COMPLEMENT FACTOR H AUTOANTIBODIES B CELL EPITOPE ANALYSIS IN AUTOIMMUNE HAEMOLYTIC UREMIC SYNDROME

Trojnár Eszter[1]

Uray Katalin[2], T. Sakari Jokiranta[3], Prohászka Zoltán[1]

[1]Füst György Komplement Diagnosztikai Laboratórium, III. Department of Internal Medicine, Semmelweis University Budapest

[2]MTA-ELTE Research Group of Peptide Chemistry

[3]University of Helsinki, Department of Bacteriology and Immunology, Haartman Institute

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 mutation 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 slight 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 altered 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 form 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 a recent publication, in which anti-CFH autoantibodies' 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 might facilitate the exploration of the autoantibody productions' mechanism and may potentially lead to diagnostic improvements. Besides, we found that multiple linear epitopes of CFH and CFHR1 determine the inhibition of antibody binding to CFH.

This work was supported by the K100687 grant of the Hungarian Research Fund.