Hemoglobins and their heredity

This article has been translated from WikiSkripta; ready for the **editor's review**.

Molecule of hemoglobin

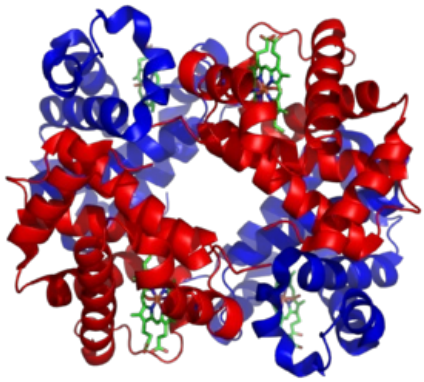
Hemoglobin is a metalloprotein that carries oxygen in the red blood cells of vertebrates. Without it, (cellular) respiration is impossible. The molecule consists of a **protein component (globin)**, which is represented by 4 polypeptide chains (always two and two are identical), and a prosthetic group - **heme** (= a pigment containing iron that binds with oxygen and enables the transport of oxygen by the hemoglobin molecule). An adult has got mainly **hemoglobin A (Adult), HbA** (98% of total Hb in an adult) in erythrocytes. Hb A contains 2 alpha chains and 2 beta chains. Globin alpha chain consists of 141 amino acids, beta chain of 146 amino acids.

Changes in the structure of hemoglobin in ontogeny

During human ontogeny, the structure of Hb in the erythrocyte changes. The molecules of all hemoglobins are tetrameric, but they differ in the composition of the chains. Heme is the same in all forms of hemoglobin, genetic variability only concerns the structure of the globin component

Types of hemoglobin and their components

Hemoglobin	Name	Chains
embryonal	Hb Gower 1	zeta 2 epsilon 2
	Hb Gower 2	alfa 2 epsilon 2
	Hb Portland	zeta 2 gama 2
fetal	HbF	alfa 2 gama 2
adult	HbA	alfa 2 beta 2
	HbA_2 (2% of total Hb in an adult)	alfa 2 delta 2



Hemoglobin structure

Changes in hemoglobin structure in ontogeny are an example of **gene expression regulation in ontogeny**. Changes in the expression of individual genes are called **globin switching**. First, the zeta and epsilon chains of globins (Hb Gower 1) are synthesized. After the expression of zeta and epsilon globins, two more types of embryonic hemoglobins are formed. Later, the zeta and epsilon genes are suppressed, and in the fetal period, mainly HbF is formed. At birth, erythrocytes contain about 70% HbF, in the following months the proportion of HbF decreases, and in adulthood, erythrocytes contain only a small amount of HbF.

The regulation of hemoglobin formation in ontogeny is linked to the localization of red blood cell formation. Embryonic hemoglobin is therefore formed in the yolk sac, fetal hemoglobin in the liver and adult hemoglobin in the bone marrow.

Fetal hemoglobin has a higher affinity for oxygen, that is, it binds and dissociates oxygen at a lower partial pressure than HbA. This feature of HbF is significant because fetal hemoglobin is oxygenated in the placenta, where the partial pressure of oxygen is lower than in the air.

Genes for globin chains

A group (cluster) of genes related to the alpha gene is located on the **16th chromosome** (16p13).

- The locus for alpha globin is quadrupled: genes alpha1, alpha2 and 2 pseudogenes – non-functional copies of alpha1 and alpha2 genes (chains of alpha1 and alpha2 globins are identical)
- The gene for zeta globin is duplicated: zeta + zeta pseudogene

A group (cluster) of genes related to the beta gene is located on the **11th chromosome** (11p15.5)

- beta gene, beta pseudogene, delta gene, gamma G gene, gamma A gene, epsilon gene

Knowledge of the structure of hemoglobin chain gene groups explains the different clinical manifestation of alpha and beta chain gene mutations. In heterozygotes, beta gene mutations affect 50% of hemoglobin chains (there is one beta gene on chromosome 11), alpha gene mutations affect only 25% of hemoglobin molecules (there are 2

copies of the alpha gene on chromosome 16), but they manifest before birth (the alpha chain is part of fetal Hb). Because both the alpha and beta chains are encoded by genes on different chromosomes (alpha on chromosome 16 and beta on chromosome 11), mutations damage either one or the other chain, never both at the same time.

Mechanism of switching the transcription of globin genes

There is a locus activation region (**LAR** – locus activation region) on both chromosomes 6-20 kb upstream of the globin genes. Transcription of genes for globin chains is activated in erythroid cells by the binding of the **NF-E1 protein** (bound to LAR) with a specific DNA binding factor (bound to the gene promoter). The DNA thus creates loops, the size of which determines the activation of the loci for the formation of embryonic, fetal and adult hemoglobin. DNA-binding factors are tissue-specific, and the localization of hematopoiesis affects the type of hemoglobin synthesis (embryonic is produced in the yolk sac, fetal in the liver, adult in the bone marrow).

Links

Source

- ŠTEFÁNEK, Jiří. *Medicína, nemoci, studium na 1. LF UK* [online]. [cit. 11. 2. 2010]. <http://www.stefajir.cz>.