Helix, Inc.
10170 Sorrento Valley Road, Suite 100
San Diego, CA 92121
Phone: 844-211-2070
Lab Director: Dr. Philip D. Cotter
CLIA: 05D2117342

DRAFT

Patient Information:	Accession:	Physician:	Report Date: **Draft**
Patient First, Patient Last	FT-XXXXXX	**Person Name**	
DOB:	Test#: FT-TSXXXXXX	Client Name	
Sex:	Order#: FT-ORXXXXXX		
MR#:	Ext Test#:	undefined, undefined undefined	
Patient#: FT-PTXXXXXX	Ext Order#:	undefined	
	Specimen Type:	Phone:	
	Collected:	Fax:	
	Received Date:		
	Authorized Date:		

DRAFT RESULTS

Carrier for **ONE** genetic condition

TEST PERFORMED

Helix Fundamental Carrier Screen

(2 Gene Panel; gene sequencing with deletion and duplication analysis)

Condition and Gene	Inheritance	Patient First, Patient Last	Partner
Spinal muscular atrophy silent carrier *SMN1*	AR	⊕ Possible Carrier c.*3+80T>G (p.?)	N/A

INTERPRETATION:

Notes and Recommendations:

- Based on these results, this individual is positive for a carrier mutation in 1 gene. Carrier screening for the reproductive partner is recommended to accurately assess the risk for any autosomal recessive conditions. A negative result reduces, but does not eliminate, the chance to be a carrier for any condition included in this screen. Please see the supplemental table for details.
- This carrier screening test does not screen for all possible genetic conditions, nor for all possible mutations in every gene tested. This report does not include variants of uncertain significance; only variants classified as pathogenic or likely pathogenic at the time of testing, and considered relevant for reproductive carrier screening, are reported. Please see the gene specific notes for details. Please note that the classification of variants can change over time.
- Patients may wish to discuss any carrier results with blood relatives, as there is an increased chance that they are also carriers. These results should be interpreted in the context of this individual's clinical findings, biochemical profile, and family history.
- Genetic counseling is recommended. Available genetic counselors and additional resources can be found at the National Society of Genetic Counselors (NSGC; https://www.nsgc.org)

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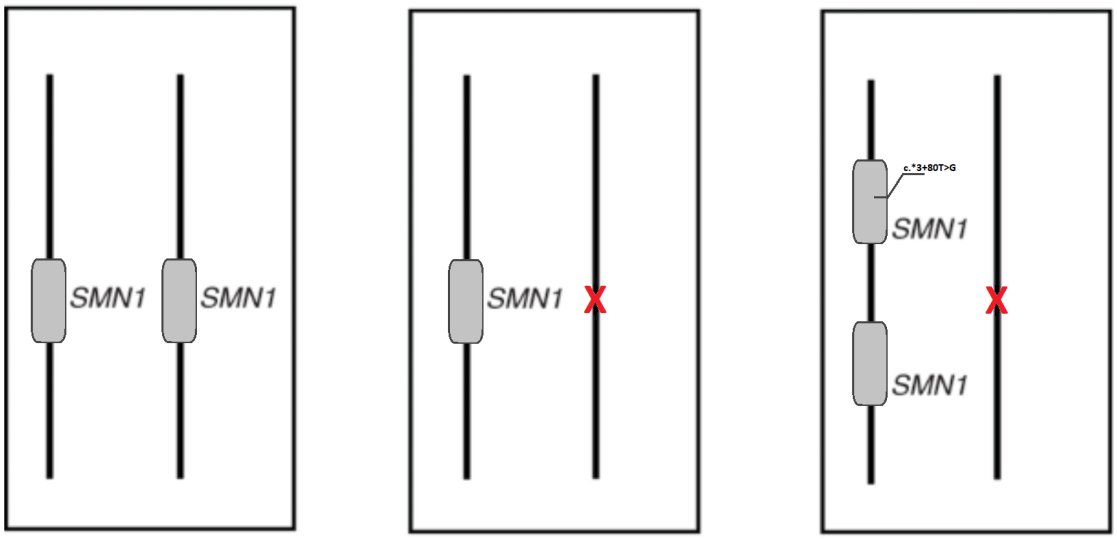
SPINAL MUSCULAR ATROPHY SILENT CARRIER

Patient	Patient First, Patient Last	Partner
Result	Possible Carrier	N/A
Variant Details	***SMN1*** (NM_000344.3) c.*3+80T>G (p.?)	N/A

What is Spinal muscular atrophy silent carrier?

Individuals typically have one copy of the *SMN1* gene on each chromosome, with carriers having a mutation in one copy that prevents normal function. A spinal muscular atrophy silent carrier is an individual who has two functional copies of the *SMN1* gene on one chromosome and zero copies of the *SMN1* gene on the other chromosome. This is a special scenario because the overall number of copies of *SMN1* may appear normal (i.e. two total copies of *SMN1*), however, that same person is considered a carrier for SMA since there are no functional copies of the *SMN1* gene on one chromosome. A person with this specific configuration of the *SMN1* genes is considered to be a "silent carrier".

Spinal muscular atrophy (SMA) affects nerve cells called motor neurons in the spinal cord and brainstem. The progressive degeneration of these nerve cells results in muscle weakness and atrophy (breakdown of muscle mass). Common symptoms include limited growth and poor weight gain, restrictive lung disease, and skeletal abnormalities, such as scoliosis or contractures of the joints. Severity and age of onset vary from severe and congenital (symptoms present at or before birth) (SMA type 0) to mild and adult-onset (SMA type 4). More than half of affected individuals have SMA type 1, in which symptoms usually start in the first 6 months of life and, without treatment, life expectancy is 2 years.



Wild type: 2 copies of *SMN1* (1+1) | Carrier: 1 copy of *SMN1* (1+0) | Silent carrier: 2 copies of *SMN1* (2+0)

For technical reasons, the chromosome with zero copies of SMN1 cannot always be directly observed in the DNA sequencing data (PubMed: 20301526, 32915251). Instead, silent carriers are observed based on the presence of two copies of the SMN1 gene and the specific variant c.*3+80T>G, which commonly occurs on the same chromosome with a duplication of the SMN1 gene. For individuals of Ashkenazi Jewish descent, c.*3+80T>G with two copies of SMN1 is considered as a positive finding for SMA carrier status (PubMed: 23788250, 36140824). While the positive predictive value of c.*3+80T>G with two copies of SMN1 can vary, nonetheless, for all other ethnic groups this variant is associated with an increased likelihood of being a carrier for SMA (PubMed: 36140824, 32066871, 36669496). Alternatively, in some individuals with c.*3+80T>G and two copies of SMN1 there is a possibility that these variants occur with a single copy of the SMN1 gene on each chromosome, and in that case the individual would not be considered a silent carrier for spinal muscular atrophy. In some cases, follow-up genetic testing of the parents of the SMN1 silent carrier may be helpful in further resolving the mutation status.

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What is my risk of having an affected child?

SMA is inherited in an autosomal recessive manner. If the patient and the partner are both carriers, the risk for an affected child is 1 in 4 (25%).

What kind of medical management is available?

It is important to provide proactive care and deliver timely intervention, as such the United States has recommended that SMA be added to state newborn screening panels, and most states, and some other countries, currently perform newborn screening for SMA. There is currently no cure for SMA, but management can include supportive, rehabilitative, and palliative care to manage symptoms and prevent complications. Treatments aim to address the effects of muscle weakness and may include dietary management and placement of a gastronomy tube (feeding tube), breathing exercises or machines to help with breathing problems, and surgical repair for scoliosis (spine curvature). Physical therapy can help with mobility, and assistive equipment such as wheelchairs or splints may also be necessary. There are FDA-approved drug and gene therapies to improve the symptoms and outcomes of SMA in some eligible individuals. Certain treatments must be given before symptoms begin in order to be effective. SMA type 3 (mild) and type 4 (adult-onset) typically do not affect life expectancy, but breathing issues are the largest cause of mortality in those with SMA types 0, 1, and 2, which occurs in infancy, childhood, or early adulthood depending on type of SMA and on treatment type and age of treatment initiation. Many drug therapies are still recent enough that their long-term effects on symptoms and life expectancy have not been studied completely, but they have been shown to greatly improve survival for those with SMA type 1. SMA treatment is an area of ongoing research; the most up-to-date information about clinical trials can be accessed from https://clinicaltrials.gov or from patient advocacy groups such as Cure SMA (https://www.curesma.org/) and the SMA Foundation (https://smafoundation.org/).

What mutation was detected?

The detected heterozygous variant was NM_000344.3:c.*3+80T>G (p.?). The detected variant NM_000344.3:c.*3+80T>G (p.?) is part of a SMN1 haplotype. In individuals with Ashkenazi Jewish heritage, the detection of this variant in concert with normal copy number of the SMN1 gene is considered positive for carrier status (PubMed: 23788250). For all other ethnic groups this variant is associated with an increased likelihood of being a carrier for SMA (PubMed: 36140824, 32066871, 36669496). This variant is located within the 3-prime untranslated region of the SMN1 gene, and has been linked with "silent carrier" status (or "[2+0]" configuration) where two copies of the SMN1 gene are present on the same chromosome and zero copies are present on the opposite chromosome. If an individual is detected as having two copies of SMN1 gene, these results would indicate that this individual may be a carrier for an SMN1 deletion on the other chromosome ("silent" carrier). The laboratory classifies this variant as pathogenic.

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GENES TESTED:

Helix Fundamental Carrier Screen - 2 Genes

This analysis was run using the Helix Fundamental Carrier Screen gene list. 2 genes were tested with 99.5% of targets sequenced at >20x coverage. For more gene-specific information and assistance with residual risk calculation, see the SUPPLEMENTAL TABLE.

CFTR, SMN1

METHODS:

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, 99.58% and 99.49% 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 FPLMv2.0 pipeline was used to analyze this specimen.

LIMITATIONS:

General Limitations

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 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. Saliva swab samples may have reduced sensitivity for CNVs and a higher CNV failure rate. 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 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.

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Gene Specific Notes and Limitations

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 conditions including isolated congenital bilateral absence of the vas deferens and CFTR-related pancreatitis are included in this analysis. *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.

Helix_FundamentalCarrierScreen_CarrierIVF_FulgentSampleReport_v3

SIGNATURE:

Example Signature

Example Director, Ph.D., CGMBS, FACMG on **04/29/2026**
Laboratory Director, Fulgent

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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To view the supplemental table describing the carrier frequencies, detection rates, and residual risks associated with the genes tested on any Beacon panel, please visit the following link:
Beacon Expanded Carrier Screening Supplemental Table