mfine /diagnostics

Choose Ultimate Coverage, Simplified Workflow, Superior Content, Deeper Analysis

Supreme Accuracy

and Cost-effectiveness for making **Clinical Decisions**

When

GENETIC

Testing Matters...

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About MFine

Everything that you need to know about MFine Limited

The Footprints

32+ Regional Laboratories

130+ Cities

Now Serving

2K+ Hospitals

10K+ Doctors

#1

7 LAKH+ PRENATAL SCREENING OF ANEUPLOIDIES
5.6 LAKH+ NEWBORN SCREENING TESTS
TO INTRODUCE ULTRA-RAPID EXOMES WITH FASTEST TAT IN INDIA
50K+ NIPT

Real Time Sample Tracker

Dedicated NGS portal offers update on the sample processing status on real time

Experienced Team

Highly experienced team of Clinical geneticist, Genetic counselor, Genome analysts, and Scientists

Lab Cities

Chennai (National Reference Lab), Pune, Mumbai, Hyderabad, Delhi NCR, Bangalore & Kolkata

NABL & CAP Accredited

~100% compliance in CAP proficiency testing (NGSE-A, NGS-A)

Why Choose Us

Market Leader in Reproductive Markers & Genomics

State of the Art National Reference Laboratory at Chennai

Wide Test Menu

A test menu of 3200+ high end tests for actionable results available under one roof

High-Quality Analysis

for precise clinical interpretation using advanced bioinformatics and AI powered tools

Comprehensive NGS solutions

Expert designed, scientifically curated panels for increased coverage of disease-associated genes to maximize diagnostic yield

Free Genetic Counseling

Pre and post test counseling by Board Certified Genetic Counselors

Report Interpretation by Clinical Geneticists and Scientists

Strong Logistics Across 130 Cities

MFine's

Next Generation Sequencing Solutions

Use Of Best-in-class Tools To Deliver Robust Content And Performance

NGS Solutions

- **Whole Genome** Sequencing
- **Whole Exome** Sequencing
- **Amplicon** Sequencing
- **300+ gene** Panels
- **Clinical Exome** Sequencing
- **RNA** Sequencing
- **Mitochondrial Genome** Sequencing

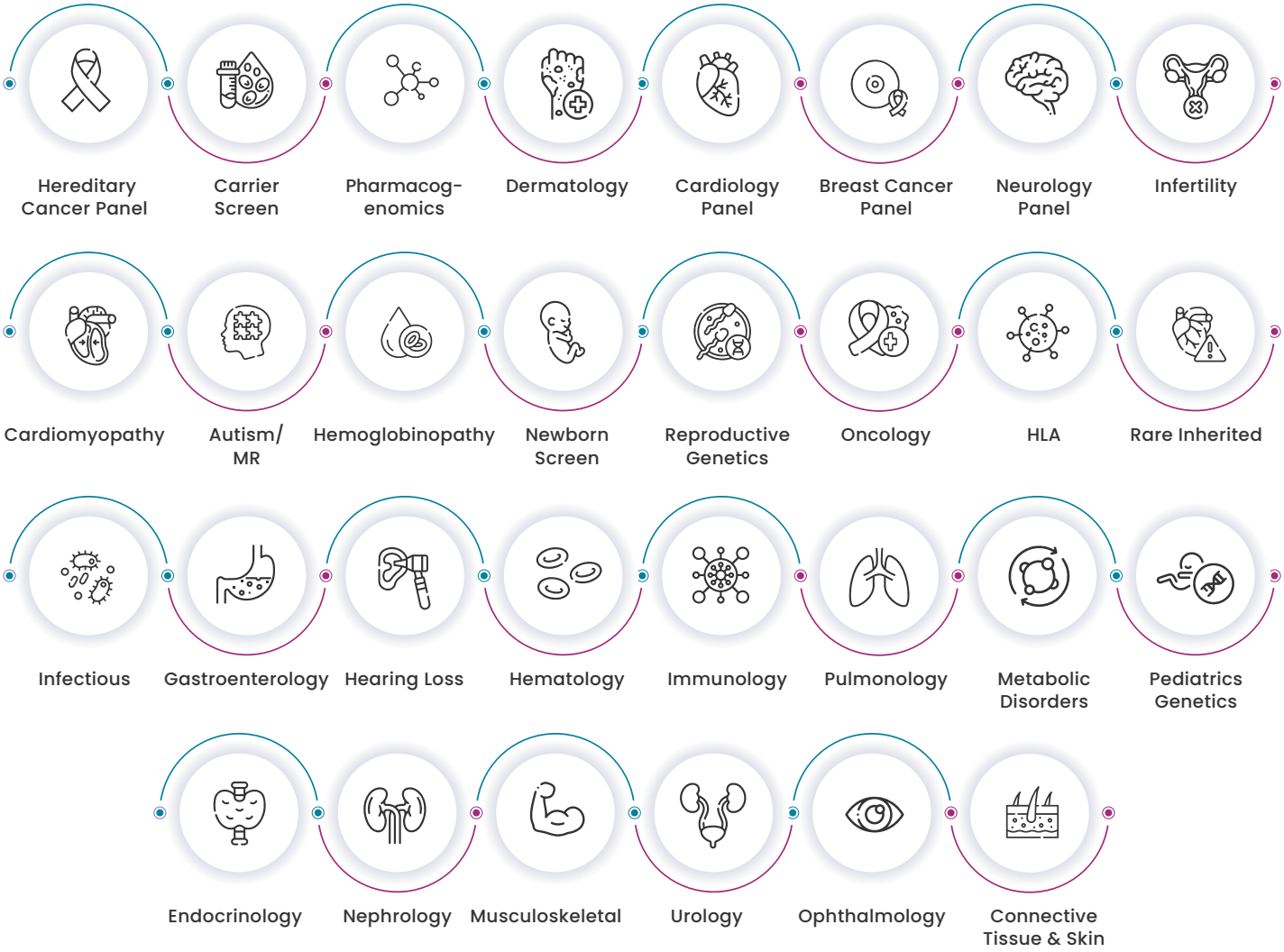
Other Services

- **Sanger** Sequencing
- **Triple repeat disorders testing** (Including Fragile X, SCA, Huntington)
- **MLPA** & Digital MLPA
- **Chromosomal** Microarray

NGS Panels

A Targeted Phenotype-Directed Approach for Testing Genetic Disorders

- Coverage of all relevant disease-causing genes
- Coverage of non-coding and coding pathogenic variants
- Includes genes necessary for differential diagnosis of syndromes with overlapping phenotype(s)



Overview

Genomic testing is a powerful way of diagnosing genetic disorders by identifying the responsible changes (also called variants) in the DNA. Genomic testing has become an efficient tool for clinicians to confirm patients' diagnosis often after their patients have experienced years of uncertainty.

Next Generation Sequencing (NGS) based on massively parallel sequencing is the most powerful platform for Genomic Testing that enables sequencing of thousands to millions of DNA molecules simultaneously offering a high throughput and coverage while reducing the sequencing cost per base.

Our NGS solutions offer unmatched breadth of high-quality sequencing combined with unmatched depth of data analysis thus enabling more accurate variant interpretation across diverse therapeutic fields.

Mfine's Exome and Genome Sequencing tests provide a comprehensive evaluation of thousands of genes by simultaneously looking for changes that are responsible for causing genetic disorders and delivering medically actionable results.

How is Genetic Testing helpful?

Empowers

- Clinicians in stating a diagnosis
- For informed reproductive decisions
- Families in evaluating the chance of recurrence.
- By enabling testing of other family members for an early intervention
- By providing a diagnosis that may help secure funding for services such as medical therapies

Guides

- About the etiology of patient's medical condition
- For short and long term medical management and care
- About future treatment options, or participation in clinical trials

Reduces

- Additional expense of unnecessary testing
- Time to diagnosis and healthcare cost
- The delays in diagnosis of around 4.8 years for rare diseases [3]

Guidelines supporting Exome Sequencing and Genome Sequencing for Clinical Evaluation

Recent evidence-based, cost effective clinical guidelines established by the American College of Medical Genetics and Genomics (ACMG) strongly recommend Exome Sequencing and Genome Sequencing as a first or second-line test for paediatric patients with:

Congenital Anomalies | **Intellectual Disability** | **Developmental Delay**

Genetic testing is particularly useful for patients with below Clinical Indications:

- Rapidly deteriorating clinical status
- Genetically heterogeneous disease, where pathogenic findings could be present in many different genes
- Exhausted currently testing options
- Unclear or atypical presentation of a genetic disorder
- Condition suggestive of a genetic disorder with a long list of differential diagnosis
- A genetic disorder with an atypical presentation
- Cardiomyopathy, epilepsy, immunodeficiencies, complex dysmorphic features, undiagnosed metabolic disorder etc

Indispensable Role of Clinicians

These are phenotype-driven test of a very large number of genes, therefore, reported results are focused on pathogenic and likely pathogenic variants in genes related to the clinical information provided.

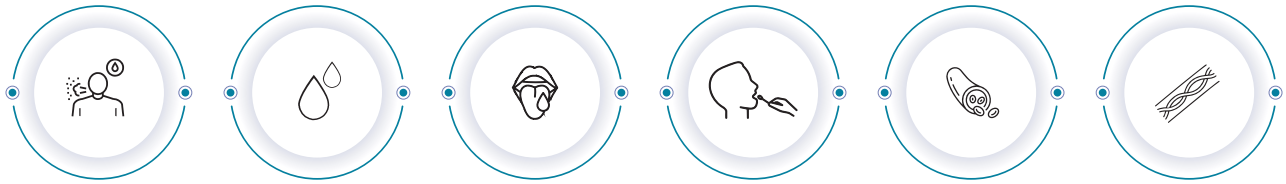
The quality of Clinical Data sent by clinicians is the keystone for accurate curation, annotation and interpretation of variants during the analysis.

The information required during the sample collection process is:

- Complete Patient History
- Three-generation medical pedigree
- Results of genomic microarray, magnetic resonance imaging (MRI), and other relevant tests
- Summary notes from genetic and specialist consultations
- Duly filled Test requisition form and informed consent

Your Trusted Partner for Genome and Exome Sequencing

GENETIC TESTING IS AVAILABLE FOR A WIDER RANGE OF SAMPLE TYPES

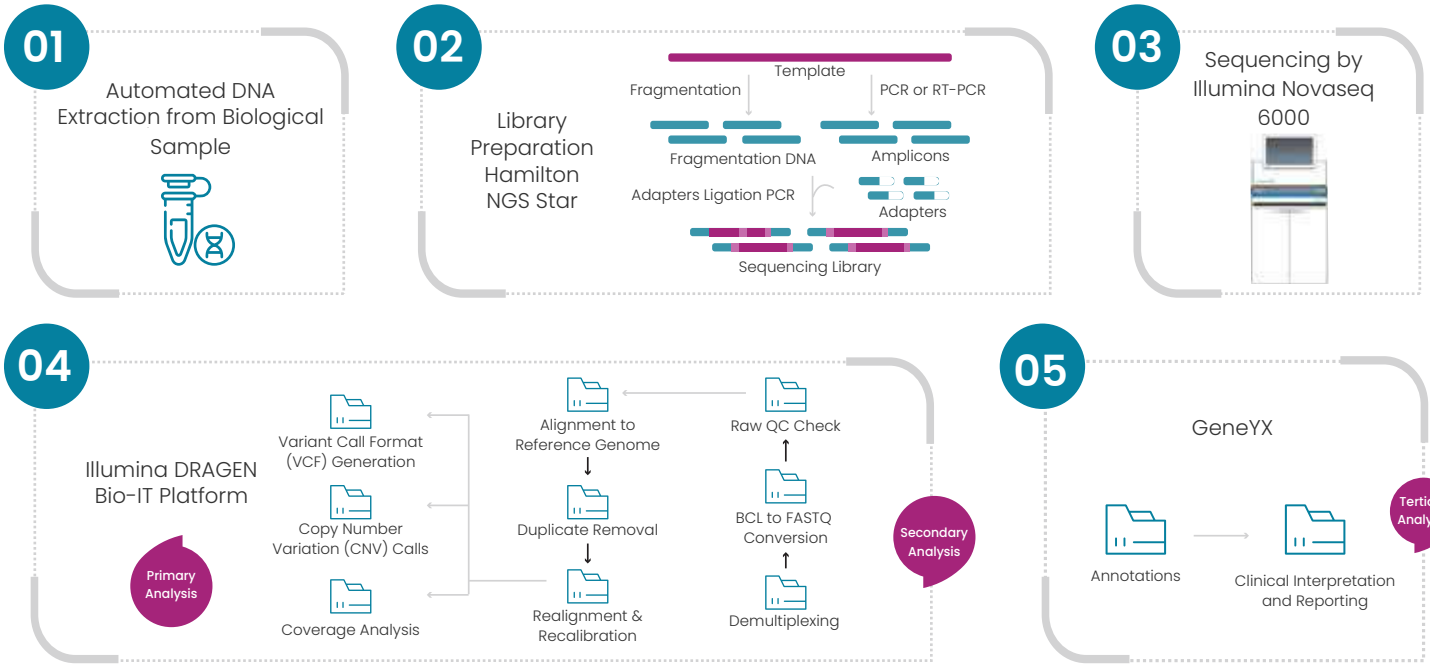


Blood/DNA | Dried Blood Spot | Saliva | Buccal Swab | AF/CVS/Tissue | Cord Blood

(Note: Maternal Cell Contamination check with Maternal Blood Sample is mandatory and offered complimentary for all prenatal samples)

Next Generation Sequencing (NGS) Process Flow

- Next generation Sequencing allows an unprecedented view into the patient's genetic makeup and has a superior diagnostic yield. Exposing complex disease patients to genome or exome testing means getting them to a diagnosis faster and saving years of uncertainty.
- Our workflow is an amalgamation of best-in-class tools integrated with machine learning and artificial intelligence, allowing us to combine clinical and genomic data to deliver actionable results.
- We make use of standard **Quality Matrices** at every step and move to the next step only when the **Quality Scores** are satisfactory.



NovaSeq 6000 provides high scalability and flexibility to accommodate diverse applications with deeper and broader coverage for a comprehensive view of the genome at a rapid turnaround time.

Hamilton NGS Star is pioneer in high-precision automated library preparation that increases workflow efficiencies, sample throughput, and quality in results.

DRAGEN is used for accurate, ultra-rapid secondary analysis of sequencing data. It offers increased genome coverage with Illumina Machine Learning and DRAGEN Graph genome mapping for an unprecedented accuracy across all read technologies for difficult-to-map regions, all benchmark regions and Major Histocompatibility Complex (MHC) regions. This enables the detection of challenging and medically relevant variants.

Geneyx, is a bioinformatics system for analyzing and interpreting somatic and germline NGS data with best-of-breed AI-based data analysis and phenotype prioritization. It integrates a machine learning tool PhenoTyper to optimize the scoring and prioritizing of variants. This enables the identification of novel biomedical insights that can significantly improve patient diagnosis and provide quick turn-around times. Automated ACMG/AMP guidelines for variant calling. Offers Cloud Data storage protection and privacy and Compliance with ACMG and ClinGen.

Genomenon uses artificial intelligence to connect the genetic mutations buried in 30 million medical research publications with patient data and 4.1 million genomic variants obtained from genetic sequencing.

Our TAT: **Ultra Rapid** (10 days), **Rapid** (15 days), **Regular** (21 days)

Standards for Variant Interpretation and Reporting:

We offer a phenotype-driven, customized analysis of variants using up-to-date clinical guidelines established by the American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP).

Variants are classified using:

- Molecular attributes Rare Protein altering Known Disease Gene
- Literature Evidence (HGMD, ClinVar, Mastermind etc)
- Public and internal population frequency databases
- Clinical records
- Comparison to parental data (when TRIO sample is available)

CNV analysis - Role in increasing diagnostic yield

Copy number variations (CNVs) represent a class of genomic variation in which large regions of the genome (>1 Kb) are duplicated or deleted.

- About 15% of affected individuals referred for clinical genetic testing carry a disease associated CNV[3]
- NGS data is a powerful tool to detect CNVs
- Our analysis automatically includes copy number variation (CNV) analysis – without extra fees. This approach reduces the associated costs, resources, and analysis time
- We make use of sophisticated CNV algorithms and analysis software like Geneyx and DRAGEN Bio-IT Platform to detect all types of CNVs, including multi-exonic, multi-genic, chromosomal aneuploidies, along with precise detection of breakpoints
- **Our customized enrichment greatly increases the diagnostic yield**

Detection of MLPA confirmed CNVs for one or more exons

GENE	CNV COORDINATE	CNV SIZE	EXONS INCLUDED	CNV TYPE
CYP21A2	Exon 1-7	1.78Mb	7	Loss
DMD	Exon 8-9	1424bp	2	Loss
BRCA1	Exon 22-23	1532bp	2	Loss
ATM	Exon 62 to 63	683bp	2	Loss

Detection of MDD MLPA and CMA confirmed CNVs for large multigene events

CNV COORDINATE	CNV SIZE (MB)	CNV TYPE
Chr5:92347-16935917	16.8	Loss
Chr2:236578744-242760597 (2q37.2-q37.3)	6.2	Loss
Chr16:105777-2571124 (16p13.3)	2.4	Gain
Chr8:30585047-145743168 (8p12.32-p24.3)	115.1	Gain
Chr20:49565166-62292849 (20q13.3-q13.33)	12.7	Gain

Genetic Testing Results:

POSITIVE

A pathogenic or likely pathogenic variant has been identified related to the patient's phenotype. Cascade testing of other family members may be required.

VARIANT OF UNCERTAIN SIGNIFICANCE

A change in the patient's DNA is present in a gene that has not been well-described. However, preliminary evidence suggests that this gene may be associated with the patient's clinical features. Additional testing for the patient and/or other family members can help in further segregation.

NEGATIVE

No clinically significant changes were found in the patient's DNA that explain the phenotype. It is possible there is a genetic variant not found under the scope of the test and further testing may help.

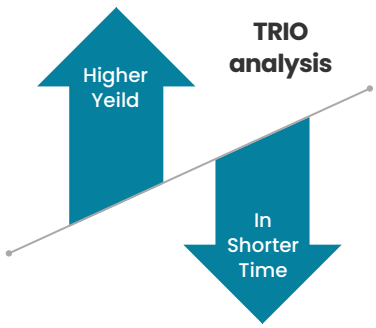
ACMG SECONDARY FINDINGS

ACMG recommended reporting of secondary findings in genes not associated with the patient's phenotype but known to cause a medically actionable health condition.

How is TRIO analysis beneficial?

TRIO is when exomes of parental samples are also sequenced simultaneously. Trio is the preferred test to diagnose an individual with an unknown Mendelian condition as:

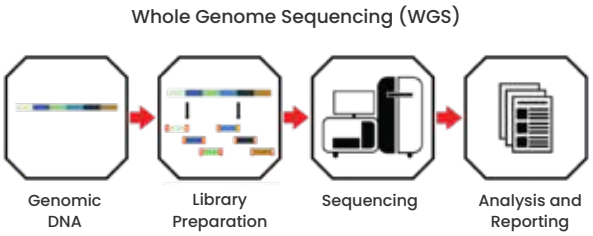
- Parental specimens are necessary to identify de novo variants and the chromosomal phase of variants and to optimally interpret patient results
- An exome wide segregation analysis can be performed
- This approach significantly increases the chances of finding the genetic cause of complex phenotypes in a shorter time
- Additional 10-15% increase in the diagnostic yield[1]. Therefore, it serves as a great way to give an early & accurate diagnosis for unclear or unexplained symptoms presented among babies admitted to Neonatal ICUs



- Joint ISPD, SMFM and PQF Position Statement and the ACMG guidelines suggests that Prenatal Exome sequencing has higher yields when samples from mother, father and fetus are analysed together as a TRIO
- Several large studies have demonstrated that exome sequencing identifies a causal variant with a higher yield for cases that specifically include other family members[4-7]

Whole Genome Sequencing (WGS)

WGS provides a high-resolution, base-by-base view of the genome. It evaluates both the exons and the introns, as well as intergenic and regulatory regions of the entire nuclear genome and the mitochondrial genome providing unparalleled coverage. It detects nearly all types of genetic variants in a single test delivering high diagnostic yields across a variety of rare genetic conditions.



WGS allows you to:

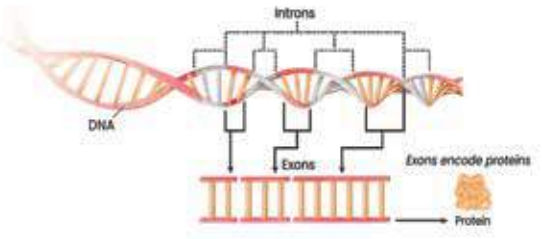
- Analyze the whole genome with uniform coverage
- Discover a broad range of genomic variants like SVs, SNVs, InDels and CNVs
- Identify previously unknown potential causative variants for future targeted studies of gene expression and regulation mechanisms.

Key Features and Performance

WHOLE GENOME COVERAGE	Highly uniform coverage of the entire nuclear genome, including both protein-coding and non-coding regions, and full mitochondrial genome
MEAN DEPTH	Greater than 90 % of the genome covered at ≥ 10 x 1000-2000x for mitochondrial genome
ADVANCED DETECTION OF NEARLY ALL TYPES OF VARIANTS IN ONE SINGLE TEST	• Genome-wide analysis of SNVs, InDels, CNVs of exon-level to cytogenomic-level, complex structural variants (SVs). • Mitochondrial heteroplasmy ≥15% is reported.
ANALYTICAL SENSITIVITY & SPECIFICITY	• Sensitivity for SNVs and InDels (≤ 50 bp) > 95 % • Specificity of > 99.9 % is guaranteed for all reported variants
TECHNICAL DETAILS	• Illumina paired-end next-generation sequencing (NGS) technology (2 x 150 bp read) • Genomes are enzymatically fragmented, and libraries are generated using NEBNext Ultra II FS DNA Kit. • More uniform coverage across both coding and non-coding regions of DNA, no selection or amplification bias exists. • 90-100 Gb of sequencing data generated for each patient
CNV COVERAGE	Reliable detection of deletions and duplications (>=5 exons) in clinically relevant genes that are related to phenotype • Single exon del/dup (51-500bp)>70% • Multi exon/whole gene(s) del/dup (100bp–10kb)>70% • Whole and partial chromosomal aneuploidies >70% • 51-99bp Insertions: >75% • 100-299bp Insertions: >70% • >300bp Insertions: >75% Note: 3-4 exon CNVs will require follow up testing
ANALYSIS PLATFORM	Secondary data analysis is performed using Illumina DRAGEN Bio-IT Platform v.4.0. Tertiary data analysis and interpretation is performed using GeneYX for SNVs and CNVs
TURNAROUND TIME	21 Days

Whole
Exome Sequencing

The exome comprises of all protein-coding regions (exons) of the approximately 20,000 genes in the human genome. Although the exome accounts for only about 1-2% of the whole genome, about 89% of all known disease-causing variants are located within the exons. Exome Sequencing primarily captures the coding regions for analysis and evaluation in order to identify the causative variant(s).



To help gain comprehensive insights into Mendelian and complex disorders, we bring to you one of the most comprehensive Whole Exome Sequencing (WES). Following design features allow detection of clinically relevant variants with superior precision:

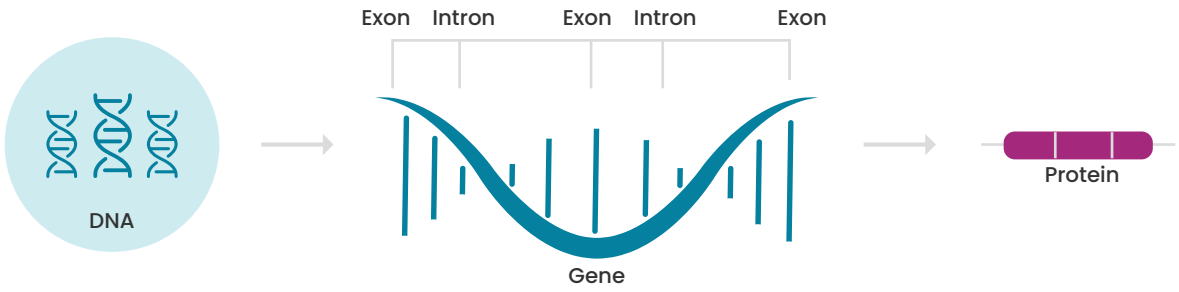
- Enhanced coverage of known disease causing genes and the inclusion of curated deep-intronic and promoter regions with spike-in probes for improved coverage of pathogenic variants
- Comprehensive copy number variant (CNV) calling from exon level (683 bp-2 exons) up to aneuploidies(155 Mb) with the use of custom breakpoint capture baits and additional spike-in probes in coding and non-coding regions

Key Features and Performance

NUMBER OF GENES ANALYSED	Protein coding regions (exons) and their flanking intronic regions (~10 bp) of the entire nuclear genome and full mitochondrial genome
MEAN DEPTH	80-100x for the nuclear genes with > 95 % of of bases covered at ≥ 20 x 1000-2000x for mitochondrial genome
UNSURPASSED DATA QUALITY	≥ 85% of bases have a sequencing quality score of ≥ Q30
ADVANCED DETECTION	Specifically designed to detect copy number variants (CNVs), single nucleotide variants (SNVs), InDels, curated deep intronic, splice-site and promoter region variants.
ANALYTICAL SENSITIVITY & SPECIFICITY	• Sensitivity for SNVs and InDels (≤ 50 bp) > 95 % • Sensitivity of CNV detection is: >90% for homozygous/Hemizygous deletions/duplications and >80% for heterozygous deletions/duplications
TECHNICAL DETAILS	• Panel size: 38.2Mb • Genome is enzymatically fragmented, and libraries are generated using TWIST comprehensive exome 2.0 kit • 7-8 Gb of sequencing data generated for each patient
SUPERIOR DESIGN	• Coverage of alternative transcripts (GENCODE, REFSEQ) • Superior coverage from major genetic databases (RefSeq, CCDS, GenCode, Clinvar and ACMG73) • Coverage of non-coding pathogenic variants for HGMD, ClinVar, Genomenon and Gencode • 100% for Mitochondrial Genome • Enhanced coverage of ~8,000 disease-associated genes
CNV COVERAGE	Single exon del/dup (51-500bp)>70% • Multi exon/whole gene(s) del/dup (100bp–10kb)>80% • Whole and partial chromosomal aneuploidies >90% • 1-2 exon CNVs Predicted by analysis will require follow up testing • For Insertions:51-99bp: >75% ; 100-299bp: >70%; >300bp: >75%
ANALYSIS PLATFORM	Secondary data analysis is performed using Illumina DRAGEN Bio-IT Platform v.4.0. Tertiary data analysis and interpretation is performed using GeneYX
TURNAROUND TIME	10 Days | 15 Days | 21 Days

Clinical
Exome Sequencing

Clinical Exome Sequencing is a custom-built solution for better coverage of disease associated genes including coding variants, deep intronic variants, splice variants and CNVs. It gives high diagnostic utility at a lower cost.



NUMBER OF GENES ANALYSED	Custom exome panel of 6800+ genes and nucleotide sequences flanking exon-Intron boundaries(~10bp) Focused in-depth coverage of genes selected from various databases with strong to moderate support on its association with disease phenotype. • 5,980 genes from OMIM (24 Oct-2021 update) • 3,686 genes from ClinVar (Dec-2021 update) • 775 genes from Decipher (version.v11.9) • 4,479 genes from DisGenNET (version.v11.9) • 2,888 genes from HPO (Dec-2021) • ACMG (59 genes; incidental finding) Designed to include all clinically relevant Coding (Exonic) region as well as known pathogenic deep non-coding (Intronic) bases and promoter regions in 740 hotspot gene regions of Clinvar
MEAN DEPTH	• 80-100x with > 95 % of of bases covered at ≥ 20 x
UNSURPASSED DATA QUALITY	• ≥ 85% of bases have a sequencing quality score of ≥ Q30
ANALYTICAL SENSITIVITY & SPECIFICITY	• Sensitivity for SNVs and InDels (≤ 50 bp) > 95 % • Specificity of > 99.9 % is guaranteed for all reported variants • Sensitivity of CNV detection is >90% for homozygous/Hemizygous deletions/duplications and >80% for heterozygous deletions/duplications
TECHNICAL DETAILS	• Genome is enzymatically fragmented, and libraries are generated using the TWIST enzymatic library preparation kit. • 3.5-5 Gb of sequencing data generated for each patient
COVERAGE	Clinically relevant protein-coding genes and intronic pathogenic mutations from ClinVar • Insertions/Single exon/ Multi exon/whole gene(s) deletion/duplication (51bp–10 kb)>95% • Whole and partial chromosomal aneuploidies >90%
ANALYSIS PLATFORM	Secondary data analysis is performed using Illumina DRAGEN Bio-IT Platform v.4.0. Tertiary data analysis and interpretation is performed using GeneYX for SNVs and CNVs
TURNAROUND TIME	10 Days | 15 Days | 21 Days

Customized Exome Panels

Our panels have been optimized to test for a wide selection of hereditary genetic disorders across different disease categories and follow a phenotype-directed approach that includes all clinically relevant genes. Additionally, we have included genes necessary for differential diagnosis of syndromes with overlapping phenotype(s).

This approach maximizes the clinical utility, de-risks panel choice, increases cost-effectiveness, and ultimately simplifies the diagnostic process.

High resolution NGS-based CNV analysis to detect larger deletions and duplications is included in all our panels at no extra cost. Deletion/duplications constitute 5–10% of disease-causing variants. By including CNV analysis in our panels, the potential of providing the most accurate diagnosis increases.

Key Features and Performance

COVERAGE	≥ 99.0 % targeted regions covered at ≥ 20 x For each gene, all SNVs described in HGMD and ClinVar, the largest public database of genotype-phenotype relationships.
SPECIFICITY	≥ 99.9 % guaranteed for all reported variants.
CNV SENSITIVITY	NGS-based copy number variations (CNV) are detected with a sensitivity of above 95 % for all homozygous deletions and heterozygous deletions / duplications spanning at least three consecutive exons. Heterozygous CNVs spanning less than three exons may not be reliably detected.
TAT	21 Days

Mitochondrial Genome Sequencing

Mitochondrial disorders are clinically heterogeneous and result from dysfunction of the mitochondrial respiratory chain. They are caused by pathogenic variants in mitochondrial DNA (mtDNA) or in nuclear genes. Mitochondrial disorders may affect a single organ, but many involve multiple organ systems particularly those that have high energy requirement like brain, skeletal muscle, heart, kidney etc.

- Using genomic DNA, the entire mitochondrial genome is amplified and sequenced using Next Generation sequencing at mean depth of 1000-2000X.
- DNA sequence is assembled and analyzed in comparison with the revised Cambridge Reference Sequence (rCRS GeneBank number NC_012920) and the reported variants listed in the MITOMAP database (http://www.mitomap.org/MITOMAP/Human/Mitoseq).
- Detection of heteroplasmy >15%
- GATK (genome analysis toolkit) best practices framework for identification of variants.

Limitations of NGS

- The available scientific knowledge about the function of all genes in the human genome is incomplete at this time.
- The test may detect presence of a genetic variant in the gene of an affected individual, but it may not be recognized as causative for the affected individual's disorder due to insufficient knowledge about the variant or the gene and its function.
- A negative result does not exclude a genetic cause for the patient's disorder.
- Some variants cannot be detected due to the presence of pseudogenes, repetitive, or homologous regions Low-level somatic variants
- Copy number variation (CNV) analysis detects deletions and duplications; in some instances, due to the size of the exons, sequence complexity, or other factors, not all CNVs may be analyzed or may be difficult to detect
- This assay does not interrogate CNVs in mitochondrial DNA.
- CNV analysis will not detect tandem repeats, balanced alterations (reciprocal translocations,robertsonian translocations, inversions, and balanced insertions), methylation abnormalities, triploidy, and genomic imbalances in segmentally duplicated regions

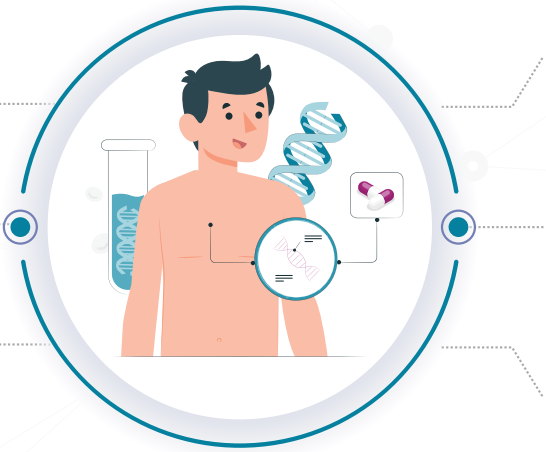
Introducing
MsurePGx

The Medical Grade Pharmacogenomic Testing

With msurePGx testing, it's possible to tailor medication plans to a patient's genetic makeup

Understand patient's responses to certain medications in a better way

Adjust and optimize the dose of certain medications



Identify the medications that may be most effective before starting treatment

Reduce the risk of adverse events for certain medications

Improve Patient Care

References:

[1] Tan TY et al. (2019) Eur J Hum Genet. 27(12):1791-1799 (PMCID: PMC6871178)
[2] Stankiewicz P et al. (2010) Annu Rev Med. ;61:437-55. (PMID: 20059347)
[3] Miller DT et al. (2010) Am J Hum Genet. ;86(5):749-64. (PMID: 20466091)
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