Human Corneal Organoids for Treatment of Corneal Injury

A novel and innovative method for generating human corneal organoids (HCOs) and their use for the treatment of corneal disease or injury.

Technology

Researchers in the Chakravarti Lab at NYU have developed a method for generating human corneal organoids (HCOs) from induced pluripotent stem cells (iPSCs). These HCOs replicate the regenerative abilities of the fetal cornea, making them a promising biomaterial for corneal wound healing and stromal repair. The HCO stroma can serve as an extracellular matrix (ECM) for tissue repair, providing a human-derived alternative to Matrigel®, which is limited in clinical use due to its mouse origin. In pilot studies, the Chakravarti group has shown that cells derived from HCOs can prevent scarring during corneal wound healing in mouse models. They also show that the HCO stromal cells introduced into decellularized human donor corneas adapt and survive, suggesting their possibility of surviving and functioning as corneal cells in future cell therapy approaches. Additionally, because these HCOs accurately replicate the 3-dimensional structure of the developing cornea, they offer an improved research tool for studying corneal development and disease. Having some features of the cornea, HCOs may also be developed into model systems to study corneal injuries and infections before extensive use of animal models.

Background

Corneal disruption is a leading cause of blindness worldwide, resulting from diseases such as keratoconus and Fuchs endothelial dystrophy, as well as from infections or injury-related scarring. The current standard treatment involves transplanting donor corneas, but this option is limited by the availability of donors. Other treatment strategies for keratoconus focus only on alleviating symptoms or slowing disease progression. Consequently, there is a critical need for new strategies to treat corneal disruption. The cornea is the outermost protective layer of the eye, consisting of a surface layer of epithelial cells, the corneal stroma made up of keratocytes, and the innermost endothelial layer. Injuries, infections, or congenital defects in any of these layers can result in decreased vision or potential blindness. Most research on corneal diseases relies on monolayers of cultured primary cells from donor tissues, which do not accurately replicate the complexity of the cornea's multiple cell types in three-dimensional space. Therefore, there is also a need for more precise research tools to better understand corneal disease and development.

Development Stage

The inventors have validated the formation of corneal layers in the HCOs using immunohistochemistry and scRNA-seq. They have also demonstrated that HCO-derived cells can facilitate corneal wound healing *in vivo* using mouse models.

Applications

Technology ID

CHA10-03

Category

Life Sciences/Platform Technology

Life Sciences/Research tools/Tissue Engineering

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- **Treatment of various corneal defects and diseases:** Potential treatment for keratoconus, Fuchs endothelial dystrophy, congenital corneal dystrophy, lattice corneal dystrophy, Avellino corneal dystrophy, infection or injury-related corneal scarring.
- **Research tool:** HCOs can be leveraged to understand the mechanisms and stages of corneal development.
- **Preclinical testing:** HCOs can be used to evaluate efficacy and toxicity during preclinical therapeutic development.

Advantages

- **Scarless wound healing:** Unique composition of the HCOs mimics fetal tissue and thus may promote scarless wound healing.
- **Alternative to donor tissue:** HCOs could be used in place of scarce donor cornea for the treatment of corneal injury.
- **Replicate fetal corneal development:** HCOs accurately replicate early corneal development and co-differentiation of all corneal cell types.
- **A xeno-free ECM material:** HCOs can serve as an alternative to mouse-derived Matrigel®, widely used to culture primary cells.
- **Scalable and robust pipeline:** This method of generating HCOs may increase yield while decreasing batch variability.

Intellectual Property

NYU has filed a provisional patent application covering the methods for improved HCO generation and their use in treatment of corneal damage and disease.

References

1. Ashworth, Sean et al. , https://pubmed.ncbi.nlm.nih.gov/39615587/