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.

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**

About 10 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 mutations can also cause Hirschsprung disease in people without Waardenburg syndrome. These mutations 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**

At least five mutations in the *EDN3* 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. *EDN3* mutations 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.

**Chromosomal Location**

Cytogenetic Location: 20q13.32, which is the long (q) arm of chromosome 20 at
position 13.32

Molecular Location: base pairs 59,300,415 to 59,325,992 on chromosome 20 (Homo
sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

**Other Names for This Gene**

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

**Additional Information & Resources**

**Educational Resources**

- Developmental Biology (sixth edition, 2000): The Neural Crest
  https://www.ncbi.nlm.nih.gov/books/NBK10065/
- Madame Curie Bioscience Database: Neural Crest and the Development of the
  Enteric Nervous System
  https://www.ncbi.nlm.nih.gov/books/NBK6273/
Clinical Information from GeneReviews

- Hirschsprung Disease Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1439

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28EDN3%5BTIAB%5D%29+OR+%28endothelin+3%5BTIAB%5D%29+OR+%28%28endothelin+3+precursor%5BTIAB%5D%29+OR+%28ET3%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D+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
  http://omim.org/entry/131242

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_EDN3.html

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=EDN3%5Bgene%5D

- HGNC Gene Symbol Report

- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:1908

- NCBI Gene

- UniProt
  https://www.uniprot.org/uniprot/P14138

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/8001160

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14669347
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4612066/

- OMIM: ENDOTHELIN 3
  http://omim.org/entry/131242
Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/27905407
Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5131347/

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14659083

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15065997

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11303518
Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1734825/

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10591209

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10231870

Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/2009762

Reviewed: May 2018
Published: August 20, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services