4. DECODING AMD: EXPLORING LIPOFUSCIN ACCUMULATION AND METABOLOMICS INSIGHTS

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Introduction. Age-related macular degeneration (AMD) represents a multifactorial, degenerative pathology of the retina, with mechanisms that remain incompletely understood. Lipofuscin accumulation is believed to play a role in these mechanisms. AMD directly affects the visual analyzer, resulting in irreversible vision loss. Metabolomics plays a crucial role in unraveling the mechanisms associated with the development and progression of this pathology.

Aim of study. To elucidate the mechanism of action and the impact of lipofuscin (LF) accumulation on the progression of the disease and additionally, to identify the interrelationship between LF and alterations in the metabolic profile.

Methods and materials. The research is grounded in a comprehensive analysis of specialized literature sourced from databases including PubMed, NCBI, and Elsevier, spanning the last 5 years. The methodology involves a constructive critical examination, aligning with the designated keywords: lipofuscin, macular degeneration, and metabolomics.

Results. LF is acknowledged as a senescence-associated pigment, gradually accumulating in various tissues, notably in the retinal pigment epithelium (RPE). With phototoxic and cytotoxic potential, LF impacts homeostasis, induces oxidative stress accompanied by lipid peroxidation, and disrupts cholesterol metabolism. It was inferred the process by which antioxidants including carotenoids, vitamin E, resveratrol could prevent and provide protection against LF cytotoxicity and oxidative stress caused by A2E. Noteworthy is the investigation of Bombyx mori, a binding protein transporting zeaxanthin (ZEA) to the RPE, mitigating oxidative stress on photoreceptors. For the transport of ZEA and lutein (LUT) to the RPE, tween-40 (special micelles) was investigated, and for carotenoids: nanoemulsion liposomes and monoclonal antibodies. As LF fluorescence intensifies with age, indicating an increase in its concentration, ZEA has the role of reducing its lifetime, thus reducing the negative consequences. Another significant factor is JS-017, aiming to degrade A2E, suppressing pro-inflammatory and pro-apoptotic actions, along with NF-κB activation, thereby safeguarding the RPE.

Conclusion. Ongoing research seeks to discern whether the accumulation of lipofuscin (LF) is the primary cause of AMD or, alternatively, a consequence of these pathologies. New studies focus on the effect of chemiexcitation in identifying treatment strategies, as this process reduces the concentration of ocular LF. Consequently, it has been shown that an optimal level of carotenoids and retinoids is necessary to decrease the risk of AMD. Thus, currently studies are based on establishing targeted treatment strategies against different forms of AMD.