Mitochondrial transfer between inner retinal neurons

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Purpose

Intraocular mitochondrial transfer has been reported across a variety of cells and tissues under both physiological and pathological conditions. Such transfer has shown broad therapeutic potential. The effectiveness of this therapy, however, is limited by a lack of understanding of the cellular and molecular mechanisms. Here, the ultrastructural features of mitochondrial transfer between inner retinal neurons discovered through retinal connectomics analysis is shown.

Methods

Retinal Connectome 2 (RC2) was built by automated transmission electron microscopy at ultrastructural (TEM) resolution. RC2 is a 0.25 µm diameter column of retina obtained from a 5-month-old female C5BL/6j mouse. The Viking application was used to visualize and annotate intra- and intrarelational features of interest in the connectome.

Results

Figure 1. Mitochondrial transfer between a bistratified ganglion cell and Amacrine cell. (A) 3D rendering (RenderApp, Patterson et al., 2019) illustrating the site of material transfer observed in the mouse inner plexiform layer between a bistratified ganglion cell (GC) and Amacrine cell (AC), as designated by the white arrow. (B) Transmission electron micrographs of material transfer in adjacent serial sections. Asterisk (*) denotes material can be defined as a mitochondrion, confirmed by the presence of cristae (+). At the transfer site, a short, electron-dense 140 nm diameter tube with a curved end (bracketed in C) is tightly associated with the inner mitochondrial membrane of one neurite and extends into a vacuole (k) within the apposing neurite formed by the plasma membranes of the two cells. Thin cytoskeletal components consistent with actin microfilaments extend into the mitochondrion (black arrows in C). Abbreviations: Ganglion Cell (GC), Amacrine Cell (AC).

Conclusion

These findings demonstrate active mitochondrial transfer between different classes of endogenous inner retinal neurons and suggest it may represent an important component of tissue homeostasis in the retina. Features of this transfer differ from previously reported mitochondrial transfer between photoreceptors upon transplantation, which may indicate cell type- or context-dependent differences in the cellular or molecular mechanisms. Our findings demonstrate active mitochondrial transfer between different classes of endogenous inner retinal neurons and suggest it may represent an important component of tissue homeostasis in the retina. Features of this transfer differ from previous reports by the Wallace and Pearson groups of material transfer between photoreceptors upon transplantation through tunneling nanotubes (Ortin-Martinez et al., 2021; Kalingyrous et al., 2021), which may indicate cell type- or context-dependent differences in the cellular or molecular mechanisms. Understanding these mechanisms could serve as a catalyst for development of novel therapeutics for disease in the retina and beyond.

Support

This work was supported by National Institutes of Health (R01 EY025128-01A1, R01 EY030193-01A1, T15 EY07109-02S1, P30 EY001798). Dr. Anderson is a Nationaleye Institute unrestricted grant to Gates Newey (R01 EY025128) and an unrestricted Grant from Research to Prevent Blindness to the Department of Ophthalmology and Visual Sciences. Funding for the JSD, JEM-1400 TEMs generously provided by the late Martin Ann Weedy and the Bloomberg Family.

Literature Cited

[References]

Commercial Disclosures: SRI, CSL, AMA, BRN, None