SIX1 Gene

Subjects: Genetics & Heredity
Contributor: Karina Chen

SIX homeobox 1

genes

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).

2. Health Conditions Related to Genetic Changes

2.1. 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.

3. 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

References

1. Kochhar A, Orten DJ, Sorensen JL, Fischer SM, Cremers CW, Kimberling WJ, SmithRJ. SIX1 mutation screening in 247 branchio-oto-renal syndrome families: arecurrent missense mutation associated with BOR. Hum Mutat. 2008 Apr;29(4):565.doi: 10.1002/humu.20714.
2. Krug P, Morinière V, Marlin S, Koubi V, Gabriel HD, Colin E, Bonneau D,Salomon R, Antignac C, Heidet L. Mutation screening of the EYA1, SIX1, and SIX5genes in a large cohort of patients harboring branchio-oto-renal syndrome callsinto question the pathogenic role of SIX5 mutations. Hum Mutat. 2011Feb;32(2):183-90. doi: 10.1002/humu.21402.
3. Mosrati MA, Hammami B, Rebeh IB, Ayadi L, Dhouib L, Ben Mahfoudh K, Hakim B,Charfeddine I, Mnif J, Ghorbel A, Masmoudi S. A novel dominant mutation in SIX1, affecting a highly conserved residue, result in only auditory defects in humans. Eur J Med Genet. 2011 Sep-Oct;54(5):e484-8. doi: 10.1016/j.ejmg.2011.06.001.
4. Ruf RG, Xu PX, Silvius D, Otto EA, Beekmann F, Muerb UT, Kumar S, Neuhaus TJ, Kemper MJ, Raymond RM Jr, Brophy PD, Berkman J, Gattas M, Hyland V, Ruf EM,Schwartz C, Chang EH, Smith RJ, Stratakis CA, Weil D, Petit C, Hildebrandt F.SIX1 mutations cause branchio-oto-renal syndrome by disruption of EYA1-SIX1-DNAcomplexes. Proc Natl Acad Sci U S A. 2004 May 25;101(21):8090-5.
5. Smith RJH. Branchiootorenal Spectrum Disorder. 1999 Mar 19 [updated 2018 Sep6]. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Stephens K, AmemiyaA, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington,Seattle; 1993-2020. Available from http://www.ncbi.nlm.nih.gov/books/NBK1380/

Retrieved from https://encyclopedia.pub/entry/history/show/12880