ALAS2 Gene

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5'-aminolevulinate synthase 2

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1. Normal Function

The *ALAS2* gene provides instructions for making an enzyme called 5'-aminolevulinate synthase 2 or erythroid ALA-synthase. This version of the enzyme is found only in developing red blood cells called erythroblasts.

ALA-synthase plays an important role in the production of heme. Heme is a component of iron-containing proteins called hemoproteins, including hemoglobin (the protein that carries oxygen in the blood). Heme is vital for all of the body's organs, although it is most abundant in the blood, bone marrow, and liver.

The production of heme is a multi-step process that requires eight different enzymes. ALA-synthase is responsible for the first step in this process, the formation of a compound called delta-aminolevulinic acid (ALA). In subsequent steps, seven other enzymes produce and modify compounds that ultimately lead to heme.

2. Health Conditions Related to Genetic Changes

2.1 Porphyria

At least two *ALAS2* gene mutations have been found in people with a form of porphyria known as X-linked dominant erythropoietic protoporphyria. Each of these mutations deletes a small amount of genetic material near the end of the *ALAS2* gene. These changes overactivate erythroid ALA-synthase, which increases the production of ALA within red blood cells. The excess ALA is converted by other enzymes to compounds called porphyrins. If these compounds build up in erythroblasts, they can leak out and be transported through the bloodstream to the skin and other tissues. High levels of porphyrins in the skin cause the oversensitivity to sunlight that is characteristic of this condition.

2.2 X-linked sideroblastic anemia

At least 50 mutations that cause X-linked sideroblastic anemia have been identified in the *ALAS2* gene. Almost all of these mutations change single protein building blocks (amino acids) in erythroid ALA-synthase. These changes impair the activity of the enzyme, which disrupts the normal production of heme in developing red blood cells. A reduction in the amount of heme prevents these cells from making enough hemoglobin. Because almost all of the iron transported into erythroblasts is normally incorporated into heme, the reduced production of heme leads to a buildup of excess iron in these cells. Additionally, the body attempts to compensate for the hemoglobin shortage by absorbing more iron from the diet. This buildup of excess iron can damage the body's organs. Low hemoglobin levels and the resulting accumulation of iron in the body's organs lead to the characteristic features of X-linked sideroblastic anemia.

3. Other Names for This Gene

- 5-aminolevulinate synthase, erythroid-specific, mitochondrial
- ALAS, erythroid
- ALAS-E
- aminolevulinate, delta-, synthase 2
- ANH1
- ASB
- HEM0_HUMAN

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