TRANSCRIPTION FACTORS, 5'-TG-3'-INERACTING FACTORS (TGIF), REGULATES TRICHOSTATIN-A MEDIATED INHIBITION OF CORNEAL SCARRING

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Purpose: Recently, we demonstrated that Trichostatin-A (TSA) inhibits transforming growth factor beta 1 (TGFβ1)-induced fibrosis (haze) in rabbit cornea in vivo. However, the molecular mechanism of this process is still unknown. This study tested the hypothesis that homeodomain transcription factors, TGIF1 and TGIF2 regulate anti-fibrotic effects of TSA in the cornea.

Methods: An established *in vitro* model of corneal scarring was used. Primary corneal fibroblast (HSF) cultures generated from donor human corneas were exposed to TGFβ1 (1ng/ml), TSA (250 or 500nM), TGFβ1 (1ng/ml)+TSA (250/500nM) or vehicle. The quantification of alpha smooth muscle actin (αSMA), TGIF1 and TGIF2 mRNA was performed with Real-time PCR and protein with immunoblotting and immunocytochemical techniques. Statistical analysis was performed using one way ANOVA. The p value < 0.05 was considered significant.

Results: This study, for the first time, demonstrates that human corneal fibroblasts express TGIF and TGIF2 and play role in corneal fibrosis modulation. TGFβ1 treatment to HSF significantly increased myofibroblasts (hallmark of corneal fibrosis) mRNA and protein levels of αSMA (myofibroblasts marker). TSA treatment showed significant decrease (60-75%; $p<.05$) in TGFβ1-induced fibrosis in human cornea in vitro. The anti-fibrotic effect of TSA was associated with a concurrent increase in TGIF and TGIF2 levels suggesting their role in the modulation of corneal fibrosis.

Conclusions: The anti-fibrotic effects of TSA in the cornea involve TGIF1 and TGIF2 transcription factors.

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