TWIST1 gene

twist family bHLH transcription factor 1

Normal Function

The *TWIST1* gene provides instructions for making a protein that plays an important role in early development. This protein is a transcription factor, which means that it attaches (binds) to specific regions of DNA and controls the activity of particular genes. Specifically, the TWIST1 protein is part of a large protein family called basic helix-loop-helix (bHLH) transcription factors. Each of these proteins includes a region called the bHLH domain, which determines the protein's 3-dimensional shape and enables it to target particular sequences of DNA. The bHLH family of transcription factors helps regulate the development of many organs and tissues before birth.

During embryonic development, the TWIST1 protein is essential for the formation of cells that give rise to bone, muscle, and other tissues in the head and face. The TWIST1 protein also plays a role in the early development of the arms and legs. Researchers believe that the TWIST1 protein regulates several genes that are known to be key players in bone formation, including the *FGFR2* and *RUNX2* genes.

Health Conditions Related to Genetic Changes

Saethre-Chotzen syndrome

More than 180 mutations in the *TWIST1* gene have been identified in people with Saethre-Chotzen syndrome. This condition is characterized by the premature fusion of certain skull bones (craniosynostosis), which prevents the skull from growing normally and affects the shape of the head and face. Abnormalities of the hands and feet are also frequent, and other body systems are less commonly affected. Some of these mutations change single DNA building blocks (nucleotides) in the *TWIST1* gene, while others delete or insert genetic material in the gene. In some cases, this condition is caused by chromosomal abnormalities (translocations or deletions) involving the region of chromosome 7 that contains the *TWIST1* gene.

TWIST1 gene mutations prevent one copy of the gene in each cell from producing any functional protein. A shortage of functional TWIST1 protein affects the development and maturation of cells in the skull, face, arms and legs. These abnormalities underlie the signs and symptoms of Saethre-Chotzen syndrome, although it is unclear exactly how a shortage of the TWIST1 protein causes specific features of the condition.

Other disorders

At least two mutations in the *TWIST1* gene have been found to cause a very rare disorder called Sweeney-Cox syndrome. This condition is characterized by widely spaced eyes (hypertelorism), abnormal eyelids and ears, unusually small bones in the face and jaw, and abnormal development or fusion of skull bones. Both mutations that cause this condition change the same amino acid in the TWIST1 protein. The abnormal protein produced from the mutated copy of the gene is thought to impair the function of the protein produced from the normal copy of the gene, severely reducing TWIST1 protein activity in developing tissues. The extreme shortage of functioning TWIST1 protein disrupts development of the skull, head, and face, resulting in the features of Sweeney-Cox syndrome.

TWIST1 gene mutations have also been found in several people with isolated craniosynostosis, which is a premature fusion of certain skull bones that occurs without the other signs and symptoms of Saethre-Chotzen syndrome or Sweeney-Cox syndrome. These mutations occur near the end of the gene in a region known as the TWIST box domain. This domain enables the TWIST1 protein to bind to and regulate a gene called *RUNX2*, which is a critical regulator of bone formation. Researchers believe that mutations in the TWIST box domain prevent the TWIST1 protein from effectively controlling the activity of the *RUNX2* gene, which disrupts the normal pattern of bone formation in the skull and leads to isolated craniosynostosis.

Other Names for This Gene

- acrocephalosyndactyly 3
- ACS3
- B-HLH DNA binding protein
- CRS1
- H-twist
- SCS
- Transcription factor TWIST
- TWIST
- twist basic helix-loop-helix transcription factor 1
- Twist Homolog
- twist homolog 1 (acrocephalosyndactyly 3; Saethre-Chotzen syndrome) (Drosophila)
- twist homolog 1 (Drosophila)
- TWST1_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of TWIST1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=7291[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28TWIST1%5BTIAB%5D%29+OR+%28TWIST+AND+craniosynostosis%5BTIAB%5D%29%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

- TWIST FAMILY bHLH TRANSCRIPTION FACTOR 1; TWIST1 (https://omim.org/entry/601622)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/7291)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=TWIST1[gene])

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Genomic Location

The *TWIST1* gene is found on chromosome 7 (https://medlineplus.gov/genetics/chromosome/7/).

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