Mini Review
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Nanodiagnostics: a revolution in biomedical nanotechnology

Abstract

The application of nanobiotechnology in molecular diagnostics is termed nanodiagnostics, and it offers new and exciting options for personalized cancer therapy. Nanomedicine involves applications of engineered nanoparticles currently under development, or longer range research which utilizes nanoparticles for cellular repairs. The incorporation of nanobiotechnology with molecular diagnostics deploys 'nanoscale probes' for detailed analysis of cell components that exist in nanoscale dimensions. Advances in nanodiagnostic technologies are being used to facilitate the discovery of therapeutic biomarkers applicable to the effective management of cancer. In this regard, medications can then be tailored specifically to the patient based on his/her unique genotype with minimal side effects. A nanodevice can be implanted in a patient for early diagnosis and prevention. Generally, nanodiagnostics confer several advantages, most importantly; tiny amounts of the material are required for faster and more sensitive analyses. The field of nanodiagnostics has, however, elicited certain ethical and public health concerns with regard to *in vivo* administration. Highlights and merits of the current nanodiagnostic technologies and their interconnection with the various nanobiotechnologies are reviewed.

Keywords: nanodiagnostics, nanobiotechnology, nanobiochips, nanobiomarkers, safety issues

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Stanley Moffatt
Regent University College of Science and Technology, Ghana

Correspondence: Stanley Moffatt, School of Medical and Allied Sciences, Regent University College of Science and Technology, Accra, Ghana, Tel +233242169839,
Email Stanley.moffatt@regentghana.net

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Introduction

Biomedical nanotechnologies are currently being applied to Nanodiagnostics, and several of them are in different phases of development. This review describes biomedical nanotechnologies that have either been deployed or have potential commercial applications in clinical diagnostics. Nanodiagnostics refer to the use of biomedical nanotechnology in diagnostics, and biomedical nanotechnology is the use of various nanotechnologies and their applications in the life sciences. These two emerging fields offer new paradigms for various medical diagnosis. This mini-review further highlights the interrelationships of biomedical nanotechnology and diagnostics in nanomedicine as shown schematically in Figure 1, with empahasis on the application of these biomedical nanotechnologies in the clinical setting.

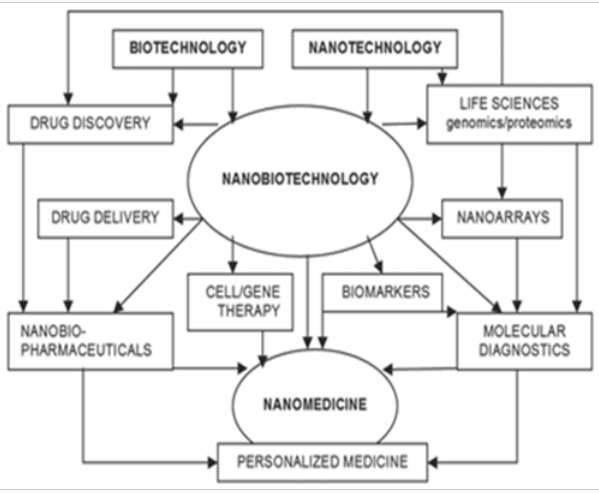

Figure 1 Inter-relationships and Contributions of Nanobiotechnology to Nanodiagnostics.

Nanotechnology-based chips

Nanotechnology could be a versatile and effective paradigm for a myriad of biochemical analyses. An example of a device that utilizes nanotechnology-based biochips and microarrays is protein nanobiochips. These nanobiochips can be adapted for point-of-care use. As a result of the challenges of spotting proteins on microarrays, protein microarrays are not widely used to study protein functions. Protein microarrays are generated by spotting cDNAs onto glass slides followed by translation into target proteins with mammalian reticulocyte. The epitope-tagged proteins allow them to be fairly immobilized. This procedure enables sufficient proteins for functional studies, ensures protein stability, and obviates the need to purify proteins. This technology has been used to characterize the regulation of Cdt1 binding to proteins, as well as map the geminin-binding domain.

Nanotechnology-based cytogenetics

Molecular cytogenetics is used to describe the chromosome structure and identification of chromosomal abnormalities related to disease. The use of fluorescent in situ hybridization (FISH) is now reaching its limit. Molecular cytogenetics is now enhanced by use of biomedical nanotechnology, e.g., use of atomic force microscopy (AFM) and quantum dot (QD) FISH. Scanning near-field optical microscopy has also been used to characterize G-bands and chromosomal probes. The fine resolution of this technique allows very small amounts of chromosomal DNA. The procedure utilizes the combination of biochemical and nanomanipulation techniques, which facilitates nanodissection and nanoextraction of the chromosomal DNA. The optical stability and narrow emission spectra of inorganic QD fluorophores make them very attractive for using FISH to study the expression of certain mRNA transcripts. QD's allow different colored probes specific for certain genetic sequences to be simultaneously excited and imaged with no artifacts.

Nanoscale identification of a single-cell or molecule

With the advent of nanotechnology, efficacious detection of single cells or a few molecules has been successful. Nanoproteomics, the application of biomedical nanotechnology to proteomics, can facilitate the detection of a single molecule of protein. Nanolaser scanning confocal spectroscopy can be used to differentiate cancer cells from closely related non-pathogenic cells. Biobarcode assays enable detection of minute amounts of proteins in body fluids by a 2D method that cannot be detected by conventional methods.[1] The mass spectrometry in solution is based on the interaction between a nanopore and solutes. As the electric current forces charged molecules (e.g. ssDNA) serially into the nanopore channel (1.5nm), the current is reduced in proportion to the size of each individual chain, allowing easy quantification of its mass. This single-molecule analysis procedure could prove useful for the characterization of biomarkers in real-time.

Nanoparticles in the discovery of biomarkers

Biomedical nanotechnology can replace the current molecular diagnostic technologies for the detection of biomarkers. The large surface area as well as the physicochemical characteristics make nanoparticles ideal candidates for detecting biomarkers. It is possible to alter the architecture of nanoparticles in order to selectively bind and sequester protein complexes and other biomarkers for later characterization using high-sensitivity nanoproteomic assays.[2] Biomarker discovery has not been a very busy area of research in biomedical nanotechnology but is likely to undergo substantial growth in the near future. Currently, polymer-coated nanoparticles has been designed and deployed for fast detection of biomarkers.[2]

Nanodiagnostics in cancer management

One of the advanced mode of imaging has been the combination of the best characteristics of QDs coated with paramagnetic lipids and silica nanoparticles to generate a single nanoparticle dual-mode MRI probe that can provide features of molecules involved in the cancer.[3] Silica nanoparticles, about 20 nm in size, are impregnated with a fluorescent dye, and iron oxide nanoparticles. The result is a 35-nm diameter nanoparticle which performs better in fluorescent imaging tests than any of the individual components. A lung tumor biomarker, polysialic acid, is linked to its antibody. The nanoparticulate complex is quickly taken up by cultured tumor cells and fluorescence microscopy.

Bioconjugated multicolor QD probes in immunohistochemistry provide a new class of biochemical labels for characterizing different cell biomarkers. Results using detailed protocols for QD-based immunohistochemistry, antibody conjugation for tissue specimens, multicolor QD staining, and biomarker quantification are now known.[4] The results demonstrate that bioconjugated QDs can be used for biomarker profiling and correlation with disease prognosis. These applications are envisaged to enhance the ability to predict the effectiveness of drug therapy in a personalized approach. The effectiveness of these protocols was demonstrated in a prostate cancer tissue. Anti-epidermal growth factor receptor (anti-EGFR)-conjugated gold nanoparticles specifically bind to cancer cells with 500% greater affinity than to non-cancerous cells.[4] The specificity of this binding result in a relatively sharper SPR absorption band with a red-shifted maximum compared with that in the presence of non-cancerous cells. Gold nanoparticles can thus be deployed in diagnosis and therapeutics by noninvasively detecting the cancer.

Nanodiagnostics in infectious diseases

The discovery of a rapid and sensitive method for detecting pathogens in patients is extremely important. Conventional diagnostic methods are however not as rapid, and also lack ultrasensitivity. Nanoparticle-based detection technologies have been developed for in-situ pathogen that can rapidly detect and quantify bacteria in specimens.[5] A single-molecule can be bioimaged using multicolor oligonucleotide-functionalized QDs as nanoprobes.[6] In the presence of target sequences, hybridization of the nanoprobes with target-specific sequences generates spectral codlings. This detection method can be used to analyze anthrax pathogens by simultaneously discovering multiple relevant sequences. A very rapid SERS-based spectroscopic assay using silver nanorods, has been developed to amplify and detect trace levels of viruses with a high degree of sensitivity.[7] With this technique, when viral DNA or RNA is scattered, the change in frequency of a the infrared laser is then measured. That frequency change is as distinct as a fingerprint and can detect spectral differences between viral strains. It is a rapid, inexpensive, and easily reproducible novel nanodiagnostic technology for viruses.

Safety issues in nanodiagnostics

Potential toxic effects are primarily a concern with *in vivo* but not *in vitro* diagnostics of nanoparticles, probably because *in vitro* diagnostics constitute the major component of laboratory diagnostics. Environmental concerns about nanoparticle pollution have been severally raised on different scientific platforms. These concerns, along the naturally present nanoparticles in the atmosphere, are being studied. A lot still remains unknown about the fate and effect of nanoparticles in the living body. Because of the huge variation in nanoparticle size, these effects are expected to vary considerably. Fluorescent label-coated QDs with calcium selenide or zinc sulfide may release toxic cadmium and zinc ions into cells. Even though capping QDs with ZnO prevents Cd2+ formation on exposure to air, UV radiation has no effect. Vigorous research is currently ongoing for better coating materials. A technically advanced imaging system has determined that coated QD fluorescent nanoprobes with Ag2S quantum dot are very sensitive *in vivo* anatomical imaging and early stage tumor diagnosis without significant cytotoxicity and disruption of cell function.[8]

It must be pointed out that while several studies about the safety of nanoparticles have been carried out, no conclusive scientific evidence has been adduced. Nevertheless, approval of *in vivo* nonmaterial for Nanodiagnostics in humans would be dependent on the empirical demonstration of nanoparticle safety. Consequently, various bioethics and safety committees have been set up to examine the effects of these nanostructures on humans and the environment.

Future prospects

Future usage of nanodiagnostics will be more effective by further miniaturizing the current biochip technology to the nanoscale level, in which the most foreseeable diagnostic application will be in blood protein analysis. The detection of these blood components in circulation as molecular fingerprints will provide a more rapid and sensitive assessment of the state of health. Nanodiagnostics could also help reduce waiting period for results. For example, patients with STDs could have their urine samples tested, and results ready by the time they are ready to see the physician, and prescriptions given immediately after that. This would drastically reduce the time spent on waiting for results, thus making the whole process less costly. In

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the next decade, genetic profiling of cancer will widely be used to overcome the current delays in cancer detection. Nanodevices in the form of nanorobotics may be for combined diagnosis and therapeutics. These devices could be implanted as a preventive measure in persons who do not manifest classic symptoms of cancer. These devices could also be employed in cancer surveillance by conducting external remote monitoring.

The deployment of these remote-sensing nanodevices however would be based on successfully detecting cancer in the early stages for timely therapeutic intervention. Such features as biodegradability ease of use and safety must also be ascertained before implantation. Ultimately, detection of biomarkers in specimens of body fluids from cancer patients, which are performed only periodically, would give way to such nanodevices because analyses conducted continuously *in vivo* would provide more accurate results. Biomedical nanotechnology in the next decade will play key roles in diagnosis, treatment and the development of personalized medicine. Because of the interrelationships of several biomedical nanotechnologies involved in Nanodiagnostics, the technicians involved in these tests would be at the forefront of decision-making in quality healthcare delivery in the future.

Conclusion

In conclusion, biomedical nanotechnology promises to extend the frontiers of current diagnostics and therapeutics, and enable the development of more personalized medicine. In the next decade, the technology would be more widely used in the rapid and more reliable diagnosis of cancer, as well as detection of infectious agents.

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None.

Conflict of interest

The author declares no conflict of interest.

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