A new world in Clinical Genetics

Where no technology has gone before…

Next-generation sequencing (NGS) has catapulted healthcare into a revolutionary genomics era.
Whole genome sequencing (WGS) is becoming one of the most widely used applications, providing the most comprehensive genetic testing available for the diagnosis of rare diseases.

WHOLE GENOME SEQUENCING

Extraordinary technological advances in NGS have made feasible WGS as a highly accessible clinical test for numerous indications.
WGS analyzes the entire coding and non-coding regions of the DNA providing detailed information of thousands of genes and intronic regions.
The gene coding regions represent only 1-2% of the entire genome of the patient and it has been demonstrated by numerous clinical studies, that variants in non-coding regions, where the regulatory information that controls gene expression is contained, are determinants in the etiology of many complex pathologies.
The information provided by WGS study increases significantly the ability to characterize these complex pathologies, especially when TRIO study is performed (index case and parents). In these cases, the diagnostic capability is superior than the available exome sequencing.

A new era in clinical diagnostics! An all-in-one solution

At this point, microarrays, NGS panels and single gene testing are focused on the analysis of known variants in specific genes and exome sequencing of only the coding regions of the DNA. In some cases, these studies are enough to identify the cause of the disease, however, due to technical limitations of these analyses, other cases remain without genetic characterization.

The sequencing of the complete genome offers a comprehensive identification of many more variants simultaneously in an all-in-one solution. WGS offers a holistic view of all DNA, in addition to detecting CNVs, translocations, splice site variants, regulatory region variants and insertions/ deletions.

WHEN IS WGS RECOMMENDED?

- Unclear or complex phenotypes with multiple differential diagnoses;
- Phenotype that does not correspond to any known genetic disease;
- Unsuccessful previous genetics testing;
- Heterogeneous disorder;
- Suspected genetic disorder with no specific genetic test available.

» Intellectual disability
Congenital anomalies
Development delay
Neurological disorders
Autism spectrum disorders
Rare diseases

Genetyca ICM has available
- Whole Genome Sequencing
- Whole Genome Sequencing Trio

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GENOME ADVANTAGES OVER EXOME

Numerous complex pediatric pathologies, such as intellectual disability, development delay or behavioral disorders, still don't have a genetic cause characterization using array CGH and exome sequencing.

Several studies have demonstrated the advantages of WGS for mutation detection. In a recent publication (1), it is demonstrated that genome sequencing allows a conclusive molecular diagnosis of 42% of the patients that had previously undergo array CGH and exome sequencing without establish a molecular diagnosis. Besides this, WGS analyses of paediatric populations has shown identification of clinically relevant variants in ~ 40% of those with autism and ~ 60% of those with intellectual disability (2).

There have been many recent successful applications of WGS in establishing the etiology of complex diseases and guiding the therapeutic decision, providing definite answers for patients with unsolved diagnoses. Clinical implementation of WGS as a primary test will provide a higher diagnostic yield than any other currently available technology and potentially reduce the time required to reach a genetic diagnosis.

SAMPLE REQUIREMENTS

5 mL of peripheral blood in EDTA tube at room temperature

COVERAGE

- Average > 99%
- Diagnostic > 97,5 %

TURNAROUND TIME

15 weeks

TECHNOLOGY AND WORKFLOW

At Genetyca ICM, WGS is performed with the most advanced technology in the market – sequencing using combinatorial Probe-Anchor Synthesis (cPAS) and DNA Nanoballs (DNB) technology developed by Complete Genomics in California. The combination of linear amplification and DNB technology reduces the error rate when compared to other NGS systems, while enhancing the signal and providing an optimal accuracy increasing the chip utilization. The large amount of data is analyzed by our team of expert bioinformatics, who perform the first filtering and identify the variants of interest. Then, our team of clinical geneticists evaluates each of these variants clearly and precisely according to the clinical context of the patient.

REFERENCES

1. Gilissen, C. et al. Genome sequencing identifies major causes of severe intellectual disability. Nature 511, 344–347 (2014).
2. Jiang, Y. H. et al. Detection of clinically relevant genetic variants in autism spectrum disorder by whole-genome sequencing. Am. J. Hum. Genet. 93, 249–263 (2013).