DNMT3A gene

DNA methyltransferase 3 alpha

Normal Function

The *DNMT3A* gene provides instructions for making an enzyme called DNA methyltransferase 3 alpha. 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, and controlling the processing of chemicals that relay signals in the nervous system (neurotransmitters). DNA methyltransferase 3 alpha is particularly important for establishing DNA methylation patterns during development before birth. The enzyme also functions in early cells that can give rise to more mature cell types. In early blood cells, called hematopoietic stem cells, the methylation patterns established by DNA methyltransferase 3 alpha promote maturation (differentiation) into different blood cell types.

Health Conditions Related to Genetic Changes

DNMT3A overgrowth syndrome

At least 16 mutations in the *DNMT3A* gene have been found to cause *DNMT3A* overgrowth syndrome. This condition is characterized by faster than normal growth before and after birth, a distinctive facial appearance, and intellectual disability.

DNMT3A gene mutations that cause *DNMT3A* overgrowth syndrome are found in all of the body's cells and lead to a decrease in normal enzyme function. Some of these *DNMT3A* gene mutations lead to a decrease in normal enzyme function. As a result, there is a reduction in DNA methylation, particularly affecting DNA methylation before birth. It is unclear how other mutations affect protein function. Decreased DNA methylation likely disrupts the normal regulation of important developmental genes, although how these change cause the specific features of *DNMT3A* overgrowth syndrome is unknown.

At least one *DNMT3A* gene alteration that causes *DNMT3A* overgrowth syndrome deletes the entire *DNMT3A* gene and multiple neighboring genes. While this deletion leads to the signs and symptoms of *DNMT3A* overgrowth syndrome, it is difficult to determine what role the other missing genes have in contributing to the development of health problems in affected individuals.

Cytogenetically normal acute myeloid leukemia

Mutations in the *DNMT3A* gene are associated with a form of blood cancer known as cytogenetically normal acute myeloid leukemia (CN-AML). While large chromosomal abnormalities can be involved in the development of acute myeloid leukemia, about half the cases do not have these abnormalities; these are classified as CN-AML. Up to one-third of people with CN-AML have a mutation in the *DNMT3A* gene.

The *DNMT3A* gene mutations involved in CN-AML are called somatic mutations; they are typically found in a small percentage of cells and the mutations are not inherited. Most change single protein building blocks (amino acids) in the DNA methyltransferase 3 alpha enzyme. Studies suggest that these changes make the enzyme less able to fully methylate DNA. It is also thought that the altered pattern of methylation in cells changes the activity of several genes; some genes that are normally silenced may be turned on. Researchers speculate that the altered gene activity prevents hematopoietic stem cells from differentiating normally, which leads to the overproduction of abnormal, immature white blood cells characteristic of acute myeloid leukemia.

Systemic mastocytosis

MedlinePlus Genetics provides information about Systemic mastocytosis

Other cancers

Somatic *DNMT3A* gene mutations are also found relatively frequently in another form of blood cancer called T-cell acute lymphoblastic leukemia. As in cytogenetically normal acute myeloid leukemia (described above), the mutations disrupt the normal pattern of methylation in cells, which blocks differentiation. It is unclear why some people with *DNMT3A* gene mutations develop acute myeloid leukemia and others develop acute lymphoblastic leukemia.

Other Names for This Gene

- DNA (cytosine-5)-methyltransferase 3A
- DNA (cytosine-5-)-methyltransferase 3 alpha
- DNA cytosine methyltransferase 3A2
- DNA MTase HsaIIIA
- DNM3A_HUMAN
- DNMT3A2
- M.HsaIIIA

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of DNMT3A (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1788[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28DNMT3A%5BTI%5D%29+OR+%28DNA-methyltransferase+3a%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)

Catalog of Genes and Diseases from OMIM

- DNA METHYLTRANSFERASE 3A; DNMT3A (https://omim.org/entry/602769)
- LEUKEMIA, ACUTE LYMPHOBLASTIC; ALL (https://omim.org/entry/613065)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1788)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=DNMT3A[gene])

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Genomic Location

The *DNMT3A* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chromosome/2/).

Last updated September 1, 2017