AB003. Deregulated autophagy and energy-deficient photoreceptors drive angiogenesis in a model of age-related macular degeneration

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Abstract: Autophagy recycles intracellular substrate in part to fuel mitochondria during starvation. Deregulated autophagy caused by dyslipidemia, oxidative stress, and aging is associated with early signs of age-related macular degeneration (AMD), such as lipofuscin and perhaps drusen accumulation. Intracellular nutrient sensors for glucose and amino acids regulate autophagy. The role of lipid sensors in controlling autophagy, however, remains ill-defined. Here we will show that abundant circulating lipids trigger a satiety signal through FA receptors that restrain autophagy and oxidative mitochondrial metabolism. In the presence of excess dietary lipids, fatty acid sensors might protect tissues with high metabolic rates against lipotoxicity, favoring their storage, instead, in adipose tissues. However, sustained exposure to lipid reduces retinal metabolic efficiency. In photoreceptors with high metabolic needs, it predisposes to an energy failure and triggers compensatory albeit pathological angiogenesis, leading to blinding neovascular AMD.

Keywords: Autophagy; age-related macular degeneration (AMD); lipid metabolism

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