PIGA gene
phosphatidylinositol glycan anchor biosynthesis class A

Normal Function

The PIGA gene provides instructions for making a protein called phosphatidylinositol glycan class A. This protein takes part in a series of steps that produce a molecule called GPI anchor. Specifically, phosphatidylinositol glycan class A is involved in the first step of the sequence, which produces an intermediate molecule called N-acetylglucosaminyl phosphatidylinositol, or GlcNAc-PI. This step takes place in the endoplasmic reticulum of the cell, a structure involved in protein processing and transport. The PIGA protein forms a complex with several other proteins, and this complex helps to start the reaction that produces GlcNAc-PI.

The GPI anchor, the ultimate product of the sequence, attaches many different proteins to the cell membrane, thereby ensuring that these proteins are available when needed at the surface of the cell.

Health Conditions Related to Genetic Changes

Paroxysmal nocturnal hemoglobinuria

Some gene mutations are acquired during a person’s lifetime and are present only in certain cells. These changes, which are called somatic mutations, are not inherited. In people with paroxysmal nocturnal hemoglobinuria, somatic mutations of the PIGA gene occur in blood-forming cells called hematopoietic stem cells. Hematopoietic stem cells produce red blood cells (erythrocytes) that carry oxygen, white blood cells (leukocytes) that protect the body from infection, and platelets (thrombocytes) that are involved in blood clotting.

Individuals with paroxysmal nocturnal hemoglobinuria have one or more PIGA gene mutations in their hematopoietic stem cells, which leads to abnormal blood cells. As the abnormal hematopoietic stem cells multiply, populations of abnormal blood cells are formed, alongside normal blood cells produced by normal hematopoietic stem cells. The proportion of abnormal blood cells in the body affects the severity of the signs and symptoms of paroxysmal nocturnal hemoglobinuria.

Researchers have identified more than 100 somatic mutations in the PIGA gene. Some of these mutations alter the numbers or types of protein building blocks (amino acids) in phosphatidylinositol glycan class A, which impair its function. Other mutations result in the insertion of a premature stop signal in the instructions for making phosphatidylinositol glycan class A. As a result, an abnormally small protein, which is usually unstable, is produced.
Simpson-Golabi-Behmel syndrome

Chromosomal Location
Cytogenetic Location: Xp22.2, which is the short (p) arm of the X chromosome at position 22.2
Molecular Location: base pairs 15,319,451 to 15,335,554 on the X chromosome (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene
• GLCNAC-PI synthesis protein
• GPI anchor biosynthesis
• GPI3
• phosphatidylinositol glycan anchor biosynthesis, class A
• phosphatidylinositol glycan anchor biosynthesis, class A (paroxysmal nocturnal hemoglobinuria)
• phosphatidylinositol-glycan biosynthesis, class A protein
• phosphatidylinositol glycan, class A (paroxysmal nocturnal hemoglobinuria)
• phosphatidylinositol N-acetylglucosaminyltransferase subunit A
• PIG-A
• PIGA_HUMAN

Additional Information & Resources
Educational Resources
• Essentials of Glycobiology (first edition, 1999): Mutations in the GPI Anchor Biosynthetic Pathway
  https://www.ncbi.nlm.nih.gov/books/NBK20711/
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28PIGA%5BTIAB%5D%29+OR+%28%28GPI3%5BTIAB%5D%29+OR+%28PIG-A%5BTIAB%5D%29+OR+%28GPI-anch+.bio+synthesis%5BTIAB%5D%29+AND+%28%28%28%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1440+days+%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- PHOSPHATIDYLINOSITOL GLYCAN ANCHOR BIOSYNTHESIS CLASS A PROTEIN
  http://omim.org/entry/311770

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_PIGA.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PIGA%5Bgene%5D
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:5277
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P37287

Sources for This Summary

- OMIM: PHOSPHATIDYLINOSITOL GLYCAN ANCHOR BIOSYNTHESIS CLASS A PROTEIN
  http://omim.org/entry/311770
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10629597

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