mfine /diagnostics

GenomeScopeNICU

for sick NICU/PICU Babies

- A Breakthrough that is Need of the Hour

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Genetic Diseases are common and leading cause of Mortality in NICU and PICU settings.[1] The disease progression can be rapid in infants, performing genetic testing at the first clinical indication can shorten the time to a diagnosis, guide immediate changes in medical management, and direct towards optimal care.

When The Clock Is Ticking...

Currently, comprehensive exome sequencing requires weeks or months to obtain actionable test results as conventional high throughput sequencing platforms run cases by batch, reducing flexibility for individual prioritized cases!

PRESENTING

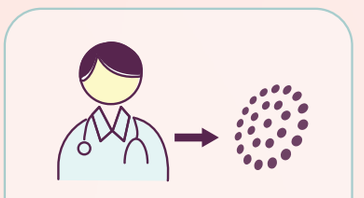
India's First Lightning Speed Gene Sequencing for

Sick NICU/ PICU Babies

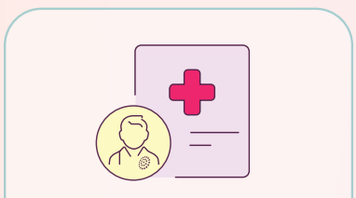
GenomeScopeNICU

MFine presents, for the first time in India, GenomeScopeNICU, Advanced Next Generation Sequencing based test panels that breaks the time barriers to give you results in JUST 5 DAYS - helping to improve outcomes in critically ill newborns by expediting an accurate diagnosis and effective treatment.

Referral Process and Patient Selection



Clinician connects to MFine Genetic Counsellor



Clinician Calls MFine Phlebotomist

On Priority Dispatch to MFine Laboratory

Day 1

- Sample Receipt at Lab (QC, TRF and Document Verification, Sample Registration)
- Sample Profiling by Dedicated GC (Case review, Phenotype Assessment, Conversion of Phenotypic Data to HPO Terms)
- Round the Clock DNA Extraction (QC on Isolated DNA)

Day 2

- Round the Clock Library Preparation (Automated with Hamilton NGS Star; Pre-capture and Post-capture QC)

Day 3

- ULTRA Rapid Mode Sequencing (Illumina Sequencer-High Coverage and Read Depth)
- Precise Variant Calling for SNV, Indel and CNV down to exon level
- Ultra-Rapid, Automated and Accurate Secondary Analysis with DRAGEN 4.0

Day 4

- Variant Analysis, Annotation and Interpretation with GeneYX, best-of-breed data analysis powered with AI and ML, Integrated with hundreds of Databases including Genomemon Mastermind
- Fully automated ACMG compliant phenotype driven variant reporting

Day 5

- Clinical Report Review by Clinical Geneticist
- Report Intimation by Genetic Counsellor

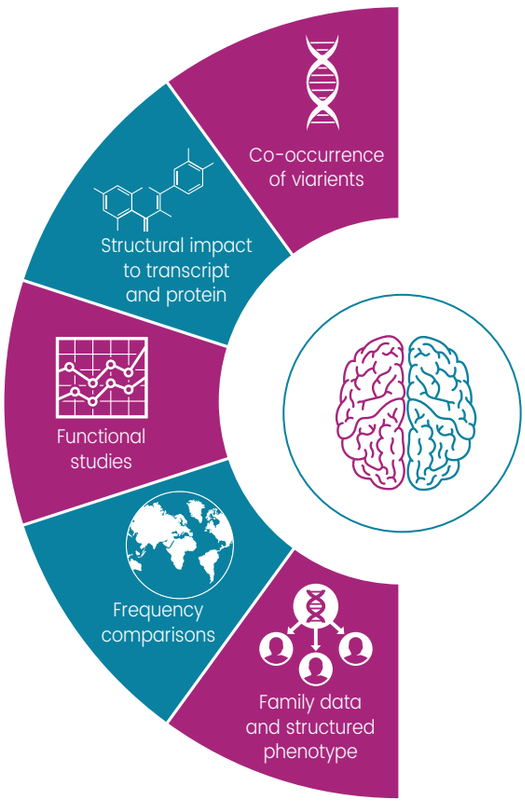
Pathogenicity Score:

Rare:
Given the severity of the Phenotype, the allele has <1% frequency in population

Protein Altering:
Most likely to have a biological consequence like Loss of Function

Know Disease Gene:
Variant present in a Gene and locus known to be associated with Mendelian Disease

Literature Evidence:
HGMD, ClinVar, Mastermind and many more

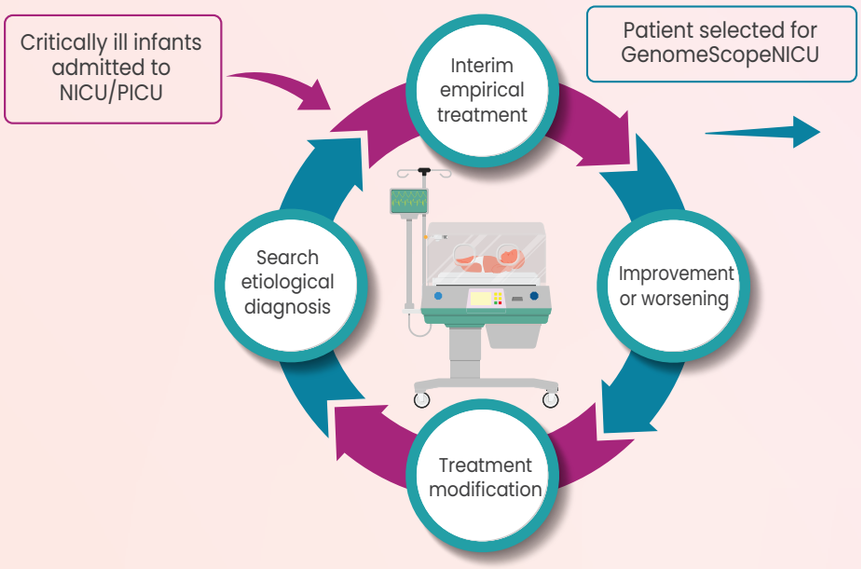


Why Choose GenomeScopeNICU?

Genetic disorders and congenital anomalies affect ~6-7% of live births, and are the leading reason for hospitalization and mortality in infants.2 Most genetic conditions do not present noticeably distinct symptomatology at early stages, especially in the neonatal stage. Choosing right genetic test can have a huge impact in:

- Reducing the NICU/PICU admission time
- Decreasing infant morbidity and hospitalization costs [12-14]
- Avoiding unnecessary diagnostic tests and invasive surgeries
- Empowering clinicians with answers to guide clinical management decisions
- Addressing parental anxiety by shortening potentially long years of diagnostic odyssey
- Optimizing medical decision making and secondary prevention
- Enabling families to connect with gene –specific support groups, enroll for clinical trials and other resources.

Paradigm Shift in NICU/PICU Standard of Care with GenomeScopeNICU



Patient selected for GenomeScopeNICU

GenomeScopeNICU Result in 5 Days

30-50% Genetic Disease Diagnosis

20-40% Precision Treatment

10-15% Avoid Mortaility and Longterm Morbidity

- Improved outcomes
- Shorter clinical stay
- Decreased cost

Improved Care with GenomeScopeNICU

Current standard of NICU/PICU care

Genetic Diagnosis takes weeks to months:
Diminishing the impact on Change in Outcome

Reference: Dimmock et al 2020, Willig et al 2015, Petrikin et al 2018

Proven Statistical Benefits Of Rapid Genetic Testing

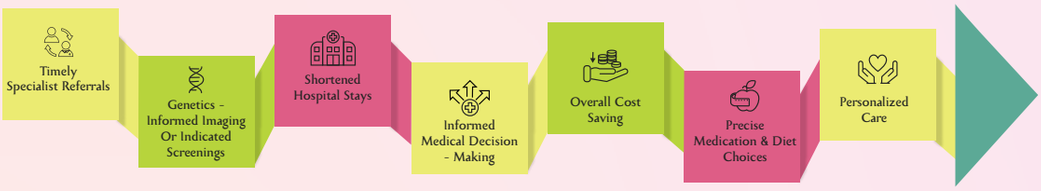
31% diagnostic yield in the Intensive Care Settings, more effective when ordered early for critically ill newborns along with parent samples.3

32% of babies who received a diagnosis from rapid genome testing had a change in clinical management.4

33% of babies who received positive results from rapid genome testing were not previously suspected of having a genetic condition.5

50% Clinical Sensitivity reported in identifying the cause of the infant's condition 1,6

Achieve more with GenomeScopeNICU Panels



Reveal more with GenomeScopeNICU Panels

The exome is estimated to encompass approximately 1% of the genome, yet contains approximately 85% of disease-causing mutations. GenomeScopeNICU is an application of Next Generation Sequencing designed to include all clinically relevant Coding (Exonic) regions as well as known pathogenic deep non-coding (Intronic) regions and nucleotide sequences flanking exon-Intron boundaries(~10bp).

- GenomeScopeNICU enables the simultaneous identification of single nucleotide variants (SNVs), gene level copy number variations (CNVs) up to aneuploidies, and small insertions or deletions (indels), as well as rare de novo mutations that may help gain comprehensive insights into Mendelian and complex disorders. This makes it possible to offer Dual Diagnosis in some cases.
- Mean depth is 80-100x with >95% of targeted regions covered at 20x;≥ 85% of bases have a Q30 sequencing quality score
- Detects SNVs and Indels with sensitivity >99%
- Offers superior coverage of major genetic databases like RefSeq, CCDS, GenCode, Clinvar, ACMG73 etc and of clinically relevant non-coding pathogenic and likely pathogenic variants

GenomescopeNICU-CES provides coverage of 6800+ genes,with focused in-depth coverage of genes selected from various databases like ClinVar, OMIM,Decipher, DisGenNET, HPO, ACMG with strong to moderate support on its association with disease phenotype. Specificity is >99% for all reported variants

GenomescopeNICU-WES provides Coverage of ~22000 genes and spiked coverage for Human Core Exome and Mitochondrial genome over noncoding regions that are known to carry pathogenic or likely pathogenic variants .This panel's high uniformity and low off-target rate deliver best-in-class sequencing efficiency.Specificity >95% for all reported variants

GenomeScopeNICU panels may also uncover pathogenic variants in genes unrelated to the patient's primary concern, but are medically actionable, known as secondary findings. The American College of Medical Genetics and Genomics (ACMG) recommends disease- causing variants in certain cancer, cardiovascular and other genes be reported, even if they are not related to the patient's condition because monitoring or early treatment may be available11. Other medically actionable incidental variants in non-ACMG genes may be reported at laboratory's discretion.

Indications for GenomeScopeNICU Testing

The diagnostic yield of whole exome sequencing has surpassed that of historically recommended tests in a clinically heterogeneous cohort.8

- Rapidly deteriorating clinical status
- Under the age of 1 year and presenting with congenital anomalies
- NICU/ PICU patients with no history of trauma, infection, or prematurity
- Unclear or atypical presentation of a genetic disorder
- Long list of differential diagnosis
- Child's medical history and physical exam findings strongly suggest that there is an underlying genetic aetiology

  Presenting with unclear symptoms which can be part of a genetic condition like Bleeding diathesis, Blood abnormalities (anaemia), Bone fragility, Failure to thrive, Heart abnormality/arrhythmia, Hepatosplenomegaly, Hypotonia, Ichthyosis/epidermolysis bullosa, Metabolic abnormalities, Microcephaly, Neutropenia, Abnormal newborn screening results, Respiratory failure, Skeletal abnormalities/craniosynostosis, Skin fragility, Unclear seizures
- Family History of unexplained neonatal deaths
- Parental Consanguinity in the background

Expert Recommended

The American College of Medical Genetics and Genomics (ACMG) recommends exome and genome testing as a first-tier test when an infant presents with congenital anomalies.8

Establishing an etiologic diagnosis in children will ensure timely implementation of precision medicine and optimal outcomes, particularly to guide weighty clinical decisions such as surgeries, extracorporeal membrane oxygenation, therapeutic selection, and palliative care.9

What Makes GenomeScopeNICU TRIO-Exome Sequencing The Better Choice?

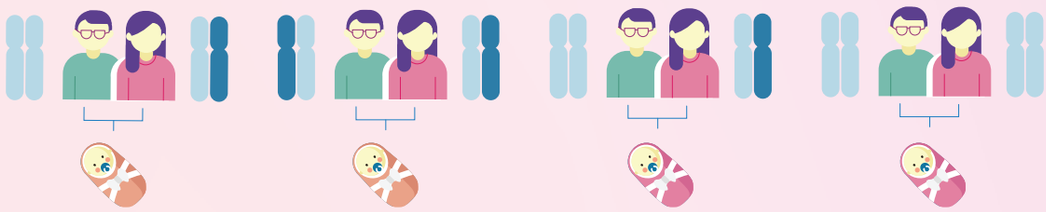
Inheritance is the process by which genetic information is passed on from parent to child. The child gets one copy of the genetic material from each of the parents.

If there is a variation in the parent's genetic material, this can also be passed on from parent to child.

Sometimes these disease-causing variations occur during Embryo development (de-novo) and are not present in the parents.

GenomeScopeNICU-TRIOExome panels offer an advanced approach for detecting inherited variations that may become a cause of illness in babies.

Modes of Inheritance of a Genetic Disease



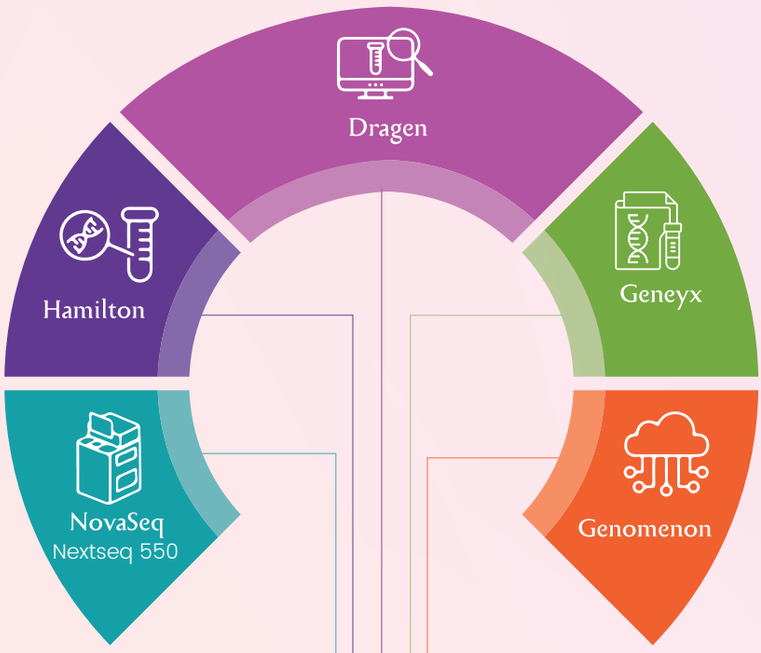
Autosomal Dominant Inheritance | Autosomal Recessive Inheritance | X-linked Inheritance | De-novo Not inherited from Parents

Because this test targets millions of genes, thousands of DNA changes (Variants) are detected which may be harmless, disease causing or have an unknown effect. Compared to GenomeScope NICU-Proband, where only the baby's DNA is analysed, GenomeScopeNICU-TRIO analyses the genetic data of the biological parents (mother and father) simultaneously along with the baby. This model offers commendable advancements including:

- Clear demarcation of the mode of inheritance (Dominant, Homozygous or Compound Heterozygous Recessive, X linked) or identification of de novo mutations in a child and aids in classification of causal variants.
- Huge reduction in the chance of finding a Variant of Unknown Significance(VOUS) where the interpretation is not always straightforward and need for follow-up testing may arise.
- Combined variant calling increases the accuracy of variant calling and ability to make variant calls in low coverage regions
- 10-15%[10] additional increase in the diagnostic yield.
- Allows the laboratory to ascertain significance of clinically relevant variants and exclude the ones which do not conform to Mendelian transmission, thereby reducing the false positive calls and narrowing down the potential candidate variants.
- As far as the cost is concerned, on the surface, it may seem like a slightly expensive option. However, considering its enormous benefits in medically actionable and timely diagnosis, the TRIO model is preferred worldwide.

MFine's Next Generation Sequencing Solutions

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



Illumina Systems 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.

Mastemind by **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.

Geneyx A clinical genetics data management platform with best-of-breed AI-based data analysis and interpretation tools. Integrated with >150 knowledgebase, it doubles the diagnostic yield 25-30% to ~60%. Increases phenotype driven interpretation from 2 to 20%. Analyses a greater percentage of the genome while significantly reducing (~ 959%) the analysis time. Offers Cloud Data storage. protection and privacy and Compliance with ACMG & ClinGen.

Phenotype-Driven Results

Actionable Next Steps

Expert Clinical Support

Extensive, Unparalleled Support

Our Clinical Geneticists, Genetic Counsellors, MD/PhD scientists, clinical and molecular genomics specialists enable us to provide clear, accurate, and meaningful test reports. Their deep knowledge helps in assisting you with any questions that you may have at various stages of the genetic testing process.

Express Genetic Counselling Services

We offer pre- and post-test genetic counselling with Board Certified Genetic Counsellor at no additional charge for patients when testing is ordered through LifeCell.

Innovation Pioneers

We have been at the forefront of genetic innovation, pioneering incorporation of new technologies and gene inclusions. Our unmatched experience enables us to offer greater diagnostic accuracy, fewer VUS (variants of uncertain significance), and data-backed answers for your patients.

PAN India Presence

Apart from the central Lab at chennai, we have 8 regional labs and 62 collection centers across India and are expanding further every day.

Proven Track Record with Assured Quality

We are a CAP, NABL and ISO 9001: 2015 laboratory associated with more than 2000 clinics. Our experience of offering Prenatal screening to more than 7,00,000 ; Newborn screening to more than 4,60,000 and Exome sequencing to more than 15,000 patients remains unparalleled!

Test Code	Test Name	Sample Requirement	Documentation Requirement	Turnaround Time
GEN0721	GenomescopeNICU WES-TRIO (*Preferred Globally)	• Dried blood spot (DBS)-for Proband • Whole Blood in lavender-top (EDTA) tubes Note: Frozen Samples are unacceptable	1. Duly Filled TRF 2. Parent's and ordering Clinician's Consent 3. Mobile Number and Email of ordering Clinician. 4. Child's age , gender and detailed Clinical History, Three generation Pedigree Chart 5. Family History and Consanguinity related information must be shared 6. Clinician's notes/ OPD cards/ Dr's prescription/ Discharge Summary 7. Reports of any investigation carried out like abnormal MRI/Echo/Ultrasound/X-Ray or metabolic test results 8. Any past genetic test results of family members detailing diagnosis/symptoms and age of onset in each relative	10 Days
GEN0725	GenomescopeNICU WES -DUO			10 Days
GEN0726	GenomescopeNICU WES- Proband			10 Days
GEN0727	GenomescopeNICU CES-TRIO			10 Days
GEN0728	GenomescopeNICU CES-DUO			10 Days
GEN0729	GenomescopeNICU CES -Proband			10 Days

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