Can human xylosyltransferase-1 serve as a biomarker and therapeutic target for corneal fibrosis?

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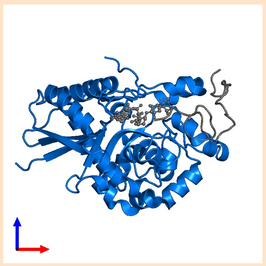
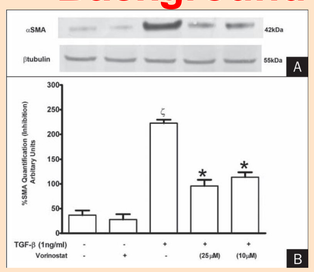
Background and Rationale

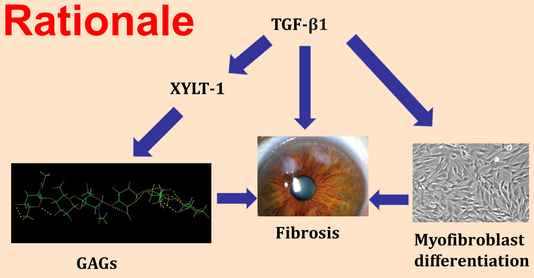


Xylosyltransferase-1



TGF-β's effects on α-SMA in corneal tissue

Tandon A, Tovey JC, Waggoner MR, et al. Vorinostat: a potent agent to prevent and treat laser-induced corneal haze. *Journal of Refractory Surgery*. 2012; 28: 285-290.



Pathways of xylosyltransferase-1 in fibrosis

Hypothesis and Objectives

Tested was the hypothesis that XYLT1 plays an important role in corneal wound healing and scarring and may allow development of newer strategies for curing corneal fibrosis. The specific aims were: 1) to characterize XYLT1 expression in normal and wounded human and rabbit corneas, 2) investigate its role in corneal wound healing, and 2) determine whether XYLT1 can serve as a biomarker for corneal fibrosis.

Materials and Methods

Materials used included normal and alkaline treated rabbit corneal tissue and normal human corneal fibroblasts (HCFs) from human donors.

Methods used included immunohistochemistry, an in vitro corneal fibrosis model utilizing transforming growth factor-beta1 (TGF-β1) treated HCFs, and quantitative polymerase chain reaction.

Results

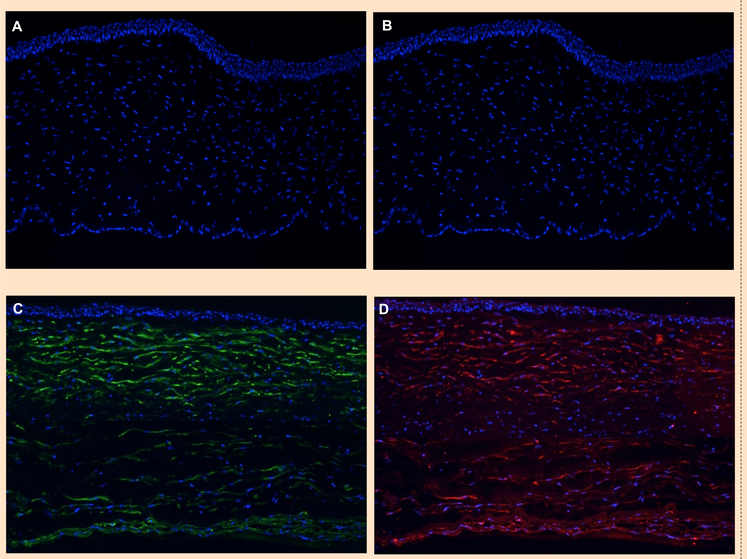


Fig 1. Rabbit cornea slides subjected to immunohistochemistry stain for α-SMA and XYLT-1 at 10X magnification. The blue (DAPI) stain is nucleus. The green stain is α-SMA and the red stain is XYLT-1. A) Naïve rabbit cornea stained for a-SMA B) Naïve rabbit cornea stained for XYLT-1 C) Alkaline injured rabbit cornea stained for α-SMA D) Alkaline injured rabbit cornea stained for XYLT-1.

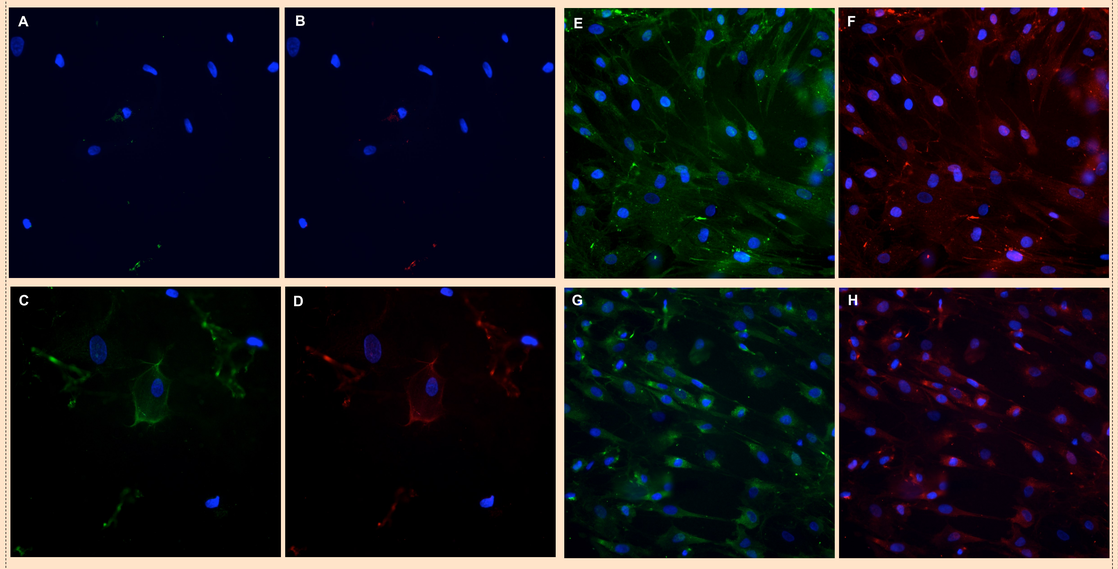


Figure 2: Normal human cornea fibroblasts treated with TGF-β1. The fixed cells were then immunohistochemically stained for α-SMA and XYLT-1. The blue (DAPI) stain is nucleus. The green stain is α-SMA and the red stain is XYLT-1. A) No treatment (NT) stained for α-SMA B) NT stained for XYLT-1 C) 24hr stained for α-SMA D) 24hr stained for XYLT-1 E) 48hr stained for α-SMA F) 48hr stained for XYLT-1 G) 72hr stained for α-SMA H) 72hr stained for XYLT-1

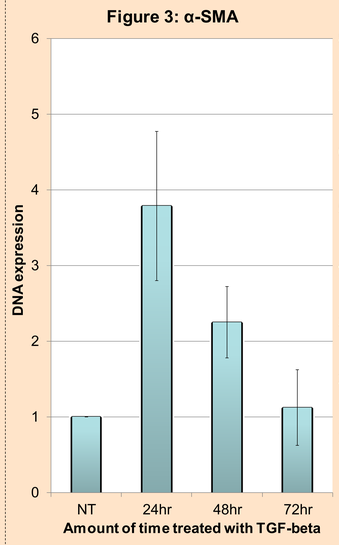


Figure 3: α-SMA targeted q-PCR of TGF-β1 treated fibroblasts

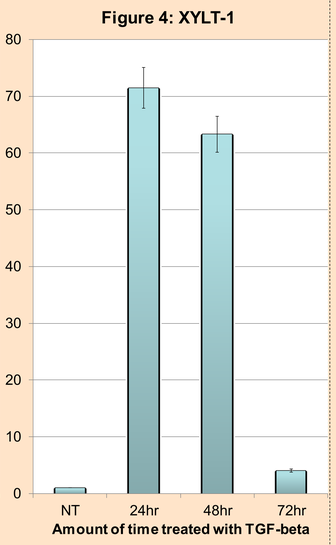


Figure 4: XYLT-1 targeted q-PCR of TGF-β1 treated fibroblasts

1.In the immunhistochemistry experiments, (both with alkaline treated rabbit cornea tissue and TGF-β1 treated normal human cornea fibroblasts) expression of XYLT-1 protein directly correlates to α-SMA protein.
2.Transforming growth factor-β1 treated HCFs showed significantly high XYLT-1 and α-SMA mRNA and protein levels (5-35 fold; $p < 0.01$) compared to untreated.
3.The qPCR results show that XYLT-1 DNA expression followed the same trend as α-SMA DNA expression as a function of time treated with TGF-β1. Results from that experiment also include roughly 30 fold higher levels of XYLT-1 DNA expression compared to α-SMA DNA expression.

Conclusions

1. Xylosyltransferase-1 appears to be a novel biomarker for corneal fibrosis.
2. XYLT-1 may be a more sensitive marker of fibrosis than α-SMA
3. XYLT-1 could be a future therapeutic target to prevent corneal fibrosis.

Acknowledgements

Primary:Ruth Kraeuchi Missouri Endowed Chair Ophthalmology Fund, University of Missouri
Partial: Veteran Health Affairs Merit (1I01BX000357), Washington DC (RRM), National Eye Institute (RO1EY17294), NIH, Bethesda MD (RRM)