Quest Diagnostics™

Helping to make earlier diagnosis possible for even the most challenging conditions

Exome testing is a well-established tool for diagnosing genetic conditions in situations where no targeted gene testing exists, or when targeted genetic testing has failed to identify the cause of disease. For many, a genetic diagnosis obviates the need for future diagnostic procedures or testing, and can inform treatment choices.

Exome testing has been shown to be successful at identifying the genetic cause of conditions when patients have multiple congenital anomalies and/or neurodevelopmental disorders. Detection rates range from about 28.8% to as high as 57.5% for this patient population.[1-7] Furthermore, in those with a genetic cause identified, 20.9% to 49% of patients had a change in their management based on the exome results.[1,8]

Exome with CNV Evaluation from Quest Diagnostics provides a new level of diagnostic and treatment possibilities positively impacting patient care and quality of life. Our test delivers exome sequencing with a mean read depth of 126X, a validated CNV evaluation, and mitochondrial genome results with a mean read depth of 550X. The exome provides a coverage of 99.6% at 20X. These leading metrics come with the added benefit of having both mitochondrial genome sequencing and CNV analysis included.

Quest's metrics, combined with our strong portfolio of cytogenetic and biochemical genetic tests that are often precursors to exome testing, make us a single source for all your testing needs, both routine and advanced testing.

Quest Diagnostics delivers the quality testing patients need. Our in-network status in most health plans helps minimize patients' out-of-pocket costs. You can order with confidence through your routine ordering channels.

Quest Diagnostics offers:

- Easy access to genetic counselors and other medical experts

- Benefit investigation, prior authorization, and financial assistance services for all third-party billed exome orders

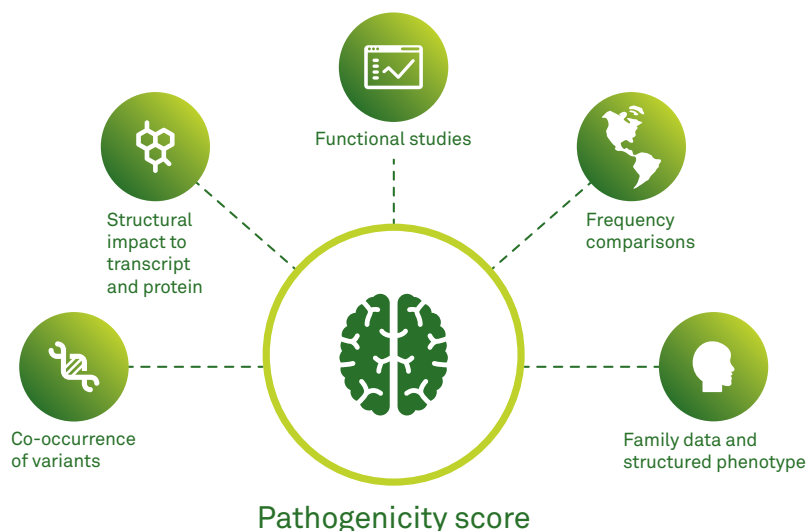- A large in-network payer base to help minimize patient risk for high out-of-pocket costs

- Convenient ways to order and receive results through Quest's Quanum™ eLabs or your institution's interfaced EMR

QuestExome.com

Standardized classification method used for variant curation and reporting

To assess the pathogenicity of genetic variants in patients, we use a rules-based, weighted process (published by our group in 2015) that is aligned with the American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP) guidelines. We conduct a thorough investigation of published research, which is then integrated with data from our internal dataset, external databases, research collaborations, and clinician-provided phenotypes. Close collaboration among our genomic variant scientists, genetic counselors, and clinical laboratory directors facilitates the collection and systemic analysis of relevant information in order to provide clinically-informative results to our clients.

For more information on the variant assessment process, please visit QuestDiagnostics.com/VariantIQ.

Functional studies

Structural impact to transcript and protein

Frequency comparisons

Co-occurrence of variants

Family data and structured phenotype

Pathogenicity score

Test code	Test name	CPT code[a]	Preferred speciment[b]	Sample specifications	Turnaround time	Specimen stability
36935	Exome with CNV Evaluation, Proband	81415	Whole Blood in lavender-top (EDTA) tubes	Adult: 8 mL (6 mL min) Pediatric (0-3 years): 2 mL (1 mL min)	6-8 weeks	Room temperature: 10 days Refrigerated: 10 days Frozen: unacceptable
36936	Exome with CNV Evaluation, Trio	81415, 81416 x2	Whole Blood in lavender-top (EDTA) tubes	Adult: 8 mL (6 mL min) Pediatric (0-3 years): 2 mL (1 mL min)	6-8 weeks	Room temperature: 10 days Refrigerated: 10 days Frozen: unacceptable
36937	Exome with CNV Evaluation, Duo	81415, 81416	Whole Blood in lavender-top (EDTA) tubes	Adult: 8 mL (6 mL min) Pediatric (0-3 years): 2 mL (1 mL min)	6-8 weeks	Room temperature: 10 days Refrigerated: 10 days Frozen: unacceptable
36939	Exome with CNV Evaluation, Family Member	Not applicable	Whole Blood in lavender-top (EDTA) tubes	Adult: 8 mL (6 mL min) Pediatric (0-3 years): 2 mL (1 mL min)	Not applicable	Room temperature: 10 days Refrigerated: 10 days Frozen: unacceptable
36938	Exome with CNV Evaluation, Reanalysis	81417	No sample needed	No sample needed	6-8 weeks	No sample needed

[a]The CPT codes provided are based on AMA guidelines and are for informational purposes only. CPT coding is the sole responsibility of the billing party. Please direct any questions regarding coding to the payer being billed.
[b]DNA will be extracted from the sample and tested for changes in multiple genes.

Learn more at QuestExome.com

Quest Diagnostics offers healthcare providers access to genetic experts who can assist in understanding how to interpret your patient's results. **For questions related to the Exome with CNV Evaluation, please contact our Genomic Client Services team at 1.866.GENE.INFO (1.866.436.3463).**

The classification and interpretation of the variant(s) identified reflect the current state of Quest Diagnostics' understanding at the time of the report. Variant classification and interpretation are subject to professional judgment, and may change for a variety of reasons, including but not limited to, updates in classification guidelines and availability of additional scientific and clinical information. This test result should be used in conjunction with the healthcare provider's clinical evaluation.

References
1. Iglesias A, Anyane-Yeboa K, Wynn J, et al. The usefulness of whole-exome sequencing in routine clinical practice. *Genet Med.* 2014;16(12):922-931. doi: 10.1038/gim.2014.58
2. Valencia CA, Husami A, Holle J, et al. Clinical Impact and Cost-Effectiveness of Whole Exome Sequencing as a Diagnostic Tool: A Pediatric Center's Experience. *Front Pediatr.* 2015;3:67.
3. Retterer K, Scuffins J, Schmidt D, et al. Assessing copy number from exome sequencing and exome array CGH based on CNV spectrum in a large clinical cohort. *Genet Med.* 2015;17(8):623-629.
4. Stark Z, Tan TY, Chong B, et al. A prospective evaluation of whole-exome sequencing as a first-tier molecular test in infants with suspected monogenic disorders. *Genet Med.* 2016;18(11):1090-1096.
5. Meng L, Pammi M, Saronwala A, et al. Use of Exome Sequencing for Infants in Intensive Care Units: Ascertainment of Severe Single-Gene Disorders and Effect on Medical Management. *JAMA Pediatr.* 2017;171(12):e173438.
6. Vissers L, 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.
7. Trujillano D, Bertoli-Avella AM, Kumar Kandaswamy K, Weiss ME, Köster J, Marais A, Paknia O, Schröder R, Garcia-Aznar JM, Werber M, Brandau O, Calvo Del Castillo M, Baldi C, Wessel K, Kishore S, Nahavandi N, Eyaid W, Al Rifai MT, Al-Rumayyan A, Al-Twaijri W, Alothaim A, Alhashem A, Al-Sannaa N, Al-Balwi M, Alfadhel M, Rolfs A, Abou Jamra R. Clinical exome sequencing: results from 2819 samples reflecting 1000 families. *Eur J Hum Genet.* 2017 Feb;25(2):176-182. doi: 10.1038/ejhg.2016.146. Epub 2016 Nov 16. PMID: 27848944
8. Soden SE, Saunders CJ, Willig LK, et al. Effectiveness of exome and genome sequencing guided by acuity of illness for diagnosis of neurodevelopmental disorders. *Sci Transl Med.* 2014;6(265):265ra168.

Image content used for illustrative purposes only. Person depicted in the content is a model.

QuestDiagnostics.com

Quest Diagnostics™