

Platelet Antigen Genotyping Panel

Human platelet antigen (HPA) genotyping is used for fetal or neonatal testing following detection of unexplained intracranial hemorrhage (ICH) or thrombocytopenia, which raises suspicion for neonatal alloimmune thrombocytopenia (NAIT; also referred to as perinatal alloimmune thrombocytopenia [PAT]).

Maternal and paternal testing is performed when the fetus or neonate is suspected to have NAIT. Women who have had a previously affected pregnancy, have a history of posttransfusion purpura, or have a sister with a previously affected pregnancy are candidates for this testing.

Disease Overview

Incidence

NAIT is the most common cause of severe thrombocytopenia in healthy term neonates and occurs in 0.3-1/1000 births.¹

- In White individuals, 80% of NAIT is caused by maternal antibodies directed against HPA-1a and ~20% is caused by antibodies directed against HPA-5b²
- Posttransfusion purpura is estimated to occur in 1/50,000-100,000 transfusions.³

Symptoms

Symptoms of NAIT can include⁴:

- Severe thrombocytopenia in an otherwise healthy newborn
- ICH in utero, at birth, or postnatally
 - Estimated to affect 7-26% of neonates with NAIT
 - ICH is fatal in 1-10% of affected neonates
 - 14-26% of ICH survivors have neurologic sequelae (eg, intellectual disability, seizures, cerebral palsy, or cortical blindness)
- Widespread petechiae or ecchymoses
- Hematoma development at injection sites
- Bleeding after circumcision

Diagnostic Issues

- NAIT results from maternal alloimmunization to paternally inherited fetal platelet antigen; maternal alloantibodies cross the placenta and cause fetal platelet destruction and thus, fetal thrombocytopenia⁵
- Because prenatal platelet typing is not routinely performed, at-risk women are typically identified only after an affected pregnancy, although some may be identified through screening because of a sister with an affected pregnancy⁶
- Recurrence risk is approximately 85%⁷ and severity may increase in subsequent pregnancies⁸
- Posttransfusion purpura is typically caused by HPA-1a antibodies in a previously sensitized HPA-1a-negative patient who is reexposed to the alloantigen as a result of transfusion⁵
- Clinical correlation between antibody titers and NAIT occurrence is not reliable⁴
- Specific paternal platelet antigens may not react with alloantibodies; genotyping allows for more accurate risk assessment and better pregnancy management
- Testing may be helpful to
 - Screen for neonatal immunization during pregnancy when parents had a previously affected pregnancy or when unexplained ICH is detected
 - Assess risk of NAIT in future pregnancies
 - Assess risk of posttransfusion purpura and thrombocytopenia

Tests to Consider

Platelet Antigen Genotyping Panel 3000193

Method: Polymerase Chain Reaction/Fluorescence Monitoring

- Use in risk assessment for NAIT
- May be ordered for parental, fetal, or neonatal genotyping

See [Related Tests](#)

Genetics

Genes

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

Alleles

- Approximately 29 different types of platelet-specific alloantigens have been identified⁹
- The more common allele is designated as “a” and the less common allele is known as “b”⁹
 - 1.6% to 4.6% of the general population are homozygous for HPA-1b⁴
 - These women are at risk for alloimmunization during pregnancy if they have a reproductive partner who is homozygous for HPA-1a or heterozygous for 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:

Antigen	Gene and Glycoprotein	Allele
HPA-1	<i>ITGB3</i> , GPIIIa	c.176T>C, p.L59P
HPA-2	<i>GP1BA</i> , GPIba	c.482C>T, p.T161M
HPA-3	<i>ITGA2B</i> , GPIIb	c.2621T>G, p.I874S
HPA-4	<i>ITGB3</i> , GPIIIa	c.506G>A, p.R169Q
HPA-5	<i>ITGA2</i> , GPIa	c.1600G>A, p.E534K
HPA-6	<i>ITGB3</i> , GPIIIa	c.1544G>A, p.R515Q
HPA-15	<i>CD109</i> , CD109	c.2108C>A, p.S703Y

Test Interpretation

Sensitivity/Specificity

- Clinical sensitivity and specificity are variable; dependent on ethnicity
- Analytical sensitivity and specificity are 99%

Results

- HPA-a/a homozygous
 - Two copies of the common “a” allele
- HPA-a/b heterozygous
 - One copy of the common “a” allele and one copy of the less common “b” allele
- HPA-b/b homozygous
 - Two 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

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9. European Molecular Biology Laboratory-European Bioinformatics Institute (EMBL-EBI). [Immuno Polymorphism Database](#). [Accessed: Apr 2020]

Related Information

[Neonatal Alloimmune Thrombocytopenia - NAIT Thrombocytopenic Disorders](#)

Related Tests

[CBC with Platelet Count 0040002](#)

Method: Automated Cell Count

[Platelet Antibodies, Indirect 0051050](#)

Method: Semi-Quantitative Enzyme-Linked Immunosorbent Assay

[Platelet Antigen 1 Genotyping \(HPA-1\) 3001170](#)

Method: Polymerase Chain Reaction/Fluorescence Monitoring

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