Preclinical development and ocular biodistribution of gemini-DNA nanoparticles after intravitreal and topical administration: Towards non-invasive glaucoma gene therapy

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Abstract

Gene therapy could offer improvement in the treatment of glaucoma compared to the current standard of lowering intraocular pressure. We have developed and characterized non-viral gemini surfactant-phospholipid nanoparticles (GL-NPs) for intravitreal and topical administration. Optimized GL-NPs (size range 150–180 nm) were biocompatible with rat retinal ganglion (RGC-5) cells with 95% viability by PrestoBlue™ assay. GL-NPs carrying Cy5-labeled plasmid DNA demonstrated distinct trafficking behavior and biodisposition within the eye in vivo after intravitreal or topical application with respect to pathways of movement and physicochemical stability. After intravitreal injection in mice, GL-NPs localized within the nerve fiber layer of the retina, whereas after topical application, GL-NPs were located in several anterior chamber tissues, including the limbus, iris, and conjunctiva. GL-NPs were thermodynamically stable in the vitreous and tear fluid and were trafficked as single, non-aggregated particles after both types of administration.

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