A40 GENETIC VARIANTS OF C1Q ARE A RISK FOR RHEUMATOID ARTHRITIS

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Background and objectives The recognition molecule of the classical pathway of complement activation, C1q, is next to its role in complement activation also implicated in protection against autoimmunity. Complete genetic deficiency of C1q predisposes strongly to autoimmunity, culminating in a Systemic Lupus Erythematosus-like disease. In this study the authors analysed whether genetic variants of C1q would predispose to rheumatoid arthritis (RA).

Materials and methods For this purpose the authors genotyped single-nucleotide polymorphisms (SNPs) in C1q in a Dutch set of RA patients and controls. The authors obtained replication in the North American RA Cohort (NARAC) and performed a meta-analysis on data from several cohorts.

Results In the discovery phase, the authors tested 13 SNPs in the C1q genes, of which 5 showed a significant association with RA. A calculation for global significance revealed a significant association for the C1q gene as a whole, which was replicated in the NARAC cohort. Further meta-analyses on several cohorts displayed a similar trend. Finally the authors screened the C1q locus in order to fine map the association, and found a set of four SNPs that associate with RA and associate with C1q serum levels in healthy individuals.

Conclusions Genetic variants in C1q, some of which associate with C1q levels, are a risk for the development of RA.