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:
Patient First, Patient Last
DOB:
Sex:
MR#:
Patient#: FT-PTXXXXXX

Accession:
FT-XXXXXX
Test#: FT-TSXXXXXX
Order#: FT-ORXXXXXX
Ext Test#:
Ext Order#:
Specimen Type:
Collected:
Received Date:
Authorized Date:

Physician:
Person Name
Client Name

undefined, undefined undefined
undefined
Phone:
Fax:

Report Date: **Draft**

DRAFT RESULTS

Carrier for **ONE** genetic condition

TEST PERFORMED

Helix Comprehensive Carrier Screen

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

Condition and Gene	Inheritance	Patient First, Patient Last	Partner
Arginase deficiency *ARG1*	AR	⊕ Carrier c.383A>G (p.Asp128Gly)	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.
- Testing for a 3 nucleotide (CGG) repeat sequence in the FMR1 gene was performed to screen for the carrier status for Fragile X Syndrome. The repeat sizes detected were: 20 and 30 repeats. These results are within the normal range. Therefore, this individual is not considered a carrier for Fragile X Syndrome.
- Testing for copy number changes in the SMN1 gene was performed to screen for the carrier status of Spinal Muscular Atrophy. The results for this individual are within the normal range for non-carriers. See Limitations section for more information.
- 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)

ARGINASE DEFICIENCY

Patient	**Patient First, Patient Last**	**Partner**
Result	⊕ Carrier	N/A
Variant Details	***ARG1*** (NM_000045.4) c.383A>G (p.Asp128Gly)	N/A

What is Arginase deficiency?

Arginase deficiency is characterized by episodic hyperammonemia of variable degrees, which rarely can be life-threatening or lethal. Individuals with this condition typically appear normal at birth and in early childhood. Affected individuals between one to three years experience deficiency in growth (slowing of linear growth) and develop spasticity, more commonly spastic diplegia, plateauing of cognitive development, and loss of developmental milestones. If left untreated, arginase deficiency usually progresses to severe spasticity, loss of ambulation, loss of bowel and bladder control, and severe intellectual disability.

What is my risk of having an affected child?

Arginase deficiency 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?

The main goals in the treatment of arginase deficiency are to lower arginine levels and to prevent hyperammonemia. People with arginase deficiency must be closely supervised by a medical team with experience treating metabolic disorders, and follow a low protein diet. They may need frequent blood tests to check arginine levels. The prognosis for people with arginase deficiency depends on many factors, including the severity of the disorder, the person's ability to follow the strict diet recommendations, and the response to treatment. It is thought that approximately 75% of people with arginase deficiency live long lives. If the disorder is not diagnosed or if a person with arginase deficiency is unable to follow the strict diet, the prognosis is poor and may include severe intellectual disability and muscle stiffness, loss of the ability to walk, and loss of bladder and bowel control.

What mutation was detected?

The detected heterozygous variant was NM_000045.4:c.383A>G (p.Asp128Gly). This variant has been reported in the homozygous state in five individuals with Arginase deficiency (PubMed: 7981719, 27038030).A functional study in *E.coli* found that this variant resulted in absent or significantly reduced RBC arginase activity (PubMed: 8902193). The laboratory classifies this variant as pathogenic.

GENES TESTED:

Helix Comprehensive Carrier Screen - 278 Genes

This analysis was run using the Helix Comprehensive Carrier Screen gene list. 278 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.

ABCA3, ABCD1, ABCC8, ACADM, ACADS, ACADVL, ACAT1, ADA, ADAMTS2, AGA, AGL, AGXT, AHI1, AIRE, ALG6, ALDH3A2, ALDOB, ALMS1, ALPL, AMT, ANO10, ARSA, ARSB, ARX, ASPA, ASL, ASNS, ASS1, ATM, ATP6V1B1, ATP7A, ATP7B, BBS1, BBS10, BBS12, BBS2, BCKDHA, BCKDHB, BCS1L, BLM, BTD, CAPN3, CC2D2A, CCDC88C, CDH23, CEP290, CERKL, CFTR, CHM, CHRNE, CLCN1, CLN3, CLN5, CLN6, CLN8, CLRN1, CNGB3, COL4A3, COL4A4, COL4A5, COL7A1, CPS1, CPT1A, CPT2, CRYL1, CTNS, CTSK, CYP11A1, CYP11B1, CYP11B2, CYP21A2, CYP27A1, CYP27B1, DCLRE1C, DBT, DHDDS, DHCR7, DLD, DMD, DNAH5, DNAI1, DNAI2, DYNC2H1, DYSF, ELP1, ERCC2, ERCC6, ERCC8, ETHE1, EVC, EVC2, EYS, F11, F9, FAH, FANCA, FANCC, FAM161A, FKRP, FKTN, FMO3, FMR1, G6PC, GAA, GALK1, GALC, GALNS, GALT, GAMT, GBA, GBE1, GCDH, GJB1, GJB2, GJB6, GLA, GLB1, GLDC, GLE1, GNE, GNPTAB, GNPTG, GNS, GRHPR, GRIP1, GUSB, HADHA, HBA1, HBA2, HBB, HGD, HGSNAT, HMGCL, HOGA1, HLCS, HPS1, HPS3, HSD17B4, HYLS1, IDS, IDUA, IL2RG, IVD, KCNJ11, L1CAM, LAMA2, LAMA3, LAMB3, LAMC2, LIPA, LOXHD1, LRP2, LRPPRC, MAN2B1, MCOLN1, MCCC1, MCCC2, MCPH1, MED17, MEFV, MESP2, MID1, MLC1, MMAA, MMAB, MMACHC, MTHFR, MTM1, MTTP, MUT, MVK, MYO7A, NAGA, NAGLU, NBN, NDUFAF5, NDUFS4, NDUFS6, NEB, NPC1, NPC2, NPHS1, NPHS2, NR0B1, NR2E3, NTRK1, OAT, OCA2, OPA3, OTC, PAH, PC, PCCA, PCCB, PCDH15, PDHA1, PEX1, PEX10, PEX12, PEX2, PEX26, PEX6, PEX7, PFKM, PHGDH, PKHD1, PLP1, PMM2, POLG, POMGNT1, POMT1, PPT1, PRF1, PROP1, PTS, PUS1, PYGM, RAG1, RAG2, RAPSN, RARS2, RMRP, RNASEH2B, RPE65, RS1, RTEL1, SACS, SCO2, SEPSECS, SGCA, SGCB, SGCD, SGCG, SGSH, SLC12A6, SLC17A5, SLC19A3, SLC22A5, SLC25A13, SLC25A20, SLC26A2, SLC26A4, SLC35A3, SLC37A4, SLC6A8, SLC7A7, SMN1, SMPD1, STAR, SUMF1, SURF1, TAT, TCIRG1, TECPR2, TF, TGM1, TH, TMEM216, TPP1, TRMU, TTPA, TYMP, USH1C, USH2A, VPS13A, VPS13B, VRK1, VSX2, WNT10A, XPA, XPC, ZFYVE26

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.

Gene Specific Notes and Limitations

ARX: Heterozygous polyalanine expansions of >7 repeats (21bp) in the ARX gene in females may not be detected by this method. *BTD:* If detected, the variant NM_001370658.1:c.1270G>C (p.Asp424His) will not be reported as this variant is associated with low disease penetrance and is primarily associated with reduced enzyme activity when homozygous. *CEP290:* Copy number analysis for exons 8-13 and exons 39-42 may have reduced sensitivity in the CEP290 gene. Confirmation of these exons are limited to individuals with a positive personal history of CEP290-related conditions and/or individuals carrying a pathogenic/likely pathogenic sequence variant. *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. *CRYL1:* As mutations in the CRYL1 gene are not known to be associated with any clinical condition, sequence variants in this gene are not analyzed. However, to increase copy number detection sensitivity for large deletions, this gene was evaluated for copy number variation. *CYP11B1:* The current testing method is not able to reliably detect certain pathogenic variants in this gene due to the interference by highly homologous regions. This analysis is not designed to detect or rule-out copy-neutral chimeric CYP11B1/CYP11B2 gene. *CYP11B2:* The current testing method is not able to reliably detect certain pathogenic variants in this gene due to the interference by highly homologous regions. This analysis is not designed to detect or rule-out copy-neutral chimeric CYP11B1/CYP11B2 gene. *CYP21A2:* Significant pseudogene interference and/or reciprocal exchanges between the CYP21A2 gene and its pseudogene, CYP21A1P, have been known to occur and may impact results. As such, the relevance of variants reported in this gene must be interpreted clinically in the context of the clinical findings, biochemical profile, and family history of each patient. LR-PCR is not routinely ordered for NM_000500.9:c.955C>T (p.Gln319Ter). Individuals with c.955C>T (p.Gln319Ter) will be reported as a Possible Carrier indicating that the precise nature of the variant has not been determined by LR-PCR and that the variant may occur in the CYP21A2 wild-type gene or in the CYP21A1P pseudogene. The confirmation test is recommended if the second reproductive partner is tested positive for variants associated with classic CAH. *DMD:* Single exon deletion/duplication analysis is limited to exons with >1 patient reported in the UMD database (http://www.umd.be/DMD/W_DMD/index.html), accessed Dec 29,2020 and all out-of-frame exons after exon 3. This includes deletion of exon 1, and duplication of exon 2, and del/dup for exons 3,6~8,11,12,17~22,43~46,48,50~56,58~63,65~70,75,76 and 78. Single-exon detection is limited to blood samples. *FMR1:* The exact size of alleles >200 CGG repeats cannot be determined; these alleles are pathogenic for X-Linked Fragile X Syndrome. Alleles with <10 repeats may fail to amplify; these alleles are benign. The repeat length for this gene may vary by +/- 1 repeat unit. Methylation is not analyzed. RP-PCR analysis of the FMR1 promoter is not routinely performed in males. Small degrees of size mosaicism, including gonadal mosaicism, may not be detected. *GALT:* The D2 "Duarte" allele is not included in this analysis. While this allele can cause positive newborn screening results, it is not known to cause clinical symptoms in any state (PubMed: 25473725, 30593450). *GBA:* The current testing method may not be able to reliably detect certain pathogenic variants in the GBA gene due to homologous recombination between the pseudogene and the functional gene. *HBA1:* Significant interference from highly homologous regions in exons 1-2 of the HBA1 gene has been recognized to occur, potentially impeding the assay's technical capability to detect pathogenic alterations during sequencing analyses. *HBA2:* Significant interference from highly homologous regions in exons 1-2 of the HBA2 gene has been recognized to occur, potentially impeding the assay's technical capability to detect pathogenic alterations during sequencing analyses. *HSD17B4:* Copy number analysis for exons 4-6 may have reduced sensitivity in the HSD17B4 gene. Confirmation of these exons are limited to individuals with a positive personal history of D-bifunctional protein deficiency and Perrault syndrome and/or individuals carrying a pathogenic/likely pathogenic sequence variant. *MTHFR:* As recommended by ACMG, the two common polymorphisms in the MTHFR gene - c.1286A>C (p.Glu429Ala, also known as c.1298A>C) and c.665C>T (p.Ala222Val, also known as c.677C>T) - are not reported in this test due to lack of sufficient clinical utility to merit testing (PubMed: 23288205). *NEB:* This gene contains a 32-kb triplicate region (exons 82-105) which is not amenable to sequencing and deletion/duplication analysis. *NPHS2:* If detected, the variant NM_014625.3:c.686G>A (p.Arg229Gln) will not be reported as this variant is not significantly associated with disease when homozygous or in the compound heterozygous state with variants in exons 1-6 of NPHS2. *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. *WNT10A:* If detected, certain common variants which are associated with autosomal dominant selective tooth agenesis are not reported. These variants are associated with low penetrance for autosomal recessive disease and are commonly found as homozygous in healthy controls.

Helix_ComprehensiveCarrierScreen_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.

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