Antioxidant Biomarkers for Early Diagnosis of Keratoconus

Novel protein biomarkers for early, non-invasive detection of keratoconus.

Technology

Researchers in the Chakravarti Lab at NYU Langone Health have recently discovered several new antioxidant biomarkers that provide a non-invasive method for diagnosing early-stage keratoconus (KC) and monitoring disease progression. Previous research has shown that the signaling pathway of NRF2, a transcription factor that regulates oxidative stress response, is dysregulated in KC patients. In published work, the NYU researchers conducted proteomic and transcriptomic studies on discarded corneal tissues obtained during surgery of keratoconus patients and detected changes in NRF2 expression and antioxidant proteins it regulates. As the tear fluid is an easily accessible ocular fluid, the investigators assessed the antioxidant glutathione peroxidase 3 (GPX3) and a byproduct of oxidative stress, malondialdehyde (MDA), in tear samples of KC patients and unaffected control volunteers. The investigators found a consistent increase in MDA and GPX3 in tear fluid of KC patients compared to control samples. These two factors may serve as biomarkers facilitating early detection and longitudinal tracking of disease progression. In conclusion, this innovative diagnostic approach paves the way for timely tracking of response to therapeutic interventions, thereby improving clinical outcomes for patients with keratoconus.

Background

The cornea is the eye's outermost protective layer, comprising three parts: a surface layer of epithelial cells, the corneal stroma made of keratocytes, and the innermost endothelial layer. Damage, infections, or congenital defects in any of these layers can lead to impaired vision or even blindness. Importantly, factors secreted by the corneal cells may be detected in the tear fluid. Keratoconus is a progressive eye disease characterized by the thinning of corneal tissue, causing the eye to bulge into a cone shape. This condition is often diagnosed in young adults and tends to worsen with age, resulting in blurred or distorted vision and increased sensitivity to light. Currently, keratoconus is diagnosed through corneal topography, measuring corneal thickness, and slit-lamp examinations, which assess the shape and integrity of the corneal surface. Biomarkers in the tear fluid may allow detection of keratoconus before other clinical phenotypes manifest, enabling clinical intervention before patients experience significant sight impairment.

Development Stage

Researchers have characterized the upregulation of these novel biomarkers in tear fluid from keratoconus patients. Future studies aim to further study these antioxidant proteins with *in vitro* systems.

Applications

Technology ID

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Category

Life Sciences/Diagnostics

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- Diagnosis (early, disease progression).
- Treatment stratification: Inform administration of therapeutic agent that reduces oxidative stress in the eye.
- Development of novel therapeutic strategies targeting anti-oxidant response.

Advantages

- Convenient collection: Non-invasive tear sampling eliminates need for costly office visit.
- Earlier detection: Biochemical changes may precede anatomical changes detectable by current imaging methods.
- Risk assessment tool: Identify individuals at risk before significant corneal changes occur, providing an opportunity for preventive measures.
- Monitor disease progression: GPX3 levels show correlation with keratoconus disease parameters (Kmax) used to assess disease severity.

Intellectual Property

NYU has filed a U.S. provisional patent application covering the method of analyzing NRF2-regulated biomarker levels in a biological sample, such as tear fluid, to diagnose keratoconus.

References

1. Shukti Chakravarti, et al. , https://iovs.arvojournals.org/article.aspx?articleid=2794154