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DQ-ASSOCIATED PROTECTION FROM TYPE 1 DIABETES: ALLELES OF HLA CLASS 2 IN PATIENTS WITH TYPE 1 DIABETES AND THEIR FAMILY MEMBERS

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In our previous study we demonstrated association between genes HLA-DRB1 and HLA-DQB1 and T1D in the Polish population. We found strong-independent associated alleles HLA-DRB1*0401 and DQB1*302, despite on statement population linkage disequilibrium among alleles of these genes. The aim of the current study was to verify a hypothesis that some alleles or haplotypes of HLA-DRB1, DQA1 and DQB1 genes increase a risk for familial aggregation of T1DM. We analysed 507 patients with IDDM derived from 80 multiplex and 325 patients from simplex families. PCR and hybridisation with SSO probes performed HLA typing for DRB1, DQA1 and DQB1 alleles. Genetic analysis demonstrated strong association allele HLA-DQB1*0302 with T1DM in Polish population as well as simplex (DM1) and multiplex (DM2) cases, compare with healthy cases (n=103). The HLA-DQB1*302 allele frequencies were27.8%vs8.7%;Pc<10-5;OR(95%CI)=4,03(3.80-4.25) and 16.3%vs8.7%;Pc<0.04;OR(95%CI)=2.04(1.79-2.89), respectively. The presence of allele HLA-DQB1*0602 has strong protective effect from T1DM in both studied groups (1.46%vs13.6%;Pc<10-5;OR(95%CI)=0.09(0.25-0.44) and 0.98vs13.6%;Pc<10-5;OR(95%CI)=0.06(0.46-0.58), respectively. Interestingly, HLA-DRB1*04 allele more often co-segregated with DM2 families as comparing the DM1 group (31.0%vs15.8%,respectively;Pc<10-5). However in both cases differences remain significant as compared to controls:Pc<10-5,OR(95%CI)=3.52(3.33-3.70) and Pc<10-5 OR(95%CI)=6.17(5.97-6.37), for DM1 and DM2 respectively. Moreover, difference in frequencies of the protective allele HLA-DQB1*0301 among DM1 and DM2 group was revealed (8.8%vs.13.7%,respectively;Pc<10-5) and protective effect of this allele remained only significant in DM1 group:8.8%vs19.9%;Pc<10-5;OR(95%CI)=0.39(0.19-0.58).Presenting results suggest it is likely that familial aggregation of T1DM is associated with lower frequency of protective alleles of HLA-DQB1 gene.

Supported by Ministry of Health grant no 16/eks/7/2002