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New insights into oxidative stress and immune mechanisms involved in age-related macular degeneration tackled by novel therapies

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Abstract

The prevalence of age-related macular degeneration (AMD) has increased in the last years. Although anti-VEGF agents have improved the prognosis of exudative AMD, dry AMD has still devastating effects on elderly people vision. Oxidative stress and inflammation are mechanisms involved in AMD pathogenesis and its progression. Molecular pathways involving epidermal growth factor receptor (EGFR), bone morphogenetic protein (BMP4) and the nuclear erythroid related factor 2 (Nrf2) are behind oxidative stress in AMD due to their participation in antioxidant cellular pathways. As a consequence of the disbalance produced in the antioxidant mechanisms, there is an activation of innate and adaptative immune response with cell recruitment, changes in complement factors expression, and modification of cellular milieu. Different therapies are being studied to treat dry AMD based on the possible effects on antioxidant molecular pathways or their action on the immune response. There is a wide range of treatments presented in this review, from natural antioxidant compounds to cell and gene therapy, based on their mechanisms. Finally, we hypothesize that alpha-1-antitrypsin (AAT), an anti-inflammatory and immunomodulatory molecule that can also modulate antioxidant cellular defenses, could be a good candidate for testing in AMD. This article is part of the special ssue on 'The Quest for Disease-Modifying Therapies for Neurodegenerative Disorders'.

Keywords: Adaptative immunity; Age-related macular degeneration; Alpha-1 antitrypsin; Innate immunity; Oxidative stress; Signaling.

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