LMBRD1 Gene

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LMBR1 domain containing 1

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1. Introduction

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 blood sugar levels in the body.

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.

2. Health Conditions Related to Genetic Changes

2.1. Methylmalonic Acidemia with Homocystinuria

At least nine mutations in the *LMBRD1* gene have been found to cause methylmalonic acidemia with homocystinuria, cblF type, one form of a disorder that causes developmental delay, eye defects, neurological problems, and blood abnormalities. *LMBRD1* gene mutations 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.

3. 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

References

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