373c Novel Triptych Polymers for Virus-Mimetic DNA Encapsulation

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The unavailability of safe and effective gene delivery vectors presents the biggest obstacle in realization of the concept of gene therapy. While the natural candidates, viruses, are capable of evoking adverse immune response and can potentially undergo recombination to regain pathogenicity, safer alternatives based on cationic polymers and lipids have failed to yield reasonable transfection efficiency so far. Thus it follows that in order to be potent a gene delivery vector should be able to closely mimic the structural and functional features of viruses while maintaining its stability and biocompatibility at various stages of delivery. We propose a novel gene delivery vector comprising an ABC triblock ("triptych") copolymer which can self-assemble in aqueous phase to form virus-mimetic DNA-encapsulation structures. The proposed polymer consists of (A) hydrophilic poly(ethylene glycol) (PEG), (B) hydrophobic poly(n-butyl acrylate) (PnBA) and (C) cationic poly(ethylene imine) (PEI). With such ABC sequence of blocks, the C block will primarily interact with the negatively charged phosphates on DNA, and the viral capsid-like morphology of the nanometers-thick membrane can be created from the A and B blocks at the outer surface of collapsed DNA. In addition, being responsive to pH changes, PEI is expected to act as a membrane fusogenic element under intracellular environment. We will present combined controlled radical and cationic polymerization techniques by which model triptych PEG-PnBA-PEI polymers have been synthesized for this study. Characterization of the nanoscale morphologies of the self-assembled structures derived from these copolymers in the presence of DNA are currently under progress by utilizing fluorescence microscopy, cryogenic transmission electron microscopy, dynamic light scattering and electrophoresis. We will discuss factors influencing the complex self-assembly processes and how they relate to the nanoscopic properties of the resultant DNA/polymer complexes. An understanding of the structure-property relationships at molecular and supramolecular levels will provide the fundamental materials science groundwork necessary for further development of a rational approach to the design and engineering of optimal multi-component DNA carriers.