HBA1 Gene

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Hemoglobin subunit alpha 1

genes

1. Introduction

The *HBA1* gene provides instructions for making a protein called alpha-globin. This protein is also produced from a nearly identical gene called *HBA2*. These two alpha-globin genes are located close together in a region of chromosome 16 known as the alpha-globin locus.

Alpha-globin is a component (subunit) of a larger protein called hemoglobin, which is the protein in red blood cells that carries oxygen to cells and tissues throughout the body. Hemoglobin is made up of four subunits: two subunits of alpha-globin and two subunits of another type of globin. Alpha-globin is a component of both fetal hemoglobin, which is active only before birth and in the newborn period, and adult hemoglobin, which is active throughout the rest of life.

Each of the four protein subunits of hemoglobin carries an iron-containing molecule called heme. Heme molecules are necessary for red blood cells to pick up oxygen in the lungs and deliver it to the body's tissues. A complete hemoglobin protein is capable of carrying four oxygen molecules at a time (one attached to each heme molecule). Oxygen attached to hemoglobin gives blood its bright red color.

2. Health Conditions Related to Genetic Changes

2.1. Alpha Thalassemia

Deletions of the *HBA1* and/or *HBA2* genes are the most common cause of alpha thalassemia. Rarely, mutations in or near these genes can also be responsible for the disease. The signs and symptoms of alpha thalassemia tend to be more severe when the disease results from mutations in the alpha-globin genes than when it is caused by deletions of these genes.

People have two copies of the *HBA1* gene and two copies of the *HBA2* gene in each cell. Each copy is called an allele. For each gene, one allele is inherited from a person's father, and the other is inherited from a person's

mother. As a result, there are four alleles that produce alpha-globin. The different types of alpha thalassemia result from the loss of some or all of these alleles.

Hb Bart syndrome, the most severe form of alpha thalassemia, results from the loss of all four alpha-globin alleles. This condition is characterized by a buildup of excess fluid in the body before birth (hydrops fetalis), a shortage of red blood cells (anemia), and an enlarged liver and spleen (hepatosplenomegaly). HbH disease, which is milder, is caused by a loss of three of the four alpha-globin alleles. HbH disease is characterized by mild to moderate anemia, hepatosplenomegaly, and yellowing of the eyes and skin (jaundice).

In Hb Bart syndrome and HbH disease, a shortage of alpha-globin prevents cells from making normal hemoglobin. Instead, cells produce abnormal forms of hemoglobin called hemoglobin Bart (Hb Bart) or hemoglobin H (HbH). These abnormal hemoglobin molecules cannot effectively carry oxygen to the body's tissues. The substitution of Hb Bart or HbH for normal hemoglobin causes anemia and the other serious health problems associated with alpha thalassemia.

Two additional variants of alpha thalassemia are related to a reduced amount of alpha-globin. Because cells still produce some normal hemoglobin, these variants tend to cause few or no health problems. A loss of two of the four alpha-globin alleles results in alpha thalassemia trait. People with alpha thalassemia trait may have unusually small, pale red blood cells and mild anemia. A loss of one alpha-globin allele is found in alpha thalassemia silent carriers. These individuals typically have no thalassemia-related signs or symptoms.

2.2. Other disorders

A condition called alpha-thalassemia-intellectual disability syndrome, chromosome 16-related (ATR-16) results from a large deletion of genetic material from the short (p) arm of chromosome 16. The signs and symptoms of this condition result from the loss of many genes, including *HBA1* and *HBA2*.

A deletion of the *HBA1* and *HBA2* genes leads to alpha thalassemia trait in most people with ATR-16. The loss of other genes causes additional features of the disorder, including intellectual disability, severely delayed language skills, an unusually small head size (microcephaly), and distinctive facial features. Affected males may also have undescended testes (cryptorchidism) and the urethra opening on the underside of the penis (hypospadias).

The signs and symptoms of ATR-16 vary depending on the size of the deletion. A particularly large deletion may include the *PKD1* gene, which is responsible for polycystic kidney disease. A loss of this gene leads to the growth of multiple cysts in the kidneys. If the deletion also includes the *TSC2* gene, an affected individual will develop tuberous sclerosis complex. This condition is characterized by the growth of noncancerous tumors in many parts of the body.

3. Other Names for This Gene

- alpha 1 globin

- alpha one globin
- alpha-1 globin
- alpha-1-globin
- CD31
- HBA-T3
- HBA_HUMAN
- hemoglobin alpha 1 globin chain
- hemoglobin alpha-1 chain
- hemoglobin, alpha 1
- MGC126895
- MGC126897

References

1. Harteveld CL, Kriek M, Bijlsma EK, Erjavec Z, Balak D, Phylipsen M, Voskamp A,di Capua E, White SJ, Giordano PC. Refinement of the genetic cause of ATR-16. HumGenet. 2007 Nov;122(3-4):283-92.
2. Harvard University: Hemoglobin Synthesis
3. Higgs DR, Weatherall DJ. The alpha thalassaemias. Cell Mol Life Sci. 2009Apr;66(7):1154-62. doi: 10.1007/s00018-008-8529-9. Review.
4. Ribeiro DM, Sonati MF. Regulation of human alpha-globin gene expression andalpha-thalassemia. Genet Mol Res. 2008 Oct 14;7(4):1045-53. Review.
5. Tamary H, Dgany O. Alpha-Thalassemia. 2005 Nov 1 [updated 2020 Oct 1]. In:Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, Amemiya A,editors. GeneReviews® [Internet]. Seattle (WA): University of Washington,Seattle; 1993-2020. Available from http://www.ncbi.nlm.nih.gov/books/NBK1435/
6. Zhang HB, Liu DP, Liang CC. The control of expression of the alpha-globin genecluster. Int J Hematol. 2002 Dec;76(5):420-6. Review.