THROMBOSPONDIN-1, A MAJOR ENDOGENOUS ACTIVATOR OF TGF-BETA IS EXPRESSED IN THE TRABECULAR MESHWORK, AND IS REGULATED BY TGF-BETA AND DEXAMETHASONE

E.R. Tamm\textsuperscript{1}, A.Ohlimann\textsuperscript{1}, C.Flügel-Koch\textsuperscript{1}, U.Welge-Lüssen\textsuperscript{2}
\textsuperscript{1} Department of Anatomy, Friedrich-Alexander-University, Erlangen-Nürnberg, Germany
\textsuperscript{2} Department of Ophthalmology, Ludwig-Maximilians-University, Munich, Germany

Background: Transforming growth factor-beta2 (TGF-beta2) is elevated in the aqueous humor of patients with primary open angle glaucoma (POAG). High levels of TGF-beta2 appear to play a role in the pathogenesis of POAG and failure of filtrating surgery. Most TGF-beta2 in the eye is present in a latent, inactive form, and the mechanisms of it’s in vivo activation are unclear. Since thromposondin-1 (TSP-1) is one of the most potent in vivo activating molecules of TGF-beta, we investigated the localization and expression of TSP-1 in the aqueous humor outflow pathways.

Design: Human eye bank tissue study

Testing/Methods/Materials: TSP-1 immunohistochemistry was performed in the eyes of human donors (6 normal and 12 with POAG). TSP-1 expression was assessed by RT-PCR and northern blotting in mRNA from fresh TM, and human TM cells in vitro. In addition, northern and western blot analyses of TM cells after incubation with TGF-beta and dexamethasone were performed.

Results: Intense TSP-1 immunolabeling was observed throughout all layers of the TM, while other ocular tissues showed no or only weak labeling. In 5 eyes with POAG, TSP-1 labeling was more intense than in normals. mRNA for TSP-1 was detected both in fresh and cultured TM cells. Incubation of TM cells with TGF-beta1 and dexamethasone caused a marked increase in TSP-1 expression.

Conclusions: TSP-1 in the TM might act as a potent local endogenous activator of TGF-beta in the aqueous humor and mediate any local effects of TGF-beta and/or dexamethasone on the outflow tissues.

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