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Review

Nanomedicine: Past, present and future – A global perspective

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ABSTRACT

Nanomedicine is an emerging and rapidly evolving field and includes the use of nanoparticles for diagnosis and therapy of a variety of diseases, as well as in regenerative medicine. In this mini-review, leaders in the field from around the globe provide a personal perspective on the development of nanomedicine. The focus lies on the translation from research to development and the innovation supply chain, as well as the current status of nanomedicine in industry. The role of academic professional societies and the importance of government funding are discussed. Nanomedicine to combat infectious diseases of poverty is highlighted along with other pertinent examples of recent breakthroughs in nanomedicine. Taken together, this review provides a unique and global perspective on the emerging field of nanomedicine.

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1. Introduction

Nanomedicine is the use of nanotechnology to bring about improvements in healthcare [1]. This involves the use of the properties of nano-scale materials, which may differ profoundly from those of the same material at a larger scale. Many biological mechanisms in the human body also occur at the nano-scale and nanoparticles, due to their small size, may potentially cross natural barriers and enter new sites different the portal of entry into the body and interact with biomolecules in the blood or within organs, tissues or cells; this may be highly advantageous for drug or gene delivery and imaging. As with all medical devices or drugs, nanomedicines are subject to regulation and monitoring and must undergo extensive characterization, toxicity assessment and clinical trials before their full potential is realized for the benefit of patients. Nanomedicine could potentially provide real breakthroughs in terms of improved and cost-effective healthcare, a crucial factor in making medicines and treatments available and affordable. This mini-review, co-authored by leading scientists hailing from the United States, Europe, Africa, and Asia, examines the emergence and current status of nanotechnology in medicine

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from different perspectives, and provides a personal perspective on the future of this field.

2. Government programs for nanotechnology research: The US perspective

The United States was the first country to initiate a formal program for government funding of research in nanotechnology. The National Nanotechnology Initiative (NNI) was launched in 2000 and has expended USD 22 billion on nanotechnology including approximately USD 1.5 billion in the President's budget request for next year (2016). NNI has four major goals: 1) advance a world-class R&D program; 2) foster the transfer of new technologies into products for commercial and public benefit; 3) develop and sustain educational resources, a skilled workforce, and a dynamic infrastructure and toolset to advance nanotechnology; and 4) support responsible development of nanotechnology. NNI funding is spread across a number of US government agencies. The top-five federal agencies in terms of funding in the 2016 budget are the National Institutes of Health (NIH), the National Science Foundation, the Department of Energy, the Department of Defense, and the National Institute of Standards and Technology. While other agencies are no doubt conducting research with relevance to nanomedicine, the primary nexus of research in nanomedicine is not surprisingly the NIH. Researchers at NIH conduct basic, applied, and clinical research within its Intramural Research Program, and NIH supports independent researchers in academia through grants and contracts through its Extramural Research Program. The NIH is made up of 27 institutes and centers, each with a specific research agenda, often focusing on particular diseases or body systems [2].

The NIH Common Fund was enacted into law by Congress through the 2006 NIH Reform Act to support cross-cutting, trans-NIH programs that require participation by at least two NIH institutes or centers or which would otherwise benefit from strategic planning and coordination. Among the programs supported by the NIH Common Fund is the Nanomedicine Initiative that has defined its goals as follows: 1) understand how the biological machinery inside living cells is built and operates at the nanoscale; and 2) use this information to re-engineer these structures, develop new technologies that could be applied to treating diseases, and/or leverage the new knowledge to focus work directly on translational studies to treat a disease or repair damaged tissue. This program began in 2005 with a national network of eight Nanomedicine Development Centers. Now, in the second half of this 10-year program, the centers best positioned to effectively apply their findings to translational studies were selected to continue receiving support. Most of the active Nanomedicine Development Centers involve researchers at more than one geographically separated academic institution that collaborate on a thematic topic. In addition to the Nanomedicine Initiative supported by the NIH Common Fund, many of the NIH institutes have their own portfolio of research in nanomedicine. The National Cancer Institute (NCI) research activities in nanomedicine are quite robust expending roughly US$150 million on this effort annually [3]. The NCI launched its own Alliance for Nanotechnology in Cancer in 2004 to advance a number of promising nanotechnologies with relevance to cancer diagnosis, treatment and prevention. Through this program, investigators have been particularly encouraged to focus on cancers where improvements in patient outcomes have been refractory to previous approaches, notably cancers of the brain, lung, ovary, and pancreas. The Alliance for Nanotechnology in Cancer has several flagship programs that are illustrative of its mission to foster innovation and collaboration across academic institutions and across scientific disciplines. These Alliance programs include: 1) Centers for Nanotechnology Excellence (CCNE); 2) Cancer Nanotechnology Platform Partnerships (CNPP); 3) Cancer Nanotechnology Training Centers (CNTC); 4) Pathway to Independence Awards (PIA) in Cancer Nanotechnology Research; and 5) the national Nanotechnology Characterization Laboratory (NCL). A more comprehensive description of these programs is beyond the scope of the present review but can be found on the Alliance website [4]. The NCL is a particularly interesting program in that it is open to the private sector. The NCL aims to speed development of nanotechnology-based products for cancer patients by performing pre-clinical characterization of nanomaterials intended for cancer therapeutics and diagnostics developed in academia, government, and industry and serves as a national resource in the translation of nanoscale particles and devices to clinical applications.

The American Society for Nanomedicine [5] is comprised of members drawn from academia, government, and industry and representing the fields of nanotechnology, engineering, and the biomedical sciences with the common goal of advancing nanomedicine research. This goal is addressed through providing an open forum of ideas and collaborative efforts, as well as close cooperation and coordination with international colleagues in nanomedicine (e.g., the European Foundation for Clinical Nanomedicine; https://www.clinam.org). The New York Academy of Sciences convened the meeting, “Nanomedicines: Addressing the Scientific and Regulatory Gap”, in 2013, to discuss recent topics in the area of nanomedicine. Experts from academia, pharmaceutical industry, nanomedical societies, and federal regulatory bodies discussed the past and present status of nanomedical research and development; to emphasize the critical lessons learned from past medical applications of nanotechnology, both successful and unsuccessful. As pointed out by the authors of the meeting report [6], “it is critical to work to close the scientific and regulatory gaps to assure that nanomedicine drives the next generation of biomedical innovation”. Doxil® was the first nanomedicine approved by the US FDA more than two decades ago. Doxil® (called Caelyx® in Europe) is a liposomal formulation of the cancer drug doxorubicin that is passively delivered to tumors via the so-called enhanced permeability and retention (EPR) effect. Subsequent to Doxil®, a number of other nanomedicines have been approved for a variety of disease indications. The NCI's Alliance for Nanotechnology in Cancer has a number of agents in clinical trials for cancer, and many more are nearing that goal. Currently, a very active area of research is active targeting of tumor cells [7]. Rather than relying only on the physicochemical properties of the agent as in the case of Doxil®, tumor-targeting nanomedicines have a targeting moiety that interacts in a specific fashion with a molecule on the targeted tumor cells. The targeting moiety is often a small molecule or protein ligand that interacts with a specific receptor on the surface of the tumor cells. A variation on this theme is the use as a targeting moiety an antibody or antibody fragment that binds to an antigen on the surface of the tumor cell. More than a dozen of such products are under development. In addition to being distinguished on the basis of their tumor-targeting molecule, these products are also distinguished on the basis of their payloads [7].

3. The innovation supply chain: The European perspective

Nanobiotechnologies and, subsequently, nanomedicine became a priority in the European R&D agenda under the European Commission's Sixth Framework Programme (FP). However, EU funding under the latter phase of FP7 and more recently under the current funding scheme Horizon2020 now gives a higher priority to translational medicine. This change is reflected by the explicit