MAYO CLINIC LABORATORIES

WHOLE EXOME SEQUENCING
ADVANCED UNDERSTANDING OF GENETIC DISEASE

For millions of individuals affected by rare diseases — 80% of which are genetic in origin[1] — knowing the underlying genetic cause is a critical first step in ending their diagnostic odyssey. Whole exome sequencing (WES) is recommended by the American College of Medical Genetics and Genomics (ACMG) as a first-line testing option to find underlying causes of rare genetic disorders in those who present with one or more congenital abnormalities or developmental delay and intellectual disability with onset prior to age 18.[2]

Mayo Clinic Laboratories' WES test uses next-generation sequencing to investigate approximately 20,000 genes in patients with suspected hereditary disorders. Not only is WES recommended to identify genetic variants in individuals with congenital abnormalities, it's also recommended for patients with clinical features or family histories suggestive of underlying genetic disease not distinguishable through other genetic tests.

Key testing

WESDX | Whole Exome Sequencing for Hereditary Disorders, Varies

Advantages

- Aligns with ACMG's evidence-based, 2021 clinical guidelines.
- Provides a comprehensive, cost-effective testing alternative to establish molecular diagnosis in individuals who might otherwise require multiple tests.
- Allows identification of genetic origin of conditions with more than one underlying cause.
- Useful for identifying rare disorders, newly described conditions, and making novel gene-disease associations.
- Optional reporting of medically actionable variants unrelated to the testing indication, including ACMG-approved secondary findings associated with hereditary cancer syndromes, cardiac syndromes, malignant hyperthermia, familial hypercholesterolemia, and others.
- Data generated from WES can be reanalyzed to detect gene-disease associations unknown at the time of original evaluation.

50%
Percentage of patients who underwent WES testing were clinically impacted[3]

36%
Percentage of patients who underwent WES testing received genetic diagnosis[4,5]

18%
Percentage of patients with diagnostic results from WES testing who received alternative treatment recommendations[6]

MAYO CLINIC LABORATORIES

Accurate answers, tailored management

Designed to detect single nucleotide variants, small insertions/deletions, and copy number variants, our precision WES test provides answers that profoundly impact a patient's medical journey.

- Covers at least 99% of bases at a read depth of over 30X.
- Sensitivity is estimated at above 99% for single nucleotide variants and above 95% for deletions up to 75 bp and insertions up to 47 bp.
- Detects multi-exon deletions/duplications. In some instances, single exon resolution can be achieved; however, the reliability of detection is variable due to isolated reduction in sequence coverage or inherent genomic complexity.

Variant identification not only enables insight into which gene(s) might be causing the disorder but can offer important information for family members about their risk for inheriting the same condition. Results also enable medical management and treatment targeted toward a specific diagnosis. Answers can put to rest a patient's search for a cause, ending the diagnostic odyssey.

Full spectrum WES testing in one laboratory

In addition to our comprehensive WES test, Mayo Clinic Laboratories offers adjunct testing for a more complete picture of the genetic landscape of patients and family members. Our full suite of testing includes:

WESDX | Whole Exome Sequencing for Hereditary Disorders, Varies

WESMT | Whole Exome and Mitochondrial Genome Sequencing, Varies

- Includes whole exome sequencing plus mitochondrial full genome analysis.

WESR | Whole Exome Sequencing Reanalysis, Varies

- Reanalysis of previously generated whole exome sequencing data.

CMPRE | Family Member Comparator Specimen for Exome Sequencing, Varies

- For family member comparator samples used to help interpret whole exome sequencing results in the patient.

FMTT | Familial Variant, Targeted Testing, Varies

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

[1]Rare Genetic Disorders. National Human Genome Research Institute. Updated April 13, 2018. Accessed October 19, 2022. https://www.genome.gov/dna-day/15-ways/rare-genetic-diseases [2]Exome and genome sequencing for pediatric patients with congenital anomalies or intellectual disability: an evidence-based clinical guideline of the American College of Medical Genetics and Genomics (ACMG). [3]Vissers LELM, van Nimwegen KJM, Schieving JH, et al. A clinical utility study of exome sequencing versus conventional genetic testing in pediatric neurology. *Genet Med.* 2017;19(9):1055-1063. [4]Clark MM, Stark Z, Farnaes L, et al. Meta-analysis of the diagnostic and clinical utility of genome and exome sequencing and chromosomal microarray in children with suspected genetic diseases. *NPJ Genom Med.* 2018;3:16. Published 2018 Jul 9. [5]Srivastava S, Love-Nichols JA, Dies KA, et al. Correction: Meta-analysis and multidisciplinary consensus statement: exome sequencing is a first-tier clinical diagnostic test for individuals with neurodevelopmental disorders. *Genet Med.* 2020;22(10):1731-1732. [6]Kuperberg M, Lev D, Blumkin L, et al. Utility of whole exome sequencing for genetic diagnosis of previously undiagnosed pediatric neurology patients. *J Child Neurol.* 2016;31(14):1534-1539.

NEWS.MAYOCLINICLABS.COM/GENETICS

SCAN to learn more

MC2775-523rev0324