Association of HLA Haplotyping with Frequent Rhinoviral Susceptibility

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Introduction

Due to the critical role of T cells in both the humoral and cell-mediated branches of the vertebrate immune system, and the function of the Human Leukocyte Antigens (HLA) in activating T cells, an association between HLA haplotypes and susceptibility to disease is inevitable. Specific HLA haplotypes have been linked with susceptibility to illnesses, including autoimmune disorders, allergies, some viral diseases, disorders of the complement system, and some neurological disorders (Goldshreyer et al., 2003). Susceptibility to numerous viral diseases, including nephropathia epidemica, mixed cryoglobulinemia, and idiopathic hemochromatosis have been positively associated with specific haplotypes of the HLA-B locus, suggesting an important connection between this locus and resistance to viral infection.

Additionally, the polymorphic nature of HLA may yield different responses from the immune system (Blasczyk et al., 1997). Different forms of some alleles may be involved in the ability of cytotoxic T (Tc) cells to recognize antigens, and could possibly cause a person to be more susceptible to becoming sick more often than normal. An association between a specific allele and an illness is determined by the Relative Risk (RR) value, which is increased by high allele frequency (Faulk & Rubenstein, 1987).

R= (P/Q) disease
R= (A/P) control

The frequency and polymorphism of HLA alleles were observed and the RR value was calculated to conclude if there was any relative risk for rhinoviral infections.

Materials and Methods

• 40 volunteers were recruited:
  - 20 with a history of frequent rhinoviral infections
  - 20 with a history of non-frequent rhinoviral infections.

• Questionnaires were given to self-report rhinoviral infection history.

• DNA samples were obtained a mouthwash rinse and purified using a QIAamp kit.

• Results were obtained through polymerase chain reaction sequence specific primer HLA haplotyping, using an Invitrogen™ SSP Unitray® kit.

• Alleles were amplified and ran through standard horizontal gel electrophoresis procedures.

• Amplification patterns were analyzed using a documentation form provided by the manufacturer.

• The patterns were observed to look for any unique alleles and/or high frequency of alleles for each group.

• The frequency of alleles were used to calculate the RR value for frequent rhinoviral infections.

Results

+HLA-B haplotypes were determined.
+Two alleles were determined for each DNA sample.
+Control bands were observed at 1200 base pairs in all wells except for wells 1 and 2, which showed control bands at 200 base pairs.
+Bands were indicative of a positive test, and the pattern of bands indicated specific alleles, which were determined by the provided documentation form.

Figure 1: DNA sample from volunteer #29 showed continuous control bands and other bands, typing for alleles B7(19) and B62(15).

Table 1: Represented alleles in those with frequent and non-frequent rhinoviral infections are presented, along with the frequency of each allele.

<table>
<thead>
<tr>
<th>Allele Frequency</th>
<th>Volunteers with a History of Frequent Rhinoviral Infections</th>
<th>Volunteers with a History of Non-frequent Rhinoviral Infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>B7</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>B8</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>B18</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>B35</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>B37(1)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>B37(2)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>B41</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>B44(12)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>B56(22)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>B57(17)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>B57(18)</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

• Alleles unique to those with histories of frequent rhinoviral infections:
  • Alleles HLA-B27 and B52(5) were unique to the group with frequent rhinoviral infections.
  • Alleles HLA-B35, B57(17), B61(40) and B75(15) were unique to the group with non-frequent rhinoviral infections.

• Common alleles included HLA-B8, B18, B37, B41, B44(12), B56(22) and B62(15).

• HLA-B7 and B41 each showed a frequency of 4 among those with frequent rhinoviral infections, and had a calculated RR value of 4:
  \[ RR = \frac{4}{20} / \frac{1}{20} = 4 \]

Discussion

Alleles shown to be unique to those with frequent rhinoviral infections suggest that these alleles possibly determine a risk for frequent rhinoviral infections. This could be due to the polymorphic nature of these alleles yielding different responses from the immune system, possibly disrupting the ability of T cells to recognize antigens. These alleles suggest a potential relationship between obtaining frequent rhinoviral infections. Individuals with these alleles would expect to have a high frequency of rhinoviral infections.

Alleles shown to be unique to the group with non-frequent rhinoviral infections suggest that these alleles possibly have a protective characteristic, and help the immune system to recognize and respond to rhinoviral infections, preventing an individual from obtaining rhinoviral infections often. These alleles suggest a potential relationship with obtaining rhinoviral infections infrequently. Consequently, individuals with these alleles would expect to have infrequent rhinoviral infections.

The alleles that were shared at the same frequency between both groups suggest that these are common alleles in the population, and do not provide any potential risk for frequency of rhinoviral infections for an individual. These alleles would be expected to be distributed evenly among the common population.

Alleles B7 and B41 had a frequency of 4 in the group of volunteers who had histories of frequent rhinoviral infections, suggesting that these alleles might be linked to frequent rhinoviral infections. The relative risk was calculated to be 4 for both B7 and B41. Because the RR value is above one, this indicates an association between these alleles and frequent rhinoviral infections. This shows that a person with either of these alleles is four times more likely to have frequent rhinoviral infections than those with a different HLA-B allele.

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References