Polymer Nano-Assemblies for Targeted Bioresponsive Cancer Delivery

The design of nanoparticles for the delivery of drugs to tumors and other specific regions of the body requires versatile chemistry and the ability to manipulate nanoparticle surfaces with the high level of control needed multiple kinds of targeting. Nanoparticle size-based targeting is based on the enhanced permeation and retention within tumor tissues, whereas molecular targeting using designed ligands, and environmentally triggered targeting can take advantage of the tumor microenvironment. The surfaces of polymeric nanoparticles provide a means to introduce mediated interactions with cells that lead to uptake of the nanoparticle, release of drugs in specific regions, and control of the intracellular trafficking of the nanoparticle. The means by which such nanostructured particle systems can be achieved using polyelectrolyte layer-by-layer assembly methods will be addressed. It is possible to design nanoparticles that consist of several nanolayers wrapped around a core materials system. These polyelectrolyte nanolayer assemblies can be generated to increase the half-life of the particle in the bloodstream by preventing adsorption of proteins via hydrated outer layers, and acting as a “stealth” layer that prevents recognition of the particle as a foreign body by the body's defense systems. On the other hand, nanolayers can be devised that facilitate cell entry in the hypoxic tumor microenvironment. Ultimately, the use of nanostructured particles that contain multiple drugs, some of which can be released with different times or profiles, will be discussed with respect to the potential impact on synergistic drug combinations for cancer. Finally, we have adapted these methods to include RNAi delivery that is highly effective, and have introduced existing methods of RNAi synthesis using rolling circle transcription to generate nanostructured particles that provide RNAi with high loading and low amounts of toxic carrier for in vivo delivery. The advantages that polymer self- and directed assembly bring to the area of nanomedicine will be discussed.