19 GENETIC VARIATION IN THE SEROTONIN RECEPTOR GENE AFFECTS IMMUNE RESPONSES

Omri Snir, Espen Hesselberg, Petra Amoudrouz, Lars Klareskog, Lars Alfredsson, Izabella Zarea-Ganji, Anca I Catrina, Leonid Padyukov, Vivianne Malmström, Maria Seddighzadeh *Rheumatology Unit, Department of Medicine at Karolinska University Hospital, Karolinska Institute, Stockholm, Sweden*

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Background and objective The function of the 5-HT2A receptor in the periphery is still largely unknown, but an increasing body of evidence shows effects of this receptor on immune responses. Rheumatoid arthritis (RA) is a common chronic inflammatory disease resulting from the complex interaction between genes and environment. Recently, the authors demonstrated that a haplotype in HTR2A, composed of the protective alleles of two SNPs (rs6314 and rs1328674) in HTR2A, is associated with protection against RA (Seddighzadeh, 2010). Our objective was to investigate whether presence of a RA-associated serotonin receptor 2A (HTR2A) haplotype (ie, TC) affect T cell and monocyte function.

Materials and methods Patients with established RA (n=379) were genotyped for two SNPs in the *HTR2A* locus, rs6314 and rs1328674, and a haplotype was defined for each individual. PBMCs from 23 patients with or without the RA-associated TC-haplotype were selected for functional studies and cultured with and without a selective HTR2A agonist (2, 5-Dimethoxy-dimethoxy-4-iodoamphetamine, DOI). The authors targeted either T cells or monocytes for stimulation with staphylococcal enterotoxin B (SEB) and lipopolysaccharide (LPS), respectively. Following stimulation, the authors assessed cytokine levels intracellularly via FACS and in supernatants via CBA.

Results Upon stimulation, T cells from TC-carrier patients produced more proinflammatory cytokines (TNFα, IFNγ and IL-17) and monocytes produced higher levels of TNFα compared to patients carrying the non-TC haplotype. TC carriers also displayed greater inhibition of cytokine production through stimulation of the serotonin receptor 2 using the agonist DOI.

Conclusion Our data demonstrate that association of RA with a distinct serotonin receptor haplotype has functional impact by affecting the immunological phenotype of T cells and monocytes.