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WHOLE GENOME SEQUENCING
COMPREHENSIVE GENETIC TESTING TO ADVANCE DIAGNOSIS

Mayo Clinic Laboratories' whole genome sequencing (WGS) test utilizes next-generation sequencing to interrogate nearly every base pair of an individual's DNA, including the mitochondrial genome.

WGS is one of the most comprehensive and cost-effective genetic testing methods for patients with clinical features that do not fit within one disorder, or for patients with a suspected genetic disorder that could have many underlying genetic causes. WGS is recommended for patients with one or more congenital anomalies, developmental delay, intellectual disability, or a suspected underlying genetic condition. While both whole exome sequencing (WES) and WGS interrogate all genes in the human genome, WGS is more comprehensive in the variant classes it can identify.

Key testing

WGSDX | Whole Genome Sequencing for Hereditary Disorders, Varies

Advantages

- Used as a first-tier test to identify a molecular diagnosis in patients with suspected genetic disorders.
- Serves as a second-tier test for patients whose previous genetic testing was negative.
- Provides a potentially cost-effective alternative to establishing a molecular diagnosis compared to performing multiple independent molecular assays.

UP TO 65%

Percentage of patients who had direct changes to care based on WES or WGS results; higher likelihood of impact dependent upon timing of testing and patient population[1,2,3]

UP TO 56%

Percentage of diagnostic yield overall; higher yields experienced when WGS is used as a first-tier test or in cohorts with specific phenotypes[1,2,3,4,5]

UP TO 30%

Percentage of increased diagnostic yield with WGS after prior negative test result, including whole exome sequencing[2,5,6]

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Finding answers for patients

As a first-tier test for diagnosing hereditary disorders, WGS detects single nucleotide variants, small insertions and deletions, copy number variants, mitochondrial genome variants, and select spinal muscular atrophy and repeat expansion variants throughout the genome. The information provided by this test can provide:

- Better understanding of the natural history/prognosis.
- Targeted management (anticipatory guidance, management changes, specific therapies).
- Predictive testing of at-risk family members.
- Testing and exclusion of disease in siblings or other relatives.
- Recurrence risk assessment.

Improving the value of testing

Our approach to WGS is returning results for an affected individual that can be compared and contextualized to results from biological parents or other informative family members when those samples are included at the time of analysis. These comparator specimens assist with result interpretation and increase the diagnostic yield of the testing. Each WGS order is carefully reviewed by a team of genetic counselors who ensure the indication for test ordering is clinically appropriate.

Beyond the test result

Our WGS test is backed by a team of laboratory scientists, genetic counselors, and clinicians who are integrated into the clinical practice at Mayo Clinic. This collaboration allows for direct consultation with practicing clinicians in instances of complex or unclear cases. WGS results are interpreted by a collaborative team who consider previous evaluations and test results from genetic studies, biochemical testing, and imaging studies as part of the genetic data review. Genetic disease experts are available to answer questions about test findings or the need for additional testing.

WGSDX | Whole Genome Sequencing for Hereditary Disorders, Varies

WGSR | Whole Genome Sequencing Reanalysis, Varies

- Reanalysis of previously generated genome sequencing data.

CMPRG | Family Member Comparator Specimen for Genome Sequencing, Varies

- For family member comparator samples used to help interpret WGS results in the patient.

FMTT | Familial Variant, Targeted Testing, Varies

- Familial testing to assess segregation of variants previously identified in a family member.

[1]NICUSeq Study Group, Krantz ID, Medne L, et al. Effect of whole-genome sequencing on the clinical management of acutely ill infants with suspected genetic disease: a randomized clinical trial [published correction appears in *JAMA Pediatr.* 2021 Dec 1;175(12):1295]. *JAMA Pediatr.* 2021;175(12):1218-1226. doi:10.1001/jamapediatrics.2021.3496 [2]100,000 Genomes Project Pilot Investigators, Smedley D, Smith KR, et al. 100,000 Genomes pilot on rare-disease diagnosis in health care — preliminary report. *N Engl J Med.* 2021;385(20):1868-1880. doi:10.1056/NEJMoa2035790 [3]French CE, Delon I, Dolling H, et al. Whole genome sequencing reveals that genetic conditions are frequent in intensively ill children. *Intensive Care Med.* 2019;45(5):627-636. doi:10.1007/s00134-019-05552-x [4]Turro E, Astle WJ, Megy K, et al. Whole-genome sequencing of patients with rare diseases in a national health system. *Nature.* 2020;583(7814):96-102. doi:10.1038/s41586-020-2434-2 [5]Carss KJ, Arno G, Erwood M, et al. Comprehensive rare variant analysis via whole-genome sequencing to determine the molecular pathology of inherited retinal disease. *Am J Hum Genet.* 2017;100(1):75-90. doi:10.1016/j.ajhg.2016.12.0036 Alfares A, Aloraini T, Subaie LA, et al. Whole-genome sequencing offers additional but limited clinical utility compared with reanalysis of whole-exome sequencing. *Genet Med.* 2018;20(11):1328-1333. doi:10.1038/gim.2018.41

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