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Patient Information:

MQ1C

Accession:
N/A

FINAL RESULTS

No carrier mutations identified

TEST PERFORMED

Custom Sonic Beacon Male Carrier Screening
(351 Gene Panel; gene sequencing with deletion and duplication analysis)

INTERPRETATION:

Notes and Recommendations:

- No carrier mutations were identified in the submitted specimen. A negative result does not rule out the possibility of a genetic predisposition nor does it rule out any pathogenic mutations in areas not assessed by this test or in regions that were covered at a level too low to reliably assess. Also, it does not rule out mutations that are of the sort not queried by this test; see Methods and Limitations for more information.
- 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. Individuals with negative test results may still have up to a 3-4% risk to have a child with a birth defect due to genetic and/or environmental factors.
- 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.
- Gene specific notes and limitations may be present. See below.
- This report does not include variants of uncertain significance.
- Genetic counseling is recommended. Contact your physician about the available options for genetic counseling.

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Quality is in our DNA

GENES TESTED:

Custom Sonic Beacon Male Carrier Screening - 351 Genes

351 genes tested (99.47% at >20x). For more gene specific information and assistance with residual risk calculation, see SUPPLEMENTAL TABLE.

ABCB11	*ABCC8*	*ABCD4*	*ACAD9*	*ACADM*	*ACADS*
ACADSB	*ACADVL*	*ACAT1*	*ACOX1*	*ACSF3*	*ADA*
ADAMTS2	*ADGRG1*	*ADK*	*AGA*	*AGL*	*AGPS*
AGXT	*AHCY*	*AHI1*	*AIPL1*	*AIRE*	*ALDH3A2*
ALDH4A1	*ALDOB*	*ALG6*	*ALMS1*	*ALPL*	*AMT*
AQP2	*ARG1*	*ARL13B*	*ARSA*	*ARSB*	*ASL*
ASNS	*ASPA*	*ASS1*	*ATM*	*ATP6V1B1*	*ATP7B*
BBS1	*BBS10*	*BBS12*	*BBS2*	*BCKDHA*	*BCKDHB*
BCS1L	*BLM*	*BSND*	*BTD*	*CAPN3*	*CASQ2*
CBS	*CCDC103*	*CCDC151*	*CCDC39*	*CDH23*	*CEP290*
CERKL	*CFTR*	*CHRNE*	*CHRNG*	*CHST6*	*CIITA*
CLN3	*CLN5*	*CLN6*	*CLN8*	*CLRN1*	*CNGA1*
CNGB1	*CNGB3*	*COL27A1*	*COL4A3*	*COL4A4*	*COL7A1*
CPS1	*CPT1A*	*CPT2*	*CRB1*	*CRYL1*	*CTNS*
CTSK	*CYBA*	*CYP11B1*	*CYP11B2*	*CYP17A1*	*CYP19A1*
CYP1B1	*CYP21A2*	*CYP27A1*	*DBT*	*DCLRE1C*	*DHCR7*
DHDDS	*DLD*	*DNAH5*	*DNAI1*	*DNAI2*	*DNAL1*
DPYD	*DUOX2*	*DUOXA2*	*DYSF*	*EIF2AK3*	*EIF2B5*
ELP1	*ERCC6*	*ERCC8*	*ESCO2*	*ETFA*	*ETFB*
ETFDH	*ETHE1*	*EVC*	*EVC2*	*EXOSC3*	*EYS*
F11	*FAH*	*FAM161A*	*FANCA*	*FANCC*	*FANCG*
FH	*FKRP*	*FKTN*	*FTCD*	*G6PC*	*GAA*
GALC	*GALE*	*GALK1*	*GALNS*	*GALT*	*GAMT*
GBA	*GBE1*	*GCDH*	*GDAP1*	*GFM1*	*GJB2*
GJB6	*GLB1*	*GLDC*	*GLE1*	*GNE*	*GNPTAB*
GNPTG	*GNRHR*	*GNS*	*GP1BA*	*GP9*	*GRHPR*
GUSB	*HADHA*	*HAX1*	*HBA1*	*HBA2*	*HBB*
HEXA	*HEXB*	*HGD*	*HGSNAT*	*HJV*	*HLCS*
HMGCL	*HOGA1*	*HPS1*	*HPS3*	*HSD17B4*	*HSD3B2*
HYAL1	*HYLS1*	*IDH3B*	*IDUA*	*IVD*	*IYD*
JAK3	*KCNJ11*	*LAMA2*	*LAMA3*	*LAMB3*	*LAMC2*
LCA5	*LHX3*	*LIFR*	*LIPA*	*LMBRD1*	*LOXHD1*
LPL	*LRPPRC*	*LYST*	*MAN2B1*	*MCCC1*	*MCCC2*
MCEE	*MCOLN1*	*MED17*	*MESP2*	*MFSD8*	*MKS1*
MLC1	*MMAA*	*MMAB*	*MMACHC*	*MMADHC*	*MPI*
MPL	*MPV17*	*MTMR2*	*MTRR*	*MTTP*	*MUT*
MVK	*MYO7A*	*NAGLU*	*NAGS*	*NBN*	*NDRG1*
NDUFAF5	*NDUFS6*	*NEB*	*NPC1*	*NPC2*	*NPHP1*
NPHS1	*NPHS2*	*NR2E3*	*NTRK1*	*OAT*	*OPA3*
OTOF	*P3H1*	*PAH*	*PANK2*	*PC*	*PCBD1*
PCCA	*PCCB*	*PCDH15*	*PDE6A*	*PDHB*	*PEX1*
PEX10	*PEX12*	*PEX2*	*PEX6*	*PEX7*	*PFKM*
PGK1	*PHGDH*	*PKHD1*	*PLA2G6*	*PLOD1*	*PMM2*
POLG	*POLR1C*	*POMGNT1*	*POMT1*	*POMT2*	*PPT1*
PQBP1	*PROP1*	*PSAP*	*PTS*	*PUS1*	*PYGM*
QDPR	*RAB23*	*RAG1*	*RAG2*	*RAPSN*	*RARS2*
RAX	*RDH12*	*RMRP*	*RPE65*	*RPGRIP1L*	*RTEL1*
SACS	*SAMHD1*	*SEPSECS*	*SERPINA1*	*SGCA*	*SGCB*

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SGCD	*SGCG*	*SGSH*	*SH3TC2*	*SLC12A3*	*SLC12A6*
SLC16A2	*SLC17A5*	*SLC22A5*	*SLC25A13*	*SLC25A15*	*SLC25A20*
SLC26A2	*SLC26A3*	*SLC26A4*	*SLC35A3*	*SLC37A4*	*SLC39A4*
SLC46A1	*SLC4A11*	*SLC5A5*	*SLC6A19*	*SLC7A7*	*SMARCAL1*
SMN1	*SMPD1*	*SPG11*	*SPG7*	*STAR*	*SUMF1*
SURF1	*TAT*	*TCIRG1*	*TECPR2*	*TFR2*	*TG*
TGM1	*TH*	*TMEM216*	*TPO*	*TPP1*	*TRDN*
TRIM32	*TRMU*	*TSFM*	*TSHB*	*TTC37*	*TTPA*
TYMP	*UGT1A1*	*USH1C*	*USH1G*	*USH2A*	*VPS13A*
VPS13B	*VPS45*	*VRK1*	*VSX2*	*WHRN*	*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, 99.50% and 99.47% 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 identified by NGS are confirmed by an orthogonal method (qPCR or MLPA), unless exceeding an internally specified and validated quality score, beyond which deletions and duplications are considered real without further confirmation. New York patients: diagnostic findings are confirmed by Sanger, MLPA, or qPCR; exception SNV variants in genes for which confirmation of NGS results has been performed >=10 times may not be confirmed if identified with high quality by NGS. Bioinformatics: The Fulgent Germline v2019.2 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 one whole

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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 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

Biotinidase deficiency: 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.

Cystic Fibrosis: 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.

GJB6-CRYL1 related nonsyndromic hearing loss, GJB6-CRYL1 related nonsyndromic hearing loss: 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 including this gene and a neighboring on gene on the panel (GJB6, also known as connexin 30), this gene was evaluated for copy number variation.

Congenital adrenal hyperplasia due to 11-beta-hydroxylase deficiency: 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.

Corticosterone methyloxidase deficiency: 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.

Congenital adrenal hyperplasia due to 21-hydroxylase deficiency: 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. The variants c.188A>T (p.His63Leu), c.844G>T (p.Val282Leu), c.1174G>A (p.Ala392Thr), and c.1360C>T (p.Pro454Ser) in CYP21A2 will not be routinely reported as these variants are primarily associated with non-classic congenital adrenal hyperplasia and low disease penetrance. Additionally, the variant c.955C>T (p.Gln319Ter) is in the region with pseudogene interference, and the probability of this variant occurring in the real gene is greater than 50%. When observed, this variant will be reported as a possible carrier without LR-PCR. The confirmation test is recommended if the second reproductive partner is tests positive for variants in CYP21A2.

Congenital hypothyroidism, DUOX2-related: DUOX2
The current testing method is not able to reliably detect variants in exons 6-8 of the DUOX2 gene (NM_014080.5) due to significant interference by the highly homologous gene, DUOX1.

Galactosemia: GALT
In general, the D2 "Duarte" allele is not reported if detected, but can be reported upon request. While this allele can cause positive newborn screening results, it is not known to cause clinical symptoms in any state. See GeneReviews for more information: https://www.ncbi.nlm.nih.gov/books/NBK1518/

Gaucher disease: 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.

Nonsyndromic hearing loss, GJB2-related: GJB2
If detected, the variant NM_004004.6:c.109G>A (p.Val37Ile) will not be reported as this variant is associated with low disease penetrance and is primarily associated with late onset and/or mild hearing loss when homozygous.

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Alpha thalassemia, Alpha thalassemia: HBA1
The phase of heterozygous alterations in the *HBA1* gene cannot be determined, but can be confirmed through parental testing.

Alpha thalassemia, Alpha thalassemia: HBA2
The phase of heterozygous alterations in the *HBA2* gene cannot be determined, but can be confirmed through parental testing.

Nemaline myopathy: NEB
This gene contains a 32-kb triplicate region (exons 82-105) which is not amenable to sequencing and deletion/duplication analysis.

Congenital nephrotic syndrome, type 2: 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.

Alpha-1 antitrypsin deficiency: SERPINA1
If detected, the variants NM_004004.6:c.109G>A (p.Val37Ile) and c.1096G>A (p.Glu366Lys) will not be reported as these variants are associated with low disease penetrance and are not associated with severe early onset disease.

Spinal muscular atrophy: 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.

Catecholaminergic polymorphic ventricular tachycardia, TRDN-related: TRDN
Due to high GC content of certain exons, copy number analysis may have reduced sensitivity for partial gene deletions/duplications of *TRDN*. Confirmation of partial gene deletions/duplications are limited to individuals with a positive personal history of cardiac arrhythmia and/or individuals carrying a pathogenic/likely pathogenic sequence variant.

Crigler-Najjar syndrome: UGT1A1
Common variants in the *UGT1A1 gene* (population allele frequency >5%) are typically not reported as they do not cause a Mendelian condition.

Odontoonychodermal dysplasia, Schopf-Schulz-Passarge syndrome: 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.

SIGNATURE:

Zhenbin Chen, Ph.D., CGMBS, DABMGG on **3/8/2022 11:46 PM PST**
Electronically signed

DISCLAIMER:

This test was developed and its performance characteristics determined by **Fulgent Genetics**. 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 **(626) 350-0537**

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or **info@fulgentgenetics.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.