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Materials for Advanced Drug Delivery in the 21st Century: A Focus Area for *Advanced Drug Delivery Reviews*

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During the second half of the 20th century much was accomplished by scientists working on the development of materials for controlled drug delivery. Examples include liposomes for passive or active targeting to sites of infection and cancer, biodegradable polymers for localized delivery of bioactive agents, water-soluble polymers for increasing the half life of therapeutic proteins and reducing immune response, linear polymers with side chains terminated in drugs, imaging agents and targeting moieties, micellar and nanoparticulate structures for encapsulation, macromolecules for delivery of nucleic acids, among others. The question is no longer whether such strategies can enhance efficacy and safety, rather how they can be improved. Three avenues of new research are conceivable: 1) advancing the clinical translation of new generations of delivery systems, 2) understanding potential alterations in mechanisms of action of therapeutic agents when they are attached, complexed or incorporated into biomaterials, and 3) designing new materials with improved properties.

Consider, for instance, the case of polymer therapeutics for cancer treatment. While the systems relying on passive targeting by enhanced permeability and retention effect have advanced to the clinic, very few containing biorecognizable moieties for active targeting are in clinical trials. Identification of new targets and preclinical work to demonstrate the superiority of this new generation of delivery systems can improve specificity and enable translation to use in human. Second, very little is known about the effect of biomaterials on altering the mechanism of action of drugs. Investigations in the past few years point that signaling pathways, gene expression profiles and drug resistance can be altered when bioactive agents are coupled with biomaterials. Further detailed mechanistic studies in this area can aid in discovering new delivery strategies with specific subcellular targets.

A third area where drug delivery can be advanced is to exploit the state of the art in materials science and nanotechnology to design novel carriers. For example, in the 90s methodologies for the recombinant synthesis of polymers emerged. More recently, ideas are being articulated about the use of nucleic acid-based materials for drug delivery. Proteins and nucleic acids are well-defined yet diverse building blocks of new materials. Artificial materials based on these well-defined motifs, as well as new chemical synthetic strategies that produce monodisperse and sequentially defined polymers, allow systematic correlation of structure with function.

Similarly, advances in nanotechnology have allowed the fabrication of nanostructures with defined size, surface functionality and geometry (such as nanorods, nanotubes, cubes, etc.). Little is known about how cells respond to these defined architectural parameters. Studies of

cellular uptake, biodistribution, biocompatibility and the utility of these constructs in drug delivery, imaging and sensing applications are emerging and can potentially lead to the design and development of new generations of delivery systems.

In the coming issues of *Advanced Drug Delivery Reviews* my goal is to present to the readers themes focusing on these and other emerging topics solicited from experts. To do so I will rely heavily on input and advice from seasoned as well as young investigators in the field.