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Correlation between the production of specific antibodies against *Borrelia burgdorferi* and particular HLA genotypes

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Background A small subset of patients infected with *Borrelia burgdorferi* does not produce *Bb* specific antibody. Our research provides additional evidence of a genetic predisposition for seronegativity in some individuals with Lyme disease.

Aim The aim of the current study was evaluation of associations between the production of specific antibodies against *Borrelia burgdorferi* and particular HLA class II.

Methods The study included 204 patients with an established diagnosis of Lyme borreliosis and 282 healthy people. The LB diagnosis was confirmed clinically, serology was tested and imposed in the Infectology Center of Latvia. Tests of *Bb*-specific immunoglobulin G and immunoglobulin M antibodies were performed using *Bb* IgG/IgM Enzyme-Linked Immunosorbent Assay and *Bb* IgG/IgM Westernblot test. HLA genotyping was performed by PCR with sequence-specific primers in the Riga Stradiņš University, Laboratory of Clinical Immunology and Immunogenetics. To analyze the correlation between the level of specific antibodies and alleles, the Mann-Whitney U test was used. In the case where three or more variables were compared, the Kruskal-Wallis Test was applied. Statistical analyses were performed with SPSS Statistics Version 21 (IBM Corporation, Illinois).

Results

Distribution of HLA -DR*-DQ* alleles in Borrelia burgdorferi specific IgM antibodies seronegative and seropositive patients with Lyme borreliosis

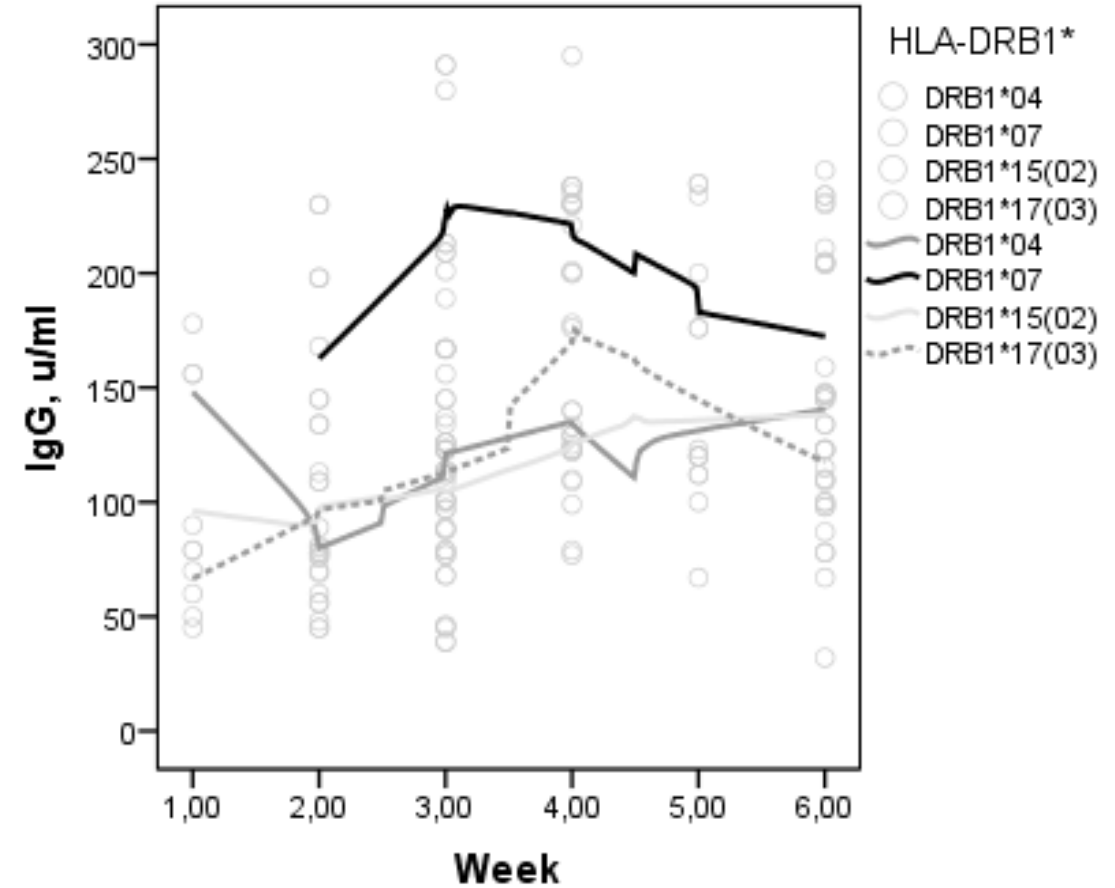
Allele HLA-	IgM seronegative LB patients (n=18) 36 alleles	IgM seropositive LB patients (n=186) 372 alleles	OR	p-value
<i>DRB1*01</i>	10 (27.7%)	37 (9.9%)	3.48	0.002
<i>DRB1*15(02)</i>	4	47	0.86	0.791
<i>DRB1*16(02)</i>	4	45	0.91	0.862
<i>DRB1*17(03)</i>	3	40	0.75	0.651
<i>DRB1*18(03)</i>	2	43	0.45	0.272
<i>DRB1*04</i>	4	29	1.48	0.486
<i>DRB1*11(05)</i>	3	13	2.51	0.153
<i>DRB1*12(05)</i>	ND	14	ND	ND
<i>DQA1*0301</i>	9 (50%)	42 (22.6%)	2.62	0.017
<i>DQA1*0401</i>	4	43	0.48	0.312
<i>DQA1*0501</i>	2	53	0.35	0.144
<i>DQB1*0301</i>	1	32	0.30	0.221
<i>DQB1*0502-4</i>	6 (33.3%)	21 (11.3%)	3.34	0.011
<i>DQB1*0601</i>	3	12	2.73	0.119
<i>DQB1*0602- 8</i>	8 (44.4%)	36 (19.4%)	2.67	0.020

Abbreviations: ND – not defined; OR (odds ratio); p-value (probability). The odds ratios (OR) were calculated by applying Mantel-Haenszel.

Results

Associations between a risk alleles and the production of specific IgG antibodies in Lyme borreliosis patients

HLA-	N	IgG, u/ml						
		Mean	Std. Deviation	Minimum	Maximum	Q1	Median	Q3
DRB1*								
<i>DRB1*04</i>	38	125.1	56.8	39.0	291.0	79.8	117.0	158.8
<i>DRB1*07</i>; p<0.001	32	192.6	52.7	100.0	291.0	136.8	204.5	230.8
<i>DRB1*15(02)</i>	51	122.7	56.2	39.0	238.0	78.0	113.0	156.0
<i>DRB1*17(03)</i> ; p=0.832	47	120.6	53.0	32.0	295.0	88.0	120.0	145.0
<i>Total</i>	168	136.0	60.9	32.0	295.0	88.3	123.0	177.5
DQA1*								
<i>DQA1*0301</i> ; p=0.914	51	132.3	60.3	32.0	295.0	89.0	119.0	178.0
<i>DQA1*0401</i>	47.0	130.0	50.6	45.0	238.0	97.0	123.0	156.0
<i>Total</i>	98	131.2	55.6	32.0	295.0	90.0	120.0	161.0
DQB1*								
<i>DQB1*0302</i> ; p=0.206	47	145.1	59.0	60.0	280.0	90.0	134.0	200.0
<i>DQB1*0502-4</i>	27	127.1	56.0	46.0	234.0	78.0	120.0	160.0
<i>Total</i>	74	138.5	58.2	46.0	280.0	88.8	133.5	190.3



Conclusions

- The lack of formation of *Borrelia burgdorferi* specific IgM antibodies in patients in the acute phase of the disease was associated with HLA-DRB1*01, -DQA1*0301, -DQB1*0502-4, -DQB1*0602-8 alleles.
- A high level of *Borrelia burgdorferi* specific IgG antibodies statistically significantly correlates with HLA-DRB1*07 allele.