# FOXC1 gene

forkhead box C1

## Normal Function

The *FOXC1* gene provides instructions for making a protein that attaches (binds) to specific regions of DNA and regulates the activity of other genes. On the basis of this action, the FOXC1 protein is called a transcription factor.

The FOXC1 protein plays a critical role in early development, particularly in the formation of structures in the front part of the eye (the anterior segment). These structures include the colored part of the eye (the iris), the lens of the eye, and the clear front covering of the eye (the cornea). Studies suggest that the FOXC1 protein may also have functions in the adult eye, such as helping cells respond to oxidative stress. Oxidative stress occurs when unstable molecules called free radicals accumulate to levels that can damage or kill cells.

The FOXC1 protein is also involved in the normal development of other parts of the body, including the heart, kidneys, and brain.

## Health Conditions Related to Genetic Changes

### Axenfeld-Rieger syndrome

More than 50 mutations in the *FOXC1* gene have been found to cause Axenfeld-Rieger syndrome type 3, a condition that primarily affects the development of the anterior segment of the eye but can also affect other parts of the body. Many *FOXC1* gene mutations reduce the amount of functional FOXC1 protein that is produced or result in a defective protein that cannot regulate the activity of other genes. Other genetic changes (such as a duplication of the *FOXC1* gene) likely increase the amount or function of the FOXC1 protein. Having either too little or too much activity of this protein disrupts the regulation of other genes needed for normal development.

Changes in the amount or function of the FOXC1 protein impairs the development of the anterior segment of the eye, leading to the eye abnormalities characteristic of Axenfeld-Rieger syndrome. In some cases, changes involving the FOXC1 protein also cause problems with development of other parts of the body.

### Peters anomaly

At least two mutations in the *FOXC1* gene have been found to cause Peters anomaly. This condition is characterized by abnormal development of the anterior segment and clouding of the cornea. The mutations that cause Peters anomaly likely disrupt the protein's ability to regulate the expression of developmental genes, especially affecting the eye. Abnormal formation of the iris, cornea, and other

structures of the anterior segment leads to the features of Peters anomaly. The *FOXC1* gene mutations that cause Peters anomaly can cause other related eye disorders, such as Axenfeld-Rieger syndrome (described above), in members of the same family.

Dandy-Walker malformation

Other disorders

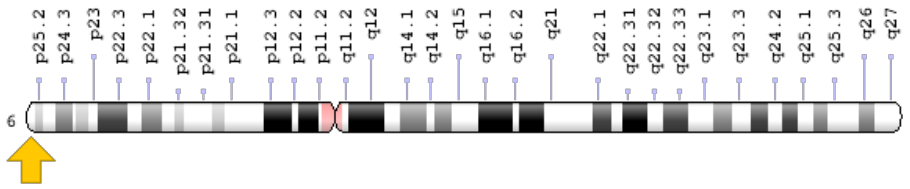
Mutations in the *FOXC1* gene have also been identified in another eye disorder called iridogoniodysgenesis type 1. Like Axenfeld-Rieger syndrome and Peters anomaly, this condition primarily involves the anterior segment of the eye. Iridogoniodysgenesis type 1 is associated with underdevelopment of the iris and an elevated risk of increased pressure in the eye (glaucoma).

*FOXC1* gene mutations have been reported in a few people with abnormalities of brain development. Mutations that change single protein building blocks (amino acids) in the FOXC1 protein have been associated with defects of the cerebellum, which is the part of the brain that is involved in coordinating movement. Additionally, deletions of genetic material from a region of chromosome 6 that includes the *FOXC1* gene and several neighboring genes have been associated with a structural abnormality of the cerebellum known as Dandy-Walker malformation.

## Chromosomal Location

Cytogenetic Location: 6p25.3, which is the short (p) arm of chromosome 6 at position 25.3

Molecular Location: base pairs 1,609,915 to 1,613,897 on chromosome 6 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)




Credit: Genome Decoration Page/NCBI

## Other Names for This Gene

- FKHL7
- forkhead box protein C1
- forkhead-related activator 3

- forkhead-related protein FKHL7
- forkhead-related transcription factor 3
- forkhead, drosophila, homolog-like 7
- forkhead/winged helix-like transcription factor 7
- FOXC1_HUMAN
- FREAC-3
- FREAC3
- myeloid factor-delta

## Additional Information & Resources

Educational Resources

- Transcriptional Control of Neural Crest Development (2010): FoxC
  https://www.ncbi.nlm.nih.gov/books/NBK53139/#s5.1

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28FOXC1%5BTIAB%5D%29+OR+%28forkhead+box+C1%5BTIAB%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+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- ANTERIOR SEGMENT DYSGENESIS 3
  http://omim.org/entry/601631
- FORKHEAD BOX C1
  http://omim.org/entry/601090

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/FOXC1ID40624ch6p25.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=FOXC1%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:3800
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:2296

- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/2296
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