# WHOLE EXOME SEQUENCING

Decode&Discover

## Decoding genetic insights with WES

MEDICOVER GENETICS

# WHAT IS **WHOLE EXOME SEQUENCING Decode&Discover**?

Medicover Genetics Whole Exome Sequencing Decode&Discover (WES Decode&Discover) analysis is a comprehensive genetic test that examines the coding regions (exons) of approximately **20,000 genes.** While exons represent only 1-2% of the human genome, 85% of all known disease-causing mutations are located in exonic regions. Accurate detection of the disease-causing mutation can lead to improved clinical management and beneficial therapies, reducing or relieving the patient's symptoms and benefiting their quality of life. Through WES analysis, diagnosis can be achieved faster, avoiding extensive, costly and lengthy serial testing.

# WHO COULD **BENEFIT** FROM THIS TEST?

- Patients with a complicated medical history that affects many organs
- Patients who have undergone previous genetic testing with inconclusive results
- Patients with a severe presentation in the neonatal or childhood period
- Patients who remain unresponsive to treatment for presumed diagnosis

# OUR **SOLUTION**

## REPORTING OPTIONS

For all WES analysis tests, data analysis can be provided in the following formats:

| PRIMARY | SECONDARY | TERTIARY | CLINICAL REPORT |
|---|---|---|---|
| FASTQ sequencing files | VCF files | VCF with annotation & classification files | Variant filtering and clinical interpretation by interdisciplinary team of experts |

## TESTING OPTIONS


Single (patient only)


Duo (patient + 1 biological parent)


Trio (patient + 2 biological parents)

Trio WES is the most commonly performed analysis providing comprehensive results with the highest diagnostic yield. In cases where only one or no biological parent is available for testing, we can perform Duo WES or Single WES, respectively. Trio WES allows simultaneous analysis for all modes of inheritance and can ascertain the significance of clinically relevant variants.

# OUR **TESTS**

## PRENATAL WES

**SAMPLE:**
DNA from chorionic villus sampling or amniotic fluid cells and EDTA blood from the parent(s)

**TURNAROUND TIME:**
2 weeks (primary, secondary, tertiary)
2-3 weeks (clinical report)

## POSTNATAL WES (INCLUDING MITOCHONDRIAL GENOME)

**SAMPLE:**
EDTA blood sample or DNA

**TURNAROUND TIME:**
2-3 weeks (primary, secondary, tertiary)
4-6 weeks (clinical report)

## COMPLETE COVERAGE: MITOCHONDRIAL GENOME

*Testing of the mitochondrial genome along with WES analysis*

Primary mitochondrial disorders develop due to mutations either in the mitochondrial DNA (mtDNA) or the nuclear DNA (nDNA). They **can manifest at any age** and are characterized by:

- diverse clinical phenotype
- complex clinical presentation
- multi-system involvement

The mtDNA mutation's type and size, localization, and the level of heteroplasmy (presence of two or more mtDNA populations within a cell) determine disease penetrance. The marked clinical variation observed in patients with mitochondrial disorders makes diagnosis **extremely challenging**.

Our Postnatal WES + Mitochondrial Genome analysis:

- detects low levels of heteroplasmy
- covers single nucleotide variants (SNV), small insertions and deletions (INDEL) and copy number variants (CNV)

***References***

*Rabbani, Bahareh et al. "The Promise of Whole-Exome Sequencing in Medical Genetics." Journal of Human Genetics vol. 59,1, 2014, 5-15.*

*Manickam, Kandamurugu, et al. "Exome and Genome Sequencing for Pediatric Patients with Congenital Anomalies or Intellectual Disability: An Evidence-Based Clinical Guideline of the ACMG." Genetics in Medicine, vol. 23, no. 11, 2021, 2029–2037.*

# WHY **RECOMMEND** TESTING?

- WES increases the chances of **finding the genetic cause** of diseases with complex and non-specific symptoms.
- **Reduces** the time and cost of a diagnosis.
- **Supports clinicians** in diagnosis and clinical management of patients.
- Provides information about **recurrence risk** (chance of having another child with a similar condition).

## CASE STUDY

Four-year-old male child presenting with short stature and neck, low-set ears, high posterior hairline and moderate intellectual disability with delayed speech and language development. He was referred for WES analysis following *ACMG guidelines.

### WES analysis results

A pathogenic, ***de novo***, heterozygous variant in exone 13 of the ***PTPN11* gene**, associated with the patient's clinical symptoms. The variant is autosomal dominant and is associated with Noonan Syndrome 1.

### WES outcome

According to the patient's clinical and genetic findings, the healthcare team could provide a diagnosis and a clinical management plan which **considered the triggers and complications of Noonan Syndrome** and the observed symptoms. Genetic counseling for future family planning was recommended for the family.

Considering the complexity of the symptoms, a WES analysis was necessary to identify the variant and the disorder.

# **SPECIFICATIONS** & **COVERAGE**

Medicover Genetics WES analysis provides **increased depth of coverage**. The test examines **adjacent non-coding sequence**, and **provides deep**, **uniform coverage** even across GC-rich regions. Medicover Genetics applies a **robust bioinformatic pipeline** and variant calling software for precise result analysis and interpretation.

### MUTATIONS COVERED
SNV, small INDEL, and CNV

### HUMAN REFERENCE GENOME
GRCh38

### MEDIAN READ DEPTH
100x

### COVERAGE
>97% over 20x

**American College of Medical Genetics and Genomics guidelines "recommend exome sequencing or genome sequencing as a first-tier or second-tier test [...] for patients with one or more congenital anomalies prior to one year of age or for patients with developmental delay/intellectual disability with onset prior to 18 years of age."*

## **BENEFITS** OF WES Decode&Discover

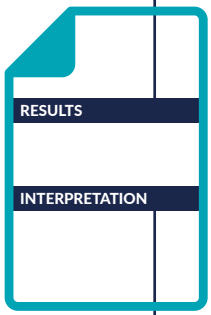
**FLEXIBLE**
3 analyses and testing options

**ACCURATE**
Validated results

**EXTENSIVE**
Examination of ~20,000 genes

**BENEFICIAL**
Can shorten the diagnostic process

## WHAT ARE THE POSSIBLE **OUTCOMES** OF THE TEST?




### CLINICALLY SIGNIFICANT VARIANT DETECTED

A pathogenic or likely pathogenic genetic variant has been identified in a gene or genes associated with the clinical characteristics provided.

### NO CLINICALLY SIGNIFICANT VARIANT DETECTED

No disease-causing genetic variant related to the clinical characteristics provided has been identified in the genes tested.

### VARIANT OF UNCERTAIN SIGNIFICANCE

A genetic change has been detected, but it is currently unknown whether that change is associated with a genetic disorder.

### SECONDARY FINDINGS

Pathogenic variants in specific genes recommended by American College of Medical Genetics and Genomics guidelines can be reported upon request and signed consent.

Summary of the results and recommendations

*Variant re-evaluation can be requested.*

## HOW TO **ORDER**?

Recommend WES analysis to your patient

Collect the sample(s)

Send the sample(s) to **Medicover Genetics**

The sample(s) will be analyzed at **Medicover Genetics** laboratories

Results will be sent to you

## MORE **QUESTIONS**?

If you have additional questions or concerns, please contact us at **info.genetics@medicover.com**

MEDICOVER GENETICS

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INTL-WES-DR-V03.1