Single Nucleotide Polymorphisms at the PRR3, ABCF1, and GNL1 Genes in the HLA Class I Region Are Associated with Graves' Ophthalmopathy

Yu-Huei Liu[1, 2], Yi-Ju Chen[2], Hsin-Hung Wu[3], Tzu-Yuan Wang[4], Fuu-Jen Tsai[1,5]

[1] Department of Medical Genetics and Medical Research, China Medical University Hospital. [2] Graduate Institute of Integrated Medicine, China Medical University, Taichung, Taiwan. [3] Department of Business Administration, National Changhua University of Education, Changhua, Taiwan. [4] Division of Endocrinology and Metabolism, College of Chinese Medicine, China Medical University, Taichung, Taiwan. [5] Department of Pediatrics and Schools of Chinese Medicine and Post-Baccalaureate Chinese Medicine, China Medical University, Taichung, Taiwan.

Graves' disease (GD) is an autoimmune disease that occurs with or without major complication Graves' ophthalmopathy (GO). This study was to investigate whether a conserved HLA class I region influenced the development of GO in patients with GD in a Taiwan-Chinese population. Four hundred sixty-eight Taiwan-Chinese patients with GD; 200 of these patients had GO, whereas 268 patients did not. Single nucleotide polymorphisms (SNPs) between the HLA-A and HLA-C loci were genotyped. Strong gender effects on the distribution of the SNPs were apparent: male GD patients carrying an A allele at rs2074503 in the PRR3 gene tended to avoid demonstrating GO (P = 0.008; OR, 0.450; 95% CI, 0.248-0.819), whereas female patients tended to show GO (P = 0.01; OR, 1.486; 95% CI, 1.098-2.012). In addition, only the female GD patients with a T allele at rs1264439 in the ABCF-1 gene tended to demonstrate GO (P = 0.005; OR, 1.539; 95% CI, 1.139-2.081). Analysis of the haplotype blocks of the SNPs rs2074505 (GNL1) and rs2074503 (PRR3) showed that haplotype HA1 was underrepresented in male GO patients (P = 0.004; OR, 0.418; 95% CI, 0.228-0.767), whereas HA-4 was underrepresented in female GO patients (P = 0.007; OR, 0.660; 95% CI, 0.490-0.895). The results suggested that SNPs at PRR3 and ABCF1 genes and the haplotype composed by SNPs at GNL1 and PRR3 between the HLA-A and HLA-C genes tended to predict GO in a gender-dependent manner in patients with GD in Taiwan.