New retinal ganglion cell subtypes emerge from single-cell RNA sequencing

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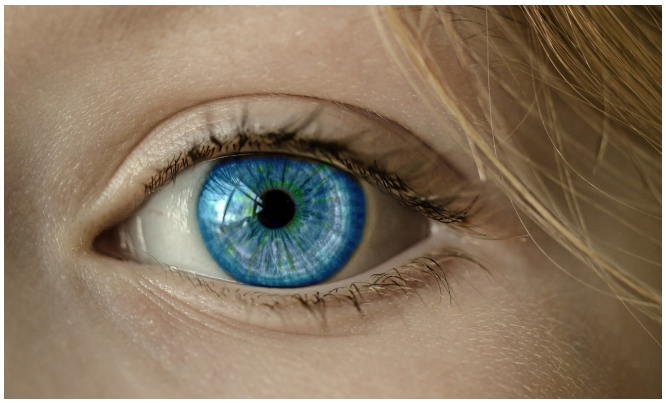

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Single-cell sequencing technologies are filling in fine details in the catalog of life. Researchers at the University of Connecticut Health Center (UConn Health) and The Jackson Laboratory (JAX) have identified 40 subtypes of retinal ganglion cells (RGCs) along with the genetic markers and transcription factors that differentiate them.

Thanks to recent advances in droplet-based single-cell RNA sequencing technologies, researchers can now isolate single cells and amplify their genetic material to probe their full complement of RNA. This makes it possible to conduct a detailed census of cells of a given type (e.g., RGCs), identifying subtle molecular differences that constitute subtypes.

RGCs convey visual data from the eye to the brain, and 30 subtypes have previously been identified. Using single-cell RNA sequencing, the research team analyzed 6,225 RGCs, detecting about 5,000 genes expressed per cell, from the left and right eyes of newborn mice. Running the resulting data through clustering algorithms resulted in the cells' classification into 40 subtypes.

Ephraim F. Trakhtenberg, Ph.D., of UConn Health's Department of Neuroscience led the research team, which includes Paul Robson, Ph.D., JAX director of single-cell biology. Their study, published in *Nature Communications*, provides new precision to a big question in biology: What constitutes a cell type or subtype?

The mammalian central nervous system is highly complex and involves the interaction of many specialized neuronal types and subtypes. The research team selected RGCs precisely because more of its subtypes have been identified to date compared to any other major neuronal cell type, and because other broad classes of retinal cell types (such as photoreceptors) have been studied at a single-cell level. Their goal was to elucidate the molecular differences between, and the markers unique to, RGC subtypes.

Besides identifying new RGC subtypes and their markers, the researchers demonstrate the amount of gene expression variability between cells needed to differentiate them into subtypes, and present a hierarchy from a cell type population to subtypes. The datasets for the study are publicly available through a user-friendly UConn Health web application, RGC Subtypes Gene Browser.

More information: Bruce A. Rheaume et al, Single cell transcriptome profiling of retinal ganglion cells identifies cellular subtypes, *Nature Communications* (2018). DOI: 10.1038/s41467-018-05134-3

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