Attenuation of bleb-fibrosis associated with glaucoma filtration surgery by PEI-decorin gene therapy

Jessica Kitchell¹, Ajay Sharma¹,³, Govindaraj Anumanthan¹,³, Rajiv R Mohan¹, ², ³

¹Department of Veterinary Medicine and Surgery, ²Mason Eye Institute, University of Missouri, Columbia, Missouri, ³Harry S. Truman Memorial Veteran Hospital, Columbia, Missouri

Rationale

• Glaucoma filtration surgery (GFS) is frequently used to treat glaucoma.
• Bleb fibrosis due to excessive wound healing is a major complication and cause for the failure of GFS.
• Transforming growth factor beta (TGFβ) is a cytokine that plays an important role in wound healing by triggering transformation of keratocytes to fibroblasts and myofibroblasts.
• In wound healing there is an excessive amount of TGFβ activity.
• Decorin, a small leucine-rich proteoglycan, is a natural inhibitor of TGFβ.

Hypothesis

We hypothesized that subconjunctival injections of decorin plasmid-PEI nanoconstructs would inhibit TGFβ activity and attenuate excessive fibrosis while improving the outcome of GFS surgery in rabbit eyes in vivo.

Methods

• GFS was performed by creating a 1.5 mm² sclerotomy on New Zealand white rabbits.
• One group received a subconjunctival injection of PEI-decorin nanoparticle plasmid polyplexes 30 minutes before GFS.
• Another group received an injection of saline solution.
• Biomicroscopy was performed on days 0, 3, 7 and 14.
• Bleb height was graded: 0 = flat; 1 = shallow/former <1 mm; 2 = elevated <2 mm; 3 = high >2 mm.
• Bleb vascularity was graded: 0 = avascular; 1 = normal vascularity; 2 = hyperemic; 3 = very hyperemic.
• Intraocular pressure (IOP) was measured using tonopen.
• Tissues were collected on day 14 for histological and immunofluorescence analysis.

Results

• The intraoperative subconjunctival decorin-PEI nanoconstructs significantly decrease postoperative fibrosis and improves the outcome of GFS.

Conclusions

The intraoperative subconjunctival decorin-PEI nanoconstructs significantly decrease postoperative fibrosis and improves the outcome of GFS. This can be seen by the decrease in bleb vascularity and IOP, along with a decrease in fibrosis markers.

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