EPAS1 Gene

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Endothelial PAS domain protein 1

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1. Normal Function

The *EPAS1* gene, often known as *HIF2A*, provides instructions for making a protein called hypoxia-inducible factor 2-alpha (HIF-2α). This protein is one part (subunit) of a larger protein complex called HIF, which plays a critical role in the body's ability to adapt to changing oxygen levels. HIF controls several important genes involved in cell division, the formation of new blood vessels, and the production of red blood cells. It is the major regulator of a hormone called erythropoietin, which controls red blood cell production.

HIF-2α is constantly produced in the body. When adequate oxygen is available, other proteins target HIF-2α to be broken down (degraded) so it does not build up. However, when oxygen levels are lower than normal (hypoxia), HIF-2α is degraded at a slower rate. Consequently, more HIF is available to stimulate the formation of new blood vessels and the production of red blood cells. These activities help maximize the amount of oxygen that can be delivered to the body's organs and tissues.

Studies suggest that the *EPAS1* gene is involved in the body's adaptation to high altitude. At higher altitudes, such as in mountainous regions, air pressure is lower and less oxygen enters the body through the lungs. Over time, the body compensates for the lower oxygen levels by changing breathing patterns and producing more red blood cells and blood vessels.

2. Health Conditions Related to Genetic Changes

2.1 Familial Erythrocytosis

At least five mutations in the *EPAS1* gene have been found to cause familial erythrocytosis, an inherited condition characterized by an increased number of red blood cells and an elevated risk of abnormal blood clots. When familial erythrocytosis results from *EPAS1* gene mutations, it is often designated ECYT4.

Mutations in the *EPAS1* gene change single protein building blocks (amino acids) in the HIF-2α protein. These changes prevent HIF-2α from interacting normally with the proteins that target it for degradation. As a result, HIF-2α is not degraded efficiently, and HIF accumulates in cells even when adequate oxygen is available. The presence of extra HIF leads to the production of red blood cells when no more are needed, resulting in an excess of these cells in the bloodstream.

3. Other Names for This Gene

- basic-helix-loop-helix-PAS protein MOP2
- bHLHe73
- class E basic helix-loop-helix protein 73
- ECYT4
- endothelial PAS domain-containing protein 1
- EPAS-1

- EPAS1_HUMAN
- HIF-1-alpha-like factor
- HIF-1alpha-like factor
- HIF-2-alpha
- HIF2-alpha
- HIF2A
- HLF
- hypoxia-inducible factor 2 alpha
- hypoxia-inducible factor 2-alpha
- member of PAS protein 2
- MOP2
- PAS domain-containing protein 2
- PASD2

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