

PAX6 gene

paired box 6

Normal Function

The *PAX6* gene belongs to a family of genes that play a critical role in the formation of tissues and organs during embryonic development. The members of the PAX gene family are also important for maintaining the normal function of certain cells after birth. To carry out these roles, the PAX genes provide instructions for making proteins that attach to specific areas of DNA and help control the activity (expression) of particular genes. On the basis of this action, PAX proteins are called transcription factors.

During embryonic development, the PAX6 protein is thought to turn on (activate) genes involved in the formation of the eyes, the brain and spinal cord (central nervous system), and the pancreas. Within the brain, the PAX6 protein is involved in the development of a specialized group of brain cells that process smell (the olfactory bulb). Additionally, researchers believe that the PAX6 protein controls many aspects of eye development before birth. After birth, the PAX6 protein likely regulates the expression of various genes in many structures of the eyes.

Health Conditions Related to Genetic Changes

Aniridia

More than 280 mutations in the *PAX6* gene have been found to cause aniridia, which is an absence of the colored part of the eye (the iris). Most of these mutations create a premature stop signal in the instructions for making the PAX6 protein and lead to the production of an abnormally short, nonfunctional protein. As a result, there is less PAX6 protein to regulate the activity of other genes.

The majority of mutations that cause aniridia occur within the *PAX6* gene; however, some disease-causing mutations occur in neighboring regions of DNA that normally regulate the expression of the *PAX6* gene, known as regulatory regions. Mutations in *PAX6* gene regulatory regions reduce the expression of the *PAX6* gene. These mutations lead to a shortage of functional PAX6 protein, which disrupts the formation of the eyes during development.

Peters anomaly

At least two mutations in the *PAX6* gene have been found to cause Peters anomaly. This condition is characterized by the abnormal development of certain structures at the front of the eye and clouding of the clear front surface of the eye (cornea). The mutations that cause Peters anomaly change single protein building blocks (amino acids) in the *PAX6* protein. These mutations reduce but do not eliminate the protein's function and are less severe than mutations that cause aniridia (described above). The mutations that cause Peters anomaly reduce the *PAX6* protein's ability to bind to DNA, disrupting its role as a transcription factor. As a result, normal development of the eye is impaired, leading to the features of Peters anomaly. The *PAX6* gene mutations that cause Peters anomaly can cause other related eye disorders in members of the same family.

Coloboma

Mutations in the *PAX6* gene can cause an eye problem called coloboma, in which there is a gap or split in one of the structures that make up the eye. The mutations that cause this abnormality occur in one copy of the *PAX6* gene in each cell. Most of these mutations change single amino acids in the *PAX6* protein. These mutations reduce but do not eliminate the protein's normal function, impairing its role as a transcription factor.

Microphthalmia

Mutations in one copy of the *PAX6* gene can cause microphthalmia, which describes eyes that are smaller than usual. These genetic changes reduce but do not eliminate *PAX6* protein function. As a result, the *PAX6* protein is less able to control the activity of certain genes involved in eye development.

WAGR syndrome

The *PAX6* gene is located in a region of chromosome 11 that is deleted in people with WAGR syndrome, which is a disorder that affects many body systems and is named for its main features: a childhood kidney cancer known as Wilms tumor, an eye problem called aniridia, genitourinary anomalies, and intellectual disability (formerly referred to as mental retardation). As a result of this deletion, affected individuals are missing one copy of the *PAX6* gene in each cell. A loss of the *PAX6* gene is associated with the characteristic eye features of WAGR syndrome, including aniridia, and may affect brain development.

Other disorders

Mutations in the *PAX6* gene can cause a variety of eye problems. Most of these mutations change single amino acids in the *PAX6* protein. These mutations reduce but do not eliminate the protein's normal function, impairing its role as a transcription factor.

In addition to microphthalmia or coloboma (described above), individuals with these relatively mild *PAX6* gene mutations may be born with pupils that are not centrally positioned in the eye (ectopia papillae) or underdeveloped optic nerves, which are the

structures that carry information from the eyes to the brain. Mild *PAX6* mutations can also result in underdevelopment of the region at the back of the eye responsible for sharp central vision (the fovea). Additional conditions caused by these *PAX6* gene mutations may be present at birth or develop later. These conditions may include a clouding of the lens of the eye (cataracts), involuntary eye movements (nystagmus), and inflammation of the front surface of the eye called the cornea (keratitis).

It is unclear why the effects of some mutations in the *PAX6* gene are limited to the eye, while other mutations affect the development of many parts of the body.

Other Names for This Gene

- AN
- AN2
- D11S812E
- MGC17209
- MGDA
- paired box gene 6
- paired box gene 6 isoform a
- paired box gene 6 isoform b
- PAX6_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PAX6 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5080\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5080[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28PAX6%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D%29>)

Catalog of Genes and Diseases from OMIM

- COLOBOMA OF OPTIC NERVE (<https://omim.org/entry/120430>)
- MICROPTHALMIA/COLOBOMA 12; MCOPCB12 (<https://omim.org/entry/120200>)
- ECTOPIA PUPILLAE (<https://omim.org/entry/129750>)
- FOVEAL HYPOPLASIA 1; FVH1 (<https://omim.org/entry/136520>)
- KERATITIS, HEREDITARY (<https://omim.org/entry/148190>)

- OPTIC NERVE HYPOPLASIA, BILATERAL (<https://omim.org/entry/165550>)
- CATARACT 9, MULTIPLE TYPES; CTRCT9 (<https://omim.org/entry/604219>)
- PAIRED BOX GENE 6; PAX6 (<https://omim.org/entry/607108>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/5080>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=PAX6\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=PAX6[gene]))

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Genomic Location

The *PAX6* gene is found on chromosome 11 (<https://medlineplus.gov/genetics/chromosome/11/>).

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