

Aptamer-mediated polymeric vehicles for enhanced cell-targeted drug delivery

Abstract

The search for smart delivery systems for enhanced pre-clinical and clinical pharmaceutical delivery and cell targeting continues to be a major biomedical research endeavor owing to differences in the physicochemical characteristics and physiological effects of drug molecules, and this affects the delivery mechanisms to elicit maximum therapeutic effects. Targeted drug delivery is a smart evolution essential to address major challenges associated with conventional drug delivery systems. These challenges mostly result in poor pharmacokinetics due to the inability of the active pharmaceutical ingredients to specifically act on malignant cells thus, causing poor therapeutic index and toxicity to surrounding normal cells. Aptamers are oligonucleotides with engineered affinities to bind specifically to their cognate targets. Aptamers have gained significant interests as effective targeting elements for enhanced therapeutic delivery as they can be generated to specifically bind to wide range of targets including proteins, peptides, ions, cells and tissues. Notwithstanding, effective delivery of aptamers as therapeutic vehicles is challenged by cell membrane electrostatic repulsion, endonuclease degradation, low pH cleavage, and binding conformation stability. The application of molecularly engineered biodegradable and biocompatible polymeric particles with tunable features such as surface area and chemistry, particulate size distribution and toxicity creates opportunities to develop smart aptamer-mediated delivery systems for controlled drug release. This article discusses opportunities for particulate aptamer-drug formulations to advance current drug delivery modalities by navigating active ingredients through cellular and biomolecular traffic to target sites for sustained and controlled release at effective therapeutic dosages while minimizing systemic cytotoxic effects. A proposal for a novel drug-polymer-aptamer-polymer (DPAP) design of aptamer-drug formulation with stage-wise delivery mechanism is presented to illustrate the potential efficacy of aptamer-polymer cargos for enhanced cell targeting and drug delivery.