Stevens Institute of Technology

Nanotechnology Graduate Program

Nanogels in Biomedical Applications

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A major bottleneck in the development of siRNA therapies is their delivery to the desired cell type or tissue, followed by effective passage across the cell membrane with subsequent silencing of the targeted mRNA. To address this problem, we describe the synthesis of poly(N-isopropylmethacrylamide) based core/shell hydrogel nanoparticles (nanogels) with surface-localized peptides that specifically target ovarian carcinoma cell lines possessing high expression levels of the Eph2A receptor. These nanogels are also demonstrated to be highly effective in the non-covalent encapsulation of siRNA, and enable cell-specific delivery of the oligonucleotides in serum-containing medium. Cell toxicity and viability assays reveal that the nanogel construct is non-toxic under the conditions studied, as no toxicity or decrease in cell proliferation is observed following delivery. Importantly, a preliminary investigation of gene silencing illustrates that nanogel-mediated delivery of siRNA targeted to the EGF receptor results in knockdown of that receptor. Excellent protection of siRNA during endosomal uptake and endosomal escape of the nanogels is suggested by these results since siRNA activity in the cytosol is required for gene silencing. We have shown that Hey cells, which overexpress the Eph2A receptor, can be targeted with Eph2A-ligand-conjugated, siRNA-loaded nanogels as indicated by the presence of green (nanogel-associated) fluorescence. In this case, the ligand is the “YSA” peptide (YSAYPDSVPMMS), which mimics the ligand ephrin-A1, a known ligand for the receptor. This presentation will expand upon these observations to discuss the efficiency of gene knockdown associated with nanogel-mediated siRNA delivery, along with some preliminary studies of clinically relevant applications in oncology. Together, these results illustrate the excellent potential of core/shell nanogels in the delivery of delicate payloads to disease sites.

Dr. Lyon began his career at Georgia Tech in January 1999 following his postdoctoral work with Professor Michael Natan at Penn State (1997-1998) and Ph.D. work at Northwestern University under the direction of Professor Joseph Hupp (1992-1996). He was promoted to Associate Professor in 2003 and Professor in 2007. Dr. Lyon’s current research involves the design of stimuli-sensitive nanogels, as well as particle assembly into higher order structures. He is the recipient of the NSF CAREER, Beckman Young Investigator, Research Corporation Research Innovation, and Camille Dreyfus Teacher-Scholar Awards, an Alfred P. Sloan Fellowship, and the National Fresenius Award.

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