Nanobiotechnology: A voyage to future?

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Abstract

Nanobiotechnology is an emerging field that is potentially changing the way we treat diseases through drug delivery and tissue engineering. Methods of targeting nanoparticles to specific sites of the body while avoiding capture by vital organs are major hurdles that need to be answered. Whether actual or perceived, the potential health hazards associated with the production, distribution and use of nanomaterial must be balanced by the overall benefit that nanobiotechnology has to offer biomedical science such as therapeutic and diagnostic applications. It would be difficult to deny the potential benefits of nanobiotechnology and stop development of research related to it since it has already begun to penetrate many different fields of research. However, nanobiotechnology can be developed using guidelines to insure that the technology does not become too potentially harmful. As Richard Feynmann has rightly predicted that "There is plenty of room at the bottom" to modify and enhance existing technologies by manipulating material properties at the nanoscale, therefore with sufficient time and research nanobiotechnology based early detection, diagnosis and treatment of various diseases may become a reality. Nanobiotechnology may bring immense paradigm shift that we would wonder that how did we live without it?

Keywords: Biotechnology, Drug delivery, In vivo, In vitro, Diagnosis, Toxicity, Tissue Engineeering.

Introduction

Scientists worldwide are continuing to discover unique properties of everyday materials at the submicrometer scale. This size domain is better known as nanometer domain and the technology concerned with this is known as nanotechnology that involves working with particles at nano level. Richard Feynman, in his classic talk "There's Plenty of Room at the Bottom - An Invitation to Enter a New Field of Physics" introduced the concept of nanotechnology in December 1959. A new branch of nanotechnology which is a rapidly advancing area of scientific and technological opportunity that applies the tools and processes of nano/microfabrication familiarly known as nanobiotechnology. In recent years this has shown lots of hope not only in diagnosis but also in monitoring, treatment and control as well as understanding of biological system. This technology is an emerging field that could potentially make a major impact not only in human health but also to animal welfare.

Various applications of nanobiotechnology

A.In drug delivery

Designing drug delivery system is challenging in terms of targeting the drug to specific sites. Controlled drug delivery strategies have made a dramatic impact in medicine. In general controlled release polymer system delivers drugs in the optimum dosage for long period, thus increasing its efficacy, maximising patient compliance, enhancing the ability to use highly toxic, poorly soluble or relatively unstable drugs. Nanobiotechnology based drug delivery system has overcome the problem such as poor solubility, drug instability in biological milieu, poor bioavailability and potential strong side effects that require drug enrichment at the site of action.

In general the drug delivery system comprises the drug, encapsulating material and surface coating agents. The drugs may be either a biological agent like RNA, DNA, protein or any pharmaceutical agent. The encapsulating material could be made from liposomes (spherical lipid bilayers), biodegradable polymers like polylactic acid (PLA), polyglycolic acid (PGA), polylactico-glycolic acid (PLGA) etc. which are biocompatible or dendrimers (tree like macromolecules with branching tendrils that reach out from a central core). Current research is aimed at improving the properties of the material such as biocompatibility, degradation rate, control over size and homogeneity of the resulting material. In order to control the targeted drug delivery of intravenously delivered nanoparticles, its interaction with macrophages must be controlled.

Nanobiotechnology is an emerging field that is potentially changing the way we treat diseases through drug delivery and tissue engineering. Methods of targeting nanoparticles to specific sites of the body while avoiding capture by vital organs are major hurdles that need to be answered. Whether actual or perceived, the potential health hazards associated with the production, distribution and use of nanomaterial must be balanced by the overall benefit that nanobiotech-nology has to offer biomedical science such as therapeutic and diagnostic applications. It would be difficult to deny the potential benefits of nanobiotech-nology and stop development of research related to it since it has already begun to penetrate many different fields of research. However, nanobiotechnology can be developed using guidelines to insure that the technology does not become too potentially harmful. As Richard Feynmann has rightly predicted that "There is plenty of room at the bottom" to modify and enhance existing technologies by manipulating material properties at the nanoscale, therefore with sufficient time and research nanobiotechnology based early detection, diagnosis and treatment of various diseases may become a reality. Nanobiotechnology may bring immense paradigm shift that we would wonder that how did we live without it? these interactions ranging from changing the size of the particle to changing surface properties. In order to decrease uptake by macrophages and to remove nonprotein adhesion, nanoparticles can be functionalized using protein repellant material such as polysaccharides, polyethylene glycol (PEG)[1]. Nonadhesive surface coatings increase the circulation time of the nanoparticles and reduced toxic effects associated with nontargeted delivery. One of the best examples of applying nanobiotechnology in solving problems in biology was the use of liposomes as drug delivery vehicles. A liposomal formulation of potent but toxic antifungal agent Amphotericin B has revolutionized the treatment of life threatening, systemic fungal infections in immunocompromised patients by allowing them to receive lethal doses of Amphotericin B with minimal risk of toxicity. Cancer therapy is being enhanced by the use of liposomal Doxorubicin which in term increases the therapeutic index of the active agent through a combination of passive tumor targeting and reduced toxicity. In this case PEG coated liposomes decreases uptake by macrophages and allows liposomes to concentrate in tumors by escaping from the leaky vasculature surrounding solid tumors through phenomenon known as the enhanced permeation and retention effect (EPR).

A significant amount of work exploring nanobiotechnological approaches for crossing blood brain barrier without sedimentation or blockade of microvasculature with minimal side effects has focused on the delivery of antineoplastic drugs to CNS e.g. Paclitaxel in PLGA nanoparticles has shown impressive results[2]. Targeted delivery of nanoparticles can be fulfilled by attaching a mAb (monoclonal antibody) or cell surface receptor ligand that binds specifically to molecules found on the surface of diseased cell, whether it may be a cancerous cell or angiogenic micro capillaries growing around malignant cells. Various targeting molecules like LH-RH, folate, thiamine, aptamers, receptor specific peptides etc. have been used successfully. Now research is much more focused on engineering multifunctional nano-construct which will eventually capable of detecting malignant cells in-vivo, pinpointing their locus in the body, destroying the diseased cells and reporting back that their payload has done its job. Such multifunctional nanodevices may enable new type of therapeutic approaches or enhanced application of existing methods to kill malignant cells.

Principles of nanobiotechnology can be applied to prevent and control a number of diseases like Brucellosis, Listeriosis, Leishmaniosis, Toxoplasmosis etc. in animals as well as humans. The causative agents of above diseases are intracellular which generally take shelter in the cells of immune system of body. Nanobiotechnology based drug delivery system that target such cells of immune system may offer new approaches to treat above dreadly diseases.

Scientists from Japan's Osaka University have enlightened on the application of nanosphere in delivering nasal vaccines. Nanosphere containing tetanus antigen when introduced to the human immune system through the mucous membrane showed significant results. Although still in its infancy, nanobiotechnology has overcome the barriers in delivering drugs and its success can be implicated through FDA approval of Rapamune (containing Sirolimus which is an immuno suppressant drug to prevent graft rejection in children after liver transplantation), Emend (contains aprepitant MK 869, for treatment of emesis with cancer chemotherapy), Abraxane (albumin bound Paclitaxel used in cancer therapy)[3].

B. Diagnosis

Nanotechnology is of great use for medical diagnosis and various nanoparticles have exhibited tremendous potential for detecting disease markers, pre-cancerous cells, fragment of viruses and other indicators.

1. Diagnosis by in-vivo method

A variety of nanosized materials have already demonstrated using imaging tumors and its microenvironment in animal models and human clinical trials. Some of the most recent works in this area uses dextran coated ultra-small super magnetic iron oxides

(USPIO) nanoparticles to image micrometastases in lymphnodes in patients with prostate cancer. Paramagnetic, Gadolinium labeled nanoparticulate dendrimers has been used to image breast cancer. Nanoparticles can be able to identify micrometatases less than two millimeter diameter in normal lymphnode, well below the typical detection limit of PET (positron emission tomography) which is thought to be the most sensitive and specific imaging technique in several clinical scenarios. Animal experiments demonstrated that nanoparticles coated with monoclonal antibody to breast carcinoma marker HER-2 (human epidermal growth factor) were able to detect tumor successfully in-vivo[4]. Management of animal breeding can be improved by using subcutaneous nanotubes. These nanotubes can be used to track estrous in animals. These tubes have the capacity to bind and detect the estradiol Ab at the time of estrous by near infrared fluorescence. The signal from the sensor could be incorporated as part of a central monitoring and control system to actuate breeding. A special charged silicon nanowire connected with antibody receptor that can detect the presence of cancer markers in the blood even if the concentration of these antigens (cancer markers) in blood is about hundred- billionth of the protein content is being synthesized recently by researchers at Harvard University.

2. Diagnosis by in-vitro method

Silicon based arrays made up of Ab-conjugated nanoware field effect transistors have been multiplexed to simultaneously detect even single copies of multiple viruses. Functionalized carbon nanotubes also serve as highly specific electronic biosensors. Various nanoscale particles also provide remarkable analytical sensitivity in a variety of in-vitro assays without the use of radio isotopes. QDs are crystalline clumps of several hundred atoms with an insulating outer shell which can serve as an effective delivery and diagnostic agent to detect quantitatively the cellular and subcellular components. Semiconducting quantum dots (QD) labeled with tumor marker Abs such as anti-HER-2 can effectively assess biopsy tissue in less time by eliminating the unnecessary steps in conventional methods. Similarly, gold nanoshells, whose optical properties also depend in a predictable manner on size, have been used to detect picogram per milliliter quantities of Abs and other biomolecules in whole blood. Nanoparticle based detection of a soluble pathogenic biomarker for Alzheimer's disease (ADDL-Amyloid beta derived diffusible ligand) is a land mark achievement. Now it is possible to detect the glucose concentration by using nanogold particle based plasmon resonance imaging technique in any body-fluid in non invasive method[5]. Nanochips can be used to check whether the patient is susceptible to heart attack by taking a drop of saliva only.

C. Nanobiotechnology in tissue engineering

Nanobiotechnology and microtechnology can be merged with biomaterials to generate scaffolds for tissue engineering that can maintain and regulate cell behaviour. Nanofabricated and microfabricated tissue engineering scaffolds have the potentials to direct cell fate as well as regulate processes such as angiogenesis and cell migration. Using micropatt-erning and nanopatterning, cell shape has also been shown to influence cell behaviour. So it is envisioned that this type of nanopatterning can be used to direct cell behaviour to induce stem cell differentiation and generate desired cell types or regulate cell behaviour within 3D scaffolds.

D. Blood substitutes based on nanobiotechnology

Stimulated by concerns of potential agents in donated blood, scientists have attempted several times to develop blood substitutes since a decade. In addition RBCs can't be sterilized to remove infective agents such as HIV, Hepatitis virus etc. Thus, substitutes for RBC are being developed. After several efforts, nanobiotechnology based blood substitutes have shown immense rays of hopes[6].

First generation RBC substitutes such as poly Hb (approved for human use in South Africa), conjugated Hb (test is under trial), cross linked molecular Hb and recombinant molecular Hb has shown encouraging results. Second generation RBC substitutes such as poly Hb-SOD-CAT (poly Hb-superoxide desmutase-catalase) and third generation complete RBC substitutes are under clinical trial.

Toxicity issues

It has been shown that nano particles can enter human body through several ports. Accidental or involuntary contact during production or use is most likely to happen through the lungs, skin or G.I.T (Gastro Intestinal Tract) from where a rapid translocation through blood stream is possible to other vital organs. This may cause altered gene expression, cytotoxicity, idiosyncrasy, and apoptosis of the cell if remain for a longer period. It may cause granuloma in skin and intestine and severe fibrosis in lungs if not cleared immediately from the body.

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