Docket #: S23-394

Single-cell analysis in living humans to understanding ocular disease mechanisms

Single-cell analysis in living humans is difficult for non-regenerative organs like the eye and brain due to biopsy damage. To solve this, Stanford researchers in the Mahajan Lab have integrated proteomics of liquid biopsies with single-cell transcriptomics from ocular cell types, tracing 5,953 proteins in the aqueous humor. They identified hundreds of cell-specific protein markers, revealing retinal degeneration in Parkinson's disease and stage-dependent cellular changes in diabetic retinopathy. AI models assessing cellular aging showed many eye diseases undergo accelerated molecular aging in specific cell types. This approach which can be applied to other organ systems, has the potential to transform molecular diagnostics and prognostics while uncovering new cellular disease and aging mechanisms

Stage of Development

- *In vivo* research – Single cell studies

Figure

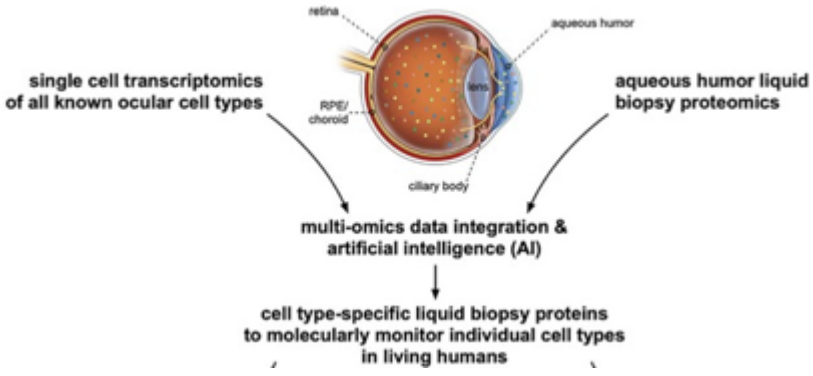

Image credit - DOI:10.1039/D3SC03623E

Applications

- **Molecular Diagnostics**
  - AI proteomic clocks for the eye to determine the biological age of the eye and specific cell types during aging and disease in living patients.
  - Assess disease mechanisms at the cell level in living patients in non-regenerative tissues such as the retina.
- **Prognostics** - Diagnose patients, select or create new therapies, design clinical trials, and interpret the relevance of animal and cell models for human disease
- **Companion diagnostic and biomarker panels** for cellular aging and disease in retinal degeneration, diabetic retinopathy, Parkinson's disease, and uveitis.
- **Personalized Medicine**
- **Eye Aging Research**

Advantages

- **Cell level analyses** in non-regenerative tissues like the retina in living patients
- **Non-Invasive Analysis**
- Proteomics clocks on cell level not organ level
- **Early Detection and Diagnostics**
- **Patient Stratification** for clinical trials
- **Patient Identification** – who will be most likely to respond to a specific therapy

Publications

- Wolf, Julian, Ditte K. Rasmussen, Young Joo Sun, Jennifer T. Vu, Elena Wang, Camilo Espinosa, Fabio Bigini et al. "Liquid-biopsy proteomics combined with AI identifies cellular drivers of eye aging and disease in vivo." *Cell* 186, no. 22 (2023): 4868-4884.

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