Counsyl

RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
4915 25th Ave E, Suite 204W
Seattle, WA 98105
Phone: (206) 588-1484
Fax: (206) 588-1484
NPI: 1306838271
Report Date: 10/04/2015

MALE
DONOR 9941
DOB: [redacted]
Ethnicity: Northern European
Sample Type: OG-510 Saliva
Date of Collection:
Date Received: 09/26/2015
Date Tested: 10/04/2015
Barcode: 55101505030113
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 9941 **(Family Prep Screen 2.0)**

RESULTS SUMMARY

NEGATIVE

No known or potential 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.
- To schedule a complimentary appointment with a genetic counselor, visit counsyl.com/my/consults/.

Copyright 2015 Counsyl, Inc
All rights reserved.

Methods and Limitations

DONOR 9941 [Family Prep Screen 2.0]: sequencing, targeted genotyping, copy number analysis, and analysis of homologous regions.

Sequencing: High-throughput sequencing is used to analyze 262 exons in 18 genes, as well as selected intergenic and intronic regions. 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 simultaneously determine the genotype of 182 variants associated with 19 diseases. 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 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 may have additional copies of a gene. Therefore, there is a small chance that a patient with a loss of function mutation may not actually be a carrier.

Copyright 2015 Counsyl, Inc
All rights reserved.

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 Counsyl test 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

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

Rebecca Mar-Heyming, PhD, DABMG

Copyright 2015 Counsyl, Inc
All rights reserved.

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. **Variant (1):** c.2207_2212del6ins7. **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):** 1288insTA, 1812-1G>A, 1898+5G>T, 2043delG, 2108delA, 2143delT, 2184insA, 2307insA, 2789+5G>A, 296+12T>C, 3199del6, 3272-26A>G, 3849+10kbC>T, 3849+4A>G, 394delTT, 405+1 G>A, 405+3A>C, 663delT, 711+5G>A, 935delA, 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*, Q996, R1066C, R1158*, R1162*, R117C, R117H, R334W, R347H, R347P, R352Q, R553*, R560T, R709*, R75*, R764*, S1196*, S1251N, S1255*, S364P, S549N, S549R(c.1645A>C), S549R(c.1647T>G), T338I, V520F, W1089*, W1204*, W1282*, Y1092X, Y122*, c.1075_1079del5ins5, c.1545_1546delTA, c.1585-1G>A, c.1766+1G>A, c.1766+1G>T, c.1923_1931del9ins1, c.2051_2052delAAinsG, c.2052delA, c.2738insG, c.274-1G>A, c.2988+1G>A, c.3039delC, c.313delA, c.325_327delTATinsG, c.3528delC, c.3536_3539delCCAA, c.3659delC, c.3744delA, c.3773dupT, c.442delA, c.489+1G>T, c.579+1G>T, c.580-1G>T, c.805_806delAT, c.948delT. **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):** IVS20+6T>C, R696P. **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.379_380dupTA, c.79delC. **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, E122K, E122Q, G25, Hb C, Hb E, Hb S, IVS-I-110, IVS-I-5, IVS-I-6T>C, IVS2-745C>G, K9Vfs*14, Q40*, W16*, c.126_129delCTTT, c.20delA, c.27dupG, c.315+1G>A, c.316-197C>T, c.316-2A>C, c.316-2A>G, c.51delC, c.92+1G>A, 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, R170W, R178H, c.1073+1G>A, c.1274_1277dupTATC, c.1421+1G>C, c.805+1G>A. **Exons:** NM_000520:1-14. **Detection rate**: Northern European > 23%.

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

Lipoamide Dehydrogenase Deficiency - **Gene:** DLD. **Variants (2):** G229C, 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.

Mucolipidosis IV - **Gene:** MCOLN1. **Variants (2):** 511_6944del, c.406-2A>G. **Exons:** NM_020533:1-14. **Detection rate**: Northern European > 10%.

NEB-related Nemaline Myopathy - **Gene:** NEB. **Variant (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. **Variant (1):** R245*. **Exons:** NM_033056:2-33. **Detection rate**: Unknown due to rarity of disease.

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

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

ANALYSIS OF HOMOLOGOUS REGIONS

Alpha Thalassemia - **Genes:** HBA1, HBA2. **Variants (13):** -(alpha)20.5, --BRIT, --MEDI, --MEDII, --SEA, --THAI or --FIL, -alpha3.7, -alpha4.2, HBA1+HBA2 deletion, Hb Constant Spring, anti3.7, anti4.2, del HS-40. **Detection rate**: Unknown due to rarity of disease.

COPY NUMBER ANALYSIS

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

TARGETED GENOTYPING

Gaucher Disease - **Gene:** GBA. **Variants (10):** D448H, D448V, L483P, N409S, R463C, R502H, R535H, V433L, c.115+1G>A, c.84dupG. **Detection rate**: Northern European 60%.

Copyright 2015 Counsyl, Inc
All rights reserved.

Counsyl

RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
NPI: 1306838271
Report Date: 10/04/2015

MALE
DONOR 9941
DOB: [redacted]
Ethnicity: Northern European
Barcode: 55101505030113

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 9941 Residual Risk	Reproductive Risk
ABCC8-related Hyperinsulinism	< 1 in 110	< 1 in 50,000
Alpha Thalassemia	Not calculated	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
Mucolipidosis 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: 3+ copies 1 in 4,800	1 in 670,000
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

Copyright 2015 Counsyl, Inc
All rights reserved.

Integrated GENETICS
LabCorp Specialty Testing Group

Client/Sending Facility:
Phoenix Sperm Bank

1492 S Mill Ave Suite 306
Tempe, AZ 85281
Ph: (602)888-7255
AZB-45

LCLS Specimen Number:	**260-944-0317-0**	Account Number:	[redacted]
Patient Name:	**9941, DONOR**	Ordering Physician:	**OLLIFFE, J**
Date of Birth:	[redacted]	Specimen Type:	**BLOOD**
Gender:	M	Client Reference:	
Patient ID:	9941	Date Collected:	09/17/2015
Lab Number:	YU15-73127 L	Date Received:	09/18/2015
Indications:	NOT GIVEN	Date Reported:	**09/25/2015**

Test: **Chromosome, Blood, Routine**

Cells Counted:	20	Cells Karyotyped:	2
Cells Analyzed:	20	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.

Chromosome analysis performed by LabCorp # Oklahoma City, CLIA 37D2002616. 840 Research Parkway, Oklahoma City, OK 73104. Laboratory Director, Peter Papenhausen, PhD.

TO: Phoenix Sperm Bank

Integrated GENETICS
LabCorp Specialty Testing Group

Client/Sending Facility:
Phoenix Sperm Bank

1492 S Mill Ave Suite 306
Tempe, AZ 85281
Ph: (602)888-7255
AZB-45

LCLS Specimen Number:	**260-944-0317-0**	Account Number:	[redacted]
Patient Name:	**9941, DONOR**	Ordering Physician:	**OLLIFFE, J**
Date of Birth:	[redacted]	Specimen Type:	**BLOOD**
Gender:	M	Client Reference:	
Patient ID:	9941	Date Collected:	09/17/2015
Lab Number:	YU15-73127 L	Date Received:	09/18/2015

[redacted]

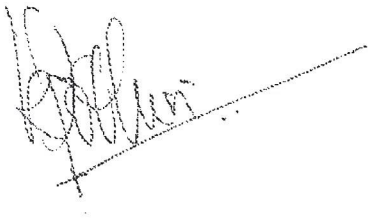
TO: **Phoenix Sperm Bank**

Integrated GENETICS
LabCorp Specialty Testing Group

Client/Sending Facility:
Phoenix Sperm Bank

1492 S Mill Ave Suite 306
Tempe, AZ 85281
Ph: (602)888-7255
AZB-45

LCLS Specimen Number:	**260-944-0317-0**	Account Number:	[redacted]
Patient Name:	**9941, DONOR**	Ordering Physician:	**OLLIFFE, J**
Date of Birth:	[redacted]	Specimen Type:	**BLOOD**
Gender:	M	Client Reference:	
Patient ID:	9941	Date Collected:	09/17/2015
Lab Number:	YU15-73127 L	Date Received:	09/18/2015



Venkateswara R Potluri, PhD
Board Certified Cytogeneticist

Arundhati Chatterjee, MD
Medical Director
Peter Papenhausen, PhD
National Director of Cytogenetics

Technical component performed by Laboratory Corporation of America Holdings,
1904 TW Alexander Drive , RTP , NC , 27709-0153 (800) 345-4363
Professional Component performed by LabCorp CLIA 45D0674994, 3701 Kirby Dr., Suite 528, Houston, TX 77098. Laboratory Director, Venkateswara R. Potluri., Ph.D.
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.**

Counsyl

RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
4915 25th Ave NE, Suite 204W
Seattle, WA 98105
Phone: (206) 588-1484
Fax: (206) 466-4696
NPI: 1306838271
Report Date: 05/15/2017

MALE
DONOR 9941
DOB: [redacted]
Ethnicity: Northern European
Sample Type: EDTA Blood
Date of Collection: 04/20/2017
Date Received: 04/25/2017
Date Tested: 05/15/2017
Barcode: 11004212111523
Indication: Egg or sperm donor

FEMALE
N/A

This is an **amended report**, from the 05/08/2017 original. Panel change.

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.

RESULTS SUMMARY

Risk Details	DONOR 9941	Partner
Panel Information	Family Prep Screen 2.0 Congenital Disorder of Glycosylation Type Ic Panel **(1 condition tested)**	N/A
All conditions tested A complete list of all conditions tested can be found on page 3.	⊖ **NEGATIVE** No disease-causing mutations were detected.	N/A

CLINICAL NOTES

- None

NEXT STEPS

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

Copyright 2017 Counsyl, Inc
All rights reserved.

Methods and Limitations

DONOR 9941 [Family Prep Screen 2.0]: sequencing with copy number analysis.

Sequencing with copy number analysis

High-throughput sequencing and read depth-based copy number analysis are 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. The region of interest (ROI) of the test comprises these regions, in addition to the 20 intronic bases flanking each exon. In a minority of cases where genomic features (e.g., long homopolymers) compromise calling fidelity, the affected intronic bases are not included in the ROI. The ROI is sequenced to high coverage and the sequences are compared to standards and references of normal variation. More than 99% of all bases in the ROI are sequenced at greater than the minimum read depth. Mutations may not be detected in areas of lower sequence coverage. Small insertions and deletions may not be as accurately determined as single nucleotide variants. Genes that have closely related pseudogenes may be addressed by a different method. *CFTR* and *DMD* testing includes analysis for both large (exon-level) deletions and duplications with an average sensitivity of 99%, while other genes are only analyzed for large deletions with a sensitivity of >75%. However, the sensitivity may be higher for selected founder deletions. If *GJB2* is tested, two large upstream deletions which overlap *GJB6* and affect the expression of *GJB2*, del(*GJB6*-D13S1830) and del(*GJB6*-D13S1854), are also analyzed. Mosaicism or somatic variants present at low levels may not be detected. If detected, these may not be reported.

Detection rates are determined by using literature to estimate the fraction of disease alleles, weighted by frequency, that the methodology is unable to detect. Detection rates only account for analytical sensitivity and certain variants that have been previously described in the literature may not be reported if there is insufficient evidence for pathogenicity. Detection rates do not account for the disease-specific rates of de novo mutations.

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 "likely" pathogenic are reported. Likely pathogenic variants are described elsewhere in the report as "likely to have a negative impact on gene function". Likely pathogenic variants are evaluated and classified by assessing the nature of the variant and reviewing reports of allele frequencies in cases and controls, functional studies, variant annotation and effect prediction, and segregation studies. Exon level duplications are assumed to be in tandem and are classified according to their predicted effect on the reading frame. Benign variants, variants of uncertain significance, and variants not directly associated with the intended disease phenotype are not reported. Curation summaries of reported variants are available upon request.

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. This test is designed to detect and report germline alterations. While somatic variants present at low levels may be detected, these may not be reported. 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 test 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*).

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

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

Copyright 2017 Counsyl, Inc
All rights reserved.

Conditions Tested

Congenital Disorder of Glycosylation Type Ic - **Gene:** ALG6. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_013339:2-15. **Detection Rate:** Northern European >99%.

Copyright 2017 Counsyl, Inc
All rights reserved.

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 9941 Residual Risk	Reproductive Risk
Congenital Disorder of Glycosylation Type Ic	< 1 in 50,000	< 1 in 1,000,000

Copyright 2017 Counsyl, Inc
All rights reserved.

Counsyl

RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
4915 25th Ave NE, Suite 204W
Seattle, WA 98105
Phone: (206) 588-1484
Fax: (206) 466-4696
NPI: 1306838271
Report Date: 01/22/2018

MALE
DONOR 9941
DOB: [redacted]
Ethnicity: Mixed or Other Caucasian
Sample Type: EDTA Blood
Date of Collection:
Date Received: 01/16/2018
Date Tested: 01/22/2018
Barcode: 11004212317626
Accession ID: CSLQVRFQG36GNQJ
Indication: Egg or sperm donor

FEMALE
N/A

Foresight™ Carrier Screen

NEGATIVE

ABOUT THIS TEST

The **Counsyl Foresight Carrier Screen** utilizes sequencing, maximizing coverage across all DNA regions tested, to help you learn about your chance to have a child with a genetic disease.

RESULTS SUMMARY

Risk Details	DONOR 9941	Partner
Panel Information	Foresight Carrier Screen 11004212317626 Custom Panel **(2 conditions tested)**	N/A
All conditions tested A complete list of all conditions tested can be found on page 3.	⊖ **NEGATIVE** No disease-causing mutations were detected.	N/A

CLINICAL NOTES

- None

NEXT STEPS

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

Copyright 2018 Counsyl, Inc
All rights reserved.

Methods and Limitations

DONOR 9941 [Foresight Carrier Screen]: sequencing with copy number analysis.

Sequencing with copy number analysis

High-throughput sequencing and read depth-based copy number analysis are 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. The region of interest (ROI) of the test comprises these regions, in addition to the 20 intronic bases flanking each exon. In a minority of cases where genomic features (e.g., long homopolymers) compromise calling fidelity, the affected intronic bases are not included in the ROI. The ROI is sequenced to high coverage and the sequences are compared to standards and references of normal variation. More than 99% of all bases in the ROI are sequenced at greater than the minimum read depth. Mutations may not be detected in areas of lower sequence coverage. Small insertions and deletions may not be as accurately determined as single nucleotide variants. Genes that have closely related pseudogenes may be addressed by a different method. *CFTR* and *DMD* testing includes analysis for both large (exon-level) deletions and duplications with an average sensitivity of 99%, while other genes are only analyzed for large deletions with a sensitivity of >75%. However, the sensitivity may be higher for selected founder deletions. If *GJB2* is tested, two large upstream deletions which overlap *GJB6* and affect the expression of *GJB2*, del(*GJB6*-D13S1830) and del(*GJB6*-D13S1854), are also analyzed. Mosaicism or somatic variants present at low levels may not be detected. If detected, these may not be reported.

Detection rates are determined by using literature to estimate the fraction of disease alleles, weighted by frequency, that the methodology is unable to detect. Detection rates only account for analytical sensitivity and certain variants that have been previously described in the literature may not be reported if there is insufficient evidence for pathogenicity. Detection rates do not account for the disease-specific rates of de novo mutations.

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 "likely" pathogenic are reported. Likely pathogenic variants are described elsewhere in the report as "likely to have a negative impact on gene function". Likely pathogenic variants are evaluated and classified by assessing the nature of the variant and reviewing reports of allele frequencies in cases and controls, functional studies, variant annotation and effect prediction, and segregation studies. Exon level duplications are assumed to be in tandem and are classified according to their predicted effect on the reading frame. Benign variants, variants of uncertain significance, and variants not directly associated with the intended disease phenotype are not reported. Curation summaries of reported variants are available upon request.

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. This test is designed to detect and report germline alterations. While somatic variants present at low levels may be detected, these may not be reported. 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 test 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*).

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

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

Copyright 2018 Counsyl, Inc
All rights reserved.

Conditions Tested

Pendred Syndrome - **Gene:** SLC26A4. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000441:2-21. **Detection Rate:** Mixed or Other Caucasian >99%.

USH2A-related Disorders - **Gene:** USH2A. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_206933:2-72. **Detection Rate:** Mixed or Other Caucasian 94%.

Copyright 2018 Counsyl, Inc
All rights reserved.

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 9941 Residual Risk	Reproductive Risk
Pendred Syndrome	1 in 7,000	< 1 in 1,000,000
USH2A-related Disorders	1 in 2,200	< 1 in 1,000,000

Copyright 2018 Counsyl, Inc
All rights reserved.

Counsyl

RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
4915 25th Ave NE, Suite 204W
Seattle, WA 98105
Phone: (206) 588-1484
Fax: (206) 466-4696
NPI: 1306838271
Report Date: 05/15/2017

MALE
DONOR 9941
DOB: [redacted]
Ethnicity: Northern European
Sample Type: EDTA Blood
Date of Collection: 04/20/2017
Date Received: 04/25/2017
Date Tested: 05/15/2017
Barcode: 11004212111523
Indication: Egg or sperm donor

FEMALE
N/A

This is an **amended report**, from the 05/08/2017 original. Panel change.

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.

RESULTS SUMMARY

Risk Details	DONOR 9941	Partner
Panel Information	Family Prep Screen 2.0 Congenital Disorder of Glycosylation Type Ic Panel **(1 condition tested)**	N/A
All conditions tested A complete list of all conditions tested can be found on page 3.	⊖ **NEGATIVE** No disease-causing mutations were detected.	N/A

CLINICAL NOTES

- None

NEXT STEPS

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

Copyright 2017 Counsyl, Inc
All rights reserved.

Methods and Limitations

DONOR 9941 [Family Prep Screen 2.0]: sequencing with copy number analysis.

Sequencing with copy number analysis

High-throughput sequencing and read depth-based copy number analysis are 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. The region of interest (ROI) of the test comprises these regions, in addition to the 20 intronic bases flanking each exon. In a minority of cases where genomic features (e.g., long homopolymers) compromise calling fidelity, the affected intronic bases are not included in the ROI. The ROI is sequenced to high coverage and the sequences are compared to standards and references of normal variation. More than 99% of all bases in the ROI are sequenced at greater than the minimum read depth. Mutations may not be detected in areas of lower sequence coverage. Small insertions and deletions may not be as accurately determined as single nucleotide variants. Genes that have closely related pseudogenes may be addressed by a different method. *CFTR* and *DMD* testing includes analysis for both large (exon-level) deletions and duplications with an average sensitivity of 99%, while other genes are only analyzed for large deletions with a sensitivity of >75%. However, the sensitivity may be higher for selected founder deletions. If *GJB2* is tested, two large upstream deletions which overlap *GJB6* and affect the expression of *GJB2*, del(*GJB6*-D13S1830) and del(*GJB6*-D13S1854), are also analyzed. Mosaicism or somatic variants present at low levels may not be detected. If detected, these may not be reported.

Detection rates are determined by using literature to estimate the fraction of disease alleles, weighted by frequency, that the methodology is unable to detect. Detection rates only account for analytical sensitivity and certain variants that have been previously described in the literature may not be reported if there is insufficient evidence for pathogenicity. Detection rates do not account for the disease-specific rates of de novo mutations.

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 "likely" pathogenic are reported. Likely pathogenic variants are described elsewhere in the report as "likely to have a negative impact on gene function". Likely pathogenic variants are evaluated and classified by assessing the nature of the variant and reviewing reports of allele frequencies in cases and controls, functional studies, variant annotation and effect prediction, and segregation studies. Exon level duplications are assumed to be in tandem and are classified according to their predicted effect on the reading frame. Benign variants, variants of uncertain significance, and variants not directly associated with the intended disease phenotype are not reported. Curation summaries of reported variants are available upon request.

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. This test is designed to detect and report germline alterations. While somatic variants present at low levels may be detected, these may not be reported. 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 test 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*).

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

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

Copyright 2017 Counsyl, Inc
All rights reserved.

Conditions Tested

Congenital Disorder of Glycosylation Type Ic - **Gene:** ALG6. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_013339:2-15. **Detection Rate:** Northern European >99%.

Copyright 2017 Counsyl, Inc
All rights reserved.

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 9941 Residual Risk	Reproductive Risk
Congenital Disorder of Glycosylation Type Ic	< 1 in 50,000	< 1 in 1,000,000

Copyright 2017 Counsyl, Inc
All rights reserved.

Counsyl

RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
4915 25th Ave NE, Suite 204W
Seattle, WA 98105
Phone: (206) 588-1484
Fax: (206) 466-4696
NPI: 1306838271
Report Date: 01/22/2018

MALE
DONOR 9941
DOB: [redacted]
Ethnicity: Mixed or Other Caucasian
Sample Type: EDTA Blood
Date of Collection:
Date Received: 01/16/2018
Date Tested: 01/22/2018
Barcode: 11004212317626
Accession ID: CSLQVRFQG36GNQJ
Indication: Egg or sperm donor

FEMALE
N/A

Foresight™ Carrier Screen

NEGATIVE

ABOUT THIS TEST

The **Counsyl Foresight Carrier Screen** utilizes sequencing, maximizing coverage across all DNA regions tested, to help you learn about your chance to have a child with a genetic disease.

RESULTS SUMMARY

Risk Details	DONOR 9941	Partner
Panel Information	Foresight Carrier Screen 11004212317626 Custom Panel **(2 conditions tested)**	N/A
All conditions tested A complete list of all conditions tested can be found on page 3.	⊖ **NEGATIVE** No disease-causing mutations were detected.	N/A

CLINICAL NOTES

- None

NEXT STEPS

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

Copyright 2018 Counsyl, Inc
All rights reserved.

Methods and Limitations

DONOR 9941 [Foresight Carrier Screen]: sequencing with copy number analysis.

Sequencing with copy number analysis

High-throughput sequencing and read depth-based copy number analysis are 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. The region of interest (ROI) of the test comprises these regions, in addition to the 20 intronic bases flanking each exon. In a minority of cases where genomic features (e.g., long homopolymers) compromise calling fidelity, the affected intronic bases are not included in the ROI. The ROI is sequenced to high coverage and the sequences are compared to standards and references of normal variation. More than 99% of all bases in the ROI are sequenced at greater than the minimum read depth. Mutations may not be detected in areas of lower sequence coverage. Small insertions and deletions may not be as accurately determined as single nucleotide variants. Genes that have closely related pseudogenes may be addressed by a different method. *CFTR* and *DMD* testing includes analysis for both large (exon-level) deletions and duplications with an average sensitivity of 99%, while other genes are only analyzed for large deletions with a sensitivity of >75%. However, the sensitivity may be higher for selected founder deletions. If *GJB2* is tested, two large upstream deletions which overlap *GJB6* and affect the expression of *GJB2*, del(*GJB6*-D13S1830) and del(*GJB6*-D13S1854), are also analyzed. Mosaicism or somatic variants present at low levels may not be detected. If detected, these may not be reported.

Detection rates are determined by using literature to estimate the fraction of disease alleles, weighted by frequency, that the methodology is unable to detect. Detection rates only account for analytical sensitivity and certain variants that have been previously described in the literature may not be reported if there is insufficient evidence for pathogenicity. Detection rates do not account for the disease-specific rates of de novo mutations.

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 "likely" pathogenic are reported. Likely pathogenic variants are described elsewhere in the report as "likely to have a negative impact on gene function". Likely pathogenic variants are evaluated and classified by assessing the nature of the variant and reviewing reports of allele frequencies in cases and controls, functional studies, variant annotation and effect prediction, and segregation studies. Exon level duplications are assumed to be in tandem and are classified according to their predicted effect on the reading frame. Benign variants, variants of uncertain significance, and variants not directly associated with the intended disease phenotype are not reported. Curation summaries of reported variants are available upon request.

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. This test is designed to detect and report germline alterations. While somatic variants present at low levels may be detected, these may not be reported. 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 test 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*).

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

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

Copyright 2018 Counsyl, Inc
All rights reserved.

Conditions Tested

Pendred Syndrome - **Gene:** SLC26A4. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000441:2-21. **Detection Rate:** Mixed or Other Caucasian >99%.

USH2A-related Disorders - **Gene:** USH2A. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_206933:2-72. **Detection Rate:** Mixed or Other Caucasian 94%.

Copyright 2018 Counsyl, Inc
All rights reserved.

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 9941 Residual Risk	Reproductive Risk
Pendred Syndrome	1 in 7,000	< 1 in 1,000,000
USH2A-related Disorders	1 in 2,200	< 1 in 1,000,000

Copyright 2018 Counsyl, Inc
All rights reserved.