HLA associations to periodontopathic bacteria

Language: English

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Istanbul

Introduction

Our previous studies revealed HLA class I- and II-associations to aggressive (AP) and chronic (CP) periodontitis (Machulla et al. 2002, Reichert et al. 2003, Stein et al. 2003). Antigenic peptides were bound by HLA molecules over specific pockets of the hypervariable peptid binding region in order to present them to T lymphocytes. In patients with advanced periodontitis, HLA class II-molecules were expressed by Langerhans cells in both oral gingival epithelium and pocket epithelium (Nunes et al. 1994). Colonization of periodontopathic bacteria and antigen specific immune response could be controlled by polymorphism of HLA alleles. That’s why an association from HLA to periodontopathic bacteria could be exist.

Fig. 1 (Hjelmström et al. 1996) Presentation of an antigenic peptide through the hypervariable binding groove of a HLA class II molecule (HLA-DQ). The T cell receptor recognises as well as structures of the HLA molecule and bound peptide. The length of the peptides vary from 13-25 amino acids.

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more Journals


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Fig. 1 (Hjelmström et al. 1996) Presentation of an antigenic peptide through the hypervariable binding groove of a HLA class II molecule (HLA-DQ). The T cell receptor recognises as well as structures of the HLA molecule and bound peptide. The length of the peptides vary from 13-25 amino acids.

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The goal of the present study was to evaluate HLA associations to A. actinomycetemcomitans (A.a.), P. gingivalis (P.g.), P. intermedia (P.i.), T. forsythensis (T.f.) and T. denticola (T.d.) in patients with both aggressive and chronic periodontitis.

**Material and Methods**

In both patient groups the smoking status, the approximal plaque index (API), bleeding on probing (BOP), pocket depth (PD), clinical attachment loss in general (CAL) and on the microbial test-sites (CALBact.) were determined. For the microbial assessment subgingival plaque samples were taken from the deepest four pockets (CALBact. > 5 mm) by means of sterile paper points. Bacterial infection was analyzed employing a PCR-rSSO microDent DNA-Strip technique (Hain Lifescience GmbH, Nehren, Germany). HLA-A, -B, -Cw, -DR, -DQ typing was performed by both CDC (Complement Depending Cytotoxicity assay, BAG, Lich, Germany) and polymerase chain reaction with sequence-specific primers (PCR-SSP, GenoVision VertriebsmbH Schwechat, Austria). Statistical calculations were carried out by Chi$^2$ testing, with Yates correction or Fishers Exact test, if appropriate. In order to determine the adjusted odds ratio (OR) of certain HLA markers for an infection with one of the periodontopathic bacteria the confounding variables age, gender, nicotine consumption and CALBact. were additional included in a logistic regression model. All patients and controls were of Caucasian descent and were unrelated and free from other general diseases known to be associated with certain HLA markers.

**Results**

AP patients were in comparison to CP patients significantly younger, more frequently smoker and A.a. positive. CP patients were significantly more infected with T.d. (Table 1).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Chronic periodontitis (CP)</th>
<th>Aggressive periodontitis (AP)</th>
<th>P values</th>
<th>AP + CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (range)</td>
<td>47 (27-68)</td>
<td>37 (15-55)</td>
<td>0.0001</td>
<td>42.5 (15-68)</td>
</tr>
<tr>
<td>females %</td>
<td>62.9</td>
<td>57.6</td>
<td>0.656</td>
<td>60.0</td>
</tr>
<tr>
<td>smoker %</td>
<td>14.3</td>
<td>48.5</td>
<td>0.002</td>
<td>30.9</td>
</tr>
<tr>
<td>API % (SD)</td>
<td>62.1 (10.5)</td>
<td>53.5 (34.8)</td>
<td>0.286</td>
<td>58.0 (29.9)</td>
</tr>
<tr>
<td>BOP % (SD)</td>
<td>64.4 (28.7)</td>
<td>71.6 (28.7)</td>
<td>0.317</td>
<td>67.8 (28.7)</td>
</tr>
<tr>
<td>PD mm (SD)</td>
<td>5.4 (1.2)</td>
<td>5.8 (1.6)</td>
<td>0.212</td>
<td>5.6 (1.4)</td>
</tr>
<tr>
<td>CAL mm (SD)</td>
<td>6.1 (1.5)</td>
<td>6.5 (1.9)</td>
<td>0.338</td>
<td>6.3 (1.7)</td>
</tr>
<tr>
<td>CAL Bact. (SD)</td>
<td>7.4 (1.8)</td>
<td>7.6 (2.0)</td>
<td>0.613</td>
<td>7.5 (1.9)</td>
</tr>
<tr>
<td>A.actinomycetemcomitans (%)</td>
<td>9 (25.7)</td>
<td>16 (48.5)</td>
<td>0.052</td>
<td>25 (36.8)</td>
</tr>
<tr>
<td>P. gingivalis (%)</td>
<td>33 (94.3)</td>
<td>26 (78.8)</td>
<td>0.079</td>
<td>59 (86.8)</td>
</tr>
<tr>
<td>P. intermedia (%)</td>
<td>22 (62.9)</td>
<td>21 (63.6)</td>
<td>0.947</td>
<td>43 (63.2)</td>
</tr>
<tr>
<td>T. forsythensis (%)</td>
<td>34 (97.1)</td>
<td>29 (87.9)</td>
<td>0.191</td>
<td>63 (92.6)</td>
</tr>
<tr>
<td>T. denticola (%)</td>
<td>35 (100)</td>
<td>29 (87.9)</td>
<td>0.050</td>
<td>64 (92.1)</td>
</tr>
</tbody>
</table>

Table 1: Demographic and clinical parameters of all investigated cohorts

The proof of P.g. was significantly positively correlated with the occurrence of P.i. and T.f.. Both, P.i. and T.f. were positively correlated with the detection of T.d. (Table 2).
The occurrence of an A.a. Infection was found to be positively associated with the haplotypes HLA-B*08:Cw*07:DRB1*03:DRB3*(DR52):DQB1*02 and HLA-DRB1*13:DRB3*(DR52):DQB1*06 as well as the HLA-B super-type Bw6. On the other hand a homozygosity for HLA-Bw4 and HLA-DRB1*13:DRB3*(DR52):DQB1*06(DQ7/DQ8) were connected with a reduced risk for an A.a. infection. The HLA markers A*02 and A*23/*24(A9) increased the infection risk for P.g. and the complex P.g., T.f., T.d., respectively. An infection with P.i. occurred less frequent in patients expressing HLA-B*51/*52(B5), HLA-DRB3*(DR52) homozygous and two combinations with HLA-DRB1*13. T.f. was negatively associated with HLA-A*33 (Table 3).

Table 2: Correlations between the five proved bacteria. *P <0.05, **P < 0.01

<table>
<thead>
<tr>
<th>HLA-</th>
<th>Number HLA positive patients</th>
<th>Microorganisms</th>
<th>Infected patients %</th>
<th>OR</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>HLA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bw6</td>
<td>55</td>
<td>A.a.</td>
<td>43,6, 7,7</td>
<td>8,2</td>
<td>0,052</td>
</tr>
<tr>
<td>B<em>08:Cw</em>07:DRB1<em>03:DRB3</em>:DQB1*02</td>
<td>8</td>
<td>A.a.</td>
<td>75,0, 31,7</td>
<td>6,2</td>
<td>0,039</td>
</tr>
<tr>
<td>DRB1<em>13:DRB3</em>:DQB1*06</td>
<td>13</td>
<td>A.a.</td>
<td>61,5, 30,9</td>
<td>4,5</td>
<td>0,029</td>
</tr>
<tr>
<td>Bw4 homozygous</td>
<td>13</td>
<td>A.a.</td>
<td>7,7, 43,6</td>
<td>0,1</td>
<td>0,052</td>
</tr>
<tr>
<td>DRB1<em>04:DRB4</em>:DQB1*03( DQ7/DQ8 )</td>
<td>11</td>
<td>A.a.</td>
<td>9,1, 42,1</td>
<td>0,2</td>
<td>0,077</td>
</tr>
<tr>
<td>A*02</td>
<td>30</td>
<td>P.g.</td>
<td>100,0, 76,3</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>A<em>23/ A</em>24 (A9)</td>
<td>14</td>
<td>P.g., T.f., T.d.</td>
<td>93,3, 71,7</td>
<td>5,5</td>
<td>0,040</td>
</tr>
<tr>
<td>B<em>51 /B</em>52 (B5)</td>
<td>8</td>
<td>P.g., T.f., T.d.</td>
<td>100,0, 75,9</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>DRB3*(DR52) homozygous</td>
<td>8</td>
<td>P.i.</td>
<td>25,0, 68,3</td>
<td>0,2</td>
<td>0,030</td>
</tr>
<tr>
<td>B<em>44:DRB1</em>13</td>
<td>4</td>
<td>P.i.</td>
<td>0,0, 67,2</td>
<td>0,01</td>
<td>0,746</td>
</tr>
<tr>
<td>DRB1<em>13:(DRB3</em>:DQB1*06) only AP group</td>
<td>6</td>
<td>P.i.</td>
<td>16,7, 74,1</td>
<td>0,07</td>
<td>0,024</td>
</tr>
<tr>
<td>A*33</td>
<td>6</td>
<td>T.f.</td>
<td>66,7, 95,2</td>
<td>0,03</td>
<td>0,025</td>
</tr>
</tbody>
</table>

Table 3: HLA associations to five periodontopathic bacteria. *OR could not be calculated

Conclusions

Single HLA markers, HLA homoygositites and HLA combinations could influence the infection with A.a., P.g., P.i., T.f. and T.d. However, the mechanisms of the HLA - bacteria association are unknown. As well as bacterial mimicry with HLA (Ebringer 1983) and HLA dependent immunoreactivity to bacterial antigens (Buckley et al. 1973, Greenberg et al. 1975) could be assumed. In addition another study revealed that HLA-B8:DR3 positive subjects showed the significant lowest levels of serum IgA (Modica et al. 1989). This finding could be related to the high incidence of an A.a. Infection among HLA-B*08:Cw*07:DRB1*03:DRB3*:DQB1*02 positive patients. Further studies about the binding of periodontopathic and protective peptides at striking HLA molecules are required.
Literature


Modica MA, Freddi S, Caruso C: Blood IgA, IgM and IgE levels are influenced by sex and HLA phenotype. Experimental and clinical immunogenetics 1989, 6, S. 251-257.


Abbreviations

HLA  human leucozyte antigen
AP  aggressive periodontitis
CP  chronic periodontitis
PCR-SSP  polymerase chain reaction with sequence-specific primers
A.a.  Actinobacillus actinomycetemcomotans
P.g.  Porphyromonas gingivalis
P.i.  Prevotella intermedia
T.f.  Tannerella forsythensis
T.d.  Treponema denticola

This Poster was submitted by OA Dr. Stefan Reichert.

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