HCFC1 gene

host cell factor C1

Normal Function

The *HCFC1* gene provides instructions for making a protein, called HCF-1, that helps regulate the activity of other genes. HCF-1 interacts with proteins called transcription factors, which attach (bind) to specific regions of DNA and help control the activity of particular genes.

A specific function of the HCF-1 protein is to control the activity of genes involved in the processing of vitamin B12 (also known as cobalamin), particularly the *MMACHC* gene. This gene plays a role in the conversion of vitamin B12 into one of two molecules, adenosylcobalamin (AdoCbl) or methylcobalamin (MeCbl). AdoCbl is required for the normal function of an enzyme known as methylmalonyl CoA mutase. This enzyme helps break down certain protein building blocks (amino acids), fats (lipids), and cholesterol. AdoCbl is called a cofactor because it helps methylmalonyl CoA mutase carry out its function. MeCbl is also a cofactor, but for an enzyme known as methionine synthase. This enzyme converts the amino acid homocysteine to another amino acid, methionine. The body uses methionine to make proteins and other important compounds.

HCF-1 helps regulate genes that are important in other cellular processes, such as progression of cells through the step-by-step process it takes to replicate themselves (called the cell cycle). This protein also plays a role in the distribution of cells in developing tissues and organs, including the brain.

Health Conditions Related to Genetic Changes

Methylmalonic acidemia with homocystinuria

At least six *HCFC1* gene mutations have been identified in individuals with methylmalonic acidemia with homocystinuria, cblX type, one form of a disorder that causes developmental delay, eye defects, neurological problems, and blood abnormalities. Individuals with this form also have severe abnormalities in the development of the skull and face (craniofacial abnormalities). These mutations occur in regions of the protein that help it to interact with other proteins. It is thought that changes in these regions prevent HCF-1 from interacting with transcription factors, which disrupts normal gene activity. Impairment of *MMACHC* gene activity, in particular, prevents normal processing and transport of vitamin B12, impeding production of both AdoCbl and MeCbl. Because both of these cofactors are missing, the enzymes that require them (methylmalonyl CoA mutase and methionine synthase) do not function normally. As a result, certain amino acids,

lipids, and cholesterol are not broken down and homocysteine cannot be converted to methionine. This dual defect results in a buildup of toxic compounds as well as homocysteine, and a decrease in the production of methionine within the body. This combination of imbalances leads to the signs and symptoms of methylmalonic acidemia with homocystinuria. Neurological and developmental problems are especially severe in individuals with cblX type, in part due to disruption of the activity of other genes normally regulated by the HCF-1 protein.

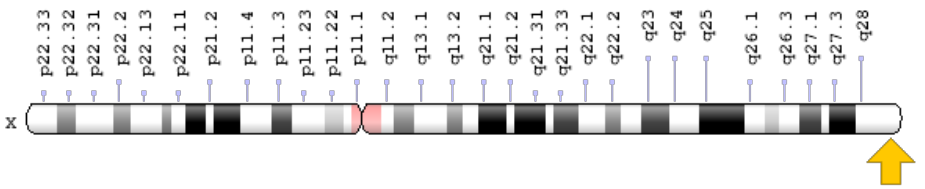
Other disorders

Mutations in the *HCFC1* gene have also been found in individuals with X-linked intellectual disability. These individuals have delayed development and other neurological problems but do not show other features of methylmalonic acidemia with homocystinuria, cblX type. The *HCFC1* gene mutations lead to production of an HCF-1 protein with reduced function. Partial reduction in this protein's function appears to disrupt normal brain development, leading to the features of X-linked disability, but does not severely impact vitamin B12 processing.

Chromosomal Location

Cytogenetic Location: Xq28, which is the long (q) arm of the X chromosome at position 28

Molecular Location: base pairs 153,947,556 to 153,972,360 on the X chromosome (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CFF
- HCF
- HCF-1
- HCF1
- HFC1
- host cell factor 1
- MGC70925

- MRX3
- PPP1R89
- protein phosphatase 1, regulatory subunit 89
- VCAF
- VP16-accessory protein

Additional Information & Resources

Clinical Information from GeneReviews

- Disorders of Intracellular Cobalamin Metabolism
  https://www.ncbi.nlm.nih.gov/books/NBK1328

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28HCFC1%5BTIAB%5D%29+OR+%28host+cell+factor+C1%5BTIAB%5D%29%29+OR+%28%28HCF-1%5BTIAB%5D%29+OR+%28HCF1%5BTIAB%5D%29+OR+%28HFC1%5BTIAB%5D%29+OR+%28MRX3%5BTIAB%5D%29+OR+%28VCAF%5BTIAB%5D%29+OR+%28VP16-accessory+protein%5BTIAB%5D%29+OR+%28host+cell+factor+1%5BTIAB%5D%29+OR+%28protein+phosphatase+1,+regulatory+subunit+89%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+1080+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- HOST CELL FACTOR C1
  http://omim.org/entry/300019

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_HCFC1.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=HCFC1%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:4839
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:3054

- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3054
- UniProt
  https://www.uniprot.org/uniprot/P51610

Sources for This Summary

- Gérard M, Morin G, Bourillon A, Colson C, Mathieu S, Rabier D, Billette de Villemeur T, Ogier de Baulny H, Benoist JF. Multiple congenital anomalies in two boys with mutation in HCFC1 and cobalamin disorder. Eur J Med Genet. 2015 Mar;58(3):148-53. doi: 10.1016/j.ejmg.2014.12.015. Epub 2015 Jan 13.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25595573
- OMIM: HOST CELL FACTOR C1
  http://omim.org/entry/300019
- Huang L, Jolly LA, Willis-Owen S, Gardner A, Kumar R, Douglas E, Shoubridge C, Wieczorek D, Tzschach A, Cohen M, Hackett A, Field M, Froyen G, Hu H, Haas SA, Ropers HH, Kalscheuer VM, Corbett MA, Gecz J. A noncoding, regulatory mutation implicates HCFC1 in nonsyndromic intellectual disability. Am J Hum Genet. 2012 Oct 5;91(4):694-702. doi: 10.1016/j.ajhg.2012.08.011. Epub 2012 Sep 20.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23000143
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3484651/
- Jolly LA, Nguyen LS, Domingo D, Sun Y, Barry S, Hancarova M, Plevova P, Vlckova M, Havlovicova M, Kalscheuer VM, Graziano C, Pippucci T, Bonora E, Sedlacek Z, Gecz J. HCFC1 loss-of-function mutations disrupt neuronal and neural progenitor cells of the developing brain. Hum Mol Genet. 2015 Jun 15;24(12):3335-47. doi: 10.1093/hmg/ddv083. Epub 2015 Mar 3.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25740848
- Parker JB, Yin H, Vinckevicius A, Chakravarti D. Host cell factor-1 recruitment to E2F-bound and cell-cycle-control genes is mediated by THAP11 and ZNF143. Cell Rep. 2014 Nov 6;9(3):967-82. doi: 10.1016/j.celrep.2014.09.051. Epub 2014 Oct 30.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25437553
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4250832/
- Yu HC, Sloan JL, Scharer G, Brebner A, Quintana AM, Achilly NP, Manoli I, Coughlin CR 2nd, Geiger EA, Schneck U, Watkins D, Suormala T, Van Hove JL, Fowler B, Baumgartner MR, Rosenblatt DS, Venditti CP, Shaikh TH. An X-linked cobalamin disorder caused by mutations in transcriptional coregulator HCFC1. Am J Hum Genet. 2013 Sep 5;93(3):506-14. doi: 10.1016/j.ajhg.2013.07.022.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/24011988
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3769968/
- Zargar Z, Tyagi S. Role of host cell factor-1 in cell cycle regulation. Transcription. 2012 Jul-Aug; 3(4):187-92. doi: 10.4161/trns.20711. Epub 2012 Jul 1. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22771988
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3654768/

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