Role of PTPN22 C1858T Gene Polymorphism in Pediatric Polyautoimmunity

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Background:
Children with more than one autoimmune disease (AID) may have a stronger genetic component than children with a single AID. PTPN22 C1858T single nucleotide polymorphism (SNP) has been associated with multiple different AIDs in adults and children, but it has not been studied in pediatric polyautoimmunity.

Objective and hypotheses
To evaluate the association of PTPN22 C1858T gene polymorphism with pediatric polyautoimmunity. We hypothesized that children with polyautoimmunity have a higher frequency of the PTPN22 C1858T SNP.

Method
A cross-sectional study was performed in 128 subjects with AIDs of pediatric-onset recruited at pediatric endocrinology, rheumatology and gastroenterology clinics at the Pontificia Universidad Católica de Chile Health Network and 98 healthy controls. Children with single AIDs included in this study had either juvenile idiopathic arthritis, type 1 diabetes, or autoimmune thyroid disease. Pediatric polyautoimmunity was defined as >1 AID. Genotyping of the rs2476601 (C1858T) PTPN22 gene SNP was performed using TaqMan SNP genotyping assay by Real Time PCR.

Results
Mean age of children with AID was 12±4.4 years and 69% were female. The C1858T allele frequencies of cases and controls showed no deviation from Hardy-Weinberg equilibrium. Genotypes CC, CT, and TT of the PTPN22 C1858T polymorphism presented frequencies of 85.2%, 13.3% and 1.6%, respectively, in the AID group, and 83.7%, 12.8%, and 2.3% in the control group (P=0.18).

The T-allele frequency was higher among patients with pediatric polyautoimmunity than children with single AID (26% vs 11%, OR=2.87, 95%CI=1.05-7.83, P=0.04).

No significant differences were found in the age of onset of autoimmunity between mono and polyautoimmune subjects (P=0.44) or between subjects with CC genotype vs. CT+TT genotypes (P=0.81).

Conclusion
Children with polyautoimmunity have a higher prevalence of the PTPN22 C1858T polymorphism, suggesting that this variant may be a risk factor for polyautoimmunity in children with AID.

Reference
6. Luis M. Gomez, Juan Manuel Anaya, Javier Martin: Genetic Influence of PTPN22 R620W Polymorphism in Tuberculosis. Human Immunology (2005); 66, 1242-1247

Table 1: C1858T polymorphism in de los 128 patients sampled

<table>
<thead>
<tr>
<th>Allele</th>
<th>Mono</th>
<th>Poli</th>
<th>Total</th>
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<tbody>
<tr>
<td>CC</td>
<td>83 (89.2%)</td>
<td>26 (74.3%)</td>
<td>109 (85.2%)</td>
</tr>
<tr>
<td>CT+TT</td>
<td>10 (10.8%)</td>
<td>9 (25.7%)</td>
<td>19 (14.8%)</td>
</tr>
<tr>
<td>Total</td>
<td>93 (100%)</td>
<td>35 (100%)</td>
<td>128 (100%)</td>
</tr>
</tbody>
</table>

Figure 1: LYP encoded by PTPN22 gene involved in immune response signaling pathway. Garth L. Burm et al.

Figure 2: T-allele frequency in patients with pediatric autoimmune disease

Figure 3: Autoimmunity age onset in patients with pediatric autoimmune disease

Figure 4: Autoimmunity age onset in patients with T-allele presence