

SHOX Gene

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short stature homeobox

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1. Normal Function

The *SHOX* gene provides instructions for making a protein that regulates the activity of other genes. On the basis of this role, the SHOX protein is called a transcription factor. The *SHOX* gene is part of a large family of homeobox genes, which act during early embryonic development to control the formation of many body structures. Specifically, the *SHOX* gene is essential for the development of the skeleton. It plays a particularly important role in the growth and maturation of bones in the arms and legs.

One copy of the *SHOX* gene is located on each of the sex chromosomes (the X and Y chromosomes) in an area called the pseudoautosomal region. Although many genes are unique to either the X or Y chromosome, genes in the pseudoautosomal region are present on both chromosomes. As a result, both females (who have two X chromosomes) and males (who have one X and one Y chromosome) have two functional copies of the *SHOX* gene in each cell.

2. Health Conditions Related to Genetic Changes

2.1. Langer mesomelic dysplasia

Langer mesomelic dysplasia results from genetic changes involving both copies of the *SHOX* gene in each cell. Deletions of this gene are the most common change responsible for this condition. Mutations in the *SHOX* gene can also cause the condition, as can deletions of nearby genetic material that normally helps regulate the gene's activity. These changes greatly reduce or eliminate the amount of SHOX protein that is produced. A lack of this protein disrupts normal bone development and growth starting before birth. The resulting skeletal abnormalities include very short stature, extreme shortening of the long bones in the arms and legs (mesomelia), and an abnormality of the wrist and forearm bones known as Madelung deformity.

2.2. Léri-Weill dyschondrosteosis

Léri-Weill dyschondrosteosis results from genetic changes involving one copy of the *SHOX* gene in each cell. Most commonly, this skeletal disorder is caused by a deletion of the *SHOX* gene. Other genetic changes that can cause the disorder include mutations in the *SHOX* gene or deletions of nearby genetic material that normally helps regulate the gene's activity. These changes reduce the amount of SHOX protein that is produced. A shortage of this protein disrupts normal bone development and growth starting before birth. The resulting skeletal abnormalities are similar to those of Langer mesomelic dysplasia, although they tend to be less severe.

2.3. Turner syndrome

Turner syndrome occurs when one normal X chromosome is present in a female's cells and the other sex chromosome is missing or structurally altered. Because the *SHOX* gene is located on the sex chromosomes, most women with Turner syndrome have only one copy of the gene in each cell instead of the usual two copies. Loss of one copy of this gene reduces the amount of SHOX protein that is produced. A shortage of this protein likely contributes to the short stature and skeletal abnormalities (such as unusual rotation of the wrist and elbow joints) often seen in females with this condition.

2.4. Other disorders

Deletions of the entire *SHOX* gene or mutations within or near the gene have been identified in some people with short stature. This short stature is usually described as idiopathic, which means it is not associated with the characteristic features of a disease or syndrome. However, some people with short stature and changes in the *SHOX* gene have been found to have subtle skeletal abnormalities.

3. Other Names for This Gene

- GCFX
- growth control factor, X-linked
- PHOG
- pseudoautosomal homeobox-containing osteogenic gene
- SHOX_HUMAN
- SS

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