12 THE EXPRESSION OF SPLICE FORMS FOR THE RHEUMATOID ARTHRITIS RISK ASSOCIATED GENE PTPN22 IS SIGNIFICANTLY DIFFERENT FOR PATIENTS COMPARED TO CONTROLS

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10.1136/annrheumdis-2011-201236.12

Background Several genetic risk factors have been revealed for rheumatoid arthritis (RA) whereof *HLA-DRB1* shared epitope alleles and *PTPN22* remains the two most undisputed for the disease. Hypotheses for how these associations confer their risk exist but the etiology is still not completely explained. The *PTPN22* risk allele is associated with a gain of function of the protein product. However, the *PTPN22* gene has alternatively spliced transcripts where at least two of the splice forms have confirmed different *PTPN22* (LYP) proteins, which may influence the proteins pathways.

Objectives Our hypothesis was that *PTPN22* splice forms may have a different expression pattern in patients compared to controls. Such an effect could enhance other effects from the associated risk alleles.

Material and methods The authors have investigated the expression of *PTPN22* splice forms in peripheral blood cells and used genotypic and phenotypic data for analysis of RA patients and controls of Caucasian origin.

Results *PTPN22* was found to be different in individuals with RA compared to controls. On average, the shorter splice form was reduced (0.8-fold, p=0.08) and the longer was increased (1.2-fold, p=0.006) for patients. This effect was further enhanced if the ratio of the transcripts for each individual was compared (1.4-fold, $p=6 \times 10^{-9}$). This finding was replicated in two independent cohorts of the total size of 165 individuals.

Conclusions The authors found important differences in expression of *PTPN22* splice forms between healthy individuals and RA patients, which may increase a gain of function that influence development of the disease. The balance between splice forms may also be of importance during immune response due to great structural differences in the encoded PTPN22 proteins.

Ann Rheum Dis: first published as 10.1136/annrheumdis-2011-201236.12 on 22 February 2012. Downloaded from http://ard.bmj.com/ on April 9, 2024 by guest. Protected by copyright.