PIGT gene

phosphatidylinositol glycan anchor biosynthesis class T

Normal Function

The *PIGT* gene provides instructions for making a protein called GPI transamidase component PIG-T (shortened to PIG-T protein). This protein is important for the attachment of certain proteins to the cell surface. Specifically, the PIG-T protein attaches (binds) a molecule called a glycosylphosphatidylinositol (GPI) anchor to various proteins inside the cell. After the GPI anchor and protein are bound, the anchor is attached to the outer surface of the cell membrane. Anchored proteins have a variety of roles, including sticking cells to one another, relaying signals into cells, and protecting cells from destruction.

Health Conditions Related to Genetic Changes

Paroxysmal nocturnal hemoglobinuria

Variants (also known as mutations) in the *PIGT* gene cause a rare form of paroxysmal nocturnal hemoglobinuria (PNH), which is a condition that affects blood cells. People with PNH have episodes of blood in the urine (hemoglobinuria) that results from the breakdown of red blood cells. Other blood cell abnormalities also occur. In addition, individuals with *PIGT*-related PNH have abnormal inflammation, which can cause recurrent aseptic meningitis (which is inflammation of the membranes surrounding the brain and spinal cord not caused by infections); a red, itchy rash (known as hives or urticaria); joint pain (arthralgia); or inflammatory bowel disease.

Affected individuals are born with a variant in one copy of the *PIGT* gene. This inherited variant is known as a germline variant and is present in every cell of the body. A second alteration that deletes the other (normal) copy of the *PIGT* gene is acquired during the person's lifetime. This second variant, known as a somatic variant, occurs in a blood-forming cell called a hematopoietic stem cell. This variant is found only in the hematopoietic stem cell and blood cells produced from that cell. Together, these *PIGT* gene variants severely reduce or eliminate the function of the PIG-T protein. As a result, GPI anchors are not attached to proteins inside cells. The GPI anchors without proteins are present at the surface of the cell. The shortage of certain proteins at the cell surface alters cell functions. Specifically, proteins that normally protect red blood cells from being broken down are missing. The red blood cells are prematurely destroyed, leading to a shortage of red blood cells (hemolytic anemia) and blood in the urine.

Studies show that GPI anchors with no attached proteins trigger inflammation in the body, leading to the inflammatory features in individuals with *PIGT*-related PNH.

Other disorders

Variants in the *PIGT* gene also cause a rare condition called multiple congenital anomalies-hypotonia-seizures syndrome 3. Affected individuals have delayed development; seizures; low muscle tone (hypotonia); distinct facial features; and abnormalities that are present from birth (congenital), typically involving the heart, bones, urinary system, or digestive system.

Individuals with this condition inherit two altered copies of the *PIGT* gene, one from each parent. The variants impair the function of the PIG-T protein, reducing the levels of proteins attached to the cell surface by GPI anchors. Researchers suspect that a shortage of proteins important for development on the surface of cells impairs the normal development of many body systems, leading to the varied signs and symptoms of multiple congenital anomalies-hypotonia-seizures syndrome 3.

Other Names for This Gene

- CGI-06
- MCAHS3
- NDAP
- neuronal development-associated protein
- phosphatidylinositol glycan, class T
- PNH2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PIGT (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=51604[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=pigt%255Btiab%255D&filter=lang.english&sort=date)

Catalog of Genes and Diseases from OMIM

- PHOSPHATIDYLINOSITOL GLYCAN ANCHOR BIOSYNTHESIS CLASS T PROTEIN; PIGT (https://omim.org/entry/610272)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/51604)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=PIGT[gene])

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