PITX1 Gene

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genes

1. Introduction

The *PITX1* gene provides instructions for making a protein that plays a critical role in development of the lower limbs. The PITX1 protein is found primarily in the developing legs and feet. The protein acts as a transcription factor, which is a protein that attaches (binds) to specific regions of DNA and helps control the activity of particular genes. Specifically, PITX1 regulates the activity of genes to direct the shape and structure of tissues in the lower limbs, including the bones, muscles, and tendons (the bands of tissue that connect muscles to bones).

The PITX1 protein is also found in the developing pituitary gland, which is a hormone-producing gland located at the base of the brain, and in an embryonic structure called the branchial arch. The PITX1 protein may play a role in formation of the pituitary gland and tissues derived from the branchial arch, such as the roof of the mouth, the jaw, and parts of the inner ear.

2. Health Conditions Related to Genetic Changes

2.1. Liebenberg syndrome

Changes in the DNA near the *PITX1* gene cause Liebenberg syndrome, a rare condition characterized by abnormal development of the arms, resulting in short fingers (brachydactyly), joint deformities called contractures that limit movement of the elbows and wrists, and other bone and muscle abnormalities. These genetic changes delete, insert, or rearrange genetic material near the *PITX1* gene; at least five such mutations have been identified in affected individuals. These changes affect regions of DNA known as regulatory elements, which help turn on or turn off genes (known as enhancers or repressors, respectively). They control when and where certain genes are active. The mutations that cause Liebenberg syndrome likely relocate enhancers that promote the activity of genes involved in upper limb development to be near the *PITX1* gene. Alternatively, mutations may remove repressors that normally turn off the *PITX1* gene during upper limb development. As a result, the *PITX1* gene is abnormally active during arm and hand development. Because the PITX1 protein normally directs lower limb structure, bones, muscles, and tendons in the arms and hands develop more like those in the legs and feet, leading to the features of Liebenberg syndrome. Development of the lower limbs is normal in people with this condition.

2.2. Other disorders

PITX1 gene mutations have been found to cause lower limb abnormalities, including an inward- and upward-turning foot (clubfoot) and absence or severe shortening of a bone in the lower leg called the tibia (tibial hemimelia). These gene mutations have also been found in people with extra toes (polydactyly), specifically a severe form of the abnormality called mirror-image polydactyly. These mutations delete a large part of the *PITX1* gene or the whole gene, or change a single protein building block (amino acid) in the PITX1 protein. Unlike the mutations that cause Liebenberg syndrome (described above), these genetic changes reduce the amount of functional PITX1 protein, which disrupts normal development of the lower limbs. The upper limbs are normal in individuals with these *PITX1* gene mutations.

3. Other Names for This Gene

- BFT
- hindlimb expressed homeobox protein backfoot
- hindlimb-expressed homeobox protein backfoot
- homeobox protein PITX1
- paired-like homeodomain 1
- paired-like homeodomain transcription factor 1
- pituitary homeo box 1
- pituitary homeobox 1
- pituitary otx-related factor
- POTX
- Ptlx
- PTX1

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