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Molecular fabrications of smart nanobiomaterials and applications in personalized medicine☆

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ABSTRACT

Recent advances in nanotechnology adequately address many of the current challenges in biomedicine. However, to advance medicine we need personalized treatments which require the combination of nanotechnological progress with genetics, molecular biology, gene sequencing, and computational design. This paper reviews the literature of nanoscale biomaterials described to be totally biocompatible, non-toxic, non-immunogenic, and biodegradable and furthermore, have been used or have the potential to be used in personalized biomedical applications such as drug delivery, tissue regeneration, and diagnostics. The nanobiomaterial architecture is discussed as basis for fabrication of novel integrated systems involving cells, growth factors, proteins, cytokines, drug molecules, and other biomolecules with the purpose of creating a universal, all purpose nanobiomedical device for personalized therapies. Nanofabrication strategies toward the development of a platform for the implementation of nanotechnology in personalized medicine are also presented. In addition, there is a discussion on the challenges faced for designing versatile, smart nanobiomaterials and the requirements for choosing a material with tailor made specifications to address the needs of a specific patient.

Contents

Abbreviations: PLGA, Poly(lactic–co-glycolic acid); PEG, poly(ethylene glycol); ECM, extracellular matrix; RES, reticuloendothelial system; MMP, matrix metallo-proteinase; BBB, blood–brain-barrier; MRI, magnetic resonance imaging; PLA, poly(lactic acid); MSCs, mesenchymal stem cells; IGF-1, insulin-like growth factor-1; bFGF, basic fibroblast growth factor.

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1. Introduction

A myriad of materials have been proposed for applications in medicine. The emphasis of this review is on biomaterials consisting of nanoscale sub-components which are non-toxic, biocompatible, non-immunogenic, biodegradable, do not use harmful chemicals for their synthesis, their degradation products are not toxic, and furthermore, have been already used or have the potential to be used for personalized therapies. It is not possible to cover all of the materials that fulfill these requirements within the length limitations of this paper however, I will present as many examples as possible for each type of material.

Currently most diseases are diagnosed in their symptomatic stages. At these late stages, multiple biochemical pathways may be affected to a different degree depending on the individual. Therefore, it is not surprising that for complex diseases the current one-size-fits-all therapies have limited success for a large percentage of the population. The business model of pharmaceutical companies is based on selling as much drugs to as many patients as possible. It is estimated that 90% of drugs currently on the market work in only ~50% of individuals. Individualized, personalized medicine allows the prescription of treatments best suited for a single patient. Personalized treatments of highly complex diseases that affect multiple organs and diverse metabolic pathways require genetic profiling and selection of the right drug for the right patient which needs to be delivered at the right time to increase drug efficiency, minimize dose side effects, and enable quick patient recovery.

The great discoveries in nanotechnology in the 1990s and the approval of patient specific therapies like Herceptin paved the way for the development of personalized therapies that would facilitate the rational use of pharmaceutical products, early disease detection, and highly efficient therapeutic interventions. In recent years, major technological advances have contributed to the effort of developing personalized therapies such as high-throughput sequencing platforms, the adoption of electronic health records, the miniaturization of existing devices, electronic data capture, the discovery of significant biological and biochemical pathways, and the realization of the importance of epigenetic modifications for the onset of a disease.

Nanomedicine includes but is not limited to the development of nanoparticles, nanofibers, and nanopatterned surfaces with applications in: (i) drug delivery in which nanoscale particles, such as polymer nanoparticles, liposomes, virosomes, and nanosuspensions or matrices consisting of nanofibers are used to control the release and to improve the bioavailability and pharmacokinetics of a therapeutic compound and also protect their payload from degradation; (ii) design and synthesis of biomaterial scaffolds for tissue regeneration that are composed of nanoscale subcomponents, such as nanofibers, which are amenable to molecular design to incorporate biologically active signal molecules; (iii) bio-imaging in which nanoparticles are used as contrast agents for magnetic resonance imaging (MRI) or ultrasound screenings providing improved contrast and favorable biodistribution; (iv) fabrication of biosensors based on nanotubes, nanowires, and/or chemically modified nanoparticles which improve the sensitivity and speed of analysis, or to measure novel, difficult to detect, analytes; (v) biomembranes for the encapsulation of electrodes, biological specimens like pancreatic islets, or other implantable devices; (vi) design and synthesis of nanoscale particles with bioactive therapeutic properties that mimic biomolecules or are novel and cannot be recapitulated by natural occurring molecules like polymer antibodies and protein/antibody modified nanoparticles.

In 1959, Feynman offered one of the first known proposals for a personalized nanomedical procedure [1]: "A friend of mine (Albert R. Hibbs) suggests a very interesting possibility for relatively small machines. He says that, although it is a very wild idea, it would be interesting in surgery if you could swallow the surgeon. You put the mechanical surgeon inside the blood vessel and it goes into the heart and looks around. It finds out which valve is the faulty one and takes a little knife and slices it out. Other small machines might be permanently incorporated in the body to assist some inadequately functioning organ." Despite ample enthusiasm and predictions about the construction of nano-robots for medical applications such nano-doctor devices are still in their infancy. However, great strides have been made in developing and testing nanoscale materials for medical applications including synthetic polymer nanoparticles, self-assembling peptide nanomaterials, self organizing polynucleotides chains, self-assembling lipids, and inorganic nanoparticles. Nanoscale materials, fibers or particles have chemical and physicochemical properties that differ from those of the bulk materials. Therefore, we need to address questions associated with toxicity of nanomaterials in biological systems before we harvest their full potential for medical applications. Nanomedicine today has branched out in hundreds of different directions, each of them embodying the key insight that the ability to structure atoms, molecules, or macromolecules at the molecular scale can bring enormous benefits in the research and practice of medicine. It is anticipated that miniaturization of medical tools will provide more accurate, controllable, versatile, reliable, cost-effective, and faster approaches to enhancing the quality of human life.

In this review a number of applications will be presented specifically focusing on the potential contribution of nanomaterials in personalized therapies. This will be followed by a description of the properties of the ideal biomaterial for nanobiomedicine and a brief survey of the current