

CONNEXIN 30 GENE TESTING

COULD MY HEARING LOSS BE CAUSED BY MUTATIONS IN THE CONNEXIN 30 GENE?

Mutations in the connexin 30 (Cx30) gene are most often seen in a person with:

- Hearing loss that was found at birth or in early childhood
- Hearing loss that is severe or profound
- Hearing loss without any other medical problems (nonsyndromic)
- Hearing loss with no identified cause
- A single mutation in the connexin 26 (Cx26) gene

Most families with this form of hearing loss are missing a large section of the DNA that includes one copy of their Cx30 gene. Usually, these families actually have a single mutation in Cx26 as well as the deletion of one of their copies of Cx30. However, some families have also been found with two copies of the Cx30 deletion and no Cx26 mutations. It appears that this form of hearing loss usually requires two mutations, but they can be two Cx26 mutations, two Cx30 deletion mutations or one of each.

Though the Cx30 deletion is usually involved in the recessive hearing loss described above, there are other kinds of Cx30 mutations that have been found to cause a dominant form of hearing loss that starts later in life. Furthermore, other dominant mutations in this gene can cause a skin disease called Hidrotic Ectodermal Dysplasia.

HOW IS THE Cx30 GENE TEST PERFORMED?

The most common Cx30 test that is offered checks to see if the DNA sample has a deletion of one, or both, copies of the Cx30 gene. Some laboratories may also examine the entire coding sequence of the gene.

HOW ARE THE RESULTS OF A Cx30 TEST INTERPRETED?

There are three possible outcomes of a Cx30 test:

1. *Two Cx30 mutations are found.* If two mutations are found, it can be assumed that the patient's hearing loss is caused by the Cx30 mutations.
2. *No Cx30 mutations are detected.* If no mutations are found, and the lab tested for the deletion and other mutations in the coding sequence, it is unlikely that the patient's hearing loss was caused by Cx30.

3. *Only one Cx30 mutation is detected.* If one mutation is detected, and the patient also has a single Cx26 mutation, it can be assumed that the combination of two mutations is causing the hearing loss. If one mutation is found and no Cx26 mutations were detected (after analyzing the whole Cx26 coding sequence) interpretation can be difficult. The most likely explanations are:
- A) The Cx30 deletion mutation may be unrelated to the deafness. It is possible for a person with hearing loss to carry a single Cx30 mutation when the real cause of the hearing loss is due to another gene or a non-genetic cause.
 - B) The test did not detect the second mutation. Even though the test for the deleted DNA and the examination of the coding sequence will detect most mutations, there are other regions of the Cx30 and Cx26 gene sequence and surrounding DNA that could contain a mutation. Unfortunately, these sequences are rarely analyzed unless a specific mutation is already known.
 - C) The mutation may act as a dominant mutation, meaning that only one mutation is required to cause hearing loss.

A catalog of all Cx30 mutations can be found at the “Connexins and Deafness” website (<http://www.crg.es/deafness>). It should be noted that the correct name of this gene is *GJB6* (gap junction beta 6). We use the protein name, connexin 30, because it is more common to the public.