



PITX2 gene

paired like homeodomain 2

Normal Function

The *PITX2* 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 PITX2 protein is called a transcription factor. The *PITX2* gene is part of a family of homeobox genes, which act during early embryonic development to control the formation of many parts of the body.

The PITX2 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 PITX2 protein also has 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 PITX2 protein is also involved in the normal development of other parts of the body, including the teeth, heart, and abdominal organs.

Health Conditions Related to Genetic Changes

Axenfeld-Rieger syndrome

More than 45 mutations in the *PITX2* gene have been found to cause Axenfeld-Rieger syndrome type 1, a condition that affects the development of the anterior segment of the eye and other parts of the body. Most *PITX2* gene mutations reduce the amount of functional PITX2 protein that is produced in cells. However, some genetic changes (such as a duplication of the *PITX2* gene) increase the amount or function of the PITX2 protein. Having either too little or too much of this protein disrupts the regulation of other genes needed for normal development.

Eye development appears to be the most sensitive to changes in PITX2 protein activity, and abnormalities of the anterior segment of the eye are the predominant features of Axenfeld-Rieger syndrome. However, changes in the amount of PITX2 protein can also lead to distinctive facial features, tooth abnormalities, and problems with development of other parts of the body in people with this condition.

Peters anomaly

At least one mutation in the *PITX2* gene has been found to cause Peters anomaly. This condition is characterized by abnormal development of the anterior segment of the eye and clouding of the cornea. This mutation (written IVS3AS,A>T,-2) alters

the way the PITX2 protein is pieced together. It is thought that this altered protein disrupts the regulation of movement of cells to their proper location in the developing anterior segment, leading to abnormal formation of the structures in this area of the eye and other features of Peters anomaly.

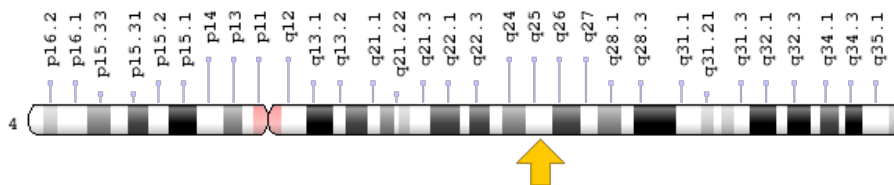
Other disorders

Mutations in the *PITX2* gene have also been identified in other eye disorders. Like Axenfeld-Rieger syndrome and Peters anomaly, these conditions primarily involve the anterior segment of the eye. Mutations in the *PITX2* gene can cause ring dermoid of the cornea, a condition associated with tumor-like growths on the cornea. Additionally, conditions that cause underdevelopment of the iris can occur, including iris hypoplasia or iridogoniodysgenesis type 2. Iridogoniodysgenesis type 2 is also associated with an elevated risk of increased pressure in the eye (glaucoma).

Chromosomal Location

Cytogenetic Location: 4q25, which is the long (q) arm of chromosome 4 at position 25

Molecular Location: base pairs 110,617,423 to 110,642,123 on chromosome 4 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- all1-responsive gene 1
- ARP1
- Brx1
- IDG2
- IGDS
- IGDS2
- IHG2
- IRID2
- Otlx2

- paired-like homeodomain 2
- paired-like homeodomain transcription factor 2
- pituitary homeobox 2
- PITX2_HUMAN
- PTX2
- RGS
- RIEG
- rieg bicoid-related homeobox transcription factor 1
- RIEG1
- RS
- solurshin

Additional Information & Resources

Educational Resources

- Transcriptional Control of Neural Crest Development (2010): Pitx2
<https://www.ncbi.nlm.nih.gov/books/NBK53140/#s6.16>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28PITX2%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+1800+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- ANTERIOR SEGMENT DYSGENESIS 4
<http://omim.org/entry/137600>
- PAIRED-LIKE HOMEODOMAIN TRANSCRIPTION FACTOR 2
<http://omim.org/entry/601542>
- RING DERMOID OF CORNEA
<http://omim.org/entry/180550>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_PITX2.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=PITX2%5Bgene%5D>

- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report#!/hgnc_id/HGNC:9005
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:5308>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/5308>
- UniProt
<https://www.uniprot.org/uniprot/Q99697>

Sources for This Summary

- Berry FB, Lines MA, Oas JM, Footz T, Underhill DA, Gage PJ, Walter MA. Functional interactions between FOXC1 and PITX2 underlie the sensitivity to FOXC1 gene dose in Axenfeld-Rieger syndrome and anterior segment dysgenesis. *Hum Mol Genet.* 2006 Mar 15;15(6):905-19. Epub 2006 Jan 31.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16449236>
- D'haene B, Meire F, Claerhout I, Kroes HY, Plomp A, Arens YH, de Ravel T, Casteels I, De Jaegere S, Hooghe S, Wuyts W, van den Ende J, Roulez F, Veenstra-Knol HE, Oldenburg RA, Giltay J, Verheij JB, de Faber JT, Menten B, De Paepe A, Kestelyn P, Leroy BP, De Baere E. Expanding the spectrum of FOXC1 and PITX2 mutations and copy number changes in patients with anterior segment malformations. *Invest Ophthalmol Vis Sci.* 2011 Jan 21;52(1):324-33. doi: 10.1167/iops.10-5309.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20881294>
- Doward W, Perveen R, Lloyd IC, Ridgway AE, Wilson L, Black GC. A mutation in the RIEG1 gene associated with Peters' anomaly. *J Med Genet.* 1999 Feb;36(2):152-5.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10051017>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1734311/>
- Footz T, Idrees F, Acharya M, Kozlowski K, Walter MA. Analysis of mutations of the PITX2 transcription factor found in patients with Axenfeld-Rieger syndrome. *Invest Ophthalmol Vis Sci.* 2009 Jun;50(6):2599-606. doi: 10.1167/iops.08-3251. Epub 2009 Feb 14.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19218601>
- Pearce WG, Mielke BC, Kulak SC, Walter MA. Histopathology and molecular basis of iridogoniodysgenesis syndrome. *Ophthalmic Genet.* 1999 Jun;20(2):83-8.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10420192>
- Reis LM, Tyler RC, Volkmann Kloss BA, Schilter KF, Levin AV, Lowry RB, Zwijnenburg PJ, Stroh E, Broeckel U, Murray JC, Semina EV. PITX2 and FOXC1 spectrum of mutations in ocular syndromes. *Eur J Hum Genet.* 2012 Dec;20(12):1224-33. doi: 10.1038/ejhg.2012.80. Epub 2012 May 9.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/22569110>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3499749/>
- Strungaru MH, Dinu I, Walter MA. Genotype-phenotype correlations in Axenfeld-Rieger malformation and glaucoma patients with FOXC1 and PITX2 mutations. *Invest Ophthalmol Vis Sci.* 2007 Jan;48(1):228-37.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17197537>

- Strungaru MH, Footz T, Liu Y, Berry FB, Belleau P, Semina EV, Raymond V, Walter MA. PITX2 is involved in stress response in cultured human trabecular meshwork cells through regulation of SLC13A3. *Invest Ophthalmol Vis Sci.* 2011 Sep 29;52(10):7625-33. doi: 10.1167/iovs.10-6967.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21873665>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3183983/>
 - Tümer Z, Bach-Holm D. Axenfeld-Rieger syndrome and spectrum of PITX2 and FOXC1 mutations. *Eur J Hum Genet.* 2009 Dec;17(12):1527-39. doi: 10.1038/ejhg.2009.93. Epub 2009 Jun 10. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19513095>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2987033/>
 - Xia K, Wu L, Liu X, Xi X, Liang D, Zheng D, Cai F, Pan Q, Long Z, Dai H, Hu Z, Tang B, Zhang Z, Xia J. Mutation in PITX2 is associated with ring dermoid of the cornea. *J Med Genet.* 2004 Dec; 41(12):e129.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15591271>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735645/>
-

Reprinted from Genetics Home Reference:
<https://ghr.nlm.nih.gov/gene/PITX2>

Reviewed: January 2014
Published: September 10, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services