HNF1A gene

HNF1 homeobox A

Normal Function

The *HNF1A* gene provides instructions for making a protein called hepatocyte nuclear factor-1 alpha (HNF-1α). The HNF-1α protein acts as a transcription factor, which means it attaches (binds) to specific regions of DNA and helps control the activity of certain genes. While this protein is found in several tissues and organs, it seems to be especially important in the pancreas and liver.

Regulation of gene activity by the HNF-1α protein is critical for the growth and development of beta cells in the pancreas. Beta cells produce and release (secrete) the hormone insulin. Insulin helps regulate blood sugar levels by controlling how much sugar (in the form of glucose) is passed from the bloodstream into cells to be used as energy. The HNF-1α protein also controls genes involved in liver development. By controlling genes that regulate cell growth and survival, the HNF-1α protein is thought to act as a tumor suppressor, which means that it helps prevent cells from growing and dividing too rapidly or in an uncontrolled way.

The structure of HNF-1α includes several important regions that help it carry out its functions. One of the regions, called the dimerization domain, is critical for protein interactions. This region allows HNF-1α proteins to interact with each other or with other proteins that have a similar structure, creating a two-protein unit (dimer) that functions as a transcription factor. Another region, known as the DNA binding domain, binds to specific areas of DNA, allowing the dimer to control gene activity.

Health Conditions Related to Genetic Changes

Maturity-onset diabetes of the young

Mutations in the *HNF1A* gene cause maturity-onset diabetes of the young (MODY), which is a group of conditions characterized by abnormally high blood glucose levels. This form of diabetes usually begins before age 30. *HNF1A* gene mutations cause the most common type of MODY, called *HNF1A*-MODY (also known as MODY3). Early symptoms are caused by high blood glucose and include frequent urination (polyuria), excessive thirst (polydipsia), fatigue, blurred vision, weight loss, and recurrent skin infections. Over time, uncontrolled high blood glucose can lead to eye and kidney problems.

HNF1A gene mutations that cause *HNF1A*-MODY occur in one of the two copies of the gene in each cell. These mutations result in production of an altered HNF-1α protein that is unable to function normally. Some changes prevent the HNF-1α protein from forming dimers; others prevent the protein from entering the nucleus where it interacts with DNA; still others prevent the transcription factor from attaching to DNA to control gene activity. These changes interrupt transcription, altering gene activity in cells. As a result, beta cell development and function are impaired. The cells are less able than normal to produce insulin in response to glucose in the blood, which means blood glucose cannot be controlled. Elevated blood glucose results in the signs and symptoms of MODY.

Rarely, individuals with *HNF1A*-MODY develop one or more noncancerous (benign) liver tumors called hepatocellular adenomas. In these individuals, a mutation occurs in the second copy of the *HNF1A* gene in liver cells. This second mutation, called a somatic mutation, is not inherited. It is unclear how the mutations cause liver cells to grow uncontrollably and form tumors.

Congenital hyperinsulinism

MedlinePlus Genetics provides information about Congenital hyperinsulinism

Type 1 diabetes

MedlinePlus Genetics provides information about Type 1 diabetes

Other disorders

Hepatocellular adenomas also occur in people without *HNF1A*-MODY (described above) . In these individuals, the tumors are associated with somatic mutations in both copies of the *HNF1A* gene. While rare, hepatocellular adenomas occur in women more frequently than in men, and most affected individuals develop a single tumor. *HNF1A*-mutated hepatocellular adenomas (also known as H-HCA) account for about 30 to 40 percent of this type of liver tumor. The *HNF1A* gene mutations that cause these tumors severely reduce or eliminate the function of the HNF-1α protein in affected liver cells. It is unclear how loss of HNF-1α function causes cells to grow uncontrollably and form tumors.

Other Names for This Gene

- HNF1 Homeobox A Gene
- LFB1
- TCF1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of HNF1A (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6927[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28HNF1A%5BTIAB%5D%29+OR+%28HNF1+homeobox+A%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+720+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- HNF1 HOMEOBOX A; HNF1A (https://omim.org/entry/142410)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/6927)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=HNF1A[gene])

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Genomic Location

The *HNF1A* gene is found on chromosome 12 (https://medlineplus.gov/genetics/chromosome/12/).

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