F5 gene

coagulation factor V

Normal Function

The *F5* gene provides instructions for making a protein called coagulation factor V. Coagulation factors are a group of related proteins that make up the coagulation system, a series of chemical reactions that form blood clots. After an injury, clots seal off blood vessels to stop bleeding and trigger blood vessel repair.

The factor V protein is made primarily by cells in the liver. The protein circulates in the bloodstream in an inactive form until the coagulation system is activated by an injury that damages blood vessels. When coagulation factor V is activated, it interacts with coagulation factor X. The active forms of these two coagulation factors (written as factor Va and factor Xa, respectively) form a complex that converts an important coagulation protein called prothrombin to its active form, thrombin. Thrombin then converts a protein called fibrinogen into fibrin, which is the material that forms the clot.

Coagulation factor V has another role in regulating the coagulation system through its interaction with activated protein C (APC). APC normally inactivates coagulation factor V by cutting (cleaving) it at specific sites. This inactivation slows down the clotting process and prevents clots from growing too large. When coagulation factor V is cleaved at a particular site (protein position 506), it can work with APC to inactivate factor VIIIa, which is another protein that is essential for normal blood clotting.

Health Conditions Related to Genetic Changes

Factor V deficiency

At least 100 variants (also called mutations) in the *F5* gene have been found to cause a rare bleeding disorder called factor V deficiency. These variants prevent the production of functional coagulation factor V or significantly reduce the amount of the protein in the bloodstream. People with this condition typically have less than 10 percent of normal levels of coagulation factor V in their blood; the most severely affected individuals have less than 1 percent. A reduced amount of functional factor V prevents blood from clotting normally, causing episodes of abnormal bleeding that can be severe. Factor V deficiency results from variants in both copies of the *F5* gene, although some people with a variant in a single copy of the gene have mild bleeding problems.

Factor V Leiden thrombophilia

Factor V Leiden is the name of a specific variant in the *F5* gene. This variant changes a single protein building block (amino acid) in the factor V protein. Specifically, it replaces the amino acid arginine with the amino acid glutamine at protein position 506 (written as Arg506Gln or R506Q). Because position 506 is one of the sites where APC normally cleaves coagulation factor V, the factor V Leiden variant slows the rate at which APC inactivates this factor. As a result, both the activated form of coagulation factor V and coagulation factor VIIIa persist longer in circulation, increasing the risk of developing an abnormal blood clot. This tendency to form abnormal clots that can block blood vessels is known as thrombophilia.

The presence of the factor V Leiden variant in one or both copies of the *F5* gene can cause thrombophilia; two copies of the variant lead to a higher risk of developing abnormal blood clots than a single copy of the variant.

Other disorders

Some people have the factor V Leiden variant (Arg506Gln) in one copy of the *F5* gene and a variant associated with factor V deficiency in the other copy of the gene in each cell. The factor V Leiden variant results in the production of an abnormal coagulation factor V protein that is resistant to inactivation by APC, while the other variant prevents the production of any coagulation factor V protein. This combination of variants is associated with an increased risk of abnormal blood clots similar to the risk associated with having two copies of the factor V Leiden variant. This rare condition is known as pseudohomozygous APC resistance or pseudohomozygous factor V Leiden.

The factor V Leiden variant is involved in some cases of a condition known as Budd-Chiari syndrome. This condition is characterized by a blockage of blood flow from the liver, which can be caused by a blood clot. People with thrombophilia, including that caused by the factor V Leiden variant, have an increased risk of developing Budd-Chiari syndrome. Signs and symptoms of the syndrome include pain in the abdomen, an abnormally large liver (hepatomegaly), and accumulation of fluid in the lining of the abdomen (ascites).

Other Names for This Gene

- blood coagulation factor V
- coagulation factor V (proaccelerin, labile factor)
- factor V

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of F5 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2153[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28factor+V%5BTI%5D%29+OR+%28coagulation+factor+V%5BTIAB%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+360+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- COAGULATION FACTOR V; F5 (https://omim.org/entry/612309)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/2153)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=F5[gene])

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Genomic Location

The *F5* gene is found on chromosome 1 (https://medlineplus.gov/genetics/chromosome/1/).

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