EDNRB Gene

Subjects: Genetics & Heredity
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Endothelin receptor type B: The EDNRB gene provides instructions for making a protein called endothelin receptor type B.

Keywords: genes

1. Normal Function

This protein is located on the surface of cells and functions as a signaling mechanism, transmitting information from outside the cell to inside the cell. The receptor interacts with proteins called endothelins to regulate several critical biological processes, including the development and function of blood vessels, the production of certain hormones, and the stimulation of cell growth and division.

Endothelin 3 (produced from the *EDN3* gene) is one of the proteins that interacts with endothelin receptor type B. During early development before birth (embryonic development), endothelin 3 and endothelin receptor type B together play an important role in neural crest cells. These cells migrate from the developing spinal cord to specific regions in the embryo, where they give rise to many different types of cells. In particular, endothelin 3 and endothelin receptor type B are essential for the formation of nerves in the intestine (enteric nerves) and for the production of specialized cells called melanocytes. Melanocytes produce melanin, a pigment that contributes to skin, hair, and eye color. Melanin is also involved in the normal function of the inner ear.

2. Health Conditions Related to Genetic Changes

2.1 Hirschsprung Disease

More than 30 mutations in the *EDNRB* gene have been found to cause Hirschsprung disease, a disorder that causes severe constipation or blockage of the intestine. Although Hirschsprung disease is a feature of another condition called Waardenburg syndrome type IV (described below), *EDNRB* gene mutations can also cause Hirschsprung disease in people without Waardenburg syndrome. People with a mutation in one of the two copies of the *EDNRB* gene tend to develop Hirschsprung disease, while people with mutations in both copies of the gene usually develop Waardenburg syndrome type IV. Most of these mutations change single DNA building blocks (nucleotides) in the gene. Changes in the *EDNRB* gene disrupt the normal function of endothelin receptor type B, preventing it from playing its usual role in the development of enteric nerves. As a result, these cells do not form normally during embryonic development. A lack of enteric nerves prevents stool from being moved through the intestine normally, leading to severe constipation or intestinal blockage.

2.2 Waardenburg Syndrome

More than a dozen mutations in the *EDNRB* gene have been identified in people with Waardenburg syndrome type IV (also known as Waardenburg-Shah syndrome). This type of Waardenburg syndrome is characterized by changes in skin, hair, and eye coloring; hearing loss; and Hirschsprung disease. Mutations in the *EDNRB* gene disrupt the normal function of endothelin receptor type B or lead to the production of an abnormally small, nonfunctional version of the protein. Because the receptor is necessary for the formation of enteric nerves and melanocytes, these cell types do not form normally during embryonic development. Missing enteric nerves in certain parts of the intestine cause the signs and symptoms of Hirschsprung disease. A lack of melanocytes affects the coloring of skin, hair, and eyes and causes the hearing loss characteristic of Waardenburg syndrome.

2.3 Cancers

Several studies have suggested that inherited variations in the *EDNRB* gene may be associated with an increased risk of melanoma, a common form of skin cancer that begins in melanocytes. However, other studies have not shown this association, and this gene's role in cancer risk remains unclear.

3. Other Names for This Gene

- ABCDS
- EDNRB_HUMAN
- endothelin receptor, non-selective type
- ETB
- ETBR
- ETRB
- HSCR
- HSCR2
- RP11-318G21.1
- WS4A

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