An association analysis of the HLA gene region in latent autoimmune diabetes in adults.

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Abstract
Aims/hypothesis Pathophysiological similarities between latent autoimmune diabetes in adults (LADA) and type 1 diabetes indicate an overlap in genetic susceptibility. HLA-DRB1 and HLA-DQB1 are major susceptibility genes for type 1 diabetes but studies of these genes in LADA have been limited. Our aim was to define patterns of HLA-encoded susceptibility/protection in a large, well characterised LADA cohort, and to establish association with disease and age at diagnosis.
Materials and methods Patients with LADA (n = 387, including 211 patients from the UK Prospective Diabetes Study) and non-diabetic control subjects (n = 327) were of British/Irish European origin. The HLA-DRB1 and -DQB1 genes were genotyped by sequence-specific PCR.
Results As in type 1 diabetes mellitus, DRB1*0301_DQB1 *0201 (odds ratio [OR] = 3.08, 95% CI 2.32–4.12, p = 1.2 × 10−16) and DRB1*0401_DQB1*0302 (OR = 2.57, 95% CI 1.80–3.73, p = 4.5 × 10−8) were the main susceptibility haplotypes in LADA, and DRB1*1501_DQB1*0602 was protective (OR = 0.21, 95% CI 0.13–0.34, p = 4.2 × 10−13). Differential susceptibility was conferred by DR4 subtypes: DRB1*0401 was predisposing (OR = 1.79, 95% CI 1.35– 2.38, p = 2.7 × 10−5) whereas DRB1*0403 was protective (OR = 0.37, 95% CI 0.13–0.97, p = 0.033). The highest-risk genotypes were DRB1*0301/DRB1*0401 and DQB1*0201/ DQB1*0302 (OR = 5.14, 95% CI 2.68–10.69, p = 1.3 × 10−8; and OR = 6.88, 95% CI 3.54–14.68, p = 1.2 × 10−11, respectively). These genotypes and those containing DRB1*0401 and DQB1*0302 associated with a younger age at diagnosis in LADA, whereas genotypes containing DRB1*1501 and DQB1*0602 associated with an older age at diagnosis.