CFI gene

complement factor I

Normal Function

The *CFI* gene provides instructions for making a protein called complement factor I. This protein helps regulate a part of the body's immune response known as the complement system. The complement system is a group of proteins that work together to destroy foreign invaders (such as bacteria and viruses), trigger inflammation, and remove debris from cells and tissues. This system must be carefully regulated so it targets only unwanted materials and does not attack the body's healthy cells. Complement factor I and several related proteins protect healthy cells by preventing activation of the complement system when it is not needed.

Health Conditions Related to Genetic Changes

Complement factor I deficiency

At least 10 mutations in the *CFI* gene have been identified in people with complement factor I deficiency, a disorder characterized by immune system dysfunction. The mutations result in abnormal, nonfunctional, or absent complement factor I.

The lack (deficiency) of functional complement factor I protein allows uncontrolled activation of the complement system. The unregulated activity of the complement system decreases blood levels of another complement protein called C3, reducing the immune system's ability to fight infections. In addition, the immune system may malfunction and attack its own tissues, resulting in autoimmune disorders.

Age-related macular degeneration

Atypical hemolytic-uremic syndrome

C3 glomerulopathy

Other disorders

Mutations in the *CFI* gene have also been found in people with glomerulonephritis with isolated C3 deposits. This condition, which may also occur in people with complement factor I deficiency, is characterized by kidney malfunction that can be serious or life-threatening. The *CFI* gene mutations identified in this disorder result in an abnormal or nonfunctional version of complement factor I. The defective protein allows uncontrolled activation of the complement system. The overactive complement

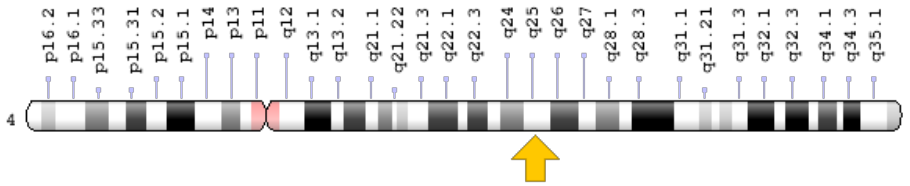
system attacks certain kidney cells, which damages the kidneys and leads to a loss of protein in the urine (proteinuria).

A common variation (polymorphism) in the *CFI* gene has also been associated with age-related macular degeneration (AMD). AMD is a leading cause of vision loss among older adults. It is characterized by damage to the retina and a loss of sharp vision (visual acuity). Researchers suggest that the *CFI* gene variation that has been associated with AMD changes the way the gene is activated (expressed). It is unclear how this change is related to the development of AMD. A combination of genetic and environmental factors likely determines the risk of developing this complex eye disorder.

Chromosomal Location

Cytogenetic Location: 4q25, which is the long (q) arm of chromosome 4 at position 25

Molecular Location: base pairs 109,731,221 to 109,802,225 on chromosome 4 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- AHUS3
- C3b-INA
- C3b-inactivator
- C3B/C4B inactivator
- C3BINA
- CFAI_HUMAN
- complement component I
- complement control protein factor I
- complement factor I heavy chain
- complement factor I preproprotein
- FI

- IF
- KAF
- Konglutinogen-activating factor
- light chain of factor I

Additional Information & Resources

Educational Resources

- Immunobiology (fifth edition, 2001): The Complement System and Innate Immunity
  https://www.ncbi.nlm.nih.gov/books/NBK27100/
- The Merck Manual for Healthcare Professionals: Complement System
  https://www.merckmanuals.com/professional/immunology-allergic-disorders/biology-of-the-immune-system/complement-system.html?qt=&sc=&alt=

Clinical Information from GeneReviews

- Genetic Atypical Hemolytic-Uremic Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1367

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28CFI%5BTIAB%5D%29+OR+%28complement+factor+I%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+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- COMPLEMENT FACTOR I
  http://omim.org/entry/217030

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_CFI.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=CFI%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:5394
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:3426

- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3426
- UniProt
  https://www.uniprot.org/uniprot/P05156

Sources for This Summary

- Baracho GV, Nudelman V, Isaac L. Molecular characterization of homozygous hereditary factor I deficiency. Clin Exp Immunol. 2003 Feb;131(2):280-6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12562389
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1808620/
- OMIM: COMPLEMENT FACTOR I
  http://omim.org/entry/217030
- Fagerness JA, Maller JB, Neale BM, Reynolds RC, Daly MJ, Seddon JM. Variation near complement factor I is associated with risk of advanced AMD. Eur J Hum Genet. 2009 Jan;17(1): 100-4. doi: 10.1038/ejhg.2008.140. Epub 2008 Aug 6.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18685559
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2985963/
- Kavanagh D, Richards A, Noris M, Hauhart R, Liszewski MK, Karpman D, Goodship JA, Fremeaux-Bacchi V, Remuzzi G, Goodship TH, Atkinson JP. Characterization of mutations in complement factor I (CFI) associated with hemolytic uremic syndrome. Mol Immunol. 2008 Jan;45(1):95-105. Epub 2007 Jun 26.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17597211
- Nilsson SC, Trouw LA, Renault N, Miteva MA, Genel F, Zelazko M, Marquart H, Muller K, Sjöholm AG, Truedsson L, Villoutreix BO, Blom AM. Genetic, molecular and functional analyses of complement factor I deficiency. Eur J Immunol. 2009 Jan;39(1):310-23. doi: 10.1002/eji.200838702.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19065647
- Ponce-Castro IM, González-Rubio C, Delgado-Cerviño EM, Abarrategui-Garrido C, Fontán G, Sánchez-Corral P, López-Trascasa M. Molecular characterization of Complement Factor I deficiency in two Spanish families. Mol Immunol. 2008 May;45(10):2764-71. doi: 10.1016/j.molimm.2008.02.008. Epub 2008 Mar 28.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18374984
- Richard I. The genetic and molecular bases of monogenic disorders affecting proteolytic systems. J Med Genet. 2005 Jul;42(7):529-39. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15994873
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1736095/
- Servais A, Frémeaux-Bacchi V, Lequintrec M, Salomon R, Blouin J, Knebelmann B, Grünfeld JP, Lesavre P, Noël LH, Fakhouri F. Primary glomerulonephritis with isolated C3 deposits: a new entity which shares common genetic risk factors with haemolytic uraemic syndrome. J Med Genet. 2007 Mar;44(3):193-9. Epub 2006 Oct 3.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17018561
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2598029/

- Vyse TJ, Morley BJ, Bartok I, Theodoridis EL, Davies KA, Webster AD, Walport MJ. The molecular basis of hereditary complement factor I deficiency. J Clin Invest. 1996 Feb 15;97(4):925-33.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8613545
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC507137/
- Vyse TJ, Späth PJ, Davies KA, Morley BJ, Philippe P, Athanassiou P, Giles CM, Walport MJ. Hereditary complement factor I deficiency. QJM. 1994 Jul;87(7):385-401. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/7922290

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/CFI

Reviewed: September 2010
Published: November 12, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services