HCFC1 Gene

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Contributor: Dean Liu

Host cell factor C1

genes

1. Introduction

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.

2. Health Conditions Related to Genetic Changes

2.1. 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.

2.2. 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.

3. 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

References

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