Inducible Adeno-Associated Virus Vector-Delivered Transgene Expression in Corneal Endothelium

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摘要

Abstract

PURPOSE: To investigate whether recombinant adeno-associated virus (rAAV) vector--mediated transgene expression is induced by inflammation in corneal endothelial cells in vivo. METHODS: The ocular anterior chamber of New Zealand White rabbits was injected with rAAV-LacZ (10(7) units of infection). Transient ocular anterior segment inflammation was induced by an intravitreal injection of lipopolysaccharide (LPS). The effect of inflammation on LacZ gene expression in corneal endothelial cells was evaluated by histochemical staining and reverse transcription-polymerase chain reaction (RT-PCR). The influence of rAAV on endothelial cell function was monitored by measuring corneal thickness. RESULTS: Inflammatory reaction peaked at 1 day after LPS treatment and, at the same time, most of the endothelial cells (91.3% plus minus 7.2%) showed prominent LacZ gene expression. The transgene expression gradually diminished to basal level (3.4% plus minus 2.1%) when the inflammation subsided at 15 days after LPS treatment. The diminished transgene expression was efficiently reactivated to a high level (86.1% plus minus 8.7%) by a second LPS injection 60 days later. Moreover, the transgene expression remained low for a long period (60 days) in the absence of LPS treatment, but was increased to high levels (87.3% plus minus 8.1%) 1 day after LPS treatment. Throughout the observation period, endothelial cell function remained intact. CONCLUSIONS: The rAAV vector can deliver genes into endothelial cells, and transgene expression is dramatically induced by inflammation. The rAAV-delivered transgene is stable and does not compromise endothelial cell function. Inducible rAAV-mediated transgene expression in corneal endothelial cells is a potential strategy in the treatment and prevention of ocular diseases