ABCD4 gene
ATP binding cassette subfamily D member 4

Normal Function

The \textit{ABCD4} gene provides instructions for making a protein that is involved in the conversion of vitamin B12 (also known as cobalamin) into one of two molecules, adenosylcobalamin (AdoCbl) or methylcobalamin (MeCbl). AdoCbl is required for the normal function of an enzyme known as methylmalonyl CoA mutase. This enzyme helps break down certain protein building blocks (amino acids), fats (lipids), and cholesterol. AdoCbl is called a cofactor because it helps methylmalonyl CoA mutase carry out its function. MeCbl is also a cofactor, but for an enzyme known as methionine synthase. This enzyme converts the amino acid homocysteine to another amino acid, methionine. The body uses methionine to make proteins and other important compounds.

The ABCD4 protein is found in the membrane that surrounds cell structures called lysosomes. Lysosomes are compartments within cells in which enzymes digest and recycle materials. In the lysosomal membrane, the ABCD4 protein interacts with another protein called LMBD1 (produced from the \textit{LMBRD1} gene). Together, these two proteins transport vitamin B12 out of lysosomes, making it available for further processing into AdoCbl and MeCbl.

Health Conditions Related to Genetic Changes

\textbf{Methylmalonic acidemia with homocystinuria}

At least five mutations in the \textit{ABCD4} gene have been found to cause methylmalonic acidemia with homocystinuria, cblJ type, one form of a disorder that causes developmental delay, eye defects, neurological problems, and blood abnormalities. \textit{ABCD4} gene mutations involved in this condition lead to production of an abnormal ABCD4 protein that is unable to function. A shortage of functional ABCD4 protein prevents the release of vitamin B12 from lysosomes, so the vitamin is unavailable for the production of AdoCbl and MeCbl. Because both of these cofactors are missing, the enzymes that require them (methylmalonyl CoA mutase and methionine synthase) do not function normally. As a result, certain amino acids, lipids, and cholesterol are not broken down and homocysteine cannot be converted to methionine. This dual defect results in a buildup of toxic compounds as well as homocysteine, and a decrease in the production of methionine within the body. This combination of imbalances leads to the signs and symptoms of methylmalonic acidemia with homocystinuria.
**Chromosomal Location**

Cytogenetic Location: 14q24.3, which is the long (q) arm of chromosome 14 at position 24.3

Molecular Location: base pairs 74,285,269 to 74,303,062 on chromosome 14 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)

![Cytogenetic Location Diagram](image)

**Credit:** Genome Decoration Page/NCBI

**Other Names for This Gene**

- 69 kDa peroxisomal ABC-transporter
- ABC41
- ATP-binding cassette sub-family D member 4
- ATP-binding cassette, sub-family D (ALD), member 4
- EST352188
- MAHCJ
- P70R
- P79R
- peroxisomal membrane protein 69
- PMP69
- PMP70-related protein
- PXMP1-L
- PXMP1L

**Additional Information & Resources**

Clinical Information from GeneReviews

- Disorders of Intracellular Cobalamin Metabolism
  https://www.ncbi.nlm.nih.gov/books/NBK1328
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28ABCD4%5BTIAB%5D%29+OR+%28ATP+binding+cassette+subfamily+D+member+4%5BTIAB%5D%29+OR+%28%2869+kDa+peroxisomal+ABC-transporter%5BTIAB%5D%29+OR+%28ATP-binding+cassette+sub-family+D+member+4%5BTIAB%5D%29+OR+%28P70R%5BTIAB%5D%29+OR+%28PMP69%5BTIAB%5D%29+OR+%28PMP70-related+protein%5BTIAB%5D%29+OR+%28PXMP1-L%5BTIAB%5D%29+OR+%28peroxisomal+membrane+protein+69%5BTIAB%5D%29+AND+%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- ATP-BINDING CASSETTE, SUBFAMILY D, MEMBER 4
  http://omim.org/entry/603214

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_ABCD4.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=ABCD4%5Bgene%5D
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:5826
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/O14678

Sources for This Summary

- OMIM: ATP-BINDING CASSETTE, SUBFAMILY D, MEMBER 4
  http://omim.org/entry/603214
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22922874
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25535791

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23141461


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