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"The onset of retinal degeneration in a mutation of membrane-type frizzled-related protein or adiponectin receptor 1 engages essential fatty acid impairments"

Abnormal lipid metabolism is the derivation of multiple retinal degenerative and blinding diseases. In the LSU Neuroscience Center, the membrane-type frizzled-related protein (MFRP), and adiponectin receptor 1 (AdipoR1) were shown to be vital to the maintenance of a healthy retinal lipidome. The two mice models of retinal degenerations *Mfrp*^{rd6} and *Adipor1 -/-* resulted in a reduction of phospholipids containing docosahexaenoic acid (DHA; 22:6) and very long-chain polyunsaturated fatty acids (VLC-PUFAs). In a pathway involving the omega 3 fatty acids eicosapentaenoic acid (EPA; 20:5) and docosahexaenoic acid (DHA; 22:6), the fatty acid elongase-4 (ELOVL4) elongates the fatty acid 28:6 into VLC-PUFAs, which are precursors to potent neuroprotective molecules known as Elovanoids. Furthermore, VLC-PUFAs are important in retaining cell structure and modulating cell signaling in the visual cycle. Thus, progressive photoreceptor cell death and the subsequent onset of retinal degeneration ensues in these *Mfrp*^{rd6} and *Adipor1 -/-* animals.

Given that these lipids are essential for proper vision, it is important to decipher the specific lipid precursors and enzymes altered by the presence of a dysfunctional MFRP or the absence of Adipor1. Using organotypic culture of retina and RPE-eyecups from *Mfrp*^{rd6}, *Adipor1 -/-*, and control animals, I am employing molecular biology approaches such as western blotting and LC-MS/MS to evaluate protein expression and lipid concentrations, respectively. Lipid levels of various fatty acid intermediates within the biochemical pathways involved in synthesizing VLC-PUFAs will be analyzed. MALDI IMS imaging of retinal sections from WT, *Mfrp*^{rd6}, and *Adipor1 -/-* will be obtained to further define differences in the retinal lipidome. These findings will help us understand the role of these proteins in maintaining retinal homeostasis.

Preliminary data showed a significant decrease in the concentration of EPA in *Adipor1 -/-* models compared to the wildtype. Conversely, there was no significant difference between DHA levels between *Adipor1 -/-* and the wildtype models. These results suggest that EPA has a prominent role in the VLC-PUFA synthesis pathway rather than DHA as previously believed. Additionally, the concentration of arachidonic acid (AA; 20:4) in the retinal membrane is significantly increased in the *Adipor1 -/-* model compared to the wildtype. This insinuates a compensatory mechanism for the decreased EPA concentration. Further experimentation with additional replicates is necessary to unveil the accurate mechanisms and pathway.