Hannes Eberhardt

The role of CFHR proteins in human autoimmune diseases

Complement is one of the first lines of defence in innate immunity and plays a crucial role in the elimination of microbes, clearance of immune complexes and damaged self cells. Complement also modulates adaptive immune responses. The complement is activated in a cascade-like manner by three major pathways, the alternative, the lectin and the classical pathway. In order to protect host cells and tissues from complement mediated destruction, the activated complement system needs tightly control. Complement factor H is a fluid phase regulator and the central regulator of the alternative complement pathway, acting on the C3-convertase. Factor H is a member of the factor H protein family, which is composed of Factor H and Complement Factor H-like protein 1 (CFHL1), as well as five Complement factor H-related proteins CFHR1, CFHR2, CFHR3, CFHR4 and CFHR5. Mutations, polymorphisms and deletions within the *CFH* gene cluster are associated with several human diseases, such as atypical hemolytic uremic syndrome (aHUS), DEAP-HUS (deficiency of CFHR proteins and antibody positive HUS), membranoproliverative glumerulonephritis type II (MPGN II) and age-related macular degeneration (AMD). The obvious correlation between dysfunctions of CFHR proteins and autoimmune diseases isn't understood so far. CFHR1 and CFHR3 deficiency is a predisposing factor for aHUS, and also for the development of autoantibodies by B-cells against factor H. Therefore the goal of the study is to address the mechanisms by which CFHR proteins are involved in the generation of autoimmune diseases, especially in the development of autoantibodies.

Publications

Eberhardt HU, Buhlmann D, Hortschansky P, Chen Q, Böhm S, Kemper MJ, Wallich R, Hartmann A, Hallström T, Zipfel PF, Skerka C (2013) Human factor H-related protein 2 (CFHR2) regulates complement activation. *PLoS One* 8(11), e78617. Details PubMed

Lesher AM, Zhou L, Kimura Y, Sato S, Gullipalli D, Herbert AP, Barlow PN, Eberhardt HU, Skerka C, Zipfel PF, Hamano T, Miwa T, Tung KS, Song WC (2013) Combination of factor H mutation and properdin deficiency causes severe C3 glomerulonephritis. *J Am Soc Nephrol* 24(1), 53-65. Details PubMed

Supervisor

Peter F. Zipfel

Co-Supervisors

Christine Skerka

Start of PhD

January 1, 2009

Doctoral Disputation

February 27, 2013