A Growing Place for Nano in Medicine

The area of nanomedicine has grown considerably since its early days, when the concepts of using nanoscale inorganic particles for imaging or adapting nanoscale carriers for targeted delivery were first introduced. The field has advanced into new areas; led to innovations in imaging, diagnostics, systemic, and localized delivery; and broached the difficult challenge of moving systems toward clinical development and translation. There remains a great deal of work in moving these technologies toward implementation, and, as pointed out by fellow associate editor Warren Chan, there is a strong need for the use of clinical samples in nanomedicine research studies and strong argument for greater and deeper pairings of physical and chemical nanoscientists to collaborate with clinicians in the field.[1] Despite these challenges, there has been gradual translation of the use of nanomaterials in medical applications, as is evident in the increasing numbers of biotech startup companies as well as more recent investments in research efforts in this area by larger and established pharmaceutical companies.

The elucidation of the important roles that nucleic acids may play in future medical applications, as well as newer accomplishments in immunological approaches to disease such as cancer vaccines, suggests a new era for drug delivery and particularly for nanomedicine for the delivery of drugs.[2−5] New advances are being made in the original pioneer areas such as cancer, and newer areas of application are being investigated at a rapid rate. These opportunities are highlighted by the submissions and discussions in the Gordon Research Conference in Drug Carriers for Medicine and Biology this August, where topics such as the application of nanomaterials for targeting of infectious disease, the cardiovascular system, and vaccines are featured. This growth and expansion is being led by developments from academic and medical research laboratories, in combination with what may be viewed as more readily attainable areas of clinical translation. Nanoparticles and other nanostructured materials systems are of strong interest to address delivery to the eye, where penetration of the corneal epithelium and blood−retinal barrier can be important. Carrier size is key to penetration of cartilage, where nanomaterials that can deliver long-term release of drugs for pain and inflammation or for stimulation of tissue regeneration may have great value. Nanomaterials that penetrate different layers of skin for transdermal delivery could yield new types of therapies and both localized and systemic treatments, particularly given the access that skin provides to the inflammatory host system. Systemic delivery of nanomaterials that can target infected tissues also provides new challenges, and a number of potential areas in neurological disease are anticipated to open up as more is understood about disorders of the brain. In general, there is a growing and expanding range of opportunities for nanomaterials systems that could provide the basis for a renaissance in materials development should these new challenges spur discovery that can be translated to patients.

As nanomedicine grows, however, we must move toward investigations that go beyond initial discovery and ultimately yield greater understanding of how nanomaterials work within cellular to physiological systems. We understand the general concept of targeting, but we do not necessarily know how to correlate it with and leverage biodistribution, bloodstream half-life, and other factors that impact drug accumulation in tumors. In general, for systemic formulations, we have learned more about the role of size in rigid nanoparticles, but there is much more to understand about the combination of size with charge and the impact of deformability in "soft" nanocarriers such as nanogels.[6] New knowledge about the role of shape in cellular uptake or nanoparticle accumulation in specific organs leads to additional questions about

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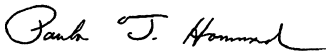
particle mechanics, presence, and distribution of surface ligands, *etc*. Despite many years of nanoparticle development for systemic delivery, we still face the challenge of liver and spleen accumulation, with few advances in lowering the engagement of macrophages and monocytes in the body. To understand many of these phenomena, we as nanoscientists must push toward a more mechanistic understanding that is more biologically and physiologically informed. Many in the field have begun to take on this task, and as we begin to study a much broader material set than the originally proposed carrier materials, there remains much to learn about the differences in these factors observed with materials of differing chemical composition, structure, morphology, size, and surface characteristics. Other challenges are newer and reflect our greater understanding of physiological response; for example, how we can design nanotherapeutics that can adapt to or compensate for changes in vascularity, endothelial, and stromal barriers and tissue or tumor morphology as disease progresses, or as disease is treated, and how can synergistic formulations of drugs be devised to achieve not only ideal loadings but also optimal independent release profiles in target tissues. Both the old and the new questions are critical to address. With greater understanding at the molecular and biological levels, we can develop more effective sets of design rules to advance this field in critical areas ranging from cancer to neurological disease.[7]

Disclosure: Views expressed in this editorial are those of the author and not necessarily the views of the ACS.



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