GPC3 gene
glypican 3

Normal Function

The GPC3 gene provides instructions for making a protein called glypican 3. This protein is one of several glypicans in humans, each of which consists of a core protein attached to long sugar molecules called heparan sulfate chains. Glypicans are anchored to the outer cell membrane, where they interact with a variety of other proteins outside the cell. Glypicans appear to play important roles in development before birth. These proteins are involved in numerous cell functions, including regulating cell growth and division (cell proliferation) and cell survival.

Several studies have found that glypican 3 interacts with other proteins at the surface of cells to restrain cell proliferation. Specifically, glypican 3 blocks (inhibits) a developmental pathway called the hedgehog signaling pathway. This pathway is critical for cell proliferation, cell specialization, and the normal shaping (patterning) of many parts of the body during embryonic development.

Researchers believe that in some cell types, glypican 3 may act as a tumor suppressor, which is a protein that prevents cells from growing and dividing in an uncontrolled way to form a cancerous tumor. Glypican 3 may also cause some types of cells to self-destruct (undergo apoptosis) when they are no longer needed, which can help keep growth in check.

Although glypican 3 is known primarily as an inhibitor of cell growth and cell division, in some tissues it appears to have the opposite effect. Research suggests that in certain types of cells, such as cells in the liver, glypican 3 may interact with proteins called growth factors to promote cell growth and cell division.

Health Conditions Related to Genetic Changes

Simpson-Golabi-Behmel syndrome

More than 50 mutations in the GPC3 gene have been identified in people with Simpson-Golabi-Behmel syndrome. This condition is classified as an overgrowth syndrome, which means that affected infants are considerably larger than normal at birth (macrosomia) and continue to grow and gain weight at an unusual rate. The condition can also be associated with a variety of other birth defects and health problems.

Most of the mutations that cause Simpson-Golabi-Behmel syndrome delete part or all of the GPC3 gene, which prevents cells from producing functional glypican 3. Other mutations insert or delete a small amount of genetic material in the gene, or change
one or a few protein building blocks (amino acids) in glypican 3. These mutations change the structure of the protein.

Mutations in the GPC3 gene prevent glypican 3 from inhibiting the hedgehog signaling pathway. The resulting overactivity of this pathway leads to an increased rate of cell growth and division starting before birth. This increased cell proliferation accounts, at least in part, for the overgrowth that occurs in Simpson-Golabi-Behmel syndrome. It is unclear how changes in hedgehog signaling contribute to the other abnormalities that can occur with this disorder.

**Chromosomal Location**

Cytogenetic Location: Xq26.2, which is the long (q) arm of the X chromosome at position 26.2

Molecular Location: base pairs 133,535,745 to 133,985,646 on the X chromosome (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)

Other Names for This Gene

- DGSX
- glypican-3
- glypican proteoglycan 3
- GPC3_HUMAN
- GTR2-2
- Intestinal protein OCI-5
- MXR7
- OCI-5
- SGBS1
Additional Information & Resources

Educational Resources

  https://www.ncbi.nlm.nih.gov/books/NBK1900/

Clinical Information from GeneReviews

• Simpson-Golabi-Behmel Syndrome Type 1
  https://www.ncbi.nlm.nih.gov/books/NBK1219

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28GPC3%5BTIAB%5D%29+OR+%28glypican+3%5BTIAB%5D%29+OR+%28glypican-3%5BTIAB%5D%29+AND+english%5Blia%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22+AND+&db=pubmed

Catalog of Genes and Diseases from OMIM

• GLYPICAN 3
  http://omim.org/entry/300037

Research Resources

• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GPC3ID156.html

• Cancer Genetics Web
  http://www.cancerindex.org/geneweb/GPC3.htm

• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=GPC3%5Bgene%5D

• HGNC Gene Family: Glypicans
  https://www.genenames.org/cgi-bin/genefamilies/set/572

• HGNC Gene Symbol Report

• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:2719

• NCBI Gene

• UniProt
  https://www.uniprot.org/uniprot/P51654
Sources for This Summary

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