Uncovering a New Avenue to Fight Retinal Diseases: Identifying Retinal Ganglion Cells as a Novel Signaling Pathway Through Fixational Eye Movements With Discovery of the ZNF385D Biomarker Group for AKB-9778 Therapeutic Intervention

Telang, Shivum (School: North Allegheny Senior High School)

Retinal degenerative diseases (RDDs) affect 300 million patients worldwide. Current imaging techniques detect RDDs in late stages after significant vision loss. Approximately 40% of Retinal Ganglion Cells (RGCs) die before structural changes are detectable on imaging, suggesting that they could serve as a novel marker of early degeneration and provide quality biomarkers. Current methods for acquiring RGC spike-trains cost more than $100,000 and are invasive, requiring ex vivo surgical implantation of electrodes into the brain. In addition, there are no known biomarkers or therapeutic solutions for RGC death. To address this, I developed the first-ever low-cost (<$150), noninvasive device using an Arducam Global Shutter and ESP32 Microcontroller that maps RGC firing rates via fixational eye movements (FEMs) and microsaccades, trained on 1,000 gaze-tracking samples. Through this pathway, I implemented a Deep SVDD model, achieving 96% prognostic accuracy 38 months earlier than SOTA imaging. To discover new biomarkers, I mapped degenerated spike-trains to RNA-seq data via manifold alignment, then performed differential gene expression analysis, and constructed Protein-Protein Interaction (PPI) networks. I found ZNF385D as a novel biomarkercausing RGC cell death. Through Magnetic-Activated Cell Sorting (MACS) and Western blotting methods, I show significant ZNF385D protein expression ($p<0.001$ & $Log2FC > 3.5$) in retinal tissue. I observed that AKB-9778 effectively inhibited ZNF385D expression via Molecular Docking (binding affinity of -9.4 kcal/mol), creating a therapeutic pathway for RDD restoration. This is the first study leveraging RGCs as a new pathway to detect and fight RDDs, and in vitro improvements could prevent vision loss for millions of patients.

Awards Won:

First Award of $6,000