# ASAH1 Gene

Subjects: Genetics & Heredity

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N-acylsphingosine amidohydrolase 1

genes

## 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 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. 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.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Farber Lipogranulomatosis

At least 20 mutations in the *ASAH1* gene have been found to cause Farber lipogranulomatosis. This condition is characterized by the buildup of fats (lipids) in cells throughout the body, particularly around the joints. Most of the mutations 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 these damaged cells lead 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.

### 2.2. Spinal Muscular Atrophy with Progressive Myoclonic Epilepsy

At least four mutations 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 mutations 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.

## 3. Other Names for This Gene

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

## References

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