LMBRD1 gene

LMBR1 domain containing 1

Normal Function

The *LMBRD1* gene provides instructions for making a protein, called LMBD1, 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 LMBD1 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 LMBD1 protein interacts with another protein called ABCD4 (produced from the *ABCD4* gene). Together, these two proteins transport vitamin B12 out of lysosomes, making it available for further processing into AdoCbl and MeCbl.

Studies suggest that the LMBD1 protein is also found in the membrane that surrounds the cell (the plasma membrane). Here, the protein appears to be involved in removing another protein called the insulin receptor from the membrane. Removal of this receptor helps regulate insulin signaling, which controls levels of blood glucose, also called blood sugar.

Another version (isoform) of the LMBD1 protein, sometimes called NESI, can also be produced from the *LMBRD1* gene. This protein interacts with a region called the nuclear export signal (NES) of a protein that forms a piece of the hepatitis D virus. It is thought that interaction with NESI aids in the assembly of the virus. The hepatitis D virus can cause liver disease, although infection is rare and requires co-infection with a related virus called hepatitis B.

Health Conditions Related to Genetic Changes

Methylmalonic acidemia with homocystinuria

Several variants (also known as mutations) in the *LMBRD1* gene have been found to cause methylmalonic acidemia with homocystinuria, cblF type, which is one form of a disorder that causes developmental delay, eye defects, neurological problems, and blood abnormalities. *LMBRD1* gene variants involved in this condition lead to production of an abnormally short LMBD1 protein that is unable to function. A shortage of functional LMBD1 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.

Other Names for This Gene

- bA810I22.1
- C6orf209
- cblF
- FLJ11240
- HDAg-L-interacting protein NESI
- hepatitis delta antigen-L interacting protein
- liver regeneration p-53 related protein
- LMBD1
- MAHCF
- NESI
- nuclear export signal-interacting protein
- probable lysosomal cobalamin transporter

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of LMBRD1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=55788[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28LMBRD1%5BTIAB%5D%29+OR+%28LMBR1+domain+containing+1%5BTIAB%5D%29%29+OR+%28%28FLJ11240%5BTIAB%5D%29+OR+%28LMBD1%5BTIAB%5D%29+OR+%28NESI%5BTIAB%5D%29+OR+%28cblF%5BTIAB%5D%29+OR+%28hepatitis+delta+antigen-L+interacting+protein%5BTIAB%5D%29+OR+%28liver+regeneration+p-53+relate

d+protein%5BTIAB%5D%29+OR+%28nuclear+export+signal-interacting+protein%5BTIAB%5D%29+OR+%28probable+lysosomal+cobalamin+transporter%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

- LMBR1 DOMAIN-CONTAINING PROTEIN 1: LMBRD1 (https://omim.org/entry/612625)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/55788)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=LMBRD1[gene])

References

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- Huang C, Jiang JY, Chang SC, Tsay YG, Chen MR, Chang MF. Nuclear exportsignal-interacting protein forms complexes with lamin A/C-Nups to mediate theCRM1-independent nuclear export of large hepatitis delta antigen. J Virol. 2013Feb;87(3):1596-604. doi: 10.1128/JVI.02357-12. Epub 2012 Nov 21. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/23175358) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3554191/)
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- Tseng LT, Lin CL, Tzen KY, Chang SC, Chang MF. LMBD1 protein serves as aspecific adaptor for insulin receptor internalization. J Biol Chem. 2013 Nov8;288(45):32424-32432. doi: 10.1074/jbc.M113.479527. Epub 2013 Sep 27. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24078630) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3820877/)

Genomic Location

The *LMBRD1* gene is found on chromosome 6 (https://medlineplus.gov/genetics/chromosome/6/).

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