nucleotide polymorphisms (SNPs), to the genetic variance of total, anti-citrullinated protein antibody (ACPA)-positive and ACPA-negative RA.

Methods A cohort of 148 twin pairs, of which at least one twin had RA, were tested for ACPA. The contribution of the HLA-DRB1 alleles and SNPs to the genetic variance was assessed by a logistic regression model with genotype-specific parameters and a random effect model representing the contribution of unobserved genetic factors.

Results In the ACPA-positive subset, the HLA SE alleles contributed 19.2% to the genetic variance, while the contribution of the protective HLA-DRB1*13 alleles was very small: 0.13%. Both SE and DRB1*13 alleles hardly contributed to ACPA-negative RA (1.52%). The contributions of the separate SNPs to the different subsets of RA were small with an average of below 1%.

Conclusion A modest amount of the genetic variance of ACPA-positive, but not ACPA-negative RA can be explained by the HLA SE alleles, while the contribution of the protective HLA-DRB1*13 alleles and non-HLA loci is very small. These results indicate that the largest part of the genetic contribution to RA remains unexplained.

3 THE CONTRIBUTION OF GENETIC RISK FACTORS OTHER THAN THE HLA SHARED EPITOPE ALLELES TO THE GENETIC VARIANCE OF RHEUMATOID ARTHRITIS

Diane van der Woude,¹ Jeanine J Houwing-Duistermaat,² Ann Morgan,³ Jane Worthington,⁴ Tom W J Huizinga,¹ Bart O Roep,⁵ René E M Toes,¹ René R P de Vries⁵ ¹Department of Rheumatology, Leiden University Medical Center, Leiden, The Netherlands; ²Department of Medical Statistics, Leiden University Medical Center, Leiden, The Netherlands; ³Leeds Institute of Molecular Medicine, University of Leeds, Leeds, UK; ⁴Arthritis Research Campaign Epidemiology Unit, University of Manchester, Manchester, UK; ⁵Department of Immunohematology and Blood Transfusion, Leiden University Medical Center, Leiden, The Netherlands

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Objective Genetic factors explain 66% of susceptibility to rheumatoid arthritis, but it is unclear how much of this genetic risk can be explained by the genetic risk factors known to date. In addition to the contribution of the HLA shared epitope (SE) alleles which the authors have quantified previously, the authors now investigated the contribution of the protective HLA-DRB1*13 alleles and of 12 replicated single