Compacted DNA nanoparticles as a non-viral delivery strategy to ocular tissues

Muna Naash
Health Sciences Center
Department of Cell Biology
University of Oklahoma, Oklahoma City (USA)

The eye is an excellent candidate for gene therapy as it is immune privileged and much of the disease causing genetics are well understood. Towards a goal of ocular gene therapy, we evaluated the efficiency of compacted DNA nanoparticles. These particles have been shown to be safe and effective in a human clinical trial and did not provoke an immune response.

Furthermore, these nanoparticles have no theoretical limitation on plasmid size and can be highly concentrated. In our study, we demonstrated that these nanoparticles can be targeted to different tissues within the eye by varying the site of injection. Almost all cell types of the eye were capable of transfection by the nanoparticle and produced robust levels of gene expression that were dose-dependent. Most impressively, subretinal delivery of these nanoparticles transfected nearly all of the photoreceptor population and produced expression levels almost equal to that of rod opsin, the highest expressed gene in the retina. For preclinical evaluation of this nanotechnology, we tested its efficacy in rescuing the phenotype in an animal model of retinitis pigmentosa with a defect in the retinal degeneration slow (RDS) gene. Three nanoparticles were designed to express wild-type-Rds in rods by the mouse opsin promoter (MOP-Rds), in rods & cones by the human red/green cone-opsin promoter (COP-Rds), and in all cells by the chicken beta actin promoter (CBA-Rds).All three particles showed high levels of transgene expression as well as functional and structural rescue of the Rds+/- phenotype. As no deleterious effects on retinal function were observed, this treatment strategy appears to be clinically promising and provides a highly efficient non-viral technology to safely deliver and express nucleic acids in the retina and other ocular tissues.