Poster 6

Modulating the mRNA Loading Capacity of Polymeric Mesoscale Nanoparticles

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Purpose

In prior work, we successfully formulated mRNA-loaded, kidney-targeted, polymeric nanoparticles, and studied their uptake kinetics and mRNA expression in vitro. The aim of these studies was to develop kidney-targeted gene therapies for kidney diseases and renal cancer. In ongoing work to maximize protein expression in vivo using rodent models, we aimed to increase the total loading of the mRNA cargo within the nanoparticle by optimization of formulation parameters.

Methods

We sought to enhance mRNA loading by modifying our original system with various biomolecules and other excipients via charge or other interactions with our polymeric nanoparticle system. To do so, we performed mRNA nanoparticle loading optimization studies and assessed them against our original formulation via Quant-iT RiboGreen assays and in vitro fluorescent protein reporter translation using renal cell lines. Thereafter, we aimed to test the biocompatibility of our modified formulation through cell viability assays, and functionality through mRNA and protein expression.

Results

Prior studies found near-complete encapsulation efficiency with 5ug- 10ug of cargo, though we found reduced encapsulation efficiency at higher loading masses. We found these particles can deliver functional mRNA into renal proximal tubular epithelial cells, with expression of a fluorescent protein reporter within one hour of incubation.

Conclusion

Modification of mesoscale nanoparticles to retain their size and surface parameters necessary for renal targeting is possible with mRNA encapsulation. Ongoing in vivo studies are aimed toward maximizing renal targeting capabilities of the nanoparticle system, as well as the renal expression of exogenous protein, with a focus on intervention in renal disease.

Keywords: Polymeric nanoparticles, mRNA loading, kidney disease, gene delivery