ABCD4 gene

ATP binding cassette subfamily D member 4

Normal Function

The *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), fat building blocks (fatty acids), 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 *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

Methylmalonic acidemia with homocystinuria

Several variants (also known as mutations) in the *ABCD4* gene have been found to cause methylmalonic acidemia with homocystinuria, cblJ type, which is one form of a disorder that causes developmental delay, eye defects, neurological problems, and blood abnormalities. Individuals with cblJ type often also have skin discoloration. *ABCD4* gene variants 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, fatty acids, and cholesterol are not broken down and homocysteine cannot be converted to methionine. This dual defect results in a buildup of toxic compounds, including 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.

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

Tests Listed in the Genetic Testing Registry

- Tests of ABCD4 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5826[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28ABCD4%5BTIAB%5D%29+OR+%28ATP+binding+cassette+subfamily+D+member+4%5BTIAB%5D%29%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+%28P79R%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%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%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; ABCD4 (https://omim.org/entry/603214)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/5826)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ABCD4[gene])

References

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- Deme JC, Hancock MA, Xia X, Shintre CA, Plesa M, Kim JC, Carpenter EP, Rosenblatt DS, Coulton JW. Purification and interaction analyses of two humanlysosomal vitamin B12 transporters: LMBD1 and ABCD4. Mol Membr Biol. 2014Nov-Dec;31(7-8):250-61. doi: 10.3109/09687688.2014.990998. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/25535791)
- Kim JC, Lee NC, Hwu PW, Chien YH, Fahiminiya S, Majewski J, Watkins D, Rosenblatt DS. Late onset of symptoms in an atypical patient with the cblJ inbornerror of vitamin B12 metabolism: diagnosis and novel mutation revealed by exomesequencing. Mol Genet Metab. 2012 Dec;107(4):664-8. doi:10.1016/j.ymgme.2012.10.005. Epub 2012 Oct 16. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23141461)

Genomic Location

The *ABCD4* gene is found on chromosome 14 (https://medlineplus.gov/genetics/chromosome/14/).

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