

Genetic Factors & AMD

Identification of genetic factors associated with the pathogenesis of AMD is an important area of ongoing research. Large genome-wide association studies have so far identified 34 genes associated with the risk of developing of AMD, however, only a small number of these genes in fact appear to have a major impact on AMD. A large risk effect has been reported for genetic variants that disrupt genes in the complement pathway, which is responsible for regulation of inflammation.^{1, 2, 3}

Genetic studies indicate that dysregulation of the complement cascade contributes significantly to the risk of AMD.³ The complement cascade is part of the innate immune system that regulates cell death and inflammatory processes.³ Polymorphisms in five key genes associated with regulation of complement cascade account for 57% of the contribution to disease risk; these include: complement factor H (CFH), complement component 2 and factor B gene (C2/CFB); complement component 3 (C3) and complement factor I (CFI).⁴

In addition, two other genes found on chromosome 10: age-related maculopathy susceptibility protein 2 (ARMS2) and HtrA serine peptidase 1 (HTRA1) have a strong impact on the susceptibility of AMD.⁵

Genetic testing does not yet generally play a role in the routine screening for AMD, or in the risk stratification of people diagnosed with the condition. As introduction of genetic testing is rolled out across the world, it is anticipated that a much deeper understanding of the genetic factors associated with development of AMD will be elucidated.

¹ Fritsche LG, Igl W, Bailey JN, Grassmann F, Sengupta S, Bragg-Gresham JL, *et al.* A large genome-wide association study of age-related macular degeneration highlights contributions of rare and common variants. *Nature genetics.* 2016;48(2): 134-143.

² Kumaramanickavel G. Age-Related Macular Degeneration: Genetics and Biology. *Asia-Pacific journal of ophthalmology.* 2016;5(4): 229-235.

³ Boyer DS, Schmidt-Erfurth U, van Lookeren Campagne M, Henry EC, Brittain C. The Pathophysiology of Geographic Atrophy Secondary to Age-Related Macular Degeneration and the Complement Pathway as a Therapeutic Target. *Retina.* 2017;37(5): 819-835.

⁴ Fritsche LG, Fariss RN, Stambolian D, Abecasis GR, Curcio CA, Swaroop A. Age-related macular degeneration: genetics and biology coming together. *Annual review of genomics and human genetics.* 2014;15: 151-171.

⁵ Seddon JM, Gensler G, Rosner B. C-reactive protein and CFH, ARMS2/HTRA1 gene variants are independently associated with risk of macular degeneration. *Ophthalmology.* 2010;117(8): 1560-1566.