

Platelet Antigen (*HPA1-HPA6* and *HPA15*) Genotyping

Indications for Ordering

Fetal or neonatal testing when

- Parents have had a prior affected pregnancy
- Unexplained intracranial hemorrhage is detected

Maternal and paternal testing when

- 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
- With posttransfusion purpura

Test Description

Polymerase chain reaction followed by fluorescent resonance energy transfer probes for human platelet antigen (HPA) alleles

- HPA-1 (GPIIIa) c.176T>C p.L59P
- HPA-2 (GPIIb) c.482C>T p.T161M
- HPA-3 (GPIIb) c.2621T>G, p.I874S
- HPA-4 (GPIIIa) c.506G>A p.R169Q
- HPA-5 (GPIa) c.1600G>A p.E534K
- HPA-6 (GPIIIa) c.1544G>A p.R515Q
- HPA-15 CD109 c.2108A>C p.Y703S

Tests to Consider

Primary test

[Platelet Antigen Genotyping Panel 0051308](#)

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

Related tests

Individual genotyping tests for NAIT risk assessment

- [Platelet Antigen 1 Genotyping \(HPA-1\) 0051309](#)
- [Platelet Antigen 2 Genotyping \(HPA-2\) 0051310](#)
- [Platelet Antigen 3 Genotyping \(HPA-3\) 0051311](#)
- [Platelet Antigen 4 Genotyping \(HPA-4\) 0051490](#)
- [Platelet Antigen 5 Genotyping \(HPA-5\) 0051312](#)
- [Platelet Antigen 6 Genotyping \(HPA-6\) 0051313](#)
- [Platelet Antigen 15 Genotyping \(HPA-15\) 0051314](#)
- [Platelet Antibodies, Indirect with Reflex to Identification 0051718](#)

Disease Overview

Incidence – NAIT occurs in 1/1,000-5,000 births

- HPA 1a and HPA 5b are believed to cause ~80% and 20%, respectively, of NAIT in Caucasians

Symptoms

- Severe thrombocytopenia in an otherwise healthy newborn
- Intracranial hemorrhage – may occur in utero, at birth, or postnatally
 - Fatal in up to one-third of individuals
 - Causes neurologic impairment in 20-30% of individuals
- Widespread petechiae or purpura
- Visceral hemorrhage – often gastrointestinal or bladder mucosa

Diagnostic issues

- Maternal immunization against fetal platelet alloantigens may result in NAIT
 - NAIT occurs when maternal IgG antibodies, directed toward paternally derived fetal alloantigens on platelets, are transferred across the placenta
- Because prenatal platelet typing is not routinely performed, at-risk women are only identified after having a previously affected pregnancy
- Recurrence rate is up to 90% in subsequent pregnancies
 - Severity may worsen with subsequent pregnancies
- Posttransfusion purpura is seen most often in women who are HPA 1a-negative and immunized during a previous pregnancy
 - Cue to possible NAIT in subsequent pregnancies
- 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 for 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

Gene – HPA

Variants

~16 different types of HPA have been identified

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

Test Interpretation

Sensitivity/specificity

- Clinical sensitivity/specificity – unknown
- Analytical sensitivity/specificity – 99%

Results

- HPA –a/a homozygous
 - Two copies of the common human platelet antigen “a” allele
- HPA –a/b heterozygous
 - One copy of the common “a” allele and one copy of the rare “b” allele
- HPA –b/b homozygous
 - Two copies of the rare human platelet antigen “b” allele

Limitations

- HPA alleles, other than the ones tested, will not be determined
- Bloody amniotic fluid specimens may give false-negative results because of maternal cell contamination
- Diagnostic errors can occur due to rare sequence variations