MAOA gene
monoamine oxidase A

Normal Function

The MAOA gene provides instructions for making an enzyme called monoamine oxidase A. This enzyme is part of a family of enzymes that break down molecules called monoamines through a chemical reaction known as oxidation. Among the monoamines broken down by monoamine oxidase A are certain chemicals that act as neurotransmitters, which transmit signals between nerve cells in the brain. Neurotransmitters are broken down when signaling is no longer needed.

Specifically, monoamine oxidase A is involved in the breakdown of the neurotransmitters serotonin, epinephrine, norepinephrine, and dopamine. Signals transmitted by serotonin regulate mood, emotion, sleep, and appetite. Epinephrine and norepinephrine control the body's response to stress. Dopamine transmits signals within the brain to produce smooth physical movements.

Monoamine oxidase A also helps break down monoamines found in the diet. It seems to be particularly important in the breakdown of excess tyramine, which is found in cheese and other foods.

Monoamine oxidase A appears to be involved in normal brain development before birth. The enzyme plays a role in the controlled self-destruction of cells (apoptosis), which is an important process in the development of many tissues and organs, including the brain.

Health Conditions Related to Genetic Changes

Monoamine oxidase A deficiency

Mutations in the MAOA gene cause monoamine oxidase A deficiency. This condition affects males almost exclusively and is characterized by mild intellectual disability and behavioral problems, including aggressive and violent outbursts. In some cases, particular foods seem to worsen symptoms of the condition. The MAOA gene mutations reduce monoamine oxidase A activity, which causes serotonin and other neurotransmitters to build up in the brain. It is unclear how this buildup leads to the signs and symptoms of monoamine oxidase A deficiency. Researchers speculate that an excess of certain neurotransmitters, particularly serotonin and norepinephrine, may impair an affected individual's ability to control his impulses, leading to aggressive outbursts. Some studies suggest that reduced monoamine oxidase A activity alters development of certain regions of the brain, which may contribute to intellectual disability and behavioral problems in people with monoamine oxidase A deficiency. Researchers suspect that a buildup of tyramine can contribute
to the problems associated with the condition, which may be why foods high in this molecule can worsen symptoms.

Other disorders

Genetic changes that affect the \textit{MAOA} gene have been linked to multiple disorders. Some of these genetic changes remove pieces of DNA (deletion mutations) that include the \textit{MAOA} gene. Deletion mutations that remove both the \textit{MAOA} gene and the nearby \textit{MAOB} gene have been found in individuals with severely delayed development of mental and motor skills, weak muscle tone (hypotonia), and repetitive hand movements. Deletion mutations that remove these two genes and another nearby gene called \textit{NDP} have also been found. The \textit{NDP} gene is associated with a condition called Norrie disease, which causes blindness and sometimes mild developmental delays and problems with other body systems. Individuals missing the \textit{MAOA}, \textit{MAOB}, and \textit{NDP} genes have severe intellectual disability, difficulty with social interactions (autism spectrum disorders), and seizures in addition to features of Norrie disease. Researchers speculate that loss of the \textit{MAOA} or \textit{MAOB} gene underlies the neurological problems in individuals with deletion mutations.

Several common genetic variants (polymorphisms) in or near the \textit{MAOA} gene have been found to affect the gene’s activity. The most studied polymorphism, called \textit{MAOA-uVNTR}, occurs in an area near the \textit{MAOA} gene, called the promoter region, that controls gene activity. In this region, a string of 30 DNA building blocks (nucleotides) is repeated, end-to-end, two to five times. Studies show that when the string of nucleotides is repeated 3.5 or four times, more monoamine oxidase A protein is produced than when the nucleotides are repeated only two or three times. For this reason, versions of DNA (alleles) with 3.5 or four repeats are referred to as high-activity alleles. Versions with only two or three repeats, which result in lower than normal amounts of monoamine oxidase A, are considered low-activity alleles. It is unclear what effect five repeats has on \textit{MAOA} gene activity.

Low-activity \textit{MAOA-uVNTR} alleles are associated with aggressive behavior. Several reports found the effect only in males, but some other reports indicate that both males and females with low-activity alleles can be prone to aggression. Some studies indicate that low-activity alleles specifically increase the risk of violence and aggression in individuals who were abused as children. Researchers are studying how these \textit{MAOA} gene polymorphisms are involved in modulating behavior and the role of environmental factors, such as childhood abuse or situations in which a person is provoked.

In contrast, high-activity \textit{MAOA-uVNTR} alleles appear to increase the risk of panic disorder in females. Panic disorder is a severe anxiety disorder characterized by episodes of overwhelming fear (panic attacks) with no obvious trigger. It is unclear how high amounts of monoamine oxidase A contribute to panic disorder.

Other polymorphisms that can affect \textit{MAOA} gene activity may also be associated with aggression. The roles of \textit{MAOA-uVNTR} and other polymorphisms are also being
studied in depression, bipolar disorder, alcoholism, drug addiction, and many other conditions.

**Chromosomal Location**

Cytogenetic Location: Xp11.3, which is the short (p) arm of the X chromosome at position 11.3

Molecular Location: base pairs 43,654,907 to 43,746,824 on the X chromosome (Homo sapiens Updated Annotation Release 109.20200228, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

**Other Names for This Gene**

- amine oxidase [flavin-containing] A isoform 1
- amine oxidase [flavin-containing] A isoform 2
- BRNRS
- MAO-A
- monoamine oxidase type A

**Additional Information & Resources**

**Educational Resources**

- Basic Neurochemistry (sixth edition, 1999): Synaptic Transmission
  https://www.ncbi.nlm.nih.gov/books/NBK27911/
- Neuroscience (second edition, 2001): The Biogenic Amines
  https://www.ncbi.nlm.nih.gov/books/NBK11035/

**Scientific Articles on PubMed**

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MAOA%5BTIAB%5D%29+OR+%28monoamine+oxidase+A%5BTIAB%5D%29+AND+%28Genes%5BMH%5D+OR+%28Genetic+Phenomena%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D
Catalog of Genes and Diseases from OMIM

- MONOAMINE OXIDASE A
  http://omim.org/entry/309850

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org Genes/GC_MAOA.html
- ClinVar
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4128
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/P21397

Sources for This Summary

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• OMIM: MONOAMINE OXIDASE A http://omim.org/entry/309850


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