Test Definition: F822B
HA F8 Intron 22 Inversion KM, B

Overview

Useful For
First-tier molecular testing for males affected with severe hemophilia A, when a familial intron 22 inversion has been previously identified

Determining hemophilia A carrier status for at-risk females, ie, individuals with a family history of severe hemophilia A due to F8 intron 22 inversion

Genetics Test Information
Detects the intron 22 inversion within the F8 gene. The intron 22 inversion mutation accounts for approximately 45% of mutations associated with severe hemophilia A.

Intron 22 inversion known mutation analysis can only be performed for individuals when an intron 22 inversion has already been identified in the family. If a mutation has not already been identified in the family, order F8INV / Hemophilia A F8 Gene, Intron 1 and 22 Inversion Mutation Analysis, Whole Blood.

Reflex Tests

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<tbody>
<tr>
<td>MATCC</td>
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Testing Algorithm
Maternal cell contamination testing will be performed for all cord blood specimens. A maternal whole blood sample with an order for MATCC / Maternal Cell Contamination, Molecular Analysis, Blood is also required to perform this test. (See Specimen Required for more details.)

The following algorithms are available in Special Instructions:

- Hemophilia Carrier Testing Algorithm
- Hemophilia Testing Algorithm

Special Instructions
- Informed Consent for Genetic Testing
- Hemophilia Carrier Testing Algorithm
- Hemophilia Testing Algorithm
- Hemophilia A Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name
Inverse Shifting-Polymerase Chain Reaction (IS-PCR)

NY State Available
Yes
Specimen

Specimen Type
Whole blood

Advisory Information
If a familial mutation has not been identified in a severely affected hemophilia A patient the F8 gene intron 1 and 22 inversion analysis (F8INV / Hemophilia A F8 Gene, Intron 1 and 22 Inversion Mutation Analysis, Whole Blood) should be ordered.

For evaluation of a patient with bleeding symptoms and no known personal history of a bleeding disorder consider BDIAL / Bleeding Diathesis Profile, Limited or the specific factor assays.

Additional Testing Requirements
Due to the complexity of testing non-peripheral blood, consultation with the laboratory is required for all cord blood samples. Order F822B / Hemophilia A F8 Gene, Intron 22 Inversion Known Mutation, Whole Blood on the cord blood specimen (only 1 sample tube required) and order MATCC / Maternal Cell Contamination, Molecular Analysis, Blood on the maternal specimen.

Necessary Information
Hemophilia A Patient Information is required, see Special Instructions. Testing may proceed without the patient information, however, the information aids in providing a more thorough interpretation. Ordering providers are strongly encouraged to fill out the form and send with the specimen.

Specimen Required
Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD) or blue top (sodium citrate)

Specimen Volume: 3 mL

Collection Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube.

Forms
1. New York Clients-Informed consent is required. Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:
   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing-Spanish (T826)
2. If not ordering electronically, complete, print, and send a Coagulation Test Request (T753) with the specimen.
Specimen Minimum Volume
1 mL

Reject Due To

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Specimen Stability Information

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<tr>
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<tr>
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Clinical and Interpretive

Clinical Information

Hemophilia A (HA) is caused by a deficiency of clotting factor VIII (FVIII). HA is an X-linked recessive bleeding disorder that affects approximately 1 in 5000 males. Males are typically affected with bleeding symptoms, whereas carrier females generally do not have bleeding symptoms but are at risk of having affected sons. Rarely, approximately 10% of carrier females have FVIII activity levels below 35% and are at risk for bleeding.

Bleeding, the most common clinical symptom in individuals with HA, correlates with FVIII activity levels. FVIII activity levels below 1% are associated with severe disease, 1% to 5% activity with moderate disease, and 5% to 40% with mild disease. In males with severe deficiency, spontaneous bleeding may occur. In individuals with mild HA, bleeding may occur only after surgery or trauma.

FVIII is encoded by the factor VIII (F8) gene. Approximately 98% of patients with a diagnosis of HA are found to have a mutation in F8 (ie, intron 1 and 22 inversions, point mutations, insertions, and deletions). The intron 22 inversion mutations account for approximately 45% of mutations associated with severe HA. These inversions are typically not identified in patients with mild or moderate HA.

Intron 22 inversion known mutation analysis is only recommended for individuals when an intron 22 inversion has already been identified in the family.

If a familial mutation has not been identified in a severely affected HA patient the F8 gene intron 1 and 22 inversion analysis (F8INV / Hemophilia A F8 Gene, Intron 1 and 22 Inversion Mutation Analysis, Whole Blood) should be ordered.

If the intron 22 inversion analysis is negative, the tested individual has not inherited the familial mutation.

It is recommended that the F8 mutation be confirmed in the affected male or obligate carrier female prior to testing at-risk individuals. Affected males are identified by FVIII activity (F8A / Coagulation Factor VIII Activity Assay, Plasma) and clinical evaluation, while obligate carrier females are identified by family history assessment. If the intron inversion assays do not detect an inversion in these individuals, additional analysis (ie, F8 sequencing) may be able
to identify the familial mutation. Of note, not all females with an affected son are germline carriers of a F8 mutation, as de novo mutations in F8 do occur. Approximately 20% of mothers of isolated cases do not have an identifiable germline F8 mutation. Importantly, there is a small risk for recurrence even when the familial F8 mutation is not identified in the mother of the affected patient due to the possibility of germline mosaicism.

Reference Values
An interpretive report will be provided.

Interpretation
The interpretive report will include assay information, background information, and conclusions based on the test results.

Cautions
Obtaining a medical genetics or hematology (coagulation) consultation prior to ordering is advisable. Consultations with the Mayo Clinic Special Coagulation Clinic, Molecular Hematopathology Laboratory, or Thrombophilia Center are available for DNA diagnosis cases. This may be especially helpful in complex cases or in situations where the diagnosis is atypical or uncertain.

Intron 22 inversion known mutation analysis is only recommended for individuals when an intron 22 inversion has already been identified in the family.

This assay detects only F8 intron 22 inversion mutations. Thus, a negative result does not exclude the presence of other mutations in F8.

The intron 22 inversion mutation targeted by this assay is found in approximately 45% of individuals with severe hemophilia A; if an intron 22 inversion has not been already identified in the family, the assay may be uninformative.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

Clinical Reference

Performance

Method Description

**Test Definition: F822B**

HA F8 Intron 22 Inversion KM, B

Performed weekly; Varies

**Analytic Time**

14 days

**Maximum Laboratory Time**

21 days

**Specimen Retention Time**

Whole Blood: 2 weeks; DNA: Indefinitely

**Performing Laboratory Location**

Rochester

**Fees and Codes**

**Fees**

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

**Test Classification**

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

**CPT Code Information**

81403

**LOINC® Information**

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