ACTIA
Inherited Genetics

MEDGENOME

Neuro Genetics

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

What is Neurogenetics?

Neurogenetic disorders have always been prominent in the practice of clinical genetics and this has increased with the advent of molecular approaches. Next-generation DNA sequencing techniques have made it possible to examine a large number of possible disease genes in a single reaction, which was impossible by previous methods. This has resulted in the rapid identification of genes involved in Mendelian Disorders. Thus, a more precise diagnosis of many neurological disorders is now possible and genetic testing can be considered earlier in the diagnostic procedure.

Prevalence

*Over 30 million people suffer from neurological disorders in India (excluding neuro infections and traumatic injuries.)**

Neurological disorders are often chronic, progressive and debilitating, and their phenotypes are genetically very heterogeneous.

What are the common Genetic Neurological Disorders (GND)?

Epileptic Disorders

- Between 6-8 million people are estimated to have epilepsy in India, with a prevalence of 5.7 per 1000
- It is most prevalent at each end of the age spectrum - the very young and the very old
- It can be syndromic or non-syndromic

Example: Benign Infantile Familial Seizures (BIFS); Lennox-Gastaut Syndrome etc.

**Gourie-Devi M. Neurol India 2014;62(6):588-98*

Neurocutaneous Disorders

- Neurological disorders that have cutaneous manifestations
- These are lifelong conditions that can cause tumors to grow inside the brain, spinal cord, organs, skin, and bones

Example: Tuberous Sclerosis (TS); Neurofibromatosis (NF) etc.

Neuromuscular Disorders

- Disorders that affect the peripheral nervous system
- These disorders affect the ability to perform voluntary movements

Example: Limb Girdle Muscular Dystrophy; Spinal Muscular Atrophy; Duchenne Muscular Dystrophy etc.

Neurodegenerative Disorders

- Involves the progressive loss of structure or function of neurons, including the death of neurons
- These diseases can be serious or life-threatening

Example: Adrenoleukodystrophy; Canavan Disease etc.

Neurometabolic Disorders

- Neurological manifestations are the prominent signs and symptoms of in-born error of metabolism
- Characterized by a lack or dysfunction of an enzyme or vitamin necessary for a specific chemical reaction in the body
- Mostly are presented in newborns and infants

Example: Maple Syrup Urine Disease, Neuronal Ceroid Lipofuscinosis, Krabbe Disease etc.

Movement Disorders

- Characterised by excess or a paucity of movement that is not connected to weakness, paralysis or spasticity of the muscles
- Affects the speed, fluency, quality and ease of movements
- Often associated with poor coordination of hands, speech, and eye movements
- Clinical presentation is complex, often variable, and sometimes even bizarre

Example: Spinocerebellar Ataxia; Tourette's Syndrome; Juvenile Parkinsonism etc.

Mitochondrial Disorders

- A clinically heterogeneous group of genetic disorders arising due to mutations in mitochondrial DNA, or nuclear DNA coding for mitochondrial components
- A group of disorders that are difficult to diagnose, because it affects each individual differently
- Symptoms can include seizures, strokes, severe developmental delays, inability to walk, talk, see, and digest food, combined with a host of other complications

Example: Mitochondrial Myopathy; Myoclonic Epilepsy with Ragged Red Fibers (MERRF) etc.

When do you need to get tested for GND?

The four means to guide clinical classification in GNDs are:

1. The earliest clinical signs referring to neuroanatomical changes or pathology specific to that disease
2. The age of onset for the clinical signs and symptoms
3. The mode of inheritance
4. Other extra-neural signs and symptoms, such as the presence of specific signs involving the eyes, skin, connective tissues, or visceral organs, etc.

Who needs to get tested?

- Individuals presenting with symptoms of neurological disease
- Individuals with family history of neurological disease
- Individuals without a family history or sporadic presentation with symptoms associated with a specific neurological disease

Why recommend Actia for patients with GND?

Actia offers a broad range of pre-designed gene mutation panels which have been developed with an in-depth understanding of genetic disorders 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 GND.

Advantages of Actia

- Expertise in genetic testing with large in-house database
- High coverage with more than 22000 genes
- Dedicated in-house lab
- High throughput NGS machines
- Screening on world-class Illumina platform
- Best-in-class methods - NGS (X10, HiSeq, MiSeq) Sanger

GND panels offered by Actia

- Muscular Dystrophy & Congenital Myopathy gene panel
- Comprehensive Neurology Panel
- Duchenne Muscular Dystrophy (DMD) deletion/duplication analysis
- Spinocerebellar Ataxia repeat expansion analysis:
  SCA1, SCA2, SCA3, SCA6, SCA7, SCA10, SCA12
- Dravet Syndrome (SCN1A) deletion/duplication analysis
- Tay-Sachs Disease (HEXA) deletion/duplication analysis
- NeuroMit (whole mitochondrial genome sequencing & neurology gene panel)
- ExomeMit (whole mitochondrial genome sequencing & neurology gene panel)
- Dystonia gene panel
- Ataxia-Telangiectasia (ATM) gene panel
- NOTCH3 (CADASIL) gene panel

What is the test methodology?

1. 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.

2. 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.

3. Fragment analysis PCR for repeat expansion analysis

These rely on detection of changes in the length of a specific DNA sequence to indicate the presence of repeat expansions.

Test sample requirements

Blood (3 ml in EDTA tubes)

Extracted DNA samples (1µg high quality DNA)

Required forms

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

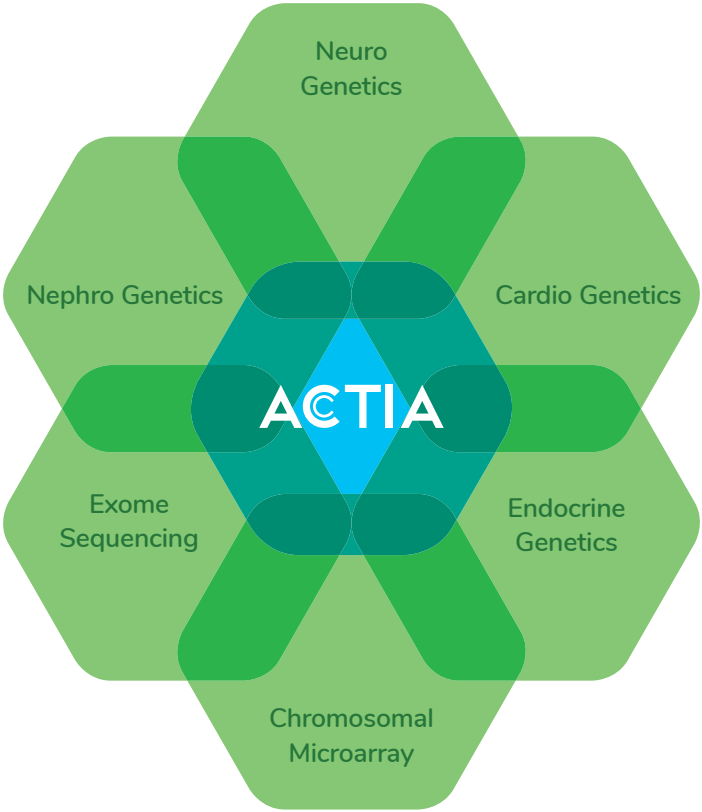
Turn Around Time (TAT)

- 21 working days for NGS
- 14 working days for MLPA
- 21 working days for Sanger Sequencing
- 7-14 working days for Fragment Analysis
- 8-15 working days for Karyotyping

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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