7 GENETIC VARIANTS OF C1Q ARE A RISK FOR RHEUMATOID ARTHRITIS

D T S L Jansen,[1] N Daha,[1] F A S Kurreeman,[1,3] S Böhringer,[2] G Stoeken-Rijsbergen,[1] J J Houwing-Duistermaat,[3] T W Huizinga,[1] R E M Toes,[1] L A Trouw[1] *[1]Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands; [2]Department of Biostatistics and Bioinformatics, Leiden University Medical Center, Leiden, The Netherlands; [3]Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Boston, Massachusetts, USA*

10.1136/annrheumdis-2011-201236.7

Introduction C1q, the recognition molecule of the classical pathway, is next to its role in complement activation also implicated in protection against autoimmunity. Both complete genetic deficiency of C1q and several SNPs are associated with development of Systemic Lupus Erythematosus. In this study, the authors analysed whether genetic variants of C1q would predispose to rheumatoid arthritis (RA).

Methods For this purpose, the authors genotyped SNPs in C1q in a Dutch set of RA patients and controls (n=845pt/1046ctr). The authors obtained replication in the NARAC and performed a meta-analysis on data from several cohorts (max n=8000pt/23262ctr). In addition, the authors linked genotypes to C1q protein levels and mRNA expression.

Results The authors tested 13 SNPs in the C1q genes, of which 5 showed a significant association with RA. The authors replicated the most significant SNP in a North American Cohort and by performing meta-analysis using additional small cohorts from the US and Greece. Imputed GWAS data displayed a similar trend. Screening the genomic area around the C1q genes revealed that the association signal was actually derived from the C1q genes and not from neighboring genes. eQTL analysis revealed that in this genomic area only SNPs in the C1q genes associate with mRNA expression levels of the C1q transcripts. Finally, the authors observed a difference in the serum levels of C1q between individuals with the genotypes of the most significant SNP.

Conclusions Genetic variants in C1q are a risk for the development of RA.