Background HLA-DRB1 is characterized by highly complex genetic variants associated with susceptibility to and autoimmune diseases including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), highlighting the primary associations of multiple amino acid changes on the epitope-binding groove of HLA-DR molecules. However, in contrast to the missense variants in HLA-DRB1, an effect of expression changes in HLA-DRB1 has been poorly understood.

Methods Both three-field HLA-DRB1 alleles (# of alleles>10) and RNA-Seq data in 48 Koreans and 357 Europeans were simultaneously analyzed to determine the most likely HLA-DRB1 genotypes in each individual and to measure allele-specific expression levels. The relative expression strength of each HLA-DRB1 allele compared to all the other alleles was calculated for contribution to phenotypes associated with amino-acid changes in HLA-DRB1.

Results Strong cis-eQTL signals of HLA-DRB1 were detected around HLA-DRB1, causing high imbalanced allelic expressions in HLA-DRB1 heterozygotes. The reported associations of HLA-DRB1 with the level of auto-citrullinated peptide (anti-CCP) autoantibodies in RA or the susceptibility to SLE were re-assessed in Korean RA (n>1,000) and SLE-control (n>5,000) genetic data, taking the relative allelic expression strength into account, and were additionally explained by the skewed allelic expressions of HLA-DRB1 in heterozygotes.

Conclusions This study identified the allele-specific expression of HLA-DRB1 that contributed to disease risk and autoantibody production in rheumatic autoimmune diseases. Funding Source(s): This study was supported by Basic Science Research Program through the National Research Foundation of Korea funded by the Ministry of Science, ICT & Future Planning (2017R1E1A1A01076388) and Korea Healthcare Technology R and D Project funded by the Ministry for Health and Welfare (HI15C3182) in Republic of Korea.

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