CHANGE-DRIVEN PLATFORMS FOR THE DELIVERY OF THERAPEUTICS

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Self-assembled block copolymer micelles are widely utilized in pharmaceutics for development of novel therapeutic and diagnostic modalities. Recently nanofabrication of polymer micelles was significantly advanced by exploring charge driven self-assembly of block copolymers containing ionic and nonionic blocks ("block ionomers"). These block copolymers react electrostatically with oppositely charged species such as polyions, proteins, surfactants, or metal ions and form block ionomer complexes (BIC). These complexes self-assemble into particles of nanoscale size and form stable aqueous dispersions. The latter enable, uniquely, encapsulation of charged therapeutic molecules. The block ionomer-metal complexes can be used as templates to synthesize a novel type of entirely hydrophilic polymer micelles with cross-linked ionic cores. These core-shell materials represent nanosized gels with the core comprising a swollen network of crosslinked polyions surrounded by a nonionic polymer shell. The stimuli-responsive behavior of nanogels can be easily controlled by selection of constituent polymer and crosslinker components to achieve a desired response at the site of action, which imparts nanogels the ability to participate actively in the intended function of the carrier system rather than being passive carriers of their cargo. Chemical functionalization of nanogels with various ligands was also explored for targeted drug delivery, triggered drug release, or preparation of composite materials. Hybrid nanogels containing hydrophobic domains in the hydrophilic cross-linked cores were designed to provide for combinatorial therapy resulting in simultaneous delivery of several anticancer drugs with very different physical properties and mechanisms of action. Further studies on the design, synthesis, and animal testing of nanogels as carriers for multidrug delivery will be described.