21 EXPRESSION OF ALTERNATIVELY SPLICED VARIANTS OF MAP2K4 GENE IN RHEUMATOID ARTHRITIS

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Background and objectives MAP2K4 encodes a mitogen activated protein kinase kinase 4 (MKK4), important for optimal activation of JNK1-3 and p38 – the two members of the MAP kinase family previously implicated in several rheumatic diseases, including rheumatoid arthritis (RA). Recently, MAP2K4 locus has been identified as being in statistical interaction with the major risk factor for RA - HLA-DRB1 shared epitope (SE) - in RA patients with anticitrullinated protein antibody (ACPA). In this study, the authors describe a novel splice variant of MAP2K4 (V2), and investigate the differential expression profile and phenotype associations of MAP2K4 splice variants in RA patients and healthy individuals.

Methods The authors performed a discovery study to detect novel splice variants of MAP2K4 in human peripheral blood cells, and obtained sequence data for variants of interest. The relative expression of MAP2K4 forms in peripheral blood was investigated for 44 RA patients and 44 controls of Caucasian ancestry and analysed against available genotypic and phenotypic data.

Results The authors detected a novel 'skipped exon' type splice variant of MAP2K4 in our study material. The MAP2K4 splice forms and were differently expressed in peripheral blood material from 88 RA cases and controls. Additionally, within the group of RA patients, a correlation was observed between MAP2K4 variants expression and phonotypical data for ACPA, rheumatoid factor, and SE.

Conclusion Our results show differential expression ratio of the canonical and alternatively spliced MAP2K4 mRNAs in RA patients compared to healthy controls. This data implies that MAP2K4 splicing and expression profile may be associated with RA pathogenesis and should be assessed as a potential biomarker in the future.