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Understanding the Genetics of Age-Related Macular Degeneration: Some Insights into the Disease Pathogenesis

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ABSTRACT Age-related macular degeneration (AMD) is a late-onset complex disorder with multifactorial etiologies. Both genetic and environmental factors play a role in the disease pathogenesis. AMD is the third leading cause of blindness in the elderly. Familial aggregation, segregation studies and linkage analysis have provided both qualitative and quantitative evidence on the genetic basis in AMD. Several candidate loci have been earlier mapped in AMD but variants in genes viz. *APOE, ABCA4, FBLN6* and *EFEMP1* harboring these loci have accounted for only a small proportion of cases. Recent screening of two major loci has led to the identification of the Complement Factor H (*CFH*) on 1q32 and *LOC387715* and *HTRA1* on the 10q26 gene cluster. Single nucleotide polymorphisms (SNPs) in *CFH* (Y402H), *LOC387715* (A69S) and a promoter variant in *HTRA1* have been associated with AMD in large case-control cohorts. These SNPs exhibited large effect sizes and high disease odds for the risk genotypes across different populations. Interestingly, these associations have been widely replicated across multiple ethnic groups worldwide indicating their potential role in the disease pathogenesis. In this review, we would outline the genetics of AMD with special emphasis on *CFH* followed by other genetic variants based on studies done by our group and colleagues worldwide. We would also provide a brief overview on the possible molecular mechanisms leading to AMD.