

LCLS Specimen Number: 049-129-0776-0
Patient Name: 12028, DONOR
Date of Birth: [REDACTED]
Gender: M
Patient ID:
Lab Number: (J16-712 L
Indications: DONOR

Account Number: [REDACTED]
Ordering Physician: J OLLIFFE
Specimen Type: BLOOD
Client Reference: B0036681055
Date Collected: 02/18/2016
Date Received: 02/19/2016
Date Reported: 03/07/2016

Test: Chromosome, Blood, Routine

Cells Counted: 20
Cells Analyzed: 20

Cells Karyotyped: 2
Band Resolution: 500

CYTOGENETIC RESULT: 46,XY

INTERPRETATION: NORMAL MALE KARYOTYPE

Cytogenetic analysis of PHA stimulated cultures has revealed a MALE karyotype with an apparently normal GTG banding pattern in all cells observed.

This result does not exclude the possibility of subtle rearrangements below the resolution of cytogenetics or congenital anomalies due to other etiologies.

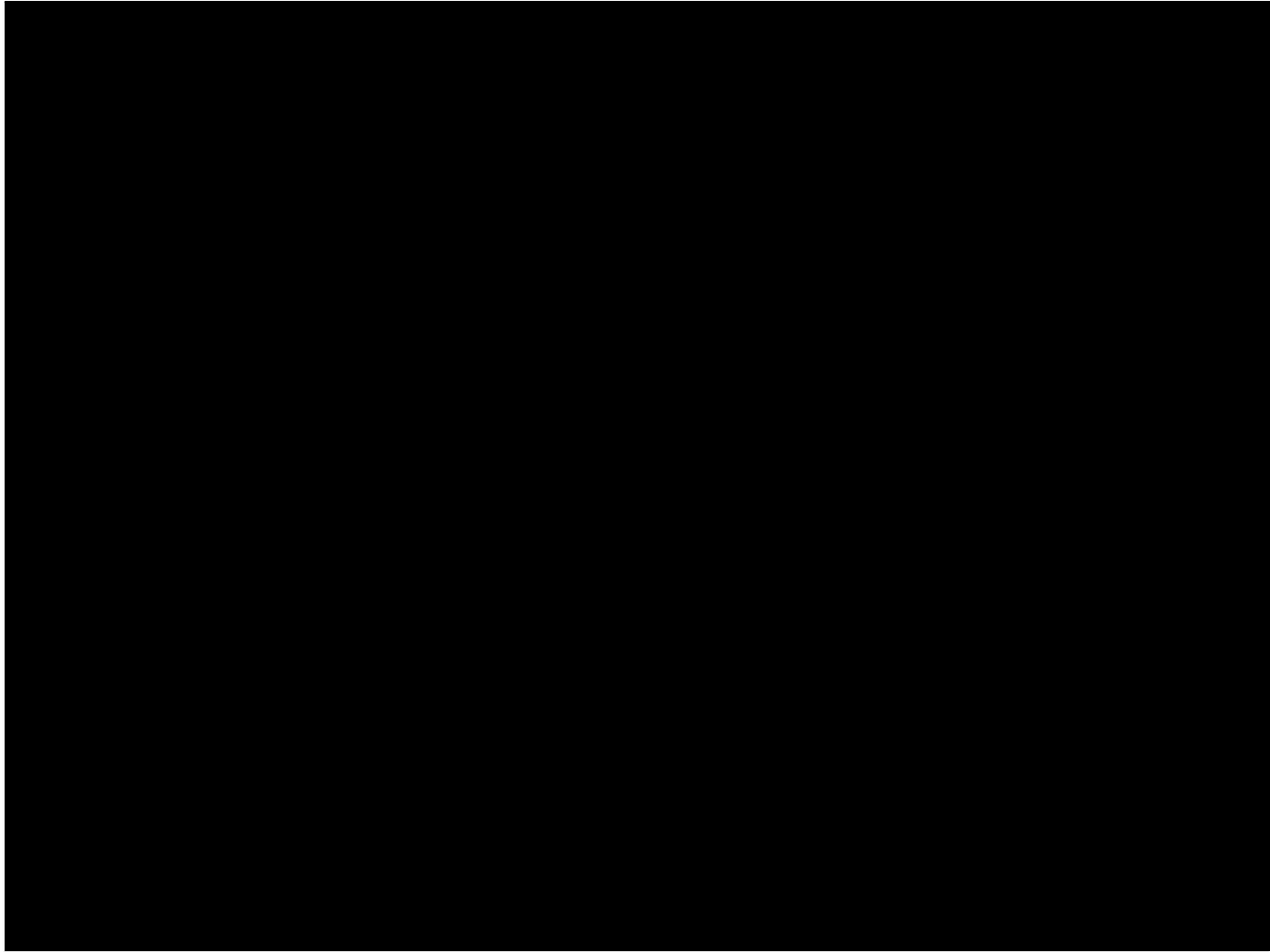


Client/Sending Facility:
Seattle Sperm Bank

4915 25th Ave Ne Ste 204
SEATTLE, WA 98105
Ph: (206)588-1484
Fax: (206) 466-4696 WAB-55

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Hiba Risheg, PhD., FACMG
Board Certified Cytogeneticist

Patricia Kandalaft, MD
Medical Director
Peter Papenhausen, PhD
National Director of Cytogenetics

Technical component performed by Laboratory Corporation of America Holdings,
550 17th Ave. Suite 200 , SEATTLE , WA , 98122-5789 (206) 861-7050

Professional Component performed by LabCorp/Dynacare CLIA 50D0632667, 550 17th Ave. Suite 200, Seattle WA 98122-5789. Medical Director, Patricia Kandalaft, MD
Integrated Genetics is a brand used by Esoterix Genetic Laboratories, LLC, a wholly-owned subsidiary of Laboratory Corporation of America Holdings.

This document contains private and confidential health information **protected by state and federal law.**



RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
4915 25th Ave NE, Suite 204W
Seattle, WA 98105
Phone: (206) 588-1484
Fax: (206) 588-1484
NPI: 1306838271
Report Date: 02/25/2016

MALE
DONOR 12028
DOB: [REDACTED]
Ethnicity: Northern European
Sample Type: EDTA Blood
Date of Collection: 02/18/2016
Date Received: 02/19/2016
Date Tested: 02/25/2016
Barcode: 11004211606727
Indication: Egg or sperm donor

FEMALE
N/A

Family Prep Screen

NEGATIVE

ABOUT THIS TEST

The Counsyl Family Prep Screen (version 2.0) utilizes sequencing, maximizing coverage across all DNA regions tested, to help you learn about your chance to have a child with a genetic disease.

PANEL DETAILS

Fundamental Plus Panel (21 conditions tested)

VERSION

DONOR 12028 (Family Prep Screen 2.0)

RESULTS SUMMARY

NEGATIVE

No known disease-causing mutations were detected. A complete list of all conditions tested can be found on page 4.

CLINICAL NOTES

- None

NEXT STEPS

- If necessary, patients can discuss residual risks with their physician or a genetic counselor.



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FEMALE
N/A

Methods and Limitations

DONOR 12028 [Family Prep Screen 2.0]: sequencing, targeted genotyping, copy number analysis, and analysis of homologous regions.

Sequencing

High-throughput sequencing is used to analyze the listed exons, as well as selected intergenic and intronic regions, of the genes in the Conditions Tested section of the report. These regions are sequenced to high coverage and the sequences are compared to standards and references of normal variation. Mutations may not be detected in areas of lower sequence coverage. On average, more than 99% of all bases in the exons listed for each gene are sequenced at the minimum read depth. Variants discovered in other exons of these genes will also be reported if they meet quality control criteria. Triplet repeats and large deletions and duplications may not be detected. Small insertions and deletions may not be as accurately determined as single nucleotide variants. Genes that have closely related pseudogenes are not well analyzed by this method.

High-throughput sequencing detects, on average, 94% of known clinically significant variants. Disease-specific detection rates and residual risks are reported as "greater than (>)" and "less than (<)" the values for targeted genotyping, respectively. More precise values are not currently available, but may become available in the future.

All variants that are a recognized cause of the disease will be reported. In addition, variants that have not previously been established as a recognized cause of disease may be identified. In these cases, only variants classified as "predicted" or "likely" pathogenic are reported. Predicted/likely pathogenic variants are described elsewhere in the report as "predicted/likely to have a negative impact on gene function". In general, predicted pathogenic variants are those which are predicted to be pathogenic based on the nature of the sequence change, while likely pathogenic variants are evaluated by reviewing reports of allele frequencies in cases and controls, functional studies, variant annotation and effect prediction, and segregation studies. Benign variants, variants of uncertain significance, and variants not directly associated with the intended disease phenotype are not reported. Literature citations validating reported variants are available upon request.

Targeted genotyping

Targeted DNA mutation analysis is used to determine the genotypes of the listed variants in the Conditions Tested section of the report. The test is not validated for detection of homozygous mutations, and although rare, asymptomatic individuals affected by the disease may not be genotyped accurately.

Copy number analysis

Targeted copy number analysis is used to determine the copy number of exon 7 of the *SMN1* gene relative to other genes. Other mutations may interfere with this analysis. Some individuals with two copies of *SMN1* are carriers with two *SMN1* genes on one chromosome and a *SMN1* deletion on the other chromosome. In addition, a small percentage of spinal muscular atrophy (SMA) cases are caused by nondeletion mutations in the *SMN1* gene. Thus, a test result of two *SMN1* copies significantly reduces the risk of being a carrier; however, there is still a residual risk of being a carrier and subsequently a small risk of future affected offspring for individuals with two or more *SMN1* gene copies. Some SMA cases arise as the result of *de novo* mutation events which will not be detected by carrier testing.

Analysis of homologous regions

A combination of high-throughput sequencing, read depth-based copy number analysis, and targeted genotyping is used to determine the number of functional gene copies and/or the presence of selected loss of function mutations in certain genes that have homology to other regions. The precise breakpoints of large deletions in these regions cannot be determined, but are estimated from copy number analysis. Patients who have one or more additional copies of the *CYP21A2* gene and a loss of function mutation may not actually be a carrier of 21-hydroxylase-deficient congenital adrenal hyperplasia (CAH). In addition, some individuals with four alpha globin genes are carriers with three genes on one chromosome and a deletion on the other chromosome. This and similar carrier states, where complementary changes exist in both the gene and a pseudogene, may not be detected by the assay.



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FEMALE
N/A

Because the true incidence of non-classic CAH is unknown, the residual carrier and reproductive risk numbers on the report are only based on published incidences for classic CAH. However, the published prevalence of non-classic CAH is highest in individuals of Ashkenazi Jewish, Hispanic, Italian, and Yugoslav descent. Therefore, the residual and reproductive risks are likely an underestimate of overall chances for 21-hydroxylase-deficient CAH, especially in the aforementioned populations, as they do not account for non-classic CAH.

Limitations

In an unknown number of cases, nearby genetic variants may interfere with mutation detection. Other possible sources of diagnostic error include sample mix-up, trace contamination, bone marrow transplantation, blood transfusions and technical errors. If more than one variant is detected in a gene, additional studies may be necessary to determine if those variants lie on the same chromosome or different chromosomes. The Family Prep Screen does not fully address all inherited forms of intellectual disability, birth defects and genetic disease. A family history of any of these conditions may warrant additional evaluation. Furthermore, not all mutations will be identified in the genes analyzed and additional testing may be beneficial for some patients. For example, individuals of African, Southeast Asian, and Mediterranean ancestry are at increased risk for being carriers for hemoglobinopathies, which can be identified by CBC and hemoglobin electrophoresis or HPLC (*ACOG Practice Bulletin No. 78. Obstet. Gynecol. 2007;109:229-37*), and additional Tay-Sachs disease testing can be performed using a biochemical assay (*Gross et al. Genet. Med. 2008;10(1):54-56*).

This test was developed and its performance characteristics determined by Counsyl, Inc. It has not been cleared or approved by the US Food and Drug Administration (FDA). The FDA does not require this test to go through premarket review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. These results are adjunctive to the ordering physician's evaluation. CLIA Number: **#05D1102604**.

LAB DIRECTORS

H. Peter Kang, MD, MS, FCAP

Rebecca Mar-Heyming, PhD, DABMG



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FEMALE
N/A

Conditions Tested

Autosomal Recessive Disorders

SEQUENCING AND TARGETED GENOTYPING

ABCC8-related Hyperinsulinism - Gene: ABCC8. **Variants (3):** 3992-9G>A, F1388del, V187D. **Exons:** NM_000352:1-39. **Detection rate:** Unknown due to rarity of disease.

Bloom Syndrome - Gene: BLM. **Variants (1):** Y736Lfs*5. **Exons:** NM_000057:2-22. **Detection rate:** Northern European > 10%.

Canavan Disease - Gene: ASPA. **Variants (4):** A305E, E285A, IVS2-2A>G, Y231*. **Exons:** NM_000049:1-6. **Detection rate:** Northern European > 53%.

Cystic Fibrosis - Gene: CFTR. **Variants (99):** 1078delT, 1288insTA, 1677delTA, 1717-1G>A, 1777A>C, 1812-1G>A, 1898+1G>A, 1898+1G>T, 1898+5G>T, 2043delG, 2055del9>A, 2108delA, 2143delT, 2183AA>G, 2184delA, 2184insA, 2307insA, 2789+5G>A, 2869insG, 296+12T>C, 3120+1G>A, 3120G>A, 3171delC, 3199del6, 3272-26A>G, 3659delC, 3667del4, 3791delC, 3849+10kbC>T, 3849+4A>G, 3876delA, 3905insT, 394delITT, 405+1 G>A, 405+3A>C, 406-1G>A, 444delA, 457TAT>G, 574delA, 621+1G>T, 663delT, 711+1G>T, 711+5G>A, 712-1G>T, 935delA, 936delTA, A455E, A559T, C524*, D1152H, E60*, E92*, F508del, G178R, G330*, G480C, G542*, G551D, G622D, G85E, I507del, K710*, L206W, M1101K, M607_Q643del, N1303K, P574H, Q1238*, Q493*, Q552*, Q890*, R1066C, R1158*, R1162*, R117C, R117H, R334W, R347H, R347P, R352Q, R553*, R560T, R709*, R75*, R764*, S1196*, S1251N, S1255*, S364P, S549N, S549R, T338I, V520F, W1089*, W1204*, W1282*, Y1092X, Y122*, c.1075_1079del5ins5. **Exons:** NM_000492:1-27. IVS8-5T allele analysis is only reported in the presence of the R117H mutation. **Detection rate:** Northern European > 91%.

Familial Dysautonomia - Gene: IKBKAP. **Variants (2):** R696P, c.2204+6T>C. **Exons:** NM_003640:19-20,26. **Detection rate:** Unknown due to rarity of disease.

Fanconi Anemia Type C - Gene: FANCC. **Variants (3):** R548*, c.456+4A>T, c.67delG. **Exons:** NM_000136:2-15. **Detection rate:** Northern European > 54%.

Glycogen Storage Disease Type Ia - Gene: G6PC. **Variants (7):** G188R, Q242*, Q347*, R83C, R83H, c.79delC, p.Y128Tfs*3. **Exons:** NM_000151:1-5. **Detection rate:** Northern European > 61%.

Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease) - Gene: HBB. **Variants (28):** -28A>G, -29A>G, -87C>G, -88C>T,

G25=, Hb C, Hb D-Punjab, Hb E, Hb O-Arab, Hb S, IVS-1-1, IVS-1-5, IVS-1-6T>C, IVS2-745C>G, K18Rfs*2, K9Vfs*14, Q40*, S10Vfs*14, W16*, c.315+1G>A, c.316-197C>T, c.316-2A>C, c.316-2A>G, c.93-21G>A, p.E7Gfs*13, p.F42Lfs*19, p.K18*, p.S73Kfs*2. **Exons:** NM_000518:1-3. **Detection rate:** Northern European > 83%.

Hexosaminidase A Deficiency (Including Tay-Sachs Disease) - Gene: HEXA. **Variants (9):** 7.6kb del, G250D, G269S, IVS7+1G>A, IVS9+1G>A, R170W, R178H, Y427Ifs*5, c.1421+1G>C. **Exons:** NM_000520:1-14. **Detection rate:** Northern European > 23%.

Joubert Syndrome 2 - Gene: TMEM216. **Variants (1):** R73L. **Exons:** NM_001173990:1-5. **Detection rate:** Unknown due to rarity of disease.

Lipoamide Dehydrogenase Deficiency - Gene: DLD. **Variants (2):** G194C, c.104dupA. **Exons:** NM_000108:1-14. **Detection rate:** Unknown due to rarity of disease.

Maple Syrup Urine Disease Type 1B - Gene: BCKDHB. **Variants (3):** E372*, G278S, R183P. **Exons:** NM_183050:1-10. **Detection rate:** Unknown due to rarity of disease.

Mucopolipidosis IV - Gene: MCOLN1. **Variants (2):** S11_6944del, IVS3-2A>G. **Exons:** NM_020533:1-14. **Detection rate:** Northern European > 10%.

NEB-related Nemaline Myopathy - Gene: NEB. **Variants (1):** c.(?_7431+1917)_(7536+373_?)del. **Exons:** NM_004543:7-8,18,25,28,33,36,45,48,54-55,58,61,71,73-74,91,94,101,111-112,114,118-119,122-123,127,129,132-135,138,140,143,146-147. **Detection rate:** Unknown due to rarity of disease.

Niemann-Pick Disease, SMPD1-associated - Gene: SMPD1. **Variants (4):** L302P, R496L, c.1829_1831delGCC, fsP330. **Exons:** NM_000543:1-6. **Detection rate:** Northern European > 38%.

Usher Syndrome Type 1F - Gene: PCDH15. **Variants (1):** R245*. **Exons:** NM_033056:2-33. **Detection rate:** Unknown due to rarity of disease.

Usher Syndrome Type 3 - Gene: CLRN1. **Variants (1):** N48K. **Exons:** NM_174878:1-3. **Detection rate:** Unknown due to rarity of disease.

Walker-Warburg Syndrome - Gene: FKTN. **Variants (1):** c.1167dupA. **Exons:** NM_001079802:3-11. **Detection rate:** Unknown due to rarity of disease.

Constant Spring, anti3.7, anti4.2, del HS-40. **Detection rate:** Unknown due to rarity of disease.

ANALYSIS OF HOMOLOGOUS REGIONS

Alpha Thalassemia - Genes: HBA1, HBA2. **Variants (13):** -(alpha)20.5, --BRIT, --MEDI, --MEDI, --SEA, --THAI or --FIL, -alpha3.7, -alpha4.2, HBA1+HBA2 deletion, Hb

COPY NUMBER ANALYSIS

Spinal Muscular Atrophy - Gene: SMN1. **Variants (1):** SMN1 copy number. **Detection rate:** Northern European 95%.

TARGETED GENOTYPING

Gaucher Disease - Gene: GBA. **Variants (10):** D409V, D448H, IVS2+1G>A, L444P, N370S, R463C, R463H, R496H, V394L, p.L29Afs*18. **Detection rate:** Northern European 60%.



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 Attn: Dr. Jeffrey Olliffe
 NPI: 1306838271
 Report Date: 02/25/2016

MALE
DONOR 12028
 DOB: [REDACTED]
 Ethnicity: Northern European
 Barcode: 11004211606727

FEMALE
 N/A

Risk Calculations

Below are the risk calculations for all conditions tested. Since negative results do not completely rule out the possibility of being a carrier, the **residual risk** represents the patient's post-test likelihood of being a carrier and the **reproductive risk** represents the likelihood the patient's future children could inherit each disease. These risks are inherent to all carrier screening tests, may vary by ethnicity, are predicated on a negative family history and are present even after a negative test result. Inaccurate reporting of ethnicity may cause errors in risk calculation. The reproductive risk presented is based on a hypothetical pairing with a partner of the same ethnic group.

Disease	DONOR 12028 Residual Risk	Reproductive Risk
ABCC8-related Hyperinsulinism	< 1 in 110	< 1 in 50,000
Alpha Thalassemia	Alpha globin status: aa/aa.	Not calculated
Bloom Syndrome	< 1 in 500	< 1 in 1,000,000
Canavan Disease	< 1 in 500	< 1 in 1,000,000
Cystic Fibrosis	< 1 in 300	< 1 in 33,000
Familial Dysautonomia	< 1 in 500	< 1 in 1,000,000
Fanconi Anemia Type C	< 1 in 340	< 1 in 220,000
Gaucher Disease	1 in 280	1 in 120,000
Glycogen Storage Disease Type Ia	< 1 in 450	< 1 in 320,000
Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease)	< 1 in 290	< 1 in 58,000
Hexosaminidase A Deficiency (Including Tay-Sachs Disease)	< 1 in 390	< 1 in 470,000
Joubert Syndrome 2	< 1 in 500	< 1 in 1,000,000
Lipoamide Dehydrogenase Deficiency	< 1 in 500	< 1 in 1,000,000
Maple Syrup Urine Disease Type 1B	< 1 in 250	< 1 in 250,000
Mucopolidiosis IV	< 1 in 500	< 1 in 1,000,000
NEB-related Nemaline Myopathy	< 1 in 500	< 1 in 1,000,000
Niemann-Pick Disease, SMPD1-associated	< 1 in 400	< 1 in 400,000
Spinal Muscular Atrophy	SMN1: 2 copies 1 in 610	1 in 84,000
Usher Syndrome Type 1F	< 1 in 190	< 1 in 150,000
Usher Syndrome Type 3	< 1 in 500	< 1 in 1,000,000
Walker-Warburg Syndrome	< 1 in 500	< 1 in 1,000,000



CARRIER SCREENING REPORT

Patient	Sample	Referring Doctor
Patient Name: Donor 12028 Date of Birth: [REDACTED] Reference #: P0611178 Indication: Chimerism Studies Test Type: NGS single gene full sequencing test	Specimen Type: Blood Lab #: 18009454NG Date Collected: 2/1/2018 Date Received: 2/2/2018 Final Report: 2/13/2018	Jeffrey Fred Olliffe, M.D. Seattle Sperm Bank 4915 25th Avenue NE Suite 204 Seattle, WA 98105 Fax: 206-466-4696

RESULT SUMMARY

NGS single gene full sequencing test

Results: No clinically significant variant(s) detected

Gene(s) analyzed: *SLC26A4*, *FAH* and *NAGLU*

Interpretation: Screening for the presence of pathogenic variants in the *SLC26A4*, *FAH* and *NAGLU* genes which are associated with Pendred syndrome, tyrosinemia, type I and mucopolysaccharidosis type IIIB, respectively, was performed by next generation sequencing and possibly genotyping for select variants on DNA extracted from this patient's sample. No clinically significant variants were detected during this analysis. This negative result does not rule out the possibility that a pathogenic variant in the genes examined is present.

Genetic counseling is recommended.

This technology may not detect all small insertion/deletions and is not diagnostic for large duplications/deletions and structural genomic variation. The coding DNA sequence of the gene plus at least five base pairs flanking splice sites were sequenced and analyzed relative to the hg19 assembly. A mutation(s) deep in intronic sequences or in untranslated regions of the gene except a portion described above or a pathogenic variant(s) in other genes not included in this test could be present in this patient. The analytical sensitivity of this test is estimated at 99% for single base substitutions and 97% overall. All potentially pathogenic variants were subjected to Sanger sequencing or genotyping by allele specific primer extension analysis for confirmation of the result. Any benign variants identified during this analysis were not reported.

Please note that this carrier screening test masks likely benign variants and variants of uncertain significance (VUS) if there are any. Only known pathogenic variants or likely pathogenic variants which are expected to result in deleterious effects on protein function are reported. If reporting of likely benign variants and VUS is desired in this patient, please contact the laboratory (tel. 212-241-2537) to request an amended report.

Comments: This test was developed and its performance characteristics were determined by Mount Sinai Genomics, Inc. It is considered acceptable for patient testing. It has not been cleared or approved by the FDA. The FDA has determined that such clearance or approval is not necessary.

Patient: Donor 12028

DOB: [REDACTED]

Lab #: 18009454NG

This type of mutation analysis generally provides highly accurate genotype information for point mutations and single nucleotide polymorphisms. Despite this level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, polymorphisms, mosaicism or other rare genetic variants that interfere with analysis. In addition, families should understand the limitations of the testing and that rare diagnostic errors may occur for the reasons described.

For Disease Specific Standards and Guidelines:

<https://www.acmg.net/>

Additional disease-specific references available upon request.

This case has been reviewed and electronically signed by Ruth Kornreich, Ph.D., Co-Laboratory Director

Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D.

Table of Residual Risks by Ethnicity

Please note: This table displays residual risks after a negative result for each of the genes and corresponding disorders. **If a patient is reported to be a carrier of a disease, their residual risk is 1 and this table does not apply for that disease.**

Disease (Inheritance)	Gene	Ethnicity	Carrier Frequency	Detection Rate	Residual Risk	Analytical Detection Rate
Mucopolysaccharidosis, Type IIIB (AR) NM_000263.3	NAGLU	Caucasian	1 in 346	59%	1 in 842	80%
		Asian	1 in 298	70%	1 in 991	>95%
		Worldwide	< 1 in 500	64%	1 in 1387	>95%
Pendred Syndrome (AR) NM_000441.1	SLC26A4	Caucasian	1 in 88	86%	1 in 622	93%
		African	1 in 76	>95%	1 in 1501	>95%
		Asian	1 in 74	83%	1 in 430	>95%
		Worldwide	1 in 80	81%	1 in 417	>95%
Tyrosinemia, Type I (AR) NM_000137.2	FAH	Caucasian	1 in 333	89%	1 in 3019	>95%
		African	1 in 478	92%	1 in 5964	>95%
		Asian	< 1 in 500	70%	1 in 1664	>95%
		Ashkenazi Jewish	1 in 143	>95%	1 in 2641	>95%
		Worldwide	< 1 in 500	82%	1 in 2773	>95%
		French Canadian - Saguenay Lac-St. Jean	1 in 25	>95%	1 in 481	>95%
		French Canadian - Other	1 in 66	>95%	1 in 1301	>95%

AR: Autosomal Recessive