Role of nanobiotechnology in the development of personalized medicine

"*Personalized medicine is the best way to integrate new biotechnologies into medicine for improving the understanding of pathomechanism of diseases, molecular diagnosis and integration with therapeutics.*"

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Personalized medicine simply means the prescription of specific treatments and therapeutics best suited for an individual taking into consideration both genetic and environmental factors that influence response to therapy [1,2]. Besides pharmacogenomics and pharmacogenetics, other -omics such as pharmacoproteomics and pharmacometabonomics are also contributing to the development of personalized medicine. Personalized medicine is the best way to integrate new biotechnologies into medicine for improving the understanding of pathomechanism of diseases, molecular diagnosis and integration with therapeutics. Nanomedicine is defined as the application of nanobiotechnology to medicine [3]. Nanobiotechnology is also making important contributions to personalized medicine through refinement of various technologies used for diagnostics and therapeutics as well as interactions among these (Figure 1).

Nanobiotechnology & biomarkers

Biomarkers play a role in personalized medicine as common reference points for diagnostics and therapeutics. A molecular biomarker is defined as an alteration of a cell on DNA, RNA, metabolite or protein level and nanotechnology is refining technologies for detection of biomarkers [4].

Nanomaterials are suitable for biolabeling, which is an important technology for biomarker studies. Water-soluble, biocompatible, fluorescent and stable silver/dendrimer nanocomposites have shown a potential for labeling cells *in vitro* as cell biomarkers. Quantum dots are stable and allow their use as molecular labels, for study of the earliest signs of cancer and to track the effectiveness of pharmaceuticals that target the cellular underpinnings of disease.

Proteomic technologies are important for discovery of biomarkers. Application of nanobiotechnology to proteomics, nanoproteomics, improves on most current protocols and facilitates analysis of low-abundant proteins and proteins that can only be isolated from limited source material. Given the variety of nanoparticle technologies that are available, it is feasible to tailor nanoparticle surfaces to selectively bind a subset of biomarkers and sequester them for later study using high-sensitivity proteomic tests [5].

Nanotechnology offers the possibility to create devices that can screen for disease biomarkers at very fast rates. The tools will be developed by identifying biomarkers for particular diseases that can then lead to diagnostic tests.

Nanobiotechnology for refining diagnostics

It is now obvious that direct analysis of DNA and protein could dramatically improve speed, accuracy and sensitivity over conventional molecular diagnostic methods. Since DNA, RNA, protein and their functional scaffolds and compartments are measured in the nanometer scale, nanobiotechnology-based approaches can provide more precise measurements. Nanobiotechnology is extending the limits of current molecular diagnostics and is facilitating point-of-care diagnosis, integration of diagnostics with therapeutics and thus advancing the development of personalized medicine [6].

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Molecular imaging is an important diagnostic modality that can be combined with therapeutics and is an important basic technology for personalizing therapy. Nanoparticulate agents, such as superparamagnetic contrast agent and perfluorocarbon nanoparticles, are being intensively studied as novel tools for molecular imaging that will enable noninvasive characterization and segmentation of patients for delivering personalized therapy [7]. Multifunctionality is the key advantage of nanoplatforms over traditional approaches as they have been employed in several biomedical imaging modalities such as optical imaging, CT, ultrasound, MRI,

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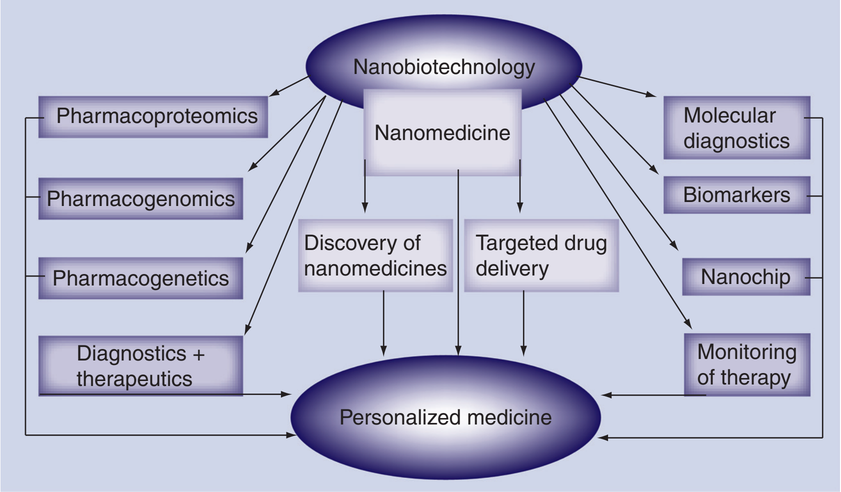

Figure 1. Relationship of nanobiotechnology and personalized medicine.

SPECT and PET [8]. Targeting ligands, imaging labels, therapeutic drugs and many other agents can all be integrated into the nanoplatform to enable for targeted molecular imaging and personalized medicine.

Discovery & delivery of personalized nanomedicines

Several nanotechnologies, including nanoparticles and nanodevices such as nanobiosensors and nanobiochips, are used to improve drug discovery and development [9]. Some of the currently used medicines are being personalized but discovery and development of some of the new medicines will take personalization into consideration at an early stage. Nanobiotechnology is already making a significant contribution to this aspect of pharmaceuticals.

Drug delivery is an important part of modern pharmaceuticals. Targeted delivery to the desired organ/site of action and passage through biological barriers are important for safe and effective use of drugs. Conjugation of nanocarriers to specific ligands and to aptamers enables specific targeting with improved clinical efficacy [10]. Nanoparticle-based improvements in drug delivery will enhance personalized medicine [11]. Nanotechnology has also made important contributions to refinements in the delivery of biological therapies such as cell and gene therapies, which are suitable for personalized treatments.

Role of nanobiotechnology in personalized oncology

Nanobiotechnology plays an important role in developing personalized approaches to the management of cancer [12]. Nanobiotechnologies will also improve detection of cancer biomarkers as a basis for devising diagnostics as well as therapeutics. Some examples of application of nanobiotechnology in improving cancer management are as follows.

$\alpha v\beta 3$-targeted paramagnetic nanoparticles have been employed to noninvasively detect very small regions of angiogenesis associated with nascent melanoma tumors [13]. Each particle is filled with thousands of molecules of the metal that is used to enhance contrast in conventional MRI scans. The surface of each particle is decorated with a substance that attaches to newly forming blood vessels that are present at tumor sites. This enables the detection of sparse biomarkers with molecular MRI *in vivo* when the growths are still invisible to conventional MRI. Earlier detection can potentially increase the effectiveness of treatment, particularly in case of melanoma. Another advantage of this approach is that the same nanoparticles used to detect the tumors can be used to deliver stronger doses of anticancer drugs directly to the tumor site without systemic toxicity. The nanoparticle MRI would enable physicians to more readily evaluate the effectiveness of the treatment by comparing MRI scans before and after treatment. This fulfills some of the important components of personalized cancer therapy: early detection, combination of diagnostics with therapeutics and monitoring of efficacy of therapy.

Dendrimers are a novel class of 3D nanoscale, core-shell structures that can be precisely synthesized for a wide range of applications including oncology. Specialized chemistry techniques enable precise control over the physical and chemical properties of the dendrimers. They are most useful in drug delivery but can also be used for the development of new pharmaceuticals with novel activities. Polyvalent dendrimers interact simultaneously with multiple drug targets. They can be developed into novel targeted cancer therapeutics. Dendrimers can be conjugated to different biofunctional moieties such as folic acid using complementary DNA oligonucleotides to produce clustered molecules, which target cancer cells that overexpress the high-affinity folate receptor [14].

Multifunctional and multiplex nanoparticles are now being actively investigated and are facilitating personalized cancer treatment [15]. When linked with biotargeting ligands, such as monoclonal antibodies, peptides or small molecules, nanoparticles can be used to target malignant tumors with high affinity and specificity. These developments provide opportunities for the progression of personalized oncology in which cancer detection, diagnosis and therapy are tailored to each individual's molecular profile [16].

Nanobiotechnology for personalized treatment of neurological disorders

Refinements in nanobiotechnologies applied to the nervous system will improve our understanding of neurological disorders and drug development as well as drug delivery for CNS disorders [17]. By improving molecular diagnosis of neurological disorders, nanobiotechnology will facilitate the integration of diagnostics with therapeutics, which is an important step in the development of a personalized approach to neurology [18]. Other ways in which nanotechnologies will contribute to the development of personalized neurology will be by development of rational therapies based on pathomechanisms of neurological disorders [19]. Targeted drug delivery to the brain by use of nanoparticles is also an important component of developing personalized treatment of neurological disorders [20].

Nanotechnology-based personalized medicine for cardiovascular disorders

The future of cardiovascular diagnosis is already being impacted by nanosystems that can both diagnose pathology and treat it with targeted delivery systems [21,22]. The dual use of perfluorocarbon nanoparticles for targeted drug delivery and molecular imaging in cardiovascular disease provides both visualization of disease states and drug delivery to the area of interest [23]. Image-based therapeutics with site-selective agents should enable verification that the drug is reaching the intended target and a molecular effect is occurring, which are important considerations for personalized therapy. Molecular imaging, as used in coronary artery disease, involves diagnostic strategies targeting biomarkers associated with the development of atherosclerotic lesions. Bioengineered nanoparticles can be utilized as transport vehicles of diagnostic or therapeutic agents for management of coronary artery disease [24].

Future prospects

Both nanomedicine and personalized medicine are already present on the clinical scene, although not officially designated as specialties of medicine. Both will continue to interact and evolve and will play an important role in shaping the future of medical practice. Safety and regulatory issues of nanomedicine are being investigated, and ethical as well as economic issues of personalized medicine are also being resolved. Not every disease requires a nanomedicine or personalized medicine and areas where these approaches are safe effective and cost effective are being identified. The ultimate aim of personalized medicine is to improve healthcare by use of new technologies. Among these, nanobiotechnology will play the most important role in integration of diagnostics with therapeutics, which is an essential component of personalized medicine.

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