EDN3 gene

endothelin 3

Normal Function

The *EDN3* gene provides instructions for making a protein called endothelin 3. Proteins in the endothelin family are produced in various cells and tissues, where they are involved in the development and function of blood vessels, the production of certain hormones, and the stimulation of cell growth and division (proliferation).

Endothelin 3 functions by interacting with another protein, endothelin receptor type B (produced from the *EDNRB* gene), on the surface of cells. During early development before birth, 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 its receptor 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.

Health Conditions Related to Genetic Changes

Hirschsprung disease

Variants (also known as mutations) in the *EDN3* 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 disorder called Waardenburg syndrome type IV (described below), *EDN3* gene variants can also cause Hirschsprung disease in people without Waardenburg syndrome. These variants change one DNA building block (nucleotide) or insert an additional nucleotide in the gene. Changes in the *EDN3* gene disrupt the normal function of endothelin 3, 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.

Waardenburg syndrome

Variants in the *EDN3* gene have been identified in people with Waardenburg syndrome

type IV (also known as Waardenburg-Hirschsprung disease or Waardenburg-Shah syndrome). This type of Waardenburg syndrome is characterized by changes in skin, hair, and eye coloring; hearing loss; and Hirschsprung disease (described above). *EDN3* gene variants change single nucleotides in the gene, preventing the production of a functional endothelin 3 protein. Because active endothelin 3 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.

Other Names for This Gene

- EDN3_HUMAN
- endothelin 3 precursor
- ET3
- HSCR4
- PPET3
- Preproendothelin-3
- RP4-614C15.1
- WS4B

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of EDN3 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1908[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28EDN3%5BTIAB%5D%29+OR+%28endothelin+3%5BTIAB%5D%29%29+OR+%28%28endothelin+3+precursor%5BTIAB%5D%29+OR+%28ET3%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- ENDOTHELIN 3; EDN3 (https://omim.org/entry/131242)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1908)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=EDN3[gene])

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Genomic Location

The *EDN3* gene is found on chromosome 20 (https://medlineplus.gov/genetics/chromosome/20/).

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