Test Definition: FIXKM

F9 Gene Known Mutation, B

Overview

Useful For

Diagnostic, targeted testing for hemophilia B when a mutation has been identified in a family member

Carrier testing of females in whom the familial *F9* genotype is known

Genetics Test Information

Documentation of the specific familial mutation must be provided with the specimen in order to perform this test.

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
MATCC	Maternal Cell Contamination, B	Yes	No

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

- Hemophilia B Patient Information
- Informed Consent for Genetic Testing
- Hemophilia Carrier Testing Algorithm
- Hemophilia Testing Algorithm
- Informed Consent for Genetic Testing (Spanish)

Method Name

Polymerase Chain Reaction (PCR)/Sanger Sequencing

NY State Available

Yes

Specimen

Specimen Type

Whole blood

Additional Testing Requirements

Due to the complexity of testing non-peripheral blood, consultation with the laboratory is required for all

cord blood samples. Order FIXKM / Hemophilia B, *F9* Gene 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 B 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

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

Gross hemolysis	OK
Gross lipemia	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Whole blood	Ambient (preferred)	7 days	
	Frozen	7 days	
	Refrigerated	7 days	

Clinical and Interpretive

Clinical Information

Hemophilia B, factor IX deficiency, is an X-linked recessive bleeding disorder with an incidence of about 1 per 30,000 live male births. It occurs as a result of mutations in the factor IX (*F9*) gene. As many as one-third of hemophiliacs have no affected family members, which reflects a high mutation rate in the *F9* gene (ie, de novo mutations). Hemophilia B affects males; however, all male offspring from an affected male will be normal. Although all female offspring of affected males will be obligatory carriers, they rarely have symptomatic bleeding. In contrast, female offspring of female carriers of hemophilia B have a 50% chance of being carriers themselves, and each male offspring has a 50% chance of being affected.

Based on factor IX activity, hemophilia B is classified as severe (factor IX activity <1%), moderate (factor IX activity 1%-5%), or mild (factor IX activity >5%-40%). In males, low factor IX activity level establishes the diagnosis of hemophilia B. However, the wide range of normal factor IX activity precludes an accurate assessment of carrier status in females, thus making molecular testing essential in assessment of carrier status.

Inhibitors to factor IX activity are estimated to occur in 5% to 8% of patients, much less than that of hemophilia A. Inhibitor risk correlates with genotype and typically occurs in patients with either partial or total deletions of the *F9* gene or in certain nonsense mutations that result in no circulating factor IX antigen. More recently, it has been observed that a subset of patients with such mutations may be at risk of experiencing anaphylactic reactions to the factor IX replacement therapy.

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.

Clinical Reference

1. Yoshitake S, Schach BG, Foster DC, et al: Nucleotide sequence of the gene for human factor IX (antihemophilic factor B). Biochemistry 1985 July 2;24(14):3736-3750

2. Giannelli F, Green PM, Sommer SS, et al: Haemophilia B: database of point mutations and short additions and deletions. Eighth edition. Nucleic Acids Res 1998 Jan 1;26(1):265-268

3. Ketterling RP, Bottema CD, Phillips JA 3rd, et al: Evidence that descendants of three founders constitute about 25% of hemophilia B in the United States. Genomics 1991 Aug;10(4):1093-1096

4. Johnsen JM, Fletcher SN, Huston H, et al: Novel approach to genetic analysis and results in 3000 hemophilia patients enrolled in the My Life, Our Future initiative. Blood Adv 2017 May;1(13):824-834 doi:10.1182/bloodadvances.2016002923

Performance

Method Description

Direct mutation analysis of leukocyte genomic DNA performed by PCR amplification of of a single region of the *F9* gene, followed by fluorescent DNA sequencing analysis utilizing an Applied Biosystems Inc (ABI) 3730*xl* DNA Analyzer.(Costa JM, Ernault P, Vidaud D, et al: Fast and efficient mutation detection method using multiplex PCR and cycle sequencing--application to haemophilia B. Thromb Haemost 2000;83[2]:244-247; Kaiser RJ, MacKellar SL, Vinayak RS, et al: Specific-primer-directed DNA sequencing using automated fluorescence detection. Nucleic Acids Res 1989;17[15]:6087-6102; Meijer P, Verbruggen, Spannagi M: Clotting factors and inhibitors: Assays and Interpretation. Chapter 33. In Laboratory Hematology Practice. Edited by K Kottke-Marchant. Wiley Blackwell Publishing. 2012, pp 435-446)

PDF Report

No

Day(s) and Time(s) Test Performed

Performed weekly; Varies

Analytic Time

21 days

Maximum Laboratory Time

28 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-Known familial variant not otherwise specified, for gene listed in Tier 1 or Tier 2, DNA sequence analysis, each variant exon

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
FIXKM	F9 Gene Known Mutation, B	69483-6

Test Definition: FIXKM

F9 Gene Known Mutation, B

Result ID	Test Result Name	Result LOINC Value
23763	F9 Known Mut Reason for Referral	42349-1
23764	F9 Known Mutation Method	49549-9
23765	F9 Known Mutation Result	38896-7
23766	F9 Known Mutation Interpretation	69047-9
37320	F9 Known Mutation Specimen Type	31208-2
23768	F9 Known Mutation Reviewed By	18771-6