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Age-related macular degeneration (AMD) is a complex blinding disease that occurs as the result of degeneration of two retinal cell types – photoreceptors and retinal pigment epithelium (RPE). The multifactorial nature of the disease, complexity of the visual system, and intersection of aging processes have hindered the field's understanding of the molecular and cellular mechanisms underlying AMD progression. Our goal – the development of first-in-class therapies for AMD – necessitates the prioritization and validation of potential targets implicated in the disease.

Our group seeks to contextualize pathways implicated in AMD pathogenesis using model organisms of relevant monogenic disease. Our model selection has been guided by proteomics analysis from AMD donor samples, which has implicated several unexpected contributors. Because these pathways are themselves causal to retinal degenerative disease, we believe that a mechanistic understanding of how they are interconnected with other pathways implicated in degeneration will inform our strategies surrounding AMD. We have collaborated with the NIBR zebrafish group to generate relevant mutants and transgenic tools that facilitate live-cell imaging of the retina at resolutions that are technically challenging to accomplish in rodents. With these tools, we can dissect fundamental pathways at a sub-cellular level to determine their impact on retinal maintenance in a manner that cannot be answered in cell culture. As we begin to better understand how these pathways contribute to retinal degeneration, we can begin to address how their modulation may be an effective therapy for the treatment of blinding disease.

Selected Publications

Cumulative mitochondrial activity correlates with ototoxin susceptibility in mechanosensory hair cells.

Pickett SB, Thomas ED, Sebe JY, Linbo T, Esterberg R, Hailey DW, Raible DW.

Elife. 2018 Dec 31;7.

Mitochondrial calcium uptake underlies ROS generation during aminoglycoside-induced hair cell death.

Esterberg R, Linbo T, Pickett SB, Wu P, Ou HC, Rubel EW, Raible DW.

J Clin Invest. 2016 Sep 1;126(9):3556-66.

ER-mitochondrial calcium flow underlies vulnerability of mechanosensory hair cells to damage.

Esterberg R, Hailey DW, Rubel EW, Raible DW.

J Neurosci. 2014 Jul 16;34(29):9703-19.

[Click here](#) for additional publications.

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List of links present in page

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