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Background and objectives Epidemiology and candidate gene studies indicate a shared genetic basis for celiac disease (CD) and rheumatoid arthritis (RA), but the extent of this sharing has not been systematically explored. Previous studies demonstrate that 6 of the established non-human leucocyte antigen (HLA) CD and RA risk loci (out of 26 loci for each disease) are shared between both diseases. The authors hypothesised that there are additional shared risk alleles, and that combining genome-wide association study (GWAS) data from each disease would increase power to identify these shared risk alleles.

Materials and methods The authors performed a meta-analysis of two published GWAS on CD (4533 cases and 10 750 controls) and RA (5539 cases and 17 231 controls), and genotyping the top associated single-nucleotide polymorphisms (SNPs) in independent set of 2169 CD cases and 2255 controls, and 2845 RA cases and 4944 controls. The authors used the gene-expression dataset of peripheral blood mononuclear cell of 1469 individuals to investigate the genotype-expression correlation of associated variants. The authors also analysed the results using various pathway analysis tools.

Results Above already established six shared loci, eight additional SNPs demonstrated $p < 5 \times 10^{-8}$ in a combined analysis of all 50 266 samples. From the 14 shared gene loci, 7 SNPs showed a genome-wide significant effect on expression of one or more transcripts in the linkage disequilibrium block around the SNP. Pathway analysis tools indicate remarkable overrepresentation of T cell signalling molecules among the shared genes.

Conclusions The authors identified 14 shared CD-RA risk loci. These associations implicate antigen presentation and T cell activation as a shared mechanism of disease pathogenesis and underscore the utility of cross-disease meta-analysis for identification of genetic risk factors with pleiotropic effects between two clinically distinct diseases.

A50 META-ANALYSIS OF GENOME-WIDE ASSOCIATION STUDIES IN CELIAC DISEASE AND RHEUMATOID ARTHRITIS IDENTIFIES FOURTEEN NON-HLA SHARED LOCI

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