POU3F4 Gene

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POU class 3 homeobox 4

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1. Introduction

The *POU3F4* gene provides instructions for making a protein that helps regulate the activity of other genes. Based on this role, the protein is called a transcription factor. The *POU3F4* gene is part of a larger family of transcription factor genes called POU domain genes. These genes play a role in determining cell types in the brain and spinal cord (the central nervous system) during early development. The proteins produced from genes in the POU domain family each include two regions, called the POU-specific domain and POU homeodomain, that bind to the DNA of other genes.

The POU3F4 protein is likely to be involved in the development of the middle and inner ear, and it is also active in certain regions of the brain before birth. Researchers are working to determine which genes are regulated by this protein.

2. Health Conditions Related to Genetic Changes

2.1. Nonsyndromic hearing loss

Mutations involving the *POU3F4* gene cause nonsyndromic hearing loss, which is a loss of hearing that is not associated with other signs and symptoms. Mutations in this gene cause a form of hearing loss designated as DFNX2, sometimes also known as Nance deafness. DFNX2 is the most common type of X-linked nonsyndromic hearing loss, accounting for about half of all cases. X-linked conditions are caused by mutations in genes on the X chromosome, which is one of the two sex chromosomes.

The signs and symptoms of DFNX2 differ in males and females. In males, this form of hearing loss begins before the child learns to speak (prelingual), becomes more severe over time, and usually involves abnormalities of both the inner ear and the middle ear (mixed hearing loss). In the middle ear, one of the small bones (the stapes) cannot move normally, which interferes with hearing. This characteristic sign of DFNX2 is called stapes fixation. During surgery to repair this abnormality, affected males are at high risk of a complication called a perilymphatic gusher, which is a leakage of fluid from the inner ear that can result in a permanent, total loss of hearing. Females with *POU3F4* gene mutations tend to be less severely affected, with little or no hearing loss and no apparent middle ear abnormalities. When hearing loss occurs, it usually begins after the child learns to speak (postlingual).

More than 50 *POU3F4* gene mutations have been found to cause DFNX2. Many of these genetic changes alter single protein building blocks (amino acids) in the POU3F4 protein or delete part or all of the *POU3F4* gene. In some cases, mutations have been found in DNA near the *POU3F4* gene. Researchers believe that this DNA may play a role in regulating the *POU3F4* gene. Mutations in or near this gene prevent cells from producing any POU3F4 protein or impair regions of the protein that are critical for binding to DNA. A lack of functional POU3F4 protein probably disrupts the normal development of structures in the middle and inner ear, leading to hearing loss.

3. Other Names for This Gene

- BRAIN-4
- brain-specific homeobox/POU domain protein 4
- Brn-4
- BRN4
- DFN3
- DFNX2

- OTF9
- PO34_HUMAN

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