Intracameral Injection of AAV-DJ.COMP-ANG1 Reduces the IOP of Mice by Reshaping the Trabecular Outflow Pathway

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PURPOSE: The angiopoietin-1 (ANG1) -TIE signaling pathway orchestrates the development and maintenance of the Schlemm's canal (SC) . In this study, we investigated the impact of adeno-associated virus (AAV) -mediated gene therapy with cartilage oligomeric matrix protein-ANG1 (COMP-ANG1) on trabecular outflow pathway.

METHODS: Different serotypes of AAVs were compared for transduction specificity and efficiency in the anterior segment. The selected AAVs encoding COMP-ANG1 or ZsGreen1 (control) were delivered into the anterior chambers of wild-type C57BL/6J mice. The IOP and ocular surface were monitored regularly. Ocular perfusion was performed to measure the outflow facility and label flow patterns of the trabecular drainage pathway. Structural features of SC as well as limbal, retinal, and skin vessels were visualized by immunostaining. Ultrastructural changes in the SC and trabecular meshwork were observed under transmission electron microscopy.

RESULTS: AAV-DJ could effectively infect the anterior segment. Intracameral injection of AAV-DJ.COMP-ANG1 lowered IOP in wild-type C57BL/6J mice. No signs of inflammation or angiogenesis were noticed. Four weeks after AAV injection, the conventional outflow facility and effective filtration area were increased significantly (P = 0.005 and P = 0.04, respectively) . Consistently, the area of the SC was enlarged (P CONCLUSIONS: Intracamerally injected AAV-DJ.COMP-ANG1 offers a significant IOP-lowering effect by remodeling the trabecular outflow pathway of mouse eyes.

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