F9 gene
coaulation 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
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.

**Chromosomal Location**

Cytogenetic Location: Xq27.1, which is the long (q) arm of the X chromosome at position 27.1

Molecular Location: base pairs 139,530,720 to 139,563,459 on the X chromosome (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)

Credit: Genome Decoration Page/NCBI

**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

Educational Resources
• Biochemistry (fifth edition, 2002): Blood clotting cascade diagram
  https://www.ncbi.nlm.nih.gov/books/NBK22589/?rendertype=figure&id=A1401

Clinical Information from GeneReviews
• Hemophilia B
  https://www.ncbi.nlm.nih.gov/books/NBK1495

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28F9%5BTI%5D%29+OR+%28factor+IX%5BMAJR%5D%29%29+AND+%28%28Genes%5BMH%5D%29%29+AND+human%5Bmh%5D+AND+%22last+1440+days%22+AND+english%5Bla

Catalog of Genes and Diseases from OMIM
• COAGULATION FACTOR IX
  http://omim.org/entry/300746

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology
• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=F9%5Bgene%5D
• Haemophilia B Mutation Database
  http://www.factorix.org/
• HGNC Gene Symbol Report
• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:2158
• NCBI Gene
• UniProt
  https://www.uniprot.org/uniprot/P00740
Sources for This Summary


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