

Capsid Mutated Adeno-Associated Virus Delivered to the Anterior Chamber Results in Efficient Transduction of Trabecular Meshwork in Mouse and Rat

Bogner B (1) , Boye SL (2) , Min SH (2) , Peterson JJ (2) , Ruan Q (2) , Zhang Z (1) , Reitsamer HA (1) , Hauswirth WW (2) , Boye SE (2)

1 Department of Ophthalmology and Optometry, SALK/Paracelsus Medical University, Salzburg, Austria.

2 Department of Ophthalmology, University of Florida, Gainesville, United States of America.

BACKGROUND: Adeno associated virus (AAV) is well known for its ability to deliver transgenes to retina and to mediate improvements in animal models and patients with inherited retinal disease. Although the field is less advanced, there is growing interest in AAV's ability to target cells of the anterior segment. The purpose of our study was to fully articulate a reliable and reproducible method for injecting the anterior chamber (AC) of mice and rats and to investigate the transduction profiles of AAV2- and AAV8-based capsid mutants containing self-complementary (sc) genomes in the anterior segment of the eye.

METHODOLOGY/PRINCIPLE FINDINGS: AC injections were performed in C57BL/6 mice and Sprague Dawley rats. The cornea was punctured anterior of the iridocorneal angle. To seal the puncture site and to prevent reflux an air bubble was created in the AC. scAAVs expressing GFP were injected and transduction was evaluated by immunohistochemistry. Both parent serotype and capsid modifications affected expression. scAAV2- based vectors mediated efficient GFP-signal in the corneal endothelium, ciliary non-pigmented epithelium (NPE) , iris and chamber angle including trabecular meshwork, with scAAV2(Y444F) and scAAV2(triple) being the most efficient.

CONCLUSIONS/SIGNIFICANCE: This is the first study to semi quantitatively evaluate transduction of anterior segment tissues following injection of capsid-mutated AAV vectors. scAAV2- based vectors transduced corneal endothelium, ciliary NPE, iris and trabecular meshwork more effectively than scAAV8-based vectors. Mutagenesis of surface-exposed tyrosine residues greatly enhanced transduction efficiency of scAAV2 in these tissues. The number of Y-F mutations was not directly proportional to transduction efficiency, however, suggesting that proteosomal avoidance alone may not be sufficient. These results are applicable to the development of targeted, gene-based strategies to investigate pathological processes of the anterior segment and may be applied toward the development of gene-based therapies for glaucoma and acquired or inherited corneal anomalies.

PLoS One. 2015 Jun 8;10(6) :e0128759. doi: 10.1371/journal.pone.0128759. eCollection 2015

PMID: 26052939

<http://www.ncbi.nlm.nih.gov/pubmed/26052939>