IgM IGOME PROFILES IN WOMEN WITH ANTIPHOSPHOLIPID SYNDROME

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Aim: Auto-antibodies with several different specificities have been described in primary anti-phospholipid syndrome (APS). Our goal was to describe global changes in the IgM repertoire of patients with APS, which can serve as a basis for future theoretical conclusions as well as a source of diagnostic profiles.

Materials and methods: To study the IgM repertoire, a phage library of random, 7-mer peptides was adsorbed onto IgM isolated from 20 patients with APS. DNA from the isolated phages was amplified and deep sequenced. The resulting sequences were compared to a library of IgM mimotopes reflecting the normal, public IgM repertoire. Longest common subsequence was used as a metric and a graph representing the relationships between the sequences at a distance threshold of 5 (at least 5 identical residues with possible deletions and insertions) was used to analyze the two libraries.

Results: When compared to mimotopes from healthy donors, 2950 7-dimensional peptide sequences were identified as mimotopes of IgM reactivity characteristic of APS patients. Their sequences are grouped into 12 clusters with very similar sequence profiles, in which short sequences of permutations of proline and leucine with N-terminal serine, threonine, methionine or histidine and C-terminal arginine predominate. BLAST-searching in the human proteome has identified a number of possible target autoantigens that are not described in the pathogenesis of APS.

Conclusion: Igome analysis of the IgM repertoire of patients with APS identifies characteristic IgM mimotope sequences which can be used to detect new autoantigens as well as to build diagnostic profiles.