1

NANOMATERIALS FOR MEDICINE

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1.1 INTRODUCTION

Nanotechnology is an interdisciplinary research area that studies the characteristics of materials at nanometer scale and developing new materials with new functionalities. Advances in nanotechnology enable us to develop new molecules and materials with more controlled chemical, physical, and biological properties. The new techniques and materials produced by using nanotechnology provide a vast array of opportunities for diagnosis and therapy of many diseases that are still considered extremely challenging by medical professionals such as cancer, Alzheimer's disease, Parkinson's disease, diabetes, and aging-related disorders. In addition, nanotechnology provides us tools to study the in-depth mechanisms of the biological machinery enabling us to learn more about the pathophysiology of the diseases. These detailed analyses can be utilized to pinpoint the exact causes behind these diseases and correct the defects in the biological machinery. Since biological machinery works at nanoscale (e.g., the diameter of DNA is 2 nm; a typical ribosome's diameter is 20–30 nm; individual collagen fibers of the extracellular matrix are ~1.5 nm in diameter and 300 nm in length), it can best be manipulated by using nanoscale materials with controlled functionalities.

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Thus, nanomaterials with controlled physical, chemical, and biological characteristics can be used for the therapy of the specific causes of the diseases.

Overall, nanomaterials serve two important purposes for medical applications: They can be utilized to understand the pathophysiology of the diseases by enhancing detailed knowledge of biological machinery and increasing diagnosis efficiency, and they can provide us novel approaches to interrupt or correct the regular biological activity depending on the disease type and the treatment strategy.

1.2 NANOSCALE MATERIAL PROPERTIES

Nanoscale is generally considered as dimensions between 0.1 and 100 nm, and nanomaterials can display extraordinary characteristics compared to their micro- or macroscale counterparts. New synthesis techniques can control shape and function of materials at the nanometer level. There are several ways to develop new materials in nanometer scale. Mainly, top-down and bottom-up approaches are the two major techniques to produce nanomaterials. In the top-down techniques, bulk materials are tailored into specific shape and size with recent high-tech tools. For example, soft-lithography techniques can craft bulk surfaces into nanostructured textures to create a high surface area and molecular contact points with the biological materials. In bottom-up approaches, small molecular building blocks are used to form more complex and higher-scale nanometer-sized materials. Both techniques have advantages and disadvantages in terms of their fabrication method and product function. In theory, it is desired to utilize both techniques in conjunction so that we can eliminate the weaknesses of each technique. Depending on the application area, either one or both of these approaches can be used to develop materials that can be used in studying pathophysiology of diseases and their diagnosis and therapy. Especially, bioinspired and biomimetic strategies yield products that can replace or accommodate activities of the natural biomolecules. Nevertheless, for effective diagnosis and therapy of diseases, it is almost crucial to first understand the molecular reasons behind disease development.

1.3 NANOMATERIALS FOR UNDERSTANDING DISEASE PATHWAYS

Biological machinery is known for its perfect balance, and runs within a complex network, which enables it to tolerate irregularities up to a certain level. Diseases occur when these irregularities cannot be tolerated, and several reasons might cause this, which are generally classified as hereditary or environmental reasons. In most cases, both of these components are the culprits behind medical problems, and it is always important to understand the changes in molecular level to decide the most appropriate treatment. For example, when an irregular activity of a protein, which can result in a disease, is detected, the necessary precautions can be taken or developed for the appropriate treatment. In some cases, protein production mechanism can be targeted to discontinue the disease-related activity. In other cases, the specific protein could be targeted and blocked; therefore the protein can be inactivated to stop the undesired activity. Since biological machinery works at the molecular level, these mechanisms can be best understood by using techniques that provide the highest sensitivity. Many of the current techniques that are used in biomedical research utilize microtechnology, which not only require higher amounts of biomolecules for analyses but also are only sensitive at microscale. On the other hand, techniques that utilize nanotechnology have recently been introduced in biomedical research and have revolutionized particular research areas. Developing DNA sequencing strategies for personalized medicine, biosensors with higher sensitivity that can be used for detection of low levels, or biomolecules and even nanoparticles that can be used for isolation for biomacromolecules such as DNA, RNA, or proteins are some of the examples of recent use of nanotechnology in understanding disease pathophysiology. On the other hand, there is an enormous amount of research in the recently published literature on developing better technologies for understanding biological events and pathways including nanomaterials for biocompatible labeling of biomolecules and cells for more efficient monitoring of activity, for tailoring nanomaterials for enhanced targeting ability (compared to regularly used antibodies), and for targeted blocking of biomolecular activity to understand their functionality in more detail. Application of these methods to biomedical research will yield in gaining more knowledge in the working mechanisms of biological machinery, and pathophysiology of diseases, and for enhancing diagnostic capabilities, all of which will in turn provide more opportunities for therapy.

1.4 NANOMATERIALS FOR THERAPY

To cure diseases with synthetic materials, the materials should be able to interact with specific biological actors in their natural environment. These biological actors can be cell surface receptors, which are mostly composed of proteins and carbohydrates; extracellular elements, such as growth factors, cytokines, or structural components like collagens; or intracellular elements, such as DNA, ribosomes, RNA, enzymes, etc. The optimal venue of interaction with biomolecules would be similar to the way they interact with their natural binding partners, so that the balance of the biological machinery can be reinstated. Therefore, the materials to be used should carry physical properties to meet the requirements for appropriate interactions. In addition to these, the materials should be functionalized with bioactive molecules. The interaction between the bioactive domain of the material and the target protein determines the stability of the complex and determines the fate of the biological activity.

Nanomaterials are used for therapy of diseases through several ways such as targeted drug/gene delivery approaches and induction of regeneration of damaged tissues by using nanomaterials. For targeted drug delivery, nanomaterials can be used as targeting molecules, as carrier systems, or as the bioactive drug itself. Aptamers, for example, are one example of how tailored nanomaterials can be used for targeting purposes. On the other hand, most of the research on nanomaterials for drug delivery has focused on developing carrier systems such as liposomes, polymeric nanoparticles, or metal-based nanoparticles. Although small-molecule drugs are the most commonly used therapeutics used for drug delivery approaches, there have been serious advances in producing tailored nanomaterial drugs, mostly in the form of small peptides or their conjugates.

The nanomaterials can be also used in regenerative medicine applications. To regenerate the tissue defects caused by diseases, materials can form an artificial three-dimensional environment to fill the gap with the bioactive signals derived from the natural healing process. The soluble factors can diffuse inside this network, and the cells in the proximity can migrate to the defect side. If correct signals and the optimum environment are provided, the tissue defect can be healed and function of the tissue can be recovered. Many polymeric materials have previously been tailored to mimic the natural biomacromolecules both physically and chemically. These materials have also been further functionalized through addition of natural biological molecules such as growth factors. On the other hand, there is a growing area of nanomaterials that are synthesized by using natural biomaterials such as peptide nanofiber systems, which can be produced through bottom-up approaches. These nanomaterials can be specifically designed to mimic natural proteins and carbohydrates to distinctively interact with particular biomacromolecules so that they induce differentiation of stem cells into specific lineages and induce functional tissue regeneration.

1.5 CHALLENGES AND FUTURE PROSPECTS

Although there have been extensive advances in developing nanomaterials for biomedical purposes, only few of them have been translated into clinics. The major limitations behind this delay are about the biocompatibility and biodegradability of nanomaterials.

One of the desired properties of the nanomaterials in the biological environment is their physicochemical stability. When a nanomaterial is injected into the blood vessels, there are several biological macromolecules that can interact with it in the environment. The noncovalent interactions including hydrogen bonds, electrostatic interactions, and van der Waals forces cause the undesired interactions in the blood. These may cause problems in the blood flow, or simply the nanomaterials cannot travel in the blood vessels, and they fail to reach to the target. In some cases, the interaction of these random molecules in the blood changes the surface chemistry or bioactivity of the nanomaterials, and they may cause undesired side reactions.

Undesired accumulation of the nanomaterials in the body and side products produced by degradation of the nanomaterials is another drawback in the use of nanomaterials for therapeutic purposes since these may cause side effects. Major areas where nanomaterials are accumulated in the body are the liver, spleen, and kidneys, which might result in metabolic problems associated with these organs, which eventually can cause organ failure.

Beyond many advances in the field of molecular biology and medicine, most molecular interactions between biomacromolecules are unknown, and our knowledge pathophysiology of diseases and the mechanisms of tissue regeneration are limited. Thus, one of the major challenges in developing and using nanomaterials for therapeutic purposes lies in the lack information on appropriate target molecular mechanisms or pathways. With more advancement in understanding of these interactions and better control on production of nanomaterials, biocompatible and bioactive nanomaterials with tightly regulated characteristics can be developed to interact with biomolecules to correct and regulate the natural biological interactions to cure diseases in the future. Beyond diagnosis, these advances can also be used to design and fabricate nanomaterials that can deliver drugs or trigger natural key reactions for regeneration purposes.

It is important to stay up to date on how nanomaterials can be used for diagnostic and therapeutic purposes by presenting specific examples from the literature. The research on biomedical nanomaterials can be classified according to their medical applications. Since nanotechnology is a fairly new technology with many unknowns, several examples of nanomaterial–biological organism interactions in terms of nanotoxicology research were demonstrated in order to stress that although nanomaterials provide a vast array of opportunities for the diagnosis and treatment of diseases, the consequences of using these new types of materials should be carefully weighed prior to their use in medical practice.