

## 4<sup>th</sup> International Conference and Exhibition on **Immunology**

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### The role of complement factor H-like and factor H-related proteins in age-related macular degeneration

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A number of genetic alterations are associated with an increased risk of developing age-related macular degeneration (AMD): The leading cause of blindness in the western World. Many of the risk modifying mutations and polymorphisms arise in genes involved in the complement cascade, part of a host's innate immune system. While much work has focused on the Y402H polymorphism in the main complement regulator factor H (FH), increasing evidence suggests this protein does not work alone in protecting Bruch's membrane in the human eye, an important site of AMD pathogenesis. Factor H-like protein 1 (FHL-1) arises from an alternative splice variation of the *CFH* gene and retains all of the regulatory activity of FH: FHL-1 is also subject to the Y402H polymorphism. Furthermore, five factor H-related (FHR) proteins also exist and share varying degrees of homology with FH. Genetic changes in the region containing the FHR genes are also associated with AMD, including a protective deletion of the FHR1 and 3 genes. Using specific antibodies and targeted mass spectrometry, we identify the significant presence of FHL-1 in Bruch's membrane. This is converse to the understanding that FH is the major regulator of complement. In this regard, we demonstrate local expression of FHL-1 and the fact that the full length FH protein is not able to diffuse through Bruch's membrane from human sera. The presence of FHR proteins also adds weight to the hypothesis that they may well compete with FHL-1 to binding sites in Bruch's membrane. An imbalance in this fine regulation based on genetics and driven via environmental or age-related factors, will lead to inappropriate complement activation and local inflammation. Here, the author will talk on current understanding of AMD pathogenesis, present new data and discuss therapeutic strategies for treating this devastating disease.

#### Biography

Simon J Clark obtained his BSc in Biochemistry (with Immunology) at the University of Aberdeen in 2002 and subsequently spent a year working in industry on the development of diagnostic tests for cardiovascular disease. In 2003 he matriculated at Oxford to begin his DPhil studies investigating the interaction of complement factor H (FH), an innate immune regulator, with endogenous sugar molecules as a mechanism for host recognition. In 2006, he moved to the Faculty of Life Sciences, University of Manchester, to study further the regulation of innate immunity on extracellular matrices and successfully identified the sugar molecules that FH binds to in Bruch's membrane, the site of AMD pathogenesis. He now works in the Faculty of Medicine and Human Sciences, University of Manchester, where he has taken up an MRC Career Development Fellowship. Recently, he identified another protein, made by alternative splicing of the *FH* gene; called factor H-like protein 1 (FHL-1) is actually the main complement regulator in Bruch's membrane. He is now focusing his work on understanding how FHL-1 and the FHR proteins contribute to immune regulation around the human body.

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