Perspective

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Designed Nanomedicine Reprogrammed the Phenotype for Preclinical Investigation

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Description

Physical scientists have developed strategies to reproducibly synthesize nanomaterials and to characterize their unique, size-dependent properties. An understanding of these fundamental physical and chemical properties is necessary for the optimal use of nanomaterials in medical applications. Nanomaterials generally consist of metal atoms, nonmetal atoms, or a mixture of metal and nonmetal atoms, commonly referred to as metallic, organic, or semiconducting particles, respectively. The surface of nanomaterials is usually coated with polymers or biorecognition molecules for improved biocompatibility and selective targeting of biologic molecules. The final size and structure of nanomaterials depend on the salt and surfactant additives, reactant concentrations, reaction temperatures, and solvent conditions used during their synthesis.

A common feature of all nanomaterials is their large ratio of surface area to volume, which may be orders of magnitude greater than that of macroscopic materials. Cutting a 1-cm cube into 1021 cubes that are each 1 nm on a side will result in the same overall volume and mass, but the surface area will be increased by a factor of 10 million. Thus, the advantage of using nanomaterials as carriers is that their surface can be coated with many molecules. Unique aspects of metal-containing materials with at least one dimension that is smaller than 100 nm are their size, shape, and compositiontunable electronic, magnetic, and optical properties.

This relationship is a direct consequence of the behavior of electrons in the nanomaterial. Electrons have two important characteristics: their spin and their ability to move in a quantized fashion between specific energy levels. Electrons are similar to tiny bar magnets, with a surrounding magnetic field that corresponds to the electron spin in an applied field. Also, after absorbing energy, electrons can generate light or heat when they move between different energy levels. In macrostructures, electrons can spin in two directions, in opposition or in alignment, and can move among many energy levels.

Role of Nano Biotechnology

The behaviour of electrons in nanostructures is more constrained and depends on the size or shape of the material or on the electrons’ interactions with the surface coating. The chemical composition of a nanomaterial determines whether one or both electron characteristics (spin and energy transition) are affected, as well as the extent of that effect. For example, all electrons in iron oxide magnetic nanoparticles (≤ 20 nm in diameter) spin in the same direction, whereas electrons in iron oxide macroparticles (>20 nm in diameter) spin in opposite directions. When these spins are aligned in the same direction, the field becomes additive, but when the electrons spin in opposite directions, the fields cancel each other out. Since the overall magnetic-field strength of a material is the sum of the magnetic fields of individual electrons, these nanoparticles have a larger, localized magnetic field as compared with that of larger particles.

Commercialization efforts in nanomedicine are picking up worldwide. We identified about 207 companies that visibly pursue nanomedicine activities—158 SMEs and startups that devote either all or a significant share of their business to the development of nanomedicines. We believe this is an underestimate of the true number, as a detailed analysis of patent data for liposomes—the area of nanomedicine with one of the longest development histories—shows that the number of companies that have filed three or more patents relating to healthcare applications of liposomes, is twice as high as the number of companies that openly communicate their involvement in this technology (e.g., on their webpage or in press releases). Therefore, we assume that the 207 companies reviewed in our study that all openly communicates their nanomedicine activities are just the tip of the iceberg. A characterizing feature of nanotechnology is its enabling function to add new functionality to existing products, making them more competitive. As measuring the added value of nanotechnology to a product is not possible, it has become common praxis in nanotechnology business studies to take the total sales of nanotechnology-enhanced products as a measure of the economic importance of nanotechnology in an industrial sector. For example, Ambisome (Gilead, Foster City, CA, USA), a liposomal formulation of the fungicide Fungizone (BristolMyers Squibb, New York) that shows reduced kidney toxicity, had total sales of $212 million in 2004. For calculating the market size. After this procedure, we estimated the total sales of the 38 identified nanomedicine products from all sectors of nanomedicine.

Nano Vehicles and Drug Carriers

Over the past decade, the first nanomedicine products have been introduced into the market. Compared with the total pharmaceutical and medical device market, nanomedicines currently constitute a tiny niche. For the most part, nanotechnology in medicine has an enabling function. In most cases, it constitutes only a functional component of a medical product; however, its great strength lies in its versatility: nanotechnology has the potential to add innovative functionality to many pharmaceutical products and medical devices. Since the beginning of this decade, the interest of the pharmaceutical and medical device industry is slowly picking up; patent activities in particular have increased in recent years. Nevertheless, the investment of corporations in the development of nanomedicines is still very cautious and is currently the biggest stumbling block for commercialization. Furthermore, the uncertainty of whether novel nanotechnology-specific medical regulations will be implemented that might add further requirements to the approval process for nanomedicines hampers their commercialization. An early clarification of this issue is important for companies planning investments in nanomedicines. Notwithstanding the commercial activities, nanomedicine is still technology driven and scientific challenges lie ahead. The chemistry of nanosized molecules is not well understood, and the manufacturing of such nanomaterials as dendrimers or pharmaceutical-grade liposomes is still costly. Furthermore, much remains to be learned about the modification of nanoscale carriers so that circulation lifetime, biodistribution and penetration of biological tissues are optimized.

The network of blood and lymphatic vessels investing the body provides natural routes for the distribution of nutrients, clearing of unwanted materials, and delivery of therapeutic agents. Superficially, however, this network appears to provide little in the way of obvious controlled and specific access to tissues, and the science of these processes has been scant. Regardless of these limitations, nanoparticulate systems provide possibilities for access to cell populations and body compartments. When injected intravenously, particles are cleared rapidly from the circulation and predominantly by the liver and the spleen (marginal zone and red pulp) macrophages.