Helix

THIS IS A DIAGNOSTIC TEST

Helix Whole Exome+ Sequencing, Trio

Patient Name: John Doe	**Patient ID:** TST23456	**Provider Name:** HELIX GENOMICS	**Order Date:** 2026-07-10
Date of Birth: 1996-02-27	**Helix ID:** HLX-34567	**Collection Date:** 2026-07-10	**Report Date:** 2026-07-17

Results NEGATIVE

This test did not detect any clinically significant variants within the analyzed gene(s).

Genetic test results should be interpreted in the context of an individual's personal medical and family history. Alteration to medical management is NOT recommended based solely on this result. It is important to note that this assay cannot detect all variants known to increase disease risk. Clinical correlation is advised.

Test Description

The Helix Whole Exome+ Sequencing test evaluates the coding regions of the human genome including the mitochondrial genome to identify genetic variants associated with the clinical features described at ordering. This test is available as Proband-only (EXPR1), Duo (EXDU1), or Trio (EXTR1). When parental samples are provided (using EPAR1 for ordering in EHR), segregation analysis is performed to aid in variant interpretation. Mitochondrial genome analysis is included by default, with heteroplasmy detection at ≥2% for blood and buccal specimens and ≥3% for saliva.

Genes Tested

All protein-coding genes in the human nuclear genome are evaluated. Analysis and reporting are guided by the clinical features (HPO terms) described at ordering. The mitochondrial genome is also analyzed.

Methods & Limitations

Extracted DNA is enriched for targeted regions and then sequenced using the Helix Exome+ (R) assay on an Illumina DNA sequencing system. Data is then aligned to a modified version of GRCh38 and all genes are analyzed using the MANE transcript and MANE Plus Clinical transcript, when available. Small variant calling is completed using a customized version of Sentieon's DNAseq software, augmented by a proprietary small variant caller for difficult variants. Copy number variants (CNVs) are then called using a proprietary bioinformatics pipeline based on depth analysis with a comparison to similarly sequenced samples. Genome-wide copy number analysis is also performed to detect clinically significant large-scale copy number changes, independent of the clinical features provided at ordering. Reportable variants in PMS2 exons 11–15 are confirmed by PacBio long reads. Both the MSH2 Boland inversion (exons 1–7) and the BRCA2 Alu insertion are detected by identifying discordant read-pairs spanning the breakpoints. The mitochondrial genome is sequenced and analyzed for variants with heteroplasmy levels ≥2% for blood and buccal specimens and ≥3% for saliva specimens; when the mother's sample is available, it is utilized for mitochondrial analysis. For Duo and Trio orders, parental samples are sequenced and used for segregation analysis to aid in variant interpretation, including identification of de novo variants. Interpretation is performed by Revvity, Inc. (CLIA #39D0673919, Address 250 Industry Drive, Suite 400 Pittsburgh, PA 15275–1017). Interpretation is based upon guidelines published by the American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP) or their modification by ClinGen Variant Curation Expert Panels when available. Interpretation is limited to the transcripts indicated on the report, +/-10 bp into intronic regions, except as noted below. Helix variant classifications include pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign, and benign. Variants classified as pathogenic, likely pathogenic, or VUS are included in the report. Variants in genes of uncertain significance are not reported unless highly suspicious. Unless a mitochondrial disorder is indicated, only pathogenic and likely pathogenic mitochondrial variants are included. All reported variants (except for VUSs with limited evidence of pathogenicity) are confirmed through secondary manual inspection of DNA sequence data or orthogonal testing. Benign and likely benign variants are not reported but are available upon request. Risk estimations and management guidelines included in this report are based on analysis of primary literature and recommendations of applicable professional societies, and should be regarded as approximations.

Based on validation studies, this assay delivers > 99% sensitivity and specificity for single nucleotide variants and insertions and deletions (indels) up to 20 bp. Larger indels and complex variants are also reported but sensitivity may be reduced. Most deletions and duplications that are at least three exons in length are reliably detected, depending on the context of the underlying sequence. This test may not detect variants in challenging regions (such as short tandem repeats, homopolymer runs, and segmental duplications), CNVs spanning fewer than 3 exons, chromosomal aneuploidy, or variants present at levels suggestive of mosaicism. Phasing will be attempted and reported, when possible. Structural rearrangements such as inversions, translocations, complex rearrangements, and gene conversions are not tested in this assay unless explicitly indicated. Additionally, deep intronic, promoter, and enhancer regions may not be covered. It is important to note that this assay cannot detect all variants known to increase disease risk, and that a negative result does not guarantee that the tested individual does not carry a rare, undetectable variant in the genes analyzed. In addition to this test, providers may order the Helix Hereditary Actionable Diseases Screen for any of the submitted samples, which reports secondary findings in accordance with ACMG recommendations. Any potential incidental findings outside of the genes and conditions evaluated will not be identified, nor reported. The results of a genetic test may be influenced by various factors, including bone marrow transplantation, blood transfusions, or in rare cases, hematolymphoid neoplasms.

Gene Specific Notes:
For specific questions regarding genes, reference transcripts, or specific regions covered, contact Helix Clinical Support at clinicalsupport@helix.com.

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Disclaimer

This test was developed and validated by Helix, Inc. with interpretation services provided by Revvity, Inc. This test has not been cleared or approved by the United States Food and Drug Administration (FDA). The Helix laboratory is accredited by the College of American Pathologists (CAP) and certified under the Clinical Laboratory Improvement Amendments (CLIA #: 05D2117342) to perform high-complexity clinical tests. This test is used for clinical purposes. It should not be regarded as investigational use only or for research use only.

Report Signed By

No signature provided

Helix's Sequence Once, Query Often® Model

When your provider orders a genetic test through Helix, we use our proprietary Sequence Once, Query Often® model to perform whole exome sequencing and analyze the specific genes related to the test. Helix securely stores your whole exome for future clinical use. With your permission, this allows your health care providers to order future medically necessary genetic tests from Helix without needing another sample. Instead, these tests are conducted through digital analysis of your stored genetic information.

To learn more about how Helix protects the privacy and security of your genetic information and learn more about your rights, please visit https://www.helix.com/privacy-and-policy-highlights .