NANOMEDICINE: A GIANT LEAP FORWARD IN DISEASE DIAGNOSIS & TREATMENT

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Abstract

Nano medicine represents a subfield of nanotechnology that uses particles in the size range of 1–1000 nm for the treatment, diagnosis, monitoring and control of various diseases. Nanoparticles, which are similar in scale to biological macromolecules such as DNA and proteins, can be used for targeted therapy through DNA, protein and drug delivery, *in vivo* imaging, and diagnostics, (as well as) for the creation of active scaffolds and implants. Recently, a dual modular system that mimics the communication-dependent recruitment of inflammatory cells to regions of disease has been developed to improve the tissue target efficiency of nanoparticles. Another more recent study has demonstrated the programming and assembly of DNA-based nanorobots that are able to carry molecular loads, transport chemical ingredients to target cells and stimulate their intracellular alterations. These sophisticated biomaterials are increasingly being incorporated into the stem cell biology field. The combination of stem cells with innovative nanotechnology holds great promise for applications in the biomedical arena.

Key Words: - Nanodentistry, Nanomedicine, Nano robots, Stem cell.

Introduction

One of the most promising applications of nanotechnology is in the field of medicine. Indeed, a whole new field of “nanomedicine” is emerging. Nanomedicine has been defined as the monitoring, repair, construction and control of human biological systems at the molecular level using engineered nano devices and nanostructures.[1] It can also be regarded as another implementation of nanotechnology in the field of medical science and diagnostics. The National Cancer Institute and the National Aeronautics & Space Administration, USA are working to develop nano-sized technologies that can detect, diagnose, and treat disease. Researchers in this field are “confident that they are going to turn healthcare inside out. “Richard Smalley, a Nobel Prize-winning chemist at Rice University, USA, described to the Congress how the potential of nanotechnology can transform medicine: Twenty years from now, nanotechnology will have given us specially engineered drugs that specifically target just the mutant cancer cells in the human body, and leave everything else blissfully alone. Cancer will be a thing of the past.[2] Nanotechnology can be defined as the science and engineering involved in the design, synthesis, characterization, and application of materials and devices whose smallest functional organization in at least one dimension is on the nanometer scale or one billionth of a meter. The prefix “nano” is derived from the Greek word for dwarf. One nanometer (nm) is equal to one-billionth of a meter, or about the width of six carbon atoms or ten water molecules. Current applications of nanotechnology in medicine range from research involving diagnostic devices and drug delivery vehicles to robots that can enter the body and perform specific tasks. In the near future, applications of nano medicine will involve engineered molecules to develop drugs, drug delivery techniques, diagnostics, medical devices and enhanced gene therapy and tissue engineering procedures.[3]

Nanoparticles can be composed of organic materials (e.g., lipids), inorganic materials (e.g., iron oxide or gold), or a combination of both types. Novel and improved nanostructured materials can be tailored by engineering (their) characteristics such as structure, stability, size, shape and surface properties in order for them to be selectively delivered to precise sites (target regions) of the body.[4] This can be achieved through passive or active targeting mechanisms: passive targeting is enabled by enhanced vascular permeability during neoangiogenesis of injured or pathological body sites, while active targeting benefits from over expression in the infectious or damaged areas of several cell surface molecules that can bind specifically to precoated nanoparticle ligands.[4,5]

The development of nanomaterials could be helpful in detecting and manipulating stem cells that will be used for tissue repair in the clinic. Nanomaterials are being used to precisely define the stem cell microenvironment through the provision of morphogenetic gradients and cell adhesion molecules, to direct stem cell fates and to provide a template for stem cells for the formation of new tissues and organs. Furthermore, internalization of nanoparticles, previously labeled with chelated ions, small molecules, metals and nanocrystals, by stem cells enables their detection by imaging. The physical, chemical and biological properties of nanomaterials can be exploited to influence proliferation, attachment, fate and differentiation of stem cells.[6]

This multidisciplinary approach allowed scientists to create a fully synthetic organ for transplantation after soaking a porous polymer nanocomposite tracheobronchial replica in a solution of bone marrow stem cells.[7] Although these new developments are encouraging, long-term studies are necessary before we can exploit such synthetic nanosystems in the clinic. For example, it is important to verify nontoxicity, exclude tumorigenic potential[8] and adverse side effects on a systemic level of nanoparticles, and study their interference with the self-renewal ability of stem cells. In addition, the pharmaceutical industry, has been reticent to engage with the cell-based regenerative medicine industry probably because of the complex regulatory and ethical issues.[9] This leads to uncertainty regarding the cost and time that will be required to successfully gain market approval for nanomedicine. The development of nanomaterials could be helpful in detecting and manipulating stem cells that will be used for repair and regeneration of periodontal tissues.

Nanomedicine as a Potential Platform for Therapeutic Applications

Applications of nanotechnologies in medicine are especially promising, and areas such as disease diagnosis, drug delivery targeted at specific sites in the body and molecular imaging are being intensively investigated and some products are undergoing clinical trials. Nanotechnology is relatively new. Although the full scope of contributions these technological advances will make in medicine is unexplored, recent advances suggested nanotechnology will have a profound impact on disease prevention, diagnosis, and treatment. The current generation of drugs is largely based on small molecules with a mass of 1000 Da or less that circulate systemically. Common deleterious consequences of systemic bio distribution include toxicity to non-target tissues, difficulty in maintaining drug concentrations within therapeutic windows, and metabolism and excretion of drugs, all of which can reduce efficacy. Drug solubility and cell permeability issues are also common with small molecules and biologics. Nanotechnology-based delivery systems could mitigate these problems by combining tissue- or organ-specific targeting with therapeutic action. Multifunctional nano-delivery systems could also combine targeting, diagnostic, and therapeutic actions. Drug bioavailability is a related problem with potential nanotechnology solutions. Nanotechnology is opening up new therapeutic opportunities for a large number of agents that cannot be used effectively as conventional oral formulations, due to poor bioavailability. In some cases, reformulation of a drug with smaller particle size may improve oral bioavailability. Nanoparticles formulations provide protection for agents susceptible to degradation or denaturation in regions of harsh pH, and also prolong the duration of exposure of a drug by increasing retention of the formulation through bio adhesion.

Another broad application of nanotechnology is the delivery of antigens for vaccination. Mucosal immunity is extremely important in disease prevention, but continues to be limited by both degradation of the vaccine and limited uptake. Recent advances in encapsulation and development of suitable animal models have demonstrated that micro and nanoparticles are capable of enhancing immunization. It has been shown that M cells in the Peyer's Patches of the distal small intestine are capable of engulfing large microparticles and recent studies have explored the benefits of nanoencapsulation.[10]

Nanomedicine as Diagnostic Purposes

Biomedical laboratory diagnosis plays a key role in today's health care. Most testing is done on a macroscopic scale, for example, in micro titer plates. Size reduction of biomedical lab tests has several advantages: Not only does it lead to a marked reduction of the sample volume needed for testing, but it also results in a marked reduction of (potentially expensive) reagents such as monoclonal antibodies. Moreover, the ability of current nanotools to measure interaction microforces between individual molecules is most promising for biomedical testing because this might eliminate the need for reagent labeling, a tedious and expensive step. Taken together, small sized sample volumes and fast reaction times bring mobile testing devices into the realm of reality. They indicate that there will be a strong trend toward point-of-care testing at the bedside or in an ambulatory setting.[11]

One of the first applications of nanomedicine will be improved fluorescent markers for diagnostic and screening purposes. Conventional fluorescent markers require complex color. Non-invasive imaging techniques had a major impact in medicine over the past 25 years or so. The current drive in developing techniques such as functional magnetic resonance imaging (MRI) is to enhance spatial resolution and contrast agents.

Nanotechnology could significantly improve diagnostic capabilities. Nanomedicine will increase the efficiency and accuracy of diagnosis from samples of body fluids. For example, some companies are attempting to develop microchips that use electrodes to identify the dielectric properties of cancerous cells, viruses, and bacteria in body fluids. Nanomedicine could result in non-invasive devices that can enter the body to determine glucose levels, distinguish between normal and cancerous tissues, and provide genetic screening for multiple diseases.[12]

Nanovehicles and drug carriers:

In addition, there are numerous engineered constructs, assemblies, architectures, and particulate systems, whose unifying feature is the nanometer scale size range (from a few to 250 nm). These include polymeric micelles, dendrimers, polymeric and ceramic nanoparticles, protein cage architectures, viral-derived capsid nanoparticles, polyplexes, and liposomes. First, therapeutic and diagnostic agents can be encapsulated, covalently attached, or adsorbed on to such nanocarriers. These approaches can easily overcome drug solubility issues, particularly with the view that large proportions of new drug candidates emerging from high-throughput drug screening initiatives are water insoluble. But some carriers have a poor capacity to incorporate active compounds (e.g., dendrimers, whose size is in the order of 5–10 nm). There are alternative nanoscale approaches for solubilization of water insoluble drugs too.[13] One approach is to mill the substance and then stabilize smaller particles with a coating; this forms nanocrystals in size ranges suitable for oral delivery, as well as for intravenous injection.[13,14] Thus, the reduced particle size entails high surface area and hence a strategy for faster drug release. Pharmacokinetic profiles of injectable nanocrystals may vary from rapidly soluble in the blood to slowly dissolving. Second, by virtue of their small size and by functionalizing their surface with synthetic polymers and appropriate ligands, nanoparticulate carriers can be targeted to specific cells and locations within the body after intravenous and subcutaneous routes of injection.[15,16] Such approaches, may enhance detection sensitivity in medical imaging, improve therapeutic effectiveness, and decrease side effects.

Some of the carriers can be engineered in such a way that they can be activated by changes in the environmental pH, chemical stimuli, by the application of a rapidly oscillating magnetic field, or by application of an external heat source.[17,18] Such modifications offer control over particle integrity, drug delivery rates, and the location of drug release, for example within specific organelles. Some are being designed with the focus on multifunctionality; these carriers target cell receptors and delivers simultaneously drugs and biological sensors.[19] Some include the incorporation of one or more nanosystems within other carriers, as in micellar encapsulation of QDs; this delineates the inherent nonspecific adsorption and aggregation of QDs in biological environments.[20] In addition to these, nano scale-based delivery strategies are beginning to make a significant impact on global pharmaceutical planning and marketing (market intelligence and lifecycle management).[21,22] Recent advances in nanoscale materials increase the potential to control stem cell fate, improve DNA and drug delivery, modulate the immune response to implanted cells, and create advanced scaffolds for the treatment of various diseases. Nanomaterials and cell-based products must be regulated and manufactured at a low-cost scale to ensure their successful application in clinics. Dental clinics could benefit in the near future from the combinatorial use of stem cells and nanostructures (e.g., creation of specific scaffolds). These devices, which will contain cells, could be implanted into damaged dental sites in order to regenerate them. However, there are serious issues concerning standardization of techniques, nanoparticles and stem cells that have to be solved before their clinical application in humans.[22]

Nanomedicine in periodontal tissue regeneration

The combination of innovative nanotechnology and stem cells with holds great promise for applications in the future periodontal regeneration. The development of either improved or innovative nano structured materials (*i.e*., on the scale of 1-1,000 nm) could be useful in manipulating stem cells by use of nanotecnology that will be used for repair and regeneration in the periodontal tissues. Nanomaterials are being used to precisely define the stem cell microenvironment through the provision of morphogenetic gradients and cell adhesion molecules, to direct stem cell fates and to provide a template for stem cells for the formation of new periodontal tissues.[23]

Conclusion

The genesis of nanomedicine can be traced to the promise of revolutionary advances across medicine, communications and human health care. The health care revolution brought about by nanomedicine could dwarf all other trends in the history of medical technology. Although the FDA should be relatively prepared for some of the earliest and most basic applications of nanomedicine in areas such as gene therapy and tissue engineering, more advanced applications of nanomedicine will pose unique challenges in terms of classification and maintenance of scientific expertise. The agency should begin to prepare now for the coming revolution in nanomedicine. There is no doubt that nanotechnology offers enormous benefits and a plethora of exciting perspectives to cell-based regenerative medicine.

Recent advances in nanoscale materials increase the potential to control stem cell fate, improve DNA and drug delivery, modulate the immune response to implanted cells, and create advanced scaffolds for the treatment of various diseases. Nanomaterials and cell-based products must be regulated and manufactured at a low-cost scale to ensure their successful application in clinics. Dentists could benefit from the use of nanoparticles to label stem cells, which, after being placed on scaffolds, could be further implanted into damaged dental tissues in order to regenerate them. The application of nanotechnology for dental purposes (nanodentistry) holds great promise as a type of personalized medicine for the management of target-specific treatment and imaging of dental tissues.

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