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Advancements in Understanding the Heterogeneity of Mammalian and Human Retinal Pigment Epithelium: Towards Unveiling the Potential of Stem Cells

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Introduction

The Retinal Pigment Epithelium (RPE) is a crucial component of the vertebrate retina, playing essential roles in maintaining retinal homeostasis, visual function, and protection against degenerative diseases. Recent research has uncovered significant heterogeneity within the RPE across species, developmental stages, and disease conditions. This article provides a comprehensive overview of the latest advancements in understanding the heterogeneity of mammalian and human RPE, with a focus on the quest for identifying RPE stem cells. We explore the diverse functions of RPE cells, molecular markers defining RPE subpopulations, and the potential implications of RPE heterogeneity in regenerative medicine and therapeutic interventions for retinal diseases. The Retinal Pigment Epithelium (RPE) is a monolayer of pigmented cells situated between the neurosensory retina and the choroid in the back of the eye. It plays multifaceted roles in supporting the function of photoreceptors, maintaining retinal integrity, and ensuring visual acuity. Recent investigations have shed light on the remarkable heterogeneity within the RPE, challenging traditional views of its cellular uniformity. This article aims to review the current understanding of RPE heterogeneity in mammalian and human systems and its implications for identifying RPE stem cells [1].

Description

The RPE exhibits functional diversity, ranging from phagocytosis of shed photoreceptor outer segments to secretion of growth factors and maintenance of the blood-retinal barrier. Recent studies have highlighted variations in these functions among RPE cells, suggesting specialized subpopulations with distinct roles in retinal physiology. Understanding the developmental origins of RPE cells is crucial for deciphering their heterogeneity. Lineage tracing studies have revealed diverse progenitor populations contributing to RPE development, including the optic cup-derived neuroepithelium and the periocular mesenchyme. These distinct origins may underlie the heterogeneity observed in adult RPE [2,3].

Advances in single-cell transcriptomics have enabled the characterization of molecular profiles of individual RPE cells. Studies have identified unique gene expression patterns and signaling pathways associated with RPE subpopulations, offering insights into their functional specialization and regulatory mechanisms. Spatial heterogeneity of RPE cells within the retina has been documented across various species. Regional differences in gene expression, morphology, and functional properties suggest localized adaptations to specific microenvironments and physiological demands. The existence of stem cell niches within the RPE has been proposed based on evidence from animal models and human tissues. These niches are hypothesized to harbor quiescent stem cells capable of self-renewal and differentiation into mature RPE cells, contributing to retinal homeostasis and repair [4].

Several candidate markers have been proposed for identifying RPE stem cells, including transcription factors, cell surface proteins, and epigenetic regulators. However, definitive markers for isolating and characterizing RPE stem cells remain elusive, necessitating further research into their molecular signatures and functional properties. RPE Replacement Therapies: The discovery of RPE stem cells holds significant promise for developing cell-based therapies for retinal degenerative diseases, such as age-related macular degeneration and retinitis pigmentosa. Strategies involving transplantation of exogenous RPE cells or activation of endogenous stem cells offer potential avenues for restoring vision and preserving retinal function. Patient-specific induced Pluripotent Stem Cells (iPSCs) derived from RPE cells provide valuable platforms for modeling retinal diseases and screening potential therapeutics. Heterogeneity within iPSC-derived RPE cultures mirrors the diversity observed in native RPE populations, enhancing their relevance for disease modelling and drug discovery [5].

Conclusion

Recent advancements in understanding the heterogeneity of mammalian and human retinal pigment epithelium have unveiled the complexity of RPE biology and its implications for regenerative medicine. The existence of stem cell niches within the RPE has been proposed based on evidence from animal models and human tissues. These niches are hypothesized to harbor quiescent stem cells capable of self-renewal and differentiation into mature RPE cells, contributing to retinal homeostasis and repair. Further elucidating the molecular and cellular mechanisms underlying RPE heterogeneity and stem cell identity is crucial for harnessing the therapeutic potential of RPE-based therapies and advancing treatments for retinal diseases.

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Conflict of Interest

There are no conflicts of interest by author.

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