Erythropoietin

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Erythropoietin is a glycoprotein cytokine, the main regulator of erythropoiesis. It has an anti-apoptotic effect, it is encoded by a gene on chromosome 7. It is responsible for the daily production of 200 billion blood cells. The primary stimulus for its formation is tissue hypoxia. During embryonic development, erythropoietin is synthesized mainly in the liver, after birth in the peritubular cells of the kidney cortex. Erythropoietin is not stored anywhere in the body, so it must be quickly synthesized when needed. It stimulates the proliferation and differentiation of cells of the red line, increases the expression of genes for transferrin, the expression of genes for globin and enzymes for heme synthesis. ⚠

Creation Regulation

Stimulation

- Prostaglandins (PGE_2),
- noradrenaline,
- growth hormone,
- thyroid hormones,
- testosterone (the cause of sex differences in the number of red blood cells and the amount of hemoglobin).

Inhibition

- estrogens.

Regulation of erythropoietin production takes place at the level of mRNA synthesis, which takes place in an "all or nothing" style. Upon hypoxemia, mRNA is synthesized, erythropoietin creates "sharp peaks" of plasma concentrations. After returning to normal oxygen levels, mRNA synthesis ceases. A rapid rise and subsequent rapid fall in plasma erythropoietin concentrations is essential for increased erythrocyte production only when needed.

Affecting Synthesis

Synthesis can be disrupted by kidney diseases, bone marrow disorders, iron and vitamins deficiency, or a side effect when administering certain drugs (e.g. cytostatics, zidovudine). During anemia or hypoxemia, erythropoietin synthesis immediately increases to more than a thousand times normal levels, increasing serum levels of erythropoietin, which subsequently stimulates the survival, proliferation and maturation of progenitor cells.

Biochemistry

The synthesis of erythropoietin itself is under the control of a sophisticated regulatory mechanism capable of detecting the amount of oxygen in the blood. The main role in it is played by a transcription factor inducible by hypoxia, the so-called **HIF-1α'** (hypoxia-inducible factor 1). During hypoxia, HIF-1α can penetrate into the kidney cell nucleus, where it dimerizes with the β subunit. It recognizes the target gene and binds to a specific sequence in the promoter part, the so-called *responsive element* (HRE – hypoxia-responsive element). By binding to the promoter, it triggers gene transcription. HIF-1 is able to activate the expression of a whole range of genes during hypoxia, and one of them is the gene encoding erythropoietin. If normoxia occurs, HIF-1 is oxidized under the catalysis of prolyl-hydroxylase and subsequently degraded by the ubiquitin-proteasome system - thus it does not fulfill its role as a transcription factor[1]. HIF-1 is not strictly a transcription factor for erythropoietin, but for a whole range of other proteins.

Mechanism of action

The effect of erythropoietin is not terminated by typical excretory organs, but directly at the site of action, i.e. in the precursor cell. Erythropoietin affects intracellular signaling after interacting with a specific receptor located on the surface of cells - the erythropoietin receptor (EPOR). It belongs to the family of cytokine receptors - receptor with tyrosine kinase activity. By binding to the receptor, endogenous or recombinantly prepared erythropoietin triggers an immediate cascade of activation reactions and at the same time causes degradation of itself and the receptor. In this way, the very short duration of the effect of erythropoietin[1] can be explained.

Links

Related Articles

- Regulation of erythrocyte production
- Erythropoietin deficiency anemia

- Ectopic production of erythropoietin

External links

- Erythropoietin (Czech Wikipedia)

Source

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References

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References

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