Nanotechnologies in Medicine

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Abstract

Nanotechnologies have unique properties, making them useful in many fields of medicine. They have many potential uses in the fields of regenerative medicine, ophthalmology, cancer treatments, bone engineering, physiotherapy, nano dentistry and more. In regenerative medicine, the specific nanotechnologies, and materials such Graphene Oxide (GO) or nanofibers can help facilitate the differentiation of stem cells. This differentiation of stem cells can be used in ophthalmology to produce healthy ocular cells for people with vision impairments. Nano-based scaffolds have a promising use for bone tissue engineering by promoting the proliferation and differentiation of stem cells. Their potential uses in orthopedic physiotherapy also includes increased bone and tendon healing. Nanotechnologies are also used as a minimally invasive form of drug delivery for cancer treatment by using passive and active forms of transport to target tumorous cells. In the field of dentistry, nanotechnologies can also help with treatments, recovery and more. Quantum dots (QD) are also a promising way of detecting disease-related biomarkers, such as detecting early signs of cancers. A lot more research needs to be done for nanotechnologies to be widely used, but nanotechnologies still remain a very promising field of research.

Keywords: Nanotechnology, medicine, regenerative medicine, dentistry, cancer therapy, bone engineering, physiotherapy

What are nanotechnologies – Nathan Vong

The vision of nanotechnologies was first introduced in 1959 by Nobel Prize-winning physicist Richard P. Feynman. Nanoscale objects correspond to 10^{-9} m of a material, with nanomaterials usually ranging from 1-100nm. In fact, materials of that size exhibit different physical properties than large-scale material, becoming a new field of science [16]. The properties of nanoparticles greatly can be tuned by controlling the size, shape, synthesis conditions, etc [17]. More recently, nanotechnologies have started to be studied for its potential uses in other fields, such as of medicine, biomedical sciences, bioengineering, food technology, biochemistry, biophysics, etc. Their unique properties make them possibly revolutionary technologies in modern medicine. This review paper will explore the current research and applications of nanotechnologies in different fields of medicine [16].

Nanotechnologies in regenerative medicine – Aly Shalaby

Numerous medical treatments remain incomplete due to the absence of advanced technology and proper tools. To address this issue, modern medicine has embraced the concept of cell therapy. This innovative approach involves utilizing viable cells as therapeutic agents with the assistance of nanotechnology tools. Cell therapy is broadly categorized into stem cell-based therapies, endogenous cell repair, cell-mediated drug delivery, and direct cell reprogramming.

Stem cell-based therapies

<u>Graphene Oxide:</u>

At the heart of cell-based therapy lies a crucial component: Graphene Oxide (GO). This carbon-based monolayer, with its unique properties, is not just mechanically robust, but also a proficient conductor of heat and electricity. By modulating integrin-mediated signaling, GO enhances embryonic stem (ES) cell self-renewal and guides ES cell differentiation into various lineages. This includes the production of dopaminergic neurons for Parkinson's Disease and hematopoietic cells for hematological disorders. Moreover, GO facilitates the differentiation of tissue-specific multipotent stem cells, such as human neural stem cells, into neurons with reduced glial cell formation. This advancement enhances the purity of stem cell-derived neurons, making them more suitable for therapeutic use, a fascinating development in the field of regenerative medicine.

Nanofibers:
The impact of the extracellular matrix (ECM) on stem cell proliferation and differentiation is an intriguing area of research. This influence led to nanofiber systems that emulate ECM properties, particularly aliphatic polyester nanofibers such as poly-ε-caprolactone (PCL). When combined with collagen, these nanofibers significantly promote the differentiation of stem cells into motor neurons, tendon-like tissue, and cardiomyocytes. This has profound implications for therapies targeting neuromuscular, musculoskeletal, and cardiac disorders. Additionally, polymers like PVDF and PHBV have been shown to enhance differentiation into neural progenitors and insulin-producing cells. Similarly, PAs have been found to improve the effectiveness of stem cell therapy in muscle and neural tissue, offering promise for the treatment of muscle and spinal cord injuries.

Nanoparticles:

Nanoparticles are used in the intracellular delivery of Bioactive Cargo, gene transfer, supporting stem cell-based therapies in vivo, and enhancing neurogenesis and cell differentiation.

Endogenous cell repair

Nanoscale technologies play a crucial role in supporting cell therapies and promoting healing by influencing cell behaviors. For instance, peptide amphiphiles imitate VEGF to stimulate angiogenesis, nanotube scaffolds assist in nerve repair, and nanofiber coatings alleviate inflammation in tendon injuries. Gold nanoparticles expedite wound healing, while conductive nanofibrous membranes enhance heart function after a heart attack. These advancements illustrate the potential of nanotechnology in regenerative medicine by modulating the body's natural cell responses.

Cell-mediated drug delivery

Nanotechnology is currently investigating cell-mediated drug delivery as a promising alternative. This involves utilizing "cellular backpacks" that are attached to macrophages to deliver drugs to the brain, thereby reducing neuroinflammation. Additionally, Sertoli cells loaded with chitosan nanoparticles have been found to efficiently target pulmonary tissues for deep lung therapy. Furthermore, research is being conducted on myeloid-derived suppressor cells (MDSCs) for extracellular vesicle-mediated gene delivery, which holds the potential for treating tumors and contributing to regenerative medicine for conditions such as stroke and Alzheimer's disease.

Direct cell reprogramming

Direct cell reprogramming allows for the alteration of cell fate without the need to pass through a pluripotent intermediate stage, creating opportunities for personalized cell therapies. By using readily available cell sources such as skin fibroblasts and bypassing induced pluripotency, direct reprogramming improves safety and effectiveness. Nevertheless, conventional methods involving viral vectors raise concerns regarding biosafety and size constraints, prompting the advancement of nanotechnologies such as nanoparticles and nanotransfection techniques to tackle these issues. [1,2,3,4]

Nanotechnologies in ophthalmology – Youssef Shalaby

Nanotechnology is also used for regenerative therapy in medicine (Lowe et al. 1). The two types of regenerative care are exogenous and endogenous. Exogenous is a cell-based treatment that is meant to replace dead cells after an injury, and endogenous allows organs to have better restorative capabilities [5]. Regenerative therapy has a great amount potential in one particular field, ophthalmology. In truth, its purpose is to replace the dead or loss ocular cells that cause reduced vision and blindness. As it is a recent topic, no end procedures were approved, but rather a direction of what to look for. Actually, the exogenous prototype consists of distributing living allogenic or autologous cells, focusing on stem cells. Nevertheless, many obstacles impede the development of this model, particularly due to the immune response of the body. In fact, the patient needs a chronic systemic immunosuppression to have an effective cell transplantation. However, this requirement can cause many disorders, which include but are not limited to the chronic graft-versus-host disease. Furthermore, different categories of nanoscaffolds are used to study ocular regenerative healing. They can be modified to have the same chemical and physical properties that imitate the natural corneal and retinal microenvironments. However, natural polymers are more suitable for cell attachment, but they have reduced mechanical strength and shorter half-life than synthetic ones.Consequently, a merging of both types of polymers is used in the transplantation process. To sum up, nanotechnology is a very effective tool for regenerative ophthalmology since it can cure blindness, but because of the lack of a concrete model, no convincing clinical trial results were published to this day [6].

Cancer and nanotherapies – Elizabeth Andriopoulos

Nanotechnology through drug delivery for cancer treatment can become a better alternative or addition to current chemotherapy, radiation and gene treatments because of its reduced toxicity, bioavailability and ultimately its availability to target tumorous cells more accurately leaving minimal side effects on normal cells. The delivery of nanoparticles through vehicles can happen in two main ways. First, through passive transport that brings the nano-therapies directly into the bloodstream to be able to reach the targeted tumor site. The second is through active transport that is powered by using different hybridized molecules along with the carrier to specifically target the tumor site. Most of the nano-therapies for cancer being studied use active transport. This includes extracellular vesicles which are useful for the targeting of brain tumors because they have the ability to cross the brain blood barrier. It also includes nanoemulsions, which use the theory of water in oil or vice versa. These are advantageous because they reduce side effects and are being studied to see if it is possible to use them without carriers. Another method is nanoparticles that are produced by inorganic molecules. There are many different subcategories such as gold, magnetic and quantum dots. Gold nanoparticles can be used to deliver small as well as large particles. Magnetic nanoparticles can be used for delivery of drugs containing metallic shells. Carbon quantum dots are fluorescent particles that have great surface functionalization and therefore have high targeting capabilities. Therefore, are super great to use for imaging. Finally, there is a method that can be given through both active and passive transport, solid lipid nanoparticles. These are made by replacing the lipid lipid bilayer by a solid lipid bilayer. The codelivery method of these particles gives them an advantage. This all being said the currently approved nano-therapeutics for cancer currently are limited. The first one in the US being Doxil which targets ovarian cancer in 1995. Now, there are currently 24 approved nanomedicine drugs for cancer treatment in the world. Researchers currently have many more undergoing the phases of clinical trials. At the same time, they are focusing on how to develop nano-therapeutics that are more effective while still only causing an accumulation in the tumor site and not in normal cells which is a tough feat since it is hard to tell the toxicity of these therapeutics [7,8].

Nanotechnology in bone engineering – Zhi Jun Liu

Nanotechnology in bone tissue engineering employs nanoparticles ranging from 10 to 100 nm to perform targeted drug delivery, label stem cells, and build longer-lasting scaffolds to enhance bone growth. Size matters when it comes to the infinite small: particles smaller than 10 nm are filtered out by the kidneys and those larger than 200 nm are phagocytosed by the spleen. First, nanoparticles called nanospheres are used to delivery drugs or growth factors for the bones. Their small size allows them to quickly adapt to stimuli from the changing environment such as pH variation, magnetic field, ultrasound, and irradiations. Scientists control the nanosphere's path and target by stimulating the nanoparticle's reacting factors. For example, supramagnetic iron oxide nanoparticles (SPIONs) convey drugs under directive of a magnetic field stimulated by a MRI, allowing efficient drug injections to favor bone growth. Moreover, nanoparticles like quantum dots, mesoporous silica, gold, and SPIONs have also been used to tag mesenchymal stem cells (MSCs). MSC are pluripotent stem cells that can differentiate into bone cells, cartilage cells, muscle cells and fat cells. However, while in vitro studies show that SPION and gold nanoparticles do not interfere with the bone forming capacity of MSC cells, other in vivo reports suggest otherwise. More research is needed in this area. Lastly, nano-based scaffold constructions allow for more compatible surface and mechanical strength necessary for enhanced cellular adhesion, stem cell differentiation, and integration to surrounding tissues. Scaffolds are temporary or permanent structures used as frameworks to support cell proliferation and differentiation to regenerate new tissues. Nano-modified scaffolds have improved surface topography, making them more efficient than classical scaffolds made of simple biodegradable polymeric materials. In short, nanotechnology in bone tissue engineering offers promising avenues to improve bone regeneration, but continued research is necessary to optimize their effectiveness in clinical applications [9][10].

Nanotechnology in physiotherapy – Huu Thien Tran

Orthopaedic Physiotherapy primarily focuses on orthopedics and treating conditions affecting the musculoskeletal system, composed of joints, muscles, bones, ligaments, and tendons. Nanotechnology is relatively new to orthopedic research, diagnostics, and treatment. However, nanotechnology has been applied in orthopedic surgery to improve surgical outcomes, enhance bone healing and growth, and reduce complications associated with orthopedic procedures and theoretically safer methods of treating the human body regarding infection rates and reducing the need for reoperations [13]. Nanotechnology can also improve drug delivery systems and create a nano-delivery system for CRISPR/Cas9 gene editing to be used more safely and efficiently in the clinic for patients with osteoarthritis and bone tumours [14]. Nanotechnology and medication delivery may also be effective for tendon healing by boosting tendon adhesion post-surgery. Additionally, nanocomposite scaffolds can be used for tendon tissue engineering as well. These scaffolds appear to meet the standards of regenerated tendons better than allografts and have demonstrated that they have increased healing and mechanical stability [12]. Nevertheless, because of the nature and complexity of nanotechnology products, cost barriers should be investigated and addressed. The high price of these products can limit their accessibility, and the current regulatory processes can be lengthy and restrict the speed at which research can be implemented. When these concerns are addressed, nanomaterials will be more accessible and see greater use in orthopedics [13].

Nanodentistry – Yiluo Fan

The prefix "nano" came from the Greek word "nannos" (dwarf), implying one billionth of a meter. Nanotechnology is therefore able to analyze structures at the nanoscale level. In dentistry, nanotechnology helps provide more accurate and better oral treatments for patients. Nanotechnology creates nanoparticles, which are in turn used in the production of nanocomposites. These composites exhibit significant durability against tooth abrasion, in which a highly polished tooth surface may maintain its smoothness for a much longer time than hybrid composites. In tissue engineering, nanoparticles improve the quality of ceramic materials, and the time needed for recovery from implantation has been significantly reduced with the use of nanoparticles. In addition, the incorporation of nanotechnology in robots also presents various potential benefits in the field of dentistry. People can coordinate nanorobots to perform movements with nanocomputers, such as navigating between teeth to assist in the patients' oral treatments. By using some specific toothpaste or mouthwash products that contain nanorobots, nanorobots can stay in a patient's mouth and perform cleaning works on the teeth's surface. Even if the person swallows them, the robots can still be turned off without any safety repercussions. In the future, scientists look forward to creating new teeth in labs (in vitro) for dental repair. The fillings used contain biological materials that are like natural teeth. Lastly, nanorobots are also expected to aid in providing permanent treatments for issues regarding dental sensitivity [15].

Using quantum dots in diagnosis and treatment – Jabin Lim

Operating at the nanoscale, medical imaging has significantly advanced medical research and treatment by enabling noninvasive visualization of internal tissues. Integrating nanoscale microparticle technology into medical imaging promises enhanced diagnostic accuracy. Experimental results indicate that image quality adjustments impact transmission rates, with images remaining stable at 60% quality, suitable for medical applications. The introduction of nanotechnology has driven the development and utilization of biosensors and nanobiosensors in biomedical sciences, facilitating the detection of disease-related biomarkers and aiding in disease identification and diagnosis. For instance, skin disease diagnosis, traditionally challenging, can now be improved with the use of multilayered perceptron with backpropagation neural networks (MLP-BPNN), sensing the chemical, physical, and biological conditions of the patient's skin with better detection specificity and sensitivity for more precise diagnosis of conditions like melanoma, nevus, psoriasis, and seborrheic keratosis. However, challenges arise from nanoparticles' size and charge, hindering efficient body clearance and potentially increasing toxicity. Quantum dots, which are nanoscale semiconductor particles ranging from 2 to 10 nanometers acting as semiconductor particles commonly composed of materials like cadmium selenide or indium arsenide could offer a solution. Emitting varied colored light, they are valuable for displays, lighting, and biological imaging. For instance, using intravenously administered quantum dots in rodent models, researchers have identified criteria for renal filtration and urinary excretion of metal-containing nanoparticles. Coatings preventing serum protein adsorption facilitate renal excretion, with a hydrodynamic diameter <5.5 nm enabling efficient elimination. Furthermore, semiconductor nanocrystal quantum dots (QDs) show promise in molecular and in vivo imaging, particularly in cancer research. Recent studies highlight QDs' applications in early detection of various cancers, including ovarian, breast, prostate, and pancreatic cancers, as well as regional lymph nodes and distant metastases [18,19,20].

Conclusion

Although, the nanotechnologies mentioned are still experimental and lack clinical trial, they remain potentially novel forms of treatments in various fields of medicine. They still require much more research before being commonly used for treatment. Further aspects of nanotechnologies that remain to be studied are their cost efficiency, their side effects and their health risks. With the development of new nanomaterials accompanied by new innovative uses for them, nanotechnologies are bound to improve a lot more, potentially becoming a crucial component in improving modern medicine.

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