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The Role of the Susceptibility Gene in the Pathogenesis of Age-Related Macular Degeneration

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Age-related macular degeneration (AMD) is the leading cause of central vision loss in the people over 60s in the world. There are two main types of age-related macular degeneration: dry form (atrophic) and the wet form (choroidal neovascularization, CNV) [1]. The most common type of AMD is the dry form and however, about 10-20% of dry forms of AMD will progress to the wet type. The risk factors such as obesity, cardiovascular disease, diabetes mellitus, alcohol use and smoking have been demonstrated to be associated with AMD, therefore , the development of AMD are multiple and complicated [2]. Although it is well recognized that the initiation of AMD involves in genetic factors, RPE cell senescence and environmental factors, the pathogenesis of AMD is still not fully understood [3]. In the editorial, we briefly summarized the resent progress in the study of the relevance of genetic background to AMD.

Previous research show that multiple susceptibility genes are associated with the development of AMD, the single nucleotide polymorphisms (SNP) is the most well studied susceptibility molecular of AMD. So far, the SNPs of apolipoprotein E (APOE), CFH , hepatic lipase–encoding gene (LIPC), C3, C2/CFB, ARMS2/Htra1, toll-like receptor-(TLR)-3 and -4, VEGFA, ABCA4, ERCC6, CX3CR1, TNFRSF10A [4-6], the genes encoding age-related macular degeneration 1 (ARMD1) and IER3/DDR1, COL8A1/FILIP1L, RAD51B, TGFBR1SLC16A8, ADAMTS9/MIR548A2, B3GALTL have been revealed to related to the pathogenesis of AMD [7].

It is recognized that CFH and Htra1 are the most prevalence SNPs associated with AMD, if the individual carries CFH Y402H or Htra1 SNPs, the risk for the development of AMD is increased significantly compared with the age matched control. Inflammation involves the pathogenesis of AMD either in the early or late stage of AMD [8], the inflammatory response in the pathogenesis of AMD is seen especially in the SNPs carrier of CFH and Htra1 [9]. In addition, Millen's study shows if there is a combination of vitamin D deficient and CFH SNPs, the risk for the development of AMD is even higher than the one who carries CFH SNPs alone, suggesting a possible synergistic effect of vitamin D deficient and CFH SNPs on the susceptibility of AMD [10]. Interesting, the major risk allele of HTRA1 in AMD patients is significantly higher in Asia [11,12]. Those results suggest that the variation of SNPs in different population is responsible for the development of AMD. Notably, a new SNP of DIAPH2 gene in the X-chromosome has been found to be a susceptibility gene of AMD. Importantly, the outcome of intravitreous injection of anti-VEGF in the treatment of CNV is affected by individual's genetic background, if the AMD patients carry Lower-risk genotypes of the CFH, ARMS2, HTRA1 and VEGF-A genes, improved visual acuity may be obtained [13]. The joint Effect of CFH and ARMS2/HTRA1 SNPs on development wet AMD is especially true in Chinese population [14]. More recently, Keenat T found that the alteration of the gene at chromosome 1 CFH-to F13B locus is also a risk factor for AMD [15].

The wet form of AMD includes Polypoidal choroidal vasculopathy (PCV) and CNV. Although no differences are found in CNV and PCV in term of the association of the genetic risk factors of CFH, HTRA1 and formyl peptide receptor 1(FPR1) [16,17], the pathogenesis of CNV is highly related to other SNPs such as super killer viralicidic activity 2-like, complement component 2. Interesting, no correlation of susceptibility of those SNPs is found in PCV patients [18]. On the other hand, the association of rs5882 near cholesteryl ester transfer protein in the patients with PCV is much higher than that in CNV [19]. Furthermore, it is found that an addition risk factor of PCV in Chinese population is linked to the SNP rs6982567 of growth differentiation factor 6 May [20]. Notably, the risk factor may be different in different phenotypes of PCV, by the allelic association and Genotype association analyses Yanagisawa demonstrates that the variants of elastin gene rs868005 is highly associated with type 2 PCV, suggesting the importance of elastin variants in the pathogenesis of PCV and possibility of the SNP may be used as marker for the differentiation of PCV phenotypes [21].

Taken together, these studies suggest that genetic abnormal contributes the pathogenesis of AMD. Understanding the pathogenesis of AMD including the roles of SNPs will promote new discovery of the treatment of AMD [22,23].

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