

ASAH1 gene

N-acylsphingosine amidohydrolase 1

Normal Function

The *ASAH1* gene provides instructions for making an enzyme called acid ceramidase. This enzyme is found in lysosomes, which are cell compartments that digest and recycle materials. Within lysosomes, acid ceramidase breaks down fats (lipids) called ceramides. Ceramides are typically found within the membranes that surround cells and play a role in regulating cell maturation (differentiation), growth and division of cells (proliferation), and controlled cell death (apoptosis). Additionally, ceramides are a component of a fatty substance called myelin that insulates and protects nerve cells. Ceramides also serve as building blocks for more complex lipids. When ceramides need to be replaced, they travel to lysosomes where acid ceramidase breaks them down into a fat called sphingosine and a fatty acid. These two breakdown products are recycled to create new ceramides for the body to use.

Health Conditions Related to Genetic Changes

Farber lipogranulomatosis

Variants (also known as mutations) in the *ASAH1* gene have been found to cause Farber lipogranulomatosis. This condition is characterized by the buildup of ceramides and other fats in cells throughout the body, particularly around the joints. Most of the variants associated with Farber lipogranulomatosis change a single protein building block (amino acid) in acid ceramidase, which severely reduces the activity of the enzyme, typically to less than one-tenth of normal. As a result, the enzyme cannot break down ceramides properly and they build up in the lysosomes of various cells, including in the lungs, liver, muscles, brain, cartilage, and bone. It is unclear how an accumulation of ceramides impairs the normal functioning of cells, but damage to the affected cells leads to the voice, skin, and joint problems that are characteristic of Farber lipogranulomatosis. Ceramides influence various cell functions, and it is likely that abnormal regulation of these processes also contributes to the features of this condition.

Spinal muscular atrophy with progressive myoclonic epilepsy

Variants in the *ASAH1* gene have been found to cause spinal muscular atrophy with progressive myoclonic epilepsy (SMA-PME). This condition is characterized by muscle

weakness and wasting (atrophy) and a combination of seizures and uncontrollable muscle jerks (myoclonic epilepsy) that begin in childhood. The *ASAH1* gene variants that cause SMA-PME result in a reduction of acid ceramidase activity to a level less than one-third of normal. The decrease in acid ceramidase activity leads to inefficient breakdown of ceramides and impaired production of its breakdown products sphingosine and fatty acids. The increase in ceramides and reduction in sphingosine and fatty acids likely play a role in the development of the features of SMA-PME, but the exact mechanism is unknown.

The reduction in acid ceramidase activity associated with SMA-PME is less than what occurs in another condition called Farber lipogranulomatosis (described above). Researchers suspect that the small amount of enzyme activity in SMA-PME allows some ceramide breakdown to occur, so the ceramides do not accumulate and damage cells as extensively as seen in Farber lipogranulomatosis. However, because SMA-PME is so rare, the effects of the enzyme changes are still unclear.

Other Names for This Gene

- AC
- ACDase
- acylsphingosine deacylase
- ASAH
- ASAH1_HUMAN
- FLJ21558
- FLJ22079
- N-acylsphingosine amidohydrolase (acid ceramidase) 1
- PHP
- PHP32

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ASAH1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=427\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=427[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28Acid+Ceramidase%5BTI%5D%29+OR+%28ASAH1%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D%29>)

Catalog of Genes and Diseases from OMIM

- N-ACYLSPHINGOSINE AMIDOHYDROLASE 1; ASAH1 (<https://omim.org/entry/613468>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/427>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=ASAH1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=ASAH1[gene]))

References

- Alayoubi AM, Wang JC, Au BC, Carpentier S, Garcia V, Dworski S, El-Ghamrasni S, Kirouac KN, Exertier MJ, Xiong ZJ, Prive GG, Simonaro CM, Casas J, Fabrias G, Schuchman EH, Turner PV, Hakem R, Levade T, Medin JA. Systemic ceramide accumulation leads to severe and varied pathological consequences. *EMBO Mol Med.* 2013 Jun;5(6):827-42. doi: 10.1002/emmm.201202301. Epub 2013 May 16. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23681708>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3779446/>)
- Dymont DA, Sell E, Vanstone MR, Smith AC, Garandeau D, Garcia V, Carpentier S, Le Trionnaire E, Sabourdy F, Beaulieu CL, Schwartzentruber JA, McMillan HJ; FORGECanada Consortium; Majewski J, Bulman DE, Levade T, Boycott KM. Evidence for clinical, genetic and biochemical variability in spinal muscular atrophy with progressive myoclonic epilepsy. *Clin Genet.* 2014 Dec;86(6):558-63. doi:10.1111/cge.12307. Epub 2013 Nov 21. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24164096>)
- Elsea SH, Solyom A, Martin K, Harmatz P, Mitchell J, Lampe C, Grant C, Selim L, Mungan NO, Guelbert N, Magnusson B, Sundberg E, Puri R, Kapoor S, Arslan N, DiRocco M, Zaki M, Ozen S, Mahmoud IG, Ehlert K, Hahn A, Gokcay G, Torcoletti M, Ferreira CR. ASAH1 pathogenic variants associated with acid ceramidase deficiency: Farber disease and spinal muscular atrophy with progressive myoclonic epilepsy. *Hum Mutat.* 2020 Sep;41(9):1469-1487. doi: 10.1002/humu.24056. Epub 2020 Jun 24. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/32449975>)
- Lucki NC, Bandyopadhyay S, Wang E, Merrill AH, Sewer MB. Acid ceramidase (ASAH1) is a global regulator of steroidogenic capacity and adrenocortical gene expression. *Mol Endocrinol.* 2012 Feb;26(2):228-43. doi: 10.1210/me.2011-1150. Epub 2012 Jan 19. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/22261821>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3275158/>)
- Mahmoud IG, Elmonem MA, Zaki MS, Ramadan A, Al-Menabawy NM, El-Gamal A, Mansour L, Issa MY, Abdel-Hamid MS, Abdel-Hady S, Khalifa I, Ibrahim A, Solyom A, Rolfs A, Selim L. ASAH1-related disorders: Description of 15 novel pediatric patients and expansion of the clinical phenotype. *Clin Genet.* 2020 Dec;98(6):598-605. doi: 10.1111/cge.13834. Epub 2020 Sep 2. Citation on PubMed (<https://www.ncbi.nlm.nih.gov/pubmed/32875576>)

- Park JH, Schuchman EH. Acid ceramidase and human disease. *Biochim BiophysActa*. 2006 Dec;1758(12):2133-8. doi: 10.1016/j.bbamem.2006.08.019. Epub 2006 Sep1. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/17064658>)
- Sands MS. Farber disease: understanding a fatal childhood disorder and dissecting ceramide biology. *EMBO Mol Med*. 2013 Jun;5(6):799-801. doi:10.1002/emmm.201302781. Epub 2013 May 13. No abstract available. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23666771>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3779442/>)
- Zhang Z, Mandal AK, Mital A, Popescu N, Zimonjic D, Moser A, Moser H, Mukherjee AB. Human acid ceramidase gene: novel mutations in Farber disease. *MolGenet Metab*. 2000 Aug;70(4):301-9. doi: 10.1006/mgme.2000.3029. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/10993717>)

Genomic Location

The *ASAH1* gene is found on chromosome 8 (<https://medlineplus.gov/genetics/chromosome/8/>).

Last updated November 10, 2021