SIX3 gene

SIX homeobox 3

Normal Function

The *SIX3* gene provides instructions for making a protein that plays an important role in the development of the eyes and front part of the brain (forebrain). This protein is a transcription factor, which means that it attaches (binds) to specific regions of DNA and helps control the activity of certain genes. The SIX3 protein regulates genes involved in several signaling pathways that are important for embryonic development. Some of these genes are turned on (activated) by the SIX3 protein and others are turned off (repressed).

One gene that is activated by the SIX3 protein is the *SHH* gene, which provides instructions for making a protein called Sonic Hedgehog. Among its many functions, Sonic Hedgehog helps establish the right and left halves (hemispheres) of the forebrain. The SIX3 protein also regulates genes involved in the formation of the lens of the eye and the specialized tissue at the back of the eye that detects light and color (the retina).

Health Conditions Related to Genetic Changes

Nonsyndromic holoprosencephaly

At least 60 mutations in the *SIX3* gene have been found to cause nonsyndromic holoprosencephaly. This condition occurs when the brain fails to divide into two hemispheres during early development. *SIX3* gene mutations are the third most common cause of nonsyndromic holoprosencephaly. Although mutations in this gene can cause mild to severe forms of the condition, they tend to result in more severe signs and symptoms than mutations in other genes that cause nonsyndromic holoprosencephaly

SIX3 gene mutations change the structure of the SIX3 protein in different ways; however, all of them disrupt the protein's ability to bind with DNA. As a result, the genes involved in normal eye and forebrain development are not properly activated or repressed. Without the correct activity of these genes, the eyes will not form normally and the brain does not separate into two hemispheres. The signs and symptoms of nonsyndromic holoprosencephaly are caused by abnormal development of the brain and face.

Coloboma

MedlinePlus Genetics provides information about Coloboma

Other Names for This Gene

- homeobox protein SIX3
- HPE2
- sine oculis homeobox homolog 3
- SIX3_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SIX3 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6496[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SIX3%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

- SIX HOMEOBOX 3; SIX3 (https://omim.org/entry/603714)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/6496)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SIX3[gene])

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Genomic Location

The *SIX3* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chromosome/2/).

Last updated September 1, 2010