UROD Gene

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Uroporphyrinogen decarboxylase.

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1. Normal Function

The *UROD* gene provides instructions for making an enzyme known as uroporphyrinogen decarboxylase. This enzyme is involved in the production of a molecule called heme. Heme is vital for all of the body's organs, although it is most abundant in the blood, bone marrow, and liver. Heme is an essential component of iron-containing proteins called hemoproteins, including hemoglobin (the protein that carries oxygen in the blood).

The production of heme is a multi-step process that requires eight different enzymes. Uroporphyrinogen decarboxylase is responsible for the fifth step in this process, in which carbon and oxygen atoms are removed from uroporphyrinogen III (the product of the fourth step) to form coproporphyrinogen III. In subsequent steps, three other enzymes produce and modify compounds that ultimately lead to heme.

2. Health Conditions Related to Genetic Changes

2.1. Porphyria

Mutations in the *UROD* gene is responsible for two forms of porphyria, porphyria cutanea tarda and hepatoerythropoietic porphyria. Porphyria cutanea tarda is the most common type of porphyria; its signs and symptoms tend to be milder and appear later in life than those of hepatoerythropoietic porphyria. When a mutation occurs in one copy of the *UROD* gene in each cell, it increases the risk of developing porphyria cutanea tarda. (Multiple genetic and nongenetic factors contribute to this form of porphyria.) Mutations in both copies of the *UROD* gene in each cell cause hepatoerythropoietic porphyria.

More than 50 *UROD* gene mutations have been associated with porphyria cutanea tarda. These mutations reduce the activity of uroporphyrinogen decarboxylase by approximately 50 percent throughout the body. As a result, compounds called porphyrins build up to toxic levels in organs and tissues, starting in the liver. This buildup, in combination with nongenetic factors such as alcohol use, smoking, certain hormones, excess iron, and hepatitis C or HIV infections, leads to this type of porphyria.

At least 10 mutations in the *UROD* gene have been identified in people with hepatoerythropoietic porphyria. A few of these mutations have also been associated with porphyria cutanea tarda. Mutations that cause hepatoerythropoietic porphyria reduce the activity of uroporphyrinogen decarboxylase to less than 10 percent of normal. A shortage of this enzyme allows compounds called porphyrins to build up in the body. These compounds are formed during the normal process of heme production, but reduced activity of uroporphyrinogen decarboxylase allows them to accumulate to toxic levels. This abnormal buildup of porphyrins leads to the characteristic features of this type of porphyria.

3. Other Names for This Gene

- DCUP_HUMAN
- UD - Uroporphyrinogen decarboxylase
- UPD
- URO-D

- Uroporphyrinogen III decarboxylase
- Uroporphyrinogen-III carboxy-lyase

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