Selina Icke (née Stippa)

Interaction of complement proteins and acute phase proteins in inflammatory processes

Damaged host cells and cellular debris must be rapidly cleared from the circulation to avoid harmful inflammatory reactions. Apparently, innate immunity and complement plays an important role in these reactions. My PhD thesis focuses on the role of human innate immune regulators (i.e. Factor H, and CFHR1 (complement Factor H related protein 1) as well as variants of CFHR1 in combination with its ligand, and the C-reactive protein. Factor H is an essential complement inhibitor, which controls the alternative pathway and CFHR1 is a regulator of the terminal pathway. CRP is a member of the pentraxin protein family which efficiently activates the classical complement pathway to the level of C3 which leads to an increased opsonization. Factor H binds CRP, and this interaction and the effect for removal of damaged particles is not completely understood and therefore needs more investigation. CFHR1 and Factor H show high sequence identity in their three C-terminal SCRs and this high degree of homology suggests related functions for CFHR1. For CFHR1 two variants are defined, which differ in at last three SCRs either by two or five amino acids. It is unclear how these amino acid exchanges affect recognition functions of the proteins such as binding to the central complement components C3b, C3d or to surfaces. Therefore CFHR1 variants with the CFHR1 and Factor H relevant amino acids are generated by in vitro mutagenesis. These proteins will be expressed, purified and analyzed for functions.

Publications

Fritsche LG, Lauer N, Hartmann A, Stippa S, Keilhauer CN, Oppermann M, Pandey MK, Köhl J, Zipfel PF, Weber BH, Skerka C (2010) An imbalance of human complement regulatory proteins CFHR1, CFHR3 and factor H influences risk for age-related macular degeneration (AMD). *Hum Mol Genet* 19(23), 4694-4704. Details PubMed

Mihlan M, Stippa S, Józsi M, Zipfel PF (2009) Monomeric CRP contributes to complement control in fluid phase and on cellular surfaces and increases phagocytosis by recruiting factor H. *Cell Death Differ* 16(12), 1630-1640. Details PubMed

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