Targeted Three-Layered Micelles and Injectable Hydrogels for Gene Delivery Systems

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Non-viral gene delivery systems have received considerable attention given the serious safety concerns associated with viral gene delivery. Cationic polymers, in particular polyethylenimine (PEI) has found widespread interest due to its high condensation and superior transfection efficiencies. However, to achieve high performance in gene therapy it requires high molecular weight (e.g. 25 k Da) PEI which is known to cause critical cytotoxicity and inefficient DNA release at the target site. To address these drawbacks, less toxic, shorter PEI (e.g. 2 k Da) was used to prepare three-layered micelles (3LM) encapsulating DNA. We have developed a dual encapsulation procedure comprising two triblock copolymers including poly(L-lactide) (PLLA) blocks, PLLA-PEI-PLLA and PLLA-PEG-PLLA. In-vitro studies have revealed that 3LM has superior DNA loading efficiency, physiological stability, reduced cytotoxicity, and pH responsive release profiles compared to common PEI/DNA polyplex. Furthermore, the biodegradable 3LM system was developed into thermo-responsive hydrogels for localized gene delivery.