DOLK gene

dolichol kinase

Normal Function

The *DOLK* gene provides instructions for making the dolichol kinase enzyme, which facilitates the final step of the production of a compound called dolichol phosphate. This compound is critical for a process called glycosylation, which attaches groups of sugar molecules (oligosaccharides) to proteins. Glycosylation changes proteins in ways that are important for their functions.

Dolichol kinase is found in the membrane of a cell compartment called the endoplasmic reticulum, which is involved in protein processing and transport. This enzyme adds a phosphate group (a cluster of oxygen and phosphorus atoms) to the compound dolichol to produce dolichol phosphate. During glycosylation, sugars are added to dolichol phosphate to build the oligosaccharide chain. Once the chain is formed, dolichol phosphate transports the oligosaccharide to the protein that needs to be glycosylated and attaches it to a specific site on the protein.

Dolichol phosphate is also needed for the formation of GPI anchors. These are complexes that attach (bind) to proteins and then bind to the outer surface of the cell membrane to ensure that the protein is available on the cell surface when needed.

Health Conditions Related to Genetic Changes

DOLK-congenital disorder of glycosylation

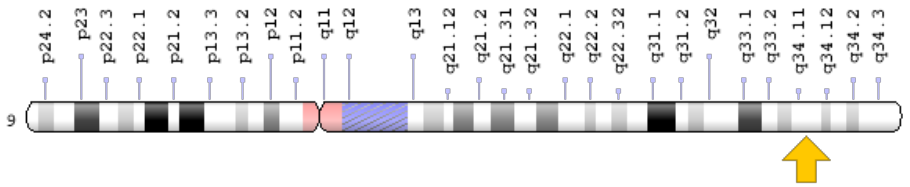
At least six mutations in the *DOLK* gene have been found to cause *DOLK*-congenital disorder of glycosylation (*DOLK*-CDG, formerly known as congenital disorder of glycosylation type Im). This condition often causes the heart to be weakened and enlarged (dilated cardiomyopathy), but it can also result in neurological problems as well as other signs and symptoms.

DOLK gene mutations change single protein building blocks (amino acids) in the dolichol kinase enzyme, leading to an enzyme with reduced or absent activity. Without properly functioning dolichol kinase, dolichol phosphate is not produced and glycosylation cannot proceed normally. In particular, a protein known to stabilize heart muscle fibers, called alpha-dystroglycan, has been shown to have reduced glycosylation in people with *DOLK*-CDG. Impaired glycosylation of alpha-dystroglycan disrupts its normal function, which damages heart muscle fibers as they repeatedly contract and relax. Over time, the fibers weaken and break down, leading to dilated cardiomyopathy. The other signs and symptoms of *DOLK*-CDG are likely due to the abnormal glycosylation of additional proteins in other organs and tissues.

Chromosomal Location

Cytogenetic Location: 9q34.11, which is the long (q) arm of chromosome 9 at position 34.11

Molecular Location: base pairs 128,945,530 to 128,947,733 on chromosome 9 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CDG1M
- DK
- DK1
- dolichol kinase 1
- KIAA1094
- SEC59
- SEC59 homolog
- TMEM15
- transmembrane protein 15

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth edition, 2002): Most Proteins Synthesized in the Rough ER Are Glycosylated by the Addition of a Common N-linked Oligosaccharide
  https://www.ncbi.nlm.nih.gov/books/NBK26841/#A2230
- Molecular Biology of the Cell (fourth edition, 2002): What Is the Purpose of Glycosylation?
  https://www.ncbi.nlm.nih.gov/books/NBK26941/#A2354
- Molecular Cell Biology (fourth edition, 2000): A Common Preformed N-Linked Oligosaccharide Is Added to Many Proteins in the Rough ER
  https://www.ncbi.nlm.nih.gov/books/NBK21744/#A4826

Clinical Information from GeneReviews

- Congenital Disorders of N-Linked Glycosylation and Multiple Pathway Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1332

Scientific Articles on PubMed

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

Catalog of Genes and Diseases from OMIM

- DOLICHOL KINASE
  http://omim.org/entry/610746

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=DOLK%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:23406
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:22845
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/22845
- UniProt
  https://www.uniprot.org/uniprot/Q9UPQ8

Sources for This Summary

- Buczkowska A, Swiezewska E, Lefeber DJ. Genetic defects in dolichol metabolism. J Inherit Metab Dis. 2015 Jan;38(1):157-69. doi: 10.1007/s10545-014-9760-1. Epub 2014 Oct 1. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/25270028
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4281381/
- OMIM: DOLICHOL KINASE
  http://omim.org/entry/610746
- Denecke J, Kranz C. Hypoglycosylation due to dolichol metabolism defects. Biochim Biophys Acta. 2009 Sep;1792(9):888-95. doi: 10.1016/j.bbadis.2009.01.013. Epub 2009 Feb 3. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19419701
- Shridas P, Waechter CJ. Human dolichol kinase, a polytopic endoplasmic reticulum membrane protein with a cytoplasmically oriented CTP-binding site. J Biol Chem. 2006 Oct 20;281(42): 31696-704. Epub 2006 Aug 21.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16923818

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