A54 THE BLIMP-1 RISK ALLELE IS ASSOCIATED WITH INCREASED SYNOVIAL INFLAMMATION IN RHEUMATOID ARTHRITIS

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10.1136/ard.2010.148965.24

Background In recent years several single-nucleotide polymorphisms (SNPs) have been associated with susceptibility to rheumatoid arthritis (RA). These SNPs were localised close to or in genes involved in several RA related pathogenic processes, including T cell activation (CD2 and CD28) and B cell differentiation (PTPN22 and PRDM1).

Objective To gain insight into the potential role of these genetic variants in pathophysiological processes in RA the authors analysed the association of these alleles with synovial tissue inflammation in RA patients.

Patients and methods RA patients underwent a mini-arthroscopy under local anaesthesia to obtain synovial biopsies. Genotyping of 14 previously validated risk alleles was done using a single Sequenom iPlex pool. In 87 patients paired synovial tissue and DNA samples passed quality control. Synovial sections were analysed by immunohistochemistry to evaluate the cell infiltrate. In 45 patients RNA was extracted from synovial biopsies RNA for microarray analysis using an oligonucleotide array covering 17 972 unique genes.

Results In carriers of the Blimp-1 risk allele the synovial infiltrate contained significantly more CD38 plasma cells (p=0.008), CD22 B cells (p=0.023), CD3 T cells (p=0.013) and CD68 sub lining macrophages (p=0.016). There was no statistically significant difference in CD55 fibroblast-like-synoviocytes and CD68 intimal macrophages. Interestingly, there was no significant difference in systemic inflammation as measured by Disease Activity Score using 28 joint counts, erythrocyte sedimentation rate and C reactive protein between patients that did or did not encode the Blimp-1 susceptibility allele. As expected, microarray analysis of the synovial tissue of patients with the Blimp-1 risk allele (n=34) showed a significant increase of several immunoglobulin encoding genes as compared to patients without the risk allele (n=11) together with an increased expression of genes involved in T and B cell activation.

Conclusion RA patients with the Blimp-1 risk allele show more synovial inflammation than those without this allele. Consistent with the role of Blimp-1 in plasma cell development, the authors found a marked increase in plasma cell numbers in patients carrying the Blimp-1 risk allele as well as increased expression of immunoglobulin encoding genes.