POSTER 118

TISSUE-SELECTIVE CONTROLLED DECORIN GENE DELIVERY IN THE RABBIT CORNEA SIGNIFICANTLY RETARDS CORNEAL ANGIOGENESIS IN VIVO

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Purpose: Recent studies have shown that decorin gene therapy inhibits neovascularization in many non-ocular tissues. We tested the efficacy of decorin gene delivery into stroma with AAV5 to impede vascular endothelial growth factor (VEGF)-induced angiogenesis in rabbit cornea in vivo.

Methods: New Zealand White rabbits were used in our study. Corneal neovascularization was induced by implanting a sucralfate-hydron pellet containing 650ng VEGF using micropocket assay. Decorin gene delivery into rabbit stroma was accomplished via topical application of 25µl AAV5 (5x10e9 vg/µl). Visual eye exam, stereomicroscopy, and slit-lamp microscopy were used to monitor corneal health. Changes in corneal neovascularization were measured with stereomicroscopy, immunocytochemistry, western blotting, and real-time PCR techniques. NIH Image J 1.38X and Adobe Photoshop software were used to quantify vasculature.

Results: AAV5 decorin gene delivery into stroma demonstrated a substantial reduction in blood vessel area compared to control corneas in a time-dependent fashion from day-3 to day-14. Stereo- and slit-lamp microscopy detected a considerable attenuation in corneal neovascularization (9.8-37.3%) in rabbit eyes in vivo with decorin gene therapy. The largest decrease in corneal angiogenesis was observed on day-10 (up to 37.3%). In addition, decorin-overexpressing rabbit corneas exhibited delayed blood vessel appearance, thinning, and retarded migration towards the cornea compared to control. Preliminary immunochemistry, western blotting, and real-time PCR data support these observations. Clinical eye examination did not reveal any significant inflammation in test or control corneas.

Conclusions: Decorin gene therapy effectively reduces corneal neovascularization in vivo. Studies are underway to delineate safety, toxicity, and doses of tested vectors.