypermethylation of promoter CpG islands and demethylation of the rest of the genome. The incidence of leukemia may increase in cases of trisomy or partial deficiency for chromosome 21. Both DNA (SV40, adenovirus, bovine papilloma virus, etc.) and RNA viruses (Epstein-Barr virus, retroviruses) can cause tumorigenesis in mammals. The loss or mutation in a gene controlling protein p53 may lead to tumorigenesis presumably due to lack of function of this suppressor gene. Genetic hybrids between the species of the platyfishes (*Xiphophorus*) are prone to develop melanoma. Approximately 30 species-crosses of tobaccos may produce tumorous offspring that form callus in vitro cultures without a requirement for phytohormones (see Fig. G31). In the *Nicotiana glauca* (2n = 24) × *N. langsdorffii* (2n = 18) hybrids, more than one locus is involved in tumor development. In the hybrids of *N. longiflora* (2n = 20) × *N. tabacum* (2n = 48), one chromosomal segment

Figure G31. Genetic tumors of interspecific tobacco hybrids. (Courtesy of Dr. H.H. Smith)

appears responsible for tumorigenesis. *N. saunderae* may inhibit the expression of tumors. In the majority of dicotyledonous and some monocotyledonous plants, agrobacterial infection and the insertion of the T-DNA of the Ti plasmid may lead to tumor formation by genetic transformation. Certain viral infections also result in tumorous growth in plants. Several insects stimulate the formation of gall tumors in plant tissues through their metabolic products. For the in vitro development of plant tumors, the additions of phytohormones (primarily natural or synthetic auxins) are required. Some cultures, however, become "habituated" after a course of culture and the exogenous auxin supply may no longer be required. The plant tumors are non-malignant. ►cancer, ►tumor, ►Knudson's two-mutation theory of cancer, ►tumor suppressor, ►carcinogens, ►SV40, ►adenoviruses, ►retroviruses, ►reverse transcription, ►retinoblastoma, ►*Agrobacterium*; Purello M et al 2001; Oncogene 20:4877; Suhardja A et al 2001 J Neurooncol 52:195; Esteller M et al 2001 Hum Mol Genet 10:3001; Smith HH 1973 Brookhaven Symp 25:309.

Genetic Vaccine: ►immunization genetic

Genetic Variability: The ability or proneness (proclivity) to hereditary change. ►mutation, ►mutator genes, ►transposable elements, ►homeostasis, ►genetic homeostasis

Genetic Variance: Genetic variance is caused by the various effects of the genotype (V_g). The variance observed is usually the phenotypic variance (V_p) that

is the outcome of the mutual action of the genotype and the environmental variance (V_e). The genetic variance itself has three components: $V_g = V_a + V_d + V_i$, where V_a is the additive genetic variance or breeding value, V_d is the dominance variance, and V_i = interactions. The interactions can be epistatic effects among the individual quantitative traits and the effect of the environment on gene expression. The additive genetic variance may be expressed also as $V_a = 2pqt^2(p[1-d] + qd)^2$ where *t* stands for displacement, The dominance variance $V_d = p^2q^2t^2(d-0.5)^2$. ►variance, ►midpoint value, ►breeding value, ►polygenes, ►gain, ►heritability, ►displacement, ►genotypic risk ratio

Genetic Variation: Hereditary differences within or between populations. Sequencing the genomes of many prokaryotic and eukaryotic organisms sheds light on earlier unforeseen variations such as SNIPS, minor duplications and deletions, and rearrangements in the chromosomes. For a review of human variations see: Serre D, Hudson TJ 2006 Annu Rev Genomics Hum Genet 7:443, http://projects.tcag.ca/variation/.

Genetical Genomics: Genetical genomics dissects regulation of transcription (Jansen RC 2003 Nature Rev Genet 4:145) by analysis of transcript expression pattern by high-throughput procedure (Jansen RC, Nap J 2001 Trends Genet 17:388) and segregation of genomic regions.

Genetically Directed Representational Difference Analysis (acronym GDRDA): GDRDA targets and identifies traits that differ between congenic lines without prior knowledge concerning their biochemical function. It determines linkage to known genes or to polymorphic DNA markers. ►congenic, ►DNA markers, RDA; Higo K et al 2000 Exp Anim 49[3]189.

Genetically Effective Cells: The cells of the germline that actually contribute to the formation of the gametes and thus to the offspring (see Fig. G32). The number of genetically effective cells can be determined in autogamous species on the basis of the segregation ratios after mutation. In case the genetically effective cell number (GECN) is 1, the segregation is either 3:1 or 1:2:1. If the GECN is 2, the segregation of dominant: recessives is 7:1, in case of GECN = 4, the expected ratio is 15:1 because only one of the cells of the germline segregates while the other cell(s) provide only non-mutant offspring. Thus, the pooled phenotypic numbers yield the 7:1 (4 + 3):1, and 15:1, (4 + 4 + 4 + 3):1 proportions. These ratios may be (slightly) altered if the transmission of the gametes carrying the recessive alleles is impaired, or if the viability of the recessive homozygotes is reduced. For the determination of GECN, the aberrant progenies should be left out of consideration. ►planning of mutation experiments, ►critical population size, ►mutation rate; Rédei GP, Koncz C 1992 In: Koncz C. et al (eds) Methods in Arabidopsis Research, World Scientific, Singapore, p 16).

Genetically Effective Population Size: ►effective population size

Genetically Modified Organisms: ►GMO, ►pest eradication

Geneticin (G418): An aminoglycoside antibiotic (see Fig. G33). ►antibiotics, ►aminoglycoside phosphotransferase, ►kanamycin, ►neomycin

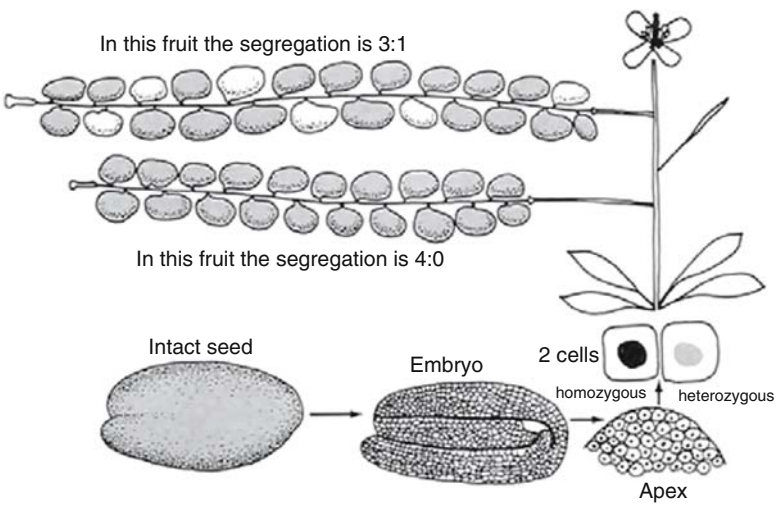

Figure G32. Segregation in case of two genetically effective cells

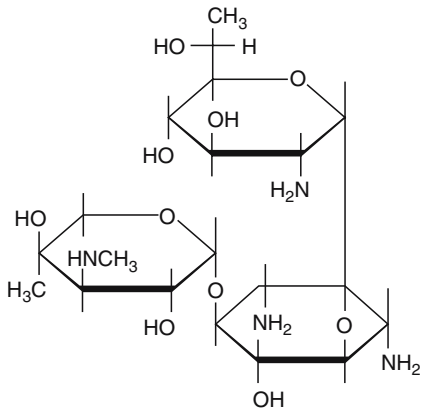

Figure G33. Geneticin

Genetics: The study of inheritance, variation, and the physical nature and function of the genetic material. William Bateson suggested the term in 1906 for the then entirely new discipline. [Professor Attila T. Szabó called my attention to a paper published in German in Brünn in 1819 (*Oekonomische Neuigkeiten und Verhandlungen* 22, April, p. 169–71) by Hungarian count Imre Festetics and used the expression "die genetische Gesätze der Natur" [the genetic rules of nature] in expounding his studies on heredity of farm animals.]

Genetics may be pursued as a basic science whose goals are only the discovery of new principle(s) and their integration into the store of knowledge. Alternatively, applied branches of genetics rely on established genetic principles and are used for agricultural (plant and animal breeding) or industrial (biotechnology) purposes, or for the improvement of human health (medical genetics). Applications of genetics are expanding into paleontology, archeology, and forensic areas. The tools of genetics are integrated today into all biological disciplines from taxonomy, evolution, cytology, development, behavior, and physiology, to biochemistry, biophysics, and molecular studies. Thus, genetics has escaped from its classical boundaries of heredity and cytology to become the core and unifying element of biology. ►heredity, ►inheritance, ►reversed genetics, ►population genetics, ►human genetics, ►medical genetics, ►clinical genetics, ►quantitative genetics, ►experiments, ►science, ►genetic engineering, ►synthetic genetics, ►criticism on genetics, ►GMO

Genetics and Privacy: The rapidly-accumulating information on risks based on various screening techniques and DNA sequencing may result in discrimination by insurance companies, potential employers, and possibly by society in general. Therefore, there is considerable concern that such information not be divulged without the consent of the individual and the privacy be legally protected. ►bioethics, ►genetic privacy; Annas GJ 2001 N Engl J Med 345(5):385.

Genetics, Chronology of: A very broad overview includes only the most important milestones of basic genetics compiled somewhat subjectively. Paraphrasing GB Shaw, who would dare to say who is greater than Shakespeare? To keep the length minimal, applied aspects of genetics are not included. (See Rédei GP 1974 Biol Zbl 93:385; chronology of medical genetics through the career of a man: Victor McKusick 2006 Annu Rev Genomics Hum Genet 7:1).

200–300 B.C. Greek Philosophers discuss heredity

1694 Camerarius recognizes sex in plants

1761 Kölreuter reports thousands of attempted and (some) successful plant hybridizations

1839 Schleiden (plants) and Schwann (animals) discover cellular organization

1865 Mendel recognizes the basic principles of inheritance

1866 Haeckel points out the role of the nucleus in heredity

1869 Galton lays down the foundations of statistics-based inheritance

1871 Miescher reports about nuclein

1873-on Mitosis, meiosis, chromosome numbers, supremacy and continuity of chromosomes are recognized

1900 Mendel's work is rediscovered

1902 Sutton proposes the chromosomal theory of inheritance

1902 Benda recognizes mitochondria

1902 Garrod reports on alkaptonuria as an inherited biochemical trait

1906 Bateson suggests the term genetics

1909 Johannsen coins the terms gene, genotype, phenotype, and explains pure lines

1909 Correns and Baur discover non-Mendelian inheritance of chloroplasts

1910–11 Morgan discovers sex-linkage and crossing over

1910 von Dungern and Hirschfeld show that blood groups are inherited

1913 Sturtevant constructs the first linear map of 6 genes of the *Drosophila* X chromosome

1913–1925 Bridges and Sturtevant discover deficiency, nondisjunction, duplication, inversion, translocation

1926 Chetverikoff and Helena Timoféeff-Ressovskaya found experimental population genetics

1926 D'Hérelle describes bacteriophages

1927 Landsteiner and Levine lay the foundations of immunogenetics

1927 Muller and then Stadler induce mutations by X-rays

1928 Griffiths observes bacterial transformation

1930-on Fisher, Wright, and Haldane, working independently, lay down the foundations of theoretical population genetics

1939-on Delbrück and Luria initiate phage genetics

1940 Beadle and Tatum conduct experiments leading to biochemical genetics and to the gene - polypeptide theory

1944 Auerbach and Robson discover chemical mutagenesis

1944 Avery, MacLeod and McCarty demonstrate that the transforming principle is DNA

1946 Lederberg and Tatum show bacterial recombination

1949 Chargaff discovers the variable base composition and A = T, G≡C relations in different DNAs

1951 McClintock discovers transposable elements

1952 Lederberg reports transduction

1953 Watson and Crick construct a valid DNA model

1955 Fraenkel-Conrat and Williams prove that RNA can also be a genetic material

1956 Kornberg shows in vitro replication of DNA

1957 Taylor in plants, and in 1958 Meselsohn and Stahl show that DNA replication is semi-conservative

1957-on Beginning of the understanding of the machinery of protein synthesis

1960 Marmur and Lane hybridize nucleic acids

1960 Barski makes somatic cell hybrids

1961 Brenner and coworkers explain the nature of the mRNA

1961 Nirenberg and Ochoa laboratories independently demonstrate the nature of the genetic code

1961 Jacob and Monod propose the operon concept

1965 Southerland discovers cAMP and opens the ways into inquiries on signal transduction and transcription factors

1969 Shapiro et al. isolate the *lac* operon

1970 Temin and also Baltimore discover reverse transcription

1970 Khorana synthesizes in vitro a tRNA gene

1971 Danna and Nathans fragment SV40 DNA by a restriction enzyme discovered by Smith and Wilcox in 1970

1972 Transformation by recombinant DNA begins in Cohen, Berg and Lobban laboratories using plasmid vectors

1977 Development of efficient DNA sequencing by Gilbert's and by Sanger's laboratories

1978 Shortle and Nathans make localized mutagenesis During the late 1970 Prusiner, S.B. isolates the "scrapie" agent", which turns out to be an unorthodox infectious, hereditary protein, the prion, in violation of the 'nucleic dogma'

1980 Capecchi et al., Ruddle et al. transform mice

1980s Christiane Nüsslein-Volhard and E. Wieschaus based on earlier studies by EB Lewis establish a new approach to developmental genetics.

1981 Schell et al. transform plants by *Agrobacterium*

1981 Cech discovers ribozymes

1983 Varmus, Bishop and others identify c-oncogenes

1985 Mullis et al. develop the PCR procedure

1989 Saiki, Walsh & Erlich initiate microarray type analysis of amplified DNA with immobilized sequence-specific probes

1995-on Sequencing of complete DNA genomes of prokaryotes and also the eukaryote yeast

By 1996 Beginning of the mass identification of the function the sequenced genes. During the 1900s RNAi, microRNA and other small Interfering RNAs have been discovered in *Caenorhabditis*, plants and other organisms by several laboratories.

1999 the almost complete sequence of the 33.4 megabase human chromosome 22 was published by 217 authors. Craig Venter's Celera group, the Berkeley, Canadian and the European Genome Projects publish the first 'complete' sequence of the *Drosophil*a genome. The sequencing of the *Arabidopsi*s genome (2000) and the human genome (2001) followed this. On Apr. 14, 2003 completion of the Human Genome Project has been announced.

1999 marks the beginning of 'modular cell biology' and the development of genetic and protein networks by Hartwell LH and co-workers, Barabási A-L, Oltvai ZN and other laboratories, culminating in detailed functional networks of lower and higher eukaryotes by the laboratories of Chant, J. in 2003 and Vidal M 2004.

From 1996 on, the interest increased on the proteome, the complete complement of cellular proteins. Their number exceeds that of the genes because of the transcripts can be processed in multiple ways. How cells and organisms function will be fully understood when all genes will be annotated and the understanding of the complex, dynamic interactions within the proteome will unfold during the coming years. (See ENCODE 2007) It is a commonplace to say that genetics progresses at a breath-taking speed. Yet it is hard to give credit to the major current developments because there are so many and they are so intertwined.

During the preceding decades geneticists tried to reveal the function of single *good* genes or of genetically controled pathways. By the turn of the millennium the field is turning toward synthesis and integration. The goal of the future research is not less than understanding the function of entire organisms

(proteome), including their descent and cooperation. In the coming years we can expect major progress in the understanding of developmental control (epigenetics), the organization and function of the nervous system, evolution, application of gene and cancer gene therapy, in developing more productive and safer agricultural plants and livestock, moving from databases to complex Information Systems. Although genetics is again in a golden age, the excitement may last indefinitely. Yet one must keep in mind the words of the immunologist Peter Medawar: wise people may have expectations but only the fools make predictions. (See Lander ES, Weinberg RA 2000 Science 287:1777).

Genetics, Digital: Digital genetics is the computer modeling of the behavior of virtual genes and their function, interaction, organization, mutation, recombination, and evolution. ►digital genes, ►avidian; Adami C 2006 Nature Rev Genet 7:109.

Genetics of Behavior: ►behavior genetics

Genetics of Cancer: ►cancer, ►genetic tumors, ►cancer gene therapy

Genetics, Public Understanding and Social Needs: In democratic societies public understanding of social and technological developments is of great importance because research and applications are influenced by the collective wisdom of individuals. Individual rights imply responsibilities. Because of rapid progress, it is increasingly more difficult to keep up with the current knowledge. Although newspapers, popular magazines, television, internet and various commercial resources are available for information transfer, the quality and trustworthiness of these resources are quite variable. Genetics knowledge is now available on the advantages and perils of various energy sources (atomic and fossil fuels), polluting industrial and agricultural chemicals (mutagens and carcinogens), drugs and side effects of medications, food processing, additives and food supplements. There is a continuous debate about the advantages and potential perils of genetically modified organisms. In the area of human health, the use of vaccination, microbial resistance to antibiotics, biological weapons, emergence of new pathogens, origin and risks of cancer, the problems of stem cell research, gene therapy, cancer gene therapy, artificial insemination, in vitro fertilization, preimplantation screening, twin studies, incest and inbreeding risks, genetic counseling, genetic testing and screening, hereditary and sporadic diseases and their penetrance and expressivity, pharmacogenetics and human individuality, race and disease prevalence, and concerns about eugenics, privacy, and ethics are areas where sound genetic information may facilitate forming relatively best opinions. The sequencing and annotation of human and other genomes are expensive for society and citizens must be able to form sound judgments. Genetic principles in forensics, such as fingerprinting, DNA analysis, and testing of blood groups are frequently discussed without adequate information for laymen. There are genetic consequences of the use of various weapon systems (nuclear, chemical, biological, and conventional). Abortion and other means of medical practices too have certain consequences in human evolution. Evolution and its relation to faith and religions are often presented with conflicting views. Obviously, it is impossible to be an expert in the broad field of genetics and its application but there is a large array of condensed information to consult in this book and references cited. Schools (elementary through college or even graduate school) do not have time enough for dealing with all the existing problems and with those yet evolving. The review of Haga SB 2006 Nature Rev Genet 7:223 discusses teaching resources for genetics.

Généthon: Research Center for Genetics and Gene Therapy (Every, France, http://www.genethon.fr/php/index.php; http://www.cephb.fr/ceph-genethon-map.html).

GeneTide: ►GeneCard

Gene-Tox: Genetic toxicology; study of factors (physical and chemical agents) that are reponsible for mutation and cancer or both. ►environmental mutagens, ►carcinogen, ►toxicogenomics, ►comparative toxicogenomics; gene-chemical interactions: http://ctd.mdibl.org/; http://toxnet.nlm.nih.gov; structure-searchable toxicity database: http://www.epa.gov/nheerl/dsstox).

GeneTrek: A method to sequence and annotate a small portion of the large genome to obtain information about its general nature (Liu R et al 2007 Proc Natl Acad Sci USA 104:11844).

GENEW (Human Gene Nomenclature Database): ►genetic nomenclature, ►gene symbols; http://www.gene.ucl.ac.uk/cgi-bin/nomenclature/searchgenes.pl.

GeneWise: GeneWise compares genomic and protein sequences. ►gene; Birney E et al 2004 Genome Res 14988; www.sanger.ac.uk/Software/Wise2/.

Genic Balance: The proportion of the sex chromosomes and autosomes has a crucial role in sex determination in some organisms (e.g., *Drosophila*). In Drosophila (1 X):(2 sets of auto-somes) means male, whereas (2X):(2 set of autosomes) = females (1:1). In general, all individuals with chromosomal ratios above 1 are females and those between 0.5 and <1 are inter-sexes.

In humans and mice, the XO is female while in *Drosophila* XO is male. In trisomics and nullisomics, the nature of the individual chromosome(s) present or absent makes a great difference in the phenotype. ►sex determination, ►trisomy, ►nullisomic, ►nullisomic compensation

Geniculate Body (geniculate nucleus): A knee-like structure in the brain where optic and auditory fibers are received.

Genie: A gene predictor program. ►GENSCAN, ►FGENE, ►MZEF; Reese MG et al 2000 Genome Res 10:529.

Genistein (4,5,7-trihydroxyflavone): A phytoestrogen (common is soybean products), an inhibitor of protein tyrosine kinases and frequently used for probing signal transduction pathways. ►leukemia BCP; X-ray crystallography: Manas ES et al 2004 Structure 12:2197.

Genital Anomaly Syndromes: In males, these syndromes may involve hypospadias or cryptorchidism or micropenis. In hypospadias the urethra may open at the lower side of the penis or between the anus and the scrotum. Cryptorchidism indicates that the testes do not descend from the abdominal cavity into the scrotum (the testicular bag). In females, commonly either the ovaries, uterus, or the fallopian tubes (connecting the ovaries with the uterus), or the vagina fail to develop normally, and clitoromegaly and fusion of the labia occur. ►hermaphroditism, ►pseudohermaphroditism, ►gonadal dysgenesis, ►Smith-Lemli-Opitz syndrome, ►Opitz syndrome, ►Wilms tumors, ►Robinow syndrome, ►Fraser syndrome, ►Wolf-Hirsch-horn syndrome, ►Bardet-Biedel syndrome, ►adrenal hyperplasia, ►trisomy, ►testicular feminization

Genius: According to the Latin meaning of the word, a genius is a guarding spirit influencing a person for better or worse. CD Darlington (1964) defined it as a person who "changes the environment of others for his own and even for succeeding generations, for his own species and even for the whole living world." Francis Galton in his book Hereditary Genius (1869) came to the conclusion that eminence is biologically inherited. Darlington had a less asserting view "the sons of great men are given the best chances with the worst results". Human intelligence cannot be exempted from the general biological laws (offspring-parent regression), although environment has great influence on the development of hereditary qualities. A good example is Marie Curie Sklodowska who became the first woman who received, along with her husband Pierre, the Nobel Prize for physics in 1903 (see Fig. G34). She received her second Nobel Prize in 1911 for chemistry. In 1935, their daughter Irene and her husband Frédérick Joliot received the Nobel Prize for chemistry, and this indicated the roles of inheritance and assortative mating on the manifestation of a genius.

Figure G34. Marie Curie Sklodowska

Albert Einstein, probably the most influential physicist in history, was a slow child (suspected to be dyslexic) and neither of his two sons matched their father although, in his words, their mother Mileva was comparable to her husband in intellectual abilities (see Fig. G35). Actually the younger son, Eduard, an aspiring psychologist died in an asylum as a schizophrenic. His brother Hans Albert became a hydraulic engineering professor. An extensive study of Nobel-laureate and literary prize-winner families suggest that outstanding creativity is not much biologically inherited rather it may be influenced primarily by the same-sex parent (Rothenberg A, Wyshak G 2004 Can J Psychiatry 49(3):185). ►human intelligence, ►musical talent; Andreasen NC 2005 The Creating Brain: The Neuroscience of Genius, Dana Press, New York.

Figure G35. Mileva and Albert Einstein wedding picture (Courtesy of Joachim Reinhardt, University of Frankfurt, Germany)

Genmap: A computer program for mapping genetic data based on least squares. ►least squares

Genocopy: A genetically determined phenotype that imitates or resembles a similar phenotype, which is controlled by another gene. ►phenocopy

Genomatron: A gene-mapping machine.

Genome: A complete single set of genes of an organism (taxonomic unit) or organelle, also the basic haploid chromosome set. The size of genomes, in rounded nucleotide numbers, varies in the different taxonomic categories (See tabulation below).

The average genome size of birds is almost 1/3 that of mammals, mainly because the avian introns are shorter. Endosymbionts usually reduce the size of their genomes during evolution. The nucleomorph of the chlorarachniophyte protist *Bigelowiella natans* is composed of only 373,000 bp representing the smallest eukaryotic nuclear genome. It has three chromosomes, 331 genes, and several very short introns in this endosymbiont within the chloroplast (Gilson PR et al 2006 Proc Natl Acad Sci USA 103:9566). The larger plant genomes contain many LTR retrotransposon families with >10,000 copies per haploid genome, whereas the smaller genomes contain few or no LTR retrotransposon families with >1,000 copies, suggesting that this differential potential for retroelement amplification is a primary

Human mitochondrion	1.7×10^3	bp
MS2 (single-stranded RNA bacteriophage)	3.5×10^3	bases
ϕ X174 (single-stranded DNA bacteriophage)	5.4×10^3	bases
SV40 (double-stranded animal DNA virus)	5.2×10^3	bp
Tobacco mosaic virus (single-strand RNA)	6.4×10^3	bases
Influenza virus (single-strand RNA, animals)	1.4×10^4	bases
λ (double-stranded DNA bacteriophage)	4.9×10^4	bp
Vaccinia virus (double-stranded DNA, animals)	1.9×10^5	bp
T2, T4 (double-stranded DNA phages)	1.7×10^5	bp
Chlamydia (bacteria)	6.0×10^5	bp
Escherichia coli bacterium	4.7×10^6	bp
Calotrix (bacteria)	1.3×10^7	bp
Saccharomyces cerevisiae (fungus, eukaryote)	1.2×10^7	bp
Ostreococcus tauri green alga	1.3×10^7	bp
Drosophila melanogaster (insect)	9.0×10^7	bp
Caenorhabditis elegans (nematode)	1.0×10^8	bp
Arabidopsis thaliana (higher plant)	$\sim 1.2 \times 10^8$	bp
Rice	$\sim 4.0 \times 10^8$	bp
Chicken	1.05×10^9	bp
Dog	$\sim 2.3 \times 10^9$	bp
Mouse	$\sim 2.6 \times 10^9$	bp
Homo sapiens	$\sim 2.9 \times 10^9$	bp
Opossum (*Monodelphis domestica*)	$\sim 3.5 \times 10^9$	bp
Toad *(Bufo bufo)*	6.0×10^9	bp
Maize (higher plant)	2.5×10^9	bp
Hexaploid wheat (n = 3x)	1.7×10^{10}	bp
Trillium luteum (higher plant)	6.5×10^{10}	bp
Fritillaria davisii (higher plant)	1.5×10^{11}	bp

factor in angiosperm genome size variation. Besides amplification of transposable elements, ejection of redundant copies by unequal homologous recombination and nonhomologous recombination determine the actual, extant genome size (Vitte C, Bennetzen JL 2006 Proc Natl Acad Sci USA 103:17638). ►mtDNA, ►chloroplasts, ►nucleomorrph, ►endosymbiont, plants: Bennett MD, Leitch IJ 1995 Ann Bot 76:113; bacterial genomes: Casjens S 1998 Annu Rev Genet 32:307; Genetica Vol 115: issue 1 (2002); ►minimal genome size, ►C value paradox, ►human genome, ►gene numbers, ►Map Viewer, ►genome sizes; http://www.cbs.dtu.dk/databases/DOGS/; ►animal genome size; http://www.genomesize.com/search.php; http://www.ensembl.org/index.html; number and organismal genomes sequenced and sequencing underway: http://www.genomesonline.org/.

Genome Analysis: Initially, genome analysis meant determining the origin of the component genomes in allopolyploid species on the basis of chromosome pairing, univalent(s) and multivalent associations, chiasma frequencies, chromosome substitution, chromosome morphology, chromosome banding, and hemizygous ineffective alleles. Today, it is used more generally for studying DNA base sequences, microsatellites, etc. (See terms under separate entries, genome elements such as►intron splice sites, ►3′ untranslated regions, ►promoters, and ►*cis*-regulatory elements, novel methods for predicting DNase I hypersensitive sites, for predicting noncoding RNA genes, including microRNA genes and their targets: Jones SM 2006 Annu Rev Genomics Hum Genet 7:315).

Genome Annotation: Identification of nucleotide sequences to reveal their function. ►annotation; Stein L 2001 Nature Rev Genet 2:P493; Devos D, Valencia A 2001 Trends Genet 17:429; Zhang MQ 2002 Nature Rev Genet 3:698; Miller W et al 2004 Annu Rev Genomics Hum Genet 5:15.

Genome Bioinformatics (http://genome.ucsc.edu/): Genome bioinformatics carries information on human, *Caenorhabditis elegans* and *C. briggsae*, mouse, rat, zebrafish, yeast, and SARS genomes, including news and updates.

Genome Conservation: Genome conservation analyses the sequence and gene content among organisms and thus provide a reliable view on phylogenesis. ►phylogeny; Kunin V et al 2005 Nucleic Acids Res 33:616.

Genome Database: ►Map Viewer; human: http://gdbwww.gdb.org; integrated microbial genomes: http://img.jgi.doe.gov/cgi-bin/pub/main.cgi; genome databases of 468 organisms: http://pedant.gsf.de.

Genome Domain: Histone modifications, transcription pattern, and DNA replication timing can define discrete active and repressed functional domains ranging from 20 kb to 1 Mb in size within the human genome (ENCODE). Active and repressed domains differ markedly from one another with respect to annotated genomic features including gene content, CpG islands, the spectrum of repetitive elements, and the density of conserved nonexonic sequences (Thurman RE et al 2007 Genome Res 17:917). ►domain, ►ENCODE

Genome Equivalent: In a genome equivalent, the mass of the DNA/RNA is the same as that of a genome.

Genome Evolution: Evolution may be based on duplication of single genes or duplication of larger chromosomal segments including hundreds of genes. The duplication may be rearranged and modified to fill a need for evolutionary advantage in the particular environment. Exons and to a lesser extent, regulatory sequences, evolve slower than introns, which contain many mutations because generally having little or no function they are not subject to selection pressure. Some of the duplicated copies may also be lost. If an organism becomes a parasite, some of its genes are no longer needed because the host can provide the required function(s). In *Salmonella enterica*, the estimated DNA loss per generation was 0.05 bp but about 50 times higher in mutants defective in repair (MutS). Deletion ranged in size from 1 to 202 kb and were not involved with repeat sequences, indicating that the losses did not depend on RecA-mediated recombination (Nilsson AI et al 2005 Proc Natl Acad Sci USA 102:12112). Within a single bacterial phylum genome, sizes vary by more by an order of magnitude, e.g., 600 kb in *Buchnera aphidicola* to 7,000 kb in *Pseudomonas fluorescence* (Ochman H 2005 Proc Natl Acad Sci USA 102:11959). The sequenced genome of *E. coli* is 4,639,221 but megabase size variations occur in different isolates. The sequenced and annotated genomes of related organisms provide opportunities for analyses of the evolutionary paths. ►genome analysis, ►evolution of the karyotype, ►evolution, ►gene evolution; Dujon B et al 2004 Nature [Lond] 430:35.

Genome Hitchhiking: ►überoperon

Genome Information Broker (GIB): A database for genomics of prokaryotes, fungi, and *Arabidopsis*. ►genomics; http://gib.genes.nig.ac.jp.

GenomeInspector: A computer program for assessing distance correlations between large sets of sequence elements, which can be used for the identification and definition of basic patterns of functional units such as

promoters and transcription factors. (See Quandt K et al 1996 Comput Appl Biosci 12:405).

Genome-Linked Viral Protein: ►VPg

Genome Mutation: Genome mutation affects chromosome numbers. ►aneuploid, ►polyploid

Genome Organization: As per genome organization, although genes are situated in a linear order within the chromosomes, temporal and hierarchial spatial arrangement of the genome affects the turning on/off the functions. ►genome, ►chromosome territories, ►transcription factories, ►DNA looping, ►chromatin, ►euchromatin, ►heterochromatin, ►repetitive DNA; Misteli T 2007 Cell 128:787.

Genome Projects: Genome projects are focused on the physical mapping and sequencing of entire genomes of humans and other higher and lower eukaryotes as well as of prokaryotes. Upon completion of these projects, a detailed inventory of all genes will become available. This in turn will facilitate new generalization of organization and function of the cells and will permit the application of the new principles and the new technologies to human economic fields, as well as for preventing and curing diseases. The complete nucleotide sequence of the four genes of the MS2 RNA virus had been determined by 1976, and by 1995 all the 1749 genes of *Haemophilus influenzae* bacterium had been sequenced. The genome of *Saccharomyces cerevisiae* yeast has also been completely sequenced.

The large eukaryotic genomes such as that of humans, containing about 3 billion bps are ordered first into sequential stretches by the use of overlapping fragments. The first step is breaking up the human chromosomal DNAs (average of 250 Mb) into 100–2,000 kb fragments and cloned them in YACs. The YACs are cleaved into an average of 40-kb fragments and cloned by cosmids. The contents of the cosmids are then cloned in 5–10-kb capacity double-stranded DNA plasmid vectors or into the single-stranded filamentous phage M13 vector of 1-kb load. The fragments at each step can be tied into contigs by "chromosome walking." The nucleotide sequences of the smaller clones can be analyzed.

The entire human genome requires a minimum of about 3,000 YAC or 20,000 BAC or 75,000 cosmid or 600,000 plasmid or 3,000,000 M13 phage clones. An alternative approach, the complete sequencing is to proceed from sequence-tagged connectors (STC). The human chromosomes would be cloned in BAC vectors and sequence 300–500 nucleotides at the ends. The 600,000 BAC end sequences represent 10% of the genome and are scattered at

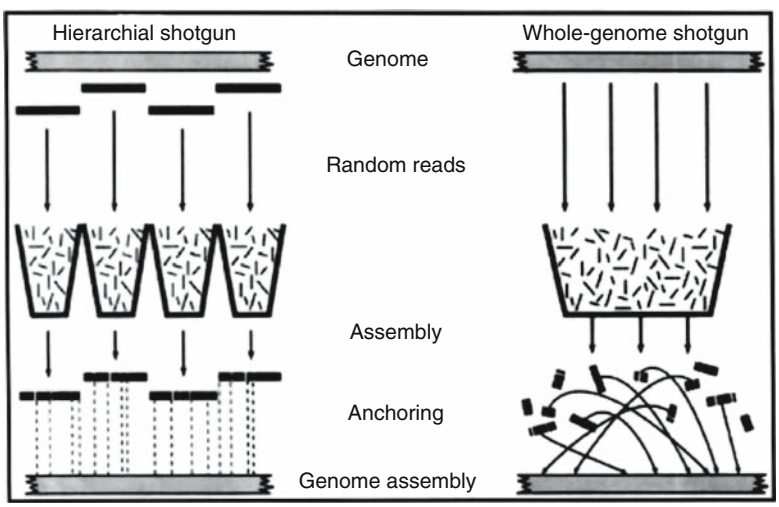

Figure G36. The human genome sequencing projects reported in Feb. 15, 2001 Science 295 and Nature [Lond] Febr. 16, 2001 used two somewhat different sequencing strategies. The *hierarchial shotgun* procedure cut up the genome into BAC clones and arranged them in a somewhat overlapping tiling path. Then after shotgun sequencing reassembled each BAC clone and then merged the sequences of adjacent clones. This had the advantage that all sequence contigs and scaffolds derived from a BAC belong to a single compartment with respect to anchoring to the genome. The *whole genome shotgun* strategy shotgun sequenced the entire genome and then reassembled the entire collection. With this method, each contig and scaffold is an independent component that had to be anchored to the genome. In general many scaffolds might have been difficult to anchor to the genome. (From Robert H. Waterston, Eric S. Lander, and John E. Sulston. 2002 Proceedings of the Natl. Acad. Sci. USA 99:3712-3716. Copyright 2002 National Academy of Sciences USA)

every 5-kb across the genome. They are called *sequence-tagged connectors* because they allow each BAC clone to be connected to about 30 others (150 kb insert/5 kb ≅ 30, Mahairas GG et al 1999 Proc Natl Acad Sci USA 96:9739). The BAC inserts are digested by a restriction enzyme to determine their size. The sequencing templates have pUC18 based plasmids with ~2-kbp templates. A "seed" BAC is sequenced and checked. A "seed" BAC is sequenced and checked against the data of sequence-tagged connectors to identify the overlapping clones.

In a following step, two BACs that show internal homology by the restriction enzyme digests and minimal overlap at their end are completely sequenced. By such a procedure the entire human genome could be sequenced in 20,000 clones. The advantage of this proposal (Venter JC Smit HO, Hood L 1996 Nature 381:364) is that some of the low-resolution mapping (YAC and cosmid steps) could be eliminated and automatic sequencing procedures could be applied, reducing cost and labors. Many groups worldwide could do the BAC clone sequencing. The already known sequence-tagged sites (STS) and expressed sequence tags (EST) could be readily located and additional genes could be easier placed. The procedure suggested would greatly facilitate the sequencing other smaller genomes of interest. The Perkin-Elmer Corporation and Craig Venter use very high efficiency DNA sequencing apparatuses (230ABI PRISM 3700) based on capillary electrophoresis (~1,000 samples/day) and robotization and to expedite the process and substantially reduce the cost of sequencing. The completed sequencing information of entire genomes reveals that homologous genes from *Saccharomyces* to *Caenorhabditis, Drosophila, Homo* and *Arabidopsis* direct the majority, but not all, of cellular functions. Yet the regulation of the functions show differences to account for the differences among these organisms. The number of genes used by the different organisms varies. Apparently and unexpectedly *Arabidopsis* needs about twice as many genes as *Drosophila* and *Caenorhabditis* relies on nearly 45% more genes than *Drosophila*. *Drosophila* has about 700 transcription factors versus 500 in *Caenorhabditis*. Among the fully sequenced microbial genomes, on the average, about 25% of the open reading frames are unique to each organism. Dunham I 2000 in Trends Genet 16:458 tabulates a chronology of the innovations facilitating the realization of the genome projects. For the best understanding of the genome sequences comparative data of many species are very helpful. Unfortunately all species cannot be sequenced because of technical and financial cost. The species to be sequenced are chosen by several criteria: (1) phylogenetic relationships, (2) relelevance to human biology, (3) economic importance, (4) genome size and characteristics, (5) developmental an organizational specialization, (6) consideration for the more ancestral evolutionary forms. Unfortunately there are hard choices and no better criteria in the organismal selection (O'Brian SJ et al 2001 Science 292:21264). By 2006 more than 400 genomes have been sequenced and many other projects are underway. ►physical mapping, ►YAC, ►cosmid, ►vectors, ►restriction enzyme, ►DNA sequencing, ►DNA sequencing automated, ►capillary electrophoresis, ►STS, ►EST, ►BAC, ►YAC, ►cosmid, ►DNA chips, ►contigs, ►seeding, ►parking, ►tiling, ►gap, ►finishing, ►clone validation, ►databases, ►shotgun sequencing, ►WGS, ►Gene Ontology, ►sequence-tagged connectors, ►scaffolds in genome sequencing, ►human genome; Venter JC et al 1998 Science 280:1540; Mullikin JC, McMurray AA 1999 Science 283:1867; Adams MD et al 2000 Science 287:2185; Waterston RH et al 2002 Proc Natl Acad Sci USA 99:3712; Myers EW et al 2002 Proc Natl Acad Sci USA 99:3712; Internet guides to the majority of genome-related databases: Nature Genet 32 suppl. 1–79 [2002]; Birney E et al 2002 Annu Rev Genomics Hum Genet 3:293; Cozzarelli NR 2003 Proc Natl Acad Sci USA 100:3021; theory of species selection criteria for sequencing: McAuliffe JD et al 2005 Proc Natl Acad Sci USA 102:7900). http://www.ncbi.nlm.nih.gov/genome/guide; sequencing projects and related resources: http://www.intlgenome.org/; http://compbio.ornl.gov/channel; published genomes: http://www.genomesonline.org/; bacterial genomes: http://xbase.bham.ac.uk/, integrated genomes: http://www.ebi.ac.uk/integr8/EBI-Integr8-HomePage.do;jsessionid = 8F34D370D1F714C23FC63A07B65D67D0.

Genome Reviews: Genome reviews contain information on sequencing and annotation of the majority of organisms: http://www.ebi.ac.uk/GenomeReviews.

GeneScan: Gene identification algorithm. Applicable to large genomes, including pertinent protein sequences. ►gene prediction; Yeh RF et al 2001 Genome Res 11:803.

GeneVar: GeneVar program is based on GeneWise and it analyzes an annotated genome, automatically identifies missed gene calls and sequence variants such as genes with disrupted reading frames (split genes) and those with insertions and deletions (indels). ►GeneWise, ►base-calling; Yu GX et al 2007 Nucleic Acids Res 35:3953.

Genome Scanning: Genome scanning comprises of cutting up the genome first by 8-bp-recognizing restriction endonuclease(s) into large fragments, followed by using more-frequent-cutter enzymes to generate physical information on the entire genome.

These fragments can then be used to establish a physical map. ►physical map, ►restriction enzyme, ►gene finding; Rouillard JM et al 2001 Genome Res 11:1453; Beekman M et al 2001 Genet Res 77:129.

Genome Sequence Database (GSDB): http://www.ncgr.org; interrupted sequences in prokaryotes: http://www-bio3d-igbmc.u-strasbg.fr/ICDS/.

Genome Sequence Sampling (GSS): In GSS, chromosomal DNA, digested with several restriction enzymes, is cloned into cosmids. Hybridization with YAC clones of the same chromosomal DNA identifies all the cosmides that contain sequences present within the YAC. The cosmids are then broken down into contigs and their ends are identified by hybridization to pure cosmid DNA. The 300–500 bps of the ends are sequenced and aligned in sequence, permitting the generation of a rather high-density physical map.

Genome Size: ►genome, ►C value paradox; Gregory TR 2005 Nature Rev Genet 6:699; animals: http://www.genomesize.com; C value of plants: http://www.kew.org/genomesize/homepage.html; fungi: http://www.zbi.ee/fungal-genomesize/; ►virus

Genome Surveys: Sequences of genomic origin, rather than cDNA (similar to EST); the sequence represented may be interrupted when compared to genomic sequence: http://www.ncbi.nlm.nih.gov/dbGSS/index.html; genomic clones and libraries: http://www.ncbi.nlm.nih.gov/genome/clone.

Genome Transplantation: ►mycoplasma

Genome-Defence Model: In the genome-defence model, generally multiple, different transposable elements occur in all organisms and their movements from one chromosomal location to another may bring about rearrangements in the genome. The cell keeps these transpositions in check by methylation of the transposase, and thus restricts deleterious alterations in the genome. (See Miura A et al 2001 Nature [Lond] 411:212).

Genomere: A hypothetical subunit of genes, proposed by Eyster WH 1924 Genetics 9:372 for explaining the behavior of unstable genes. Demerec M 1935 Bot Rev 1:233 has argued against the plausibility of the existence of such particles, and the term has been abandoned. ►unstable genes

GenomeScan: A gene identification algorithm (Yef R-F et al 2001 Genome Res 11:803).

Genometrics: Biometric analysis of chromosomes. ►biometry, ►genomics; Roten C-A H et al 2002 Nucleic Acids Res 30:142); http://www.unil.ch/dmf/page14997_en.html.

Genome-Wide Analysis: ►GWA

Genome-Wide Functional Analysis: In genome-wide functional analysis, in contrast to hitting genes by random mutations, the procedures aim at specific genes by homologous recombination mediated gene replacement. Unfortunately, the efficiency of the latter procedure is quite variable among different organisms. An alternative approach is the use of RNAi (~300 nucleotide long double-stranded precursors), which can be injected, fed, or transferred by the use of plasmids into *Caenorhabditis* or *Drosophila*. In contrast to flies and worms, the introduction of long dsRNA in mammalian cells induces a non-sequence-specific interferon response and shutdown of translation. This response can however be bypassed by the direct introduction of Dicer products of short interfering RNAs.

The SID-1 protein (systemic RNA interference-deficient) of *C. elegans* may greatly facilitate the uptake (Feinberg EH, Hunter CP 2003 Science 301:1545). Insertional mutagenesis, degron, peptide aptamer inhibitors, or other function specific tags are also useful. The perturbed genes may be detected by high-throughput optical devices such as automatic microscopes, particle-size counters, reporter genes, fluorescent labels, FRET analysis, and cell sorters. Z-factor determinations may be a useful statistical device to assess the significance of differences of quantitative measurements. ►RNAi, ►insertional mutation, ►targeting genes, ►degron, ►aptamer, ►synthetic lethal, ►FRET, ►cell sorter, ►Z, ►mutagenesis, ►genetic networks, ►networks, ►small-world networks, ►probabilistic graphical models of cellular networks, ►synthetic genetic array, ►GAIN; Carpenter AE, Sabatini DM 2004 Nature Rev Genet 5:11; Friedman A, Perrimon N 2004 Curr Opin Genet Developm 14:470; technique for use in mouse: Wu S et al 2007 Nature Genet 39:922.

Genome-Wide Location Analysis: The genome-wide location analysis or genome-wide binding analysis reveals the genes bound in vivo by transcriptional regulators of the genome. The procedure may be epitope tagging and microarray hybridization. The 2343 promoter regions of the 6270 genes of yeast were found to bind one or more of the 106 transcriptional regulators. On the average, each regulator was found to bind 38 promoter regions. The Abf1 regulator bound 181 promoter sites. The Thi2 activator of thiamine biosynthesis, however, bound only three promoters. 295 combinations of two or more regulators may bind to common sets of promoters, thus regulating yeast genes in response to specific environmental inputs. The regulators may function in a sequential manner in which, one regulator may affect the promoter of a second regulator, which in turn may regulate a third promoter

and so on. Also, by inserting—by homologous recombination—structural genes fused to green fluorescent protein markers, the subcellular location of various proteins and groups of proteins can be determined (Huh W-K et al 2003 Nature [Lond] 425:686). The abundance of individual proteins detected by similar optical means is >50 to 10^6 molecules/yeast cell (Ghaemmaghami S et al 2003 Nature [Lond] 425:737). ►transcription factors, ►epitope tagging, ►microarray hybridization, ►ABF-1, ►genetic networks; GAIN; Lee TI et al 2002 Science 298:799; Jorgenson E, Witte JS 2006 Nature Rev Genet 7:885.

Genomewise: A program for the analysis of gene structure across cDNA and EST-defined spliced structure; it is suitable for annotation. ►GeneWise; Birney E et al 2004 Genome Res 14988.

Genomic Clone: A genomic clone is prepared from chromosomal DNA, rather than from cDNA. ►genomic DNA, ►cDNA; http://www.ncbi.nlm.nih.gov/genome/clone.

Genomic Control: A statistical method for the estimation of population structure in a manner somewhat similar to case-control design or transmission disequilibrium tests. ►case-control design, ►transmission disequilibrium test; Bacanu SA et al 2000 Am J Hum Genet 66:1933.

Genomic Disorder: A genetically determined disease caused by deletions, duplications, inversions, translocations, transpositions in chromosomes.

Genomic DNA (gDNA): The native DNA including exons, introns and spacer sequences (versus the processed genes which are transcribed from mRNA to DNA by reverse transcription and have only the coding sequences). ►processed genes, ►reverse transcription

Genomic Exclusion: Genomic exclusion takes place in the ciliate *Tetrahymena pyriformis* in case one of the two mates has a defective genome (micronucleus) that is therefore not included in the meiotic progeny. The first progeny becomes heterokaryotic, having only the normal diploid micro-nucleus and an old macronucleus that is genetically not concordant with the micronucleus. After subsequent matings the normal micronucleus forms a macronucleus concordant with its own genetic constitution. As a result the strain is purged from the defect. ►conjugation *Paramecia*; Cole ES et al 2001 J Eukaryot Microbiol 48(3):266.

Genomic Formulas: n = haploid, 2n = diploid, 3n = triploid etc. and n−1 or 2n−2 = nullisomic, 2n−1 monosomic, 2n + 1 = trisomic, 2n + 2 = tetrasomic, etc., where n = haploid chromosome number. The basic chromosome number, however, is x and the diploids may be 2x = 2n. ►polyploids, ►aneuploids

Genomic Fractionation: ►RDA

Genomic Hybridization: ►comparative genomic hybridization

Genomic Library: A set of cloned genomic DNAs; it is expected that a good library includes at least one copy of all the genes of a particular genome. ►cloning, ►genome, ►fragment recovery probability

Genomic Medicine: Genomic medicine studies genetic variations in human populations concerning the genetic bases of disease. It is based on single nucleotide polymorphisms, oligonucleotide microarrays, molecular characterization of drug responses, etc. It uses global genomic information in connection clinical data to assess individual risks and multidimensional analysis for efficient management of disease. It combines predictive, preventive, and personalized medicine. ►SNIP, ►drug discovery, ►medical genetics, needs and some available resources for practicing physicians: Guttmacher AE et al 2007 Nature Rev Genet 8:151.

Genomic Mistmatch Scanning: ►GMS

Genomic Profiling: The detection of concurrent occurrence of multiple generic variations that predispose humans to a particular disease. Identification of such genetic factors may assist in personalized medication and preventive means of health maintenance. The currently suggested commercial procedures have not yet been adequately tested. Although genomic profiling may have significance in the future, at present it is not entirely safe to follow some of the recommendations. (See Haga SB et al 2003 Nature Genet 34:347; http://www.genovations.com/home/index.html; http://www.bankdna.com/).

Genomic Prospecting: Searching of diverse species (e.g., different mammalian genomes) for DNA sequences, which could alleviate human disease with the aid of gene therapy. ►gene therapy; O'Brien SJ 1995 Nature Med 1:742.

Genomic Screening: Genomic screeing is used for the localization of genetics markers (genes). For *random genomic screening*, usually anonymous polymorphic markers are employed. For *directed genomic screening*, specific polymorphic markers, which have already been located in the vicinity of a targeted gene(s) are suitable. The best markers are easy to recognize, are highly heterozygous, and have established chromosomal location. In human genetics, the Généthon (http://www.genethon.fr/genethon_en.html) map containing more than 5,000 dinucleotide

markers covering the entire genome by ~2 cM average spacing is used. Alternatively, the Cooperative Human Linkage Project (CHLC, http://www.chlc.org) covers the genome by 3600 tri- and tetranucleotide markers with an average spacing of 1 cM. The Utah Human Genetics Institute (http://www.genetics.utah.edu/home.html) has developed tetranucleotide markers at 10–15 cM spacing. These spacings are average and are not evenly distributed. The standard sets of markers are called *mapping sets*. Using lod scores, a value of 3 is considered to be significant. In case when two genes are tested, the lod score probability may be corrected for more accuracy and should be $3 + \log 2 \approx 3.3$, and in case of say 20 genes it should be $3 + \log 20 \approx 4.3$. Sib pair data sets may be evaluated with the aid of the chi^2 procedure and the appropriate degrees of freedom, but general probability may be determined by using lod = $(\chi^2)/4.605$. ($2\ln 10 \approx 4.605$, and converts the lod scores to χ^2 with 1 degree of freedom. Lod score of 3 corresponds to a P value of 0.001, and $\chi^2 \approx 4.605 \times 3 \approx 13.83$). Jianfeng Xu et al. (1998) present the justification for the very high significance level of 0.001 as follows. If the human genome is 3000 cM and it is divided into sixty 50 cM segments and the studied locus is in one of them, then the chance for the location of this gene is $1/60 \approx 0.02$. In other words, under this assumption, the *a priori* chance of linkage for any single locus is ~2%. According to Bayes' theorem, with a lod score of 3, the posterior probability for linkage is about 95%, a conventional limit for level of significance. Usually these linkage data are loaded with false positive results and the best statistical procedures have not been agreed upon or generally accepted. Directed genomic screening may identify *locational candidate regions* where the investigated genetic difference is likely to be situated. As a general rule large relative risk, determined by λ_S is very helpful in locating genes. ►physical mapping, ►mapping, ►minisatellite, ►microsatellite, ►microarrays, ►lod score, ►chi square, ►candidate gene, ►λ_S, ►Bayes' theorem

Genomic Stress: Genomic stress, such as dissimilar genetic backgrounds in hybrids, in vitro cell culture, etc., may activate dormant transposable elements and cause genetic instability. ►transposable elements, ►somaclonal variation

Genomic Subtraction: A method that removes from wild type DNA all the sequences that are present in a deletion mutant, but retains the wild type DNA sequences corresponding to the deletions by denaturing a mixture of wild type and biotinylated mutant DNA. Allowing the mix to reassociate, the biotinylated sequences are subtracted by several repeated cycles of binding to avidin-coated polystyrene beads (that have great affinity for biotin). The remaining (non-biotinylated) DNA is wild type and contains only the sequences that were deleted in the mutant but present in the wild type. This DNA can then be amplified by PCR and studied by standard techniques of sequencing. This method also permits the isolation of genes affected by the deletion (caused by, e.g., ionizing radiation). ►physical mutagens, ►gene isolation, ►biotinylation, ►avidin, ►PCR, ►DNA sequencing, ►RDA, ►RFLP subtraction, ►subtractive hybridization; Kingsley PD et al 2001 Dev Growth Differ 43(2):133.

Genomic Variation: Genetic variation, chromosomal rearrangements, polyploidy, copy number estimates, and human genome variation: http://www.sanger.ac.uk/humgen/cnv/data/.

Genomics: The study of the molecular organization of genomic DNA and physical mapping. *Structural genomics* studies the folds of macromolecules, the three-dimensional shape of biological molecules with the aid of physical instruments (X-ray crystallography, etc.) and bioinformatics, and classifies these molecules into functional families (see Fig. G37).

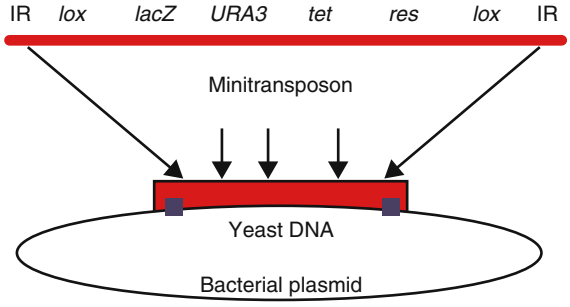

Figure G37. Identification of gene function

Biochemical genomics studies pools of purified proteins and the corresponding open reading frames (ORF). This is accomplished by generation and expression, e.g., a large set of glutathione-ORF fusion proteins are purified and mapped to a specific ORF and the proteins are further analyzed in subpools (Martzen MR et al 1999 Science 286:1153). *Chemical genomics* studies the effects of small molecules to ascertain their modulating effects on cellular states or on gene expression, preferably in high-throughput systems (Stegmaier K et al 2004 Nature Genet 36:257). The *functional genomics/physiological*

genomics deals with genome-wide functional analyses and integration of structure of the DNA and the molecular function and interaction of genes and gene products (Wu LF et al 2002 Nature Genet 31:255; Liang P et al 2002 Physiol Genomics 9:15). After the completion of sequencing of the organisms, interest is now turning to the determination of the function(s) of genetics. Such studies can now be conducted with high-throughput procedures (see diagram modified after Ross-Macdonald P et al 1999 Nature [Lond] 402:413). These types of methods can identify the function of thousands of ORFs in combination with macroarray analysis. This area of study integrates genetics, molecular biology, biochemistry, pharmacology (*pharmacogenomics*: designing drugs that best fit the genetic constitution of an individual), agriculture, medicine, and other disciplines. In 1996 alone, a half million patents were proposed from the field. *Epigenomics* studies the interaction between proteomes and genomes, global patterns of methylation, and methylation signals, and surveys this type of information in different species. *Comparative genomics/phylogenomics* seeks to determine (i) the number of distinct protein families encoded by different genomes, (ii) the distribution of the coding genes within the genomes and (iii) and how many of the genes are shared by the different genomes (Ureta-Vidal A et al 2003 Nature Rev Genet 4:251). *Orthogenomics* deals with the genomes of orthologous descent whereas *paragenomics* studies paralogous genomes. The study includes the composition and organization of protein domains in the different organisms. *Genetical genomics* involves expression profiles and marker-based fingerprints of each individual in a segregating population. The data are analyzed by QTL methods (Jansen RC, Nap JP 2001 Trends Genet 17:388).*Computational genomics* quantitatively or qualitatively measures a property of interest in ten or more inbred mouse strains. Genetic factors are then computationally identified in genomic regions where the pattern of genetic variation correlates with the distribution of trait values among the inbred strains analyzed. The extent of correlation between the trait values and strain groupings within each haplotype block is determined by analysis of variance (Wang J et al 2005 Trends Genet 21:526). *Nutrigeno*mics has the goal to reveal the consequences of macro- and micronutrients on health and disease on different genotypes (Müller M, Kersten S 2003 Nature Rev Genet 4:315). *Toxicogenomics* seeks understanding the complexities in the biological system responding to toxic, mutagenic and carcinogenic factors. Special consideration is given to homologies of genes involved in controlling disease in the human genome, to sharing fundamental functions such as the cell cycle and structure, cell adhesion, signaling, apoptosis, neuronal controls and the defense system (immune reactions). Finished genomic sequence is contiguous and has no more errors than 1/10,000 bases. ►genomic DNA, ►DNA sequencing, ►DNA chips, ►macroarray analysis, ►microarray hybridization, ►maldi/tof/ms, ►physical mapping, ►mass spectrometer, ►genome projects, ►gene numbers, ►duplications, ►proteome, ►SAGE, ►biotechnology, ►genetic engineering, ►ORF, ►*Cre/Lox*, ►knockin, ►X-ray diffraction analysis, ►orthology, ►paralogy, ►comparative genomics, ►TWINSCAN, ►bioinformatics, ►analysis of variance; Craig AG, Hoheisel JD 1999 Automation: Genome and Functional Analyses. Academic Press, San Diego, California; Trends Guide to Bioinformatics, Sup. Elsevier, 1998, Rubin GM et al 2000 Science 287:2204; Koonin EV 2001 Curr Biol 11:R155; Reboul J et al 2001 Nature Genet 27:227; Gopal S 2001 Nature Genet 27:337; genometrics; Meyerowitz EM 2002 Science 295:1482; Aardema MJ, MacGregor JT 2002 Mutation Res 499:13; human genomics reviews: Human Mol Genet 15 Rev. issue 1; http://www.functionalgenomics.org.uk/; chemical genomics: http://www.genome.jp/kegg/; http://gib.genes.nig.ac.jp; public population genomics: http://www.p3gconsortium.org/; structural genomics targets: http://www.ysbl.york.ac.uk/sgTarget/; agriculturally relevant species: http://www.agbase.msstate.edu; plant genomes: http://mips.gsf.de/projects/plants.

Genomics-Guided Transgenes (GGT): GGT are homologous genes obtained from native species or from related species. GGTs are expected to provide useful features to crops without potential drawbacks of induced mutant genes. ►transgene, ►GMO; Strauss SH 2003 Science 300:61.

Genomotyping: Genomotyping hybridizes the DNA of a particular strain/isolate to the genome of a sequenced standard line to assess the difference between the two.

Genophore: gene string not associated with large amounts of protein (bacterial chromosome). (See Ris H, Chandler BL 1963 Cold Spring Harbor Symp Quant Biol 18:1).

Genotator: is a program for sequence annotation and gene finding. ►gene prediction, ►annotation of the genome; http://www.fruitfly.org/~nomi/genotator/user-manual.html.

Genotoxic Chemicals: Genotoxic chemicals cause gene mutation, chromosomal aberration, and cancer. Genotoxic stress activates cell cycle checkpoints to allow time for repair, if possible. The most recommended tests involve bacterial mutation assays, in vitro test for chromosomal damage using mammalian

cells (rodent hematopoietic cells), and in vitro assay of mouse lymphoma *tk* $^{+/-}$ cells (MLA). Molecular effects of genotoxic chemicals can be assessed by single nucleotide polymorphism analysis. ►gene-tox, ►databases, ►environmental mutagens, ►mutagen assays, ►SNIP, ►cell cycle, ►checkpoint, ►pharmaceuticals; Müller L et al 1999 Mutation Res 436:195.

Genotype: The genetic constitution, the full set of genes.

Genotype Elimination: In genotypic elimination, statistical algorithms are used for the identification of genotypes that are inconsistent with the pedigree information. (See O'Connell JR, Weeks DE 1999 Am J Hum Genet 65:1733).

Genotypic Frequencies: ►Hardy-Weinberg theorem

Genotypic Mixing: In genotypic mixing, after infecting a cell with viruses of different genotypes, in a single viral capsid more than one type of viral DNA may be included. ►rounds of matings

Genotypic Risk Ratio (GRR): The total number of offspring affected/twice the number of affected homozygotes. ►genetic hazards, ►risk, ►genetic risk, ►empirical risk, ►displacement

Genotypic Segregation: ►trinomial distribution

Genotypic Value: A quantitative genetics term indicating the genetically determined component (G) of the phenotypic variation; phenotypic value (P) = G + E, where (E) stands for environmental variation. ►midpoint, ►breeding value, ►additive effects

Genotyping: Identification of the genotypic constitution at one or more loci by genetic, molecular, immunological, or any other means using cells, tissues, or whole organisms. Single-sperm genotyping permits detection of recombination in humans at large scale and sheds light on the extent of linkage disequilibrium. Naturally, this procedure does not reveal recombinational differences among females, if any. Quite commonly RFLP, mini- and microsatellites, trinucleotide repeats, single nucleotide polymorphism, and PCR are used. Immobilizing DNA on silicon chips and the use of MALDI has developed high-throughput methods. Statistical methods based on inheritance are available for the detection of genotyping errors (Douglas JA et al 2002 Am J Hum Genet 70:487; Sobel E et al 2002 Am J Hum Genet 70:496). ►genotype, ►RFLP, ►SNIP, ►PCR, ►minisatellite, ►microsatellite, ►trinucleotide repeats, ►DNA chips, ►microarray hybridization, ►MALDI, ►haplotype analysis, ►GWA; Tang K et al 1999 Proc Natl Acad Sci USA 96:10016; Ranade K et al 2001 Genome Res 11:1262; Beaulieu M et al 2001 Nucleic Acids Res 29:1114; Wolfe JL et al 2002 Proc Natl Acad Sci USA 99:11073; genotyping errors and estimation of errors: Pompanon F et al 2005 Nature Rev Genet 6:847; Wang L et al 2007 Adv Exp Med Biol 593:105.

Gens (plural gentes): Organisms with shared relations (a sub-race).

GENSAT (http://www.gensat.org/login.jsp): is a gene expression atlas of the central nervous system.

Genscan: is a gene predictor program. (See Burle C, Karlin S 1997 J Mol Biol 268:78, http://genes.mit.edu/GENSCAN.html).

GENT Algorithm: The GENT algorithm generates contigs from optical mapping data. ►contig, ►optical mapping; Mathe C et al 1999 J Mol Biol 285:1977.

Gentamycin (gentamycin): A broad-spectrum aminoglycoside antibiotic. Gentamicin may facilitate reading through nonsense termination codons during translation. It may cause irreversible hearing loss that is preventable by aspirin (see Fig. G38). (See New England J Med 354:1856; ►readthrough, formula).

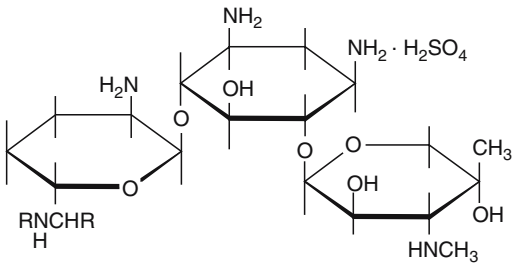

Figure G38. Gentamycin sulphate

Genus: A taxonomic category including usually several species of common descent. e.g., *Drosophila* (genus) *melanogaster* (species), the fruitfly most commonly used in genetics studies. Some genera are monotypic, however, inasmuch as they consist of a single species, e.g., *Arabidopsis*. ►species

Genus (in statistics): A topologically invariant property of a surface defined as the largest number of nonisotopic simple closed curves that can be drawn on the surface without separating it, i.e., the number of handles on the surface (Tuminello M 2005 Proc Natl Acad Sci USA 102:10421).

Gene2XML: A program, which converts ENTREZ GENE ASN1 into XML. ►ASN.1, ►XML; ftp.ncbi.nih.gov/toolbox/ncbi\\s\\do5(t)ools/converters/by\\s\\do5(p)rogram/gene2xml/

GEO (Gene Expression Omnibus): The GEO lists genes by name, type, organism, database, etc. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gds.

Geographic Isolation: Geographically isolated populations cannot exchange genes because physical distance or other physical factors (mountain ranges, lakes, etc.) keep them apart. ►speciation

Geographical Race: A topologically separate population with distinctive gene frequencies.

Geological Age: ►evolutionary clock

Geological–Evolutionary Time Periods: (∼ millions of years ago) formation of the Earth—4600—origin of Life—3000—Cambrian—600—Ordovician—450—Silurian—410—Devonian—345—Carboniferous—280—Permian—225—Triassic—190—Jurassic—135—Cretacious—65—Eocene—36—Oligocene—Miocene—13—Pliocene—3—Pleistocene—0.01→ Recent. ►Archeozoic, ►Pterozoic, ►Paleozoic, ►Mesozoic, ►Cenozoic, ►origin of life, ►evolution prebiotic, ►extinction, ►evolution of the genetic code, ►missing link

Geometric Mean: ►mean

Geometric Progression: A series of elements increasing by the same factor, e.g., 2, 6, 18, 54 (i.e., by a factor of 3 in this example). ►arithmetic progression

Geometric Solids: (see Fig. G39).
Surface: □ $6a^2$; □ 2(ab + ac + bc); □ 2rπ((h + r); □ base surface + [(ah)/2 × n
□ rπ(r + s); □ side areas × 4; □ π[r^2 + (r + r1)s + r^2]
Volume: □ a^3; □ a × b × c; □ r^2πh; □ base surface × h; □ (r^2πh)/3,
□ h/3(axa) $\sqrt{(axa)(a1xa1)}$ + (a1xa1); □ (πh)/3) (r^2 + rxr1 + (r1)^2
*SPHERE: surface: 4r^2π; volume: (4/3)r^3π (π ≅ 3.132857). ►circle

George III: This mad king of England (1738–1820) might have been a victim of porphyria. ►porphyria

Geotropism: Growth influenced by gravity; positive (+) geotropism directed toward and negative (−) away from gravity. Plant roots grow downward (+) and the shoots upward (−).

GEP: Guanine nucleotide exchange proteins.

Gephyrin (93 kDa): Peripheral nervous system membrane protein binding the inhibitory β subunit of the motor neural glycine receptor to tubulin in the cytoskeleton encoded in human chromosome 14 (Heilig R et al 2003 Nature [Lond] 421:601). It is also used for a co-factor that regulates molybdenum-dependent enzymes. ►cytoskeleton, ►tubulin, ►neuron; Sola M et al 2001 J Biol Chem 276:25294.

Geranyl Pyrophosphate: A precursor of farnesyl pyrophosphate. Two molecules of farnesyl pyrophosphate join by the pyrophosphate end and squalene is formed through the elimination of both pyrosphosphates. Squalene is then cyclicized to form lanosterol before being converted into cholesterol. ►prenylation, ►cholesterols

GERBICH (Ge blood group): The Ge blood group is distinguished by its encoding β and γ sialoglycoproteins (glycophorins). These red blood cell membrane proteins are suspected of being the receptors of the *Plasmodium falciparum* merozoite (malaria-causing protozoon). ►blood group, ►malaria; Mayer DC et al 2001 Proc Natl Acad Sci USA 98:5222.

Gerbil: *Gerbillus cheesmani* 2n = 38; *Gerbillus gerbillus* 2n = 43 male, 42 female.

Germ: (Pathogenic) microorganism or an initial cellular structure capable of differentiation and development into a special organ or organism.

Germ Cells: The reproductive (sex) cells of eukaryotes, such as spores, eggs, and spermatozoa. The spores frequently come about by non-sexual processes such as the conidia of fungi and may not function like sex cells. The egg and spermatozoa are direct or indirect products of meiosis that have undergone a process of differentiation without division, e.g., the spermatozoa of animals arise from the spermatids and the sperms of plants are formed by post-meiotic division of the microspore nuclei. The eggs of animals arise by an additional division of the haploid secondary oocytes.

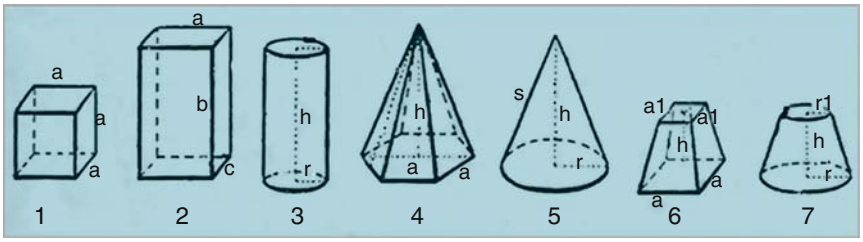

Figure G39. Geometric solids

Primordial germ cells of animals are sexually undifferentiated and can develop into oogonia or spermatogonia by mitosis before the meiotic path is set. Retinoic acid causes germ cells in the ovary to enter meiosis and initiates oogenesis. In the fetal testis, a retinoid-degrading enzyme (CYP26B1) retards meiosis and ultimately spermatogenesis takes place. Thus retinoid levels specify germ cell fate during gonad development (Bowles J et al 2006 Science 312:596). In mice,the *Stra8* gene (stimulated by retinoic acid 8) controls the transition into meiosis in both sexes. In females *Stra 8* is expressed in embryonic ovaries just before meiosis whereas in males it is expressed in the testes after birth (Koubova J et al 2006 Proc Natl Acad Sci USA 103:2474).

Primordial germ cells of mouse obtained from fetuses 8.5 p.c. when transplanted into the seminiferous tubules of infertile mice permitted the production of fertile offspring (Chuma S et al 2005 Development 132:117). The spermatogonial stem cells of animals can divide throughout life and produce spermatozoa. Adult testicular germ cells of the fish, trout (*Oncorhyncus mykiss*), contain spermatogonial stem cells, which when transplanted into the peritoneal cavity of newly hatched male or female embryos differentiated into functional spermatozoa in males and into functional eggs in the female recipients, and were capable of producing normal offspring (Okutsu T et al 2006 Proc Natl Acad Sci USA 103:2725). The egg of plants is formed through three divisions from one of the haploid megaspores. ►gametogenesis, ►germ plasm, ►conidia, ►egg, ►sperm, ►spore, ►megaspore, ►microspore, ►histone variants, ►protamaines, ►embryoid body, ►p.c.; Raz E 2003 Nature Rev Genet 4:690; Santos AC, Lehmann R 2004 Current Biol 14:R578; germline transmission of genetically modified primordial germ cells: van de Lavoir M-C et al 2006 Nature [Lond] 441:766; conserved gametogenesis transcriptome in humans mouse and rat: Chalmel F et al 2007 Proc Natl Acad Sci USA 104:8346; genome browser: http://www.germonline.org/index.html.

Germ Layers: Gastrulation forms the most inner layer, *endoderm*, the surface layer, *ectoderm* (epithelium), and the in-between mesenchyme cell layer the *mesoderm*. Some embryologists attribute the differentiation to the neural crest. ►gastrula, ►neural crest

Germ Plasm: Development (in *Drosophila*) begins with the formation of the primordial germ cells also called pole cells. The syncytial nuclei congregate at the posterior segment of the pole. Cellularization begins after about two hours. During gastrulation, the germ cells move to the embryonic gonad and form the germline stem cells. In both males and females, after four rounds of cell divisions 16 cells are formed. In the male, all 16 contribute to sperm formation. In the female these 16 cells remain interconnected but only one becomes an oocyte, while the 15 others become polyploid nurse cells and nourish the oocyte. The oocyte proceeds with meiosis. About 80 maternal (somatic) follicle cells surround the oocyte and nurse cells. The development of the germ plasm (the cytoplasmic determinants of the germ cells) is controlled by the interacting products of a series of genes. ►morphogenesis in *Drosophila*, ►germ cells, ►germline, ►germplasm, ►*Drosophila*

German (germen): Closely related, such as having the same parents. ►cousin german

German Measles: ►rubella virus

Germarium: The location of the pro-oocytes which through mitotic divisions gives rise to the oocysts, one of which, becomes the oocyte. ►oocyte primary, ►karyosome

Germinal Center: A group of naive (uncommitted) B cells. When activated by a specific antigen, they may develop into either memory B cells after antigen selection or become plasma cells. In the presence of interleukin-1,-10, and CD40 ligands they become memory B cells. By removal of CD40 ligand, the cells differentiate into plasma cells. A rapidly growing center also includes antigen-specific helper T cells. CD21 may be required for the B cells to survive in the germinal center. The germinal center has an open structure that enables competitition for rare high-affinity B cells to participate in antigen responses (Schwickerts T et al 2007 Nature [Lond] 446:83). ►T lymphocyte, ►clonal selection, ►antigen, ►CD40, ►CD21, ►plasma cell, ►memory immunological, ►OBF, ►somatic hypermutation, ►B lymphocyte; Schebesta M et al 2002 Curr Opin Immunol 14:216.

Germinal Choice: Germinal choice is the idea that parents should not necessarily rely on their own gametes for producing offspring but adopt eggs, sperms, or even fertilized eggs from superior gene pools as a practical measure of positive eugenics. ►sperm bank, ►in vitro fertilization, ►eugenics, ►ART; Stock G 2005 Reprod Biol Online 10(1):27.

Germinal Mutation: Germinal mutation occurs in the germline, gonads, or in the gametes. ►germline, ►gonad, ►gamete

Germinal Vesicle: The large nucleus of the amphibian oocyte. This nucleus contains the three eukaryotic

RNA polymerases and can also transcribe exogenous (microinjected) DNA. The oocyte then translates the mRNAs into a variety of proteins. ►in vitro translation systems

Germinoma: The neoplasm of the male or female gonads. ►gonad

Germline: The cell lineage that contributes to the formation of the gametes. In the majority of animals, the germline is determined very early in the zygote although the embryonic stem cells have pluripotent capability. In mice, the germ cells originate from extra-embryonic ectoderm under the influence of an inducible transmembrane protein encoded by the *fragilis* gene. Then gene *stella* is expressed in the cells that are restricted to the germline. The latter gene represses homeobox genes in the cells and thus they retain pluripotency (Saitou M et al 2002 Nature [Lond] 418:293). The segregation of the germline from the soma line involves the degradation of CCCH finger proteins in the soma by the ZIF-1 protein complex, which interacts with cullin-dependent ubiquitination system. In the germline, the PAR-1 kinase protects these proteins (DeRenzo C et al 2003 Nature [Lond] 424:685).

According to some views, plants do not have germline, certainly not in the sense of animals, because the generative cell lineage is not set aside definitely in early development and plant cells may retain totipotency for almost the entire life of the individuals. Nevertheless, by "fate maps", the cell lineages giving rise to megaspores and microspores of plants can be traced to origin. In *Drosophila*, for the development of the germline the product of the *nanos* (*na*) gene locus is essential. In animals, the germline progenitor cells and gonadal somatic cells form the embryonic gonads, which develop into gamete-producing organs. In the embryonic gonads of *Drosophila*, 101 genes are expressed preferentially out of which 39 were expressed predominantly in the germline, whereas 58 in the somatic cells and 45 genes in both lineages (Shiegenobu S et al 2006 Proc Natl Acad Sci USA 103:13728). If mutation occurs in the germline, the genetically mosaic tissue may produce different gametes. Some mutations, which appear recessive in the somatic tissues may display reversal and function as dominant. In such cases, selection is possible before the formation of the gametes. ►cell lineages, ►*Drosophila* life cycle, ►genetically effective cell number, ►morphogenesis in *Drosophila*, ►germ plasm, ►gonads, ►gametogenesis, ►stem cells, ►somatic embryogenesis, ►CCCH protein, ►cullin, ►PAR, ►ubiquitin, ►Keimbahn for illustration; Lin H 1997 Annu Rev Genet 31:455; Saffman EE, Lasko P 1999 Cell Mol Life Sci 55:1141; Extavour C, García-Bellido A 2001 Proc Natl Acad Sci USA 98:11341; Crittenden SL et al 2002 Nature [Lond] 417:660.

Germline Transcripts (sterile RNA): Gerline transcripts are not translated into protein. These specific guanine-rich RNAs are transcribed from the immunoglobulin heavy chain S (switch) sequences in the B lymphocytes. These RNAs of 1 to 10-kb in length and containing repeats of 20 to 100 bp, anneal with the cytosine-rich DNA template. The sterile transcripts—although have similar overall structure—are specific for each switch sequence preceding a heavy chain gene, and each mediates in cis position class switching of a specific heavy chain gene. It has been hypothesized that these RNA-DNA hybrids are the recognition sites for the endonuclease that cuts the DNA double strands in the process of class switching. ►immunoglobulins, ►antibody gene witching, cis arrangements; Tracy RB et al 2000 Science 288:1058.

Germplasm (Keimplasma): The sum of the genetic determinants transmitted through the gametes to the progeny. In a broader sense, it is used for the designation of a collection of genotypes of organisms usable as plant and animal breeding resource. ►genotype, ►germ plasm

Gerontology: The clinical, biological, and sociological study of aging. ►aging, ►apoptosis, ►Hayflick's limit

Gerstmann-Sträussler Disease (GSD): A chromosome 20p12-pter dominant brain disease with substantial similarities to the Creutzfeldt-Jakob disease. There are some apparent differences inasmuch that in GSD there are numerous multicentric tuft-like plaques in the cerebral and cerebellar cortex, in the basal ganglia, and in the white matter of the brain. GSD appears to involve a greater recurrence risk than the Creutzfeldt-Jakob disease. ►Creutzfeldt-Jakob disease, ►scrapie, ►prion, ►encephalopathies, ►encephalopathy bovine spongiform

Gestation: The time from fertilization of the ovum (ova) to the delivery of the newborns in viviparous animals. The average term of gestation, in days: opossum 13, hamster 17, mouse 19, rat 21, rabbit 31, giant kangaroo 39, dog 61, cat 63, guinea pig 68, sow 114, sheep and goat 151, Virginia deer 215, Rhesus monkey 164, chimpanzee 238, woman 267, cow 284, mare 340, and elephant 624. There may be substantial deviations from these averages. Some of the differences in literature data are due to either biological or developmental variations, or the information indicates the time between ovulation and birth. ►hatching time in poultry

Gestational Drive (green beard effect): As per gestational drive, maternal genes recognizing and favoring special genes of the offspring, already during gestation, and favoring or disfavoring a genetic constitution may lead to consequences somewhat similar to meiotic drive. Population geneticists do not generally accept the concept. ►meiotic drive, ►green beard effect

GFAP (glial fibrillary acidic protein): GFAP affects myelination of the peripheral nerve cells and brain and its defect causes long-term depression. ►myelin, ►depression, ►leukemia, ►inhibitory factor; Headley SA et al 2001 J Comp Pathol 125(2–3):90.

GFF (General Feature Format): A document software format for finding in higher organisms a variety of recognition methods that give scores to likely signals (starts, splice sites, stops, motifs, etc.) or to extended regions (exons, introns, protein domains etc.), and then combine these to give complete gene, RNA transcript, or protein structures. Normally, the combination step is done in the same program as the feature detection, often using dynamic programming methods. To enable these processes to be decoupled, a format called GFF ("Gene-Finding Format" or "General Feature Format") was proposed as a protocol for the transfer of feature information. (See http://www.sanger.ac.uk/Software/formats/GFF/GFF_Spec.shtml).

GFP: ►green fluorescing protein

GGAs: Proteins that sort mannose phosphate receptors (MPR) into vesicles budding from the transgolgi network (TGN). The proteins are eventually delivered to endosomal and lysosomal compartments. The GGA is composed of a VHS (VPS27, Hrs, STAM) domain at the NH_2 end and a GAT domain that is flexibly hinged to a GAE domain at the carboxyl end. The GGA is moved to the transgolgi membrane after the GAT (transporter) domain interacts with the ARF-GTP (ADP-ribosylation factor–guanosine triphosphate) complex on the TGN membrane. The VHS domain binds the acidic cluster dileucine motif (ACLL) of the MPR. The GGA recruits at the GAE hinge a clathrin triskelion and accessory proteins γ-synergin (controling clathrin-coated vesicle traffic) and the endosome fusion regulator protein rabaptin 5. ►mannose phosphate receptor, ►transgolgi network, ►endocytosis, ►lysosome, ►triskelion; Tooze SA 2001 Science 292:1663.

γ-Glutamyl Carboxylase (GGC): The enzyme required for the post-translational modification of vitamin K dependent proteins used for blood clotting and bone proteins. ►vitamin K-dependent blood clotting factors

GH: Growth hormone such as the hGH (human, encoded in 17q22-q24) or rGH (rat) growth hormones. ►hormone response elements, ►hormones, ►pituitary dwarfness, ►growth hormone relapsing hormone, ►GHRH, ►GHRHR

Ghost: An empty phage capsid without its genetic material. Also, electronic noise.

Ghost QTL: An erroneous localization result obtained by QTL analysis. ►QTL

G_h: G protein with GTP-binding signaling function and transglutaminase activity. ►G-protein

Ghrelin: An acetylated, 28-amino acid secretagogue produced in the hypothalmus that releases growth hormone from its receptor. It promotes feeding and is an antagonist of leptin. Ghrelin regulates neuropeptide Y and agouti-related protein neurons. The fatty acid synthase inhibitor, C75, blocks the synthesis of ghrelin. Oxyntomodulin suppresses it. ►secretagogue, ►growth hormone pituitary, ►leptin, ►agouti, ►neuropeptide Y, ►obesity, ►obestatin, ►oxyntomodulin; Inui A 2001 Nature Rev Neurosci 2:551; Hosoda H et al 2003 J Biol Chem 278:64; Hu Z et al 2005 Proc Natl Acad Sci USA 102:3972.

GHRH (growth hormone release hormone, 20q11.2): GHRH stimulates the release of growth hormones from the pituitary. Antagonists of GHRH receptors suppress cancerous proliferation. Somatostatin inhibits growth hormone secretion. ►animal hormones, ►pituitary, ►somatostatin, ►brain human, ►GH; GHRH antagonists with improved antitumor activity: Zarandi M et al 2006 Proc Natl Acad Sci USA 103:4610.

GHRHR (growth hormone-releasing hormone receptor, 7p15-p14): GHRHR results in dwarfism. Several variants are known. ►dwarfism, ►GH; Szepesházi K et al 2001 Endocrinology 142:4341.

gi: An identification number in the GenBank data base that is used in addition to the accession number. This permits a closer identification of later discovered variations in a particular sequence to which—as new information becomes available for that particular DNA—a string of gi-s may be added. ►accession number, ►asn.1, ►GenBank, ►identifier syntax

G_i Protein: A member of the trimeric G-protein family; it activates adenylate cyclase and thus opens K^+ channels. The βγ subunits activate the ERK/MAPK signal transduction path through tyrosine kinase. This pathway responds positively to RAS and antagonized by RAP1. ►G-proteins, ►signal transduction, ►adenylate cyclase, ►ion channels, ►RAS, ►RAP1

GI_{50}: A chemical dose that provides 50% growth inhibition, e.g., for a certain cancer cell line.

Giant Axonal Neuropathy (GAN, 16q24): A recessive sensory and motor disease of the central and peripheral nervous system. Its onset is at early childhood and usually causes death by late adolescence of curly haired individuals. It causes swelling of the axons due to a defect in the protein gigaxonin affecting the axonal cytoskeleton. Gigaxonin binds to

ubiquitin-activating enzyme E1 through its amino-terminal BVTB domain, and the carboxyterminal kelch repeat interacts with the light chain of microtubule-associated protein 1B (MAP1B). Overexpression of gigaxonin enhances the degradation of MAP1B, and loss of gigaxonin has the opposite effect (Allen E et al 2005 Nature [Lond] 438:224). A similar disease also afflicts some German Shepherd dogs. ►neuropathy, ►BTB, ►microtubule, ►kelch motif

Giant Chromosomes: Polytenic chromosomes and lampbrush chromosomes. ►lampbrush chromosomes, ►polytenic chromosomes, ►salivary gland chromosomes

G

Giant Platelet Syndrome (Bernard-Soulier syndrome, 22q11.2, 17pter-p12): The giant platelet syndrome is caused by deficiency of a major platelet glycoprotein (glycoprotein Ib-β, GP1BB), resulting in a bleeding disorder. ►thrombophilia, ►May-Hegglin anomaly, ►thrombocytopenia

Giardia: *Giardia* is an intestinal protozoan parasite causing sensitive people severe, debilitating diarrhea and abdominal pain (see Fig. G40). It generally infests through unsanitized water. Its genome is less than 12 Mb. The *G. lamblia* genome is tightly packaged. Bidirectional transcription is a common feature and produces, not only the appropriate downstream sense transcript, but also leads to the production of either an upstream sense transcript (for promoters between genes in a head-to-head arrangement) or an upstream sterile antisense transcript (for promoters between genes in a head-to-tail arrangement). Bidirectional transcription seems to contribute to the abundance of sterile antisense transcripts observed (Teodorovic S et al 2007 Nucleic Acids Res 35:2544). The cells do not have mitochondria but mitosomes. ►mitosome, ►*Entamoeba*, ►*Trichomonas*; Adam, RD 2007 Clin Microbiol Rev 14: 447.

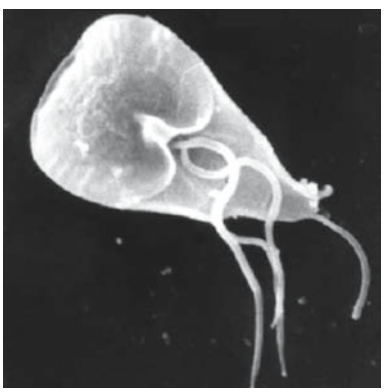

Figure G40. Giardia (Courtesy of CDC Public Health Image Library)

GIB: ►Genome Information Broker (http://gib.genes.nig.ac.jp).

Gibberella fujikuroi: A plant-pathogenic fungus that produces by its normal metabolism the plant hormones gibberellins. ►plant hormones

Gibberellins: ►plant hormones, ►*Gibberella fujikuroi*, ►dwarfism, ►florigen;Rojas MC et al 2001 Proc Natl Acad Sci USA 98:5838; Richards DE et al 2001 Annu Rev Plant Physiol Mol Biol 52: 67; Olszewski N et al 2002 Plant Cell 14:S61; genes and enzymes in fungi and plants; Tudzynski B 2005 Appl Microbiol Biotechnol 66:597 (see Fig. G41).

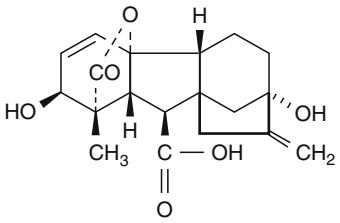

Figure G41. Gibberellic acid

Gibbon: ►Pongidae, ►primates

Giemsa Stain: The Giemsa stain contains azure II, azure-eosin, glycerol, and methanol. The dark bands appear to be poor in GC and the light, rich in GC content. ►G banding, ►chromosome banding, ►rye; Niimura Y, Gojobori T 2002 Proc Natl Acad Sci USA 99:797.

Gierke's Disease: ►glycogen storage disease type I

GIFT (gamete intrafallopian transfer): A method of artificial insemination. ►artificial insemination, ►ART

GIGA: Prefix for 10^9 size or quantity.

GigAssembler: An algorithm suitable for preparing the human genome working draft, including about 88% of the 400,000 initial contigs. ►contig, ►human genome, ►genome projects; Kent WJ, Haussler D 2001 Genome Res 11:1541.

Gilbert Syndrome: A very common human chromosome 2, dominant hyperbilirubinemia, similar to the Criggler-Najjar syndrome and probably controlled by genes allelic to it. ►Criggler-Najjar syndrome, ►Dubin-Johnson syndrome, ►hyperbilirubinemia

Gilles de la Tourette Syndrome: ►Tourette disease

Gillespie Equation: The Gillepsie equation can be used to estimate the stochastic regulation of chemical reactions, including interacting gene systems. The paper cited here presents a computational simpler

form. (See Gillespie DT 2001 J Chem Phys 115:1716).

Gin: An invertase. ►invertases

Ginger (*Zingiber officinale,* 2n = 2x = 22): Perennial rhizome spice. It dilates blood vessels, relieves pain, reduces flatulence, increases perspiration, and it is a stimulant. ►phenolics

Ginkgo biloba: An ornamental tree in the USA. Its leaves are considered as herbal medicine for neurological disorders associated with aging such as Alzheimer disease, hearing and memory loss, attention deficit, etc. Its flavonoids appear to be effective scavangers of free radicals. Microarray hybridization was found to reveal higher level of tyrosine/threonine phosphatase and other mRNAs involved in up-regulation of activity in the brain cortex of mice upon consuming leaf extracts. Ginkgos are very old species. (See Watanabe CMH et al 2001 Proc Natl Acad Sci USA 98:6577; Zhu Z, Zheng S 2003 Nature [Lond] 423:821).

GIP: A G protein subunit, and a potential oncoprotein. ►G protein, ►oncoprotein

GINS: One of the accessory factors for replication by DNA polymerases ε and α; it is a heterotetrameric complex consisting of Sld5, Psf1 (partner of Sld5-1), Psf2, and Psf3. ►SLD; Chang YP et al 2007 Proc Natl Acad Sci USA 104:12685.

GIP (glucose-dependent insulinotropic polypeptides): GIPs mediate insulin secretion. (See Hinke SA 2001 Biochim Biophys Acta 1547:143).

Giraffe (*Giraffa camelopardalis*): 2n = 30; the *Okapia johnstoni* is 2n = 45.

Girdle Bands: Concentric rings of thylakoids. ►chloroplasts, ►thylakoids

GIRK (G-protein-gated inwardly rectifying K^+ channel): A heterotrimeric guanine nucleotide-binding protein. ►ion channels, ►G proteins; Seeger T, Alzheimer C 2001 J Physiol 535[pt 2]:383.

GIS (gene identification signature): See Liu T-B, Ruan Y 2005 Nature Meth 2:105; ►transcriptome

GISH: Genomic in situ hybridization (see Fig. G42). It may identify chromosomes in species hybrids and reveal crossovers among homoeologues. ►in situ hybridization, ►FISH, ►genome, ►homoeologous chromosome

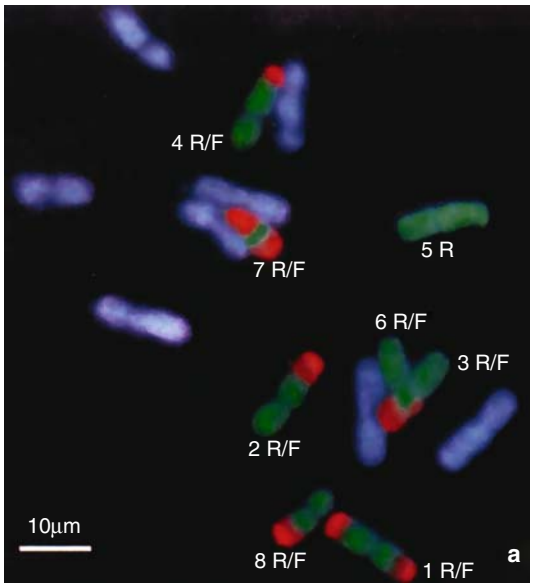

Figure G42. GISH. Introgression of *Allium fistulosum* chromosomes into *A. cepa,* mediated by bridging cross to *A. roylei*. The *A. fistulosum* chromosomes are labeled red (biotin, CY3), *A. roylei* shows green fluorescence (FITC) and *A. cepa* chromatin is blue (DAPI). (From Khrustaleva LI, Kik C 2000 Theor Appl Genet 100:17–26. Copyright Springer Vlg, 2000)

GIS-PET: Gene-identification signature analysis using paired-end ditags. Paired-end ditags from the two ends of each expressed transcript (18 bp from 5′ end and 18 bp from 3′ end) are extracted, concatenated, and subjected to sequencing analysis. ►GIS, ►paired-end diTag

giSNP (genetically indistinguishable SNP): About 50% of SNPs in human chromosome 20 shows at least one SNP partner in perfect linkage disequilibrium within < 20 kb clusters. Such giSNPs may make difficult the association mapping of disease genes. (Lawrence R et al 2005 Genome Res 15:1503). ►SNIPs, ►linkage disequilibrium

Gitelman Syndrome (16q13): Hypocalciuria, hypomagnesemia, and hypertension. ►Bartter syndrome, ►Liddle syndrome, ►hypoaldosteronism, ►hypertension, ►hypokalemia

GITR (glucocorticoid-induced tumor necrosis factor receptor-related, 1p36.3): GITR regulates cell proliferation, differentiation, and cell survival. Its ligand is AITR (activation-inducible TNFR). ►TNF; Nocentini G et al 2000 DNA Cell Biol 19(4):205.

GIY-YIG: A family of homing endonuclease with a GIY (X_{10-11})-YIG amino acid motif. These enzymes occur in T4 bacteriophage, either free, or within mobile group I introns. They occur in fungal and algal

mitochondrial introns and in algal chloroplasts. ►homing endonucleases; Chevalier BS, Stoddard BL 2001 Nucleic Acids Res 29:3757.

Glanzmann's Disease: A variety of blood platelet anomalies determined by autosomal recessive genes. The overall symptoms include bleeding under the skin (ecchimosis), tiny, round and flat purplish (later yellow or blue) spots under the skin caused by blood release (petechia), bleeding of the tooth gum (gingiva), nosebleeds (epistaxes), gastrointestinal bleeding, excessive uterine bleeding (menorrhagia), or bleeding from the uterus at irregular intervals (metrorrhagia). The platelets may appear normal yet their number is reduced (thrombocytopenia). Sometimes the size of the platelets increases and their shape becomes abnormal and they appear isolated rather than aggregated. ►platelet abnormalities, ►hemophilias, ►von Willebrand disease, and other terms under separate entries.

Glast: Na^+-dependent transporters of glutamate and aspartate; GLASTs may have 68% homology with another glutamate transporter GLT. β-Lactam antibiotics increase the expression of glutamate transporters and may protect against some neurological diseases (Rothstein JD et al 2005 Nature [Lond] 433:73). ►transporters, ►β-latamase, ►antibiotics, ►neurological disorders; Gegelashvili G et al 2001 Progr Brain Res 132:267; structure of *Pyrococcus* homolog: Yarnol D et al 2004 Nature [Lond] 431:811.

Glaucoma: Glaucoma may be controlled by autosomal dominant or recessive genes and may be manifested at birth, during juvenile years, or in adults (see Fig. G43). The incidence of the different forms may vary from 10^{-4} to a couple of percent in the general population, usually presenting a higher risk in adult life. The most general features are opacity of the eye lens caused by a gray gleam on the iris and an increased intraocular pressure, which eventually distorts the vision. In the early stages or in any mild forms, the anterior chamber of the eye is open (open angle glaucoma). This stage may pass into an intermittent form that may be transient but can last for several months, and eventually the angle becomes closed resulting in great pressure and swelling of the cornea accompanied by substantial pain. Eventually, if untreated, total blindness may follow.

Figure G43. Glaucoma. (From Bergsma, D. ed. 1973 Birth Defects. Atlas and Compendium. National Foundation-March of Dimes)

Testing the eye (intraocular) pressure before the visible onset of the condition may monitor it. In some cases, the increased intraocular pressure does not result in glaucoma and in some individuals glaucoma develops without eye pressure. In the early stages, the majority of people are unaware of the disease. The penetrance and expressivity of this disease is highly variable. The basic defect is degeneration of the optic nerve in the retinal ganglion cells. Amyloid β (Aβ) has an important role in retinal ganglion cell apoptosis (Guo L 2007 Proc Natl Acad Sci USA 104:13444). Radiation treatment of the receiver (1000 rad in two doses to whole body) and syngeneic (T cell-depleted) bone marrow injection from donor was found to provide very successful treatment in mice (Anderson MG et al 2005 Proc Natl Acad Sci, USA 102:4566). The most common forms of glaucoma are not monogenic but show complex inheritance due to multiple genetic and environmental factors. The gene (GLC1A) coding for juvenile open angle glaucoma (JOAG) was assigned to human chromosome 1q23-q25. GLC1B is at 2cen-q13 and GLC1C at 3q. The GC3B (buphtalmos) locus is at 1p36. The gene encodes the trabecular (supportive connective tissue) meshwork-inducible glucocorticoid response (TIGR) or myocilin. The dominant glaucoma at 6p25 encodes a forkhead type transcription factor. For early detection of glaucoma, the endothelial leukocyte adhesion molecule (ELAM-1, 1q23-q25) test has been suggested. ►eye diseases, ►syngeneic, ►FKH, ►amyloids, ►Axenfeld-Rieger anomaly; Jacobson N et al 2001 Hum Mol Genet 10:117; Libby RT et al 2005 Annu Rev Genomics Hum Genet 6:15.

GLC: ►gas liquid chromatography

Gle1: ►RNA export, ►export adaptors

Gleason Score: A classification of prostate cancer on the basis of histology with predictive value for progression. (See Gleason DF 1992 Hum Pathol 23:273; prostate cancer).

Gleevec (Glivec, Imatinib, STI-571): An inhibitor of Abelson murine leukemia virus oncogene-encoded tyrosine kinase and an anticancer drug effective against some sarcomas and hematopoietic cancer (see Fig. G44). In some cases, cardiac failure may result from this drug. It is an inhibitor of platelet-derived growth factor receptor (PDGFR) and cancers where this growth factor is involved. Resistance may arise to the drug through mutation in the kinase domain. The new drug BMS-3548725, however, is effective against most of the cells resistant to Gleevec (Shah NP et al 2004 Science 305:399). Recently,

some physicians reported improvement of diabetes II in a few patients treated by Gleevec. The drug seems to be a potent inhibitor of differentiated myeloid leukemic cells (CML), but does not deplete leukemic stem cells (Michor F et al 2005 Nature [Lond] 435:1267). A new generation of inhibitor of CML is Desatinib. For gastrointestinal tumors, Sutent may replace Imatinib. ►hematopoiesis, ►leukemia, ►diabetes, ►genetic medicine, ►biomarkers; Capdeville R et al 2002 Nature Rev Drug Discovery 1:493.

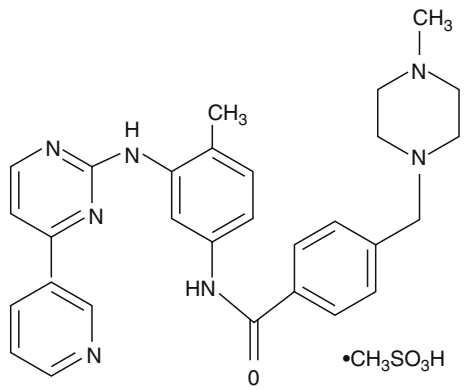

Figure G44. Gleevec

GLGF Repeats: Same as DHR domain or PDZ domain. (See Tochio H et al 2000 J Mol Biol 295:225).

GLI1 Oncogene (glioma): GLI1 has been located to human chromosome 12q13. It is highly amplified in gliomas. GLI2 in chromosome 2q14 (appears homologous to the *Krüppel* gene of *Drosophila* encoding a DNA-binding protein, regulating embryo morphogenesis). Similarly, GLI2 is also expressed in embryonal carcinomas but not in late developing ones. GLI3 (7q13) is apparently not an oncogene but it is involved in the Greig syndrome and in the Pallister Hall syndrome. Other homologous genes were also found in the human genome, altogether six loci in five different chromosomes. Some of the homologs (GLI4, 8q24.3) are denoted as HKR (human Krüppel). Gli transcription factors are suspected in the transduction of sonic hedgehog signals. Carboxy-terminal deletions in Gli3 facilitate its association with SMADs. ►oncogenes, ►Krüppel, ►Greig's cephalopolysyndactyly syndrome, ►Pallister-Hall syndrome, ►Rubinstein-Taybi syndrome, ►nevoid basal cell carcinoma, ►*hedgehog*, ►*sonic hedgehog*, ►syndactyly, ►polydactyly, ►DNA-binding protein domains, ►SMAD, ►glioma; Kim Y-S et al 2002 J Biol Chem 277:30901.

Gliadin: ►zein, ►glutenin

Glial Cell (neuroglia): Glial cells can be either astrocytes or oligodendrocytes or microcytes; the first two have supportive roles, the latter phagocytize the waste products of the nerves. Glial cells modulate synaptic transmission though an acetylcholine binding protein. ►FGF, ►acetylcholine

Glimmer: A program for locating (bacterial) genes based on interpolated Markov models. ►ORF, ►Markov chain statistics; Salzberg SL et al 1998 Nucleic Acids Res 26:544; http://glimmer.sourceforge.net/.

Glioma: A tumor of the tissues supporting the nerve cells (astrocytes) but it may spread beyond these. The glioma may be benign yet the malignant forms lead to rapid death. The most active glioma (glioblastoma multiformis, GBM) develops by an interaction of Ras and Akt in mice. GBM, although highly heterogeneous, can be grouped into rapidly progressing and slow progressing groups on the basis of expression ~70 genes, especially FABP7, and it can serve as a prognostic marker (Liang Y et al 2005 Proc Natl Acad Sci USA 102:5814). Gliomas seem to secrete glutamate that activates the NMDA receptors and further facilitates the expansion of the tumor. Surgery, radiation treatment supplemented with chemotherapy, and gene therapy with adenoviral vector carried herpes simplex virus thymidine kinase (HSVTK) and gancyclovir are used, but none give entirely satisfactory results. Bone morphogenetic protein inhibits glioblastoma stem cell proliferation (Piccirillo SGM et al 2006 Nature [Lond] 444:761). ►cancer gene therapy, ►GLI oncogene, ►angiogenesis, ►adenovirus, ►gancyclovir, ►RAS, ►Akt, ►FABP, ►NMDA, ►p110α, ►CD133, ►bone morphogenetic protein; Lam PYP, Breakfield XO 2001 Hum Mol Genet 10:777; Holland EC 2001 Nature Rev Genet 2:120; Takano T et al 2001 Nature Med 7:1010.

glnA: Bacterial glutamine synthase.

glnAp2, glnAp1: Major and minor glutamine synthase promoters, respectively, in bacteria.

Global Genetic Effects: Global genetic effects involve most or all of the genome. With the availability of microarray hybridization a very large number of gene loci can be studied (Rockman MV, Kruglyak L 2006 Nature Rev Genet 7:862). ►microarray hybridization, ►QTL

Global Single Cell Reverse Transcription-Polymerase Chain Reaction (GSC RT-PCR): The aim of the GSC RT-PCR method is to determine differences in gene expression among individual cells within a population of cells. This may be of interest for determining the process of metastasis, changes in gene expression during development, etc. A description of the procedure

can be found: Brailo LH et al 1999 Mutation Res Genomics 406:45. Although much difference is detectable among different cells, the components of the procedure introduce substantial variations too. ►microarray hybridization, ►SAGE

Globins: Ancestral protein molecules that diverged over a billion years ago into the oxygen-carrying muscle protein myoglobin and into the respiratory hemoglobins of the red blood cells. The neuroglobin, encoded at human chromosome 14q24, is expressed predominantly in the brain. The hemoglobin α locus is at human chromosome 16pter-p13.3, the β locus is at 11p15.5, δ is at 11p15.5, θ is at 16pter-13.3, the ζ is at 16pter-p13.3, and the ε is at 11p15.5. ►myoglobin, ►hemoglobin, ►leghemoglobin, ►haptoglobin, ►LCR, ►thalassemia, evolution of globins: Vinogradov SN et al 2005 Proc Natl Acad Sci USA 102:11385; http://globin.cse.psu.edu/.

Globo H: A glycoceramide present in breast cancer, ovarian, gastric, pancreatic, endometrial, prostate and small cell lung carcinomas. It may be employed in cancer vaccines. ►cancer gene therapy; Keusch JJ et al 2000 J Biol Chem 275:25315.

Globoid Cell Leukodystrophy: ►Krabbe's leukodystrophy

Globoside: Glycosphingolipid with the most common structure: acetylgalactoseamine-galactose-galactose-glucose-ceramide. ►sphingolipids, ►ceramides; Puri V et al 2001 J Biol Chem 154:535.

Globozoospermia (round-headed spermatozoa): A developmental anomaly caused by the loss of α' subunit of casein kinase II. This enzyme has many substrates and is involved in numerous metabolic controls. (See Larson KL et al 2001 J Androl 22 (3):424).

Globulin: Salt-soluble proteins with many diverse cellular functions.

Glofish: A genetically modified zebrafish expressing a red fluorescent protein transgene under a muscle-specific promoter, a pet novelty. ►transgene, ►zebrafish

Glomerulocystic Kidney Disease, Hypoplastic, Familial (GCKD, 17 cen-q21.3): Dominant mutations in the hepatocyte nuclear factor-1-β gene causing chronic renal failure, renal cysts and diabetes-like symptoms. ►HNF, ►kidney diseases

Glomerulonephritis: An autosomal dominant kidney disease associated with very sparse hairs and red lesions due to dilation of the blood vessels (telangiectasis). This disease (membrano proliferative glomerulonephritis) is frequently associated with reduced levels of C3 complement component. More recent information indicates that the FcγR (fragment crystalline gamma receptor) of the antibody molecule is the most critical factor in the disease. Complement factor H-deficient mice showed significant reduction of nephritis if deficient in C5 but not in C6. Antimurine C5 antibody reversed renal injury (Pickering MC et al 2006 Proc Natl Acad Sci USA 103:9649). The dominant IgA nephropathy (6q22-q23) occurs at a frequency of 1×10^{-3} and may cause death in ~20% of the afflicted, despite dialysis. ►hair, ►kidney diseases, ►skin diseases, ►telangiectasis, ►complement, ►antibody, ►immunoglobulins, ►gene copy number

Glomerulosclerosis, Focal and Segmental, Familial: Glomerulosclerosis involves increased urinary protein excretion and decreasing kidney function or even morbid kidney defects. The α-actinin gene at human chromosome 19q13.1 may be one of the causes for the stronger than normal binding of this protein to filamentous actin. Another dominant locus is in chromosome 11q22-q24 (encoding a transient receptor potential cation channel) and a recessive steroid-resistant NPHS2 gene has been assigned to 1q25-q31. The latter locus encodes the transmembrane protein podocin. ►actinin, ►actin, ►kidney diseases; Winn MP et al 2005 Science 308:1801.

Glomerulus (plural glomeruli): Cluster of blood vessels or nerve fibers.

Gloves: Gloves are frequently recommended for laboratory work when handling hazardous material or when contamination by hands must be avoided. Remember that surgical latex gloves easily develop invisible holes and permit unseen contamination of the hands. (Mercury penetrates latex disposable gloves in 15 seconds.) Latex gloves may cause (serious) allergic reactions to about 10% of the regular users and food allergies may aggravate it. Longer than 15-minute use of a latex glove may result in leakage. Organic solvents damage some plastic gloves and they may develop holes easily. For most operations neoprene gloves provide the greatest safety. For very hazardous material, the use of double gloves may be advisable. Washing hands after the removal of the gloves is recommended. (See laboratory safety).

GLT: ►GAST

Glucagon: A polypeptide hormone secreted by the α cells of the pancreas when the level of blood glucose sinks below a certain level. The hormone then increases the concentration of blood sugar by breaking down glycogen with the cooperation of epinephrine. ►epinephrine, ►animal hormones, ►cAMP, ►diabetes mellitus

Glucan: A polymer (repeating units) of glucose, the same as glucosan. ►glucosan

Glucanase: Glucan-digesting enzyme. ►glucan, ►host–pathogen relation

Glucocorticoid: A kidney cortex hormone which regulates carbohydrate, lipid, and protein metabolism, muscle tone, blood pressure, the nervous system, etc. It inhibits the release of adrenocorticotropin, slows down cartilage synthesis, and mitigates inflammation, allergy and various immunological responses. Cortisol (hydroxycortisone) is an important natural glucocorticoid, whereas dexamethasone is a synthetic product that is two orders of magnitude more potent than cortisol. The glucocorticoid-mediated immunosuppression involves the activation of the IκBα gene and an increase of its cytoplasmic protein product. When the nuclear regulator factor NF-κB is active (because of the expression of TNF), its inhibitor, the IκBα protein is degraded and NF-κB moves into the nucleus and activates the immune system. Dexamethasone—in contrast with natural glucocorticoids—causes an increased transcription of IκBα. Thus, the NF-κB translocation to the nucleus is inhibited, leading to less nuclear NF-κB and reduction of inflammation because the immune system is suppressed. Familial and sporadic glucocorticoid deficiencies are caused by defective adrenocorticotropic hormone receptors. Glucocorticoids can affect serotonin levels and brain function. The deficiency of the glucocorticoid receptor (94-kDa, encoded at 5q31) causes cortisol and dexamethasone resistance. The melanocortin unresponsiveness is due to receptor deficiency at 18p11.2. The glucocorticoid receptor is an indispensable transcription factor, and it can attach to naked DNA as well as to nucleosomal structures. ►adrenocorticotropin, ►NF-κB, ►IκB, ►cortisol, ►dexamethasone, ►opiocortin, ►immunosuppression, ►apoptosis, ►Cushing syndrome, ►calreticulin, ►immunophilins, ►GRE, ►stress, ►serotonin, ►allergy

Glucocorticoid Response Elements (GRE): GREs are located generally about 100 to 2,000 nucleotide pairs upstream from the transcription initiation site (the human growth hormone response element is within the transcribed region). These elements, such as the mammary tumor virus (MTV), metallothionein (MTIIA), tyrosine oxidase (TO), and the tyrosine amino transferase receptor element, respond to different activating proteins as indicated by their names. Despite differences in structure they share a consensus: CGTACANNNTGTTCT. ►hormone response elements, ►regulation of gene activity, ►DNA looping, ►mammary tumor virus, ►metallothionein, ►tyrosine aminotransferase; Herrlich P 2001 Oncogene 20:2465.

Glucogenic Amino Acids: Glucogenic amino acids can be converted into glucose or glycogen through pyruvate (alanine, cysteine, glycine, serine, tryptophan), α−ketoglutarate (arginine, glutamine, histidine proline), succinyl CoA (isoleucine, methionine, threonine, valine), fumarate, (phenylalanine, tyrosine) and oxaloacetate (asparagine, aspartate). ►amino acids

Glucokinase (GK): GK phosphorylates glucose to form glucose-6-phosphate. Heterozygosity for GK mutation in the fetus may cause mild hyperglycemia and may reduce insulin secretion by the fetus resulting in reduced intrauterine growth. In case of maternal glucokinase mutation, hyperglycemia stimulates fetal insulin secretion and increase in growth. ►insulin; Grimsby J et al 2003 Science 301:370.

Gluconeogenesis: Gluconeogenesis is the synthesis of sugars from non-carbohydrate precursors (such as oxalo-acetate, pyruvate, citrate, malate, TORC).

Glucosan (polyglucosan): Different types of polysaccharides (starch, glycogen, cellulose) containing repeating glucose subunits.

Glucose (glycose): A 6-carbon sugar (dextrose), an aldohexose. Besides being a source of energy, it induces and represses many genes. In chemostat cultures of yeast on galactose media, by small pulses of glucose additions, ∼25% of the genes changed their expression (monitored by microarrays) primarily due to five transcription factors (Ronen M, Botstein D 2006 Proc Natl Acad Sci USA 103:389). Glucose influx triggers gene expression changes in hepatocytes to suppress endogenous glucose production and convert excess glucose into glycogen or fatty acids to be stored in adipose tissue. This process is controlled by insulin. Glucose also regulates the activity of ChREBP, a transcription factor that modulates lipogenesis. Glucose binds and stimulates the transcriptional activity of the liver X receptor (LXR), a nuclear receptor that coordinates hepatic lipid metabolism (Mitro N et al 2007 Nature [Lond] 445:219). ►galactose [for formula], ►insulin, ►lipidogenesis

Glucose Effect: A form of catabolite repression when as long as glucose is available in the nutrient medium, the synthesis of enzymes involved in the utilization of other carbohydrates is prevented. The preferential growth on, e.g., glucose is followed by a temporary pause before the utilization of another carbon source is commonly called *diauxic growth*. Glucose may act at three levels: (1) inhibits the uptake of inducer molecules by relying on the dephosphorylated component of the phosphoenolpyruvate-dependent

glucose phosphotransferase. (2) Lowers the level of cAMP and its receptor and activates indirectly adenylate cyclase. (3) Increases the level of catabolites that repress the synthesis of inducible enzymes. In fungi, the mechanism of glucose effect may be mediated through the function of hexokinase. In yeast, *SNF1* (sucrose non-fermenting) encoding a transactivator protein (protein threonine/serine kinase) gene can relieve *SUC* and *GAL* glucose repression. The Mig1/CREA Zinc-finger DNA-binding protein, Glc7 protein phosphatase and the Tup1 general suppressor have also been implicated in the regulation. Two glucose signaling loci (*gsf1* and *2*) also affect the glucose repression of *SUC2* and *Gal10*. Glucose suppression has been analyzed in prokaryotes and lower and higher eukaryotes, animals as well as plants. The *PRL1* locus of *Arabidopsis* encodes an α-importin WD protein that regulates glucose/sucrose sensitivity as well as hormone responses in the plant. ►feedback control, ►repression, ►catabolite repression, ►Zinc finger, ►Tup1, ►WD-40, ►SW1, ►transactivator, ►*SUC2*, ►*GAL*; Ronne H 1995 Trends Genet 11:12; Németh K et al 1998 Genes & Development 12:3059; Stülke J, Hillen W 1999 Curr Opin Microbiol 2:195; Rolland F et al 2002 Plant Cell 14:S185.

Glucose Induction: Glucose sensors *SNF* and *RGT1* genes monitor glucose in the cell membrane of yeast. Glucose most likely causes a conformation change in these proteins by attaching to their N-terminal domains outside the cell membrane. Both of these are transmembrane proteins with their C-terminus tail within the cytoplasm. That tail probably recruits the Hxt glucose transporters. The transcriptional suppressor Zn-finger protein, Rgt1, represses the *HXT* glucose transporter genes and the SCF^{Grr1} complex inhibits Rgt1 (regulator of transport) when a low concentration of glucose appears in the culture medium. (SCF is an acronym for Skp1, Cdc53 and Cdc34; it includes an F-box protein. Grr is a Cdc34-dependent protein factor of ubiquitination of cyclins). Then, HXT genes are activated. When the level of sucrose is increased beyond a certain level, the Mig1 suppressor system becomes active. When the concentration of glucose becomes high, Rgt1 turns into an activator of HXT1. ►glucose effect, ►SNF, ►SCF, ►Skp, ►Cdc34, ►Cdc53, ►F-box, ►glucose transporters; Vaulont S et al 2000 J Biol Chem 275:31555.

Glucose Repression: ►glucose effect

Glucose Tolerance Test: ►diabetes

Glucose Toxicity: Normally, insulin regulates the physiological range of glucose in the cells. When the level of glucose is raised for a longer period of time, glucose toxicity results. Glucose may generate reactive oxygen species (ROS). Antioxidants as well as binding transcription factors PDX-1/STF and RIPE-3b1 to the insulin promoter may increase insulin production and reduce toxicity. (See Shimoi K et al 2001 Mutation Res 480–481:371).

Glucose Transporters: GLUT (12p13.3) is a 49-kDa protein involved in moving glucose. GLUT2 (3q26.1-q26.3) is another solute/sugar carrier (Fanconi-Bickle syndrome). GLUT1 (1p35-p31.3) mediates sugar transport to the brain across the blood/brain barrier membrane. The GLUT4 (17p13) defect seems to be involved in the resistance to insulin in diabetes type 2. GLUT5 (1p36.2) is a fructose transporter. GLUT10 (20q13.1) deficiency upregulated TGF. ►diabetes, ►BBB; Brown GK 2000 J Inherit Metab Dis 23:237; Coucke PJ et al 2006 Nature Genet 38:452.

Glucose-Galactose Malabsorption (GGM): ►SGLT

Glucose-6-Phosphate Dehydrogenase: The first enzyme in the pentosephosphate pathway that converts G-6-P into 6-phosphoglucone-δ-lactone (see Fig. G45). The final product of the pathway is D-ribose-5-phosphate, and NADPH is also generated. Although about 90% of the cellular glucose in mammals is converted to lactate by glycolysis, 10% is driven through the pentose phosphate path and this is the principal reaction to provide the erythrocytes with NADPH for the reduction of glutathion. The deficiency of the enzyme caused by Xq28-chromosomal genes was first identified as a hemolytic anemia caused by the antimalarial drug 8-aminoquinoline. Most of the afflicted individuals are essentially asymptomatic until exposed to drugs such as certain analgesics, sulfonamides, antimalarial drugs (atabrine), quinine, etc., or afflicted by other diseases (see Fig. G46). G-6-P dehydrogenase deficiency is widespread in human populations, probably because the heterozygotes and hemizygous males are protected against falciparum malaria by a 46–58% reduction of the infectious disease. Heterozygotes (XX) may display lyonization. In the Jewish populations of Kurdistan, Caucasus, and Iraq, the frequency of the defect reached 58.2, 28.0 and 24.8%, respectively, whereas in geographical areas free of malaria it was generally less than 2%. Cavalli-Sforza and Bodmer estimated that G-6-P dehydrogenase deficiency conveyed an extremely high 0.15% selective advantage against malaria (Saunders MA et al 2002 Genetics 162:1849). A similar sequence is situated in human chromosome 17 and it may be a pseudogene. ►analgesic, ►malaria, ►selection coefficient, ►selection conditions, ►pentose phosphate pathway, ►glycolysis, ►glutathion, ►glycogen storage

diseases, ►atabrine; Tishkoff SA et al 2001 Science 293:455; http://www.rubic.rdg.ac.uk/g6pd/.

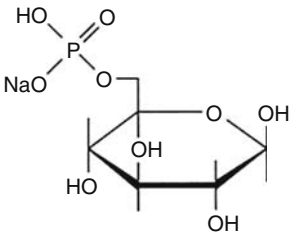

Figure G45. Glucose-6-phosphate

Figure G46. G-6-P deficient erythrocyte peripheral "BITE"

Glucose-Phosphate Isomerase: ►phosphohexose isomerase

Glucosidase (GCS1): An enzyme that digests 1,2-N-linked glycoproteins and other glycose linkages; in humans it is encoded in chromosome 2p13-p12. ►acid maltase, ►Pompe diseases, ►Gaucher disease

Glucosides: When D-(+) glucose is treated with an alcohol (methanol) and HCl, methyl D-(+)glucoside is formed that still has one methyl group attached, yet its properties resemble that of an acetal. Acetals may be formed from aldehydes and they are common in different plants. Cardiac glucosides present in plants such as *Digitalis, Scilla*, etc. have cardiotonic effect (strengthen heart function) and used as medicine. Many of the plant glucosides are highly toxic and cause anorexia (loss of appetite), nausea, vomiting, salivation, diarrhea, headache, drowsiness, delirium, hallucinations, and possibly death. Glycosides linked to cyanides also occur in common food plants such as beans, apricot, and almond seed, etc. Forage plants such as Sudan grass, white clover, etc. may contain enough cyanide to kill a 50 kg animal if it eats 1 to 2 kg fresh plant material. Through plant breeding efforts, the synthesis of the glucoside (lotoaustralin) may be blocked or the production of the enzyme linamarase may reduce the toxicity. ►lotoaustralin, ►cyanide; Tattersall DB et al 2001 Science 293:1826.

Glucosylation: Attaching glucose to another molecule. Defective N-glycosylation is the cause of mucolipidosis II and impacts the immune systems. Glycosylation has many important consequences on plant metabolism. ►mucolipidosis, ►glycosylation, ►congenital disorders of glycosylation; Lowe JB 2001 Cell 104:809; congenital disorders: Jaeken J, Matthijs G 2007 Annu Rev Genomics Hum Genet 8:261.

Glucuronic Acid: A derivative of uronic acid (a derivative of glucose) and it is present in glucosaminoglycans (see Fig. G47). ►mucopolysaccharidosis, ►GUS

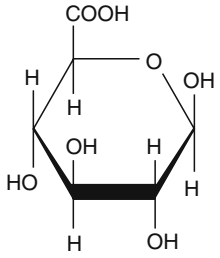

Figure G47. D-glucuronic acid

Glume: The lower-most bract of the grass florets (see Fig. G48). The glume is generally free from the fruit, in some cases however, it may be firmly associated with the kernels.

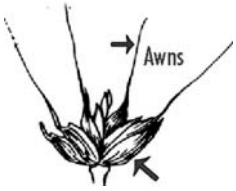

Figure G48. Glumes

GluR: ►glutamate receptor

GLUTs: Insulin-dependent glucose transporters encoded by the genes SLC. GLUT may be homologous to the cJun amino-terminal kinase-interacting protein JIP. MAPK81P1 (11p11.2-p12), a potential SLC transactivator, may be a major gene for type-2 diabetes. There are also several other glucose transporters. ►insulin, ►MAPK, ►diabetes, ►MODY, ►MAPK; Doege H et al 2001 Biochem J 359[pt2]:443)

Glutamate ($HOOCCH[NH_2]CH_2CH_2CONH_2$): An uncharged derivative of glutamic acid, which also has a key role as a nitrogen donor in the cell. The glutamate neurotransmitter activates the glutamate receptors (iGluR) regulating ion uptake and (mGluR) nerve synaptic strength and frequency. Mitochondrial glutamate facilitates insulin secretion. ►amino acids, ►glutamine, ►glutamate synthase, ►glutamate synthetase, ►neurotransmitter

Glutamate Decarboxylase Deficiency Disease (GAD): A pyridoxine-dependent epilepsy. The two enzymes require the cofactor pyridoxal phosphate. These enzymes convert glutamic acid into γ-aminobutyric acid (GABA) that controls neurotransmission in vertebrates and invertebrates. The phenotype is autosomal recessive (GAD1 at 2q31, GAD2 at 10p11.23). ►epilepsy, ►GABA, ►amino acid metabolism

Glutamate Dehydrogenase (M_r 330,000): Glutamate dehydrogenase catalyzes oxidative deamination of glutamate in the mitochondria, resulting in the formation of α–ketoglutarate. The reaction requires NAD^+ or $NADP^+$ as cofactors and is regulated allosterically by GTP and ADP. Then in turn, α–ketoglutarate and ammonia may again form glutamate. If the concentration of NH_3 is low, glutamate dehydrogenase cannot function to an appreciable extent. In such a case, NH_3 plus glutamate are converted to glutamine by non-adenylylated glutamine synthetase. In the presence of high amount of NH_3, *glutamine synthetase* is adenylylated and becomes inactive and in this form it represses its own synthesis (autoregulation). In its non-adenylylated state (when the level of ammonia is low), it represses *glutamate dehydrogenase* instead. From glutamine and α–ketoglutarate, glutamate can be synthesized by *glutamate synthase* in the presence of $NADPH + H^+$. Glutamate synthase also serves as an inducer for tryptophan permease, which together with tryptophan transaminase may also contribute to glutamate synthesis. In its non-adenylylated state, glutamine synthetase activates also the histidine utilization operon (*hut*). This operon also yields glutamate and ammonia. In humans, a small multienzyme family codes this enzyme (GLUD); its level is relatively high in the brain. The principal and functional *GLUD1* is located in human chromosome 10q23. This gene is homologous to mouse locus *Glud-2* in chromosome 14. ►UTase, ►glutamate synthase, ►olivopontocerebellar atrophy, ►autoregulation

Glutamate Formiminotransferase: An autosomal recessive deficiency of this enzyme leads to the accumulation of formiminoglutamate and folic acid in the urine and in the serum causing physical and mental retardation (see Fig. G49). ►amino acid metabolism, ►mental retardation

Glutamate Oxaloacetate Transaminase (GOT2): GOT2 is encoded in human chromosome 16q21 but the protein is mitochondrially located. In many plants and lower animals, the enzyme is mitochondrially coded. Pseudogenes were found at two locations in human chromosome 1 and in chromosome 12. ►mtDNA, ►aspartate aminotransferase mitochondrial, ►tyrosine aminotransferase

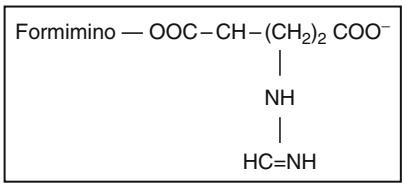

Figure G49. Formiminoglutamate

Glutamate Receptors (GluR): GluR are cation channels mediating the post-synaptic current in the central neurons. Certain mutations in GluR-B subunits lead to increased calcium uptake and concomitant seizures if, e.g., the position 586 arginine prevents editing of pre-mRNA. The glutamate receptors are tetrameric. GluR genes with 63% to 16% homology to animal GluRs have been identified in both monocot and dicot plants with role in light signal transmission. ►neurotransmitters, ►NMDA, ►GABA, ►ion channels; Borges K, Dingledine R 2001 J Biol Chem 276:25929.

Glutamate Synthase: Glutamate synthase catalyzes the reaction that leads to: α-ketoglutarate + glutamine + $NADPH + H^+ \rightarrow$ 2 glutamate + $NADP^+$. The result of the combined action of glutamate synthetase and glutamate synthase in bacteria is:

α-ketoglutarate + $NH4^+$ + NADPH + ATP → L-glutamate + $NADP^+$ + ADP + Pi

►glutamate dehydrogenase, ►glutamine, ►autoregulation

Glutamate Synthetase: Glutamate synthetase in *E. coli* is a ca. 800,000 M_r protein containing flavin, iron, and S^{2-}. ►glutamate synthase, ►glutamate dehydrogenase, ►glutamic acid, ►glutamine, ►autoregulation

Glutamate Transporter: ►GLAST

Glutamate-Pyruvate Transaminase (GPT1): GPT1 catalyzes the reversible reaction:

The soluble enzyme is encoded in human chromosome 8q24.2-qter. Cytosolic and mitochondrial forms exist. It is also called alanine aminotransferase (AAT1). ►amino, ►acid metabolism; ►glutamine; ►alanine aminotransferase

$$HOOCCH_2CH_2COCOOH + CH_3CH(NH_2)COOH \leftrightarrows HOOCCH_2CH_2CH(NH_2)COOH + COOHCOCH_3$$

α – ketoglutaric acid L-alanine L-glutamic acid pyruvic acid

Glutamic Acid: $HOOC.CH(NH_2).CH_2.CH_2.COOH$ (L(+), amino-glutaric acid)

Glutaminase (GLS): An enzyme converting glutamine into glutamic acid and it has been mapped to human chromosome 2q32-q34. It is activated by phosphate and may affect the neurotransmitter role of glutamate. ►amino acid metabolism, ►glutamine, ►glutamic acid

Glutamine: $HOOC\text{-}CH(NH_2)\text{-}(CH_2)_2\text{-}C(O)NH_2$. ►glutamic acid

Glutamine Amidotransferases: A group of enzymes with two domains, one binds glutamine and the other binds another molecule. After cleaving ammonia from glutamine they transfer it to the other substrate, generally in the presence of ATP.

Glutamine-Repeat Diseases: ►Huntington's chorea, ►Kennedy disease, ►dentatorubral-pallidoluysian atrophy, ►olivopontocerebral atrophy, ►Macho-Joseph disease, ►fragile sites, ►trinucleotide repeat

Glutamyl Ribose-5-Phosphate Glycoproteinosis: An ADP ribose protein hydrolase deficiency resulting in proteinuria and neurological disorders. It is also regarded as a lysosomal storage disease. It may be X-linked. ►lysosomal storage diseases

Glutamyl-tRNA Synthetase (QARS): The enzyme charging the cognate tRNA with glu-tamic acid; it is encoded in human chromosome 1q32-q34. ►aminoacyl tRNA synthetase

Glutaraldehyde: ►fixatives

Glutaredoxin: Glutaredoxin catalyzes NADPH-dependent reduction of disulfides usually in a complex with glutathione and glutathione reductase. ►thioredoxin, ►DsbA

Glutaricacidemia (GA): GAI autosomal recessive (19p13.2) glutaryl-CoA dehydrogenase deficiency results in increase in glutaric acid in the blood and in the urine resulting in neurodegenerative disorders. GAIC encoded in human chromosome 4q32-qter involves deficiency in the electron transfer flavoprotein oxidoreductase. GAIIA (15q23-q25) causes the excretion, besides glutaric acid, also lactic, ethylmalonic, isovaleric and different forms of butyric acids. Similarly, an X-linked (Xq26-q28) acyl-CoA dehydrogenase deficiency results in the abnormal excretion of glutaric and other organic acids. ►glutaricaciduria, ►aminoacidurias

Glutaricaciduria: An autosomal recessive glutaryl-CoA dehydrogenase deficiency leading to accumulation of glutaric acid in the urine, degeneration of the nervous system, and impairment of muscle functions. Limiting amino acid intake may alleviate the symptoms. An autosomal dominant form (15q23-q25) was identified as a defect in an electron-transfer flavoprotein. Some glutaricacidemias are also called glutaricaciduria, e.g., glutaryl-CoA dehydrogenase deficiency (GAI, 19p13.2). Glutaricaciduria IIC (GAIIC) was assigned to 4q32-qter. ►neuromuscular diseases, ►aminoacidurias, ►glutaricacidemia

Glutathione: Glutathione or γ-L-glutamyl-L-cysteinyl-glycine is a reducing agent that protects SH groups in proteins. About 10% of the blood glucose is oxidized to 6-phosphogluconate by glucose-6-phosphate dehydgrogenase (G6PD) using $NADP^+$, and the reducer NADPH keeps glutathione reduced. Deficiency of G6PD results in destruction of red blood cells and thus anemia. Glutathione is indispensable for development. Protozoa with anaerobic metabolism lack glutathione and mitochondria. ►glucose-6-phospate dehydrogenase; Meister A 1988 J Biol Chem 263:17205; Spector D et al 2001 J Biol Chem 276:7011.

Glutathione Peroxidase (GPX1): GPX1 was assigned to human chromosome 3p21.3 (earlier it was assigned to 3q11). Its deficiency causes hemolysis and jaundice. The frequency of the GPX1 gene is >0.5 in Mediterranean Jewish populations but it is < 0.2 in Northern Europeans. Locus GPX2 is in 14q24.1, GPX2 is in 5q32-q33.1, and GPX4 is in 19p13.3. The ailment may also be caused by selenium-deficient diet. ►hemolytic anemia, ►glutathione reductase, ►glutathione synthetase, ►deficiency

Glutathione Reductase (GSR): The GSR gene was located to human chromosome 8p21. Its deficiency results in hemolytic anemia. In insects thioredoxin substitutes for GSR. ►hemolytic anemia

Glutathione Synthetase Deficiency: A form of human chromosome 20q11.2 recessive hemolytic anemia and/or 5-oxyprolinuria. It may also result in excess metabolic pyroglutamic acid in the urine and in a variety of ailments. GST2 (γ-glutamylcysteine synthetase) gene was assigned to human chromosome 6p12 also causes hemolytic anemia. ►hemolytic anemia, ►glutathione, ►anemia

Glutathione-S-Transferases (GST): A family of enzymes metabolizing and detoxifying mutagens and carcinogens (some alkylating agents, cisplatin, carbonyl, peroxide, and epoxide groups) GST 3 was assigned to 11q13, GST2 to 6p12, GST1, GST4, GST5 all at 1p13.3. GSTPL (glutathione transferase-like enzyme) is encoded in 12q13-q14. These enzymes, despite different locations of the coding units, show homology. GST is also used for protein labeling. It is extremely stable and facilitates the solubilization of proteins fused with. ►multidrug resistance, ►cisplatin

Glutathionuria (GGT): A recessive defect (human chromosome 22q11.1-q11.2) in γ-glutamyl transpeptidase enzyme and accumulation of glutathione in the urine.

Gluten: A mixture of several seed proteins in cereals. The main fractions are the alcohol-soluble gliadin and the alkali-soluble glutenin. The proportion of the components is genetically determined and defines nutritional value and baking quality. ►glutenin, ►zein

Glutenin: Glutenin is about half of the seed storage protein in wheat; it is soluble in 70% ethanol and alkali but insoluble in water. It is a polymer of extremely large molecular weight, up to tens of millions. Its composition bears similarity to the muscle protein titin, comprising about 27,000 amino acid residues. The similarities based on (PEVK) proline, glutamate, valine, and lysine sequences may be attributed to the fact that both proteins require great elasticity in the bread dough. It was (indirectly selected by humans) to retain gas bubbles in the dough to return to the original position after extension. In wheat, gliadin occurs with glutenin. The former conveys resistance to extension while the latter provides the softness and viscosity of the dough. ►gluten, ►gliadin, ►celiac disease, ►*Triticum*, ►resilin; Kobrehel K et al 1992 Plant Physiol 99:919.

Glycan: A general old term for polysaccharides. Glycans associated with proteins have very important role in the cell (immune system, transport, etc.) and defects in their synthesis or association are involved in a large number of human diseases (galactosemia, fucosidosis, etc). ►lectins, ►polysaccharide, ►immune response; Lowe JB, Marth JD 2003 Annu Rev Biochem 72:643; bacterial glycans in immune response: Comstock LE, Kasper DL 2006 Cell 126:847; glycans technologies: Prescher JA, Bertozzi CR 2006Cell 126:851.

Glycemia: Blood sugar content.

Glycerol ($CH_2OH—CHOH—CH_2OH$): An intermediate in carbohydrate and lipid biosynthesis.

Glycerol Kinase Deficiency (GKD, Xp21-p21.2): Physical and mental retardation, osteoporosis, myopathy, eye defects, and hypergycerolemia. Chromosomal deletions may overlap with several other genes in the region of the X chromosome. ►contiguous gene syndrome; Gaudet D et al 2000 Am J Hum Genet 66:1558.

Glycerophospholipid: Glycerophospholipids are formed when fatty acids are esterified to glycerol and a polar alcohol is linked to it by phosphodiester bond. They are parts of cell membranes (synonymous with phosphoglycerides).

Glycine Biosynthesis: Glycine (NH_2CH_2COOH) is synthesized by hydroxymethyltrans-ferase from serine ($HOCH_2CH(NH_2)COOH$), while tetrahydrofolate is converted to N^5,N^{10} methylene tetrahydrofolate. The transferase gene has been located to human chromosome 12q12-q14, whereas the tetrahydrofolate cyclases are in human chromosomes 8q21, 18-qter. Glycine is synthesized alternatively from CO2 and NH4 by glycine synthase in the liver of vertebrates. ►glycinemia ketotic, ►hyperglycinemia

Glycine max (soybean): A leguminous plant (basic chromosome number 20). The seed contains 20 to 23% oil and its protein content (meal) may exceed 40%. It is one of the most important source for vegetable oil products and textured proteins for human food. Also, it is used as supplements to animal feed mixtures.

Glycinemia, Ketotic (PCC): PCC is caused by two genes at two human chromosomal locations (PCCB at 3q21-q22 and PCCA at 13q32). The biochemical defect is propionyl-CoA carboxylase deficiency. This enzyme's primary known role is the generation of D-methyl-malonyl-CoA, which is epimerized into the L form and subsequently by a mutase—with vitamin B12 cofactor—to succinyl-CoA. These processes concommitantly somehow produce ketosis, hypoglycemia, and hyperglycinemia. The symptoms are growth retardation, vomiting, lethargy, protein intolerance, low level of neutrophilic leukocytes, reduction in platelet number, etc. ►ketoacidosis, ►amino acid metabolism, ►glycine biosynthesis, ►methylmalonicaciduria, ►hyperglycinemia

Glycocalyx: A carbohydrate-rich membrane glycoprotein-lipid layer of prokaryotic and eukaryotic cell surface.

Glycoform: Proteins with differences in glycosylation. ►glycosylation

Glycogen: The main storage polysaccharide in animal cells. About 7% of the wet weight of the liver is glycogen and glycogen is present in the muscle cells too. It is branched at every 8 to 12 residues. As needed, glycogen is hydrolyzed into glucose to supply energy, with the aid of enzymes that are associated with its granular form. Glycogen is synthesized from glucose-6-phosphate by first being changed into glucose-1-phosphate by phosphoglucomutase. Then UDP-glucose pyrophosphorylase converts G-1-P and UTP into UDP-glucose and pyrophosphate (PPi). Glycogen synthase then converts UDP-glucose into glycogen. *Glycogen synthase a* is the dephosphorylated active form of the enzyme, whereas the phosphorylated *glycogen synthase b* is inactive. The reaction requires a primer of α1–4 polyglucose and the protein glycogenin. The branching is generated by

branching enzymes amylo-(1→4) to (1→6) transglycolase or glycosyl-(4→6) transferase. The glycogen metabolism is regulated by glucagon and insulin in the liver and mainly by epinephrine and insulin in the muscles. The level of glucagon is regulated by cAMP. *Glycogen synthase kinase-3* regulates glycogen and protein synthesis by insulin and modulates transcription factor AP-1, CREB, the dorso-ventral patterning of embryogenesis, and apoptosis. ►epinephrine, ►insulin, ►diseases, ►AP, ►CREB, ►Akt, ►PTG; Weston CR, Davis RJ 2001 Science 292:2439.

Glycogen Storage Diseases: Several hereditary defects have been identified as being associated with the synthesis and catabolism of glycogen: 1. von *Gierke's disease* (type I glycogen storage disease, 17q21) involves a deficiency of glucose-6-phosphatase, determined by an autosomal recessive gene (see Fig. G50). The patients develop liver enlargement (hepatomegaly as indicated by the extended abdomen, see photo), subnormal level of blood sugar content (hypoglycemia), increased levels of ketone bodies (acetone) in tissues and fluids (ketosis), as well as high amounts of lactic and uric acids in the blood. 2. *Type II glycogen disease* (Pompe disease, GAA, chromosome 17q25.2-q25.3) is determined by an autosomal recessive condition causing a deficiency of lysosomal α-1,4-glucosidase (acid maltase). Infants develop excessive enlargement of the heart (cardiomegaly) because of the deposition of glycogen in the lysosomes and, under severe conditions, in the heart. By the age of two they succumb to cardiorespiratory failure. The defect can be diagnosed prenatally from amniocentesis. A milder form of the disease exists, with prolonged survival. Intravenous injection of the normal GAA gene in an adenovirus vector construct significantly alleviated the disease in a mouse model. 3. *Type III glycogen disease* (see Forbes disease) is also caused by autosomal recessive (1p21) mutations. The basic physiological defects involve, in variable forms, the glycogen debranching process. The symptoms are not as severe as in Type II disease and the patients may survive longer; with age some of the symptoms may even be somewhat alleviated. 4. *Type IV disease* involves a 3p21 recessive defect of the glycogen branching enzymes. The progressive destruction of liver cells is accompanied by an increase in connective tissues and the liver substance (cirrhosis). An increase in the size of the liver and spleen and accumulation of fluids in the abdominal cavity (ascites) results in death before age two. 5. In *Type V McArdle's disease* (chromosome 11q13), the homozygosity of autosomal recessive glucose-6-phosphate translocase gene causes variable symptoms accompanied by glycogen accumulation. Phosphorylating activity in the muscle tissues is deficient. Painful cramps accompanying physical exercise are the first symptom of the disease, the onset of which is around age 20. There is no hypoglycemia or increase of lactate in the blood but some patients excrete myoglobins in the urine. 6. *Type VI* (chromosome 14q21-q22) patients accumulate glycogen and some show reduced phosphorylating activity. 7. *Type VII disease* (Tarui disease), determined by chromosome 12q13.3 recessive genes, resembles Type V disease but the patients have reduced phosphofructokinase activity as well. 8. *Type VIII* glycogen storage disease is caused by a Xp22.2-p22.1-chromosomal recessive gene and thus affects primarily males. It is based on a leukocyte phosphorylase b activation deficiency. Some glycogen diseases involve multiple enzyme defects. These diseases are frequently associated with muscle weakness and various other adverse effects. ►glucose-6-phosphate dehydrogenase, ►glycogen, ►epilepsy, ►acid maltase deficiency, ►neuromuscular disease, ►enzyme replacement therapy

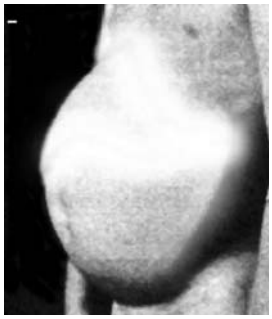

Figure G50. Glycogen storage diseases

Glycogen Synthase: ►glycogen

Glycogenosis: The term "glycogenosis" is used to designate glycogen storage diseases. ►glycogen storage

Glycolipid: A lipid with a carbohydrate group. Glycolipids are derivatives of sphingosine with one or more sugar. ►sphingosine

Glycolysis: The catabolic pathway from carbohydrates to pyruvate; anaerobic breakdown of glucose for the synthesis of ATP. ►Embden-Meyerhof pathway, ►pentose monophosphate shunt

Glycome: The sugar chains in the cell, including glycosylated proteins, chaperones, and lipids. The size of glycomes exceeds that of proteins by orders of magnitude. Large numbers of human diseases are caused by disorders of the glycome (Freeze HH 2006 Nature Rev Genet 7:537). ►glycosylation, ►phosphomannomutase deficiency, ►phosphomannose isomerase, ►glycosyltransferases, ►mannosyltransferases, ►glycosidase, ►lissencephaly,

►Ehlers-Danlos syndrome, ►exostosis, ►Kniest dysplasia, ►glycolipids, ►mucolipidoses, ►mucopolysaccharidosis, ►galactosemia, ►fructose intolerance, ►Marfan syndrome, ►muscular dystrophy; ►Walker-Warburg syndrome, ►thrombocytopenia, ►leucopenia, ►leukotrienes, ►epilepsy; http://www.glycosciences.de/; http://www.glyco.ac.ru/bcsdb/.

Glycophorin: A 131 amino acid transmembrane glycoprotein. Serological glycophorin assays have been developed to detect somatic mutations. Glycophorin-spectrin/actin bridge determines membrane shape and stability. ►spectrin, ►actin; Gerber D, Shai Y 2001 J Biol Chem 276:31229.

Glycoprotein: Proteins with covalently linked carbohydrate(s). ►proteoglycan; http://www.cbs.dtu.dk/databases/OGLYCBASE/.

Glycosaminoglycan (synonym mucopolysaccharide): A heteropoly-saccharide alternating *N*-acetylglucosamine + uronic acid and *N*-acetylgalactosamine + uronic acid (glucuronic acid). This family of compounds includes chitins, chondroitin sulfate, heparan, heparin, hyaluronic acid, keratans, and keratin (see Fig. G51). Chemokines interact with glycosaminoglycans and play roles in inflammation, and in developmental and homeostatic functions. ►exostosis, ►mucopolysaccharidosis, ►proteoglycan, ►chemokines, ►glucuronic acid, ►hyaluronidase deficiency; Constantopolous G, Dekaban AS 1975 Clin Chim Acta 59[3]:321; Handel TM et al 2005 Annu Rev Biochem 74:385.

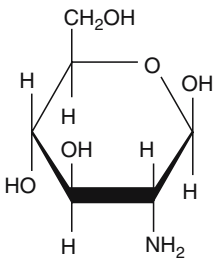

Figure G51. Glucosamine

Glycose: The generic name of monosaccharides, e.g., glucose, fructose, mannose, etc.

Glycosidase: Glycosidase digests glycosidic bonds and transfers of glycosyl moieties from a donor sugar to an acceptor of another sugar or other molecule(s).

Glycosidic Bond: A sugar linked to either alcohol or purine, or pyrimidine or sugar through an oxygen or nitrogen atom. (See conformation maps: http://www.glycosciences.de/modeling/glycomapsdb/).

Glycosome: Peroxisomes (microbodies) filled with glycolytic enzymes. ►glycolysis, ►microbody

Glycosphingolipids: Glycosphingolipids are present in plasma membrane rafts and caveolae and play an important role in differentiation and development ►sphingolipid, ►caveolae, ►RAFT

Glycosuria: An incompletely recessive defect in glycose reabsorption by the kidney, resulting in high sugar level in the urine. ►phlorizin, ►disaccharide intolerance

Glycosylases: Enzymes involved in excision of damaged purines and pyrimidines from the sugar-phosphate backbone of DNA. Different enzymes work on different bases (see Fig. G52). The uracil-DNA glycosylases (human gene UNG, chromosome 12q23-q24) remove uracils formed by spontaneous or induced deamination of cytosine, to avoid U-G mispairing potentially leading to GC→AT transitions.

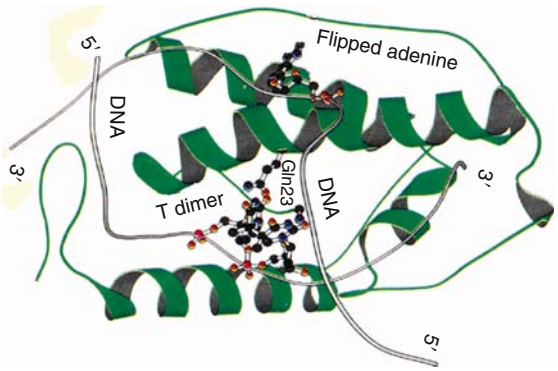

Figure G52. T4-pdg (pyrimidine dimer glycosylase/AP lyase, a TDG) X-ray crystal structure as a ribbon diagram. The DNA is distorted and the flipped-out adenine and the thymine dimer are shown as ball and sticks. The 3′ and 5′ indicate the directions of the DNA strands. Gln23 is a mutant amino acid residue. (Courtesy of Lloyd, RS, see also McCullogh AK et al 1999 Annu Rev Biochem 68:266)

It works in the nucleus and the mitochondria as well. The thymine-DNA glycosylase (TDG/UDG, 12q24.1) is one of the most efficient of these repair enzymes. The enzyme pushes and pulls out the improper uracil nucleotide from the major groove of the DNA. Subsequently,

TDG excises U, AP endonuclease cleaves the DNA backbone, deoxyribo-phosphodiesterase removes the 5′-phosphate group, and DNA polymerase β replaces the correct nucleotide and ligase finishes the job. It has been estimated that in a human cell 100 to 500 cytosine residues are deaminated daily. MUG (mismatch-specific uracil DNA glycosylase, human

chromosome 12) removes uracil/thymine when mispaired with guanine. The human hSMUG1 operates primarily at single strands of DNA during replication and transcription. MBD4 glycosylase (3q21) may remove mismatched U or T nucleotides. The 3-methyladenine-DNA glycosylase (gene AAG/MPG, chromosome 16p-telomere) works on N-3- and N-7 methylation adducts of purines (including hypoxanthine) and cyclic adducts. The pyrimidine hydrate-DNA glycosylase removes damaged or altered pyrimidines. OGG1 (oxoguanine glycosylase, 3p25.3/ 3p26.2) removes 8-oxoguanine across cytosine. MYH (1p32.1-p34.3) glycosylase excises adenine when misincorporated across oxoguanine. The formamidopyrimidine-DNA glycosylase (NTHL1, 16p13.3-p13.2) excises oxidatively damaged purines such as 8-oxyguanine, 8-hydroxyguanine, thymine glycol, and cytosine glycole, but requires the cofactor XPG (xeroderma pigmentosum G, 13q33). This DNA glycosylase also removes deaminated 5-methylcytosines that are common in eukaryotic DNA. All these excision repair enzymes maintain the working conditions of the human cells each of which suffers more than 10,000 damages each day. The yeast or *E. coli* glycosylases have similar functions but the proteins involved are different in size. ►excinucleases; ►AP endonucleases; ►endonuclease III; ►endonuclease VIII; ►DNA repair; ►mismatch repair; ►transition; ►adduct; ►base flipping; ►X-ray repair; ►RAD27; ►pyrimidine dimer; ►cyclobutane ring; McCullough AK et al 1999 Annu Rev Biochem 68:255; Hollis T et al 2000 Mutation Res 460:201; Ischenko AA, Saparbaev MK 2002 Nature [Lond] 415:183; MuTM glycosylase: Banerjee A et al 2006 Science 311:1153.

Glycosylation: The attachment of sugars to proteins either through a hydroxyl group of serine or threonine (O-glycosylation, Ser[Thr]-O-GlcNAcylation), or to the amide group of an asparagine (N-glycosylation). Glycosylated proteins have many different types of cellular functions. O-glycosylation occurs in proteins of the nuclear pore, in RNA polymerase II, transcription factors, oncoproteins (tumor suppressors), chromatin proteins, microtubule-associated proteins, cytoskeletal binding proteins, tyrosine phosphatase, SV40 T antigen, estrogen receptors, etc. Some antibiotics (tunicamycin) interfere with the process. Glycosylation increases the stability of proteins and may facilitate antigen recognition, appropriate folding, signal transduction, nerve function, etc. It plays an important role in the function of the immune system in the reproductive cell paths and several other health-related metabolic functions. A search for glycosylation in the Human Gene Mutation Data Base revealed 77 genes with 142 glycosylation mutations that seem to affect disease susceptibility (Vogt G et al 2005 Nature Genet 37:692). ►glycoform, ►glycosylation, ►glycome, ►sialic acid, ►mycobacterium; Rudd PM et al 2001 Science 291:2370; Lübke T et al 2001 Nature Genet 28:73; Varki A 2006 Cell 126:841; glycosylation in health and disease: Ohtsubo K, Marth JD. 2006 Cell 126:855; glycobiology reviews: Nature [Lond] 446:1030–1051.

Glycosyltransferases: Enzymes adding glucose to proteins and lipids involved in the formation of lipopolysaccharides used for bacterial cell wall. The ABO blood group alleles also encode glycosyltransferases (also the B gene product adds galactose). These enzymes shape the cell surface, determine cell to cell contacts, play some role in cancer, and have an important function in various sphingolipidoses. ►sphingolipidoses, ►ABO blood group; Cosgrove DJ 1999 Annu Rev Plant Physiol Plant Mol Biol 50:391; may catalyze reversible reactions: Zhang C et al 2006 Science 313:1291.

Glyoxalase: Glyoxalase I adds SH group from glutathione to the aldehyde carbonyl of methylglyoxal. The thioester product is then hydrolyzed by glyoxalase II (see Fig. G53). Glyoxal: OHCCHO. Methylglyoxal: CH_3COCHO. ►enzyme design

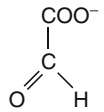

Figure G53. Glyoxylate

Glyoxylate Cycle: The glyoxylate cycle converts acetate into succinate and finally to carbohydrate. ►Krebs-Szentgyörgyi cycle

Glyoxysome: Vesicles in plant seeds and special type of microbodies (peroxisomes) in plants mediate the conversion of fatty acids to succinic acid to produce peroxiacetyl CoA and glucose through the glyoxylate cycle. ►microbody, ►glyoxylate cycle

Glyphosate: ►herbicides, ►GMO

Glypicans: Transmembrane proteins with phosphatidyl inositol distal to the membrane and heparan sulphate outside but proximal to the membrane. Glypican-1, -3, -5 are encoded at human chromosomes 2q35-q37, Xq26, and 13q31-q32, respectively. In mice, glypican-3 regulates a quantitative trait locus (QTL) involved in the body mass determination (Oliver F et al 2005 PLoS Biol 3(5):e135). ►phosphatidylinositol, ►heparan sulphate, ►syndecan, ►Simpson-Golabi-Behmel syndrome; Filmus J, Selleck SB 2001 J Clin Invest 108[4]:497.

GLYT: Glycine-specific transporters to the nervous system; they may be inhibitory neurotransmitters through a ligand-gated Cl^- channels, activated by glycine or may modulate glutamate-mediated neurotransmission. ►transporters, ►ion channels; Hanley JG et al 2000 J Biol Chem 275:840.

GM: ►GMO

GMENDEL: A computer program for analysis of segregation and linkage. (See Hered J 81:407 [1990]).

GM1-Gangliosidosis: ►gangliosidosis type I

GM2-Gangliosidosis: ►Tay-Sach disease, ►Sandhoff disease

GM3-Gangliosidosis: ►gangliosidosis type III, ►Sandhoff disease

GM3 Synthase: GM3 synthase produces gangliosides and glycolipids. Homozygous mutations cause infantile-onset epilepsy. ►epilepsy; Simpson MA et al 2004 Nature Genet 36:1225.

GMHT: (genetically modified herbicide-tolerant plants) have an agronomic advantage by facilitating the elimination of undesirable weeds from crops but they may adversely affect the population of wild birds that feed on weed seeds. ►GMO

GM-CSF: The granulocyte–macrophage colony stimulating growth factor is a lymphokine. ►lymphokines, ►macrophage, ►granulocyte, ►MCSF, ►M-CSF, ►G-CSF; Collins SJ et al 2001 Blood 98:2382.

GMO: Genetically modified organisms; a name actually used for transgenic plants and animals (see Fig. G54). Consumers may oppose genetically modified (GM) food, fearing that the products may cause allergic reactions (e.g., Brazil nut albumins in transgenic soybean). The modified organisms develop antibiotic resistance (in case antibiotic resistance genes were used in the transformation vectors) or the transgene may be transcribed and translated into harmful substances. Lectins and alkaloids in the GMO may create human or environmental hazards (e.g., transmitting glyphosate herbicide-resistance by cross-pollination to weeds [*Cruciferae*], harming useful insects [e.g., neuropteran lacewings] or other species such as the Monarch butterfly [by Bt]). Ecologists have expressed concerns about the potential selective advantage of genetically modified plants in the natural environment. In a 10-year-long study of rape, maize, beet, and potato carrying various transgenes, it was found, however, that in general these were no more invasive than conventional crops (Crawley MJ et al 2001 Nature [Lond] 409:682). Although the actual extent of cross-pollination between transgenic and wild type plants is difficult to determine, indirect assessment may be feasible and useful (Wilkinson MJ et al 2003 Science 302:457).

Figure G54. Monarch (*Danaus*) butterfly larva

Transgenic rice producing more β-carotene and accumulating more iron may not entail any danger, but can reduce malnutrition, anemia, and some kinds of blindness in the underdeveloped areas of the world. It is worth considering that the transgenic organisms may be easier, cheaper, and safer to produce because of they offer resistance to pests and diseases and facilitate the curtailing of hunger. The extensive use of chemical pesticides may be reduced. Insect-resistant GM rice yields more and protects the health of farmers because pesticides do not harm the workers (Huang J et al 2005 Science 308:688). These opposing facts may mandate some regulations and/or labeling of the products and further research to clarify the cost/benefit dilemmas. Genetically modified proteins in excess of 0.1% are detectable by ELISA and PCR detects DNA modifications when present at 0.01% in the sample. By 2005, more than 12% of the crops were transgenic and the acreage has been increasing since, without any evidence of harm to the consumer (Raven PH 2005 Proc Natl Acad Sci USA 102:13003).

Rainbow trout (*Onorhynchus*) or salmon carrying engineered growth hormone genes may grow dramatically larger, especially the non-domesticated forms, which had not been subjected to selection for increased productivity. Genetically engineered cows may produce milk with higher β- and κ-casein (Brophy B et al 2003 Nature Biotechn 21:157). One study of cattle produced by somatic cloning (offspring obtained by transfer of somatic cell nuclei into enucleated eggs and subsequent pregnancy and birth) was analyzed in detail in comparison with sexually produced progeny for the normal milk composition, including antibodies. No significant differences were detected. In the comparative analysis of the meat no significant differences were found, except higher fatty acid components in the muscles and the increase mesentery fat (in the membranes covering internal organs) of the modified animals. Internal organs were histologically analyzed for possible pathological changes and abnormalities. In the kidney and urinary ducts, calculi (mineral stones) were found in the clones but these were often detected in normal beef

cattle. This relatively small-scale study does not indicate differences beyond the range of natural variations of the breeds (Tian XC et al 2005 Proc Natl Acad Sci USA 102:6261). Another study with potatoes transgenic for insulin-type fructans (sucrose: sucrose 1-fructosyl transferase and fructan:fructan 1-fructosyltransdferase) indicated overall substantial similarity in composition compared to the non-transgenic (original) cultivar, as demonstrated by gas chromatography, capillary electrophoresis, and mass spectrometry (Catchpole GS et al 2005 Proc Natl Acad Sci USA 102:14458).

One must keep in mind that a type of genetic modification, selection, raised the sugar content of beets from ~2% to ~20% from the middle of the eighteenth century to the present. Similarly, purposeful plant breeding increased maize production from about 1.25 metric tons/hectare to ~15 tons since the 1930s. The "green revolution" doubled cereal production since the 1960s. Nevertheless, even today about 40,000 children die daily from malnutrition-related diseases. Obviously, technological progress will involve a trade-off. The only question is whether it is worth the exchange. There was a general fear in the 1970s about the use of recombinant DNAs even for laboratory purposes. Most of these fears turned out to be unfounded but certain types of genetic engineering (e.g., using toxin genes) can be carried out only in a highly controlled environment and only when there is a special, justified need. The arguments against and for genetically modified organisms must be based on scientifically validated facts, rather than on political views or preconceived notions. Existing information indicates relatively fast (100–150 days) decomposition of most (60–70%) of the Bt toxin in soil and even in plant tissues. Paracelsus/Theophrastos of Hohenheim (1493–1541), the 'Luther of Medicine', remarked: "Guilty is he who does not know it properly and who does not apply it properly" (see Fig. G55).

Figure G55. Paracelsus

Interestingly, William Shakespeare in his play *Winter's Tale* (1611) (Act. 4, Scene 4) addressed the problem of genetically modified organisms:

"POLIXENES
Say there be;
Yet Nature is made better by no mean
But Nature makes that mean: so, over that art
Which you say adds to Nature is an art
That Nature makes. You see, sweet maid; we marry
A gentler scion to the wildest stock,
And make conceive a bark of baser kind
By bud of nobler race: this is an art
Which does mend Nature change it rather, but
The art itself is Nature." (I am indebted to Professor AT Szabó for calling my attention to this quotation).

The genetic and ethical problems relevant to inheritable genetic modification of humans can be accessed on the WEB: http://www.aaas.org/spp/sfrl/projects/germline/report.pdf. ►Asilomar conference, ►biohazards, ►pollen, ►chloroplast genetics, ►recombinant DNA and biohazards, ►xenotransplantation, ►targeting genes, ►stem cells, ►nuclear transplantation, ►transplantation of organelles, ►biotechnology, ►*Bacillus thüringiensis*, ►Bt, ►gene therapy, ►input trait, ►pest eradication, ►refuge, ►RBF, ►terminator technology, ►T-GURT, ►patent, ►fructans; Wolferbarger LL, Phifer PR 2000 Science 290:2088; Quist D, Chapela IH 2001 Nature [Lond] 414:541; Dale PJ et al 2002 Nature Biotechnol 20:567; Hare PD, Chua N-H 2002 Nature Biotechn 20:575; Vasil IK 2003 Nature Biotechnol 21:849; environmental contamination: Stewart CN et al 2003 Nature Rev Genet 4:806; transgenic livestock: Clark J, Whitelaw B 2003 Nature Rev Genet 4:825; public concerns with GMOs: Hailds R, Kinderlerer J 2003 Nature Rev Genet 4:819; http://www.nbiap.vt.edu; www.usia.gov/topical/global/biotech; http://usbiotechreg.nbii.gov/; http://www.colostate.edu/programs/lifesciences/TransgenicCrops.

GMP: Guanosine monophosphate.

GMS (genomic mismatch scanning): A method designed to scan large genomic DNA samples for differences in order to identify alterations, e.g., those responsible for hereditary disease. The principles are as follows: two DNA samples (diseased and healthy) are digested with restriction endonuclease. Fragments of one of the samples are methylated. Then both samples are denatured and allowed to hybridize. From re-annealed DNA only those strands are subjected to further study, which are hybrids (i.e., one of the two strands is methylated but other is not). These hybrids are exposed to bacterial mismatch repair enzymes that recognize mismatches and at that site nick the unmethylated strand. The nicked strands

are then removed and the intact duplexes retained. These would be expected to include the desired marker(s). The method is very elegant in principle but cannot yet be applied to the very complex human genome with great amount of redundancy and complexity. Single genetic regions can, however, be studied with the aid of array hybridization. ►RDA, ►mismatch repair, ►genetic screening, ►array hybridization; Mirzayans F, Walter MA 2001 Methods Mol Biol 175:37.

Gnotobiota: The known microbes (animals and plants) associated with laboratory animals. The animals might be raised under germfree conditions and infected with a single, specific bacterium.

GnRHA (gonadotropin-releasing hormone agonist): When administered at a constant rate, GnRHA shuts down mammalian reproductive functions and induces a condition resembling the menopause. It can be employed as a fertility-controlling agent but must be supplemented with periodic treatments with other hormones to prevent menopause-like side effects. It can be also used to save an implanted ovum or zygote by preventing ovulation. GnRHA has many other medical applications. ►gonadotropin releasing factor, ►egg donation, ►in vitro fertilization, ►ART, ►menopause, ►menstruation; Smitz J et al 1992 Hum Reprod 1:49.

GNRP (guanine nucleotide releasing protein): It is involved in signal transduction with RAS and affect several cellular functions. A rather detailed review of its basic function is in Quilliam RL et al 2002 Progr Nucleic Acid Res Mol Biol 71:391). GNRP, when activated by receptor tyrosine kinase in the signal transduction pathway, a RAS protein switch is turned on. ►RAS, ►signal transduction; Marshall M 1995 Mol Reprod Dev 42[4]:493.

GO: A dormant stage of cell divisions in fission yeast. ►cell cycle, ►*Schizosaccharomyces pombe*

GO: ►gene ontology

G_o Protein: A subunit of the trimeric G-protein; it activates K^+ channels and shuts down Ca^{2+} ion channels. Mutations in the gene encoding it cause behavioral anomalies in *Caenorhabditis* similar to those caused by a defect in the serotonin receptor. The main symptoms are hyperactivity, premature egg laying, and male impotence due to defects in neuronal and muscle functions. ►signal transduction, ►ion channels, ►serotonin, ►G_α

GO Units: ►gene ontology

Goat (*Capra hircus*): 2n = 60. It was probably the first large herbivorous domesticated animal. (See MacHugh DE & Bradley DG 2001 Proc Natl Acad Sci USA 98:5382, http://locus.jouy.inra.fr/cgi-bin/lgbc/mapping/common/intro2.pl?Base=goat).

Goat-Sheep Hybrids: The domesticated sheep (*Ovies aries*, 2n = 54) can be impregnated by the domesticated goat (*Capra hircus*, 2n = 60), but the hybrid embryo rarely develops normally although, occasionally some hybrids do grow up. ►animal species hybrids; Hancock JL et al 1968 J Reprod Fertil3:29; Ilbery PL et al 1967 Aust J Biol Sci 20:1245.

GOBASE: An organelle genome database. ►organelle genetics, ►OMIA; http://megasun.bch.umontreal.ca/gobase/; http://gobase.bcm.umontreal.ca/.

GOGAT: Glutamine-2-oxoglutarate transferase. ►nitrogen fixation

Goiter, Familial: A collection of various metabolic anomalies involving enlargement of the thyroid gland that may become obvious by viewing the neck. The defect may involve various dominant or recessive mutations in the thyroglobulin gene. The thyroglobulin gene (TG) is located in human chromosome 8q24 extending to about 300-kb genomic DNA, containing 37 exons and large introns. The dimeric thyroglobulin protein has a molecular weight of ca. 660,000. This protein is iodinated at tyrosine residues to form mono- and diiodotyrosines. *Thyroxine* is a tetraiodothyronine but *triiodothyronine* is also formed upon activation by peroxidase. The iodinated proteins are transported by the blood, increase the metabolism, and regulate the function of the nervous system, kidney, liver and heart. *Hyperthyroidism* occurs due to the overproduction of iodinated thyroglobulin hormones, resulting in goiter, fast heart rate, fatigue, muscular weakness, heat intolerance and sweating, tremors, and emotional instability. Excessive secretion of thyroid hormones is referred to by the synonymous *Graves* or *Basedow* disease, with susceptibility controlled by several sites (14q31, 6p21, 7q, 8q, 10q, 2q33, 20q13, Xq21). The New Graves Disease maps to 18q21. The latter condition may or may not be genetic, although its frequency may be quite high (0.008). The basic defect may involve autoimmunity of the receptor of the hormone. *Hypothyroidism* is the consequence of the underproduction of the thyroid hormone, resulting in fatigue, lethargy, low metabolism, cold-sensitivity, and menstrual problems in females. This condition may lead to *cretenism*, which is most commonly caused by failure of releasing *thyrotropin*, the glycoprotein thyroid-stimulating hormone of the anterior pituitary. Cretenism also means an arrest of physical and mental development, and is caused by this hormonal deficiency.

Hypothyroidism may also lead to deafness. Defects in deiodination of iodotyrosines could also cause hypothyroidism. *Permanent congenital hypothyroidism* has a prevalence of ~3 to 4 × 10^{-4} in newborns and unless it is caused by hypothalmic or pituitary defects, it is accompanied by over-expression of the thyroid-stimulating hormone and lower-than-normal thyroid function or thyroid dysgenesis. Thyroid therapy is required within the first two months to prevent neurological damage (cretinism). In some cases, mutation of the Pax8 gene at human chromosome 2q12-q14 has been detected. PAX8 seems to be required for the differentiation of endoderm primordia into thyroxin-producing follicular cells. Goiter-like diseases are known in the majority of mammals. Thyroxine binding globulin is encoded in human chromosome Xq28 and a thyroxin binding serum globulin is autosomal. The multinodular goiter—with 5:1 female:male ratio—has been assigned to Xp22. ►hyperthyroidism, ►Hashimoto disease, ►animal hormones, ►tyrosine, ►thyroid stimulating hormone, ►PAX, ►NIS, ►Pendred syndrome, ►CTLA-4; Tomer Y et al 1997 J Clin Endocr Metab 82:1645; Vaidya B et al 2000 Am J Hum Genet 66:1710.

Gold Standard Test: The gold standard test in clinical trial involves (i) random allocation of the treatment, (ii) concurrent control and (iii) double blind trial of the drug or the treatment. ►double-blind test

Goldberg-Hogness Box: ►Hogness box

Goldenhar Syndrome: Autosomal dominant and recessive forms with different expressions of facial and other developmental deformities.

Golgi Apparatus: Flat vesicles (cisternae) containing cellular storage and transport material involved in glycosylation, sulfation, proteolysis, etc., in animals (see Fig. G56). Although the model shown indicates transport in one direction, evidence is accumulating for transport by the cisternae from the cell membrane toward the endoplasmic reticulum. The *coat protein I* (COPI) and SNARE seem to play important role in the transport. The homologous structures in plants are frequently called dictyosomes. Some of the Golgi structures are located next to endoplasmic reticulum and are called *cis Golgi*; others occur at a distance (*trans Golgi*). In these vesicles, some proteins are modified after the completion of their synthesis in the endoplasmic reticulum. In the stacked fragments, some of the functions seem compartmentalized (Yano H et al 2005 Proc Natl Acad Sci USA 102:13467). The Golgi complex is inherited by fragmentation of the elements into small vesicles, which are distributed at random during mitosis. According to more recent observations, the distribution may not be entirely random. The fragments were found to aggregate around the mitotic spindle pole and the motor proteins pulled them into the daughter cells. After cytokinesis, Cdc2 supposedly phosphorylates the

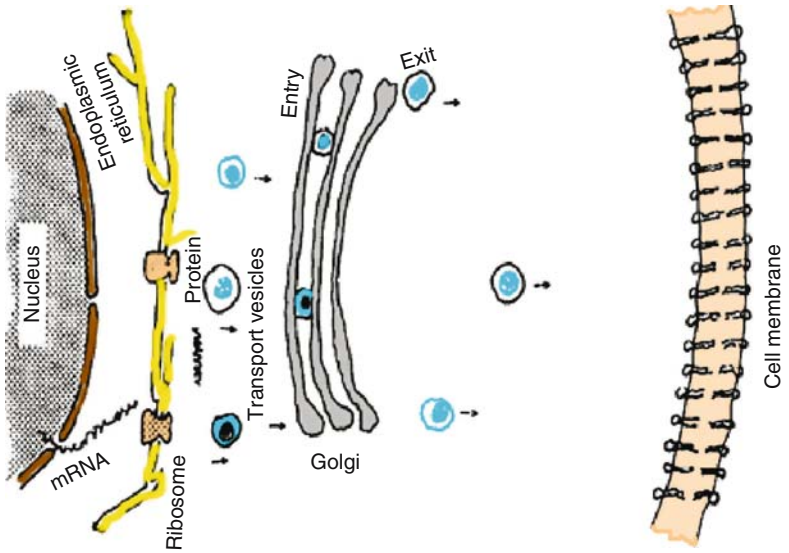

Figure G56. Transport function of the Golgi apparatus. From the nucleus, through the nuclear pores, mRNA reaches the ribosomes sitting on the endoplasdmic reticulum (ER). The protein synthesized may enter the lumen of the ER with the assistance of a signal peptide transfer particle-mediated system. The proteins may emerge then in transport vesicles to enter the Golgi at the cis side end, exit at the" bulbous" ends of the stacked membrane vesicles. In the golgi the proteins are glycosylated and modified post-translationally

p115 receptor and then of the fragments the Golgi structure is reconstituted probably via the endoplasmic reticulum. The exact mechanisms are not generally agreed upon, however.

►endoplasmic reticulum, ►dictyosome, ►cell structure, ►trans-Golgi network, ►cis-Golgi, ►RAB oncogene, ►SNARE; Allan BB, Balch WE 1999 Science 285:63; Roth MG 1999 Cell 99:559; Müsch A et al 2001 EMBO J 20:2171; Allan VJ et al 2002 Nature Cell Biol 4:E236; Shorter J, Warren G 2002 Annu Rev Cell Mol Biol 18:379; Golgi maturation: Losev E et al 2006 Nature [Lond] 441:1002; Matsuura-Tokita K et al 2006 Nature [Lond) 441:1007.

G_{olf}-Protein: A trimeric G-protein; stimulating cAMP in the control of olfactory neurons. ►G-proteins, ►olfactory, ►olfactogenetics

GOMBO Syndrome: Autosomal recessive growth retardation with eye, brain, skeletal, and mental defects. ►growth retardation

Gomori's (Gömöri's) Stain: Gomori's stain is used primarily for histological localization of phosphatases and lipases in sectioned specimens by the light microscope. The trichrome stain contains, in 200 mL H_2O, chromotrope 2R (2[phenylazo]chromotropic acid) 1.2 g, fast green o.6 g, phosphotungstic acid 1.6 g, and glacial acetic acid 2mL. ►stains, ►histochemistry; Gomori G 1950 Am J Clin Path 20:665.

Gonadal Dysgenesis: The failure of normal differentiation of the gonads (ovary, testis). It is a common cause of sterility in aneuploids. Gonadal dysgenesis of XY chromosomal constitution occurs in mammalian females. They have "streak gonads" and fail to develop the secondary sexual characteristics. Gonadal neoplasias are frequent in these individuals. It has been shown that the testis-determining factor resides in a Y-chromosomal segment and either deletion or base substitution may lead to an inactive human SRY (Yp11.3) product, a DNA binding protein involved in testis determination. Transfection of the TDY (the mouse homolog of SRY) DNA into XX mouse was found to induce male development. Gonadal dysgenesis may occur also in XX females, which have higher than normal level of gonadotropins and underdeveloped male gonads. In XY females (GDXY, Xp22.11–21.2) gonadal dysgenesis causes multiple developmental anomalies and hypermuscular appearance. Premature ovarian failure (2p21-p26) is a mutation in the follicle-stimulating hormone receptor. The cause of the dysgenesis may reside either in autosomal recessive genes or in the sex chromosomes. Mutation in the human desert hedgehog (12q12-q31.1) may lead to partial gonadal dysgenesis and neuropathy. ►H - Y antigen, ►FSH, ►testicular feminization, ►Swyer syndrome, ►Turner syndrome, ►Smith-Lemli-Opitz syndrome, ►hermaphroditism, ►pseudohermaphroditism, ►SRY, ►SOX, ►campomelic dysplasia, ►gonad, ►hedgehog, ►sex reversal

Gonadoblastoma: A rare type of neoplasm containing germ cell, immature Sertoli-like cells, and cells resembling the granulosa cell of the ovarian follicles. Mutation in a 1–2 Mb fragment encoding the testis-specific protein (TSPY) near the centromere in the short arm of the human Y chromosome may be responsible for it. ►Frasier syndrome

Gonadotropin: A group of hormones that regulate gonadal and placental functions. ►MSAFP, ►GnRHA, ►puberty

Gonadotrophin: Same as gonadotropin.

Gonadotropin-Releasing Factor: ►luteinizing hormone-releasing factor

Gonadotropin-Releasing Hormone Agonist: ►GnRHA

Gonads: The organs of gametogenesis, such as ovary and testis. In *Drosophila*, the male gonad includes about 15, the female about 12 cells that further proliferate during embryonic differentiation, and there are 60–110 primordial germ cells by the late instar stage (see Fig. G57). In the mouse, the primordial germ cells appear seven days after mating (dpc). In the female, the primordial germ cells stop mitosis 13–15 dpc and meiosis is initiated immediately. Spermatogenesis begins 5–6 days after birth and on the 9th day proleptotene spermatocytes appear.

By day 18, haploid spermatids are formed followed by spermiogenesis. The general pattern of gonadal development is similar in mammals too, as shown in the diagram. The testes and the ovary differentiate from sex neutral structures. From the Müllerian ducts, the fallopian tube, and at its base the uterus develops, while the primitive gonad is converted into the ovary. From the Wolffian duct, the vas deferens, and at is base the seminal vesicles are formed, and the primitive gonad is converted into testis. In the drawing (for saving space) only half of the female and male sexual apparatus is shown. At the undifferentiated stage, the steroidogenic factor, SF-1, the Wilms tumor 1 Zinc-finger protein, and the homeobox gene Lim-1 are important. During the sexual differentiation stage, the Y chromosomal testis determining gene, SRY, the autosomal male sex differentiation factors SOX9, glucoprotein WNT4 (female), WT1 (male), SF-1, and a general sexual differentiation factor, DMRT1 play key roles.

Müllerian inhibitory substance inhibits testosterone synthesis in the female, whereas promotes it in the male. The Dax-1 protein (originally considered as an

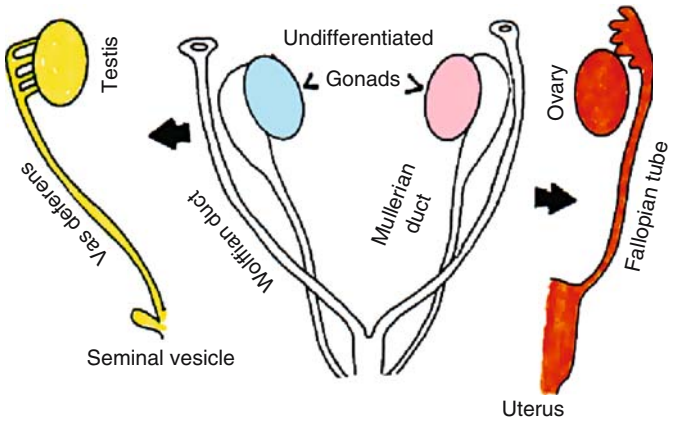

Figure G57. Gonads. The diagram was redrawn after H. Eldon Sutton & RP Wagner 1985 Genetics. A Human Concern. Macmillan, New York

ovary promoting substance) at higher dosage suppresses male development. The InsL3 protein has a role for the gubernaculum (a ligament) facilitating the descent of the testes into the testicular bag, the scrotum. Numerous other proteins are also involved. ►Müllerian duct, ►Wolffian duct, ►gametogenesis, ►cell cycle, ►germline, ►dpc, ►mismatch repair, ►sex, ►sex reversal, ►GDNF, ►puberty; Roberts LM et al 1999 Am J Hum Genet 65:933; Koopman P 2001 Curr Biol 11:R481; Mackay S 2000 Int Rev Cytol 200:47; Kobayashi A, Behringer RR 2003 Nature Rev Genet 4:969; Brennan J, Capel B 2004 Nature Rev Genet 5:509; http://www.germonline.org/.

Gonidia: Specialized asexual reproductive cells.

Gonioblast: A cell resulting from asymmetric division in the germline; the original stem cell gives rise by division to a new stem cell and to the gonioblast, which is destined for differentiation.

Gonochorism: As per gonochorism, normally the species has separate male and female individuals. ►dioecious, ►hermaphrodite

Gonocytes: Progenitors of the spermatogonia. ►spermatogonia, ►gametogenesis

Gonosome: The sex chromosomes as distinct from the autosomes. ►autosome, ►sex chromosome

Gonotaxis: A genetically controlled ability of eggs or spermatozoa to be preferentially involved in the formation of a zygote. ►meiotic drive

Gonzalo of Spain: A great grandson of Queen Victoria of England who inherited from his grandmother, Beatrice, the classic X-chromosomal hemophilia gene and died by hemorrhage in an automobile accident at age 20. ►hemophilia, ►anticoagulation factors, ►Queen Victoria

Good Genes: The expression "good genes" has a double meaning: (i) genes that are advantageous for the individual or for evolution (eugenics), and (ii) genes with good penetrance and expressivity and thus facilitating analysis of their inheritance and function. ►penetrance, ►expressivity

Goodness of Fit Test: ►chi square

Goodpasture Syndrome: An autosomal recessive autoimmune reaction of the basement membrane of the renal glomeruli and the lung. The basic defect is in the α-chain of collagen type 4. Although some cases indicated familial occurrence, most likely they were exposed to similar (viral, bacterial hydrocarbon) environmental factors. ►autoimmune disease, ►collagen, ►basement membrane, ►Wegener granulomatosis; Papiris SA et al 2007 Critical Care 11:213)

GOOSE: *Anser anser*, 2n = 80.

Gooseberry (*Ribes* spp): Tart berry fruits; 2n = 2x = 16.

Gopher: Genetic information databases, accessible through INTERNET electronic networks. Software for gopher is free and can be obtained with FTP (file transfer protocol) by gopher@boombox.micro.umn.edu. (The name comes from a ground squirrel).

Gordon Syndrome (PHA2A, 1q31-q42): The Gordon syndrome involves hypertension and high salt concentration in the blood with normal filtration rate in the kidneys. It is also called pseudohypoaldosteronism II. Similar disorders occur at 17q21-q22 and 12p13. ►hypertension, ►pseudohypoaldosteronism, ►Liddle syndrome

Gorilla: ►Pongidae, ►primates

Gorlin-Chaudhry-Moss Syndrome: A very rare autosomal recessive craniofacial dysostosis (head malformation), excessive hairiness, heart and lung defect

(patent ductus), and hypoplasia (reduced growth) of the female external genitalia. ►hypertrichosis, ►craniosynostosis

Gorlin-Goltz Syndrome ►nevoid basal cell carcinoma

Gossypium: (cotton): A member of the *malvaceae* family of plants. Economically the most important are the long staple upland species, *G. hirsutum* (2n = 4x = 52) that produces 95% of the cotton fibers, and *G. barbadense*, an extra long staple (Sea Island; Egyptian) cotton (also a tetraploid), contributes about 5% of the world fiber. There are 30 diploid species. *G. herbaceum* and *G. arboreum* carry the *A* genome and are the only diploids with spinnable lint. The *B* genome is represented by North-African and Cape Verde Islands species. The *C* genome occurs in Australian diploids. *D* genome plants occur in Mexico, Peru, Galopagos Islands, and the USA. The *E* genome species occur in North Africa, Arabia, and Pakistan. The *F* genome is represented by a single African species. The new world tetraploids contain the *A* and *D* genomes. Most of the cottons are naturally cross-pollinated but tolerate inbreeding. The various genomes are distinguished primarily on the basis of chiasma frequencies and the number of univalents in the species hybrids, although some chromosome morphological differences also exist. The seed of the plants would be potentially useful for food but it contains the toxic gossypol (terpenoids), which provides protection against herbivorous insects. RNAi technology can disrupt gossypol biosynthesis in cottonseed by interfering with the expression of the δ-cadinene synthase gene during seed development (see Fig. G58). This genetic modification does not affect gossypol level in the leaves but reduces it to apparently safe level in the seeds. (Sunilkumar G et al 2006 Proc Natl Acad Sci USA 103:18504; ►terpene; http://www.tigr.org/tdb/tgi/.

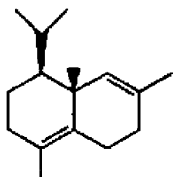

Figure G58. Cadinene

Gout: A complex hereditary disorder of the joints leading to arthritis caused by overproduction and/or underexcretion of uric acid. In one autosomal recessive gout, glucose-6-phosphatase is deficient. In the X-linked gout, hypoxanthine-guanine phosphoribosyl transferase deficiency exists (see Fig. G59). Some gouts are associated with increased turnover of nucleic acids. Autosomal dominant and polygenic forms are also known. Gout may be asymptomatic initially but at later stages the joints and the kidney may become permanently injured. (See Fig. G59). The first sign is pain in the great toe but it may spread to other parts of the foot and also to the wrists and other body parts. The prevalence may vary in different populations from 0.2 up to 10%. The serum urate level may vary from 6 to over 9 mg/100 mL serum. Generally, fewer women than men suffer from it, but in women the gout may be more sever and destructive. If the diet is very low in proteins, gout may not appear. The uric acid crystals (urate) activate the Hageman factor in the viscous fluid (synovia) of the joints that in turn sets into motion a series of events leading to inflammation. Uric acid crystals activate the inflammasome (Martinon F et al 2006 Nature [Lond] 440:237). In chickens that lack the Hageman factor or in dogs with suppressed number of leukocytes (leukopenia), the inflammatory reaction fails, indicating the role of these factors in gout attack. After the first attack, the gout symptoms apparently disappear for weeks or many months, only to return with greater strength. The chronic arthritic gout may produce ulcerating tophi (a chalky urate deposit) in the joint and may cause severe deformation of the affected area. Urates may be deposited also in kidneys, cartilage, and bone tissues. Tophi may be present at the fingertips, palms, soles, eyelids, nasal cartilages, and in the eye. Rarely, it is also observed in and on the penis, the aorta, on the heart wall (myocardium), valves, tongue, the entrance of the larynx (epiglottis), and vocal cords. Urate deposits occur in between the vertebral disks and cartilages. There is very little or any urate in the spinal cord or in the nervous system. In the kidney medulla, urate crystals may accumulate and kidney stones may be formed (lithiasis) in 20 to 40% of the affected persons. Gout is frequently associated with obesity, and hyperuricemia is common in case of diabetes mellitus. Hyperlipoproteinemia and high triglyceride levels are common in gout. Alcoholism may aggravate hyperuricemia. Serum urate levels are about the same in people of European origin, in North-American Indians, Hawaiians, Japanese, and Chinese. In some Polynesians and Australian aborigines and South-American Indians, the urate level may be higher. Overproduction of uric acid is correlated to the availability of L-glutamine and phosphoribosyl-1-pyrophosphate that are rate-limiting precursors in purine biosynthesis. Uric acid is dramatically overproduced in case of (partial) deficiency of hypoxanthine-guanine-phosphoribosyltransferase (HPRT). Glucose-6-phosphatase and glutathione reductase also increase uric acid synthesis.

Exposure to lead may increase the occurrence of gouty arthritis due to inflammation of the kidney (saturnine gout). Starvation, Down's syndrome, and psoriasis (a skin disease causing silvery scaling and plaques) may increase uricemia. Acute attacks of gout may be successfully treated with colchicine and allopurinol, an inhibitor of xanthine oxidase. Both of these compounds may be highly toxic. Gout due to genetically determined factors is called primary gout, the secondary gout is the result of ingestion of certain chemicals and drugs. Many famous historical persons were apparently afflicted by gout: Medici, Newton, Darwin, Luther, Calvin, Benjamin Franklin, Cotton Mather (who reported plant hybrids in America in 1721), and others. Recently by the use of scanning electronmicroscopy in the mummified finger tip of the Holy Roman Emperor Charles V (King Charles I of Spain), uric acid crystals were positively identified after almost a half a millennium, explaining the cause of the illness of this powerful ruler (Ordi J et al 2006 New England J Med 355:516). His seated pose on a special chair, painted by the famous artist Titian, also supports other historical records of his debilitating affliction. ►Lesch-Nyhan syndrome, ►colchicine, ►antihemophilic factors, ►Hageman factor, ►inflammasome; Chen SY et al 2001 Metabolism 50:1203.

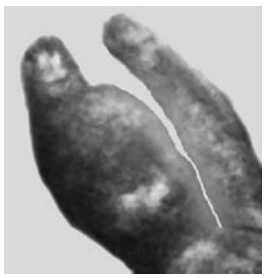

Figure G59. Gouty fingers

gp: In general, the abbreviation for glycoprotein; the gp is usually followed by a number.

gp: Gene of phage, e.g., the first gene of λ phage entering the capsid is *gpNu*.►lambda phage

GP32 Protein (of phage T4): GP32 protein is required for (i) configuration of the single-strand DNA (ssDNA) to accommodate the replisome, including DNA polymerase, (ii) to melt adventitious secondary structures, (iii) to protect ssDNA from nucleases, and (iv) to facilitate homologous recombination. ►replication fork, ►replisome

gp39: Same as the CD40 ligand.

gp120: The HIV glycoprotein that activates B lymphocytes with receptors carrying variable heavy chain (V_H3) immunoglobulins. ►HIV, ►immunoglobulins, ►B lymphocytes

gp130: A ~101-kDa (without glycosylation) subunit of the interleukin 6 family receptors, encoded at 5q21. It is a signal transducer chain for IL-6, IL-11, LIF, OSM, and CNTF. ►interleukins, APRF; Chow D-c et al 2001 Science 291:2150.

Gp190: A ~121-kDa (without glycosylation) subunit of various cytokine receptors, encoded at 5p12-p13.

GPA: Genes of yeast homologous to Gα cDNAs, involved in mammalian G-protein coding. GPA1 protein is 110-, and GPA2 is 83-amino-acid longer at the N termini than the mammalian proteins. GPA1 may be involved in mating signal transduction, GPA2 controls cAMP level. GPA1 (α subunit of G-protein) plays a negative role (growth arrest) in mating signal transduction, whereas the *STE4/STE18* (β, γ subunits) are responsible for a positive transducing signal (enhancement) for mating. ►G proteins, ►cAMP, ►STE, ►mating type determination in yeast

GPCR (G protein-linked receptors): ►signal transduction

G6PD: The glucose-6-phosphate dehydrogenase deficiency is responsible for one type of hemolytic anemia in humans; it is controlled by a sex-linked recessive gene (map location X28). It catalyzes the reaction G6P + TPN^+ + H_2O ⇆ 6-phosphogluconic acid + TPNH + H^+. ►Zwischenferment, ►glutathione, ►glucose-6-phosphate dehydrogenase, ►malaria

GPI Anchors: Glycosyl-phosphatidylinositol cell surface-membrane proteins.

G1ps: G1 (gap 1) pre-synthetic phase (preceding S phase) of mitosis. ►cell cycle, ►mitosis

GPR: Co-receptors of HIV and SIV. ►acquired immunodeficiency syndrome

G-Quadruplexes: Four-stranded guanine-rich structural elements of the telomeres. G-quadruplexes may be directly involved in gene regulation at the level of transcription. In promoter regions of more than 40% of the human genes (1 kb upstream of the transcription start site), one or more quadruplex motifs exist. The promoter quadruplexes are strongly associate with nuclease hypersensitive sites. Regions of the human genome that are both nuclease hypersensitive and within promoters show 230-fold enrichment of quadruplex elements, compared to the rest of the genome (Huppert JL, Balasubramanian S 2007 Nucleic Aids Res 35:406). ►telomeres, ►telomerase, ►promoter, ►tetraplex; Parkinson GN et al 2002 Nature [Lond] 417:876.

G_q-Protein: A member of the trimeric G-protein family; activates phospholipase C-β and responds to

acetylcholine. ►G-proteins, ►signal transduction, ►phospholipase; ►acetylcholine, ►acetylcholine receptors

Graafian Follicle: Small sac-like structures on the ovary of mammals containing a mature egg (secondary oocyte). The release of the egg is called ovulation and afterwards the follicle is transformed into a corpus luteum. ►luteinization, ►corpus luteum

Gradient Centrifugation: A technique of separation of cells, subcellular organelles, and macromolecules on the basis of their density and shape by centrifugation. High-speed centrifuges may separate the larger particles while for macromolecules ultracentrifuges are used. The medium of separation may be sucrose, percol, cesium salts, etc. The material is placed on the top of the medium, which is made in various concentrations in steps; i.e., first we place in the centrifuge tube 60% sucrose, layer on top of it 40%, then 20% solutions. Alternatively, cesium salts may be used at an average density of the macromolecule. In the latter case, during high-speed centrifugation the medium forms a continuous density gradient. In either case, the material will accumulate either at the top of the step (layer) which has higher density than the substance to be separated or it will accumulate as a band in the medium that corresponds to the density of the macromolecule (DNA, ribosomes, viral particles). ►ultracentrifuge, ►buoyant density, ►DNA density

Grading Up: In the process of grading up an animal breed is repeatedly backcrossed with males of another, more desirable livestock to improve its productivity and/or quality. ►gain

Gradualism: As per gradualism, evolution is supposed to proceed by slow acquisition of adaptive mutations in the Darwinian sense. (See Darwinian evolution; punctuated evolution).

Graeco-Latin Square: An experimental design similar to the Latin Square (see Fig. G60). Three or more variates, e.g., A, B, C, each are tested under three or more different treatments, e.g., 1, 2, and 3, and the results are usually evaluated by analysis of variance. One such arrangement is shown in the box. ►Latin Square, ►analysis of variance, ►factorial experiments

A_1	B_2	C_3
B_3	C_1	A_2
C_2	A_3	B_1

Figure G60. Layout of simple Graeco-Latin square

Graft: Transplantation of plant or animal tissues by surgical means.

Graft Hybrid: Chimera produced by fusion of two genetically different cells in tissues. The followers of the Mitchurin, Lysenko, and Glushchenko's group of Soviet ideologues postulated non-chimeric type graft hybrids. They referred to them also as vegetative hybrids, and claimed that grafting alters the hereditary material of both graft and scion. These claims were not reproducible by appropriate methods of experimentation, and several of the results were due either to ignorance or deliberate deception. When the mitchurinian experiments were re-examined under well-defined conditions, no acceptable evidence indicated the existence of vegetative hybridization (Stubbe H 1954 Kulturpflanze 2:185; Böhme H 1957 Ztschr Pflanztg 38:37). Certainly, viruses can be transmitted between stock and scion by grafting and this may result in an altered phenotype. But, this can hardly be considered a genetic alteration. Infection of plant (or other cells) by genetic vectors containing foreign genes can result in transgenic individuals because of the transfer of DNA. The "plastic substances" of vegetative hybridizers have no substance in the twenty-first century when all assertions need proof to become acceptable. The assertion (Liu Y 2006 Adv Genet 56:101) that doubts about graft hybridization were "squarely contradicted by a substantial body of reliable experimental evidence (Landman 1963)" is not justified in view of the experiments reviewed and the conclusions of Landman (1963 BioScience 43:696) who does not even mention graft hybridization, although he reviews old and new evidences for inheritance of acquired characters, including "epinucleic inheritance". Liu acknowledges, "Further evidence will be required to elucidate molecular mechanisms underlying graft hybridization". Unfortunately, even the data on graft hybridization are highly questionable. Linnaeus stated already in 1735 "Knowledge… built on opinion only, will not stand". Unsubstantiated findings are not just scientifically unacceptable but may be very detrimental to applications in agriculture or medicine. ►acquired characters

Graft Inheritance: ►cortical inheritance

Graft Rejection (GVHD): The manifestation and result of histoincompatibility between transplanted tissues: host-versus-graft disease. If oocytes of an individual mouse are stimulated to parthenogenetic development, histocompatible tissue can be produced (Kim K et al 2007 Science 315:482). ►cytotoxic T cells, ►HLA, ►MHC, ►mixed lymphocyte reaction, ►microcytotoxicity assay, ►therapeutic cloning, ►graft-versus-host disease, ►stem cells, ►MHC

GVDH (graft versus hoist disease): ►graft rejection

Grafting: Grafting transfers one piece of tissue or an organ from one place to another within the body or to another body. Horticulturists have practiced grafting of plants as a means of propagation. Grafted roses and other ornamentals, as well as fruit trees assure the maintenance of genetic uniformity in the grafts where multiplication by seed would produce a heterogeneous offspring because of heterozygosity at multiple loci. Some grafts are horticulturally advantageous because the rootstock may be resistant to soil-born pests and can secure crops in more valuable varieties of *Vitis vinifera* grapes. *Vitis rotundifolia*, a wild grape stock, may be 20 fold more resistant to the *Dactylosphaera vitifolii* root parasite than the standard varieties. Grafting may be used to propagate inviable plants on appropriate stocks and to study the physiological interactions between scion and stock in such complex processes as flowering response, etc. Macromolecules such as viruses may move from stock to scion through plasmodesmata. mRNA may move through the phloem and mutant phenotype may be expressed in the scion. ►transplantation, ►grafting in medicine, ►graft hybrids; Kim M et al 2001 Science 293:287.

Grafting in Medicine: Grafting is practiced in modern medicine by transplanting skin, kidneys, liver, heart and other organs. Allografts are generally incompatible with the host immune system. The immune response is controlled by a large number of genes that are part of the major histocompatibility gene families. Experimental studies on tissue transplantation are carried out with inbred strains of mice (see congenic resistant). The histocompatibility genes are codominant and F_1 hybrids between different inbred lines may accept graft from both parents, whereas the two parental lines may be incompatible with each other. F_1 hybrid generally accepts grafts also from the offspring from the later generation. The incompatibility is inherited in a Mendelian manner and 3/4 of the F_2 individuals are compatible with one or the other parent and 1/4 are not. If the number of independent histocompatibility loci is (n), $(3/4)^n$ = the number of histocompatible individuals in F_2 and in a backcross it is $(1/2)^n$. There are some confounding factors, however. Within some highly inbred lines, skin grafts from male to female may be rejected but not from female to male. This may be due to "male-specific" antigens encoded by the Y chromosome. Also, tumor tissues may be rejected when skin grafts are accepted because of tumor-specific antigens. Heterotopically (placed to a non-regular position) transferred hearts and kidneys may be accepted when skin grafts are rejected. Even apparently accepted graft may produce very low level of antibodies. Allogeneic inhibition may also occur, i.e., parental animals fail to accept transplants from their offspring, but the offspring may accept the transfer from that parent. Most of these principles of grafting were derived from studies on inbred mice strains. Grafts have another interest for medicine with the discovery of the regenerative capacity of stem cells. ►HLA, ►allogeneic, ►mixed lymphocyte reaction, ►microcytotoxicity assay, ►therapeutic cloning, ►stem cells, ►zoonosis, ►cell therapy, ►organ culture; Quisenberry PJ et al 2001 Ann NY Acad Sci 938:54.

Graft-Versus-Host Disease (GvH): GvH may arise when the grafted tissue damages the host because of the immune reaction. GvH may also be beneficial by eradicating the residual leukemia cells though the mediation of T cells and the HLA molecules of the major histocompatibility system. ►graft rejection, ►HLA, ►TIP; Kärre K 2002 Science 295:2029.

GRAIL: A gene locator/annotation program. ►gene prediction

Gram Molecular Weight: Grams of a compound equal to its molecular weight: mole.

Gram Negative/Gram Positive: Classification of bacteria depending on retention of the Gram stain (gentiana violet after an iodine stain, and then extracted by acetone or alcohol) (see Fig. G61). The outer membrane of the Gram-positive bacteria (stain blue-purple) does not have lipopolysaccharides but these are present in the membrane of Gram-negative bacteria (stain pink-red). The cell wall of Gram-positive bacteria contains peptidoglycans and teichoic acid. *Gram-positive bacteria*: *Streptococci, Staphylococci, Pneumococci, Corynebacterium, Mycobacterium*, *Bacillus anthracis*, *B. cereus*, *Listeria, Actinomyces, Streptomyces*, etc. *Gram-negative bacteria*: *Neisseria*, *Enterobacteriaceae* (*E. coli, Salmonella, Shigella*), *Haemophilus, Bordatella, Yersinia, Vibrio cholerae, Pseudomonas, Brucella, Proteus, Campylobacter, Legionella*, etc. ►peptidoglycan, ►teichoic acid

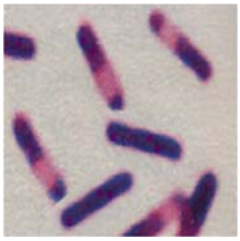

Figure G61. Gram-positive cells

Gram Stain: ►bacteria, ►Gram negative/Gram positive

Gramene (rice and other grasses database): http://www.gramene.org.

Grana (sing. granum): Dark green pile of flattened membrane vesicles (thylakoids) in the chloroplasts (see Fig. G62). ►chloroplast, ►chloroplast genetics

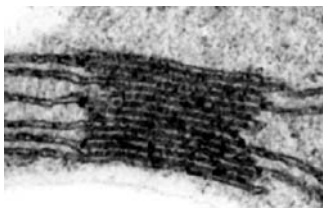

Figure G62. Granum

Grandchildless-Knirps Syndrome: In *Drosophila*, maternal effect genes cause embryonic lethality by eliminating pole cells and one or more abdominal segments. ►morphogenesis, ►pole cells, ►maternal effect genes

Granddaughter Design: An analysis of genetic linkage of quantitative loci to (usually) DNA markers among the granddaughters. The markers are identified in grandsires and sons but quantitative analysis is carried on the daughters of sons. ►QTL, ►least squares, ►RFLP, ►maximum likelihood method applied to recombination; Weller JI et al 1990 J Dairy Sci 73:2525; Cappieters W et al 1998 Genetics 149:1547)

Grande: The wild type cells of yeast in comparison with the petite mitochondrial mutants deficient in respiration. ►petite, ►mtDNA

Granin: Calcium-binding acidic proteins (21 to 76-kDa) in the Golgi network. Their function is processing secreted proteins and they are subject to processing by converting into biologically active peptides. The granin consensus bears similarity to breast cancer gene proteins, BRCA1 and 2. ►Golgi, ►breast cancer; Rosa P, Gerdes HH 1994 J Endocrinol Invest 17[3]:207.

Grantham's Rule: Highly expressed genes preferentially use, from the synonymous codons, those that have a pyrimidine at the third position of the triplets. ►genetic code, ►codon usage, ►synonymous codons; Grantham R et al 1981 Nucleic Acids Res 9:r43.

Grantham's Classification: Classification of amino acids on the basis of substitution frequencies in proteins, atomic weight ratio of non-C elements in end groups or rings to C atoms in side chains, polarity, and mol volume. Substitution frequencies agree much better with the chemical properties than with the minimum base differences in their codons. Fixation of mutations involving non-similar amino acids is relatively rare. (See Grantham R 1974 Science 185:862).

Granule Exocytosis: ►cytotoxic T cells

Granulocyte-Macrophage Colony Stimulating Growth Factor: GM-CSF (18–30-kDa monomeric glycoprotein, encoded at human chromosome 5q21-q32) activates the cells of the granulocyte pathway. Binding of GM-CSF to its receptor dimerizes the receptor and leads to activation of the Jak-STAT pathway of signal transduction. A small nucleotide, SB 247464, may serve as a non-peptidyl inducer of the oligomerization of the receptor. It may be involved in the maturation or function of special antigen presenting cells. ►lymphokines, ►neutropenia, ►signal transduction, ►antigen presenting cell; Tian SS et al 1996 Blood 88:4435; Roth MD et al 2000 Cancer Res 60:1934; Trapnell BC, Whitsett JA 2002 Annu Rev Physiol 64:775.

Granulocytes (polymorphonuclear leukocyte): Specialized white blood cells such as neutrophils, eosinophils, and basophils. They contain numerous lysosomes and secretory vesicles (granules) and play an important role in the defense system of the animal body. ►lysosome, ►neutrophils, ►eosinophils, ►C/EBP

Granulomatous Disease, Chronic (CGD): A group of X-chromosomal (Xp21.1) recessive conditions involving chronic infections, based on defects in NADPH-oxidase subunits of the neutrophils and other phagocytotic leukocytes. If the normal enzyme is activated it generates superoxide that is converted to antimicrobial hydrogen peroxide. The 91-kDa-membrane glycoprotein, a phagocyte oxidase ($gp91^{phox}$, $p47^{phox}$, $p40^{phox}$, $p67^{phox}$), is a part of the cytochrome b system. The autosomal (16q24) recessive type is deficient in cytochrome b α-subunit (CYBA) and the neutrophil cytosol factor deficiency (NCF1) form is located in chromosome 7q11.23. A third CGD (NCF2) was assigned to 1q25. The Duchenne muscular dystrophy gene may involve CGD and several other genes have bearing on the disease. ►neutrophil, ►leukocyte, ►superoxide dismutase, ►hydrogen peroxide, ►McLeod syndrome, ►muscular dystrophy, ►contiguous gene syndrome; Grizot S et al 2001 J Biol Chem 276:21627.

Granulolysin: ►cytotoxic T cell

Granum in Chloroplasts (plural grana): The multilayered thylakoids appear as dark "grains" in the chloroplasts viewed by the light microscope. ►chloroplasts, ►chloroplast genetics; see photo at grana.

Granzymes: Cytotoxic T cell serine proteases and perforin responsible for apoptosis by activating the precursor (CPP32) of the protease cleaving poly (ADP-ribose) polymerase. Granzyme B is activated in T cells and in the active form cytolytic $CD8^+$ T cells (CTL) destroy infecting particles. Besides Granzyme A and B, perforin is important for the action of CTLs. Granzymes cleave lamins and may be responsible for cytolysis. Granzyme A initiates mitochondrial damage leading to apoptosis (Martinvalet D et al 2005 Immunity 22:355). ►CTL, ►ICE, ►apoptosis, ►perforin, ►caspase, ►cathepsin, ►lamins; Kam CM et al 2000 Biochim Biophys Acta 1477:307; Zhang D et al 2001 Proc Natl Acad Sci USA 98:5746.

Grapefruit: *Citrus paradisi*, 2n = 18, 27, 36. Grapefruit juice has beneficial dietary value because of high antioxidant content and lowering the level of blood plasma lipids (Gorinstein S et al 2005 J Agric Food Chem 53:3223). Because of furanocoumarin/bergamottin content, it may interfere with or increase intestinal absorption of several drugs (statins, antihistamins, calcium channel blockers, cyclospoprin, sildenafil, multidrug transporter P-glycoproteins, etc.) and the fruit and the drugs should not be taken simultaneously or within several hours of each other. ►bergamottin, ►drug interaction; Romiti N et al 2004 Life Sci 76:293; Bailey DG, Dresser GK 2004 Am J Cardiovasc Drugs 4(5):281; drug interaction with grapefruit juice: Anonymous 2005 Obstet Gynecol 105(2):429.

Grapes: *Vitis vinifera*, 2n = 38; the *Muscadina* species, 2n = 2x = 40. The condensed tannins/proanthocyanidins, which are a products of the flavonoid pathway in red wines have protective effects against heart disease involving ventricular fibrillation and tachycardia (Pataki T et al 2002 Am J Clin Nutr 75:894). ►resveratrol; diversity and history of grape wines: This P et al 2006 Trends Genet 22:511; Sandler M, Pinder R (eds) 2002 Wine: A Scientific Exploration. Taylor & Francis, London, UK; http://mpss.udel.edu/grape/.

Grapes, Seedless: Normal diploids but a gene prevents the division of the embryo, presumably because of shortage of hormones (stenospermocarpy). ►seedless fruits

Graph Theory: Graph theory represents metabolic or genetic networks as nodes (vertices) connected by links of edges (arcs). The graph theory has many applications, including in biology. ►networks, ►genetic networks; Wilson R, Beineke L 2004 Topics In: Algebraic Graph Theory, Cambridge Univ. Press, New York, Solymosi J 2005 Proc Natl Acad Sci USA 102:8075.

Grasses (cultivated for herbage): Blue grass (*Poa pratensis*) 2n = 36–123; Italian ryegrass (*Lolium multiflorum*) 2x = 14; meadow fescue (*Festuca pratensis*) 2x = 14; orchardgrass (*Dactylis glomerata*) 4x = 28; perennial ryegrass (*Lolium perenne*) 2x = 14; smooth brome (*Bromus inermis*) 8x = 56; tall fescue (*Festuca arundinacea*) x = 7, 2n = 42; timothy (*Phleum pratense*) 6x = 42. ►gramene

Grasshoppers (*Orthoptera*): Grasshoppers are suitable objects of cytological and evolutionary investigations because of the large size and number of chromosomes. (n = 13 to 57 in males that are of XO constitution); *Melanopus differentialis* 2n = 24. The variation in chromosome number is supposed to be due to chromatin reorganization rather than to polyploidy. (See http://www.haibei.org/brim/grashopp/look.asp).

Gratuitous Inducer: A substrate analog of an inducible enzyme that may trigger transcription of the gene concerned, such as IPTG (isopropyl thiogalactoside) for the *Lac* operon, although it is not metabolized by the *z* gene of the operon. ►inducer, ►*Lac* operon; Horton N et al 1997 J Mol Biol 265:1.

Grauzone: A female meiosis regulatory WD type Zinc-finger protein distantly related to Cdc20 that binds to the cortex promoter during meiosis and early embryo development. Meiosis fails when it mutates. ►WD-40, ►DNA-binding proteins, ►CDC20; Harms E et al 2000 Genetics 155:1831; Chu T et al 2001 Genesis 29:141.

Graves Disease (Grave's disease): ►goiter

Gravitropism: A tendency of plant organs such as roots to grow in the direction of terrestrial gravitation. The mechanism of this response is unclear although amyloplasts and other cytoplasmic characteristics have been suggested as possible receptor sites. ►statolith, ►phototropism; Kato T et al 2002 Plant Cell 14:33; Yano D et al 2003 Proc Natl Acad Sci USA 100:8589.

Gravity: Either hypo- or hypergravity may cause chromosomal damage in human cells.

Gray Crescent: A pale area in some amphibian eggs, opposite to the sperm entry; at this point will the dorsal parts be initiated. ►dorsal

Gray Matter: A butterfly-shaped neuronal tissue of the hippocampus; it is surrounded by the axonal *white matter*. Its anomalies may lead to psychomotor retardation, seizures that are resistant to anticonvulsant therapy. Some of the hereditary infantile seizures respond dramatically to large doses of vitamin B_6 (pyridoxine). Differences in the frontal gray matter of individuals are under genetic control and increased

size appears positively correlated with cognitive abilities. ►brain human, ►neuron; Thompson PM et al 2001 Nature Neurosci 4:1253.

Gray Units: Units of ionizing radiations; 1 Gy = 100 rad absorbed dose. ►R, ►rad, ►rem, ►Sievert

GRB (growth factor receptor-bound protein): A vertebrate adaptor protein with SH2 and SH3 binding domains; it is a downstream receptor kinase. It mediates the activation of guanine nucleotide exchange (GTP⇆GDP) on RAS, a homolog of the *Drosophila* protein DRK. ►DRK, ►signal transduction, ►SH2, ►SH3; Jahn T et al 2001 J Biol Chem 276:43419; Kessels HWHG et al 2002 Proc Nat Acad Sci USA 99:8524.

GRE (glucocorticoid receptor element): GRE is situated upstream from the TATA box gene regulatory tract. ►backtracking, ►glucocorticoid, ►glucocorticoid response element; Herrlich P 2001 Oncogene 20:2465.

Greek Alphabet (with Roman counterparts): (see Table G5).

Greek-Key: A protein configuration where β-sheets are connected across the end of a barrel. ►barrel

Green Beard Effect: An idea that some unique traits are specially favored by the parents' altruistic behavior during evolution. In general, other individuals of the population, irrespective whether they carry it themselves, recognize the "green beard" gene (gene product). ►gestational drive, ►kin selection, ►altruistic behavior; Dawkins R 1976 The Selfish Gene, Oxford Univ. Press, New York, Nee S 1989 J Theor Biol 141:81; Sinervo B et al 2006 Proc Natl Acad Sci USA 103:7372.

Green Processes: Green processes do not have serious environmental impacts.

Green Fluorescent Protein: ►aequorin, ►Renilla GFP, ►drFP583

Green Revolution: The development of new plant (cereal crop) varieties which, because of the shorter and stronger stems and improved disease resistance, permitted more intensive agricultural practices (use of higher doses of fertilizers, irrigation, etc.) and resulted in 2–3 fold increases in grain yield. (See Khush GS 2000 Nature Rev Genet 2:815; Evenson RE, Gollin D 2003 Science 300:758).

Greenberg Dysplasia: ►hydropsectopic calcification–motheaten skeletal dysplasia

Greenhouse Gases: Greenhouse gases are faulted as the main causes of global warming. Carbon dioxide and methane were thought to be primarily responsible.

Table G5. The Greek and corresponding Roman characters

Greek			Roman
	α	alpha	a
	β	beta	b
Γ	γ	gamma	G g
Δ	δ	delta	D d
	ε	epsilon	e
	ζ	zeta	z
	η	eta	e
Θ	$\theta\ \vartheta$	theta	Th th
	ι	iota	i
	κ	kappa	k
Λ	λ	lambda	L l
	μ	mu	m
	ν	nu	n
Ξ	ξ	xi	X x
	o	omicron	o
Π	π	pi	P p
	ρ	rho	r
Σ	σ	sigma	S s
	τ	tau	t
	υ	upsilon	y
Φ	ϕ	phi	F f
	χ	chi	ch
Ψ	ψ	psi	Ps ps
Ω	ω	omega	O o

Therefore, extended forestation was believed to be able to reduce CO_2 level in the atmosphere. Now it appears that green plants produce large amounts of methane that counteracts the beneficial effects of forestation (Lowe DC 2006 Nature [Lond] 439:149; Keppler F et al 2006 Nature [Lond] 439:187). Thus, President Ronald Reagan's ridiculed remarks about plants being the cause of warming of the globe appears prescient.

Greig's Cephalopolysyndactyly Syndrome (GCPS): GCPS is dominant in the short arm of human chromosome 7p13. It involves polysyndactyly and malformation of the head without mental defects. Molecular analysis indicates that the anomaly is concerned with GLI3 oncogen, a CREB-binding

protein. The protein product of the *cubitus inrruptus* locus of *Drosophila,* involved in the regulation of limb development is also a homolog. ►hedgehog, ►Rubinstein-Taybi syndrome, ►GLI oncogene, ►morphogenesis in *Drosophila,* ►polydactyly, ►polysyndactyly, ►Pallister-Hall syndrome, ►cubitus interruptus

Grey Matter: ►gray matter

Grid: A surface evenly lined by parallel horizontal and vertical lines, such as, e.g., in microarray slides.

GRID (general repository for protein interaction database): http://biodata.mshri.on.ca/grid/.

Gridding: Aligning spots on a grid. ►grid

GRIM (gene associated with interferon-retinoic acid-induced cell mortality): ►interferon, ►retinoic acid; Zhang J et al 2003 Proc Natl Acad Sci USA 100:9342.

GRIP (glutamate receptor interacting protein): GRIP contains seven PDZ domains interacts with C end and links AMPA to other proteins. GRIP lacks catalytic functions. ►AMPA, ►CARM; van Beeren HC et al 2000 FEBS Lett 481:213.

Griscelli Syndrome: Recessive 15q21 mutation causing anomalous pigmentation and T lymphocyte and macrophage function aberrations (hemophagocytic syndrome). The basic defect is in the RAB27A guanosine triphosphate-binding protein. Defects at the same site may also involve myosin 5a, a motor protein. The former lesion involves immune defects, the latter is concerned with neurological impairment. The hypopigmentation and the immunological problems appear to be related to lysosomal defect. ►RAB, ►lysosomes, ►Warburg micro syndrome; Anikster Y et al 2002 Am J Hum Genet 71:407; Stinchcombe J et al 2004 Science 305:55.

Griseofulvin: Strong inhibitor of fungal mitosis but weak as human spindle microtubule inhibitor and displays relatively low toxicity (see Fig. G63). It has been used against ringworm infections. In human tumor cells, it blocks cell cycle progression at G2/M and can cause apoptosis and it is a potential anticancer drug (Panda D et al 2005 Proc Natl Acad Sci USA 102:9878).

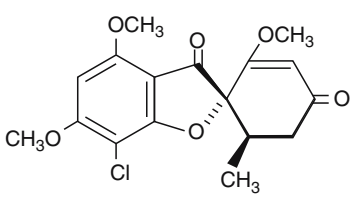

Figure G63. Griseofulvin

GRK1 (rhodopsin kinase): GRK1 is involved in the desensitization of G protein-mediated signaling. ►rhodopsin, ►GRK2

GRK2 (G protein-coupled receptor kinase 2): GRK2 controls signaling from activated receptors to downstream effectors. (See for crystal structure: Tesmer VM et al 2005 Science 310:1686).

GRM: General regulator of mating type in yeast in cooperation with PRTF. ►mating type determination in yeast, ►PRTF

gRNA (guide RNA): gRNA has a role in the kinetoplast, mitochondrial DNA of some protozoa. It mediates the pan edited primary RNA transcripts substantially by modified U additions or deletions but some short sequences (50–100 bases) may remain homologous to the primary transcript. These sequences are apparently anchored to the 3′-end and thus pairing may get started. Additional homology may occur in the middle (20–30 bases) and at the 5′-end (ca. 10 bases). These gRNAs may serve as templates for editing. The process requires a series of enzymatic steps. Free uridine triphosphates are the source of the Us inserted and they are added to the 3′ ends generated by enzymatic cleavage. ►kinetoplast, ►*Trypanosoma*, ►*Leischmania*, ►RNA editing, ►pan editing, ►mtDNA; Müller UF et al 2001 EMBO J 20:1394; Bloom D et al 2001 Nucleic Acid Res 29:2950; Decatur WA, Fournier MJ 2003 J Biol Chem 278:695.

grow: Hamster gene activated by mitogens ►KC, ►N51, ►MGSA

GROα: ►melanoma growth-stimulating factor

GroEL: A homo-tetradecameric chaperonin, composed of 57 kDa subunits of three functional domains each, arranged as a hollow cylinder of two stacked rings with seven-fold symmetry in *E. coli*. It binds to the smaller GroES molecule. GroEL and GroES are encoded in the same operon of *E. coli* (see Fig. G64). Although the information for folding resides in the primary structure of proteins, the GroEL–GroES complex facilitates the realization of this potential. In *E. coli*, ~250 proteins interact with GroEL but most of these can utilize the upstream chaperone trigger factor and DnaK for folding (Kerner MJ et al 2005 Cell 122:209). ►chaperone, ►chaperonin, ►protein folding, ►DnaK, ►trigger factor; Feltham JL, Gierash LM 2000 Cell 100:193; Farr GW et al 2000 Cell 100:561.

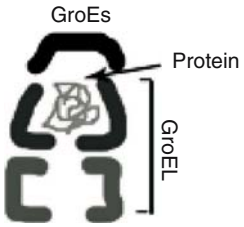

Figure G64. GroES and GroEL structure

GroES: A 10-kDa monomer. (See diagram).

Groucho: In *Drosophila*, groucho is a somewhat limited in scope corepressor protein responsible for extra bristles and ocelli above the eyes of the flies. It can act with Hairy, Engrailed, and Dorsal although the interacting domains in Hairy and Engrailed are different. Its mammalian homologue is TLE1 and it is structurally and functionally related to Tup1 of yeast. ►corepressor, ►ocellus, ►Tup1, ►engrailed, ►hairy [morphogenesis in *Drosophila* {30}], ►dorsal [morphogenesis in *Drosophila* {3}]

Groundnut (peanut, *Arachis hypogea*): About 40 – 70 species, 2n = 2x = 20; some have higher ploidy. Some people are allergic to peanut protein that binds immunoglobulin (IgE) in the intestinal mucosa resulting in histamine release, which may cause contraction of the smooth muscles of the airways and anaphylactic reaction. It should be promptly counteracted by epinephrine to prevent serious consequences that may include death. (See Burow MD et al 2001 Genetics 159:823).

Ground State: Stable, normal, not excited form of an atom, molecule, or gene.

Group Selection: Group selection may occur when the behavior of individuals influences their own fitness and the fitness of related individuals and is selected by Nature accordingly. ►altruistic behavior, ►kin selection, ►nepotism

Group Transfer Potential: Ability of a compound to donate an activated group (e.g., phosphate or acyl).

Growth: ►cell growth, ►growth curve, ►exponential growth, ►invasive growth

Growth Cone: The tip of growing axons. ►axon

Growth Curve: Cell multiplication may start at an exponential rate under ideal conditions for proliferation, then it reaches a stationary phase (growth flattens) and only maintenance of the cell population takes place (S curve) (see Fig. G65). The exponential growth is named so because an exponent of base 2 can mathematically define the growth. Thus, after 10 divisions of a cell the expected number is 2^{10}. In case the initial cell number was 100, after exponential growth, the number of cells 10 generations later would be $2^{10} \times 100 = 1024 \times 100$. Alternatively, growth may decline and the level of the population decreases. In higher organisms, such growth curves can be observed only in isolated cell cultures. In differentiated tissues the growth has structural limitations.

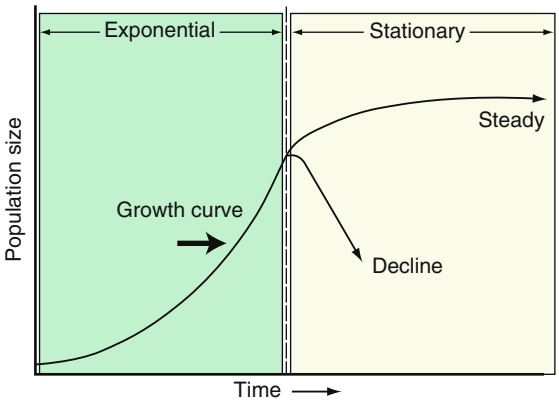

Figure G65. Growth curve

Growth Factors: ►FGF, ►PDGF, ►EGF, ►IGF-I, ►IL-2, ►IL-3, ►NGF, ►TGF, ►erythropoietin, ►cell cycle, ►growth hormone pituitary, ►brassinosteroids, ►epidermis

Growth Hormone, Pituitary: The gene complex for the hormone is in human chromosome 17q23-q24 and encodes a 190 amino acid protein, human growth hormone (hGH), and also the somatotropin, a chorionic growth hormone (191 amino residue with ≈85% homology to hGH), and a growth hormone-like protein (GHL, 22-kDa). The expression of the hormone gene complex is regulated by the 33-kDa growth hormone transcription factor (GHF1) and growth factor response protein (GFRP1). The hGH is released by a 44-amino acid growth hormone-release factor (GHRF) encoded at chromosome 20p12. ►pituitary dwarfness, ►pituitary, ►brain human, ►secretagogue, ►ghrelin, ►Rowley-Rosenberg syndrome, ►Gapo syndrome, ►prion

Growth Hormones: Growth hormones and receptors are associated with many cellular proliferative processes and nuclear localization of the growth hormone receptors is associated with various typoes of cancer (Conway-Campbell BL et al 2007 Proc Natl Acad Sci USA 104:13331). ►animal hormones, ►plant hormones, ►nuclear receptors

Growth Retardation: Reduction in the rate of increase in size, cell multiplication, differentiation and development. ►retardation, ►Rowley-Rosenberg syndrome, ►GAPO syndrome, ►Gombo syndrome

Growth-Associated Kinase: An M-phase histone-1 kinase, functions at its peak in mitotic M phase but its activity ebb at other phases; it is also active during meiosis. ►histones, ►mitosis

GRP: Heat shock glycoproteins of the HSP family. GrpE is itself not a chaperone but as ADP-ATP exchanges factor it is part of the DnaJ-DnaK chaperone complex of prokaryotes and the replication machinery of phage lambda. Its homologs are present in prokaryotes as well as in the mitochondria of yeast, insects, and mammals. The mammalian Grp94 (member of the Hsp90 family of proteins) chaperones are a small number of proteins and are suspected to be involved in antigen presentation and tumor rejection. ►heat-shock proteins, ►HSP, ►DnaK, ►Mge1, ►Droe1, ►Hsp90, ►antigen processing and presentation, ►endoplasmic reticulum

GRP: General receptors of phosphoinositides. ►phosphoinositides

Grunstein-Hogness Screening: Grunstein-Hogness screening involves in situ lysis of bacterial colonies on nitrocellulose filters (or other membranes) and non-covalent attachment of the probe DNA to that support medium. ►Benton-Davis plaque hybridization, ►probe; Elvin P et al 1988 Br J Cancer 57:36.

G_s Protein: A stimulatory G protein; when bound to GTP it stimulates the activity of adenylate cyclase, the membrane bound enzyme, which generates cAMP. G_s has α, β and γ subunits, the GTP/GDP binding site being on the α subunit. When GDP is at the nucleotide-binding site, adenylate cyclase activity ceases. Displacement of GDP and replacement by GTP (mediated by the hormone, epinephrine) restores the active form. At this stage, the α sub-unit with bound GTP dissociates from β and γ. ►G-proteins, ►adenylate cyclase, ►signal transduction, ►oogenesis

GSC (genome structure correction): A method to adapt statistical tests to make fewer assumptions about the distribution of features on the genome sequence. This provides a conservative correction to standard tests. ►genome sequence sampling

GSC RT-PCR: ►global single cell reverse transcription-polymerase chain reaction

GSD (genetically significant dose): GSD determines the effectivness of a mutagenic exposure. ►mutation rate, ►doubling dose, ►genetic hazards, ►genetic load, ►mutation spontaneous

GSEA (gene set enrichment analysis): GSEA detects modest but coordinate expression of groups of functionally related genes. The relevant genes are ranked according to difference in expression between two conditions of interest. The null hypothesis is that the expression is random between the two groups. The alternative hypothesis is that the rank of the affected individuals of the pathway members is associated with the diagnostic criteria used for the characterization. The extent of the association is measured by a non-parametric test. The maximum enrichment score (MES) is evaluated after random permutation of the diagnostic labels between the groups. The actual MES is than compared to the distribution of the enrichment score over all pathways tested. Subramanian A et al (2005 Proc Natl Acad Sci USA 102:15545) described an improved version and the procedure (software) is freely made available. On the basis of microarray information, the genome-wide factors involved in a pathway, e.g., leukemia or lung cancer can be predicted. ►null hypothesis, ►cluster analysis; Mootha VK et al 2003 Nature Genet 34:267.

GSH: Reduced glutathione. ►glutathione

GSK3 (glycogen synthase kinase 3β): A protein encoded by *Drosophila* gene *zeste white* (z^{W3}, chromosome 1–1); homologous proteins are present in other animals. It is assumed that GSK is mediating a step in the intestinal polyposis carcinogenic pathway. It also regulates global protein synthesis. GSK3β is involved in the induction of mammalian neurogenesis in embryonic stem cells targeted by 4,6-disubstitited pyrrolopyrimidine (Ding S et al 2003 Proc Natl Acad Sci USA 100:7632). GSK-3β mediates the establishment and maintenance of neuronal polarity and its inhibitors may be suitable targets to promote the generation of new axons after neural injury (Jiang H et al 2005 Cell 120:123). Therapeutic concentration of lithium (LiCl) inhibits GSK-3α by interfering with the γ-secretase cleavage of amyloid precursor protein (APP). GSK-3α also phosphorylates the tau protein, the main component of the neurofibrillary tangles in Alzheimer disease. Thus GSK-3α may control two steps in the development of Alzheimer disease (Phiel CJ et al 2003 Nature [Lond] 423:435). Levels of Akt-GSK3β reduction appear to be a factor in schizophrenia (Emamamian ES et al 2004 Nature Genet 36:131). AKT-activated GSK also regulates apoptosis. The anti-apoptotic BCL-2 family proteins control the permeabilization of the outer membrane of the mitochondria, whereas the pro-apoptotic BAX and BAK are required for permeabilization. GSK-3 phosphorylates MCL-1 (member of the BCL-2 family of proteins), leading to its degradation by the proteasome and facilitating the release of cytochrome c and apoptosis (Maurer U et al 2006 Mol Cell

21:749). ►polyposis adenomatous intestinal, ►translation initiation, ►conductin, ►GBP, ►Alzheimer disease, ►tau, ►secretase, ►stem cell, ►AKT oncogene, ►neurogenesis, ►adipocyte, ►apoptosis, ►cleft palate, ►BCL-2, ►BAX, ►BAK, ►epiloia

GSM (genetic sexing mechanism): A method of insect control by producing translocation between the Y chromosome and the X chromosome. The Y translocation serves as a dominant selectable marker and reduces the fertility of the female. ►genetic sterilization, ►autosexing

GSMA (genome search meta-analysis): A linkage analysis procedure based on non-parametric ranking of lod scores or other recombination values. ►lod score, ►non-►parametric tests, ►meta-analysis of linkage, ►affected-sib-pair; Levinson DF et al 2003 Am J Hum Genet 73:17.

gsp: c-oncogene; its product is the α-subunit of G-proteins. ►G-, ►c oncogene

GSP: Gene-specific primer. ►directed mutation, ►c-oncogene

GSS: ►genome sequence sampling

G_{ST}: An index of genetic diversity similar to F_{ST}. (See F; Nei M 1973 Proc Natl Acad Sci USA 70:3321).

GST: ►glutathione-*S*-transferase

GSTB (Genome Sequence Data Bank): The GSTB maintains nucleotide sequence information on genes and clones ►GenBank; ►NCBI

GT – AG RULE (Chambon's rule): The Chambon's rule states that the first two and the last two nucleotides of introns are GT and AG, respectively; some exceptions are known. ►intron, ►exon

GTL (genome to life): A US Department of Energy project that aims to shed light on the biological mechanisms of microbes and microbial systems under dynamic conditions, in order to use the information for assisting public needs in solving problems of health and the environment. (See http://DOEGenomesToLife.org/).

G_t-Protein (transducin): A member of the trimeric G-protein family; it activates cGMP phosphodiesterase in photoreceptors. ►G-proteins; ►rhodopsin

GTBP (G/T mismatch-binding protein): GTBP is encoded in human chromosome 2 and its mutations lead to genetic instability at single nucleotide sites. ►mismatch, ►DNA repair, ►hereditary nonpolyposis colorectal cancer

GTF (general transcription factors): Proteins that are required for the initiation of transcription by RNA polymerase I (TFIs), RNA polymerase II (TFIIs), and RNA polymerase III (TFIIIs). ►transcription factors

GTP: Guanosine triphosphate (see Fig. G66).

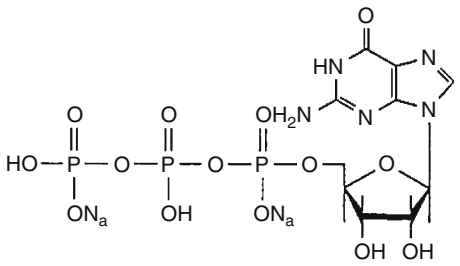

Figure G66. GTP

GTPase: ~60 proteins mediating the conversion of GTP into GDP. These enzymes regulate translation, signal transduction, cytoskeletal organization, vesicle transport, nuclear import, and protein translocation across membranes, etc. Two different GTPases may modulate each other's activity. ►RAS, ►RAC, ►RHO, ►RAB, ►RAN, ►RASA, ►dynamins, ►Arf, ►GAP, ►GEF, ►SAR, ►G proteins; Yang Z 2002 Plant Cell 14:S375.

GTPase-Activating Protein (GAP): GAP increases GTP hydrolysis to GDP by several orders of magnitude in signal transduction. ►signal transduction

GTP Binding Protein Superfamily: The GTP binding protein superfamily includes transitional factors, transmembrane signaling proteins, Ras proteins, and tubulins. ►signal transduction, ►E region of GTP-binding proteins

GTP Cyclohydrolase Deficiency (14q22.1-q22.2): The recessive deficiency of guanosine triphosphate cyclohydrolase I results in hyperphenylaninemia because tetrahydrobiopterin is not converted into dihydroneopterin triphosphate by a process requiring GTP. The disorder involves low urinary pterines, serotonin, and dopamine levels. The afflicted individuals show convulsions, muscular hypotonia of the trunk but hypertonia of the limbs. Oral L-erythro-tetrahydrobiopterin may alleviate some of the symptoms. ►phenylalanine, ►hyperphenylalaninemia, ►pteridines, ►biopterin, ►serotonin, ►dopamine, ►hypotonia, ►hypertonia

Guam Disease: An autosomal dominant complex syndrome displaying the characteristics of amyotrophic lateral sclerosis, Parkinsonism, and dementia, and discovered in Guam. Environmental conditions such a low calcium and magnesium in the diet and consumption of the Cycas plants seem to favor toxic metal accumulation in the central nervous

system and appears to favor the onset. ►neurodegenerative diseases

Guanidinium Chloride: Guanidinium chloride is used in molecular genetics similarly to guanidinium isothiocyanate for isolation of undegraded RNA. ►RNA extraction

Guanidinium Isothiocyanate: Guanidinium isothiocyanate is used for the isolation of RNA. It breaks up cells, dissociates nucleoproteins, and inactivates tough RNase enzymes (at 4 M solutions) in the presence of the reducing agent β-mercaptoethanol. ►RNA extraction

Guanine: The purine base in DNA and RNA (see Fig. G67). ►glycosylases

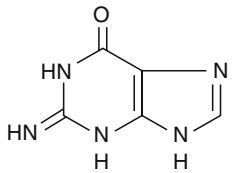

Figure G67. Guanine

Guanine Methyltransferase: The guanine methyltransferase methylates the mRNA cap. ►cap

Guanine Nucleotide Binding Protein (16q13, 6q21.3, 20q13.2, 7q21, 22q11.2, 1p13, 3p21, 19p13): The guanine nucleotide binding protein mediates signal transduction on G proteins.

Guanine Nucleotide-Exchange Protein (11p23.3, 19q13.3): The guanine nucleotide-exchange protein catalyze the reaction GTP⇆GDP. The large Rho family of G proteins generally contains a Dbl (MCH2) domain and a pleckstrin homology (PH) domain. ►G protein, ►MCH2, ►Rho, ►brefeldin

Guanine Nucleotide Releasing Protein (GNRP, 11q13): GNRP hydrolyzes GTP, bound to G proteins, into GDP. ►signal transduction

Guanosine: The nucleoside of guanine.

Guanosine Tetraphosphate, Guanosine Penta Phosphate (ppGpp, pppGpp): ppGpp and pppGpp are effectors of the stringent response. ►stringent response; Chatterji D, Ojha AK 2001 Curr Opin Microbiol 4:160.

Guanylate Cyclase: Guanylate cyclase mediates the formation of cyclic guanosine monophosphate, cGMP.

Guanylic Acid: Guanine nucleotide.

Guanylyl Transferase: Guanylyl transferase attaches GTP to the mRNA cap. ►cap, ►GTP

Guard Cell: ►stoma

Guard Hypothesis: The guard hypothesis postulates that the requirement for a specific protein to activate the plant resistance gene when it encounters an avirulence gene of a pathogen and it guards against the suppression of the plant defense mechanism by any bacterial effector.

Guava (*Psidium guajava*): Subtropical, tropical, small, allogamous fruit tree; 2n = 2x = 22.

Guessmer: Usually 30–7-base long synthetic oligonucleotides representing limited degeneracy and using neutral bases (inosine) at sites of ambiguity. The nucleotide sequence is generated on the basis of information of amino acid sequences in the protein. This label can be used for screening for specific coding sequences (genes). If the codons would be picked at random, the synthetic sequence would represent at least 76% homology by chance, but by considering codon usage of the organism, the homology may be over 90%. The probes are labeled with the aid of polynucleotide kinase or primer extension with the Klenow fragment. ►probe, ►primer extension; O'Farrell PA et al 1997 Biochem Biphys Res Commun 239:810.

Guest Peptide: ►CD tagging

Guest RNA: ►CD-tagging

Guest Tag: ►CD-tagging

Guide RNA: Guide RNA chaperones the alignment of splicing by attaching either to the intron or to the exon sequences of the transcript. ►RNA editing, ►gRNA, ►intron, ►splicing; Kabb AL et al 2001 Nucleic Acids Res 29:2575.

Guillain-Barré Syndrome: A sporadic or familial autosomal dominant. It is a de-myelinating neuropathy arising after infection by *Campylobacter jejuni*. ►*Campylobacter*

Guillardia: A filamentous alga.

Guinea Pig: *Cavia porcellus*, 2n = 64 (see Fig. G68).

Figure G68. Guinea pig

Gunther Disease: ►porphyria (erythropoietic porphyria, 10q25.2-q26.3)

GURT: ►T-GURT

GUS: The tetrameric glycoprotein acid hydrolase, ß-glucuronidase enzyme (gene) is frequently used as a reporter for the in vivo testing of promoters, identifying site-specific expression, or monitoring the excision of transposable elements. Several substrates of the enzyme are useful for releasing a blue color upon activity of GUS. Deficiency of the enzyme in mammals leads to lysosomal storage diseases. ►lysosomal storage diseases, ►gene fusion, ►reporter gene, ►aging; Jefferson RA et al 1987 EMBO J 6:3901; Schenk PM et al 2001 Plant Mol Biol 43:399.

Gustatory: "Gustatory" refers to something involving the sensation of taste. ►taste

Gustducin: ►taste

Gut: The gastrointestinal tract or the developmentally primitive (early) digestive tract composed of fore-, middle-, and hindgut sections. The mammalian gut endoderm forms different 'buds' giving rise to the liver, lung, pancreas, thyroid, and gastrointestinal tissues. The developmental fates are determined by the additional growth factors recruited. The microbial flora (10 to 100 trillion microbes/gut) has important function in gastrointestinal health and disease, and substatial variations exist in these populations among individuals (Eckburg PE et al 2005 Science 308:1635; Bäckhead F et al 2005 Science 307:1915). ►microbiome, ►oral bacterial films

Guthrie Test: Guthrie test detects phenylketonuria because if the blood contains phenylalanine, the analog β-2-thienylalanine does not interfere with the growth of *Bacillus subtilis*. ►phenylketonuria, ►genetic screening

Guthrie Cards: Guthrie cards are used for genetic testing/screening of newborns—from dry blood samples—for about 30 hereditary disorders.

Gutless/Gutted Vector: Usually a viral vector without nearly any viral gene, which would have been required for viral replication. Such vectors require helpers for trans-complementation and propagation. ►HDAd

Guttation: In the process of guttation, water ascending through the xylem vessels of plants may drop from the leaves when relative humidity increases. ►transpiration, ►cohesion-tension

Guttmacher Syndrome (preaxial deficiency, postaxial polydactyly and hypospadias, 7p15-p14.2): A special hand-foot-genital syndrome, apparently due to mutation in the HOXA13 gene. ►polydactyly, ►hypospadias, ►hand-foot-genital syndrome; Guttmacher AE 1993 Am J Med Genet 46:219.

GVG: A transcription factor constructed of the yeast GAL4 DNA-binding domain, the trans-activation domain of herpes virus VP16, and the hormone-binding domain of the glucocorticoid receptor. ►galactose utilization, ►VP16, ►glucocorticoid response elements, ►dexamethasone

GW Body (GWBs): 182-kD proteins characterized by multiple glycine (G)-tryptophan (W) repeats and an RNA recognition motif that binds messenger RNAs and have a role in mRNA degradation (Eystathioy T et al 2003 RNA 9:1171).

GWA (genome-wide association, GWAS): GWAS uses mapping linkage to the level of expression across a genome(s). The analysis may involve various markers, including single-nucleotide polymorphism, and determines the regression of the markers and the trait of interest (Evans DM, Cardon LR 2006 Trends Genet 22:350). Statistical and computer programs are now available for studying the association between known phenotypes and molecular biology markers (Pearson JW et al 2007 Amer J Hum Genet 80:126). This relatively new approach is less expensive for the analysis of complex traits than direct genotyping although it may be adversely affected by microarray-based errors (McGregor S 2007 Eur Hum Genet 15:501). A GWA study of British populations in 2007, including 2,000 individuals for each of seven major diseases and a shared set of 3,000 controls, identified 24 independent association signals at $P < 5 \times 10^{-7}$: one in bipolar disorder, one in coronary artery disease, nine in Crohn's disease, three in rheumatoid arthritis, seven in type 1 diabetes, and three in type 2 diabetes. The information indicates that this is a new powerful approach for understanding human pathophysiology (Nature [Lond] 447:661). ►QTL, ►genotyping, ►microarray hybridization, ►human subjects privacy protection; US federal guidelines concerned with GWA: http://grants.nih.gov/grants/gwas/index.htm; privacy proteection: Lowrance WW, Collins FS 2007 Science 317:600.

Gy: Gray units of radiation; 1 Gy = 100 rad. ►rad

Gy: Billion years of geological time.

Gymnosperm (*Coniferophyta*): Plants with seeds, which are not enclosed in an ovary. Typical representatives are the pine trees (2n = 24).

Gymnothecium: The fruiting body of some ascomycetes fungi; it may cause skin infections. ►perithecium, ►cleistothecium, ►ascogonium

Gynander: Same as gynandromorphy, *Drosophil*a gynandromorph image from Morgan T et al 1925 Bibliographia Genetica 2:1.

Gynandromorph: Sex mosaic (part male/part female); same as gynander. They are the result of the loss one of the X-chromosomes during development of *Drosophila* and other organisms where the XO chromosomal constitution leads to the development of male phenotypic characteristics (see Fig. G69). The loss of the X-chromosome reveals the recessive alleles present in the remaining homolog. These sex mosaic individuals can be exploited for fate mapping. The right side of the diagram of the fly shows male characteristics and has a ruby eye because the left sector is X0. The left side depicts like female (XX). ►fate mapping, ►lyonization, ►variegation; Szabad J, Fajszi C 1982 Genetics 100:61.

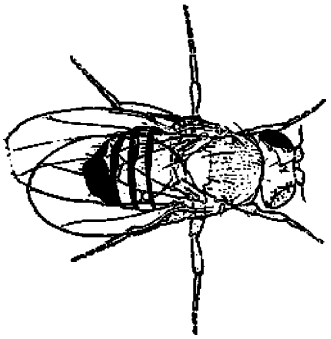

Figure G69. Gynandromorph

Gynecomastia: Increased development of the mammary gland of males caused either by estrogen accumulation and/or reduction of testosterone (see Fig. G70). Deficiency of a gene encoding hydroxysteroid dehydrogenase III (9q22) and increased expression of the cytochrome P450 (CYP, 15q21.2) aromatase subunit may be responsible for pseudohermaphroditism and gynecomastia. X-linked inheritance with male transmission has also been suggested. A transient mild form may not be abnormal during puberty. Several statues of the young pharaoh, Tutankhamen (fourteenth century BC), reveals bilateral gynecomastia and the somewhat bloated stomach suggests the likelihood of celiac disease (see Fig. G71). Gynecomastia can be corrected by plastic surgery (Yavuz M et al 2006 Ann Plast Surg 57 [4]:370). ►pseudohermaphroditism male, ►Klinefelter syndrome, ►Kennedy syndrome, ►animal hormones, ►steroid dehydrogenase/ hydroxysteroid dehydrogenase; ►aromatase; black and white photo showing a young male with gynecomasty on one side of his chest; photo by courtesy of Dr. C. Stern.

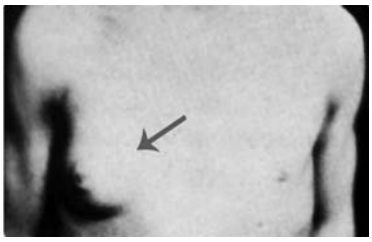

Figure G70. Gynecomastia

Figure G71. Tutankhamen

Gynodioecious: A gynodioecious population consists of both hermaphroditic and female individuals, and is generally determined by nuclear and mitochondrial genes. ►hermaphrodite; Taylor DR et al 2001 Genetics 158:833.

Gynoecium: The carpels and structures enclosed by them in flowers. ►fruits; Ferrándiz C et al 1999 Annu Rev Biochem 68:321.

Gynogenesis: Reproduction by parthenogenesis, i. e., the sperm does not fertilize the egg but stimulates the cleavage of the unreduced egg (pseudogamy). Also, embryos developed by transfer of male pronuclei into the egg, and thus diploid are called *gynogenones*, in contrast to *parthenogenones* (gynogenotes), which arise from parthenogenesis. ►apomixis, ►parthenogenesis, ►androgenesis, ►EP

Gypsy: A somewhat diverse ethnic group migrating from the Indian subcontinent north and southward, presumably before the ninth century, to Asia and to Egypt, and from there to most of the northern hemisphere, although they are now found all over the world. Their Indian origin is asserted by orally transmitted legends. Linguistic evidence indicates Sanskrit roots. Y chromosomal and mtDNA information

support Indian origin. Their ethnic identity has been preserved by cultural and genetic isolation. Haldane JBS (1935) used ABO blood type frequencies to show that the Hungarian Gypsies are more closely related to some Eastern Indian populations than to that of Hungary although some of them lived in that country since the early fifteenth century. They prefer to be called Roma. ►ethnicity; Kalaydjieva L et al 2001 Eur J Hum Genet 9[2]:97; Gresham D et al 2001 Am J Hum Genet 69:1314.

Historical vignettes

"William Curtis, British botanist, described a weed called *Arabidopsis thaliana* as having 'no particular virtues or uses'. More than 200 years later, he could not have been proved more wrong."

The Guardian, UK, quoted after Jane Alfred, Editor of Nature Rev. Genet. 2001, 2:86.

Herman N Eisen 2001 in Annu. Rev. Immunol. 19:1

"…the self-correcting character… is inherent in the scientific enterprise. This aspect of science seems at times to be utterly incomprehensible to journalists, politicians, and the public at large—as I was to find out painfully many years later…"

Gypsy Retroposon: ►copia, ►insulator

Gyrase: A DNA topoisomerase II that reverses the direction of coiling in DNA, resulting in negative supercoiling. ►DNA replication, ►transcription, ►supercoiling, ►topoisomerase; Gellert M et al 1979 Proc Natl Acad Sci USA 76:6289; Kirchhausen T et al 1985 Cell 3:933; Williams NL, Maxwell A 1999 Biochemistry 38:13502.