SLC11A2 gene
solute carrier family 11 member 2

Normal Function

The SLC11A2 gene provides instructions for making a protein called divalent metal transporter 1 (DMT1). Four different versions (isoforms) of the DMT1 protein are produced from the SLC11A2 gene. Each isoform is specific to one or more tissues, but some form of the DMT1 protein is found in all tissues. The primary role of the DMT1 protein is to transport positively charged iron atoms (ions) within cells; however, the protein can transport some other metal ions as well.

In a section of the small intestine called the duodenum, the DMT1 protein is located within finger-like projections called microvilli. These projections absorb nutrients from food as it passes through the intestine and then release them into the bloodstream. In all other cells, including immature red blood cells called erythroblasts, DMT1 is located in the membrane of endosomes, which are specialized compartments that are formed at the cell surface to carry proteins and other molecules to their destinations within the cell. DMT1 transports iron from the endosomes to the cytoplasm so it can be used by the cell.

Health Conditions Related to Genetic Changes

Hypochromic microcytic anemia with iron overload

At least seven mutations in the SLC11A2 gene have been found to cause hypochromic microcytic anemia with iron overload. This condition is characterized by a shortage of red blood cells (anemia) that is apparent at birth. The red blood cells that are produced are abnormally small (microcytic) and pale (hypochromic). There is also progressive accumulation of iron in the liver.

Most SLC11A2 gene mutations that cause this condition change single protein building blocks (amino acids) in the DMT1 protein. These mutations lead to reduced production of the DMT1 protein, decreased protein function, or impaired ability of the protein to get to the correct location in cells. In erythroblasts, a shortage of DMT1 protein diminishes the amount of iron transported within cells, even though there is an abundance of iron in the blood. As a result, the development of healthy red blood cells is impaired, leading to a shortage of these cells. In the duodenum, a shortage of DMT1 protein decreases iron absorption. To compensate, cells increase production of functional DMT1 protein, which increases iron absorption. Because the red blood cells cannot use the iron that is absorbed, it accumulates in the liver, eventually impairing liver function. The lack of iron in red blood cells and the accumulation of
Iron in the liver lead to the signs and symptoms of hypochromic microcytic anemia with iron overload.

**Chromosomal Location**

Cytogenetic Location: 12q13.12, which is the long (q) arm of chromosome 12 at position 13.12

Molecular Location: base pairs 50,952,263 to 51,028,335 on chromosome 12 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

**Other Names for This Gene**

- DCT1
- divalent cation transporter 1
- DMT-1
- DMT1
- natural resistance-associated macrophage protein 2
- NRAMP 2
- NRAMP2
- solute carrier family 11 (proton-coupled divalent metal ion transporter), member 2
- solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2

**Additional Information & Resources**

**Educational Resources**

- Biochemistry (fifth edition, 2002): Oxygen Binding Induces Substantial Structural Changes at the Iron Sites in Hemoglobin
  https://www.ncbi.nlm.nih.gov/books/NBK22596/#A1348

- Madame Curie Bioscience Database: A Glimpse into the Mechanism of Metal-Ion Uptake
  https://www.ncbi.nlm.nih.gov/books/NBK6091/#A23429
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SLC11A2%5BTIAB%5D%29+OR+%28%28divalent+metal+transporter+1%5BTIAB%5D%29+OR+%28DMT1%5BTIAB%5D%29+OR+%28NRAMP2%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+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- SOLUTE CARRIER FAMILY 11 (PROTON-COUPLED DIVALENT METAL ION TRANSPORTER), MEMBER 2
  http://omim.org/entry/600523

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SLC11A2.html
- ClinVar
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4891
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P49281

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21871825

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16439678

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19786204
  *Citation on PubMed*: https://www.ncbi.nlm.nih.gov/pubmed/16584902

  *Citation on PubMed*: https://www.ncbi.nlm.nih.gov/pubmed/16085548

  *Citation on PubMed*: https://www.ncbi.nlm.nih.gov/pubmed/16091455

- OMIM: SOLUTE CARRIER FAMILY 11 (PROTON-COUPLED DIVALENT METAL ION TRANSPORTER), MEMBER 2  
  http://omim.org/entry/600523

  *Citation on PubMed*: https://www.ncbi.nlm.nih.gov/pubmed/23177986

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