Poster 23

Development of Mesoscale Lipid Nanoparticle Formulation for Targeted Nucleic Acid Delivery to the Kidneys

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Purpose

Nanoparticles in the mesoscale size range (300 – 400 nm) have been shown to selectively target the proximal tubular epithelial cells in the kidneys. Such a drug delivery platform has the potential to improve the accumulation of kidney therapeutics at the disease site while also reducing off-target effects. However, kidney targeting of mesoscale nanoparticles has so far only been demonstrated with polymeric carriers. The purpose of this work was to develop a lipid-based mesoscale nanoparticle formulation, which can later be applied for targeted delivery of nucleic acids for kidney disease treatment.

Methods

Mesoscale lipid nanoparticles (MLNP) with siRNA cargo have been formulated with an ionizable lipid, a phospholipid, cholesterol, and a PEGylated lipid using the nanoprecipitation method. Modifications of the formulation composition and process parameters have been applied to optimize the nanoparticle size. MLNP size and polydispersity index were characterized via dynamic light scattering and zeta potential via electrophoretic light scattering. siRNA encapsulation efficiency was measured using a fluorescence-based RNA-quantitation assay. MTT assay has been applied to test the MLNP cytotoxicity.

Results

Lipid nanoparticle formulation with a size in the mesoscale range has been obtained through an increase in total lipid concentration, modification of lipid molar ratio, an increase in ion concentration, and modification of mixing parameters. Lipid composition has also been optimized to achieve stable PEGylation required for kidney targeting. Treatment with the optimized MLNP formulations encapsulating non-targeting siRNA and IL-6 siRNA has shown no effect on the viability of renal epithelial cells, which demonstrated that this formulation is non-cytotoxic and suitable for further experimentation.

Conclusion

In conclusion, we have formulated a mesoscale lipid nanoparticle optimized for targeted nucleic acid delivery to the renal epithelial cells. The MLNP formulation has shown preliminary indications of safety, and further in vitro and in vivo studies will be conducted to demonstrate the efficacy of nucleic acid delivery to the renal cells.

Keywords: lipid nanoparticles, kidney targeting, nucleic acid delivery