SIX5 gene

SIX homeobox 5

Normal Function

The *SIX5* 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 SIX5 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; and the kidneys. Researchers have also found the SIX5 protein in the adult brain, heart, eyes, and muscles used for movement (skeletal muscles).

Health Conditions Related to Genetic Changes

Branchiootorenal/branchiootic syndrome

At least four mutations in the *SIX5* gene have been found 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. BOR syndrome is considered part of a disease spectrum with a condition known as branchiootic (BO) syndrome, which has many of the same features as BOR syndrome except for kidney (renal) malformations.

Researchers now question whether mutations in the *SIX5* gene cause BOR syndrome. Some affected individuals originally reported to have mutations in this gene were later found to have mutations in the *EYA1* gene as well. Researchers suspect that the *EYA1* gene mutations may be the actual cause of the condition in these people.

Each of the identified *SIX5* gene mutations changes a single protein building block (amino acid) in the SIX5 protein, which alters this protein's interactions with the protein produced from the *EYA1* gene. Because this protein interaction is necessary for the activation of certain genes during embryonic development, it is possible that the altered SIX5 protein disrupts development before birth. The major signs and symptoms of BOR syndrome result from abnormal development of the second branchial arch, ears, and

kidneys.

Congenital anomalies of kidney and urinary tract

MedlinePlus Genetics provides information about Congenital anomalies of kidney and urinary tract

Other Names for This Gene

- BOR2
- DM locus-associated homeodomain protein
- DMAHP
- dystrophia myotonica-associated homeodomain protein
- homeobox protein SIX5
- sine oculis homeobox homolog 5
- SIX5_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SIX5 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=147912[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SIX5%5BTI%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

Catalog of Genes and Diseases from OMIM

- SIX HOMEOBOX 5; SIX5 (https://omim.org/entry/600963)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/147912)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SIX5[gene])

References

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Genomic Location

The *SIX5* gene is found on chromosome 19 (https://medlineplus.gov/genetics/chromosome/19/).

Last updated March 1, 2016