HNF1B Gene

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HNF1 homeobox B

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1. Introduction

The *HNF1B* gene provides instructions for making a protein called hepatocyte nuclear factor-1 beta (HNF-1β). This protein attaches (binds) to specific regions of DNA and regulates the activity of other genes. Based on this role, the protein is called a transcription factor. The HNF-1β protein is one 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 HNF-1β protein is found in many organs and tissues, including the lungs, liver, intestines, pancreas, kidneys, genital tract, and urinary tract and is thought to play a role in their development. The HNF-1β protein is important for development and function of the kidneys and 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.

2. Health Conditions Related to Genetic Changes

2.1. Maturity-onset diabetes of the young

Mutations in the *HNF1B* gene cause maturity-onset diabetes of the young (MODY). MODY is a group of conditions characterized by abnormally high blood sugar that usually begins before age 30. *HNF1B* gene mutations cases a type of MODY known as renal cysts and diabetes (RCAD) syndrome (also known as *HNF1B*-MODY or MODY5). In addition to diabetes, people with RCAD typically also have kidney abnormalities (primarily fluid-filled sacs called cysts). Affected individuals may also have abnormalities of the pancreas, liver, or genital tract; or a condition called gout, which is a form of arthritis.

HNF1B gene mutations involved in RCAD occur in one copy of the gene in each cell. The changes reduce the amount of functional HNF-1β protein. A shortage of this transcription factor disrupts the activity of genes that direct the development and function of certain tissues and organs. In the pancreas, these changes prevent normal beta cell function. The cells are less able than normal to produce insulin in response to sugar in the blood, leading to diabetes. In the kidneys, altered HNF-1β activity results in the formation of cysts or other abnormalities.

2.2. 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 a type of maturity-onset diabetes of the young (MODY) called renal cysts and diabetes (RCAD) syndrome (described above). Other features of 17q12 deletion syndrome include abnormalities of the urinary tract and reproductive system, delayed development, impaired thinking (cognitive) ability, 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 HNF-1β 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 RCAD syndrome in people with 17q12 deletion syndrome.

2.3. 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 tract but without other features of 17q12 deletion syndrome (described above) or RCAD 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 HNF-1β 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 HNF-1β 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 tract are affected in these individuals.

2.4. 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 (described above) 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 HNF-1β 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.

3. 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

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