SLC40A1 Gene

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solute carrier family 40 member 1

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1. Normal Function

The *SLC40A1* gene provides instructions for making a protein called ferroportin. This protein is involved in the process of absorbing iron that the body receives from food. Ferroportin transports iron obtained from the diet that is absorbed through the walls of the small intestine into the bloodstream. The iron is carried by the blood to the tissues and organs of the body. Ferroportin also transports iron out of specialized immune system cells (called reticuloendothelial cells) that are found in the liver, spleen, and bone marrow. The amount of iron absorbed during digestion depends on the amount of iron transported from intestinal and reticuloendothelial cells.

The amount of ferroportin available to transport iron is controlled by another iron regulatory protein, hepcidin. Hepcidin attaches (binds) to ferroportin and causes it to be broken down when the body's iron supplies are normal. When the body is low on iron, hepcidin levels decrease and more ferroportin is available to transport iron into the bloodstream so it can be delivered to tissues throughout the body.

2. Health Conditions Related to Genetic Changes

2.1. Hereditary hemochromatosis

Researchers have identified more than 37 mutations in the *SLC40A1* gene that cause a form of hereditary hemochromatosis called ferroportin disease, which is also sometimes referred to as type 4 hemochromatosis. This form of the disorder usually begins during adulthood. Hereditary hemochromatosis is a disorder that causes the body to absorb too much iron from the diet. The excess iron accumulates in, and eventually damages, the body's tissues and organs.

Almost all *SLC40A1* gene mutations change a single protein building block (amino acid) in ferroportin. Abnormal ferroportin proteins cannot transport and release iron from intestinal or reticuloendothelial cells. As a result, the regulation of iron levels in the body is impaired, resulting in iron overload and damage to tissues and organs in the body that is characteristic of hereditary hemochromatosis.

2.2. African iron overload

Some studies have indicated that a particular variation in the *SLC40A1* gene slightly increases the risk of increased iron stores in people of African descent, which may lead to African iron overload. This effect seems to be more pronounced in men, which may be related to sex differences in the processing of iron.

The *SLC40A1* gene variation associated with increased iron stores replaces the amino acid glutamine with the amino acid histidine at position 248 in the ferroportin protein sequence and is written as Gln248His or Q248H. It is found in 5 to 20 percent of people of African descent but is not generally found in other populations. The Q248H variation may affect the way ferroportin helps to regulate iron levels in the body, resulting in an increased risk of African iron overload. People with the variation may inherit an increased risk of this condition, but not the condition itself. Not all people with this condition have the variation in the gene, and not all people with the variation will develop the disorder.

3. Other Names for This Gene

- Ferroportin 1
- FPN1

- HFE4
- IREG1
- Iron regulated gene 1
- Iron-regulated transporter 1
- MTP1
- S40A1_HUMAN
- SLC11A3
- Solute carrier family 11 (proton-coupled divalent metal ion transporters), member 3
- solute carrier family 40 (iron-regulated transporter), member 1

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