Transcriptome profiling reveals novel expression markers that predispose patients to develop post-photorefractive keratectomy corneal haze

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Abstract

Photorefractive keratectomy is an excimer laser [1] based ablation surgery of corneal surface used for correcting refractive errors. Corneal haze is the result of an aggressive wound healing response with an incidence rate [2] of 1.44% post PRK, making it an important health burden. Studies thus far have only focused on molecular alterations post haze development. Since the corneal epithelium is an important mediator of the stromal haze response, we studies its role in predisposing subjects to develop aberrant wound healing response. Corneal epithelium samples collected intra-operatively from clinically healthy patients during PRK. This epithelium from 6 eyes that developed haze postoperatively and 10 eyes of age matched controls without haze were compared. Gene expression microarrays were performed for the mRNA samples followed by ontological analysis of underlying molecular pathways. The identified targets were validated in an independent set of post haze epithelial samples from 3 subjects with PRK induced haze. In vitro studies were done on HCE cells for differential dose of TGFβ for inflammatory markers, corneal structure & fibrosis associated genes and regulators of signal transduction. In addition, loss and gain of function studies was performed using PREX1 as a novel, prototype target. Mean age of groups was 25-28 years. A total of 1100 up and 1700 down regulated genes were revealed by microarray. Alterations in Oxidative stress, ECM-Receptor interactions, Wnt signaling pathway and CXC motif containing chemokines contributes to cellular proliferation and wound healing, which is observed in in vitro model. In cornea novel target PREX1, an oxidative stress gene, when over expressed exhibits faster wound closure in HCE cells with and without TGFβ. Loss of function using PREX1 shRNA shows reduced wound closure. Our study shows that novel genes are involved in pathogenesis of post PRK haze. PREX1 over expression results in faster wound healing and modulating these pathways can prevent haze post PRK in future.

References


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