**HLA CLASS II GENETICS OF EASTERN CROATIAN COELIAC DISEASE PATIENTS**

S. Marczi1,2, S. Tokić1, M. Štefanić1,2, Lj. Glavaš-Obrovac2, A. Bugarin1, I. Mihaljević1,2

1Clinical Institute of Nuclear Medicine and Radiation Protection, University Hospital Centre Osijek, Croatia, 2Faculty of Medicine, J.J. Strossmayer University, Osijek, Croatia

Genetic predisposition to coeliac disease (CD) is primarily attributed to DQ2 and DQ8 heterodimers encoded by HLA-DQA1\*0501/DQB1\*02 and HLA-DQA1\*0301/DQB1\*0302 loci. In order to investigate these associations in Eastern Croatian population, 23 unrelated children diagnosed with CD were typed for HLA-DRB1, -DQA1 and -DQB1 alleles by sequence specific oligonucleotide probe (PCR-SSP) method. Allele and haplotype frequencies (EM algorithm) were compared to data obtained from previously typed, unrelated, healthy Croatian controls (n=119) by using Fisher exact test and relative risks (RR, Woolf-Haldane method). CD susceptibility was strongly associated with DQA1\*0505 (RR=126.5, p<0.0001), DQB1\*02 (p=0.007, RR=2.51, 95% confidence interval 1.56-4.27), DQA1\*0501-DQB1\*02 [28.3% in patients vs. 8.05% in controls, p=0.022, RR=3.22 (1.92-5.26)] and DQA1\*0505-DQB1\*03(DQ7) [21.7% vs. 0%, p=0.001, RR=7.69 (5.26-10)]. In contrast, DQB1\*06 locus [p=0.014, RR=0.16 (0.03-0.81)] conferred the protection against CD. The presence of DQ2 α1\*05:01/β1\*02 heterodimer in a single dose in cis increased the risk of CD fourfold [p=0.001, RR=3.97, CI (2.1-7.5)], whilst the absence of both DQ2/DQ8 heterodimers reduced the risk of CD threefold [p=0.0005, R=0.35 (0.18-0.68)]. The results suggest a major role of DQ7.5, DQ2.5 and DQ8.1 haplotypes in CD susceptibility in Eastern Croatian population. Large sample and high resolution testing are required for in-depth dissection of allelic heterogeneity and epistasis at DQ6 locus.