SDHAF2 Gene

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succinate dehydrogenase complex assembly factor 2

genes

1. Normal Function

The *SDHAF2* gene provides instructions for making a protein that interacts with the succinate dehydrogenase (SDH) enzyme. The SDHAF2 protein helps a molecule called FAD attach to the SDH enzyme. FAD is called a cofactor because it helps the enzyme carry out its function. The FAD cofactor is required for SDH enzyme activity.

The SDH enzyme plays a critical role in mitochondria, which are structures inside cells that convert the energy from food into a form that cells can use. Within mitochondria, the SDH enzyme links two important pathways in energy conversion: the citric acid cycle (or Krebs cycle) and oxidative phosphorylation. As part of the citric acid cycle, the SDH enzyme converts a compound called succinate to another compound called fumarate.

Succinate, the compound on which the SDH enzyme acts, is an oxygen sensor in the cell and can help turn on specific pathways that stimulate cells to grow in a low-oxygen environment (hypoxia). In particular, succinate stabilizes a protein called hypoxia-inducible factor (HIF) by preventing a reaction that would allow HIF to be broken down. HIF controls several important genes involved in cell division and the formation of new blood vessels in a hypoxic environment.

The *SDHAF2* gene is a tumor suppressor, which means it prevents cells from growing and dividing in an uncontrolled way.

2. Health Conditions Related to Genetic Changes

2.1. Hereditary paraganglioma-pheochromocytoma

At least one mutation in the *SDHAF2* gene has been identified in people with hereditary paraganglioma-pheochromocytoma type 2. People with this condition have paragangliomas, pheochromocytomas, or both. These noncancerous (benign) tumors are associated with the nervous system. The mutation replaces a protein building block (amino acid) in the SDHAF2 protein. Specifically, the amino acid glycine is replaced with the amino acid arginine at position 78 (written as Gly78Arg or G78R). The interaction between the mutated SDHAF2 protein and

the SDH complex is impaired, and attachment of the FAD cofactor is decreased. As a result, the SDH enzyme is nonfunctional. Because the mutated SDH enzyme cannot convert succinate to fumarate, succinate accumulates in the cell. Excess succinate abnormally stabilizes HIF, which also builds up in cells. Excess HIF stimulates cells to divide and triggers the production of blood vessels when they are not needed. Rapid and uncontrolled cell division, along with the formation of new blood vessels, can lead to the development of tumors in people with hereditary paraganglioma-pheochromocytoma.

3. Other Names for This Gene

- C11orf79
- FLJ20487
- hSDH5
- PGL2
- SDH assembly factor 2
- SDH5
- SDHF2_HUMAN
- succinate dehydrogenase assembly factor 2, mitochondrial
- succinate dehydrogenase subunit 5, mitochondrial

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