EPM2A gene

EPM2A, laforin glucan phosphatase

Normal Function

The *EPM2A* gene provides instructions for making a protein called laforin. Although this protein is active in cells throughout the body, it appears to play a critical role in the survival of nerve cells (neurons) in the brain.

Studies suggest that laforin has multiple functions within cells. To carry out these functions, laforin interacts with several other proteins, including malin (which is produced from the *NHLRC1* gene). These proteins are part of complex networks that transmit chemical signals and break down unneeded or abnormal proteins. Additionally, laforin may act as a tumor suppressor protein, which means that it keeps cells from growing and dividing in an uncontrolled way.

Laforin and malin likely play a critical role in regulating the production of a complex sugar called glycogen. Glycogen is a major source of stored energy in the body. The body stores this sugar in the liver and muscles, breaking it down when it is needed for fuel. Researchers believe that laforin and malin may prevent a potentially damaging buildup of glycogen in tissues that do not normally store this molecule, such as those of the nervous system.

Health Conditions Related to Genetic Changes

Lafora progressive myoclonus epilepsy

More than 50 mutations in the *EPM2A* gene have been identified in people with Lafora progressive myoclonus epilepsy. Many of these mutations change single protein building blocks (amino acids) in the laforin protein. Other mutations delete or insert genetic material in the *EPM2A* gene. Almost all mutations in this gene prevent cells from producing any laforin or lead to the production of a nonfunctional version of the protein.

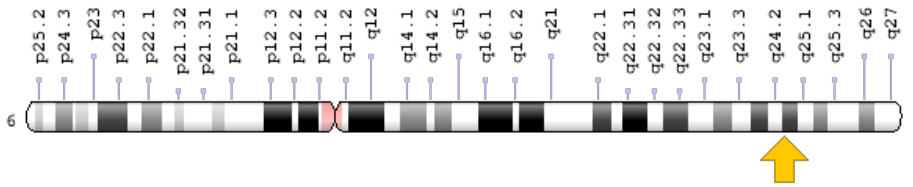
It is unclear how mutations in the *EPM2A* gene lead to the major features of Lafora progressive myoclonus epilepsy. Studies suggest that a loss of laforin prevents cells from regulating the production of glycogen. As a result, distinctive clumps called Lafora bodies form within many types of cells. Lafora bodies are made up of an abnormal form of glycogen (called polyglucosan) that cannot be broken down and used for fuel. Instead, polyglucosans build up to form clumps that can damage cells. Neurons appear to be particularly vulnerable to this type of damage. Although Lafora bodies are found in many of the body's tissues, the signs and symptoms of Lafora progressive myoclonus epilepsy are limited to the nervous system.

Researchers are uncertain how a loss of functional laforin contributes to the formation of Lafora bodies. However, a lack of this protein ultimately results in the death of neurons, which interferes with the brain's normal functions. The degeneration of neurons likely underlies the seizures, movement abnormalities, intellectual decline, and other neurological problems seen with Lafora progressive myoclonus epilepsy.

Chromosomal Location

Cytogenetic Location: 6q24.3, which is the long (q) arm of chromosome 6 at position 24.3

Molecular Location: base pairs 145,382,540 to 145,736,023 on chromosome 6 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- epilepsy, progressive myoclonus type 2, Lafora disease (laforin)
- epilepsy, progressive myoclonus type 2A, Lafora disease (laforin)
- EPM2
- EPM2A_HUMAN
- laforin
- LD
- LDE
- MELF

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Glycogen Metabolism https://www.ncbi.nlm.nih.gov/books/NBK21190/

Clinical Information from GeneReviews

- Progressive Myoclonus Epilepsy, Lafora Type
  https://www.ncbi.nlm.nih.gov/books/NBK1389

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28EPM2A%5BTIAB%5D%29+OR+%28laforin%5BTIAB%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

- EPM2A GENE
  http://omim.org/entry/607566

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_EPM2A.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=EPM2A%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:3413
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:7957
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/7957
- The Lafora Progressive Myoclonus Epilepsy Mutation and Polymorphism Database
  http://projects.tcag.ca/lafora/
- UniProt
  https://www.uniprot.org/uniprot/O95278

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