PIGN gene

phosphatidylinositol glycan anchor biosynthesis class N

Normal Function

The *PIGN* gene provides instructions for making an enzyme called GPI ethanolamine phosphate transferase 1. This enzyme takes part in a series of steps that produce a molecule called a glycophosphatidylinositol (GPI) anchor. A GPI anchor attaches to many different proteins inside the cell, which are known as GPI-anchored proteins. After a GPI anchor binds to a protein, the GPI anchor attaches itself to the outer surface of the cell membrane, ensuring that the GPI-anchored protein is available when it is needed. A GPI anchor is made up of many different pieces and is assembled in a cell structure called the endoplasmic reticulum, which is involved in protein processing and transport.

GPI-anchored proteins have a variety of roles, which include helping cells attach to one another (cell adhesion), relaying signals into the cells (cell signaling), and protecting cells from foreign invaders (cellular immunity).

Health Conditions Related to Genetic Changes

Fryns syndrome

Variants (also called mutations) in the *PIGN* gene have been found to cause Fryns syndrome in some people. This condition affects the development of many parts of the body. Most people with Fryns syndrome have a defect in the muscle that separates the abdomen from the chest cavity (the diaphragm). The most common defect is a congenital diaphragmatic hernia, which is a hole in the diaphragm that develops before birth. Additional signs and symptoms can include distinctive facial features and abnormalities of the fingers and toes.

Most of the *PIGN* gene variants that are associated with Fryns syndrome cause cells to produce a shortened version of the enzyme that does not function properly. These variants are known as "loss-of-function variants" because they reduce the amount of functional GPI ethanolamine phosphate transferase 1 enzyme that is available to modify the GPI anchor. As a result, the GPI anchor cannot deliver proteins to their proper places on the cell membrane. This disrupts critical developmental pathways, which leads to the signs and symptoms seen in people with Fryns syndrome.

Other disorders

Variants in the *PIGN* gene can also cause a condition called multiple congenital anomalies-hypotonia-seizures syndrome 1 (MCAHS1). Many of the signs and symptoms seen in people with MCAHS1 overlap with those seen in people withFryns syndrome. However, people with MCAHS1 typically do not have a congenital diaphragmatic hernia. Many of the *PIGN* gene variants that cause MCAHS1 lead to changes in single protein building blocks (amino acids) in the GPI ethanolamine phosphate transferase 1 enzyme. Though the features seen in people with MCAHS1 are typically considered to be less severe than those seen in people withFryns syndrome, individuals with MCAHS1 usually do not survive past early childhood. People with MCAHS1 have variants in both copies of the *PIGN* gene.

Some people with *PIGN* gene variants have neurologic signs and symptoms that are similar to those seen in people with Fryns syndrome or MCAHS1 without having all of the features of these disorders. These individuals may have weak muscle tone (hypotonia), developmental delays, intellectual disabilities, movement disorders, and seizures. Researchers are working to learn more about the range of features that can be associated with changes in the *PIGN* gene.

Other Names for This Gene

- MCD4
- Phosphatidylinositol glycan anchor biosynthesis class N protein
- PIG-N

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PIGN (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=23556[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=PIGN+gene&filter=datesearch.y_10)

Catalog of Genes and Diseases from OMIM

- PHOSPHATIDYLINOSITOL GLYCAN ANCHOR BIOSYNTHESIS CLASS N PROTEIN; PIGN (https://omim.org/entry/606097)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/23556)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=PIGN[gene])

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