Formulation of CRISPR Cas-9 loaded polymeric mesoscale nanoparticles for renal-targeted gene therapy

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CRISPR Cas-9 systems are a molecular mechanism of gene editing that may enable gene therapies in renal diseases and kidney cancer. Earlier studies have shown reduction of gene expression in renal carcinoma, though specific targeting of these molecules to the kidneys is difficult. Prior work has demonstrated liposomal delivery of CRISPR Cas-9. In our prior work, we developed mesoscale nanoparticles (MNPs) which can specifically target renal tubules and exhibit controlled release of nucleic acid therapeutics. In this work, we investigated the ability to maintain the physicochemical properties of MNPs which enable renal targeting while encapsulating functional CRISPR-Cas9 gene editing mechanisms. As a proof of concept, we have synthesised MNPs with a single guide RNA (sgRNA) and Cas-9 protein to target green fluorescent protein (GFP) and evaluated their functionality in vitro using stably transfected renal carcinoma cells expressing GFP. In vitro studies by fluorescence imaging and RT q-PCR demonstrated substantial reduction in GFP expression upon exposure to these CRISPR Cas-9 loaded nanoparticles. Since many kidney cancers and renal diseases involve chromosomal alterations and gene mutations, in the future we aim to target these genes using CRISPR Cas-9 and correct the mutations with high precision and thus reduce the progression of the disease.