Medicine and Dentistry, Queen Mary University of London, London, UK; ⁹Department of Clinical Medicine, Trinity Centre for Health Sciences, Trinity College Dublin, St James's Hospital, Dublin, Ireland; ¹⁰Genetics and Genomics Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, US National Institutes of Health, Bethesda, Maryland, USA; ¹¹European Laboratory for Food Induced Disease, University of Naples Federico II, Naples, Italy; ¹²Unità di Aterosclerosi e Trombosi, IRCCS Casa Sollievo della Sofferenza, S Giovanni Rotondo, Foggia, Italy; ¹³Department of Experimental Medicine, Sapienza University of Rome, Rome, Italy; ¹⁴Department of Gastroenterology, Hepatology and Immunology, Children's Memorial Health Institute, Warsaw, Poland; ¹⁵Department of Pathology, Children's Memorial Health Institute, Warsaw, Poland; ¹⁶Celera, Alameda, California, USA; ¹⁷Department of Medicine, Division of Genetics, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA; ¹⁸Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands; ¹⁹The Feinstein Institute for Medical Research, North Shore-Long Island Jewish Health System, Manhasset, New York, USA; ²⁰Arthritis Research Campaign (arc) – Epidemiology Unit, The University of Manchester, Manchester, UK; ²¹Department of Medicine, University of Toronto, Mount Sinai Hospital and University Health Network, Toronto, Ontario, Canada; ²²Rheumatology Unit, Department of Medicine, Karolinska Institutet at Karolinska University Hospital Solna, Stockholm, Sweden

10.1136/ard.2010.148965.20

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

Alexandra Zernakova,¹⁻³ Eli A Stahl,^{3,4} Gosia Trynka,⁵ Soumya Raychaudhuri,^{4,6,7} Eleanora Festen,⁵ Lude Franke,^{5,8} Rudolf S N Fehrmann,⁵ Fina A S Kurreeman,^{1,3,4} Brian Thomson,⁴ Namrata Gupta,⁴ Jihane Romanos,⁵ Ross McManus,⁹ Anthony W Ryan,⁹ Graham Turner,⁹ Elaine F Remmers,¹⁰ Luigi Greco,¹¹ Rene Toes,¹ Elvira Grandone,¹² Maria Cristina Mazzilli,¹³ Anna Rybak,¹⁴ Bozena Cukrowska,¹⁵ Yonghong Li,¹⁶ Paul I W de Bakker,^{3,4,17,18} Peter K Gregersen,¹⁹ Jane Worthington,²⁰ Katherine A Siminovitch,²¹ Lars Klareskog,²² Tom W J Huizinga,¹ Cisca Wijmenga,⁵ Robert M Plenge^{3,4} ¹Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands; ²Department of Medical Genetics, University Medical Centre Utrecht, Utrecht, The Netherlands; ³Division of Rheumatology, Immunology, and Allergy, Brigham and Women's Hospital, Boston, Massachusetts, USA; ⁴Broad Institute, Cambridge, Massachusetts, USA; ⁵Genetics Department, University Medical Centre Groningen and University of Groningen, Groningen, The Netherlands; ⁶Center for Human Genetic Research, Massachusetts General Hospital, Boston, Massachusetts, USA; ⁷Division of Genetics, Brigham and Women's Hospital, Boston, Massachusetts, USA; ⁸Blizard Institute of Cell and Molecular Science, Barts and The London School of