PSAP gene
prosaposin

Normal Function

The PSAP gene provides instructions for making a protein called prosaposin. This protein is involved in a number of biological functions, including the development of the nervous system and the reproductive system. Prosaposin is the precursor of four smaller proteins called saposin A, B, C, and D, which are produced when prosaposin is broken up (cleaved).

The individual saposins are found in cellular structures called lysosomes, which are the cell's recycling centers. The saposins help lysosomal enzymes break down fatty substances called sphingolipids.

The saposin B protein works with several enzymes to break down sphingolipids. Its most critical biological role seems to be associated with the enzyme arylsulfatase A. This enzyme is involved in breaking down a subgroup of sphingolipids called sulfatides, especially in the nervous system's white matter, which consists of nerve fibers covered by myelin. Myelin is a substance that insulates and protects nerves. Saposin B may also play a role in transporting lipids to the outer surface of the cell so they can be recognized by the immune system.

The saposin C protein works with the enzyme beta-glucocerebrosidase to break down another sphingolipid called glucocerebroside. Saposins A and D are also involved in processing sphingolipids.

Health Conditions Related to Genetic Changes

Metachromatic leukodystrophy

In a small number of individuals with metachromatic leukodystrophy, a disorder that causes deterioration of nervous system functions, researchers have identified PSAP gene mutations that result in a shortage (deficiency) of the saposin B protein. This deficiency interferes with the breakdown of sulfatides. As a result, these substances can accumulate to toxic levels in the nervous system.

The buildup of sulfatides gradually destroys myelin, the covering that protects nerves and promotes the efficient transmission of nerve impulses. Destruction of myelin leads to a loss of white matter (leukodystrophy) and impairment of nervous system function, resulting in the signs and symptoms of metachromatic leukodystrophy.
Other disorders

In a few individuals, mutations in the PSAP gene interfere with the function of the saposin C protein, resulting in a disorder that resembles a severe form of Gaucher disease. Signs and symptoms of this condition include neurological problems and abnormal enlargement of the liver and spleen (hepatosplenomegaly). Without adequate saposin C activator protein, the glucocerebrosidase enzyme cannot break down glucocerebroside effectively. As a result, glucocerebroside accumulates in the body’s tissues as it does in the classic form of Gaucher disease. A few PSAP gene mutations have also been identified in individuals with signs and symptoms resembling another leukodystrophy called Krabbe disease.

In addition, a few mutations in the PSAP gene have been identified that prevent the production of more than one of the saposin proteins. Individuals with these mutations have massive accumulation of sphingolipids in their nervous system and other organs. This accumulation results in very severe neurological disease, respiratory problems, and hepatosplenomegaly.

Chromosomal Location

Cytogenetic Location: 10q22.1, which is the long (q) arm of chromosome 10 at position 22.1

Molecular Location: base pairs 71,816,298 to 71,851,251 on chromosome 10 (Homo sapiens Updated Annotation Release 109.20200228, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- Prosaposin (sphingolipid activator protein-1)
- prosaposin (variant Gaucher disease and variant metachromatic leukodystrophy)
- prosaptides
- SAP1
- SAP2 (sphingolipid activator protein-2)
- SAP_HUMAN
- SGP-1 (sulfoglycoprotein-1)
Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Lysosomal Disease
  https://www.ncbi.nlm.nih.gov/books/NBK28215/
  https://www.ncbi.nlm.nih.gov/books/NBK20729/#A1383

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28PSAP%5BTIAB%5D%29+OR+%28prosaposin%5BTIAB%5D%29+OR+%28%28SAP1%5BTIAB%5D%29+OR+%28%28prosaposin%5BTIAB%5D%29+OR+%28%28PSAP%5BTIAB%5D%29+AND+%28%28%28Genes%5BMH%5D%29+OR+%28%28Genetic+Phenomena%5BMH%5D%29+OR+%28%28PSAP%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- COMBINED SAPOSIN DEFICIENCY
  http://omim.org/entry/611721
- GAUCHER DISEASE, ATYPICAL, DUE TO SAPOSIN C DEFICIENCY
  http://omim.org/entry/610539
- KRABBE DISEASE, ATYPICAL, DUE TO SAPOSIN A DEFICIENCY
  http://omim.org/entry/611722
- PROSAPOSIN
  http://omim.org/entry/176801

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/PSAPID42980ch10q22.html
- ClinVar
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:5660
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P07602

page 3
Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19955343

- Basic Neurochemistry (sixth edition, 1999): Lysosomal Disease
  https://www.ncbi.nlm.nih.gov/books/NBK28215/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17616409

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15856305

  https://www.ncbi.nlm.nih.gov/books/NBK20729/#A1383

- OMIM: GAUCHER DISEASE, ATYPICAL, DUE TO SAPOSIN C DEFICIENCY 
  http://omim.org/entry/610539

- OMIM: PROSAPOSIN 
  http://omim.org/entry/176801

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/23319190

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/22652185 
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3534739/

Reprinted from Genetics Home Reference: 

Reviewed: February 2013 
Published: March 31, 2020