Investigation: HLA class II alleles in patients with Borrelia burgdorferi infection

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Introduction. Lyme borreliosis is a very actual disease in the recent years, and its incidence rate in Latvia is one of the highest in Europe.

The Lyme borreliosis incidence rates per 100,000 population in neighbouring countries in 2008 (see table):

There are some similarities between the bacterial agents and HLA molecules because an immune response to infection develops one way or another in the body. There are many hypotheses about the direct role of HLA molecules in the pathogenesis of infection. Clarifying the polymorphism of HLA immunogenetic molecular markers may identify regularities in the development and pathology and develop a new approach to treating these diseases.

Incidence	The Republic of Belarus	Estonia	Latvia	Lithuania	Russia
Lyme borreliosis	6.6	106.0	21.5	34.0	5.4

Objective. To determine HLA-DR, -DQ molecules in patients with clinical, epidemiological and laboratory approved Lyme borreliosis diagnosis.

Materials and methods. The study included 20 patients with clinical stage erythema migrans and 20 control (healthy) persons. The clinical diagnosis was confirmed at the Infectology Center of Latvia. Immunogenetic examinations were performed at the Riga Stradiņš University Immunogenetic and Clinical Immunology Laboratory. HLA genotyping was performed through PCR-SSP method. The significance of differences in individual subtypes between patients and controls was assessed by Mantel–Haenszel test and Fisher exact correction for small numbers.

Results. Typing of all sixteen -DR and sixteen -DQ alleles was investigated. The predisposition to Lyme disease is associated with HLA-DRB1 *17(03) (OR 7,5; p<0,044) and DRB1 *15 (OR 5,21; p<0,132) (Table 1). For the -DRB1 *18(03) allele, the evidence is controversial (Fig. 1).

HLA-DQA1*0201, -DQA1*0501 and DQB1*0201 were shown to be considerably increased in patients, although the difference was no longer significant when the p value was not corrected for the number of alleles (Fig. 1). And, the allele DRB1*13 (OR 0,27; p<0,233) was lower in Borreliosis patients and significantly higher in controls (Table 1). The distribution of alleles in the patients included in this study follows the world tendency: DRB1 *17(03) was the most frequent allele in Caucasian population.

Table 1. **The frequency of HLA -DR, -DQ alleles in patients and controls**

Allele **DRB1**	Patients (%)	Controls(%)	OR (95%CI)	*P-values*	Allele**DQA1**	Patients(%))	Controls(%)	OR (95%CI)	*P-values*	Allele**DQB1**	Patients(%)	Controls(%)	OR (95%CI)	*P-values*
***03**	15	20	0,87	0,806	***0101**	25	40	0,69	0,553	*0201	45	30	2,04	0,224
***07**	15	25	0,68	0,451	***0102**	15	10	1,84	0,516	***0301**	10	20	0,56	0,52
***08**	5	15	0,37	0,371	***0103**	10	25	0,44	0,335	***0302**	45	50	1,08	0,886
***09**	10	15	0,77	0,577	*0201	20	10	2,53	0,291	***0303**	10	15	0,77	0,783
***13**	5	20	0,27	0,233	*0501	40	25	2,15	0,217	***0305**	10	20	0,56	0,52
*15	20	5	5,2	0,132	***0401/ 0601**	25	40	0,69	0,553	***0501**	5	15	0,37	0,39
***17(03)**	30	5	**7,5**	0,049	–	–	–	–	–	***0601**	5	15	0,37	0,39

Abbreviations: OR (odds ratio), P (probability).

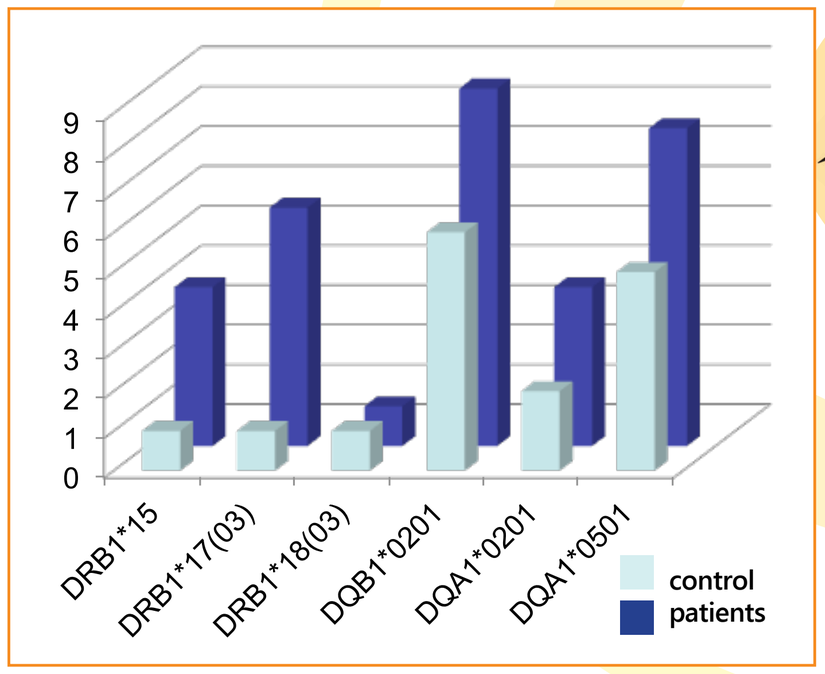
HLA disease – protective alleles

- DRB1* • *07, *08, *13;
- DQA1* • *0103;
- DQB1* • *0501, *0601;

HLA disease – associated alleles

- DRB1* • *17(03), *15;
- DQA1* • *0201, *0501, *0102;
- DQB1* • *0201;

Fig. 1. **The frequency of HLA -DR, -DQ alleles in patients and controls from Latvia**



Conclusions.

- The HLA-DRB1*17(03) and -DRB1*15 – contributes definitely to a genetic predisposition to Borrelia burgdorferi infection in Latvian population.
- The HLA-DQA1*0201, -DQA1*0501 and DQB1*0201 were shown to be considerably increased in Borreliosis patients.
- And, the allele DRB1*13 was smaller in Borreliosis patients and significantly higher in controls.
- This data suggest that HLA-DR, -DQ molecules may have a considerable effect on susceptibility/ or protection to Lyme borreliosis.

2010/0200/2DP/2.1.1.2.0/10/APIA/VIAA/006