UNDERSTANDING GENETIC HEARING LOSS AND THE IMPORTANCE OF GENETIC TESTING

REGENERON
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Learn about

- Congenital hearing loss
- Genetics of hearing loss
- The importance of genetic testing

Discover more online at: learngeneticheartingloss.com

THE FIRST STEPS ON YOUR FAMILY'S HEARING LOSS JOURNEY

Worldwide 1 in 500 babies
are born with congenital hearing loss[1]

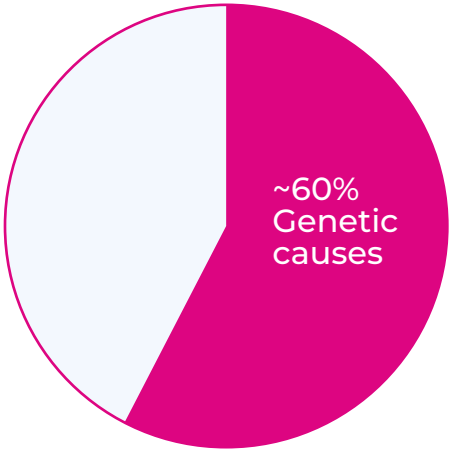
What is congenital hearing loss?

Congenital hearing loss occurs when a baby is born deaf or hard of hearing.

Congenital hearing loss occurs when a baby is born deaf or hard of hearing. There are a number of causes of hearing loss in newborns including infections, premature birth, low birth weight, and genetics.[2]

Finding out that your child has hearing loss can be overwhelming. One of the first steps you can take is to explore whether your child's congenital hearing loss could be due to a genetic cause.

Genetic variations are the leading cause of congenital hearing loss[3]



What is a gene?

Genes are the blueprints providing instructions on how to make proteins for the body.

What is a protein?

Proteins are molecules responsible for performing vital functions in our cells.

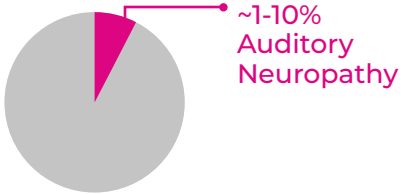
How can genetic variations cause hearing loss?

Specific variations in our genes can cause incorrect coding of proteins. Some proteins are essential for hearing and, if nonfunctional or missing, can cause congenital hearing loss.

THE MOST COMMON CAUSE OF GENETIC AUDITORY NEUROPATHY SPECTRUM DISORDER

Up to 10% of children diagnosed with hearing loss at birth have auditory neuropathy, usually due to genetic variants.[4]

Children diagnosed with hearing loss at birth



The absence of a protein called otoferlin can result in auditory neuropathy spectrum disorder (ANSD). Otoferlin is the most common genetic protein variation that causes this type of hearing loss.

What is Auditory Neuropathy Spectrum Disorder (ANSD)?

ANSD is a hearing condition where the inner ear is able to successfully detect sound but is unable to send sound from the ear to the brain.

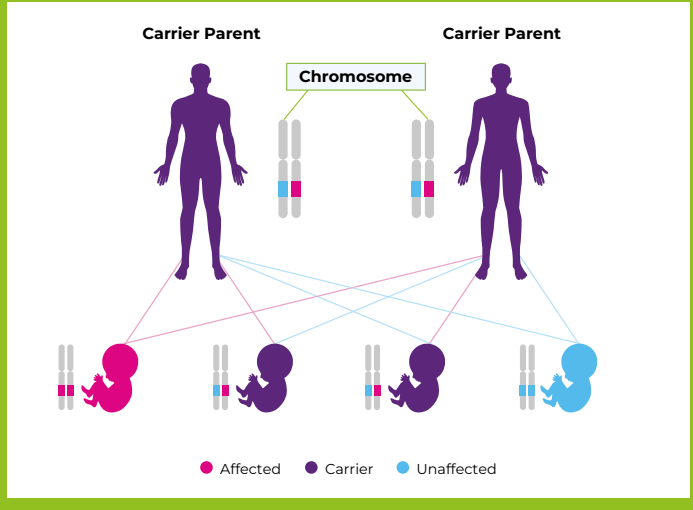
Otoferlin/OTOF

Otoferlin protein is created by the *OTOF* gene. Variations in this gene can lead to profound hearing loss.

HOW IS GENETIC HEARING LOSS PASSED TO A CHILD?

We all inherit two copies of each of our genes, one from each parent. In most cases of otoferlin-related ANSD, a child inherits one non-working copy of the *OTOF* gene from each of their parents, known as an autosomal recessive inheritance pattern.

AUTOSOMAL RECESSIVE INHERITANCE

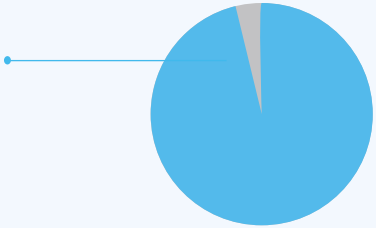


25% chance of inheriting this condition if each parent has one copy of the genetic variant

Parents of a child with this kind of hearing loss are unlikely to know they each carry one copy of the OTOF genetic variant because both may not have been genetically tested, and they don't themselves experience this kind of hearing loss.

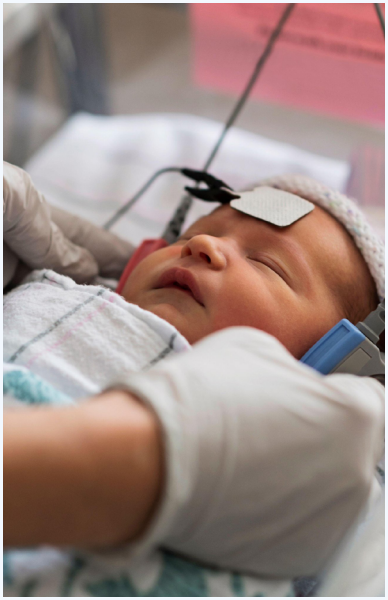
UNDERSTANDING THE IMPACT OF VARIANTS OF THE OTOF GENE

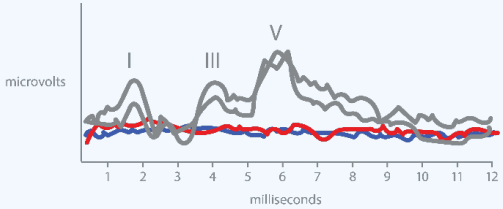
Children with two non-functioning copies of the *OTOF* gene



95% of people who inherit two non-functioning copies of the OTOF gene have severe to profound hearing loss.[5]

OTOFERLIN MAKES IT POSSIBLE FOR THE EAR CELLS RECEIVING SOUND TO COMMUNICATE WITH THE BRAIN





These ABR test results[6] show babies with:

1. Typical hearing (grey lines) have peaks (I, III, V) at different time points, indicating sound is being sent from the ear to the brain successfully.

2. Non-functioning Otoferlin (red/blue lines) have no ABR response, indicating disrupted or no sound is being sent from the ear to the brain.

What is an Auditory Brainstem Response (ABR) Test?

ABR tests are used to assess how well sound travels along the network of nerves from the ear to the brain. The ABR test is painless and noninvasive. The clinician places sticker electrodes on the child's forehead and ear region, and the sounds are played through headphones to see if sound is traveling properly from the ear to the brain.

Approximately 95% of all babies born with non-functioning otoferlin deficiency have an absent ABR (no measurable peaks) suggesting profound hearing loss due to inability for sound to travel from the ear to the brain.[5]

THE IMPORTANCE OF GENETIC TESTING

Genetic testing can help identify the cause of congenital hearing loss early, and aid families in understanding options for addressing hearing loss.

Potential benefits of genetic testing include:

- Identifying if hearing loss is genetic.
- May help clinician with guiding care of childhood hearing loss.
- Accessing current and future investigational gene therapy clinical trials for genetic hearing loss, if qualified.
- Opportunity to support research that will enable better understanding of genetic hearing loss and development of potential therapies.

A genetic test requires a single mouth swab and, in most cases, detect the most common genetic variants associated with congenital hearing loss.

REFERENCES

[1] www.who.int/news-room/facts-in-pictures/detail/deafness
www.cdc.gov/ncbddd/hearingloss/data.html

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[3] Morton CC, Nance WE. Newborn hearing screening—a silent revolution. N Engl J Med. 2006;354(20):2151-2164

[4] De Siati RD, et al. Auditory Neuropathy Spectrum Disorders: From Diagnosis to Treatment: Literature Review and Case Reports. J Clin Med. 2020 Apr 10;9(4):1074.

[5] *OTOF*-Related Deafness
www.ncbi.nlm.nih.gov/books/NBK1251/

[6] *Vogl et.al. EMBO J. 2016;35(23):2536–2552.*

For more information about genetics of hearing loss, how to access no-cost, non-invasive genetic testing, and how to support research on investigational gene therapies, please visit:

learngeneticheargingloss.com

We're here to support you every step of the way through your family's hearing loss journey. Regeneron is also dedicated to developing gene therapies that could, if proven in clinical trials, offer additional options for children with hearing loss to be able to hear.

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