SIX1 gene
SIX homeobox 1

Normal Function

The SIX1 gene is part of a group of similar genes known as the SIX gene family. Genes in this family provide instructions for making proteins that bind to DNA and control the activity of other genes. Based on this role, SIX proteins are called transcription factors.

The SIX1 protein interacts with several other proteins, including the protein produced from the EYA1 gene, to regulate the activity of genes that are important for normal development. Before birth, these protein interactions appear to be essential for the normal formation of many tissues. These include the second branchial arch, which gives rise to tissues in the front and side of the neck; the ears; the kidneys; the nose; a gland called the thymus that is part of the immune system; and muscles used for movement (skeletal muscles).

Health Conditions Related to Genetic Changes

Branchiootorenal/branchiootic syndrome

At least nine mutations in the SIX1 gene have been identified in people with branchiootorenal (BOR) syndrome, a condition that disrupts the development of tissues in the neck and causes malformations of the ears and kidneys. A few SIX1 gene mutations have also been found to cause branchiootic (BO) syndrome, which includes many of the same features as BOR syndrome except for kidney (renal) malformations. The two conditions are otherwise so similar that researchers often consider them together (BOR/BO syndrome or branchiootorenal spectrum disorders). In some cases, the same SIX1 gene mutation causes BOR syndrome in some members of a family and BO syndrome in others.

Most of the known SIX1 gene mutations change single protein building blocks (amino acids) in the SIX1 protein. Some of these mutations prevent the SIX1 protein from interacting with other proteins, such as the protein produced from the EYA1 gene. Other mutations affect the ability of SIX1 protein to bind to DNA. Both of these functions are necessary for the SIX1 protein to regulate gene activity during embryonic development. When the SIX1 protein is faulty, it impairs the normal development of many tissues before birth. The major signs and symptoms of BOR/BO syndrome result from abnormal development of the second branchial arch, the ears, and (in BOR syndrome) the kidneys.

Congenital anomalies of kidney and urinary tract
Chromosomal Location

Cytogenetic Location: 14q23.1, which is the long (q) arm of chromosome 14 at position 23.1

Molecular Location: base pairs 60,643,421 to 60,649,489 on chromosome 14 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

Other Names for This Gene

• BOS3
• homeobox protein SIX1
• sine oculis homeobox (Drosophila) homolog 1
• sine oculis homeobox homolog 1
• sine oculis homeobox homolog 1 (Drosophila)
• SIX1_HUMAN
• TIP39

Additional Information & Resources

Educational Resources

• Developmental Biology (sixth edition, 2000): Transcription Factors
  https://www.ncbi.nlm.nih.gov/books/NBK10023/#A763

Clinical Information from GeneReviews

• Branchiootorenal Spectrum Disorder
  https://www.ncbi.nlm.nih.gov/books/NBK1380

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28SIX1%5BTIAB%5D%29+OR+%28DFNA23%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22+AND+human%5Bdp%5D
Catalog of Genes and Diseases from OMIM

- SIX HOMEBOX 1
  http://omim.org/entry/601205

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/SIX1ID42302ch14q23.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SIX1%5Bgene%5D
- HGNC Gene Symbol Report
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:6495
- NCBI Gene
- UniProt
  https://www.uniprot.org/uniprot/Q15475

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15141091
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC419562/

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301554

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  https://ghr.nlm.nih.gov/gene/SIX1

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