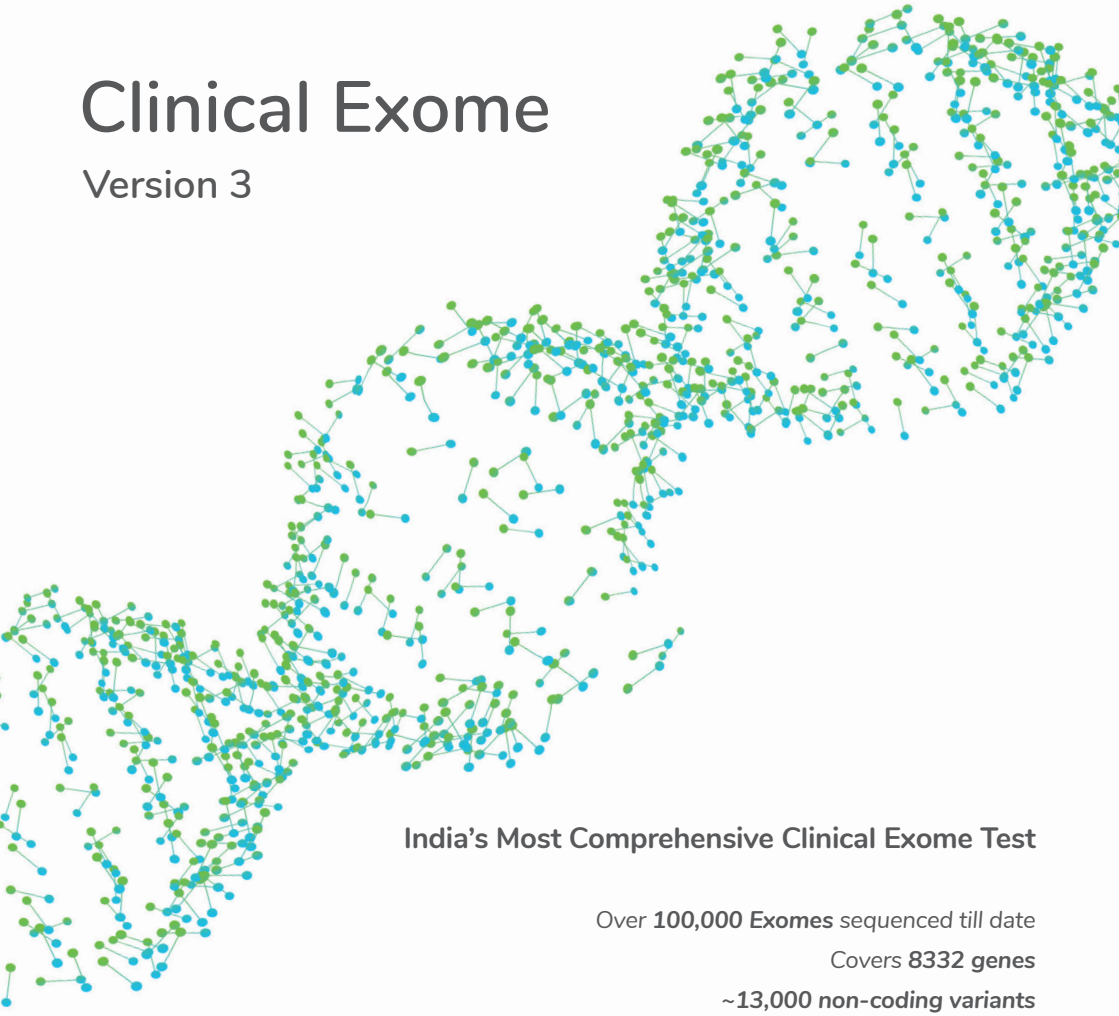
ACTIA
Inherited Genetics

MEDGENOME

Clinical Exome

Version 3



India's Most Comprehensive Clinical Exome Test

*Over **100,000 Exomes** sequenced till date*

*Covers **8332 genes***

~13,000 non-coding variants

***CNV** detection*

Reports Reviewed By Clinical Geneticist

Free Post Test Genetic Counselling

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

Actia

Inherited Genetics

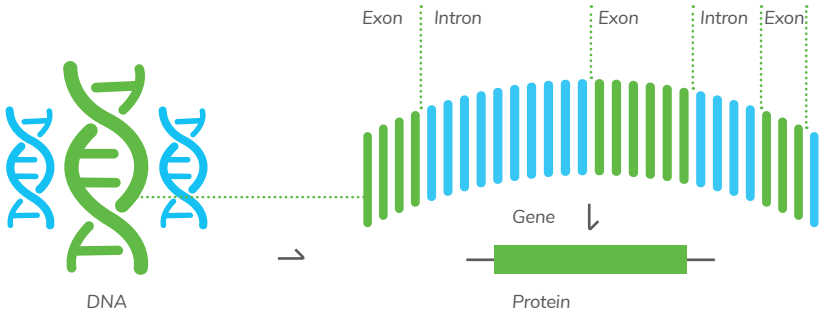
The understanding of pathology at a molecular level is critical for identification of many diseases and their subtypes. Precision in diagnosis, including the identification of disease subtypes directly influences treatment and patient outcomes.

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.

What is Clinical Exome?

Clinical Exome is a DNA test that can identify the molecular basis of a genetic disorder in individuals with a genetically heterogeneous disease and/or an atypical presentation of a genetic disorder. This comprehensive clinical exome covers ~8332 genes including the most relevant disease-associated genes from OMIM, HGMD, ClinVar and SwissVar.

Exome's are the protein coding region of the genome and comprise 1-2% of the genome



When to consider a Clinical Exome test?

Clinical/Diagnostic Evaluation
Detailed clinical and family history
Evaluation of non genetic causes
Additional test if required for differential diagnosis

Genetic Diagnosis Known
Single gene/multigenic panel/ clinical exome or chromosomal microarray based on Diagnosis

Example:
- DMD – MLPA followed by point mutation screening
- Glycogen storage disease Multigenic panel/clinical exome

Genetic Diagnosis Unknown
Clinical exome/Whole exome/microarray based on the clinical suspicion

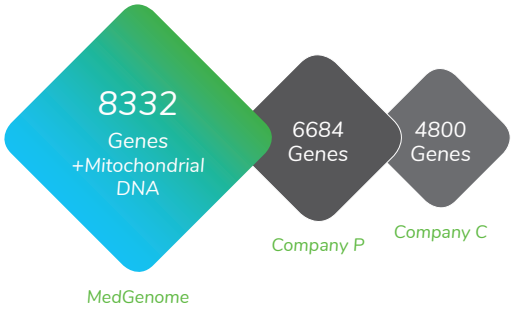
Example:
- EIEE (Early Infantile Epileptic Encephalopathy- Multigenic panel/clinical exome preferably Trio as several de novo mutations are reported
- Syndromic ID- Microarray followed by clinical exome/Whole exome

Indications for prescribing clinical exome testing

- Clinical finding or family history is suggestive of underlying genetic aetiology
- Screening of genetically heterogeneous diseases
- Patient with undiagnosed genetic disease (diagnostic odyssey)
- To facilitate medical intervention and/or treatment
- To confirm the suspected genetic diagnosis
- To guide reproductive planning and assessment of recurrence risk
- For prognosis (based on family history)

MedGenome Clinical Exome Version 3

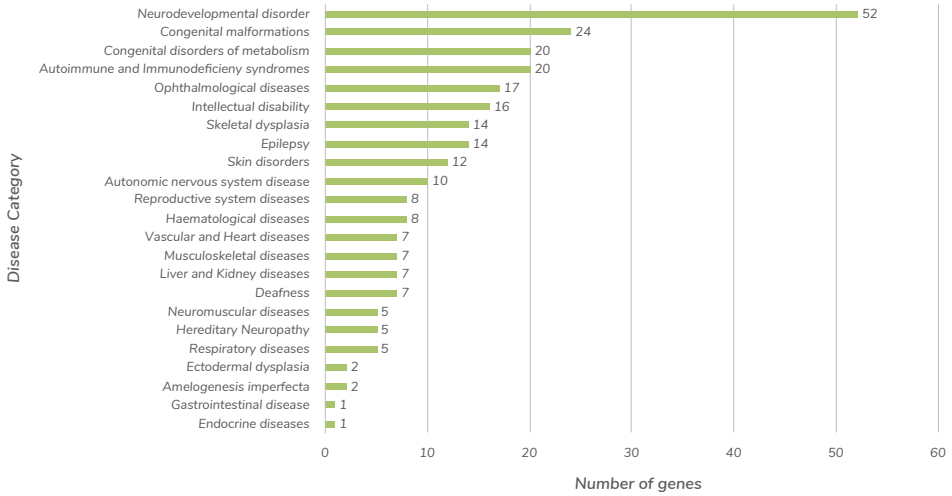
MedGenome's Clinical Exome is already India's Most Comprehensive Clinical Exome Test. Our enhanced Clinical Exome Version 3 (MedGenome CE V3) offers better coverage, superior sensitivity and specificity.



Do the additional genes make a difference?

Inherited developmental diseases are genetically heterogeneous and are individually rare. Thus, additional disease associated genes increase the potential for better diagnosis.

- Approximately 2000 additional genes are present in MedGenome CE V3
- More than 1000 genes unique to MedGenome CE V3 are associated with disease phenotypes in OMIM, HGMD or Clinvar
- Including ~260 genes with known molecular basis in OMIM with ≥ 98% coverage at 20x depth of coverage



Disease phenotype details of 264 OMIM genes which are unique in MedGenome CEV3

Why MedGenome CE V3 is superior

Coverage: *Clinical phenotypes associated with 3977 OMIM genes, 5849 HGMD genes and 4284 ClinVar genes*

Enhanced coverage of disease genes: *Additional coverage of genes wherein pathogenic mutations have been reported in HGMD and ClinVar*

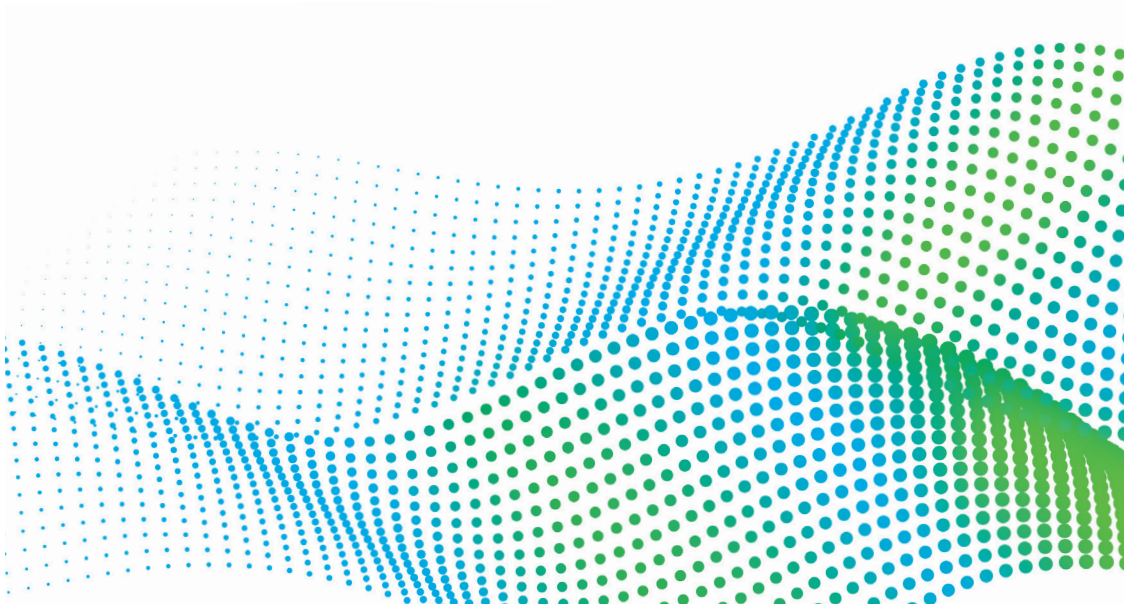
Mutations in Non-coding regions: *Coverage of disease causing pathogenic mutations ~13,000 from HGMD in non-coding and promoter regions of the genes*

Mitochondrial: *Coverage of complete mitochondrial genome (both coding and non-coding genes)*

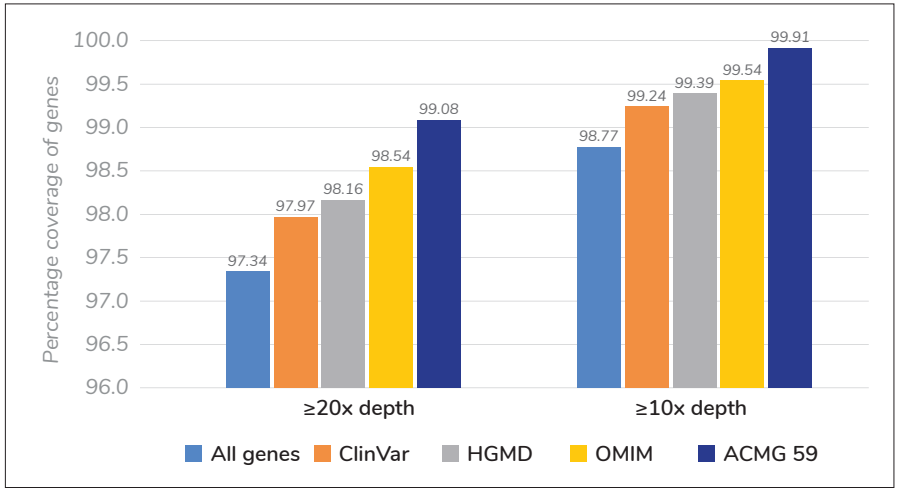
Enriched targets: *Additional probes for improved CNV detection*

Proficiency: *Requisite quality control steps throughout the workflow from the laboratory sample processing which ensures the interpretation ensures consistency, validity and accuracy of results (CAP predictive testing 99.8% accuracy)*

CNV: *CNV detection increases the diagnostic yield without any additional test*



Coverage



Representation of average coverage of genes (n=100) in MedGenome CEV3 based on disease associated gene source HGMD, CLinVar, OMIM, ACMG 59

Clinical Exome Test including CNV

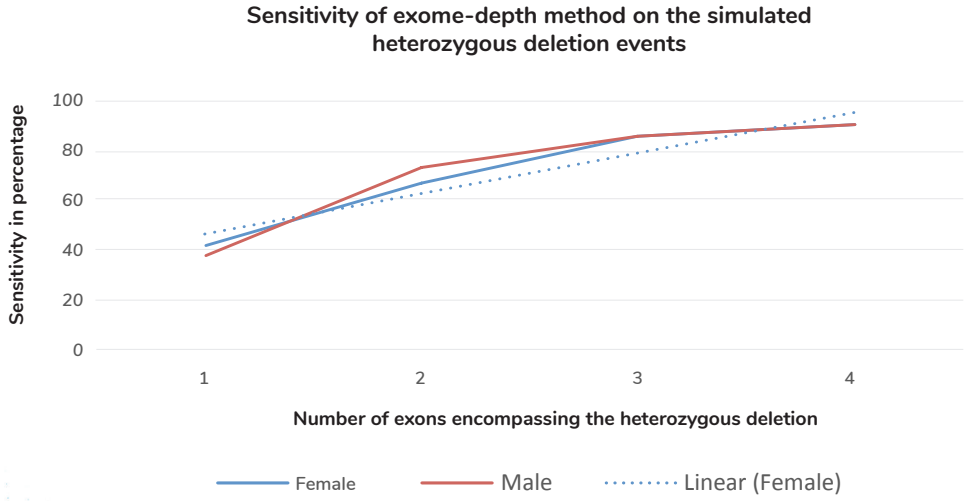
MedGenome CE V3 proprietary exome depth method enables CNV detection on NGS data for:

- Single and multi-exon aberrations
- Deletions and duplications
- Both reported and novel events

Sensitivity:

- Heterozygous deletion/duplication for >200bp: ~75%
- Homozygous deletion: >90%
- Detection of CNVs as small as 300 bp*

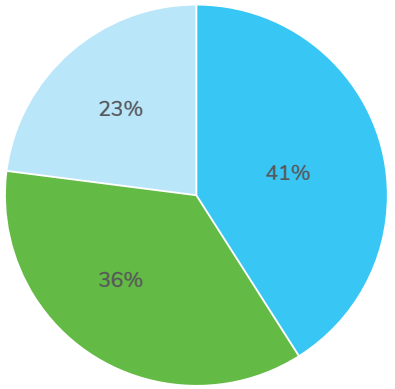
** Sensitivity of CNV detection varies with length of the region and sequencing depth*



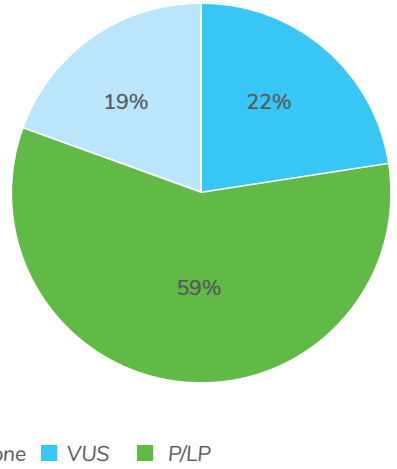
Sensitivity based on performance evaluation of Exome-Depth method based on simulation of ~10,700 events covering ~78 samples.

Sensitivity

The detection of the significant variants varies based on the clinical diagnosis and underlying genetic aetiology. The diagnostic yield of Medgenome CE V3 is comparable to those reported in literature 36% The diagnostic yield of familial samples with strong family history are higher compared to proband only analysis*



Diagnostic yield based on 14637 samples



Diagnostic yield in trio/familial (n=250)

** Percentage of molecular diagnosis varies based on the underlying phenotype*

Why recommend Clinical Exome?

- Comprehensive and efficient method of analysing DNA to identify the genetic cause of diseases or disabilities
- Can be leveraged for several autosomal dominant, recessive and X-linked disorders
- Cost-effective especially for broad spectrum of genetic disorders with overlapping phenotype
- Reporting of clinically relevant disease-causing gene mutations based on OMIM \ and / or HGMD
- Detection of both novel and reported mutations
- Better diagnostic yield through:
  - High sequencing accuracy
  - High quality variant calling
  - Clarity in interpretation

Clinically relevant for a range of disorders across:

- Rare Diseases
- Inherited Cancers
- Neurology
- Cardiology
- Endocrinology
- Nephrology
- ENT

and others

MedGenome CE V3 test details

	Medgenome Clinical Exome V3
Panel size	~29 Mb
Number of genes	8332 (includes 10bp flanking sequences to CDS)
Panel coverage	80-100x
Coverage at >20x	≥ 95%
Annotation source	ClinVar, HGMD, Ensembl, OMIM, RefSeq and literature

Clinical exome	Single	Trio	Carrier testing
Sample	Proband	Parents and proband	Couple
Sample requirements	 Whole blood or extracted DNA of good quality	 Whole blood or extracted DNA of good quality	 Whole blood or extracted DNA of good quality
TAT	28 working days	28 working days	28 working days
Segregation Studies	On request in the parents by Sanger sequencing	This is done as part of the analysis	On request in the affected/unaffected family members by Sanger sequencing

Reporting of results

The clinical and sequenced data is systematically evaluated and reviewed by experienced analyst and clinical geneticist. The results are reported based on the recommendations of American College of Medical Genetics (2015).

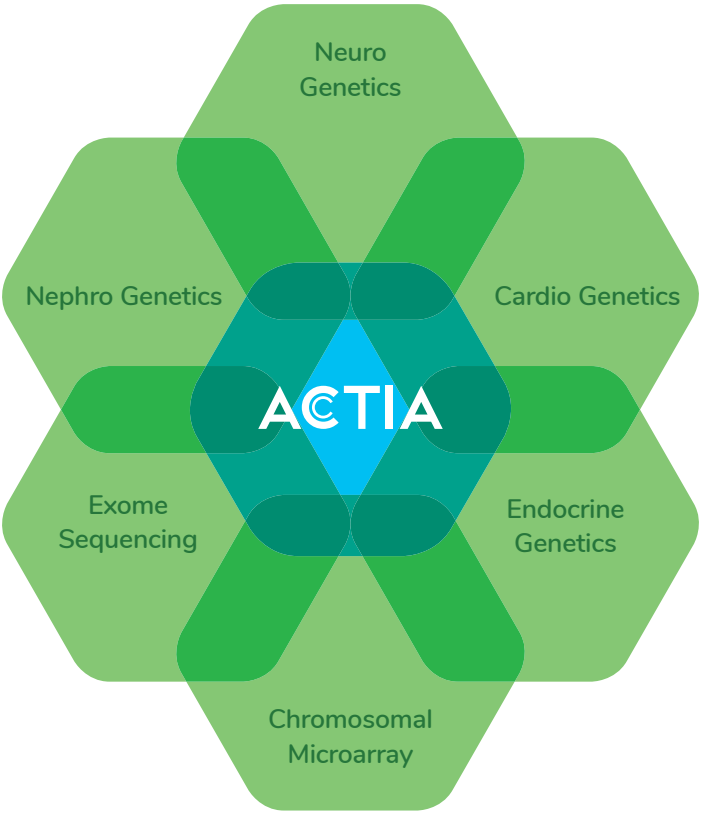
We ensure the best available support for your patients and families via:

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

Free genetic counselling

MedGenome offers all your patients FREE pre & post-test genetic counselling with our expert and certified genetic counsellors. This genetic counselling will enable patients to:

- Make an informed decision
- Understand risk if any
- Discuss the implications of the results
- Connect them to resources or support groups



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