PHOX2A gene

paired like homeobox 2A

Normal Function

The *PHOX2A* gene provides instructions for making a protein that is found in the nervous system. This protein acts early in development to help promote the formation of nerve cells (neurons) and regulate the process by which the neurons mature to carry out specific functions (differentiation).

Most of researchers' knowledge about the PHOX2A protein comes from studies in animals. From these studies, it is clear that the protein plays a critical role in the development of the autonomic nervous system, which controls involuntary body functions such as breathing, blood pressure, heart rate, and digestion. The PHOX2A protein is also involved in the formation of certain nerves in the head and face (cranial nerves). Specifically, it appears to be critical for the development and function of cranial nerves III and IV, which emerge from the brain and control many of the muscles that surround the eyes (extraocular muscles). These muscles direct eye movement and determine the position of the eyes.

Health Conditions Related to Genetic Changes

Congenital fibrosis of the extraocular muscles

At least four mutations in the *PHOX2A* gene can cause congenital fibrosis of the extraocular muscles (CFEOM). These mutations are responsible for a form of the disorder called CFEOM2, which has been identified in several families of Middle Eastern descent.

Most of the mutations that cause CFEOM2 result in the production of an abnormally short, nonfunctional version of the PHOX2A protein. A lack of this protein prevents the normal development of several cranial nerves and the extraocular muscles they control. Abnormal development and function of these muscles leads to the characteristic features of the disorder, including restricted eye movement and related problems with vision. Although the PHOX2A protein plays an important role in autonomic nervous system development, *PHOX2A* mutations do not seem to affect the function of this part of the nervous system.

Other Names for This Gene

- aristaless homeobox homolog
- aristaless homeobox protein homolog
- ARIX
- arix homeodomain protein
- ARIX1 homeodomain protein
- CFEOM2
- FEOM2
- MGC52227
- NCAM2
- paired like homeobox 2a
- paired mesoderm homeobox protein 2A
- paired-like homeobox 2a
- PHX2A_HUMAN
- PMX2A

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PHOX2A (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=401[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28PHOX2A%5BTIAB%5D%29+OR+%28ARIX%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

- PAIRED-LIKE HOMEOBOX 2A; PHOX2A (https://omim.org/entry/602753)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/401)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=PHOX2A[gene])

References

- Benfante R, Flora A, Di Lascio S, Cargnin F, Longhi R, Colombo S, Clementi F, Fornasari D. Transcription factor PHOX2A regulates the human alpha3 nicotinicreceptor subunit gene promoter. J Biol Chem. 2007 May 4;282(18):13290-302. doi:10.1074/jbc.M608616200. Epub 2007 Mar 7. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17344216)
- Bosley TM, Oystreck DT, Robertson RL, al Awad A, Abu-Amero K, Engle EC. Neurological features of congenital fibrosis of the extraocular muscles type 2with mutations in PHOX2A. Brain. 2006 Sep;129(Pt 9):2363-74. doi:10.1093/brain/awl161. Epub 2006 Jun 30. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16815872)
- Hasan KB, Agarwala S, Ragsdale CW. PHOX2A regulation of oculomotor complexnucleogenesis. Development. 2010 Apr;137(7):1205-13. doi: 10.1242/dev.041251. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20215354) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2835333/)
- Heidary G, Engle EC, Hunter DG. Congenital fibrosis of the extraocularmuscles. Semin Ophthalmol. 2008 Jan-Feb;23(1):3-8. doi:10.1080/08820530701745181. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18214786)
- Nakano M, Yamada K, Fain J, Sener EC, Selleck CJ, Awad AH, Zwaan J, MullaneyPB, Bosley TM, Engle EC. Homozygous mutations in ARIX(PHOX2A) result incongenital fibrosis of the extraocular muscles type 2. Nat Genet. 2001Nov;29(3):315-20. doi: 10.1038/ng744. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11600883)
- Pattyn A, Morin X, Cremer H, Goridis C, Brunet JF. Expression and interactionsof the two closely related homeobox genes Phox2a and Phox2b during neurogenesis. Development. 1997 Oct;124(20):4065-75. doi: 10.1242/dev.124.20.4065. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/9374403)
- Yazdani A, Chung DC, Abbaszadegan MR, Al-Khayer K, Chan WM, Yazdani M, GhodsiK, Engle EC, Traboulsi EI. A novel PHOX2A/ARIX mutation in an Iranian family withcongenital fibrosis of extraocular muscles type 2 (CFEOM2). Am J Ophthalmol. 2003Nov;136(5):861-5. doi: 10.1016/s0002-9394(03)00891-2. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/14597037)

Genomic Location

The *PHOX2A* gene is found on chromosome 11 (https://medlineplus.gov/genetics/chromosome/11/).

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