

## 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.<sup>1</sup>

- In White individuals, 80% of NAIT is caused by maternal antibodies directed against HPA-1a and ~20% is caused by antibodies directed against HPA-5b<sup>2</sup>
- Posttransfusion purpura is estimated to occur in 1/50,000-100,000 transfusions.<sup>3</sup>

#### Symptoms

Symptoms of NAIT can include<sup>4</sup>:

- 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 thrombocytopenia<sup>5</sup>
- 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 pregnancy<sup>6</sup>
- Recurrence risk is approximately 85%<sup>7</sup> and severity may increase in subsequent pregnancies<sup>8</sup>
- 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 transfusion<sup>5</sup>
- Clinical correlation between antibody titers and NAIT occurrence is not reliable<sup>4</sup>
- 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

### Genetics

#### Genes

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

#### 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](#)

## Alleles

- Approximately 29 different types of platelet-specific alloantigens have been identified<sup>9</sup>
- The more common allele is designated as “a” and the less common allele is known as “b”<sup>9</sup>
  - 1.6% to 4.6% of the general population are homozygous for HPA-1b<sup>4</sup>
  - 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> , GPIIb	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

1. Lieberman L, Greinacher A, Murphy MF, et al. [Fetal and neonatal alloimmune thrombocytopenia: recommendations for evidence-based practice, an international approach.](#) *Br J Haematol.* 2019;185(3):549-562.
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4. Espinoza JP, Caradeux J, Norwitz ER, et al. [Fetal and neonatal alloimmune thrombocytopenia.](#) *Rev Obstet Gynecol.* 2013;6(1):e15-e21.
5. Heikal NM, Smock KJ. [Laboratory testing for platelet antibodies.](#) *Am J Hematol.* 2013;88(9):818-821.

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7. Mella MT, Eddleman KA. [Neonatal alloimmune thrombocytopenia.](#) *Intern J Clin Trans Med.* 2015;3;29-40.
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## Related Information

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

## Related Tests

[Platelet Antibodies, Indirect 0051050](#)

**Method:** Semi-Quantitative Enzyme-Linked Immunosorbent Assay

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