AB009. The age-related macular degeneration genetic-risk promotes pathogenic subretinal inflammation

Florian Sennlaub

Institut de la Vision, Sorbonne Universités, Paris, France

Abstract: Mononuclear phagocytes (MP) comprise a family of cells that include microglial cells (MC), monocytes, and macrophages. The subretinal space, located between the RPE and the photoreceptor outer segments, is physiologically devoid of MPs and a zone of immune privilege mediated, among others, by immunosuppressive RPE signals. Age-related macular degeneration (AMD) is a highly heritable major cause of blindness, characterized by a breakdown of the subretinal immunosuppressive environment and an accumulation of pathogenic inflammatory MPs. Studies in mice and humans suggest that the AMD-associated APOE2 isoform promotes the breakdown of subretinal immunosuppression and increased MP survival. Of all genetic factors, variants of complement factor H (CFH) are associated with greatest linkage to AMD. Using loss of function genetics and orthologous models of AMD, we provide mechanistic evidence that CFH inhibits the elimination of subretinal MPs. Importantly, the AMD-associated CFH402H isoform markedly increased this inhibitory effect on microglial cells, indicating a causal link to disease etiology. Pharmacological acceleration of resolution of subretinal inflammation might be a powerful tool for controlling inflammation and neurodegeneration in late AMD.

Keywords: Age-related macular degeneration (AMD); complement factor H (CFH); subretinal inflammation

doi: 10.21037/aes.2018.AB009

Cite this abstract as: Sennlaub F. The age-related macular degeneration genetic-risk promotes pathogenic subretinal inflammation. Ann Eye Sci 2018;3:AB009.