Whole Exome Sequencing in genetic diseases

The clinical / clinical pathology partnership that benefits patients
Whole Exome Sequencing ("WES") in diagnostic practice

The term “genetic disease” embraces a wide range of pathologies. The identification of causal variants facilitates clinical diagnosis and prognosis, patient management, genetic counselling and, in some cases, the adjustment of therapeutic care to individual patient needs.

The conventional step-by-step sequencing approach (gene by gene or panel by panel), which sometimes follows complex decision trees, is gradually being replaced by “Whole Exome Sequencing” as a first-tier technique, in an increasing number of indications\(^1\)\(^-\)\(^2\).

Whole Exome Sequencing makes it possible to sequence, in a single step, all of the coding regions of the human genome (containing more than 85% of pathogenic mutations) at an affordable price.

As a first-tier technique, WES provides:

- time-saving compared to carrying out a series of gene panels,
- a diagnostic test for patients where the clinical examination does not enable the clinician to identify the gene/panel of genes to be tested,
- retrophenotyping in atypical clinical pictures,
- an improved diagnostic yield compared to the gene panel.
The “Whole Exome” test by Eurofins Biomnis

In the laboratory

- A dedicated team of clinical pathologists, technicians and bioinformatics specialists
- Continuous biopathological support, from the implementation of the test to the interpretation of the results.

Sequencing

- ~98% 30X*
- > 99% sensitivity**

At the end of the analytical process

- An interpretation of an average of 30,000 variants in consultation with the clinician
- Provision of raw data (fastQ, VCF, BAM and quality report) via a secure interface
- Report with detailed results within an optimised period of 6 weeks

Why Eurofins Biomnis?

- Specialised medical pathology laboratory
- ISO 15189 accreditation (CAP standard equivalent)
- Authorisation to perform constitutional genetics tests
- Certified clinical pathologists
- Expertise in sequencing techniques in diagnostic practice

The clinical/clinical pathology partnership that benefits patients

One of the challenges of exome sequencing is the interpretation of variants.

To actively involve partner clinicians and clinical pathologists in the interpretation of data, Eurofins Biomnis provides access to SeqOne, a secure bioinformatics platform.

*target Refseq + 2 base pairs
**data calculated from SNV’s from NIST reference samples, for 40 million pairs of reads generated.
SeqOne, for optimal diagnostic performance

Thanks to this platform, a joint interpretation with Eurofins Biomnis or an autonomous interpretation is possible. This ensures optimal diagnostic performance (laboratory experience and literature\(^3\)).

Why SeqOne?

- **Simplicity of interpretation**: intuitive platform and possibility of joint interpretation
- **Search for pathogenic variants**: prioritisation of pathogenic variants by AI and by phenotype, automated ACMG score calculation and detailed investigation with specific databases.
- **Customised features**: solo or trio analysis, OMIM pro version database and private annotation management
- **Safety and Quality**: coverage control, health data host (HDS), and CE IVD certification
- **Training and assistance**: support in the handling of the tool and ongoing operational support.

The data is accessible and available to the clinician at all times, which allows:

- reanalysis, when if required;
- use of data for research.
3 interpretation options/solutions

Whole Exome Test by Eurofins Biomnis

Basic interpretation report

Access to the bioinformatics interface

1. Eurofins Biomnis interpretation

2. Joint interpretation

3. Autonomous interpretation

Partner Clinicians & clinical pathologists

Detailed interpretation report

References


## Whole Exome Sequencing & Access to the interpretation interface

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<th>Detailed report</th>
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<td>Turnaround</td>
<td>6 weeks for a negative result</td>
<td>4 weeks</td>
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<td>Extended deadline if additional examinations necessary</td>
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<tr>
<td>Indications</td>
<td>intellectual disability, neurodevelopmental disorders, syndrome-based disorders, clinical pictures which do not directly suggest a specific gene test or gene panel, or negative result for these primary tests, organ damage (kidney, heart, etc.).</td>
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<tr>
<td>Sample</td>
<td>Solo: 5 mL EDTA whole blood or DNA sample</td>
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<td></td>
<td>Duo/Trio: 5mL EDTA whole blood or DNA sample from relative</td>
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<td>Conservation &amp; transport</td>
<td>Room temperature</td>
<td></td>
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<tr>
<td>Technique</td>
<td>Exome sequencing + bioinformatics pipeline</td>
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<td>B34-INTGB Test request form available on <a href="http://www.eurofins-biomnis.com">www.eurofins-biomnis.com</a> &gt; Test guide &gt; Analysis code EXOME</td>
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<td>Complementary test</td>
<td>Study of relative persons by Sanger sequencing: 5 mL EDTA whole blood or DNA sample from relative</td>
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