

## DNMT1 gene

DNA methyltransferase 1

### Normal Function

The *DNMT1* gene provides instructions for making an enzyme called DNA methyltransferase 1. This enzyme is involved in DNA methylation, which is the addition of methyl groups, consisting of one carbon atom and three hydrogen atoms, to DNA molecules. In particular, the enzyme helps add methyl groups to DNA building blocks (nucleotides) called cytosines.

DNA methylation is important in many cellular functions. These include determining whether the instructions in a particular segment of DNA are carried out or suppressed (gene silencing), regulating reactions involving proteins and fats (lipids), and controlling the processing of chemicals that relay signals in the nervous system (neurotransmitters).

DNA methyltransferase 1 is active in the adult nervous system. Although its specific function is not well understood, the enzyme may help regulate nerve cell (neuron) maturation and specialization (differentiation), the ability of neurons to move (migrate) and connect with each other, and neuron survival.

### Health Conditions Related to Genetic Changes

#### Autosomal dominant cerebellar ataxia, deafness, and narcolepsy

At least four *DNMT1* gene mutations have been identified in people with a nervous system disorder called autosomal dominant cerebellar ataxia, deafness, and narcolepsy (ADCADN). Features of this disorder include difficulty coordinating movements (ataxia), hearing loss caused by abnormalities of the inner ear (sensorineural deafness), and excessive daytime sleepiness (narcolepsy). Cognitive decline occurs as the disorder progresses. Numbness, tingling, or pain in the arms and legs (sensory neuropathy) can also occur. Affected individuals usually survive into their forties or fifties.

The *DNMT1* gene mutations associated with this disorder affect a region of the DNA methyltransferase 1 enzyme, known as the targeting sequence, that helps direct the methylation process to the correct segments of DNA. As a result of these mutations, methylation is abnormal, which affects the expression of multiple genes. Maintenance of the neurons that make up the nervous system is disrupted, leading to the signs and symptoms of ADCADN.

## Hereditary sensory and autonomic neuropathy type IE

At least 10 *DNMT1* gene mutations have been identified in people with another nervous system disorder called hereditary sensory and autonomic neuropathy type IE (HSAN IE).

As in ADCADN, (described above), people with HSAN IE have sensorineural deafness, sensory neuropathy, cognitive decline, and a shortened lifespan. However, they typically do not have the ataxia or narcolepsy that occurs in ADCADN, and the sensory neuropathy begins earlier in life in people with HSAN IE. Seizures can also occur in this disorder.

*DNMT1* gene mutations that cause HSAN IE, like those that cause ADCADN, affect the targeting sequence of the DNA methyltransferase 1 enzyme. However, most of the mutations that cause HSAN IE occur in a part of the gene called exon 20 and affect one end of the enzyme's targeting sequence, while the mutations that cause ADCADN are mostly in a nearby part of the gene called exon 21 and affect the other end of the enzyme's targeting sequence.

As a result of the *DNMT1* gene mutations, methylation is abnormal and maintenance of the neurons that make up the nervous system is impaired. However, it is not known how the mutations cause the specific signs and symptoms of HSAN IE, or how mutations affecting the targeting sequence of the DNA methyltransferase 1 enzyme can cause either HSAN IE or ADCADN.

## Charcot-Marie-Tooth disease

MedlinePlus Genetics provides information about Charcot-Marie-Tooth disease

## Cancers

Several normal variations (polymorphisms) in the *DNMT1* gene have been associated with an increased risk of cancer, including cancers of the breast and stomach. These variations, which are found in cells throughout the body and can be passed on from parent to child, may affect the activity of the DNA methyltransferase 1 enzyme and its role in gene silencing. Changes in the silencing of particular genes can lead to abnormal cell growth and division and increase the risk of cancer.

In addition, increased activity (overexpression) of the *DNMT1* gene has been identified in certain brain cancers called gliomas. The genetic changes involved in this overexpression are somatic, which means that they occur only in the tumor cells and are not inherited. Researchers suggest that overexpression of the *DNMT1* gene may result in methylation and silencing of genes called tumor suppressors. When tumor suppressor genes are silenced, cells can grow and divide unchecked, which can lead to cancer.

## **Other Names for This Gene**

- AIM
- CXXC finger protein 9

- CXXC-type zinc finger protein 9
- CXXC9
- DNA (cytosine-5)-methyltransferase 1
- DNA (cytosine-5)-methyltransferase 1
- DNA methyltransferase HsaI
- DNA MTase HsaI
- DNMT
- DNMT1\_HUMAN
- HSN1E
- m.HsaI
- MCMT

## **Additional Information & Resources**

### Tests Listed in the Genetic Testing Registry

- Tests of DNMT1 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1786\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1786[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28DNMT1%5BTI%5D%29+OR+%28DNA+-methyltransferase+1%5BTI%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+720+days%22%5Bdp%5D%29%29%29>)

### Catalog of Genes and Diseases from OMIM

- DNA METHYLTRANSFERASE 1; DNMT1 (<https://omim.org/entry/126375>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/1786>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=DNMT1\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=DNMT1[gene]))

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## Genomic Location

The *DNMT1* gene is found on chromosome 19 (<https://medlineplus.gov/genetics/chromosome/19/>).

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