

## 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.

### **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**

#### Tests Listed in the Genetic Testing Registry

- Tests of PSAP ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5660\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5660[geneid]))

#### Scientific Articles on PubMed

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

## Catalog of Genes and Diseases from OMIM

- PROSAPOSIN; PSAP (<https://omim.org/entry/176801>)
- GAUCHER DISEASE, ATYPICAL, DUE TO SAPOSIN C DEFICIENCY; GDSAPC (<https://omim.org/entry/610539>)
- COMBINED SAPOSIN DEFICIENCY; PSAPD (<https://omim.org/entry/611721>)
- KRABBE DISEASE, ATYPICAL, DUE TO SAPOSIN A DEFICIENCY; KRBSAPA (<https://omim.org/entry/611722>)

## Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/5660>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=PSAP\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=PSAP[gene]))

## **References**

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## Genomic Location

The *PSAP* gene is found on chromosome 10 (<https://medlineplus.gov/genetics/chromosome/10/>).

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