Platelet Antigen Genotyping Panel

Human platelet antigen (HPA) genotyping is used for fetal or neonatal testing when unexplained intracranial hemorrhage or thrombocytopenia is detected, or when parents have had a previously affected pregnancy.

Maternal and paternal testing is performed when the fetus or neonate is suspected to have neonatal alloimmune thrombocytopenia (NAIT, also referred to as perinatal alloimmune thrombocytopenia [PAT]).

Women planning a pregnancy who have a sister with a previously affected pregnancy or who have had posttransfusion purpura are also candidates for this testing.

Disease Overview

Incidence

NAIT is the most common cause of severe thrombocytopenia in healthy term neonates and occurs in 1/1,000-5,000 births.

- In Caucasians, 80% of NAIT is caused by maternal antibodies directed against HPA-1a and ~20% is caused by antibodies directed against HPA-5b.
- Posttransfusion purpura occurs in 1/50,000-100,000 transfusions.

Symptoms

- Severe thrombocytopenia in an otherwise healthy newborn
- Intracranial hemorrhage in utero, at birth, or postnatally
  - Fatal in 5-10% of affected neonates
  - Intellectual disability, seizures, cerebral palsy, or cortical blindness in up to 25% of survivors
- Widespread petechiae or purpura
- Visceral hemorrhage – often of gastrointestinal or bladder mucosa

Diagnostic Issues

- Maternal immunization against fetal platelet alloantigens may result in NAIT, which is caused by maternal-fetal HPA incompatibility and alloantigens on platelets transferred across the placenta
- Because prenatal platelet typing is not routinely performed, at-risk women are identified only after an affected pregnancy
- Recurrence risk is up to 90% and severity may increase in subsequent pregnancies
- Posttransfusion purpura is most common in women who are HPA-1a negative and immunized during a previous pregnancy
- Clinical correlation between antibody titers and NAIT occurrence is not reliable
- Specific paternal platelet antigens are demonstrated to react with alloantibodies in only 50% of cases
  - Genotyping allows for more accurate risk assessment and better pregnancy management
• Testing may be helpful to
  ○ Screen neonatal immunization during pregnancy when parents had prior affected pregnancy or when unexplained intracranial hemorrhage is detected
  ○ Assess risk of NAIT in future pregnancies
  ○ Assess risk of posttransfusion purpura and thrombocytopenia

Genetics

Genes

HPA genes (*ITGB3, GP1BA, ITGA2B, ITGA2, and CD109*)

Alleles

Approximately 29 different types of platelet-specific alloantigens have been identified.

• The more common allele is designated as "a" and the less common allele is known as “b”.
  ○ 2% of Caucasian women are homozygous for HPA-1b.
    • These women are at risk for alloimmunization during pregnancy if her reproductive partner is homozygous HPA-1a or heterozygous HPA-1a/b and contributes the HPA-1a allele to the fetus.

Test Description

Multiplex polymerase chain reaction (PCR) followed by fluorescence monitoring to detect HPA alleles:

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Gene and Glycoprotein</th>
<th>Allele</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPA-1</td>
<td><em>ITGB3</em>, GPIIIa</td>
<td>c.176T&gt;C, p.L59P</td>
</tr>
<tr>
<td>HPA-2</td>
<td><em>GP1BA</em>, GPIba</td>
<td>c.482C&gt;T, p.T161M</td>
</tr>
<tr>
<td>HPA-3</td>
<td><em>ITGA2B</em>, GPIIb</td>
<td>c.2621T&gt;G, p.I874S</td>
</tr>
<tr>
<td>HPA-4</td>
<td><em>ITGB3</em>, GPIIIa</td>
<td>c.506G&gt;A, p.R169Q</td>
</tr>
<tr>
<td>HPA-5</td>
<td><em>ITGA2</em>, GPIa</td>
<td>c.1600G&gt;A, p.E534K</td>
</tr>
<tr>
<td>HPA-6</td>
<td><em>ITGB3</em>, GPIIIa</td>
<td>c.1544G&gt;A, p.R515Q</td>
</tr>
</tbody>
</table>

Test Interpretation

Sensitivity/Specificity

• Clinical sensitivity/specificity – variable, dependent on ethnicity
• Analytical sensitivity/specificity – 99%

Results
HPA-a/a homozygous
- 2 copies of the common “a” allele

HPA-a/b heterozygous
- 1 copy of the common “a” allele and 1 copy of the less common “b” allele

HPA-b/b homozygous
- 2 copies of the less common “b” allele

Limitations

- HPA genes and variants, other than those tested, will not be detected
- Bloody amniotic fluid specimens may give false-negative results due to maternal cell contamination
- Diagnostic errors can occur due to rare sequence variations

References


Related Tests

**Platelet Antigen 1 Genotyping (HPA-1) 3001170**
Method: Polymerase Chain Reaction/Fluorescence Monitoring

**Platelet Antibodies, Indirect 0051050**
Method: Semi-Quantitative Enzyme-Linked Immunosorbent Assay

**CBC with Platelet Count 0040002**
Method: Automated Cell Count

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology. 500 Chipeta Way, Salt Lake City, UT 84108 | (800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com
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