SACS gene
sacs in molecular chaperone

Normal Function

The SACS gene provides instructions for producing a protein called sacsin. Sacsin is found in the brain, skin cells, muscles used for movement (skeletal muscles), and at low levels in the pancreas, but the specific function of the protein is unknown. Research suggests that sacsin plays a role in organizing proteins into bundles called intermediate filaments. Intermediate filaments provide support and strength to cells. In nerve cells (neurons), specialized intermediate filaments called neurofilaments comprise the structural framework that establishes the size and shape of nerve cell extensions called axons, which are essential for transmission of nerve impulses to other neurons and to muscle cells.

Health Conditions Related to Genetic Changes

Autosomal recessive spastic ataxia of Charlevoix-Saguenay

About 200 mutations in the SACS gene have been found to cause autosomal recessive spastic ataxia of Charlevoix-Saguenay, commonly called ARSACS. ARSACS is a condition affecting muscle movement that is characterized by abnormal tensing of the muscles (spasticity), problems with balance and coordination (cerebellar ataxia), and reduced sensation and weakness in the arms and legs (peripheral neuropathy).

Two SACS gene mutations have been found frequently in people with ARSACS from the Charlevoix-Saguenay region of Quebec, Canada. One of these mutations deletes a DNA building block (nucleotide) called thymine at position 6594 in the SACS gene (written as 6594delT). This mutation is found in more than 90 percent of people with ARSACS in Quebec. The other mutation replaces the nucleotide cytosine with the nucleotide thymine at position 5254 in the SACS gene (written as C5254T). Both of these mutations lead to production of a sacsin protein that is abnormally short and nonfunctional.

Mutations causing ARSACS in people outside of Quebec are varied and usually unique to that person or family. Most of these mutations either delete one or more nucleotides or replace one nucleotide with another nucleotide in the SACS gene. Mutations in the SACS gene result in the production of an unstable sacsin protein that does not function normally. It is unclear how the abnormal sacsin protein affects the brain and skeletal muscles but it likely impairs normal organization of intermediate filaments in cells, particularly neurofilaments, and disrupts neuron function. This decreased neuronal signaling may result in the signs and symptoms of ARSACS.
Chromosomal Location

Cytogenetic Location: 13q12.12, which is the long (q) arm of chromosome 13 at position 12.12

Molecular Location: base pairs 23,328,827 to 23,433,728 on chromosome 13 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ARSACS
- DNAJC29
- KIAA0730
- PPP1R138
- SACS_HUMAN
- sacsin
- spastic ataxia of Charlevoix-Saguenay (sacsin)
- SPAX6

Additional Information & Resources

Clinical Information from GeneReviews

- ARSACS
  https://www.ncbi.nlm.nih.gov/books/NBK1255

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SACS%5BTIAB%5D%29+AND+%28spastic+ataxia%5BALL%5D%29+OR+%28sacsin%5BTIAB%5D%29+AND+%28Genes%5BMH%5D+OR+Genetic+Phenomena%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D
Catalog of Genes and Diseases from OMIM

- SACSIN
  http://omim.org/entry/604490

Research Resources

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

- HGNC Gene Symbol Report

- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:26278

- NCBI Gene

- UniProt
  https://www.uniprot.org/uniprot/Q9NZJ4

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10655055

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/30332300

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11788093

- OMIM: SACSIN
  http://omim.org/entry/604490

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16961075

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17853117

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