1597ΔC Polymorphism and Preterm Birth in African-American Mothers

Christopher Peterson, Anthony Torres, MD, Michael Benson, Martin Kharrazi, PhD, Michelle Pearl, PhD

Introduction

Natural killer cells are of particular interest during pregnancy, as they account for 70% of all lymphocytes in the placenta. Thus, abnormalities in natural killer (NK) cells have been implicated in pre-term birth, the leading cause of infant mortality. A suggested causative factor is a deletion at nucleotide 1597 in the HLA-G gene, which codes for the HLA-G histocompatibility antigen. HLA-G is of interest as: it is a rare “non-classical” antigen predominantly produced by fetal cells, and HLA-G polymorphisms have been implicated in another pregnancy disorder: preeclampsia. The interaction between HLA-G antigen on trophoblasts and inhibitory killer-immunoglobulin like receptor (KIR) 2DL4 on natural killer cells produces an inhibitory effect on the natural killer cell.

Maternal DNA was amplified using quantitative (“real-time”) PCR (qPCR), which can quantify target sequences of DNA. Each sample was run twice with primers positive (1597ΔC) and negative (HLA-G, or 1597) for the deletion. Peaks at approx. 88°C signified the deletion, and peaks at 77 °C (with absence of a positive peak) signified absence of the deletion.

Results

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Normal C/C</th>
<th>Deletion Δ/C</th>
<th>Deletion Δ/Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Individuals</td>
<td>630</td>
<td>81</td>
<td>2</td>
</tr>
<tr>
<td>Frequency</td>
<td>88.36%</td>
<td>11.36%</td>
<td>0.28%</td>
</tr>
</tbody>
</table>

Conclusion

We are confirming the association between 1597ΔC and pre-term birth in this population, and a positive association would suggest that mothers possessing the deletion are at risk for delivering pre-term. As this is a double-blind study, we are unaware which genotypes correlate with pre-term birth. We are currently awaiting completion of the statistical analysis by the California Department of Health.

References

4. Loisel, Dagan A.; Billstrand, Christine; Murray, Kathleen; Patterson, Kristen; Chaiworapongsa, Tinnakorn; Romero, Roberto and Ober, Carol. "The Maternal HLA-G 1597 deltaC Null Mutation is Associated with Increased Risk of Pre-Eclampsia and Reduced HLA-G Expression During Pregnancy in African-American Women". Molecular Human Reproduction. 19.3 (2013):144-152.