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DQ POLYMORPHISM IN JUVENIL ONSET DIABETES MELLITUS

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Recently stronger association of insulin dependent diabetes mellitus (IDDM) with certain HLA AQ alleles has focused attention on the DQA1 and DQB1 genes as susceptibility determinants. We studied DQB1 and DQB1 polymorphism in 10 Egyptian families (53 individuals) having one or more members suffering from IDDM, and comparing results with 14 age and sex matched controls.

Extracted DNA was dot blotted on nylon membrane and then hybridized with sequence specific oligonucleotides (SSO)labelled with digoxiginine. Detection was carried out by chemiluminescence

DQA1 0301, -201, 0302 and DQB 1 0201, 0302, and 0501 alleles were statistically significantly increased in patients compared to the control group (Z 1, 96)

DQA1 0301 and DQB1 0201 alleles were present in (50% and 40% of parents)
respectively, suggesting increased susceptibility and genetic predisposition to develop IDDM

DQA1 0301 and DQB1 0302 alleles were higher in non diabetic offspring (72.7% and 27.3%) respectively having increased risk to develop IDDM.

We have pointed out certain new susceptible alleles significantly increased in our patients and not recorded in other ethnic population these are the DQA1 0201, 0302 and DQB1 0501 alleles .

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THE ASSOCIATION OF HLA-ANTIGENS WITH INSULIN-DEPENDENT DIABETES MELLITUS (IDDM) IN SAINT-PETERSBURG (RUSSIA).

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The importance of hereditary predisposition to IDDM is confirmed by its association with immunogenetic markers of MHC. However, the exist differences in these associations depend on the region where the investigations were performed. Thats why the study of associations IDDM with HLA-antigens in different populations is actual.

We have determined serologicaly HLA-A,-B,-C and -DR specificities for 77 St.Petersburg IDDM patients (18 male and 59 female) and also their parents and siblings. The control group included 250 healthy individuals. Our study have revealed the considerable increased frequencies of HLA-A9(42,9% vs 24,4% in control), B8(29,9% vs 13,2%), B15(27,3% vs 8,4%), B16(19.5% vs 8,8%), DR3(48,1% vs 22,8%) and DR4(80,5% vs 21,2%). According our dates the highest risk of development IDDM is connected with presence in phenotype the combination HLA-DR3/DR4 (33,8% vs 0).

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HLA-DQB1 genotyping of IDDM in Latvia

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We investigated 119 children with IDDM and 165 controls. The HLA-DQB1 typing method was described (M.Sjoroos et al., Biotechniques,1995;18:870). The frequencies of the defined four DQB1 alleles in IDDM patients and controls are shown in Table.

HLA-DQB1 alleles	IDDM patients n	%	controls n	%	RR
0201	83	69.7	54	32.7	4.75
0302	82	68.9	16	9.7	20.63
0301	18	15.1	73	44.2	0.22
0602/0603	3	2.5	86	52.1	0.02

According to the results, in Latvian population DQB1*0302 alleles are associated with the strong, but DQB1*0201 alleles - with the weak predisposition to IDDM. DQB1*0301 alleles are associated with the weak, but DQB1*0602/0603 alleles - with the strong protection against IDDM. The genotyping of four alleles of the HLA-DQB1 locus can be useful for determination of the risk of disease and for screening of IDDM susceptibility in the Latvian population.

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HLA GENETIC MARKERS OF IDDM IN BURIAT POPULATION.

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The frequencies of class II HLA alleles (DRB1, DQA1, DQB1) were studied in Buriat population group (Orient origin) living in South-Eastern Sibiria. IDDM cases in Buriats are tenfold lower as compared to that of other populations (mainly Caucasians) of the region.

HLA genotyping was performed using mSSP (mixed SSP) an original variant of SSP developed in our laboratory and undergone quality control in frame of the XII IHWC.

The genotyping of IDDM Buriat patients revealed that HLA-DRB04 (50%) and HLA-DRB1-07 (21%) are the most frequent in them. We should note that 45% of the patients with DRB1-04 in genotype were homozegous. DR-03 being the second "classical" IDDM marker of DRB1 is rearly identified both in IDDM and "healthy" Buriat subjects.

DQA1 0301 allele (being "classical" IDDM marker) is highly increased (64,3%) in IDDM Buriat patients whereas DQA1 0501 is virtually at the control level.

As for 0302 and 0201 alleles of DQB1 gene only DQB1-0201 is significantly increased (23.8%) in Buriat IDDM patients. "Unsignificant" increase of DQB1-04 (19%) is revealed in Buriat IDDM patients as compared to the control (8,3%). The peculiar HLA-association and low number of IDDM cases in Buriat is being discussed.

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Immunogenetic Heterogeneity in type I (Insulin-Dependent)Diabetes Among the Tunisian population . HLA DR , HLA DQ ,C4 and Organ specific Auto-antibodies

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The frequency of HLA DR antigens , as well as the prevalence of islet cell , isulin auto-antibodies and other auto-immunity disorders , were investigated in Tunisian patients with insulin -dependent diabetes (IDDM) and were compared with family members (sibs) and healthy control subjects .

A good correlation between HLA DR3/DR4 heterozygous phenotypes and the presence of ICA in patients with IDDM and thier unaffected sibs was observed in the Tunisian population . In fact , this heterozygous is found in 63.3 % of ICA postive diabetic patients and in 44.4 % of ICA positive unaffected sibs , whereas , HLA DR3/HLA DR4 antigens were noted in only 22.9% of ICA negative of diabetic patients and in no ICA negative unaffected sibs.

In this work , we also summarized the distribution of HLA DR antigens in patients with IDDM who presented auto-immune disorders other tha ICA .

In this studies , we used above technique for typing the HLA DQ A1 *alleles in Tunisian diabetic patients . The frequency of HLA DQA1*0301was greatly increased compared with the control group . This was in agreement with previously published data in Caucasian and Japanese isulin dependent diabetes mellitus .

The polymorphism of the C4A and C4B genes was investigated also in Tunisian population patients with IDDM . Multiplex families were analysed .

Using RFLP analysis , we confirmed the high frequency of C4 nul alleles . We also observed that most of these alleles were genes deleted in IDDM patients compared with the controls (72.23% vs 20% for C4AQ0 and 70.07% vs 16.70 for C4BQ0).

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CLASS 1 MHC ASSOCIATION WITH NON-INSULIN DEPENDENT DIABETES IN MAORI WITH RENAL FAILURE.

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MHC associations with non-insulin dependent diabetes mellitus (NIDDM) have been described in a number of non-European races. The New Zealand Maori have a very high incidence of NIDDM which often leads to renal failure.

All Maori with NIDDM were identified from the Auckland renal database. Tissue typing had been performed by standard serological methods on 45 of these patients for transplant work-up. HLA types were confirmed by reviewing the original laboratory worksheets and the diabetic diagnosis by reviewing the clinical notes. 576 normal Maori were used as the control population.

A 2 x 2 Chi square method was used for statistical analysis.

The broad groups HLA-A10 (rel risk 2.6) and HLA-B40 (rel risk 3.0) were significantly associated with NIDDM ($p<0.05$).

Class I MHC relationships with NIDDM have been found in many non-European races. These races are genetically homogeneous and the HLA associations may provide a further marker for the development of NIDDM.