

Helix Family Variant Testing

Patient Name: Jane Doe	Patient ID: XXXXXX	Provider Name: Client Client	Order Date: 04-24-2026
Date of Birth: 01-01-1990	Helix ID: HELIX123456	Collection Date: 04-24-2026	Report Date: 04-30-2026

Results NEGATIVE

Targeted testing for a known familial variant was requested. The variant, c.2862C>G (p.Tyr954Ter) in the MSH6 gene, was not identified in this individual. This determination was made using the NM_000179.3 transcript. This test did not detect any clinically significant variants within the analyzed gene(s). Only MSH6 was analyzed.

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

Helix Family Variant Testing is a targeted test to identify the presence or absence of one or more specific variants previously identified as being present in a family member. The entire gene will be evaluated and therefore additional variants determined to be pathogenic or likely pathogenic within the gene ordered will also be included in the report. Variants of uncertain significance (VUS) will not be included except in cases where the variant specified in the order is determined to be a VUS. A separate order is required for variants in separate genes.

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. Reportable variants in PMS2 exons 12-15 are confirmed by PacBio long reads. The MSH2 Boland inversion (exons 1-7) is detected by identifying discordant read-pairs spanning the presumed breakpoint. 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. 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. Based on validation studies, this assay delivers > 99% sensitivity to multi-exon CNVs and > 90% sensitivity to single-exon CNVs. This test may not detect variants in challenging regions (such as short tandem repeats, homopolymer runs, and segment duplications), sub-exonic CNVs, chromosomal aneuploidy, or variants in the presence of mosaicism. Phasing will be attempted and reported, when possible. Structural rearrangements such as inversions, translocations, 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 genes analyzed. Any potential incidental findings outside of these genes and conditions 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.

Results do not rule out the presence of other variants related to this condition. Results may include incidental findings within the gene that are determined to be pathogenic or likely pathogenic.

Gene Specific Notes:
N/A

Disclaimer

This test was developed and validated by Helix, 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 or for research.

Report Signed By

Matt Ferber, Ph.D. FACMG

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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>.

SAMPLE