Helix Fundamental Carrier Screen

Item	Description
Test Name	Helix Fundamental Carrier Screen
Test Type	Carrier Screening
Catalog Number	FNCM1
Procedure Code	H000725-7
Test Description	This panel evaluates *CFTR* and *SMN1* for carrier status.
Genes Tested	*CFTR, SMN1*
Genetics Information	This test utilizes next-generation sequencing to detect single nucleotide variants, insertions and deletions up to 20 bp, and copy number variants in genes associated with autosomal recessive disorders.
Indications For Testing	Prenatal or preconception risk assessment for individuals who are pregnant or planning to conceive.
Clinical Descriptions	This panel includes the two genes that the American College of Medical Genetics and Genomics recommends all individuals who are pregnant or planning a pregnancy be tested for as a Tier 1 screen.
Interpretation	All detected variants are evaluated according to American College of Medical Genetics and Genomics recommendations. Variants are classified based on known, predicted, or possible pathogenicity and reported with interpretive comments detailing their potential or known significance.
Reclassification Of Variants	Helix reviews variant classifications annually when they arise in routine processes and upon request from providers. The timing of re-review depends on clinical risk. Providers can request a variant re-review by contacting Helix Customer Support. If a classification by Helix is updated, Helix identifies affected past patients and issues revised reports. Updated results are communicated to providers prior to results being uploaded to the EHR, and patients are notified through the EHR patient portal.
Variant Evaluation	Variant classification is performed using the guidelines set forth by the American College of Medical Genetics and Genomics and the Association for Molecular Pathology, with modifications as suggested by domain specific Expert Panels of the Clinical genome Resource (ClinGen) when available. Variant pathogenicity is categorized as benign, likely benign, variant of uncertain significance (VUS), likely pathogenic, or pathogenic.
Turnaround Time - Standard	Typically 7 to 21 days
Turnaround Time - Requery (SOQO®)	Typically 7 to 21 days
Available In NY State	Yes
Test Classification	This test was developed, and its performance characteristics determined, by Fulgent Therapeutics LLC in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

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Item	Description
Performing Laboratory Information	Fulgent Therapeutics LLC CLIA Laboratory Number: 05D2043189 Laboratory Hours of Operation: Monday-Friday (7AM-5PM PST) Saturday (8AM-3PM PST) Address: 4399 Santa Anita Ave., El Monte, CA 91731 Healthcare professionals may contact Helix directly to discuss results: Helix Customer Service: (844) 211-2070 Email: clinicalsupport@helix.com
Regulatory Information	CLIA Complexity: High Test Classification: Non-Waived/ Laboratory Developed Test
CLIA Category	Chemistry / Routine Chemistry

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- *(CFTR)* Cystic Fibrosis
- *(SMN1)* Spinal muscular atrophy

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Methods & Limitations for Helix Fundamental Carrier Screen

Genomic DNA was isolated from the submitted specimen indicated above (if cellular material was submitted). DNA was barcoded, and enriched for the coding exons of targeted genes using hybrid capture technology. Prepared DNA libraries were then sequenced using a Next Generation Sequencing technology. Following alignment to the human genome reference sequence (assembly GRCh37), variants were detected in regions of at least 10x coverage. For this specimen, 99.66% and 99.61% of coding regions and splicing junctions of genes listed had been sequenced with coverage of at least 10x and 20x, respectively, by NGS or by Sanger sequencing. The remaining regions did not have 10x coverage, and were not evaluated. Variants were interpreted manually using locus specific databases, literature searches, and other molecular biological principles. To minimize false positive results, any variants that do not meet internal quality standards are confirmed by Sanger sequencing. Variants classified as pathogenic, likely pathogenic, or risk allele which are located in the coding regions and nearby intronic regions (+/- 20bp) of the genes listed above are reported. Variants outside these intervals may be reported but are typically not guaranteed. When a single pathogenic or likely pathogenic variant is identified in a clinically relevant gene with autosomal recessive inheritance, the laboratory will attempt to ensure 100% coverage of coding sequences either through NGS or Sanger sequencing technologies ("fill-in"). All genes listed were evaluated for large deletions and/or duplications. However, single exon deletions or duplications will not be detected in this assay, nor will copy number alterations in regions of genes with significant pseudogenes. Putative deletions or duplications are analyzed using Fulgent Germline proprietary pipeline for this specimen. Bioinformatics: The Fulgent Germline v2019.2 pipeline was used to analyze this specimen.

These test results and variant interpretation are based on the proper identification of the submitted specimen, accuracy of any stated familial relationships, and use of the correct human reference sequences at the queried loci. In very rare instances, errors may result due to mix-up or co-mingling of specimens. Positive results do not imply that there are no other contributors, genetic or otherwise, to future pregnancies, and negative results do not rule out the genetic risk to a pregnancy. Official gene names change over time. Fulgent uses the most up to date gene names based on HUGO Gene Nomenclature Committee (https://www.genenames.org) recommendations. If the gene name on report does not match that of ordered gene, please contact the laboratory and details can be provided. Result interpretation is based on the available clinical and family history information for this individual, collected published information, and Alamut annotation available at the time of reporting. This assay is not designed or validated for the detection of low-level mosaicism or somatic mutations. This assay will not detect certain types of genomic aberrations such as translocations, inversions, or repeat expansions other than specified genes. DNA alterations in regulatory regions or deep intronic regions (greater than 20bp from an exon) may not be detected by this test. Unless otherwise indicated, no additional assays have been performed to evaluate genetic changes in this specimen. There are technical limitations on the ability of DNA sequencing to detect small insertions and deletions. Our laboratory uses a sensitive detection algorithm, however these types of alterations are not detected as reliably as single nucleotide variants. Rarely, due to systematic chemical, computational, or human error, DNA variants may be missed. Although next generation sequencing technologies and our bioinformatics analysis significantly reduce the confounding contribution of pseudogene sequences or other highly-homologous sequences, sometimes these may still interfere with the technical ability of the assay to identify pathogenic alterations in both sequencing and deletion/duplication analyses. Deletion/duplication analysis can identify alterations of genomic regions which include one whole gene (buccal swab specimens and whole blood specimens) and are two or more contiguous exons in size (whole blood specimens only); single exon deletions or duplications may occasionally be identified, but are not routinely detected by this test. When novel DNA duplications are identified, it is not possible to discern the genomic location or orientation of the duplicated segment, hence the effect of the duplication cannot be predicted. Where

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deletions are detected, it is not always possible to determine whether the predicted product will remain in-frame or not. Unless otherwise indicated, deletion/duplication analysis has not been performed in regions that have been sequenced by Sanger.

Gene Specific Notes:
CFTR: Analysis of the intron 8 polymorphic region (e.g. IVS8-5T allele) is only performed if the p.Arg117His (R117H) mutation is detected. Single exon deletion/duplication analysis is limited to deletions of previously reported exons: 1, 2, 3, 11, 19, 20, 21. CFTR variants primarily associated with CFTR-related isolated congenital bilateral absence of the vas deferens and CFTR-related pancreatitis are not included in this analysis. CFTR variants with insufficient evidence of being cystic fibrosis mutations will not be reported either. SMN1: The current testing method detects sequencing variants in exon 7 and copy number variations in exons 7-8 of the SMN1 gene (NM_022874.2). Sequencing and deletion/duplication analysis are not performed on any other region in this gene. About 5%-8% of the population have two copies of SMN1 on a single chromosome and a deletion on the other chromosome, known as a [2+0] configuration (PubMed: 20301526). The current testing method cannot directly detect carriers with a [2+0] SMN1 configuration, but can detect linkage between the silent carrier allele and certain population-specific single nucleotide changes. As a result, a negative result for carrier testing greatly reduces but does not eliminate the chance that a person is a carrier. Only abnormal results will be reported.

Disclaimer:
This test was developed, performed, and its performance characteristics determined by Fulgent Therapeutics LLC (CAP# 8042697, CLIA# 05D2043189), 4399 Santa Anita Ave., El Monte, CA 91731. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. Since genetic variation, as well as systematic and technical factors, can affect the accuracy of testing, the results of testing should always be interpreted in the context of clinical and familial data. For assistance with interpretation of these results, healthcare professionals may contact us directly at 844-211-2070 or by email at clinicalsupport@helix.com. It is recommended that patients receive appropriate genetic counseling to explain the implications of the test result, including its residual risks, uncertainties and reproductive or medical options.

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Targeted Genes & Methodology for Helix Fundamental Carrier Screen

The following applies to the Helix Fundamental Carrier Screen. Testing is performed to evaluate for the presence of variants in coding regions and extending to +/- 20 base pairs of adjacent intronic sequences on either side of the coding exons of the genes analyzed. In addition, the analysis will cover select non-coding variants, as listed below. Next-generation sequencing is performed to test for the presence of small variants and copy number variants in the genes analyzed. Confirmation of select reportable variants may be performed by alternate methodologies based on internal laboratory criteria.

This list is current from December 2025 to the present. This document is intended to highlight additional evaluations for variants of high clinical interest as well as technical limitations. For questions regarding genes, reference transcripts, or specific regions covered, contact Helix Customer Service at (844) 211-2070.

Genomic Build: GRCh37
Catalog Number: FNCM1

Gene	Transcript	Technical Limitations
CFTR	NM_000492.4	Analysis of the intron 8 polymorphic region (e.g. IVS8-5T allele) is only performed if the p.Arg117His (R117H) mutation is detected. Single exon deletion/duplication analysis is limited to deletions of previously reported exons: 1, 2, 3, 11, 19, 20, 21. CFTR variants primarily associated with CFTR-related isolated congenital bilateral absence of the vas deferens and CFTR-related pancreatitis are not included in this analysis. CFTR variants with insufficient evidence of being cystic fibrosis mutations will not be reported either.
SMN1	NM_000344.3	The current testing method detects sequencing variants in exon 7 and copy number variations in exons 7-8 of the SMN1 gene (NM_022874.2). Sequencing and deletion/duplication analysis are not performed on any other region in this gene. About 5%-8% of the population have two copies of SMN1 on a single chromosome and a deletion on the other chromosome, known as a [2+0] configuration (PubMed: 20301526). The current testing method cannot directly detect carriers with a [2+0] SMN1 configuration, but can detect linkage between the silent carrier allele and certain population-specific single nucleotide changes. As a result, a negative result for carrier testing greatly reduces but does not eliminate the chance that a person is a carrier. Only abnormal results will be reported.

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