

Overview

Useful For

Genetic confirmation of a factor X deficiency diagnosis with the identification of a known or suspected pathogenic alterations in the *F10* gene

Carrier testing for close family members of an individual with a factor X deficiency diagnosis

This test is **not intended for** prenatal diagnosis.

Genetics Test Information

This test detects pathogenic alterations within the *F10* gene to delineate the underlying molecular defect in a patient with a laboratory diagnosis of factor X deficiency, a rare bleeding disorder.

The gene target for this test is:

Gene name (transcript): *F10* (GRCh 37 [hg19] NM_000504)

Chromosomal location: 13q34

Testing Algorithm

[Genetic testing for factor X deficiency \(F10D\)](#) should only be considered after coagulation screening is performed and if factor X activity is less than 65% of normal (Note: reference ranges may vary depending on the locally established reference range).

Genetic testing for F10D is indicated if:

-Factor X clotting activity is reduced (less than 80% of normal)

-Acquired causes of factor X deficiency have been excluded (eg, liver disease, warfarin therapy, vitamin K deficiency, systemic amyloidosis, and inhibitors)

Special Instructions

- [Informed Consent for Genetic Testing](#)
- [Informed Consent for Genetic Testing \(Spanish\)](#)

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- [Rare Coagulation Disorder Patient Information](#)

Method Name

Custom Sequence Capture and Targeted Next-Generation Sequencing (NGS) followed by Polymerase Chain Reaction (PCR) and Sanger Sequencing when appropriate

NY State Available

Yes

Specimen**Specimen Type**

Varies

Ordering Guidance

The clinical workup for factor X deficiency (F10D) begins with special coagulation testing for factor X. Order F_10 / Coagulation Factor X Activity Assay, Plasma.

Shipping Instructions

Ambient and refrigerated specimens **must** arrive within 7 days of collection, and frozen specimens must arrive within 14 days.

Collect and package specimen as close to shipping time as possible.

Necessary Information

[Rare Coagulation Disorder Patient Information](#) is required. 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

Submit only 1 of the following specimens:

Specimen Type: Whole blood

Container/Tube:

Preferred: Lavender top (EDTA)

Acceptable: Yellow top (ACD) or light-blue top (3.2% sodium citrate)

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**

Specimen Stability: Ambient (preferred)/Refrigerated/Frozen

Specimen Type: Extracted DNA

Container/Tube: 1.5- to 2-mL tube

Specimen Volume: Entire specimen

Collection Instructions:

1. Label specimen as extracted DNA and source of specimen.
2. Provide indication of volume and concentration of the DNA.

Specimen Stability: Frozen (preferred)/Refrigerated/Ambient

Forms

1. [Rare Coagulation Disorder Patient Information \(T824\)](#) is required. Fax the completed form to 507-284-1759.
2. **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:

-[Informed Consent for Genetic Testing \(T576\)](#)

-[Informed Consent for Genetic Testing-Spanish \(T826\)](#)

3. If [not ordering electronically, complete, print, and send a Coagulation Test Request \(T753\)](#) with the specimen.

Reject Due To

Gross hemolysis OK
Gross lipemia OK

Specimen Minimum Volume

Blood: 1 mL

Extracted DNA: 100 mcL at 50 ng/mcL concentration

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)	7 days	
	Frozen	14 days	
	Refrigerated	7 days	

Clinical & Interpretive
Clinical Information

Factor X (FX) deficiency (F10D) is a bleeding diathesis of variable severity that may appear at any age, although more severely affected patients, who typically have FX activity less than 1%, present early in life. Symptoms include umbilical stump bleeding, intracranial hemorrhage, gastrointestinal bleeding, joint bleeds, and hematomas. The most severe clinical symptoms are uncommon in a patient with FX activity levels greater than 2%. Regardless of disease severity, the most common bleeding symptom is nose bleeds. Menorrhagia occurs in more than half of women with F10D but miscarriages are not common. Antepartum and postpartum hemorrhage are reportedly common in women with F10D and also has been reported in heterozygous females.

F10D is estimated to affect 1 in 1,000,000 people. If genetic, F10D is inherited in an autosomal recessive manner. Both males and females may be affected.

Hereditary F10D results from defects in the concentration or function of coagulation FX, a vitamin-K dependent protein synthesized in the liver that is essential for stopping blood loss after injury. FX circulates in blood plasma as an inactive zymogen. It is activated by either the intrinsic or extrinsic pathway and is the most important activator of prothrombin, which has multiple roles in the hemostatic response to injury.

The *F10* gene produces coagulation FX. Alterations in the *F10* gene can interfere with the production of coagulation FX, leading to lower levels of the factor in blood (type I F10D) or dysfunctional factor protein that is produced in normal amounts (type II F10D). The bleeding tendency in F10D is variable and does not always correlate with circulating FX antigen levels. In general, however, lower FX activity levels predict a higher risk for bleeding. FX activity of less than 1% of normal is associated with severe F10D, activity of 1% to 5% of normal is associated with moderate disease, and a FX activity of 6% to 10% is associated with mild disease. Of note, normal, full-term newborn infants or healthy premature infants may have decreased levels (greater than or equal to 15% to 20% of normal), which may not reach adult levels for greater than or equal to 180 days after birth.

Acquired deficiency of FX is more common than hereditary F10D. Causes of acquired (non-genetic) F10D that should be excluded prior to genetic testing include liver disease, warfarin therapy, vitamin K deficiency, and (rarely) inhibitors. Acquired isolated F10D is seen in 6% to 14% of individuals with primary amyloidosis. Other conditions associated with acquired isolated F10D include underlying malignancy, especially acute myeloid leukemia, and respiratory infection. Conditions associated with acquired F10D should be considered prior to genetic testing.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Evaluation and categorization of variants is performed using the most recent published American College of Medical Genetics and Genomics (ACMG) recommendations as a guideline. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.

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.

Cautions

Clinical:

Some individuals may have a variant that is not identified by the methods performed. The absence of a variant, therefore, does not eliminate the possibility of factor X deficiency or a related disorder. This assay does not distinguish between germline and somatic alterations, particularly with variant allele frequencies significantly lower than 50%. Test results should be interpreted in context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Technical Limitations:

Next-generation sequencing (NGS) may not detect all types of genetic variants. Additionally, rare variants (ie, polymorphisms) may be present that could lead to false-negative or false-positive results. Therefore, test results should be interpreted in the context of activity and antigen measurements, clinical findings, family history, and other laboratory data. If results do not match clinical findings, consider alternative methods for analyzing these genes, such as Sanger sequencing or large deletion/duplication analysis. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

If multiple alterations are identified, NGS is not able to distinguish between alterations that are found in the same allele ("in cis") and alterations found on different alleles ("in trans"). This limitation may complicate diagnosis or classification and has implications for inheritance and genetic counseling. To resolve these cases, molecular results must be correlated with clinical history, activity and antigen measurements, and family studies.

Unless reported or predicted to cause disease, alterations found deep in the intron or alterations that do not result in an amino acid substitution are not reported. These and common alterations (ie, polymorphisms) identified for this patient are available upon request.

Reclassification of Variants Policy:

At this time, it is not standard practice for the laboratory to systematically review likely pathogenic variants or variants of uncertain significance that are detected and reported. The laboratory encourages health care providers to contact the laboratory at any time to learn how the status of a particular variant may have changed over time.

Clinical Reference

1. Brown DL, Kouides PA: Diagnosis and treatment of inherited factor X deficiency. *Haemophilia*. 2008 Nov;14(6):1176-1182
2. Karimi M, Menegatti M, Afrasiabi A, et al: Phenotype and genotype report on homozygous and heterozygous patient with congenital factor X deficiency. *Haematologica*. 2008 Jun;93(6):934-938
3. Lee G, Duan-Porter W, Metjian AD: Acquired, non-amyloid related factor X deficiency: review of the literature. *Haemophilia*. 2012 Sep;18(5):655-663
4. Mumford AD, Ackroyd S, Alikhan R, et al: Guidelines for the diagnosis and management of the rare coagulation disorders: a United Kingdom Haemophilia Centre Doctors' Organization guidelines on behalf of the British Committee for Standards in Haematology. *Br J Haematol*. 2014 Nov;167(3):304-326
5. Nance D, Josephson NC, Paulyson-Nunez K, et al: Factor X deficiency and pregnancy: preconception counseling and therapeutic options. *Haemophilia*. 2012 May;18(3):e277-285
6. Palla R, Peyvandi F, Shapiro AD: Rare bleeding disorders: diagnosis and treatment. *Blood*. 2015 Mar;125(13):2052-2061
7. Menegatti M, Peyvandi F: Factor X deficiency. *Semin Thromb Hemost*. 2009 Jun;35(4):407-415

Performance

Method Description

Next-generation sequencing (NGS) and/or Sanger sequencing are performed.

Regions of homology, high guanine-cytosine (GC)-rich content, and repetitive sequences may not provide accurate sequence. Therefore, all reported alterations detected by NGS in these regions are confirmed by an independent reference method. However, this does not rule out the possibility of a false-negative result in these regions.

Sanger sequencing is used to confirm alterations detected by NGS when appropriate. (Unpublished Mayo method)

PDF Report

No

Specimen Retention Time

Whole Blood: 2 weeks; DNA: Indefinitely

Performing Laboratory Location

Rochester

Fees & Codes**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 US Food and Drug Administration.

CPT Code Information

81479

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
F10NG	F10 Gene, Full Gene NGS	92990-1

Result ID	Reporting Name	LOINC®
113052	F10NG Result	50397-9
113045	Interpretation	69047-9
113046	Alterations Detected	82939-0

113047	Additional Information	48767-8
113048	Method	85069-3
113049	Disclaimer	62364-5
113050	Panel Gene List	48018-6
113051	Reviewed By	18771-6