HNF4A Gene

Subjects: Genetics & Heredity
Contributor: Dean Liu

Hepatocyte nuclear factor 4 alpha

Keywords: genes

1. Introduction

The *HNF4A* gene provides instructions for making a protein called hepatocyte nuclear factor-4 alpha (HNF-4α). This protein plays an important role in the function of certain tissues and organs in the body. The HNF-4α protein acts as a transcription factor, which means it attaches (binds) to specific regions of DNA and helps control the activity of particular genes.

The HNF-4α protein controls genes that are especially important for development and function 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-4α protein also controls genes involved in normal liver functions.

The structure of the HNF-4α protein includes several important regions. One of the regions, called the dimerization domain, is critical for protein interactions. This region allows molecules of HNF-4α to interact with each other, 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.

2. Health Conditions Related to Genetic Changes

2.1. Maturity-Onset Diabetes of the Young

Mutations in the *HNF4A* gene cause maturity-onset diabetes of the young (MODY), which is a group of conditions characterized by abnormally high blood sugar levels. MODY usually begins before age 30. *HNF4A* gene mutations cause a type called *HNF4A*-MODY (also known as MODY1). Often babies with this condition are heavier than average when they are born, and they may have unusually low blood sugar levels. Symptoms of high blood sugar, which usually begin in childhood or early adulthood, include frequent urination (polyuria), excessive thirst (polydipsia), fatigue, blurred vision, weight loss, and recurrent skin infections. Over time, uncontrolled high blood sugar can lead to eye and kidney problems.

HNF4A gene mutations result in production of an altered HNF-4α protein that is unable to function normally. Some changes prevent the HNF-4α protein from forming dimers; others prevent the attachment of additional proteins that aid in transcription; 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 sugar in the blood, which means blood sugar cannot be controlled. Elevated blood sugar results in the signs and symptoms of MODY

3. Other Names for This Gene

- HEPATOCYTE NUCLEAR FACTOR 4-ALPHA
- HNF4-ALPHA
- HNF4A gene
- NR2A1
- Nuclear Receptor Subfamily 2, Group A, Member 1

- TCF14
- TRANSCRIPTION FACTOR 14, HEPATIC NUCLEAR FACTOR

References

1. Rha GB, Wu G, Chi YI. Probing the effect of MODY mutations near theco-activator-binding pocket of HNF4α. Biosci Rep. 2011 Oct;31(5):411-9. doi:10.1042/BSR20110013.
2. Singh P, Tung SP, Han EH, Lee IK, Chi YI. Dimerization defective MODYmutations of hepatocyte nuclear factor 4α. Mutat Res. 2019 Mar;814:1-6. doi:10.1016/j.mrfmmm.2019.01.002.
3. Yamagata K. Roles of HNF1α and HNF4α in pancreatic β-cells: lessons from amonogenic form of diabetes (MODY). Vitam Horm. 2014;95:407-23. doi:10.1016/B978-0-12-800174-5.00016-8. Review.

Retrieved from https://encyclopedia.pub/entry/history/show/12528