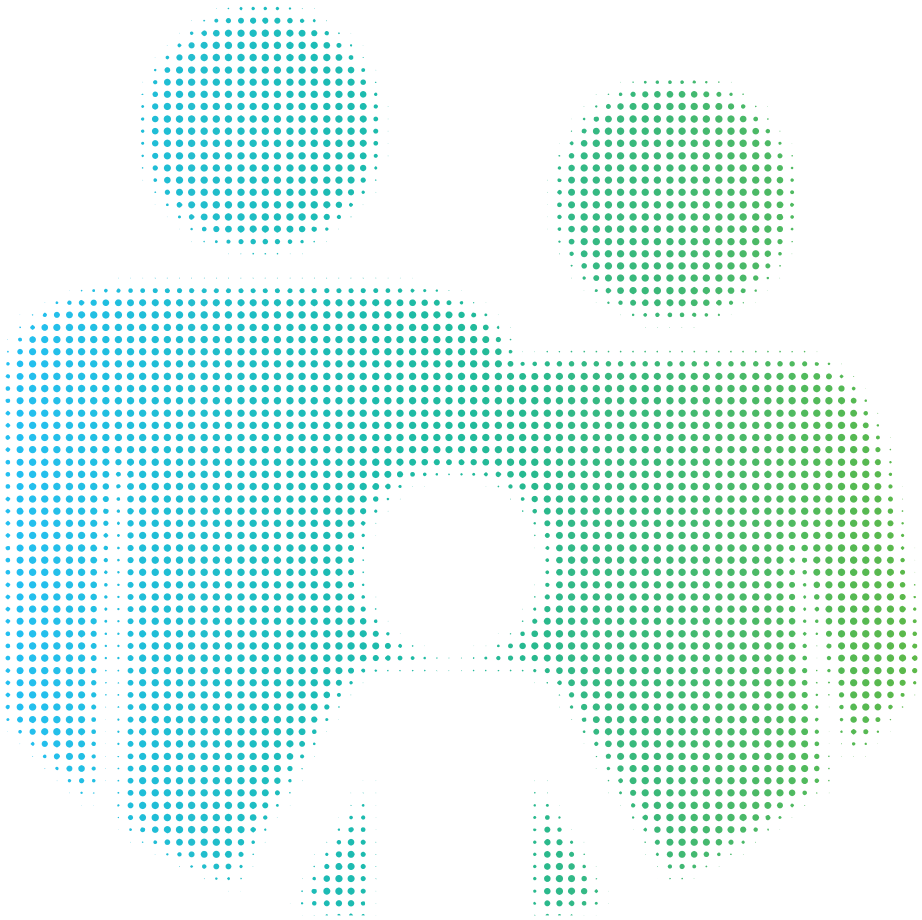
ACTIA
Inherited Genetics

MEDGENOME

Trio Exome Analysis



CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

Actia

Inherited Genetics

The understanding of pathology at a molecular level is critical for identification of many diseases and their subtypes. Precision in diagnosis, including the identification of disease subtypes directly influences treatment and patient outcomes.

Actia from MedGenome provides an end-to-end integrated solution to clinical genomics in India and is highly focused on the Indian population. Actia has been delivering actionable genetic insights for inherited genetic conditions enabling happier outcomes.

Background

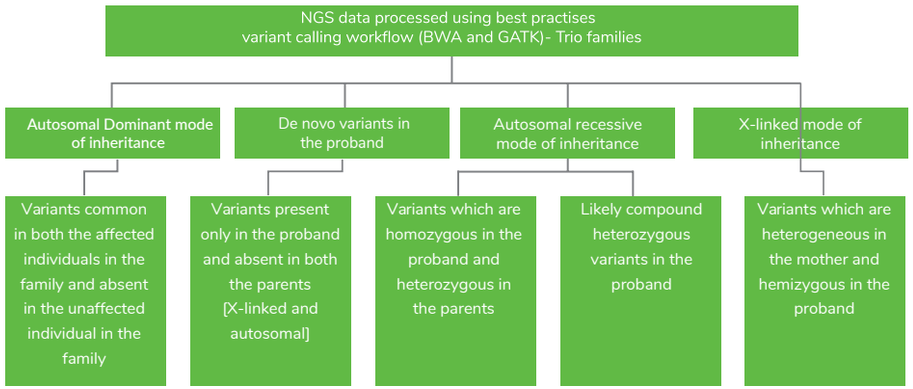
Exome sequencing is rapidly becoming a common molecular diagnostic test for individuals with rare genetic disorders. It is important to diagnose a disease at the earliest to offer a better treatment / management to the patient. Despite the recognized clinical value of exome-based diagnostics, methods for comprehensive genomic interpretation sometimes remain inconclusive. The main challenge in Next Generation Sequencing (NGS) studies, is in handling the large genetic data, is to distinguish false positive variants from true pathogenic variants. Trio study design (father, mother, and child) can identify inherited/non-inherited or de novo mutations in a child and aids in classification of putative causal variants.

What is a Trio Exome Analysis?

NGS based Trio Exome Analysis family pedigrees offers a powerful approach for the identification of causal mutations for inherited diseases. Trio Exome Analysis can be used to identify variants inherited from the parents causing recessive disease or dominant disease. Additionally, de novo variants that occur in the offspring but are not present in either of the parents can also be detected.

Trio Exome Analysis using whole exome/clinical exome sequencing facilitates analyses of thousands of genes simultaneously to identify genetic alterations like insertions/deletions (indels), single nucleotide variants (SNVs) and copy number variations (CNVs). This familial analysis based approach also helps in excluding variants, which do not conform to Mendelian transmission, thereby reducing false positive calls and narrowing down the potential candidate variants.

The overall diagnostic yield of Trio Exome Analysis exome sequencing has a 5-10% increase compared to analyzing proband only.



What are the situations where Trio Exome test can be used?

The test is used only where the individual's medical examination, laboratory findings and family history suggest underlying genetic etiology. This test can be done for one or more of the following reasons:

- *Patient with undiagnosed genetic disease (extensive evaluation and multiple genetic tests, without identifying the etiology)*
- *To facilitate medical intervention, treatment etc*
- *To guide reproductive planning and assessment of recurrence risk Screening of genetically heterogeneous diseases (where the same disease or condition can be caused by several genes)*
- *Prognosis (based on family history)*
- *Where there is no other alternate technique to confirm the diagnosis and to end the diagnostic odyssey*
- *Trio analysis may aid in better management of the patients and prenatal diagnosis where possible*
- *Further, it can be implemented where definitive clinical diagnosis is not possible due to clinical heterogeneity, especially those with rare congenital disorders where identifying the causal variant by traditional methods is not feasible.*

What are the advantage that MedGenome's Trio Exome test?

Mendelian inconsistency QC to assess the relatedness based on variants obtained

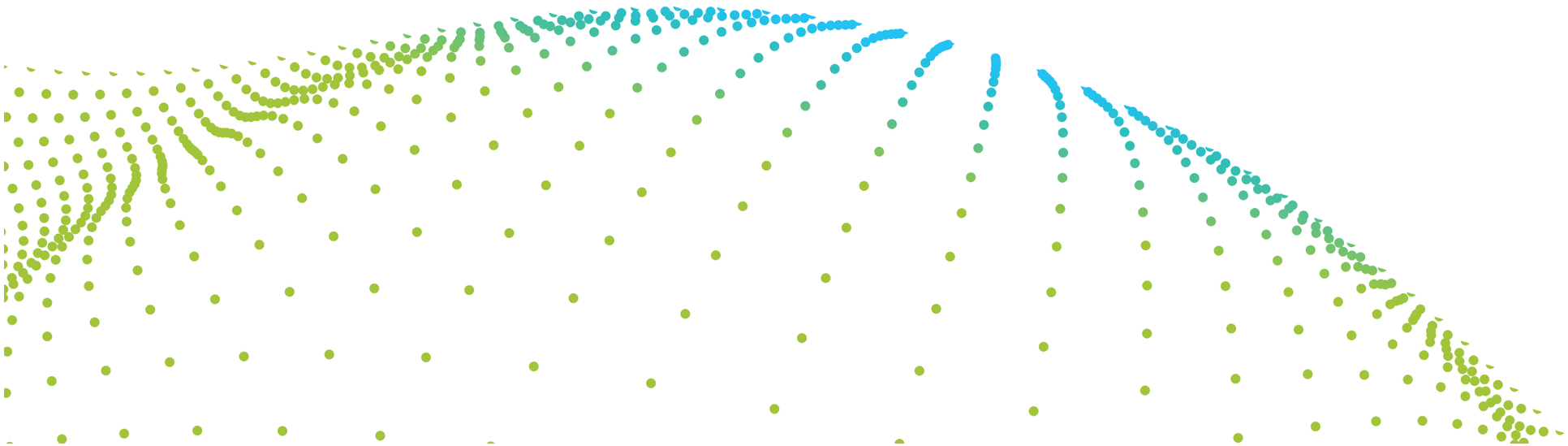
Combined variant calling increases the accuracy of variant calling and ability to make variant calls in low coverage regions

Better diagnostic yield compared to analyzing single proband sample

Simultaneous analysis for all modes of inheritance i.e. autosomal recessive, autosomal dominant and de novo variants

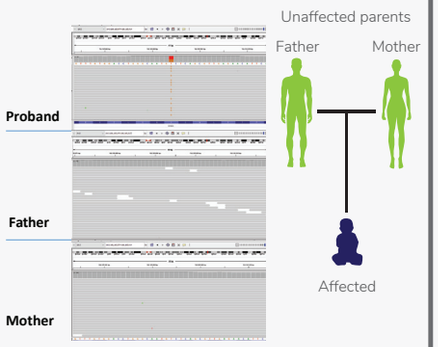
Prioritization of variants based on patient phenotype

Ability to ascertain significance of clinically relevant variants especially compound heterozygous and de novo variants



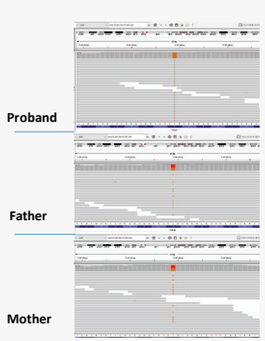
Examples:

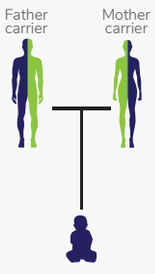
Figure 2



Denovo Mutation in proband

Figure 3





The homozygous variant observed in the proband was detected in the heterozygous state in both the parents.

Note: Triplet repeat expansions, translocations cannot be detected by this methodology. Genetic changes present outside of the targeted region will not be detected

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.

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

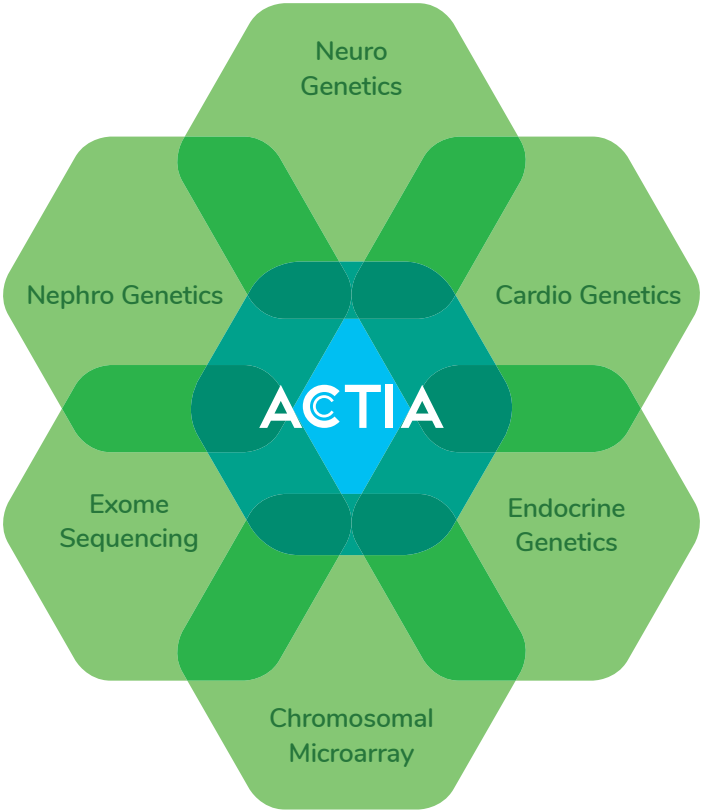
- 3 weeks for NGS

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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