Chemical Engineering Thesis Defense

Aminoglycosides-derived lipopolymer nanoparticles for delivery of mRNA

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Abstract

The advancement of efficient drug delivery systems has the potential to enhance the prognosis of numerous pathological states. Aminoglycosides have been utilized as antibacterial agents and are deemed appealing as monomers for the advancement of polymeric materials in diverse applications. The utilization of in vitro transcribed messenger RNA (mRNA) has surfaced as a promising therapeutic platform in recent times. To fulfill its commitment, it is imperative to achieve efficient delivery of mRNA to precise cell types and tissues. In recent times, Lipid nanoparticles and polymeric nanoparticles have been identified as promising vehicles for the delivery of short-interfering RNAs (SiRNA), plasmid DNAs (pDNA), and other small molecule drugs and have progressed to clinical trials. However, there are some limitations to the use of LNPs in mRNA delivery including stability, limited loading capacity, cellular uptake variability, etc. Nonetheless, the potential of LNPs to transport mRNA remains largely unexplored. In this study, we present an account of the creation of novel amphiphilic nanoparticles derived from aminoglycosides, which have been proven in the past as an efficient carrier for the delivery of plasmid DNA and small molecules and small interfering RNAs, for mRNA delivery. From the library of aminoglycoside-derived lipopolymers, we have picked the lead lipopolymers NRC6, PRC6, and PGC18 and their parental polymers NR, PR, and PG for the delivery of mRNA. The complexes of lipopolymers and mRNA were made with different ratios of lipopolymers to mRNA. The appropriate binding ratios of lipopolymers and mRNA were determined by gel electrophoresis. The complexes were characterized using dynamic light scattering (DLS) and zeta potential. Cell-based assays indicated that aminoglycoside-derived LPNs are attractive vehicles for the delivery of mRNA for different applications in medicine and biology including cancer.

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