DOLK Gene

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Contributor: Vivi Li

Dolichol Kinase

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1. 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.

2. Health Conditions Related to Genetic Changes

2.1 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.

3. Other Names for This Gene

- CDG1M
- DK
- DK1
- dolichol kinase 1
- KIAA1094

- SEC59
- SEC59 homolog
- TMEM15
- transmembrane protein 15

References

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