

results in impaired accessibility to the N-terminal, the SCR6-8 and the C-terminal functional domains of FH. In this respect, having impaired all its functionalities, the FH-R1210C mutant is equivalent to a partial FH deficiency, which is well documented that is not associated with a particular disease. Carriers of the FH-R1210C mutation may develop aHUS, AMD or C3G, but the final outcome is determined by their overall genetic risk to these diseases, which is set up by known additional genetic and/or environmental factors. These data illustrate the relevance of understanding the functional consequences of the disease-associated mutations.

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B cell epitope analysis of factor H autoantibodies in autoimmune haemolytic uremic syndrome

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Introduction: One of the most common factors evoking acute renal failure in children is hemolytic uremic syndrome (HUS). A rare form of HUS is mediated by autoantibodies against complement factor H (CFH). In patients with anti-CFH autoantibodies deletion of CFH related proteins (CFHR), most often CFHR3–1 is observed. CFH domains 19–20 and the homologous ones of CFHR1 differ only in two amino acids, but these minor differences could affect the binding sites for the autoantibodies. To understand the origin of anti-CFH autoantibodies the exploration of their B cell epitope specificities would provide essential data, therefore our aim was to carry out the B-cell epitope mapping of anti-CFH autoantibodies, and to investigate the inhibitory effect of CFHR1 domains 4–5 on antibody binding to CFH.

Methods: We analyzed 5, anti-CFH IgG positive HUS patients' sera taken in the first episode of the disease. As control sera of healthy children and patients' sera from remission was used. The binding of antibodies to overlapping synthetic peptides representing selected regions of CFH and CFHR1 was measured by ELISA method. We used competitive ELISA technique to investigate antibody binding to CFH in presence of CFH domains 19–20 and CFHR1 domains 4–5.

Results: In healthy controls enhanced reactivity was measured in three regions of CFH (AA1142–1156, AA1182–1196, AA1202–1216). Serum samples of HUS patients contained antibodies to these 3 regions and to two additional (AA1157–1171, AA1177–1191) regions as well. Increased antibody binding was detected in patients' sera to CFHR1, too. Although in competitive assays CFH showed significantly stronger inhibition than CFHR1, both were capable to maximally inhibit antibody binding to CFH.

Conclusion: Our results corroborate recent results, in which anti-CFH autoantibody binding was also reported to multiple regions of factor H in healthy controls and in HUS patients. However, we describe here for the first time specific B-cell epitopes localized on the 19th and 20th CCP domains of factor H in aHUS patients. Further analysis of these data may facilitate the exploration of the mechanism of autoantibody production and may lead to diagnostic improvements. Besides, we found that multiple linear epitopes of CFH and CFHR1 determine the inhibition of antibody binding to CFH.

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Plasma levels of the serine proteases and associated proteins of the lectin pathway are altered in patients with SLE

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Objective: Systemic lupus erythematosus (SLE) is a complex autoimmune disease where the complement system plays a key role in the pathogenesis. The proteins of the lectin pathway of complement activation are involved in inflammation and we therefore wished to examine the potential role of these proteins in SLE. In this pilot study, we present results on quantification of mannan-binding lectin (MBL) associated serine proteases (MASPs) and MBL associated proteins (MAPs) in patients with SLE. The data was compared to age and gender matched healthy controls and analyzed for associations to characteristic SLE manifestations and disease activity scores.

Methods: Plasma was obtained from a cross-sectional cohort of 58 SLE patients, from whom we prospectively collected demographic, clinical and biochemical data. For comparison, blood samples were collected from 65 age and gender matched healthy blood donors. Using in house developed time resolved immuno-fluorometric assays (TRIFMA), plasma levels of MASP-1, -2, -3, MAP19 and MAP44 were determined. The Mann–Whitney test was used to compare plasma protein levels of in patients and controls and Spearman correlation analysis was used for correlation analysis.

Results: Plasma concentrations in patients were found to be higher than controls regarding MASP-1, MASP-3 and Map44 (*p* values respectively 0.0001, 0.0003 and 0.0013), and lower for Map19 (*p* 0.0001). A negative correlation was found between low levels of C3 and plasma levels of Map19 ($r = -0.3907$, $p = 0.0035$) and a positive correlation was seen between plasma levels of anti-dsDNA-antibodies and Map19 ($r = 0.3289$, $p = 0.0133$).

Conclusion: In SLE patients we found altered plasma concentrations of several MASPs and MAPs complement proteins. The changes were associated with characteristic clinical and biochemical SLE manifestations, which indicate that proteins of the lectin pathway play a role in the pathogenesis of SLE.

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Generation of highly specific monoclonal antibodies for the determination of complement factor H-related 5 plasma levels

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Background: Factor H (FH) is a regulator of the alternative pathway of the complement system, to ensure protection against complement activation on host tissue. Genetic variations in the CFH region are associated with several complement-mediated diseases, such as age-related macular degeneration and atypical hemolytic uremia. Next to variations in FH itself, also polymorphisms in the highly homologous FH-related proteins (FHRs) are linked to disease, such as susceptibility for meningococcal disease. Although



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