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Editorial

Recent progress in non-viral nucleic acids delivery

A major goal of nucleic acid based therapies is to treat inherited and acquired disorders by adding, correcting, suppressing or replacing genes (Abbas et al., 2008). Advantages of non-viral vectors for delivering nucleic acid based therapies include ease of scale-up, storage stability and improved quality control. The most promising non-viral vectors have been liposomes and cationic polymers which complex with nucleic acids such as siRNA and plasmid DNA to form lipoplexes or polyplexes (Wang et al., 2011). Advances in the development of this technology have included pegylation to increase circulation times and impart stealth-like properties to the vector and attachment of cell targeting or cell binding ligands to increase nucleic acid delivery efficiency. Other improvements have included new formulation strategies to enhance protection of the nucleic acids against enzymatic degradation, to improve stability in the presence of serum and to optimize eventual release capabilities. An additional major goal of researchers has been to design non-viral vectors with desirable cytotoxicity and reduced immunogenicity characteristics.

In this special theme issue, we have assembled manuscripts from an outstanding group of researchers that are leaders in the effort to optimize non-viral vectors and overcome several challenges and barriers to translating use of non-viral vectors into the clinic. This theme issue includes comprehensive reviews by Amiji (Xu et al., 2011), Torchilin (Wang et al., 2011) and Patil (Kapoor et al., 2011) that present recent progress in non-condensing polymeric nanoparticles, condensing cationic polymer based nanoplexes and the physico-chemical characterization of lipid based delivery systems for siRNA. Original research articles in this theme issue focus on the development and testing of nucleic acid delivery systems. For example, Pun and colleagues discuss the development of a reducible HPMA-co-oligolysine copolymer for nucleic acid delivery (Shi et al., 2011). Mallapragada and colleagues discuss the development a temperature-responsive pentablock copolymer that is designed to deliver DNA and prolong gene expression by forming a thermogelling release depot after subcutaneous or intratumoral injection (Zhang et al., 2011). Kwon and colleagues present a biodegradable hybrid recombinant block copolymer for non-viral gene delivery that is capable of appreciable transfections with low toxicity (Chen et al., 2011). Ghandehari and colleagues carry out a comparative study between silk-elastin like protein polymer hydrogels and poloxamer gels for matrix-mediated viral gene delivery (Price et al., 2011). Berkland and colleagues demonstrate the utility of calcium condensed cell penetrating peptide (TAT) complexes for efficient gene silencing with reduced toxicity (Baoum et al., 2011). Salem and colleagues describe the development of a mannosylated pegylated polyethylenimine for siRNA delivery and the development of optimized dextran–polyethylenimine conjugates for plasmid DNA delivery (Jiang and Salem, 2011; Kim et al., 2011). Kissel and colleagues show that the transfection efficiency of amphiphilic biodegradable hy-PEI-g-PCL-b-PEG copolymers is dependent on graft density of the PCL-b-PEG chains (Zheng et al., 2011). Finally Szoka and colleagues show that asymmetric 1-alkyl-2-acyl phosphatidylcholine is a helper lipid that is necessary for enhanced non-viral gene delivery (Huang et al., 2011).

Appropriately for the *International Journal of Pharmaceutics*, the studies presented in this special theme issue carry out thorough physico-chemical characterizations of the delivery systems being developed and highlight limitations and future directions necessary for these systems to overcome current bottlenecks and challenges. As Vladimir Torchilin alludes to in his review, design of new nucleic acid delivery systems must incorporate consideration of the balance between gene packing and release, the need to increase circulation times following administration and ensuring greater stability and reduced toxicity. The papers presented in this special theme issue show some of the progress that has been made in these areas.

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