F12 Gene

Subjects: Genetics & Heredity
Contributor: Vivi Li

Coagulation factor XII

Keywords: genes

1. Normal Function

The *F12* gene provides instructions for making a protein called coagulation factor XII. Coagulation factors are a group of related proteins that are essential for normal blood clotting (coagulation). After an injury, clots protect the body by sealing off damaged blood vessels and preventing further blood loss. Factor XII circulates in the bloodstream in an inactive form until it is activated, usually by coming in contact with damaged blood vessel walls. Upon activation, factor XII interacts with coagulation factor XI. This interaction sets off a chain of additional chemical reactions that form a blood clot.

Factor XII also plays a role in stimulating inflammation, a normal body response to infection, irritation, or other injury. When factor XII is activated, it also interacts with a protein called plasma prekallikrein. This interaction initiates a series of chemical reactions that lead to the release of a protein called bradykinin. Bradykinin promotes inflammation by increasing the permeability of blood vessel walls, allowing more fluids to leak into body tissues. This leakage causes the swelling that accompanies inflammation.

2. Health Conditions Related to Genetic Changes

2.1 Hereditary Angioedema

At least two mutations in the *F12* gene are associated with hereditary angioedema type III. These mutations change single protein building blocks (amino acids) in factor XII, which increases the activity of the protein. As a result, more bradykinin is produced, which allows additional fluids to leak through blood vessel walls. The accumulation of fluids in body tissues leads to the episodes of swelling in people with hereditary angioedema type III.

2.2 Other Disorders

Approximately 20 mutations in the *F12* gene that cause factor XII deficiency have been identified. Factor XII deficiency is an inherited condition characterized by a shortage of factor XII in the blood. Individuals with this condition usually do not experience abnormal bleeding or other symptoms. Factor XII deficiency is typically discovered during routine blood testing because reduced levels of factor XII cause the blood to take longer to clot in a test tube. Most of the mutations that cause factor XII deficiency change single amino acids, which alters the structure of factor XII. It remains unclear why individuals with factor XII deficiency do not experience abnormal bleeding like those with deficiencies of other coagulation factors.

3. Other Names for This Gene

- coagulation factor XII (Hageman factor)
- FA12_HUMAN
- HAE3
- HAEX
- HAF
- Hageman factor

References

1. Cichon S, Martin L, Hennies HC, Müller F, Van Driessche K, Karpushova A,Stevens W, Colombo R, Renné T, Drouet C, Bork K, Nöthen MM. Increased activity ofcoagulation factor XII (Hageman factor) causes hereditary angioedema type III. AmJ Hum Genet. 2006 Dec;79(6):1098-104.
2. Dewald G, Bork K. Missense mutations in the coagulation factor XII (Hagemanfactor) gene in hereditary angioedema with normal C1 inhibitor. Biochem BiophysRes Commun. 2006 May 19;343(4):1286-9.
3. Lombardi AM, Bortoletto E, Scarparo P, Scapin M, Santarossa L, Girolami A.Genetic study in patients with factor XII deficiency: a report of three newmutations exon 13 (Q501STOP), exon 14 (P547L) and -13C>T promoter region in threecompound heterozygotes. Blood Coagul Fibrinolysis. 2008 Oct;19(7):639-43. doi:10.1097/MBC.0b013e32830d8629.
4. Martin L, Raison-Peyron N, Nöthen MM, Cichon S, Drouet C. Hereditaryangioedema with normal C1 inhibitor gene in a family with affected women and men is associated with the p.Thr328Lys mutation in the F12 gene. J Allergy ClinImmunol. 2007 Oct;120(4):975-7.
5. Renné T, Gailani D. Role of Factor XII in hemostasis and thrombosis: clinical implications. Expert Rev Cardiovasc Ther. 2007 Jul;5(4):733-41. Review.
6. Schmaier AH. The elusive physiologic role of Factor XII. J Clin Invest. 2008Sep;118(9):3006-9. doi: 10.1172/JCI36617. Review.
