DOLK-congenital disorder of glycosylation

Description

DOLK-congenital disorder of glycosylation (*DOLK*-CDG, formerly known as congenital disorder of glycosylation type Im) is an inherited condition that often affects the heart but can also involve other body systems. The pattern and severity of this disorder's signs and symptoms vary among affected individuals.

Individuals with *DOLK*-CDG typically develop signs and symptoms of the condition during infancy or early childhood. Nearly all individuals with *DOLK*-CDG develop a weakened and enlarged heart (dilated cardiomyopathy). Other frequent signs and symptoms include recurrent seizures; developmental delay; poor muscle tone (hypotonia); and dry, scaly skin (ichthyosis). Less commonly, affected individuals can have distinctive facial features, kidney disease, hormonal abnormalities, or eye problems.

Individuals with *DOLK*-CDG typically do not survive into adulthood, often because of complications related to dilated cardiomyopathy, and some do not survive past infancy.

Frequency

DOLK-CDG is likely a rare condition; at least 18 cases have been reported in the scientific literature.

Causes

DOLK-CDG is caused by mutations in the *DOLK* gene. This gene provides instructions for making the enzyme dolichol kinase, 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. During glycosylation, sugars are added to dolichol phosphate in order 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.

Mutations in the *DOLK* gene lead to the production of abnormal dolichol kinase 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.

Learn more about the gene associated with DOLK-congenital disorder of glycosylation

- DOLK

Inheritance

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- CDG1M
- Congenital disorder of glycosylation, type Im
- DK1 deficiency
- Dolichol kinase deficiency
- DOLK-CDG

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: DK1-congenital disorder of glycosylation (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1835849/)

Genetic and Rare Diseases Information Center

- Congenital disorder of glycosylation (https://rarediseases.info.nih.gov/diseases/10307/index)
- DK1-CDG (https://rarediseases.info.nih.gov/diseases/12393/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- CONGENITAL DISORDER OF GLYCOSYLATION, TYPE Im; CDG1M (https://omim.org/entry/610768)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28dolichol+kinase%29+OR+%28DOLK%29%29+AND+%28congenital+disorder+of+glycosylation%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

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