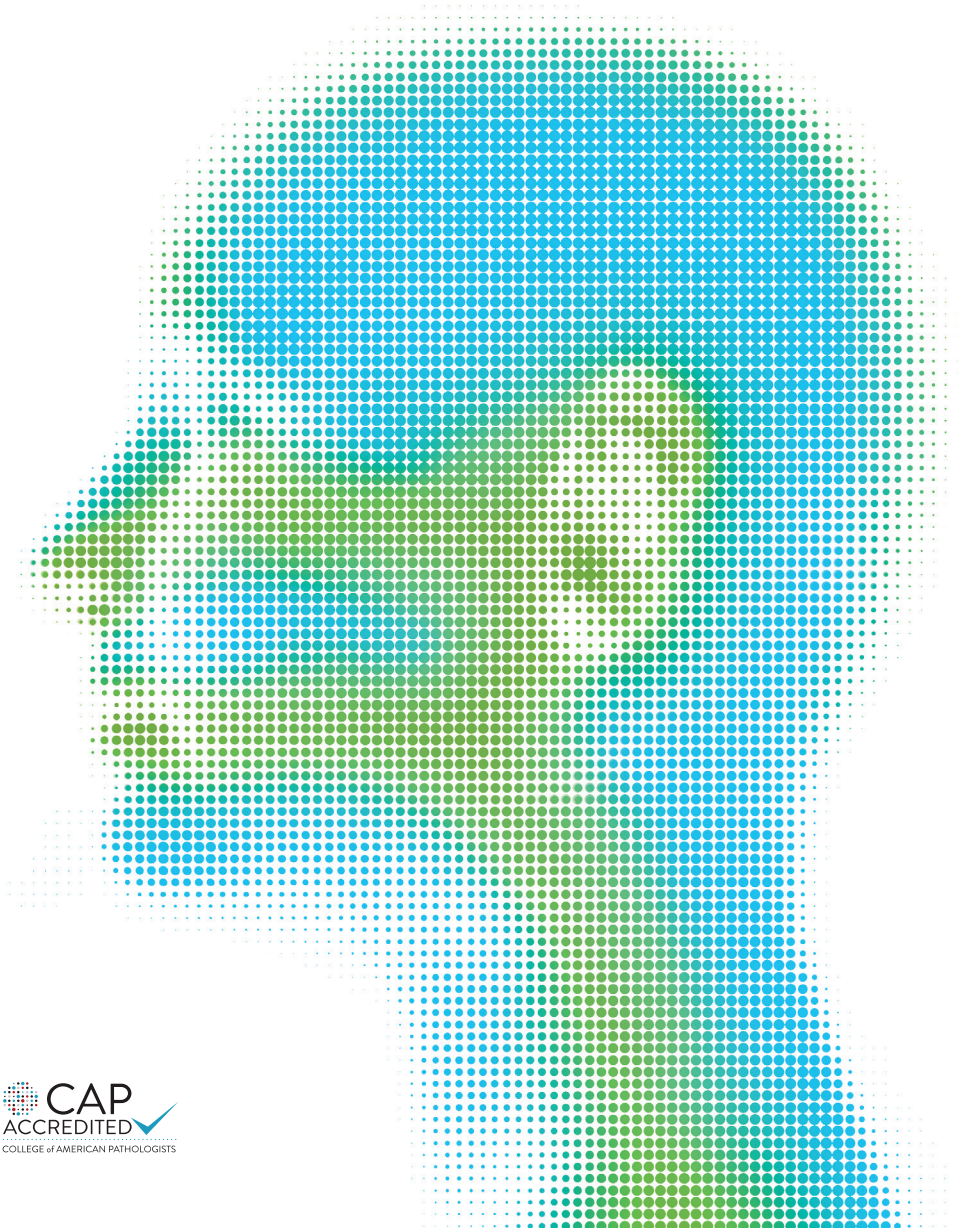
ACTIA
Inherited Genetics

MEDGENOME

ENT Genetics



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COLLEGE of AMERICAN PATHOLOGISTS

What is ENT Genetics?

- *One of the most common birth defects is congenital deafness affecting as many as 3 in every 1,000 babies born*
- *Inherited genetic defects play an important role in congenital hearing loss, contributing to about 60% of deafness occurring in infants*
- *It is also likely that genetics plays an important role in hearing loss in the elderly*
- *Hearing loss and deafness can be due to Inherited genetic defects, medical problems, environmental exposure, trauma and medications*

Prevalence

- *Hearing loss is the most common birth defect and the most prevalent sensorineural disorder.*
- *One of every 500 newborns has bilateral permanent sensorineural hearing loss*
- *The prevalence increases to 3.5 per 1000 during adolescence.*[1]
- *The prevalence of deafness in India is fairly significant and is the second most common cause of disability.*
- *The estimated prevalence of adult-onset deafness was found to be 7.6% and childhood-onset deafness was found to be 2%.*[2]
- *Approximately 63 million people (6.3%) in India suffer from significant auditory loss (WHO, 2009a).*

1. *Morton CC, Nance WE., Newborn hearing screening--a silent revolution. N Engl J Med. 2006 May 18; 354(20):2151-64.*
2. *Denise Yan, Abhiraami Kannan-Sundhari, Subramanian Vishwanath, Jie Qing, Rahul Mittal, Mohan Kameswaran, and Xue Zhong Liu., The Genetic Basis of Nonsyndromic Hearing Loss in Indian and Pakistani Populations. Genet Test Mol Biomarkers. 2015 Sep 1; 19(9): 512–527.*

What are the common Genetic Hearing Disorders ?

Non-syndromic

- *Accounts for approximately 70% of inherited hearing loss*
- *80% of non-syndromic hearing impairment cases have an autosomal recessive mode of inheritance*
- *20% are caused by autosomal-dominant genes*
- *Less than two percent of cases are caused by X-linked and mitochondrial genetic malfunctions*

Syndromic

- *Hearing impairment is associated with other clinical abnormalities*
- *15 to 30% of hereditary hearing impairments are syndromic*
- *Over 400 syndromes are known to include hearing impairment*

These can be further classified as:

- *Syndromes due to cytogenetic or chromosomal anomalies*
- *Syndromes transmitted in classical monogenic or Mendelian inheritance*
- *Syndromes due to multi-factorial influences*
- *Syndromes due to a combination of genetic and environmental factors*

Why do you need to test for Genetic ENT Disorders

- Most of deafness that occur prelingual has a genetic cause and often inherited in autosomal recessive manner. Over 80% of these non-syndromic deafness cases are as a result of mutation in a single gene and are called monogenic.
- Most commonly mutated gene in deafness patients is GJB2 and the carrier rate in the general population for pathological GJB2 mutation is quite high. About 20% of cases and is most often postlingual and less than 1% of cases, the inheritance occurs through the X-chromosome or the mitochondria.[3]
- More than 100 genes are known to cause deafness, either in isolation or as part of a syndrome. About 70% of cases are non-syndromic and are monogenic in nature while the other 30% of cases are syndromic and associated with additional physical findings along with hearing loss in one of the clinical components.[4]
- Very often clinical symptoms are not always the product of the same genetic variation. Hence, confirmation of a clinical diagnosis through genetic testing which allows to specific investigation can optimise treatment regimens and such findings helps in proper genetic counselling leading to immediate medical/family management.
- In many cases, genetic testing will clarify the cause of an individual's deafness, provide information on the likelihood of related health issues, and also establish the risk to other family members and future generations.

When do you need to get tested for Genetic ENT Disorders

- In most of the cases a genetic test can be performed soon after the on-set of clinical symptoms and a clinical diagnosis.
- Genetic test can also be performed even before the on-set of the symptoms to identify if an individual is carrying any pathological mutation.
- Deafness as a disease inherits mostly in recessive fashion and carrier rate is quite high in genes like GJB2. At times genetic testing for a healthy individual is also be advised in view of family history of deafness.

3. Cryns K, Van Camp G, Deafness genes and their diagnostic applications. Audiol Neurootol. 2004 Jan-Feb; 9(1):2-22.
4. Toriello HV, Reardon W, Gorlin RJ. Hereditary Hearing Loss and its Syndromes. Oxford University Press, Inc; Oxford: 2004.

Who needs to get tested?

- Individuals presenting with the most common symptoms of ENT-related disorders such as hearing loss/impairment
- Individuals with a standard preliminary test showing the possibility of hearing loss
- Individuals with a positive family history of an ENT disease
- Individuals without a positive family history but with symptoms resembling a specific disease indication
- Prenatal testing is recommended only in families with affected individuals with prior molecular/genetic testing

Why Recommend Actia for Patients with Genetic ENT Disorders

Actia offers a broad range of pre-designed gene mutation panels which have been developed with in-depth disease understanding of the genetic disorder incorporating the latest research in that particular domain.

New updated technologies, helpful customer service, and clear result interpretation along with counselling sessions with our expert genetic counsellors, make us equipped to provide you the best available support for your patients and families with Genetic ENT Disorders

Actia offers the following ENT gene panel tests

1. Connexin-26 (GJB2) deletion/duplication analysis
2. Connexin-26 (GJB2) gene analysis
3. Deafness gene panel
4. Mondini defect (SLC26A4) gene analysis
5. Waardenburg syndrome gene panel

Test methodology

Next Generation Sequencing (NGS)

Using genomic DNA extracted from blood, the coding regions of all the genes are captured and sequenced simultaneously by NGS technology on an Illumina platform. The sequence data that is generated is aligned and analyzed for sequence variants.

Multiplex Ligation-dependent Probe Amplification (MLPA)

Deletion and duplication analysis of genomic DNA is carried out by MLPA. This method allows for the amplification of multiple targets with only a single primer pair.

Test sample requirements

Blood (3-5ml in EDTA tubes)

or

Extracted DNA samples
(1µg high quality DNA)

Required forms

- Relevant clinical information including all the clinical presentations and symptoms
- Test request form

Turnaround time

The time taken for generating a clinical report will be maximum of

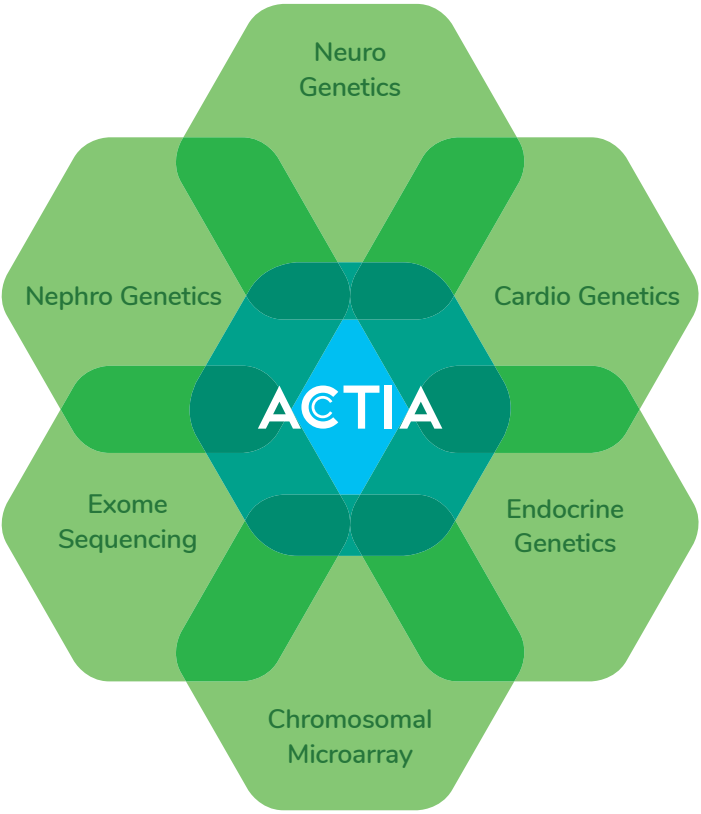
- 6 weeks for NGS
- 3 weeks for MLPA
- 3 weeks for Sanger Sequencing

Free genetic counselling

Actia offers all your patients FREE pre & post test genetic counselling with our expert and certified genetic counsellors.

Best available support for your patients and families via

- Latest technologies
- Helpful customer service
- Clear result interpretation
- Counselling sessions with our Genetic Counsellors



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