Evidence for a role of angiopoietin-like 7 (ANGPTL7) in extracellular matrix formation of the human trabecular meshwork: implications for glaucoma

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The trabecular meshwork tissue controls the drainage of the aqueous humor of the eye. A dysfunctional trabecular meshwork leads to an altered fluid resistance, which results in increased intraocular pressure (IOP) . IOP is the major risk factor of glaucoma, the second-leading cause of blindness in the developed world. In the search for genes altered by glaucomatous insults, we identified angiopoietin-like7 (ANGPTL7) , a member of the ANGPTL family. Although structurally related to the angiopoietins, ANGPTL7's function is poorly understood.

Because ANGPTL7 is secreted and because extracellular matrix (ECM) deposition and organization is critical for aqueous humor resistance, we investigated the effect of ANGPTL7 on relevant trabecular meshwork ECM genes and proteins. We find that overexpression of ANGPTL7 in primary human trabecular meshwork cells altered the expression of fibronectin, collagens type I, IV & V, myocilin, versican, and MMP1. ANGPTL7 also interfered with the fibrillar assembly of fibronectin.

Finally, we find that silencing ANGPTL7 during the glucocorticoid insult significantly affected the expression of other steroid-responsive proteins. These results indicate that ANGPTL7 modulates the trabecular meshwork's ECM as well as the response of this tissue to steroids. Together with previous findings, these properties strengthen ANGPTL7's candidacy for the regulation of IOP and glaucoma.

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