Macaque study provides insights for future clinical diagnosis and treatment of glaucoma

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Schematic diagram illustrating possible mechanisms of APOE in trabecular meshwork degeneration with aging. Credit: Jian Wu, Chaoye Wang, Shuhui Sun, Tianmin Ren, Lijie Pan, Hongyi Liu, Simeng Hou, Shen Wu, Xuejing Yan, Jingxue Zhang, Xiaofang Zhao, Weihai Liu, Sirui Zhu, Shuwen Wei, Chi Zhang, Xu Jia, Qi Zhang, Ziyu Yu, Yehong Zhuo, Qi Zhao, Chenlong Yang, Ningli Wang
A study, titled "Single-cell transcriptomic Atlas of aging macaque ocular outflow tissues" appearing in *Protein & Cell*, delves into the age-related changes in the trabecular meshwork (TM) of macaques, which are vital for regulating intraocular pressure and maintaining eye health.

The TM undergoes significant changes with age, leading to diseases such as primary open-angle glaucoma. By analyzing the single-cell RNA sequencing data, the researchers identified various cell types and their aging-related transcriptional changes.

The focus was on the increased expression of the APOE gene and its impact on TM function, particularly its role in mitochondrial dysfunction and extracellular matrix regulation.

These findings provide a comprehensive understanding of the molecular mechanisms underlying TM aging and its contribution to glaucoma.

Key findings from the study include:

1. **Cellular composition and aging**: The study identified 12 distinct cell types in the TM tissues, including trabecular meshwork cells, perivascular cells, pericytes, myofibroblasts, neurons, vascular endothelial cells, macrophages, B cells, T/NK cells, and others. Aging was associated with significant changes in the proportions of these cell types, with neurons and immune cells showing the most pronounced alterations.

2. **Mitochondrial dysfunction**: Mitochondrial dysfunction emerged as a prominent feature of aging TM cells. Gene ontology analysis highlighted the impact of aging on mitochondrial metabolic processes, oxidative phosphorylation, and ATP production. These changes suggest that impaired mitochondrial function is a critical factor in the aging of TM
tissues.

3. **Apoe gene and aging**: The APOE gene was identified as a key differentially expressed gene in aging TM cells. The study demonstrated that silencing the APOE gene could enhance cell migration and reduce apoptosis by affecting the PI3K-AKT pathway and extracellular matrix components. This finding indicates that APOE plays a significant role in TM aging and presents a potential target for therapeutic interventions.

4. **Implications for glaucoma**: The research provides valuable insights into the molecular mechanisms driving the increased incidence of glaucoma with age. The findings suggest that aging-related changes in TM cells, particularly those involving mitochondrial dysfunction and the APOE gene, contribute to the pathogenesis of glaucoma. This understanding could lead to new strategies for diagnosing and treating age-related ocular diseases.

This study offers a comprehensive single-cell transcriptomic atlas of aging trabecular meshwork tissues in macaques, revealing crucial molecular and cellular alterations associated with aging.

The identification of 12 distinct cell types and the detailed analysis of their aging-related transcriptional changes provide a deeper understanding of the aging process in ocular outflow tissues. Mitochondrial dysfunction and the upregulation of the APOE gene were highlighted as key features of aging TM cells.

The research suggests that targeting the APOE gene and improving mitochondrial function could be potential therapeutic approaches for age-related ocular diseases like glaucoma. Overall, these findings enhance our knowledge of the molecular mechanisms underlying TM aging and pave the way for future clinical interventions.

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