

Anti-Connective Tissue Growth Factor Antibody Treatment Reduces Extracellular Matrix production in Trabecular Meshwork and Lamina Cribrosa cells

Wallace DM, Clark AF, Lipson K, Andrews D, Crean J, O'Brien CJ.

PURPOSE: We have previously demonstrated elevated levels of Connective Tissue Growth Factor (CTGF/CCN2) in the aqueous humour (AqH) of pseudoexfoliation glaucoma (PXFG) patients when compared to cataract controls. Furthermore, there is a significant trabecular meshwork (TM) and lamina cribrosa (LC) fibrotic phenotype associated with glaucoma possibly driven by CTGF. The purpose of this study was to investigate the potential of anti-CTGF immunotherapy in glaucoma.

METHODS: Primary TM and LC cells were cultured from human donors with (GTM/GLC) and without (NTM/NLC) primary open angle glaucoma (POAG). AqH samples from PXFG, POAG and control cataract patients were applied to N/GTM and N/G LC cells in the presence or absence of a therapeutic, humanized monoclonal anti-CTGF antibody FG-3019 (10µg/ml) (FibroGen Inc.). Hydrogen peroxide, (H₂O₂) was also used as a stimulus. Expression of fibrotic genes (fibronectin-1, fibrillin-1, CTGF, collagen 1A1 and α-smooth muscle actin) was assessed by q-PCR. Protein expression of collagen 1A1 and α-smooth muscle actin was examined in N/G TM cells by SDS-PAGE. The modulatory effect of FG3019 (10µg/ml) and IgG (10µg/ml) were also assessed.

RESULTS: Treatment of cells with AqH from PXFG & POAG patients and H₂O₂ induced a significant (P<0.05) increase in expression of fibrotic genes. **CONCLUSIONS:** FG-3019 is effective in blocking extracellular matrix production in TM and LC cells thus supporting a role for the use of anti-CTGF immunotherapy in the treatment of glaucoma.

Invest Ophthalmol Vis Sci. 2013 Nov 7. pii: iovs.13-12494v1. doi: 10.1167/iov.13-12494.

PMID: 24204045

<http://www.ncbi.nlm.nih.gov/pubmed/24204045>