SACS gene

sacsin 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.

Other Names for This Gene

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

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SACS (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=26278[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28SACS%5BTIAB%5D%29+AND+%28spastic+ataxia%5BALL%5D%29+OR+%28sacsin%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+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- SACSIN; SACS (https://omim.org/entry/604490)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/26278)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SACS[gene])

References

- Engert JC, Berube P, Mercier J, Dore C, Lepage P, Ge B, Bouchard JP, MathieuJ,

Melancon SB, Schalling M, Lander ES, Morgan K, Hudson TJ, Richter A. ARSACS, aspastic ataxia common in northeastern Quebec, is caused by mutations in a newgene encoding an 11.5-kb ORF. Nat Genet. 2000 Feb;24(2):120-5. doi:10.1038/72769. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/10655055)

- Gentil BJ, Lai GT, Menade M, Lariviere R, Minotti S, Gehring K, Chapple JP,Brais B, Durham HD. Sacsin, mutated in the ataxia ARSACS, regulates intermediatefilament assembly and dynamics. FASEB J. 2019 Feb;33(2):2982-2994. doi:10.1096/fj.201801556R. Epub 2018 Oct 17. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/30332300)
- Mercier J, Prevost C, Engert JC, Bouchard JP, Mathieu J, Richter A. Rapiddetection of the sacsin mutations causing autosomal recessive spastic ataxia ofCharlevoix-Saguenay. Genet Test. 2001 Fall;5(3):255-9. doi:10.1089/10906570152742326. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11788093)
- Takiyama Y. Autosomal recessive spastic ataxia of Charlevoix-Saguenay. Neuropathology. 2006 Aug;26(4):368-75. doi: 10.1111/j.1440-1789.2006.00664.x. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16961075)
- Takiyama Y. Sacsinopathies: sacsin-related ataxia. Cerebellum.2007;6(4):353-9. doi: 10.1080/14734220701230466. Epub 2007 Feb 28. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17853117)

Genomic Location

The *SACS* gene is found on chromosome 13 (https://medlineplus.gov/genetics/chromosome/13/).

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