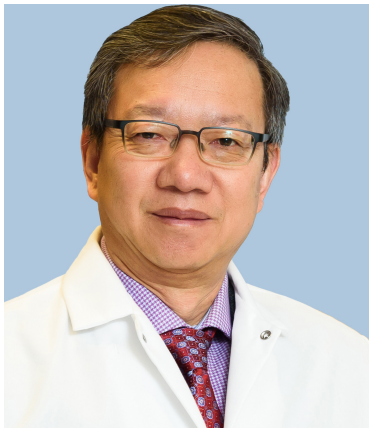
化生研セミナーのお知らせ

Smart ionizable lipid nanoparticles for nucleic acid delivery



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Abstract

Nucleic acid based therapeutics have been developed for correction and/or regulation of genetic activities and functions, including gene editing, gene replacement, RNA interference, and mRNA vaccine to treat human diseases. Safe and efficient delivery of nucleic acids into target cells is still the main obstacle for their broad clinical applications. In 2007, our lab first proposed the concept of pH-sensitive amphiphilic endosomal escape and reductive cytosolic release of nucleic acids to design smart, multifunctional pH-sensitive protonatable or ionizable lipids for highly efficient delivery of nucleic acids. The key components of these lipids include a pH-sensitive ionizable amino head group, two distal lipid tails, and two cross-linkable thiols, which together facilitate self-assembly with nucleic acids to form stable smart lipid nanoparticles (LNP) without helper lipids for local or systemic delivery. A multifunctional ionizable lipid, ECO, was identified as a lead lipid for translational development. The ECO based LNP or ELNP is able to sense and respond to environmental changes during the delivery process for targeted delivery, endosomal escape in response to the pH decrease, and reductive dissociation for cytoplasmic release. ELNP has been explored for delivery of siRNA and miRNA for cancer therapy, plasmid DNA for treating inherited retinal genetic disorders, CRISPR/Cas9 for gene editing, and mRNA for vaccine.

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