HNF1B gene

HNF1 homeobox B

Normal Function

The *HNF1B* gene provides instructions for making a protein that attaches (binds) to specific regions of DNA and regulates the activity of other genes. On the basis of this role, the protein produced from the *HNF1B* gene is called a transcription factor. The HNF1B protein is part of a large group of transcription factors called homeodomain proteins. The homeodomain is a region of the protein that allows it to bind to DNA.

The HNF1B protein is found in many organs and tissues, including the lungs, liver, intestines, pancreas, kidneys, reproductive system, and urinary tract. Researchers suspect that this protein may play a role in the development of many of these parts of the body.

Health Conditions Related to Genetic Changes

17q12 deletion syndrome

17q12 deletion syndrome is a condition that results from the deletion of a small piece of chromosome 17 in each cell. Signs and symptoms of 17q12 deletion syndrome can include abnormalities of the kidneys (particularly fluid-filled sacs, called cysts, in the kidneys) and a form of diabetes called maturity-onset diabetes of the young type 5 (MODY5). The combination of kidney cysts and MODY5 is sometimes referred to as renal cysts and diabetes (RCAD) syndrome. Other features of 17q12 deletion syndrome include abnormalities of the urinary tract and reproductive system, delayed development, intellectual disability, and behavioral or psychiatric disorders. The health problems associated with 17q12 deletion syndrome vary widely, even among affected members of the same family.

The part of chromosome 17 that is deleted is on the long (q) arm of the chromosome at a position designated q12. This region of the chromosome contains at least 15 genes, including *HNF1B*. A deletion of this region results in a loss of one copy of the *HNF1B* gene in each cell, leading to a reduced amount of HNF1B protein. A shortage of this protein likely disrupts the regulation of genes that are necessary for the normal development of several organs, including the kidneys and pancreas. Studies suggest that a loss of one copy of the *HNF1B* gene underlies the kidney and urinary tract abnormalities, as well as MODY5, in people with 17q12 deletion syndrome.

Congenital anomalies of kidney and urinary tract

Mutations within the *HNF1B* gene are found in people with abnormalities of the kidneys and other structures of the urinary system but without other features of 17q12

deletion syndrome (described above). These abnormalities vary in severity and are grouped together as congenital anomalies of kidney and urinary tract (CAKUT). The most severe CAKUT abnormalities can cause kidney damage and life-threatening kidney failure.

Mutations associated with CAKUT occur in one copy of the *HNF1B* gene in each cell. Many change single protein building blocks (amino acids) in the HNF1B protein. Others lead to an abnormally shaped protein or prevent the production of any functional protein from one copy of the gene. A shortage of functional HNF1B protein likely disrupts the regulation of genes that help direct development of the kidneys and urinary tract. It is unclear why only structures of the urinary system are affected in these individuals.

Prostate cancer

Other disorders

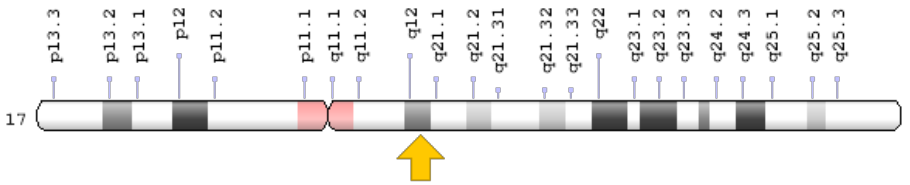
HNF1B gene mutations can also cause abnormalities of multiple organ systems. Some of the features associated with *HNF1B* gene mutations are the same as those of 17q12 deletion syndrome (described above), including RCAD syndrome and abnormalities of the urinary tract, reproductive system, and other organs. Like the signs and symptoms of those syndromes, the health problems associated with *HNF1B* gene mutations vary widely among affected individuals. However, unlike 17q12 deletions, mutations in the *HNF1B* gene have not been found to cause delayed development, intellectual disability, or behavioral or psychiatric disorders.

More than 200 mutations in the *HNF1B* gene have been identified. As in CAKUT (described above), the mutations lead to a shortage of functional HNF1B protein, which likely disrupts the regulation of genes that are necessary for the normal development of several organs. It is unclear why these mutations can affect different organ systems in different people.

Chromosomal Location

Cytogenetic Location: 17q12, which is the long (q) arm of chromosome 17 at position 12

Molecular Location: base pairs 37,686,431 to 37,745,059 on chromosome 17 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- FJHN
- hepatocyte nuclear factor 1B
- HNF-1-beta
- HNF-1B
- HNF1 beta A
- HNF1beta
- HNF2
- homeoprotein LFB3
- HPC11
- LF-B3
- LFB3
- TCF-2
- TCF2
- transcription factor 2, hepatic
- VHNF1

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): Homeodomain Proteins Constitute a Special Class of Helix-Turn-Helix Proteins
  https://www.ncbi.nlm.nih.gov/books/NBK26806/#A1240
- RareRenal: HNF1B – Patient Information
  https://rarerenal.org/patient-information/hnf1b-patient-information/
- The Genetic Landscape of Diabetes (2004): MODY5: Caused by a Mutation in Transcription Factor TCF2 (HNF1B)
  https://www.ncbi.nlm.nih.gov/books/NBK1666/#A891

Clinical Information from GeneReviews

- 17q12 Recurrent Deletion Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK401562

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28HNF1B%5BTIAB%5D%29+OR+%28HNF1+homeobox+B%5BTIAB%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

- HNF1 HOMEOBOX B
  http://omim.org/entry/189907

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_HNF1B.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=HNF1B%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:11630
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:6928
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/6928
- UniProt
  https://www.uniprot.org/uniprot/P35680

Sources for This Summary

- Bockenhauer D, Jaureguiberry G. HNF1B-associated clinical phenotypes: the kidney and beyond. Pediatr Nephrol. 2016 May;31(5):707-14. doi: 10.1007/s00467-015-3142-2. Epub 2015 Jul 8. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26160100
- Clissold RL, Shaw-Smith C, Turnpenny P, Bunce B, Bockenhauer D, Kerecuk L, Waller S, Bowman P, Ford T, Ellard S, Hattersley AT, Bingham C. Chromosome 17q12 microdeletions but not intragenic HNF1B mutations link developmental kidney disease and psychiatric disorder. Kidney Int. 2016 Jul;90(1):203-11. doi: 10.1016/j.kint.2016.03.027. Epub 2016 May 24.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/27234567
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4915913/
- El-Khairi R, Vallier L. The role of hepatocyte nuclear factor 1β in disease and development. Diabetes Obes Metab. 2016 Sep;18 Suppl 1:23-32. doi: 10.1111/dom.12715. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/27615128
- Ferrè S, Igarashi P. New insights into the role of HNF-1β in kidney (patho)physiology. Pediatr Nephrol. 2018 Jul 1. doi: 10.1007/s00467-018-3990-7. [Epub ahead of print] Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/29961928
- OMIM: HNF1 HOMEOBOX B
  http://omim.org/entry/189907
- Laffargue F, Bourthoumieu S, Llanas B, Baudouin V, Lahoche A, Morin D, Bessenay L, De Parscau L, Cloarec S, Delrue MA, Taupiac E, Dizier E, Laroche C, Bahans C, Yardin C, Lacombe D, Guigonis V. Towards a new point of view on the phenotype of patients with a 17q12 microdeletion syndrome. Arch Dis Child. 2015 Mar;100(3):259-64. doi: 10.1136/archdischild-2014-306810.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25324567
- Mefford HC, Clauin S, Sharp AJ, Moller RS, Ullmann R, Kapur R, Pinkel D, Cooper GM, Ventura M, Ropers HH, Tommerup N, Eichler EE, Bellanne-Chantelot C. Recurrent reciprocal genomic rearrangements of 17q12 are associated with renal disease, diabetes, and epilepsy. Am J Hum Genet. 2007 Nov;81(5):1057-69.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17924346
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2265663/
- Verhave JC, Bech AP, Wetzels JF, Nijenhuis T. Hepatocyte Nuclear Factor 1β-Associated Kidney Disease: More than Renal Cysts and Diabetes. J Am Soc Nephrol. 2016 Feb;27(2):345-53. doi: 10.1681/ASN.2015050544. Epub 2015 Aug 28. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26319241
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4731131/
- van der Made CI, Hoorn EJ, de la Faille R, Karaaslan H, Knoers NV, Hoenderop JG, Vargas Poussou R, de Baaij JH. Hypomagnesemia as First Clinical Manifestation of ADTKD-HNF1B: A Case Series and Literature Review. Am J Nephrol. 2015;42(1):85-90. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/26340261

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/HNF1B

Reviewed: November 2018
Published: June 25, 2019

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