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

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Background and Rationale

Fig 1. Rabbit cornea slides subjected to immunohistochemistry stain for α1-SMA and the red stain is XYLT1. A) No treatment (NT) B) NT stained for α1-SMA C) 24hr stained for α1-SMA D) 24hr stained for XYLT1 E) 48hr stained for α1-SMA F) 48hr stained for XYLT1 G) 72hr stained for α1-SMA H) 72hr stained for XYLT1

1. In the immunohistochemistry experiments, (both with alkaline treated rabbit cornea tissue and TGF-β1 treated normal human cornea fibroblasts) expression of XYLT1 protein directly correlates to α1-SMA protein.
2. Transforming growth factor-β1 treated HCFs showed significantly high XYLT1 and α1-SMA mRNA and protein levels (5-35 fold; p <0.01) compared to untreated.
3. The qPCR results show that XYLT1 DNA expression followed the same trend as α1-SMA DNA expression as a function of time treated with TGF-β1. Results from that experiment also include roughly 30 fold higher levels of XYLT1 DNA expression compared to α1-SMA DNA expression.

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 cornea tissue and normal human cornea 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 2: Normal human cornea fibroblasts treated with TGF-β1. The fixed cells were then immunohistochemically stained for α1-SMA and XYLT1. A) No treatment (NT) B) NT stained for α1-SMA C) 24hr stained for α1-SMA D) 24hr stained for XYLT1 E) 48hr stained for α1-SMA F) 48hr stained for XYLT1 G) 72hr stained for α1-SMA H) 72hr stained for XYLT1

Fig 3: α1-SMA targeted q-PCR of TGF-β1 treated fibroblasts

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

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 α1-SMA.
3. XYLT-1 could be a future therapeutic target to prevent corneal fibrosis.

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