To: Example Client
123 Example Street
Allentown, PA 18106
United States

Referred by:
Dr. Example Physician

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EXTENDED CARRIER SCREENING PANEL

DATE RECEIVED: 1/2/2021 **DATE REPORTED:** 1/14/2021 **DATE COLLECTED:** 1/1/2021

Patient Name	DOB	Patient ID #
Example, Patient	2/23/1985	X00123
Test Request	**Specimen Type**	**Your Code**
Extended Carrier Screening Panel	Peripheral blood	M1234567

DISORDER:	RESULTS:	INTERPRETATION:
Fragile X Syndrome	NEGATIVE FMR1: c.-129CGG[29]; [31]	**No evidence of abnormal CGG repeat number; Reduced carrier risk for Fragile X or Fragile X associated disorders.**
Spinal Muscular Atrophy	NEGATIVE SMN1: 2 copies SMN2: 2 copies	**No evidence of abnormal copy number in the SMN1 or SMN2 gene; Reduced carrier risk for SMA.**
All other disorders	NEGATIVE	**No other pathogenic/likely pathogenic variant was detected. Reduced carrier risk for the other tested disorders.**

BACKGROUND

This test is designed to detect carriers of the disorders listed in the Genes Tested section below. These disorders are mostly severe, childhood onset disorders with autosomal recessive or X-linked inheritance. This test is intended for pre/post-conception carrier screening and is not intended for diagnostic testing. Genetic counseling is recommended for interpretation of test results. For additional information, please contact HNL Genomics (CTGT) at 484-244-2900 or visit our website at www.CTGT.net.

METHODOLOGY

Next generation sequencing (NGS) and copy number variation analysis (CNV): All coding exons and exon boundaries of the genes on the common carrier screening panel, plus two intronic CFTR variants (c.1680-886A>G and c.3718-2477C>T), were targeted using the Agilent SureSelect hybridization capture method and were sequenced using an Illumina MiSeq next generation sequencer. Sequences were aligned to the human genome reference build GRCh37/hg19 and variants were called. All exons are routinely covered by at least 40 sequence reads. Due to high homology between the gene pairs, variants are not routinely called in SMN1/2 exons 1-6 or HBA1/2 exon 1-2. Additionally, the NGS data is used to analyze all coding exons for copy number variations (CNV). CNV detection limit is typically a single exon. This analysis does not detect rearrangements that do not result in copy number variation. Classification of the clinical significance of detected variants is performed based on professional guidelines. Pathogenic and likely pathogenic variants are included in this report. Variants of uncertain significance, likely benign variants, and benign variants are not reported. The CFTR polyT variant (5T, 7T, 9T) is only reported if the Arg117His variant is present on the same allele.

Fragile X repeat analysis: Analysis of the FMR1 gene includes determination of the number of CGG repeats in the 5'UTR of FMR1. The repeat region was amplified using polymerase chain reaction (PCR) with a fluorescence labeled primer and the PCR products were sized by capillary gel electrophoresis. If these results show a repeat number of greater than 44 or a single allele in a female specimen, an additional assay using a CGG repeat-primed PCR method will be performed to verify the repeat number.

- This test was developed and its performance characteristics determined by HNL Genomics (CTGT). It has not been cleared or approved by the FDA. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. CTGT is certified under CLIA since 2004.

Reported repeat number may vary by +/- two repeats. The interpretation of Fragile X test results is based on the number of CGG repeats detected, using the following ranges: <45 repeats is Negative, 45-54 repeats is the Intermediate range, 55-200 repeats is a Premutation, and >200 repeats is a Full Mutation.

Spinal muscular atrophy analysis: Analysis of the SMN1 and SMN2 genes includes determination of the number of copies of SMN1 and SMN2 exon 7 and assessment of the presence of the SMN1 c.*3+80T>G SNP (g.27134T>G, see Luo: PMID 23788250). All coding exons and exon boundaries of the SMN1 and SMN2 genes were targeted using the Agilent SureSelect hybridization capture method and were sequenced using an Illumina MiSeq next generation sequencer. Sequences were aligned to the human genome reference build GRCh37/hg19 and copy number was determined by an algorithm which compares the patient sample to a set of reference samples and uses that data to calculate 0, 1, 2, or 3 copies of SMN1 and SMN2 exon 7. Individuals with two or more copies of SMN1 generally have a low carrier risk. The genotype at SMN1 position c.*3+80 was also determined as the presence of a G at this position correlates in certain populations with increased risk of being a silent carrier with two copies of SMN1 on the same allele.

Limitations: Although DNA sequencing, copy number variation analysis, and PCR fragment length analysis are highly sensitive methodologies, mutation detection may not be 100%. Mosaic variants, non-coding/intronic variants, variants in regions/genes not included in this test, and chromosomal rearrangements that do not result in copy number variation may not be detected by this test. The number of copies of SMN1 and SMN2 on each allele is not determined. Additionally, variant classification may change over time as more information becomes available. False positive or false negative results are rare but may occur for various reasons, including but not limited to, pseudogene interference, sex chromosome abnormalities, rare genetic variants interfering with primer binding, unusual allelic configurations, blood transfusions, and bone marrow transplantation. A negative test result reduces, but does not eliminate, the chance that this individual is a carrier for the disorders tested by this panel.

GENES TESTED

Gene	Accession	Disorder	MIM	Inheritance
ACADM	NM_000016	Medium-chain acyl-CoA dehydrogenase deficiency	201450	AR
ARSA	NM_000487	Metachromatic leukodystrophy	250100	AR
ARSB	NM_000046	Mucopolysaccharidosis type VI (Maroteaux-Lamy)	253200	AR
ASPA	NM_000049	Canavan disease	271900	AR
ASS1	NM_000050	Citrullinemia	215700	AR
BCKDHA	NM_000709	Maple syrup urine disease, type Ia	248600	AR
BCKDHB	NM_183050	Maple syrup urine disease, type Ib	248600	AR
BLM (RECQL3)	NM_000057	Bloom syndrome	210900	AR
BTD	NM_000060	Biotinidase deficiency	253260	AR
CFTR	NM_000492	Cystic Fibrosis Congenital bilateral absence of vas deferens	219700 277180	AR AR
DHCR7	NM_001360	Smith-Lemli-Opitz syndrome	270400	AR
DMD	NM_004006	Duchenne muscular dystrophy Becker muscular dystrophy Cardiomyopathy, dilated, 3B	310200 300376 302045	XLR XLR XL
ELP1 (IKBKAP)	NM_003640	Familial dysautonomia	223900	AR
FANCC	NM_000136	Fanconi anemia C	227645	AR
FMR1	NM_002024	Fragile X syndrome Fragile X tremor/ataxia syndrome Premature ovarian failure 1	300624 300623 311360	XL XL XL
G6PC	NM_000151	Glycogen storage disease Ia	232200	AR
GAA	NM_000152	Glycogen storage disease II	232300	AR
GALC	NM_000153	Krabbe disease	245200	AR
GALE	NM_000403	Galactose epimerase deficiency	230350	AR
GALK1	NM_000154	Galactokinase deficiency with cataracts	230200	AR
GALT	NM_000155	Galactosemia	230400	AR
GAMT	NM_000156	Cerebral creatine deficiency syndrome 2	612736	AR
GATM	NM_001482	Cerebral creatine deficiency syndrome 3	612718	AR
GBA	NM_001005741	Gaucher disease, type I Gaucher disease, type II Gaucher disease, type III Gaucher disease, type IIIC Gaucher disease, perinatal lethal	230800 230900 231000 231005 608013	AR AR AR AR AR
GLA	NM_000169	Fabry disease	301500	XL

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HBA1 HBA2	NM_000558 NM_000517	Alpha thalassemia Hemoglobin H disease Hemoglobin Bart's hydrops fetalis syndrome	604131 613978 236750	AR AR AR
HBB	NM_000518	Beta thalassemia Sickle cell anemia	613985 603903	AR AR
HEXA	NM_000520	Tay-Sachs disease	272800	AR
HFE	NM_000410	Hemochromatosis	235200	AR
IDS	NM_000202	Mucopolysaccharidosis II	309900	XLR
IDUA	NM_000203	Mucopolysaccharidosis Ih Mucopolysaccharidosis Ih/s Mucopolysaccharidosis Is	607014 607015 67016	AR AR AR
IVD	NM_002225	Isovaleric acidemia	243500	AR
MCOLN1	NM_020533	Mucolipidosis IV	252650	AR
MMACHC	NM_015506	Methylmalonic aciduria with homocystinuria, cblC type	277400	AR
OTC	NM_000531	Ornithine transcarbamylase deficiency	311250	XLR
PAH	NM_000277	Phenylketonuria	261600	AR
PHKA2	NM_000292	Glycogen storage disease, type IXa	306000	XLR
PHKG2	NM_000294	Glycogen storage disease IXc	613027	AR
PKHD1	NM_138694	Polycystic kidney disease 4, with or without hepatic disease	263200	AR
PYGL	NM_002863	Glycogen storage disease VI	232700	AR
SLC37A4	NM_001164277	Glycogen storage disease Ib Glycogen storage disease Ic	232220 232240	AR AR
SLC6A8	NM_005629	Cerebral creatine deficiency syndrome 1	300352	XLR
SMN1	NM_022874	Spinal muscular atrophy 1 Spinal muscular atrophy 2 Spinal muscular atrophy 3 Spinal muscular atrophy 4	253300 253550 253400 271150	AR AR AR AR
SMN2	NM_022876	Modifier of spinal muscular atrophy	253400	--
SMPD1	NM_000543	Niemann-Pick disease, type A Niemann-Pick disease, type B	257200 607616	AR AR
SUMF1	NM_182760	Multiple sulfatase deficiency	272200	AR

For additional information, please contact HNL Genomics

(CTGT) at 484-244-2900. Sincerely yours,

Kerry Kocher Brown, Ph.D., FACMG

This test was developed and its performance characteristics determined by Connective Tissue Gene Tests. It has not been cleared or approved by the FDA. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. CTGT is certified under CLIA since 2004.