

## F9 gene

coagulation factor IX

### Normal Function

The *F9* gene provides instructions for making a protein called coagulation factor IX. Coagulation factors are a group of related proteins that are essential for the formation of blood clots. After an injury, clots protect the body by sealing off damaged blood vessels and preventing further blood loss.

Coagulation factor IX is made in the liver. This protein circulates in the bloodstream in an inactive form until an injury that damages blood vessels occurs. In response to injury, coagulation factor IX is activated by another coagulation factor called factor XIa. The active protein (sometimes written as coagulation factor IXa) interacts with coagulation factor VIII and other molecules. These interactions set off a chain of additional chemical reactions that form a blood clot.

### Health Conditions Related to Genetic Changes

#### Hemophilia

Mutations in the *F9* gene cause a type of hemophilia called hemophilia B. More than 900 alterations in this gene have been identified. The most common mutations change single DNA building blocks (base pairs) in the gene. A small percentage of mutations delete or insert multiple base pairs or rearrange segments of DNA within the gene.

Mutations in the *F9* gene lead to the production of an abnormal version of coagulation factor IX or reduce the amount of this protein. The altered or missing protein cannot participate effectively in the blood clotting process. As a result, blood clots cannot form properly in response to injury. These problems with blood clotting lead to excessive bleeding that can be difficult to control. Mutations that completely eliminate the activity of coagulation factor IX result in severe hemophilia. Mutations that reduce but do not eliminate the protein's activity usually cause mild or moderate hemophilia.

Several mutations near the beginning of the *F9* gene sequence cause an unusual form of hemophilia known as hemophilia B Leyden. People with these mutations are born with very low levels of functional coagulation factor IX, but hormonal changes cause the levels of this protein to increase gradually during puberty. As a result, adults with hemophilia B Leyden rarely experience episodes of abnormal bleeding.

## Warfarin sensitivity

MedlinePlus Genetics provides information about Warfarin sensitivity

## Other disorders

Several rare mutations in the *F9* gene cause an increased sensitivity (hypersensitivity) to a drug called warfarin. This medication is an anticoagulant, which means it is used to prevent the formation or growth of abnormal blood clots. Warfarin works by reducing the amount of active factor IX and three other coagulation proteins.

The mutations responsible for warfarin hypersensitivity each change a single base pair in the *F9* gene. These mutations do not cause hemophilia B, and people with these genetic changes only have bleeding problems if they are treated with warfarin. Warfarin reduces the amount of coagulation factor IX to very low levels in these individuals, which prevents the blood from clotting normally and can lead to recurrent, severe bleeding problems. To avoid these complications, people with warfarin hypersensitivity can be treated with other anticoagulant medications.

## **Other Names for This Gene**

- Christmas factor
- coagulation factor IX (plasma thromboplastic component, Christmas disease, hemophilia B)
- FA9\_HUMAN
- Factor 9
- FIX
- HEMB
- Plasma thromboplastin component
- PTC

## **Additional Information & Resources**

### Tests Listed in the Genetic Testing Registry

- Tests of F9 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2158\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2158[geneid]))

### Scientific Articles on PubMed

- PubMed ([https://pubmed.ncbi.nlm.nih.gov/?term=%28%28F9%5BTI%5D%29+OR+%28factor+IX%5BMAJR%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D\)](https://pubmed.ncbi.nlm.nih.gov/?term=%28%28F9%5BTI%5D%29+OR+%28factor+IX%5BMAJR%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D)))

## Catalog of Genes and Diseases from OMIM

- COAGULATION FACTOR IX; F9 (<https://omim.org/entry/300746>)

## Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/2158>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=F9\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=F9[gene]))

## **References**

- Bolton-Maggs PH, Pasi KJ. Haemophilias A and B. *Lancet*. 2003 May24;361(9371):1801-9. doi: 10.1016/S0140-6736(03)13405-8. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12781551>)
- Bowen DJ. Haemophilia A and haemophilia B: molecular insights. *Mol Pathol*.2002 Apr;55(2):127-44. doi: 10.1136/mp.55.2.127. Erratum In: *Mol Pathol* 2002Jun;55(3):208. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11950963>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1187163/>)
- Chu K, Wu SM, Stanley T, Stafford DW, High KA. A mutation in the propeptide of Factor IX leads to warfarin sensitivity by a novel mechanism. *J Clin Invest*. 1996Oct 1;98(7):1619-25. doi: 10.1172/JCI118956. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/8833911>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC507595/>)
- Giangrande P. Haemophilia B: Christmas disease. *Expert Opin Pharmacother*. 2005Aug;6(9):1517-24. doi: 10.1517/14656566.6.9.1517. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/16086639>)
- Kristensen SR. Warfarin treatment of a patient with coagulation factor IX propeptide mutation causing warfarin hypersensitivity. *Blood*. 2002 Oct1;100(7):2676-7. doi: 10.1182/blood-2002-06-1753. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/12360981>)
- Lillicrap D. The molecular basis of haemophilia B. *Haemophilia*. 1998Jul;4(4):350-7. doi: 10.1046/j.1365-2516.1998.440350.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9873754>)
- Oldenburg J, Kriz K, Willemin WA, Maly FE, von Felten A, Siegemund A, Keeling DM, Baker P, Chu K, Konkle BA, Lammle B, Albert T; Study Group on Hereditary Warfarin Sensitivity. Genetic predisposition to bleeding during oral anticoagulant therapy: evidence for common founder mutations (FIXVal-10 and FIXThr-10) and an independent CpG hotspot mutation (FIXThr-10). *Thromb Haemost*.2001 Mar;85(3):454-7. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/11307814>)
- Oldenburg J, Quenzel EM, Harbrecht U, Fregin A, Kress W, Muller CR, Hertfelder HJ, Schwaab R, Brackmann HH, Hanfland P. Missense mutations at ALA-10 in the factor IX propeptide: an insignificant variant in normal life but a decisive cause of bleeding during oral anticoagulant therapy. *Br J Haematol*. 1997Jul;

98(1):240-4. doi: 10.1046/j.1365-2141.1997.2213036.x. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/9233593>)

- Ulrich S, Brand B, Speich R, Oldenburg J, Asmis L. Congenital hypersensitivity to vitamin K antagonists due to FIX propeptide mutation at locus -10: a (not so) rare cause of bleeding under oral anticoagulant therapy in Switzerland. *Swiss Med Wkly*. 2008 Feb 23;138(7-8):100-7. doi: 10.4414/smw.2008.12022. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/18293119>)
- Zogg T, Brandstetter H. Activation mechanisms of coagulation factor IX. *Biol Chem*. 2009 May-Jun;390(5-6):391-400. doi: 10.1515/BC.2009.057. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/19361276>)

## Genomic Location

The *F9* gene is found on the X chromosome (<https://medlineplus.gov/genetics/chromosome/x/>).

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