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WHOLE EXOME SEQUENCING

DESIGNED FOR DEEPER COVERAGE & PRECISE DIAGNOSIS

Artificial Intelligence & machine learning powers improved **SNV/Indels & CNV** detection

Covers all 16,659 base pairs & 37 genes of the **mitochondrial genome**

Uniform coverage with a mean depth of >80-100X. **6Gb-7Gb** data/sample

Covers **>20,250 Genes** with **protein-coding regions,** several **non-coding variants** & **intron-exon boundaries**

State of the art **bioinformatics analysis pipelines** designed for accuracy

Clinical grade variant annotations with industry leading annotation sources

Reviewed by **clinical geneticist**

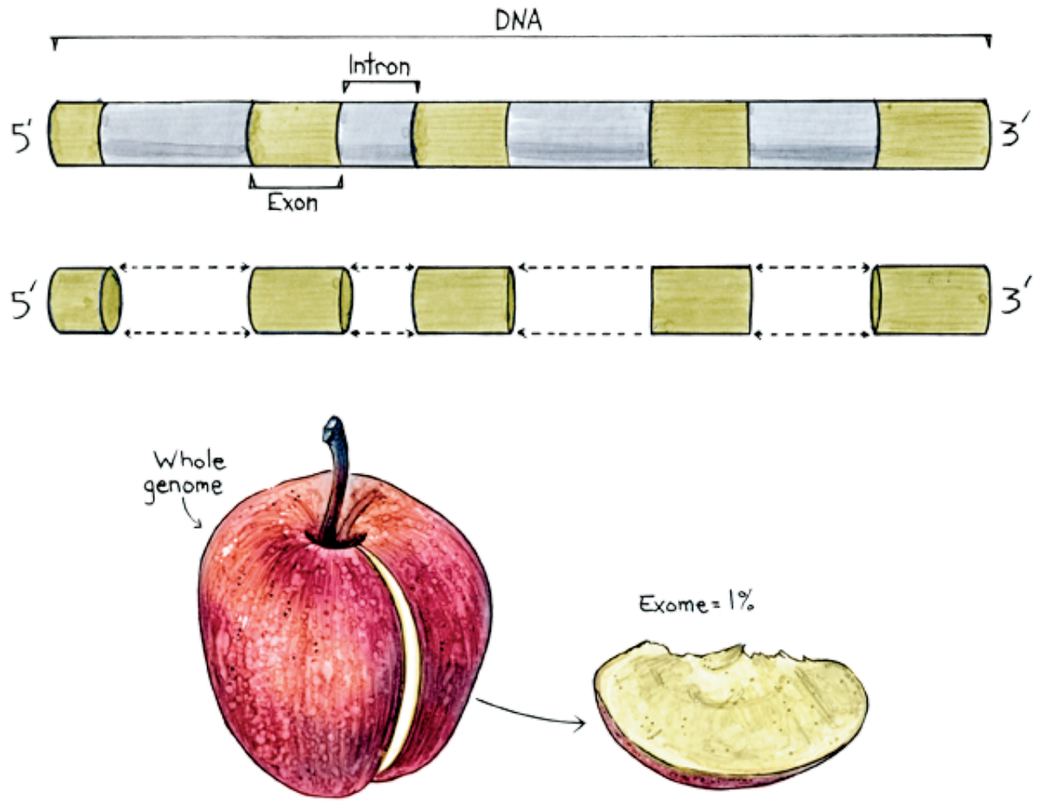
High Performance Exome Built on Advanced and Proven Technology

The complete genomic information within a sample or individual is known as the whole genome. Exons are the genome's protein-coding regions and are collectively known as the exome.

Whole Exome Sequencing (WES) assay is a widely used method that involves sequencing the complete coding region of the genome. It is designed to examine all the coding regions and splice junctions of the genome.

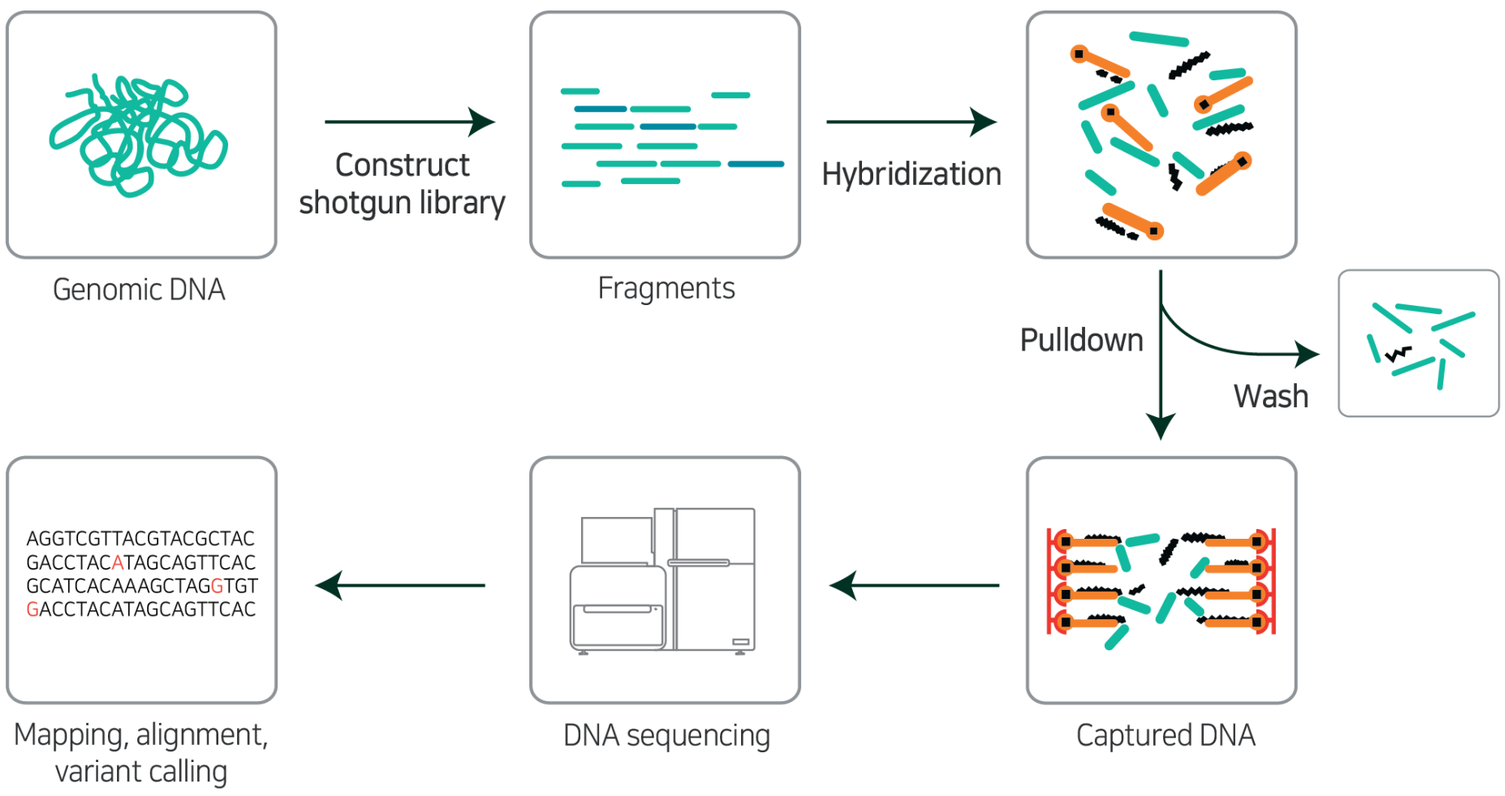
Exome sequencing using exome enrichment can efficiently identify coding variants (**SNVs/Indels/CNVs**)across a broad range of applications, including population genetics, genetic disease, and cancer studies.

When looking for an answer, something to explain the underlying cause of a disease, researchers often turn to the genome. With more than 3.2 billion bases in the human genome, the first and most financially viable step is to narrow the search to portions most likely to be informative. To do this, researchers can extract specific portions of the genome for sequencing with target enrichment panels. Picking the right panel is key to collecting quality, informative data.



Researchers have two options at this stage: small and targeted panels (Clinical exome) or whole exome panels. Whereas panels of “clinically relevant” targets offer a narrow and cost-effective view of specific genes, Whole Exome Sequencing (WES) provides a dramatically increased perspective of the genetic landscape. With this broader view, researchers can parse through the data for known pathogenic variants, or piece together patterns that allude to novel gene-phenotype discoveries. **Therein lies the power of WES: It provides a breadth of data that can be used for a myriad of applications.**

"Spiked coverage over noncoding regions that are known to carry pathogenic or likely pathogenic variants enhances our exome panel’s discovery power."



Whole exome sequencing assay, Designed to maximize diagnostic yield

Complete new design that maximizes coverage of clinically relevant regions from the ClinVar database while including updated coverage of protein-coding regions from **CCDS**, **RefSeq** and **GENCODE**.

Powered by machine learning-based probe design and an improved probe-printing process, this exome panel spans a **36.5 Mb** target region of the human genome. The panel delivers excellent enrichment performance for more uniform coverage, lower GC bias, meaning this panel can help detect complex targets containing high, or low, levels of GC content.

Covers all 16,659 base pairs & **37 genes of the mitochondrial genome.** Sequencing depth optimized for **Heteroplasmy detection.**

Covers **>20,250** Genes with protein-coding regions, several non-coding variants & intron-exon boundaries.

Bioinformatics: Artificial intelligence (AI) & Machine learning (ML) based **Illumina DRAGEN Bio-IT Platform** provides super-fast, accurate, comprehensive, ultra-efficient analysis & Robust **CNV** calling/classification.

Clinical grade variant annotations through industry leading annotation sources and automated ACMG classification.

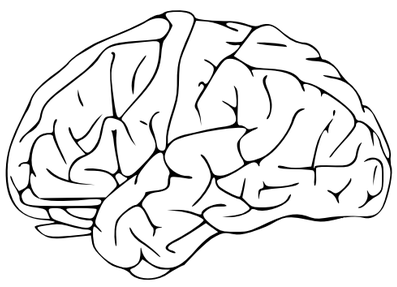
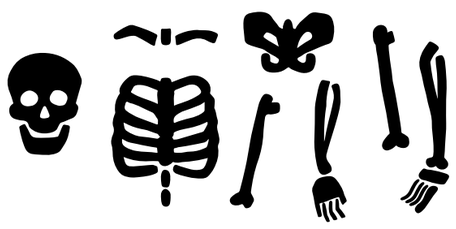
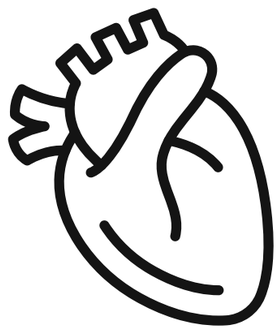
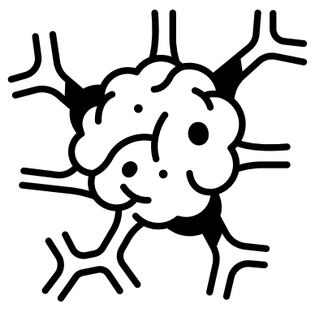
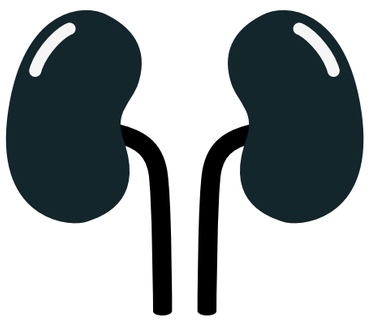
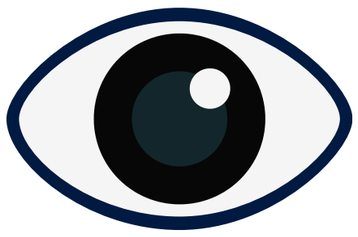
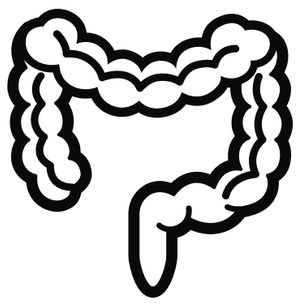
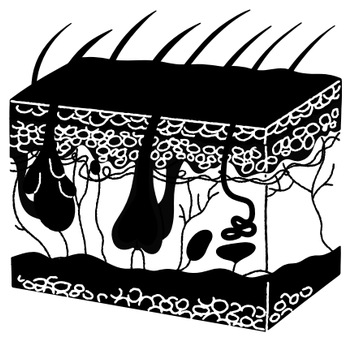
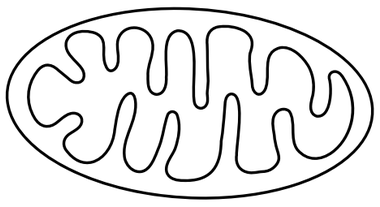
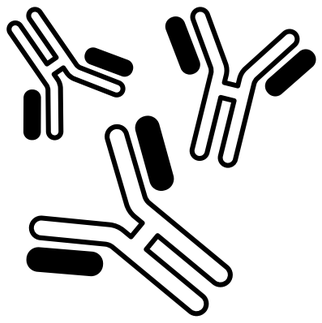
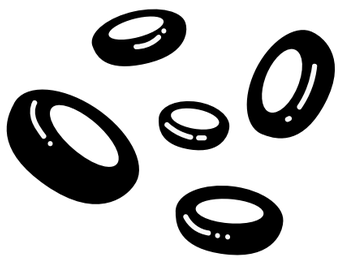
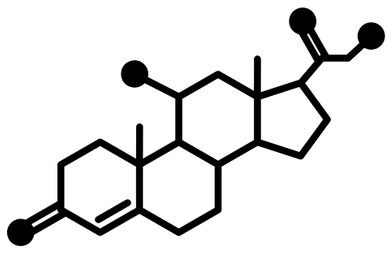
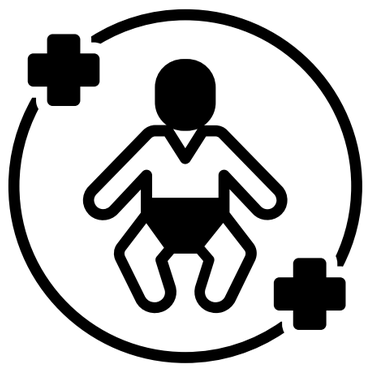
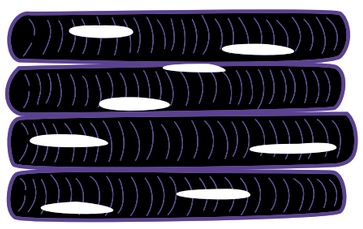
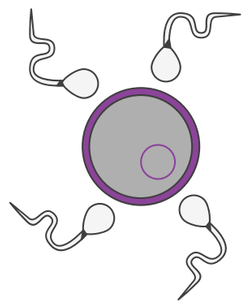
"Genetic information of patients is carefully interpreted by our team of geneticists, utilising highly sophisticated AI backed variant prioritization tools, latest publications, up-to-date databases, Population databases, In-silico prediction tools & Internal variant databases."

"Most commercially available exome panels cover nearly all gene-coding sequences in the genome But, one key and critical differentiating factor is how deeply they cover specific genes. While some whole-exome panels focus on providing particularly deep coverage over genes that are relevant to cancer development, inherited disorders, or other such conditions, this panel provides deep coverage over all genes that have been linked to clinical phenotypes, enabling translational research on a wide range of conditions. "

Who benefits from WES?

WES is most suitable for individuals :

- Complex phenotypes with multiple differential diagnoses
- Genetically heterogeneous disorders
- Suspected genetic disorders where a specific genetic test is not available
- Inconclusive previous genetic testing
- To guide reproductive planning and assessment of recurrence risk
- To facilitate prognosis

 Neurology	 Malformations	 Cardiology	 Hereditary Cancer
 Nephrology	 Ophthalmology	 Gastroenterology	 Dermatology
 Mitochondrial Disorders	 Immunology	 Hematology	 Endocrinology
 Metabolic Disorders	 Pediatrics	 Muscles	 Reproductive Health

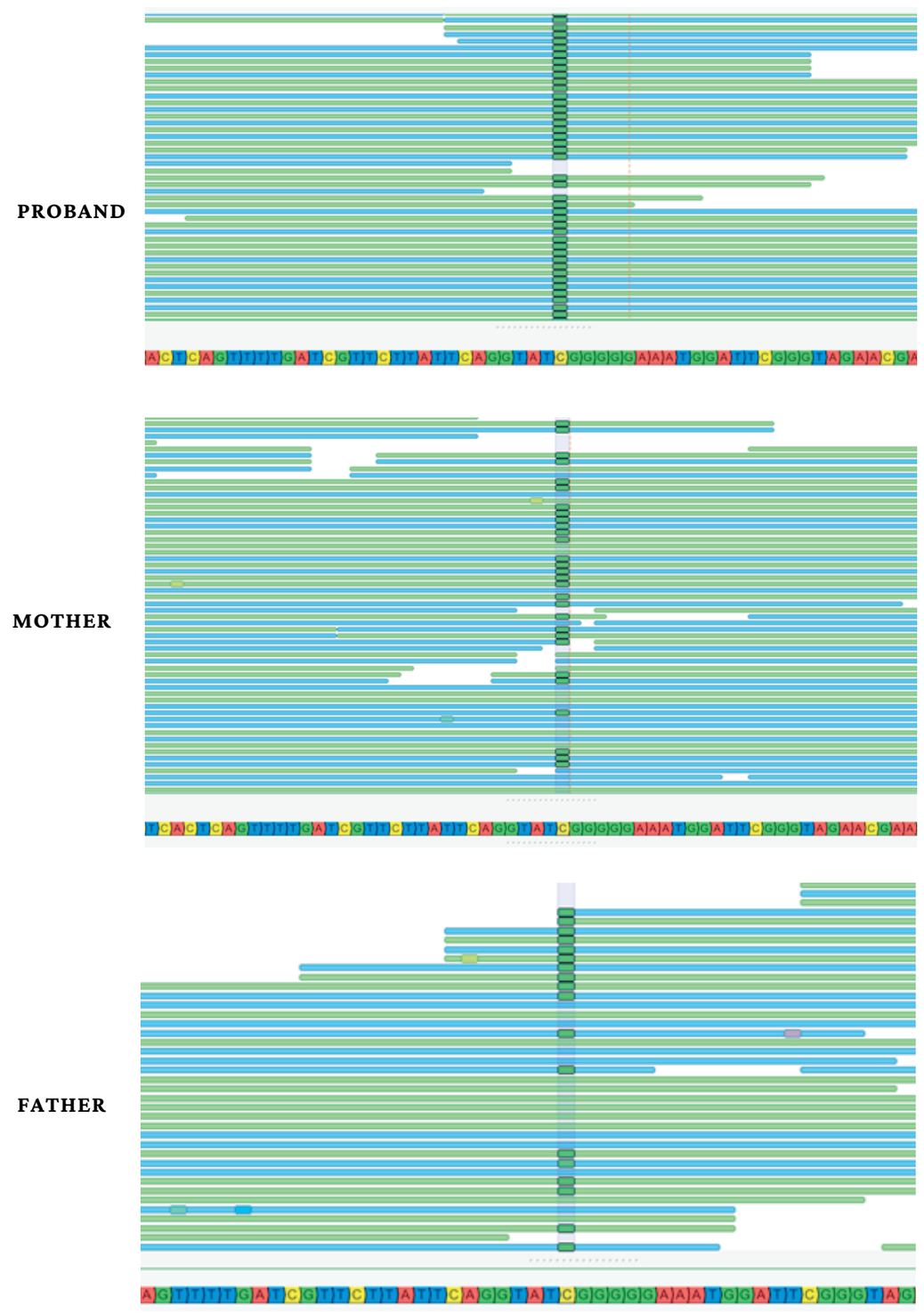
Case studies

Trio Whole Exome analysis

Trio-Exome sequencing analysis differs from single proband's Exome sequencing as it not only examines a baby's genetic data but also that of its biological parents. This technique may cost slightly more, but it provides a **12-15% increase in the diagnostic yield compared to Singleton-Exome sequencing,** making it a more cost-effective option for undiagnosed cases. This advanced technology expedites the diagnostic journey for critically ill babies by identifying differences between the DNA of the affected baby and its unaffected parents. These differences are variations (**such as insertions/deletions** (indels)**, single nucleotide variants** (SNVs)**, and copy number variations** (CNVs)) associated with different genetic conditions that can be passed down from parents to their children, making the parents carriers of the condition.

This approach helps exclude variants that do not conform to Mendelian transmission, reducing false positive calls and narrowing down potential candidate variants.

By comparing the DNA sequence of both the baby and its parents to the reference sequences, geneticists can identify variations that may be linked to the baby's medical concern. This thorough analysis reduces the chance of error and specifically targets potential disease-causing variations. In summary, trio-exome sequencing offers an advanced approach to detecting inherited variations that could become a cause of illness in babies, making it extremely beneficial for undiagnosed cases after Singleton-Exome sequencing.



"2.5 Years male child presented with global developmental delay, seizures, Muscle wekness, hypotonia and cerebral atrophy. Trio whole exome sequencing was offered."

Gene & Transcript	Location	Variant	Zygosity/ Inheritance	OMIM Phenotype	Clinical Significance
Proband BCS1L(+) NM_004328.5	Exon 4	c.325C>G (p.Arg109Gly)	Homozygous /Autosomal Recessive	Mitochondrial complex III deficiency, nuclear type 1	**Likely Pathogenic**
Mother BCS1L(+) NM_004328.5	Exon 4	c.325C>G (p.Arg109Gly)	Heterozygous /Autosomal Recessive		
Father BCS1L(+) NM_004328.5	Exon 4	c.325C>G (p.Arg109Gly)	Heterozygous /Autosomal Recessive		

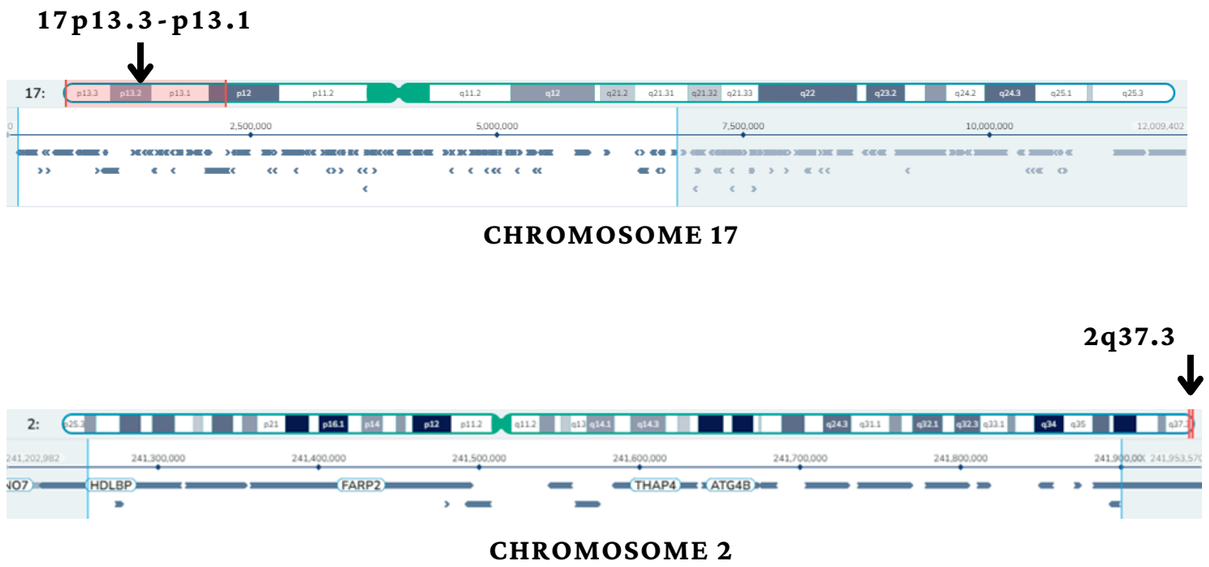
**Genetic test results are reported based on the recommendations of American College of Medical Genetics*

CNV - Copy Number Variations (Deletion/Duplication)

Copy-number variation is a common source of genomic variation and an important genetic cause of disease. Microarray-based analysis of copy-number variants (CNVs) has become a first-tier diagnostic test for patients with neurodevelopmental disorders, with a diagnostic yield of 10–20%. With advances in NGS methods, CNV screening is possible with whole exome studies as well.

Using specialized, integrated Probes & Sophisticated, Optimized bioinformatics algorithms for analyzing CNVs along with SNV/Indels on Whole exome sequencing platform can be quick, cost effective screening alternative.

Sensitivity of detecting CNVs is 75-99% depending on the length and zygosity (heterozygous/homozygous) of the deleletion/duplication status.



"7 Years Male child presented with Global developmental delay; Walking-1 1/2 years; Social anxiety; goes to special school; history of one episodes of Seizers at age of 1.3 Years: was on anti epileptic drug for 2 years."

Whole Exome sequencing Results:

Chromosome & CNV type	Cytoband	Genomic Cordinates	Size/ Zygosity	Genes	Clinical Significance
Chr 17 (Duplication)	17p13.3-13.1	Chr17: 137,590 - 6,830,376	6.7 Mb Heterozygous Duplication	169 Genes	**Pathogenic**
Chr 2 (Deletion)	2q37.3	Chr2: 241,256,183-241,900,369	644 Kb/ Heterozygous Deletion	20 Genes	**Pathogenic**

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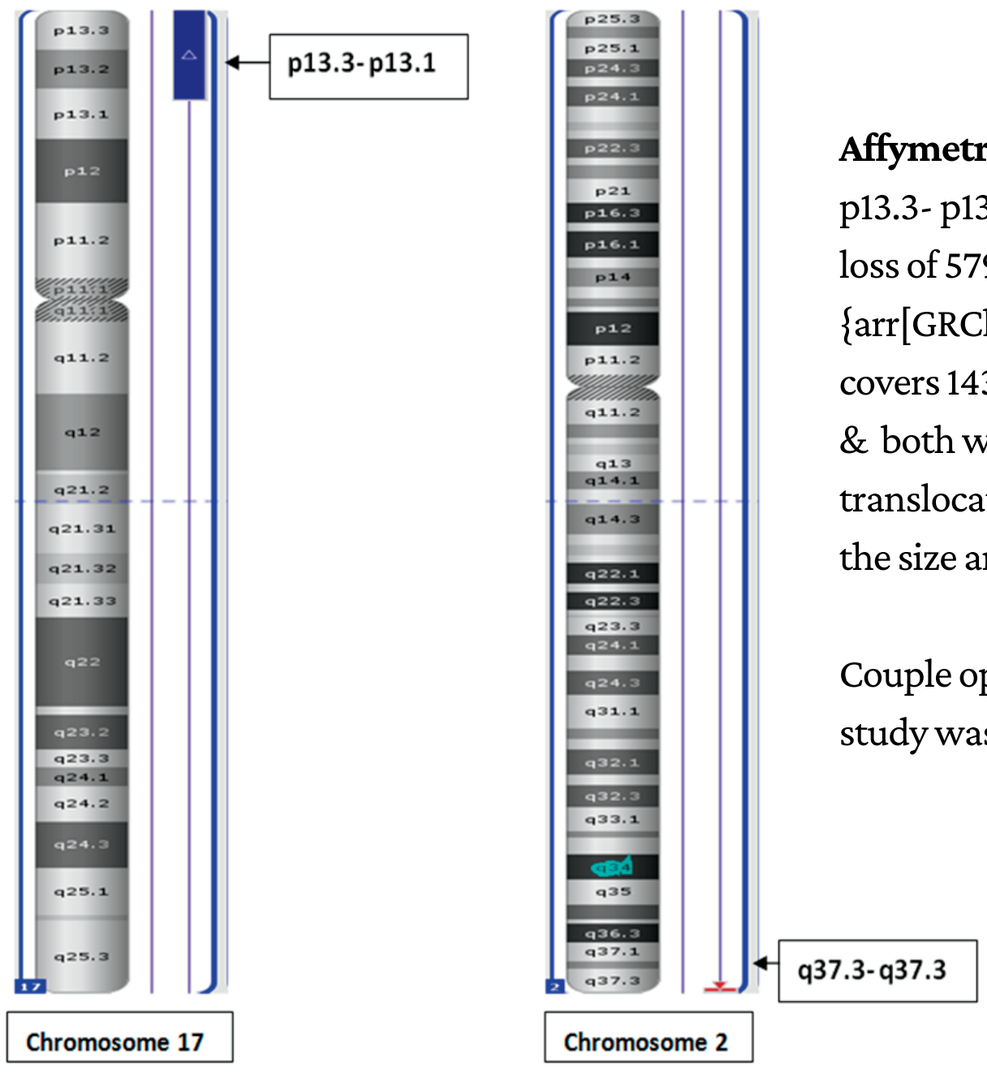


Affymetrix CytoScan Optima 315k analysis shows a gain of 7,400Kb on cytoband p13.3- p13.1 on chromosome 17 {arr[GRCh37]17p13.3p13.1(526_7,400,815)x3} and loss of 579Kb on cytoband q37.3- q37.3 on chromosome 2 {arr[GRCh37]2q37.3(242,204,286_242,783,384)x1}. Reported copy number variant covers 143 OMIM genes on Chromosome 17 and 12 OMIM genes on chromosome 2 & both were classified as Pathogenic. This results is suggestive of unbalanced translocation. The severity of the condition and the signs and symptoms depend on the size and location of the duplication and deletion and which genes are involved.

Couple optical mapping using BIONANO or High resolution couple karyotyping study was recommended to understand inheritance pattern.

Microdeletion detected in whole exome analysis

Clinical Indication: The Proband (4 Years years, Male child) was also suspected for global developmental delay, autism spectrum disorder (ASD).

Results: The submitted sample shows Heterozygous deletion on chromosome 7. A 1.4 Mb deletion was detected at cytoband q11.23(73,303,397-74,706,433) on chromosome 7 including 25 coding genes known as William syndrome.

Kreatech Williams-Beuren region probe is optimized to detect copy numbers of the ELN gene region at 7q11. The 7q22 region specific FISH probe at 7q22 is included as control probe. Normal: ELN Two Orange, control Two Green. Abnormal: ELN One Orange, control Two Green.

Whole Exome sequencing Results:

Chromosome & CNV type	Cytoband	Genomic Cordinates	Size/ Zygosity	Genes	Clinical Significance
Chr 7 (Deletion)	7q11.23	chr7:73,303,397-74,706,433	1.4 Mb Heterozygous Deletion	25 Genes	**Pathogenic**

**Genetic test results are reported based on the recommendations of American College of Medical Genetics*

DMD deletions - Prenatal case

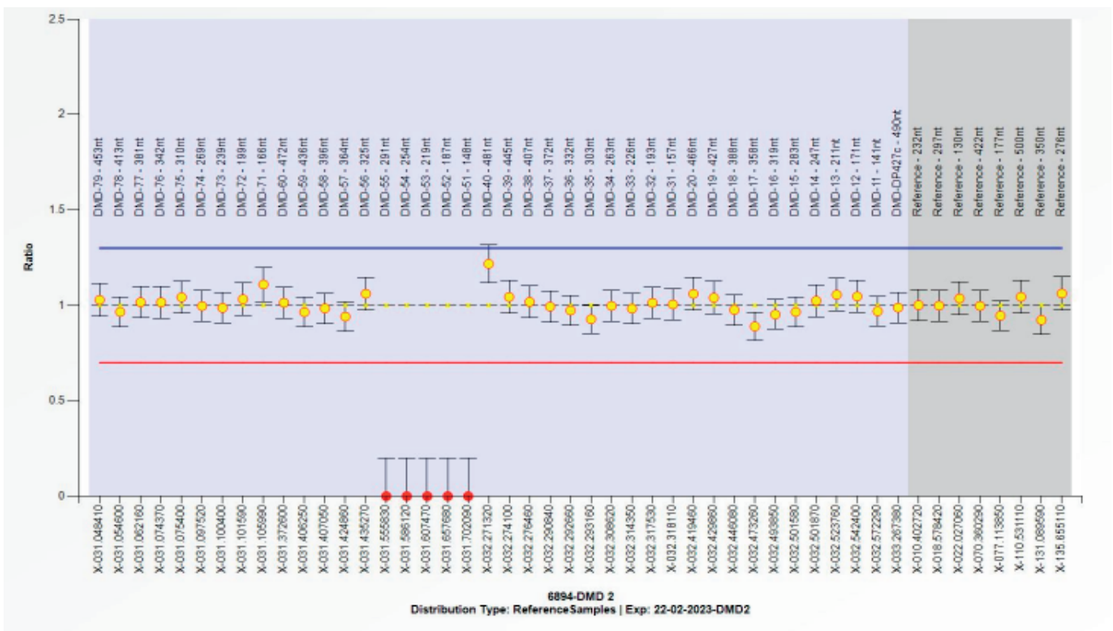
Clinical Indication: 16 weeks Prenatal ultrasound detected Fetus with multiple abnormality. ?Skeletal deformities

Result: The submitted sample shows Hemizygous deletion of Exon 51-55 on gene DMD. A 162.1 Kb deletion detected on cytoband Xp21.1. Results were confirmed with MLPA study. Gender was confirmed.

Whole Exome sequencing:

Chromosome & CNV type	Location	Cordinates	Size/ Zygosity	Genes	Clinical Significance
Chr X (Deletion)	Exon 51-55	c.7200-?_8027+?	162.1 Kb Hemizygous Deletion	1 Gene (DMD)	**Pathogenic**

MLPA result confirms the hemizygous deletion



also Know about our 154 gene NGS panel

COMPREHENSIVE HEREDITARY CANCER ASSAY

Early detection can save life.
Regularly check yourself and get a mammogram.

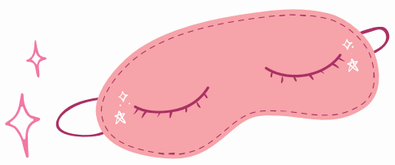
CANCER CHANGES YOUR LIFE.

Ways to Reduce

Risk for Breast Cancer

Keeping a Healthy Weight

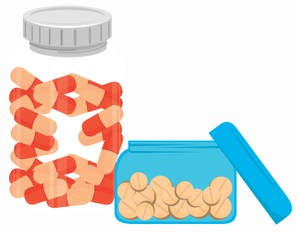
Exercising Regularity



Getting Enough Sleep

Limiting Alcohol Intake, Don't Smoke

Breastfeeding Your Babies



Avoid Post-Menopausal Hormones

WE'RE RAISING AWARENESS...

Get support at www.sngenelab.com