March 17, 2015

Seattle Sperm Bank
4915 25th Ave Ne Ste 204
SEATTLE, WA 98105

Test Results of: 9854, DONOR
DOB: [redacted] Sex: M
Collected on: 03/12/2015
Received on: 03/12/2015
Reported on: 03/17/2015

Patient ID#:

Branch Number: WAB55
Account Number: [redacted]
Specimen Number: 071-129-1072-0
Specimen Type: Blood

Physician: OLLIFFE J

Test: Cystic Fibrosis, DNA Analysis

RESULTS: Negative for 32 mutations analyzed

INTERPRETATION:
This individual is negative for the mutations analyzed. This negative result may need further interpretation depending on the clinical indication. This result reduces but does not eliminate the risk to be a CF carrier.

COMMENTS:
The detection rate varies with ethnicity and is listed below. The presence of an undetected mutation in the CF gene cannot be ruled out. In the absence of family history, the remaining risk that a person with a negative result could have at least one CF mutation is listed in the table. If there is a family history of CF, these risk figures do not apply. As detailed information regarding this individual's family history would permit a more accurate assessment of this individual's risk to be a carrier of cystic fibrosis, please contact LabCorp-Esoterix at (888) 690-3935 for a revised report.

Mutation Detection Rates among Ethnic Groups	Detection rates are based on mutation frequencies in patients affected with cystic fibrosis. Among individuals with an atypical or mild presentation (e.g. congenital absence of the vas deferens, pancreatitis) detection rates may vary from those provided here:	
Ethnicity	**Carrier risk reduction when no family history**	**Detection Rate**
Ashkenazi Jewish	1/26 to 1/834	97%
Caucasian (non-Hispanic)	1/25 to 1/240	90%
African-American	1/65 to 1/207	69%
Hispanic	1/46 to 1/168	73%
Asian	1/94 to 1/208	55%

This interpretation is based on the clinical and family relationship information provided and the current understanding of the molecular genetics of this condition.

MUTATIONS ANALYZED:

G85E	A455E	S549N	R1162X	711+1 G→T	2184delA	3876delA
R117H	ΔI507	S549R	W1282X	1078delT	2789+5 G→A	3905insT
R334W	ΔF508	G551D	N1303K	1717-1 G→A	3120+1 G→A	
R347H	V520F	R553X	394delTT	1898+1 G→A	3659delC	
R347P	G542X	R560T	621+1 G→T	2183AA→G	3849+10kb C→T	

METHODS/LIMITATIONS:
DNA is isolated from the sample and tested for the 32 CF mutations on the Universal Array Platform (Luminex). Regions of the *CFTR* gene are amplified enzymatically and subjected to a solution-phase multiplex allele-specific primer extension with subsequent hybridization to a bead array and fluorescence detection. Polymorphisms F508C, I506V, and I507V are included in this panel to rule out false positive deltaF508 homozygotes. Reflex testing of 5T is included in the panel for R117H interpretation. False positive or negative results may occur for reasons that include genetic variants, blood transfusions, bone marrow transplantation, erroneous representation of family relationships or contamination of a fetal sample with maternal cells. The assay provides information intended to be used for carrier screening in adults of reproductive age, as an aid in newborn screening, and as a confirmatory test for another medically established diagnosis in newborns and children. The test is not intended for use in fetal diagnostic testing, pre-implantation screening, or for any stand-alone diagnostic purposes without confirmation by another medically established diagnostic product or procedure.

REFERENCES:
1. Updates on Carrier Screening for Cystic Fibrosis, (2011) Am J Ob Gynecol 117(4):1028-1031.
2. Watson, et al. (2004) *Genet Med* 6:387-91
3. Richards, et al. (2002) *Genet Med* 4:379-391
4. Preconception and prenatal carrier screening for cystic fibrosis: (2001)ACOG.ACMG publication

Results Released By: Samuel H. Pepkowitz, M.D., Medical Director
Report Released By: Samuel H. Pepkowitz, M.D., Medical Director

Samuel H. Pepkowitz, MD
Medical Director, Esoterix

LabCorp - Esoterix
4301 Lost Hills Road, Calabasas Hills, CA, 91301 (888) 690-3935

Integrated GENETICS
LabCorp Specialty Testing Group

Client/Sending Facility:
Seattle Sperm Bank

4915 25th Ave Ne Ste 204
SEATTLE, WA 98105
Ph: (206)588-1484
Fax: (206) 588-1485 WAB-55

LCLS Specimen Number:	**071-129-1072-0**	Account Number:	[redacted]
Patient Name:	**9854, DONOR**	Ordering Physician:	**J OLLIFFE**
Date of Birth:	[redacted]	Specimen Type:	**BLOOD**
Gender:	M	Client Reference:	B0019646637
Patient ID:		Date Collected:	03/12/2015
Lab Number:	(J15-819 L	Date Received:	03/13/2015
Indications:	DONOR	Date Reported:	**03/24/2015**

Test: **Chromosome, Blood, Routine**

Cells Counted:	15	Cells Karyotyped:	5
Cells Analyzed:	5	Band Resolution:	550

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.

Integrated GENETICS
LabCorp Specialty Testing Group

Client/Sending Facility:
Seattle Sperm Bank

4915 25th Ave Ne Ste 204
SEATTLE, WA 98105
Ph: (206)588-1484
Fax: (206) 588-1485 WAB-55

LCLS Specimen Number:	**071-129-1072-0**
Patient Name:	**9854, DONOR**
Date of Birth:	[redacted]
Gender:	M
Patient ID:	
Lab Number:	(J15-819 L
Account Number:	[redacted]
Ordering Physician:	**J OLLIFFE**
Specimen Type:	**BLOOD**
Client Reference:	B0019646637
Date Collected:	03/12/2015
Date Received:	03/13/2015

[redacted]

Integrated GENETICS
LabCorp Specialty Testing Group

Client/Sending Facility:
Seattle Sperm Bank

4915 25th Ave Ne Ste 204
SEATTLE, WA 98105
Ph: (206)588-1484
Fax: (206) 588-1485 WAB-55

LCLS Specimen Number: 071-129-1072-0
Patient Name: **9854, DONOR**
Date of Birth: [redacted]
Gender: M
Patient ID:
Lab Number: (J15-819 L

Account Number: [redacted]
Ordering Physician: **J OLLIFFE**
Specimen Type: **BLOOD**
Client Reference: B0019646637
Date Collected: 03/12/2015
Date Received: 03/13/2015

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 (800) 676-8033
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.

Integrated GENETICS
LabCorp Specialty Testing Group

SMN1 Copy Number Analysis

Patient Name: Donor 9854
[redacted]
Age: 21 yrs
Gender: Male

803037 / 803038
Seattle Sperm Bank
4915 25th Avenue East
Suite 204W
Seattle, WA 98105
USA

Specimen #: 62801602-1
Case #: 62693601 Patient ID #: 62341145
Date Collected: 03/12/2015 Date Received: 03/13/2015

Referring Physician: Jeffrey Olliffe
Genetic Counselor:

Specimen Type: Peripheral Blood

Clinical Data: Carrier Test/Gamete donor

Client Lab ID #:
Hospital ID #:
Specimen ID #:
Specimen(s) Received: 1 - Yellow (ACD) 7 ml round bottom tube(s)
Ethnicity: Caucasian

RESULTS: SMN1 copy number: 2 (Reduced Carrier Risk)

INTERPRETATION:

This individual has an SMN1 copy number of two. This result reduces but does not eliminate the risk to be a carrier of SMA. Ethnic specific risk reductions based on a negative family history and an SMN1 copy number of two are provided in the Comments section of this report.

COMMENT:

Spinal muscular atrophy (SMA) is an autosomal recessive disease of variable age of onset and severity caused by mutations (most often deletions or gene conversions) in the survival motor neuron (SMN1) gene. Molecular testing assesses the number of copies of the SMN1 gene. Individuals with one copy of the SMN1 gene are predicted to be carriers of SMA. Individuals with two or more copies have a reduced risk to be carriers. (Affected individuals have 0 copies of the SMN1 gene.)

This copy number analysis cannot detect individuals who are carriers of SMA as a result of either 2 (or very rarely 3) copies of the SMN1 gene on one chromosome and the absence of the SMN1 gene on the other chromosome or small intragenic mutations within the SMN1 gene. This analysis also will not detect germline mosaicism or mutations in genes other than SMN1. Additionally, de novo mutations have been reported in approximately 2% of SMA patients.

Carrier Frequency and Risk Reductions for Individuals with No Family History of SMA				
Ethnicity	**Detection Rate[1]**	**Prior Carrier Risk[1]**	**Reduced Carrier Risk for 2 copy result**	**Reduced Carrier Risk for 3 copy result**
Caucasian	94.8%	1:47	1:834	1:5,600
Ashkenazi Jewish	90.5%	1:67	1:611	1:5,400
Asian	93.3%	1:59	1:806	1:5,600
Hispanic	90.0%	1:68	1:579	1:5,400
African American	70.5%	1:72	1:130	1:4,200
Asian Indian	90.2%	1:52	1:443	1:5,400
Mixed or Other Ethnic Background	For counseling purposes, consider using the ethnic background with the most conservative risk estimates.			

METHOD/LIMITATIONS: Specimen DNA is isolated and amplified by real-time polymerase chain reaction (PCR) for exon 7 of the SMN1 gene and the internal standard reference genes. A mathematical algorithm is used to calculate and report SMN1 copy numbers of 0, 1, 2 and 3. Based upon this analysis, an upper limit of 3 represents the highest degree of accuracy in reporting SMN1 copy number with statistical confidence. Sequencing of the primer and probe binding sites is performed on all fetal samples and samples with one copy of SMN1 by real-time PCR to rule out the presence of sequence variants which could interfere with analysis and interpretation. False positive or negative results may occur for reasons that include genetic variants, blood transfusions, bone marrow transplantation, erroneous representation of family relationships or contamination of a fetal sample with maternal cells.

REFERENCES:
1. Sugarman EA, Nagan N, Zhu H, et al. Pan-ethnic carrier screening and prenatal diagnosis for spinal muscular atrophy: clinical laboratory analysis of >72,400 specimens. Eur J Hum Genet 2012; 20:27-32. 2. Prior TW, et al. Technical standards and guidelines for spinal muscular atrophy testing. Genet Med 2011; 13(7): 686-694.

Electronically Signed by: Jane W. Thuo, Ph.D., FACMG, on 03/17/2015
Reported by: /

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) 588-1484
NPI: 1306838271
Report Date: 01/26/2016

MALE
DONOR 9854
DOB: [redacted]
Ethnicity: Mixed or Other Caucasian
Sample Type: OG-510 Saliva
Date of Collection: 01/12/2016
Date Received: 01/18/2016
Date Tested: 01/23/2016
Barcode: 55101505040527
Indication: Screening for genetic disease carrier status

FEMALE
N/A

This is an **amended report**, from the 01/23/2016 original. Panel change requested.

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

55101505040527 Custom Panel **(3 conditions tested)**

VERSION

DONOR 9854 **(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 3.

CLINICAL NOTES

- None

NEXT STEPS

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

Methods and Limitations

DONOR 9854 [Family Prep Screen 2.0]: sequencing and targeted genotyping.

Sequencing: High-throughput sequencing is used to analyze 36 exons in 3 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 5 variants associated with 3 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.

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.

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

Conditions Tested

Autosomal Recessive Disorders

SEQUENCING AND TARGETED GENOTYPING

Alpha-1 Antitrypsin Deficiency - **Gene:** SERPINA1. **Variant (1):** Z allele. **Exons:** NM_000295:2-5. **Detection rate**: Mixed or Other Caucasian > 95%.

PEX1-related Zellweger Syndrome Spectrum - **Gene:** PEX1. **Variants (2):** G843D, I700Yfs*42. **Exons:** NM_000466:1-24. **Detection rate**: Mixed or Other Caucasian > 68%.

Steroid-Resistant Nephrotic Syndrome - **Gene:** NPHS2. **Variants (2):** R138*, R138Q. **Exons:** NM_014625:1-8. **Detection rate**: Mixed or Other Caucasian > 33%.

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 9854 Residual Risk	Reproductive Risk
Alpha-1 Antitrypsin Deficiency	< 1 in 680	< 1 in 93,000
PEX1-related Zellweger Syndrome Spectrum	< 1 in 350	< 1 in 160,000
Steroid-Resistant Nephrotic Syndrome	< 1 in 600	< 1 in 950,000

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: 08/15/2017

MALE
DONOR 9854
DOB: [redacted]
Ethnicity: Unknown / Not Reported
Sample Type: EDTA Blood
Date of Collection: 08/09/2017
Date Received: 08/10/2017
Date Tested: 08/15/2017
Barcode: 11004212187644
Indication: Egg or sperm donor

FEMALE
N/A

Foresight™ Carrier Screen

POSITIVE: CARRIER

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 9854	Partner
Panel Information	Foresight Carrier Screen Universal Panel Minus X-Linked **(102 conditions tested)**	N/A
POSITIVE: CARRIER GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness **Reproductive Risk: 1 in 130** **Inheritance: Autosomal Recessive**	**CARRIER*** NM_004004.5(GJB2):c.101T>C(M34T) heterozygote	The reproductive risk presented is based on a hypothetical pairing with a partner of the same ethnic group. Carrier testing should be considered. See "Next Steps".

*Carriers generally do not experience symptoms.

No disease-causing mutations were detected in any other gene tested. A complete list of all conditions tested can be found on page 6.

CLINICAL NOTES

- Ethnicity unknown or not reported for DONOR. Risk calculation is based on the assumption of Northern European ancestry.

NEXT STEPS

- Carrier testing should be considered for the diseases specified above for the patient's partner, as both parents must be carriers before a child is at high risk of developing the disease.
- Genetic counseling is recommended and patients may wish to discuss any positive results with blood relatives, as there is an increased chance that they are also carriers.

Counsyl has renamed its products effective July 19, 2017. The Family Prep Screen is now the Foresight Carrier Screen. The new names now appear on all communications from Counsyl. If you have any questions, please contact Counsyl directly.

Counsyl

RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
NPI: 1306838271
Report Date: 08/15/2017

MALE
DONOR 9854
DOB: [redacted]
Ethnicity: Unknown / Not Reported
Barcode: 11004212187644

FEMALE
N/A

POSITIVE: CARRIER

GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness

Reproductive risk: 1 in 130
Risk before testing: 1 in 4,200

Gene: GJB2 | **Inheritance Pattern:** Autosomal Recessive

Patient	DONOR 9854	No partner tested
Result	✚ Carrier	N/A
Variant(s)	NM_004004.5(GJB2):c.101T>C(M34T) heterozygote	N/A
Methodology	Sequencing with copy number analysis	N/A
Interpretation	This individual is a carrier of GJB2-related DFNB1 nonsyndromic hearing loss and deafness. Carriers generally do not experience symptoms. M34T is associated with a variable presentation, ranging from clinically asymptomatic to severe hearing loss.	N/A
Detection rate	>99%	N/A
Exons tested	NM_004004:1-2.	N/A

What is GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness?

DFNB1 nonsyndromic hearing loss and deafness is an inherited condition in which a person has mild to severe hearing loss from birth. It is caused by mutations in GJB2 (which encodes the protein connexin 26) and GJB6 (which encodes connexin 30). The condition is not progressive, meaning that it does not worsen over time.

The word “nonsyndromic” refers to the fact that there are no other symptoms or systems of the body involved with the disease. Unlike some other forms of hearing loss, DFNB1 nonsyndromic hearing loss and deafness does not affect balance or movement.

The degree of hearing loss is difficult to predict based on which genetic mutation one has. Even if members of the same family are affected by DFNB1 nonsyndromic hearing loss and deafness, the degree of hearing loss may vary among them.

How common is GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness?

In the United States, the United Kingdom, France, Australia, and New Zealand, approximately 14 in 100,000 people have DFNB1 nonsyndromic hearing loss and deafness. Roughly 1 in 33 people are carriers of the mutation that causes the condition.

How is GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness treated?

People with DFNB1 nonsyndromic hearing loss and deafness may show improvement by using hearing aids. For people with profound deafness, cochlear implants may also be helpful. They may also want to consider enrolling in an educational program for the hearing impaired.

What is the prognosis for a person with GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness?

While a person with GJB2-related DFNB1 nonsyndromic hearing loss and deafness will have mild to severe hearing loss, it does not affect lifespan and does not affect any other part of the body.

Methods and Limitations

DONOR 9854 [Foresight Carrier Screen]: sequencing with copy number analysis, spinal muscular atrophy, and analysis of homologous regions.

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.

Spinal muscular atrophy

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. This is more likely in individuals who have 2 copies of the *SMN1* gene and are positive for the g.27134T>G SNP, which affects the reported residual risk; Ashkenazi Jewish or Asian patients with this genotype have a high post-test likelihood of being carriers for SMA and are reported as carriers. The g.27134T>G SNP is only reported in individuals who have 2 copies of *SMN1*.

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 genes cannot be determined, but are estimated from copy number analysis. High numbers of pseudogene copies may interfere with this analysis.

If *CYP21A2* is tested, 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). 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. If *HBA1*/*HBA2* are tested, some individuals with four alpha globin genes may be carriers, with three genes on one chromosome and a deletion on the other chromosome. This and similar, but rare, carrier states, where complementary changes exist in both the gene and a pseudogene, may not be detected by the assay.

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

Conditions Tested

21-hydroxylase-deficient Congenital Adrenal Hyperplasia - **Gene:** CYP21A2. Autosomal Recessive. Analysis of Homologous Regions. **Variants (13):** CYP21A2 deletion, CYP21A2 duplication, CYP21A2 triplication, G111Vfs*21, I173N, L308FfsX6, P31L, Q319*, Q319*+CYP21A2dup, R357W, V281L, [I237N;V238E;M240K], c.293-13C>G. **Detection Rate:** Ethnicity Unknown 96%.

ABCC8-related Hyperinsulinism - **Gene:** ABCC8. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000352:1-39. **Detection Rate:** Ethnicity Unknown >99%.

Alkaptonuria - **Gene:** HGD. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000187:1-14. **Detection Rate:** Ethnicity Unknown >99%.

Alpha Thalassemia - **Genes:** HBA1, HBA2. Autosomal Recessive. Analysis of Homologous Regions. **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.

Alpha-1 Antitrypsin Deficiency - **Gene:** SERPINA1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000295:2-5. **Detection Rate:** Ethnicity Unknown >99%.

Alpha-mannosidosis - **Gene:** MAN2B1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000528:1-23. **Detection Rate:** Ethnicity Unknown >99%.

Alpha-sarcoglycanopathy - **Gene:** SGCA. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000023:1-9. **Detection Rate:** Ethnicity Unknown >99%.

Andermann Syndrome - **Gene:** SLC12A6. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_133647:1-25. **Detection Rate:** Ethnicity Unknown >99%.

ARSACS - **Gene:** SACS. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_014363:2-10. **Detection Rate:** Ethnicity Unknown 99%.

Aspartylglycosaminuria - **Gene:** AGA. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000027:1-9. **Detection Rate:** Ethnicity Unknown >99%.

Ataxia with Vitamin E Deficiency - **Gene:** TTPA. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000370:1-5. **Detection Rate:** Ethnicity Unknown >99%.

Ataxia-telangiectasia - **Gene:** ATM. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000051:2-63. **Detection Rate:** Ethnicity Unknown 98%.

Bardet-Biedl Syndrome, BBS1-related - **Gene:** BBS1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_024649:1-17. **Detection Rate:** Ethnicity Unknown >99%.

Bardet-Biedl Syndrome, BBS10-related - **Gene:** BBS10. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_024685:1-2. **Detection Rate:** Ethnicity Unknown >99%.

Beta-sarcoglycanopathy - **Gene:** SGCB. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000232:1-6. **Detection Rate:** Ethnicity Unknown >99%.

Biotinidase Deficiency - **Gene:** BTD. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000060:1-4. **Detection Rate:** Ethnicity Unknown >99%.

Bloom Syndrome - **Gene:** BLM. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000057:2-22. **Detection Rate:** Ethnicity Unknown >99%.

Canavan Disease - **Gene:** ASPA. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000049:1-6. **Detection Rate:** Ethnicity Unknown 98%.

Carnitine Palmitoyltransferase IA Deficiency - **Gene:** CPT1A. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_001876:2-19. **Detection Rate:** Ethnicity Unknown >99%.

Carnitine Palmitoyltransferase II Deficiency - **Gene:** CPT2. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000098:1-5. **Detection Rate:** Ethnicity Unknown >99%.

Cartilage-hair Hypoplasia - **Gene:** RMRP. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exon:** NR_003051:1. **Detection Rate:** Ethnicity Unknown >99%.

Citrullinemia Type 1 - **Gene:** ASS1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000050:3-16. **Detection Rate:** Ethnicity Unknown >99%.

CLN3-related Neuronal Ceroid Lipofuscinosis - **Gene:** CLN3. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_001042432:2-16. **Detection Rate:** Ethnicity Unknown >99%.

CLN5-related Neuronal Ceroid Lipofuscinosis - **Gene:** CLN5. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_006493:1-4. **Detection Rate:** Ethnicity Unknown >99%.

CNGB3-related Achromatopsia - **Gene:** CNGB3. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_019098:1-18. **Detection Rate:** Ethnicity Unknown >99%.

Cohen Syndrome - **Gene:** VPS13B. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_017890:2-62. **Detection Rate:** Ethnicity Unknown 97%.

Congenital Disorder of Glycosylation Type Ia - **Gene:** PMM2. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000303:1-8. **Detection Rate:** Ethnicity Unknown >99%.

Congenital Disorder of Glycosylation Type Ib - **Gene:** MPI. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_002435:1-8. **Detection Rate:** Ethnicity Unknown >99%.

Congenital Finnish Nephrosis - **Gene:** NPHS1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_004646:1-29. **Detection Rate:** Ethnicity Unknown >99%.

Costeff Optic Atrophy Syndrome - **Gene:** OPA3. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_025136:1-2. **Detection Rate:** Ethnicity Unknown >99%.

Cystic Fibrosis - **Gene:** CFTR. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000492:1-27. IVS8-5T allele analysis is only reported in the presence of the R117H mutation. **Detection Rate:** Ethnicity Unknown >99%.

Cystinosis - **Gene:** CTNS. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_004937:3-12. **Detection Rate:** Ethnicity Unknown >99%.

D-bifunctional Protein Deficiency - **Gene:** HSD17B4. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000414:1-24. **Detection Rate:** Ethnicity Unknown 98%.

Dihydropyrimidine Dehydrogenase Deficiency - **Gene:** DPYD. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000110:1-23. **Detection Rate:** Ethnicity Unknown 98%.

Factor XI Deficiency - **Gene:** F11. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000128:2-15. **Detection Rate:** Ethnicity Unknown >99%.

Familial Dysautonomia - **Gene:** IKBKAP. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_003640:2-37. **Detection Rate:** Ethnicity Unknown >99%.

Familial Mediterranean Fever - **Gene:** MEFV. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000243:1-10. **Detection Rate:** Ethnicity Unknown >99%.

Fanconi Anemia Type C - **Gene:** FANCC. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000136:2-15. **Detection Rate:** Ethnicity Unknown >99%.

FKTN-related Disorders - **Gene:** FKTN. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_001079802:3-11. **Detection Rate:** Ethnicity Unknown >99%.

Galactosemia - **Gene:** GALT. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000155:1-11. **Detection Rate:** Ethnicity Unknown >99%.

Gaucher Disease - **Gene:** GBA. Autosomal Recessive. Analysis of Homologous Regions. **Variants (10):** D409V, D448H, IVS2+1G>A, L444P, N370S, R463C, R463H, R496H, V394L, p.L29Afs*18. **Detection Rate:** Ethnicity Unknown 60%.

GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness - **Gene:** GJB2. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_004004:1-2. **Detection Rate:** Ethnicity Unknown >99%.

Glutaric Acidemia Type 1 - **Gene:** GCDH. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000159:2-12. **Detection Rate:** Ethnicity Unknown >99%.

Glycogen Storage Disease Type Ia - **Gene:** G6PC. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000151:1-5. **Detection Rate:** Ethnicity Unknown >99%.
Glycogen Storage Disease Type Ib - **Gene:** SLC37A4. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_001164277:3-11. **Detection Rate:** Ethnicity Unknown >99%.
Glycogen Storage Disease Type III - **Gene:** AGL. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000642:2-34. **Detection Rate:** Ethnicity Unknown >99%.
Glycogen Storage Disease Type V - **Gene:** PYGM. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_005609:1-20. **Detection Rate:** Ethnicity Unknown >99%.
GRACILE Syndrome - **Gene:** BCS1L. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_004328:3-9. **Detection Rate:** Ethnicity Unknown >99%.
HADHA-related Disorders - **Gene:** HADHA. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000182:1-20. **Detection Rate:** Ethnicity Unknown >99%.
Hb Beta Chain-related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease) - **Gene:** HBB. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000518:1-3. **Detection Rate:** Ethnicity Unknown >99%.
Hereditary Fructose Intolerance - **Gene:** ALDOB. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000035:2-9. **Detection Rate:** Ethnicity Unknown >99%.
Herlitz Junctional Epidermolysis Bullosa, LAMA3-related - **Gene:** LAMA3. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000227:1-38. **Detection Rate:** Ethnicity Unknown >99%.
Herlitz Junctional Epidermolysis Bullosa, LAMB3-related - **Gene:** LAMB3. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000228:2-23. **Detection Rate:** Ethnicity Unknown >99%.
Herlitz Junctional Epidermolysis Bullosa, LAMC2-related - **Gene:** LAMC2. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_005562:1-23. **Detection Rate:** Ethnicity Unknown >99%.
Hexosaminidase A Deficiency (Including Tay-Sachs Disease) - **Gene:** HEXA. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000520:1-14. **Detection Rate:** Ethnicity Unknown >99%.
Homocystinuria Caused by Cystathionine Beta-synthase Deficiency - **Gene:** CBS. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000071:3-17. **Detection Rate:** Ethnicity Unknown >99%.
Hypophosphatasia, Autosomal Recessive - **Gene:** ALPL. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000478:2-12. **Detection Rate:** Ethnicity Unknown >99%.
Inclusion Body Myopathy 2 - **Gene:** GNE. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_001128227:1-12. **Detection Rate:** Ethnicity Unknown >99%.
Isovaleric Acidemia - **Gene:** IVD. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_002225:1-12. **Detection Rate:** Ethnicity Unknown >99%.
Joubert Syndrome 2 - **Gene:** TMEM216. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_001173990:1-5. **Detection Rate:** Ethnicity Unknown >99%.
Krabbe Disease - **Gene:** GALC. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000153:1-17. **Detection Rate:** Ethnicity Unknown >99%.
Lipoamide Dehydrogenase Deficiency - **Gene:** DLD. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000108:1-14. **Detection Rate:** Ethnicity Unknown >99%.
Maple Syrup Urine Disease Type 1B - **Gene:** BCKDHB. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_183050:1-10. **Detection Rate:** Ethnicity Unknown >99%.
Medium Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADM. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000016:1-12. **Detection Rate:** Ethnicity Unknown >99%.
Megalencephalic Leukoencephalopathy with Subcortical Cysts - **Gene:** MLC1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_015166:2-12. **Detection Rate:** Ethnicity Unknown >99%.
Metachromatic Leukodystrophy - **Gene:** ARSA. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000487:1-8. **Detection Rate:** Ethnicity Unknown >99%.
Mucolipidosis IV - **Gene:** MCOLN1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_020533:1-14. **Detection Rate:** Ethnicity Unknown >99%.
Mucopolysaccharidosis Type I - **Gene:** IDUA. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000203:1-14. **Detection Rate:** Ethnicity Unknown >99%.
Muscle-eye-brain Disease - **Gene:** POMGNT1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_017739:2-22. **Detection Rate:** Ethnicity Unknown 96%.
NEB-related Nemaline Myopathy - **Gene:** NEB. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_001271208:3-80,117-183. **Detection Rate:** Ethnicity Unknown 92%.
Niemann-Pick Disease Type C - **Gene:** NPC1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000271:1-25. **Detection Rate:** Ethnicity Unknown >99%.
Niemann-Pick Disease, SMPD1-associated - **Gene:** SMPD1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000543:1-6. **Detection Rate:** Ethnicity Unknown >99%.
Nijmegen Breakage Syndrome - **Gene:** NBN. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_002485:1-16. **Detection Rate:** Ethnicity Unknown >99%.
Northern Epilepsy - **Gene:** CLN8. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_018941:2-3. **Detection Rate:** Ethnicity Unknown >99%.
PCDH15-related Disorders - **Gene:** PCDH15. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_033056:2-33. **Detection Rate:** Ethnicity Unknown 93%.
Pendred Syndrome - **Gene:** SLC26A4. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000441:2-21. **Detection Rate:** Ethnicity Unknown >99%.
PEX1-related Zellweger Syndrome Spectrum - **Gene:** PEX1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000466:1-24. **Detection Rate:** Ethnicity Unknown >99%.
Phenylalanine Hydroxylase Deficiency - **Gene:** PAH. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000277:1-13. **Detection Rate:** Ethnicity Unknown >99%.
PKHD1-related Autosomal Recessive Polycystic Kidney Disease - **Gene:** PKHD1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_138694:2-67. **Detection Rate:** Ethnicity Unknown >99%.
Polyglandular Autoimmune Syndrome Type 1 - **Gene:** AIRE. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000383:1-14. **Detection Rate:** Ethnicity Unknown >99%.
Pompe Disease - **Gene:** GAA. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000152:2-20. **Detection Rate:** Ethnicity Unknown 98%.
PPT1-related Neuronal Ceroid Lipofuscinosis - **Gene:** PPT1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000310:1-9. **Detection Rate:** Ethnicity Unknown >99%.
Primary Carnitine Deficiency - **Gene:** SLC22A5. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_003060:1-10. **Detection Rate:** Ethnicity Unknown >99%.
Primary Hyperoxaluria Type 1 - **Gene:** AGXT. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000030:1-11. **Detection Rate:** Ethnicity Unknown >99%.
Primary Hyperoxaluria Type 2 - **Gene:** GRHPR. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_012203:1-9. **Detection Rate:** Ethnicity Unknown >99%.
PROP1-related Combined Pituitary Hormone Deficiency - **Gene:** PROP1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_006261:1-3. **Detection Rate:** Ethnicity Unknown >99%.
Pseudocholinesterase Deficiency - **Gene:** BCHE. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000055:2-4. **Detection Rate:** Ethnicity Unknown >99%.
Pycnodysostosis - **Gene:** CTSK. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000396:2-8. **Detection Rate:** Ethnicity Unknown >99%.
Rhizomelic Chondrodysplasia Punctata Type 1 - **Gene:** PEX7. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000288:1-10. **Detection Rate:** Ethnicity Unknown >99%.

Salla Disease - **Gene:** SLC17A5. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_012434:1-11. **Detection Rate:** Ethnicity Unknown 98%.
Segawa Syndrome - **Gene:** TH. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000360:1-13. **Detection Rate:** Ethnicity Unknown >99%.
Short Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADS. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000017:1-10. **Detection Rate:** Ethnicity Unknown >99%.
Sjogren-Larsson Syndrome - **Gene:** ALDH3A2. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000382:1-10. **Detection Rate:** Ethnicity Unknown 97%.
Smith-Lemli-Opitz Syndrome - **Gene:** DHCR7. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_001360:3-9. **Detection Rate:** Ethnicity Unknown >99%.
Spinal Muscular Atrophy - **Gene:** SMN1. Autosomal Recessive. Spinal Muscular Atrophy. **Variant (1):** SMN1 copy number. **Detection Rate:** Ethnicity Unknown 95%.
Steroid-resistant Nephrotic Syndrome - **Gene:** NPHS2. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_014625:1-8. **Detection Rate:** Ethnicity Unknown >99%.
Sulfate Transporter-related Osteochondrodysplasia - **Gene:** SLC26A2. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000112:2-3. **Detection Rate:** Ethnicity Unknown >99%.
TPP1-related Neuronal Ceroid Lipofuscinosis - **Gene:** TPP1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000391:1-13. **Detection Rate:** Ethnicity Unknown >99%.
Tyrosinemia Type I - **Gene:** FAH. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000137:1-14. **Detection Rate:** Ethnicity Unknown >99%.
Usher Syndrome Type 3 - **Gene:** CLRN1. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_174878:1-3. **Detection Rate:** Ethnicity Unknown >99%.
Very Long Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADVL. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000018:1-20. **Detection Rate:** Ethnicity Unknown >99%.
Wilson Disease - **Gene:** ATP7B. Autosomal Recessive. Sequencing with Copy Number Analysis. **Exons:** NM_000053:1-21. **Detection Rate:** Ethnicity Unknown >99%.

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.

†Indicates a positive result. See the full clinical report for interpretation and details.

Disease	DONOR 9854 Residual Risk	Reproductive Risk
21-hydroxylase-deficient Congenital Adrenal Hyperplasia	1 in 1,400	1 in 310,000
ABCC8-related Hyperinsulinism	1 in 11,000	< 1 in 1,000,000
Alkaptonuria	1 in 6,800	< 1 in 1,000,000
Alpha Thalassemia	Alpha globin status: aa/aa.	Not calculated
Alpha-1 Antitrypsin Deficiency	1 in 2,700	1 in 300,000
Alpha-mannosidosis	1 in 35,000	< 1 in 1,000,000
Alpha-sarcoglycanopathy	1 in 45,000	< 1 in 1,000,000
Andermann Syndrome	< 1 in 50,000	< 1 in 1,000,000
ARSACS	< 1 in 44,000	< 1 in 1,000,000
Aspartylglycosaminuria	< 1 in 50,000	< 1 in 1,000,000
Ataxia with Vitamin E Deficiency	< 1 in 50,000	< 1 in 1,000,000
Ataxia-telangiectasia	1 in 8,200	< 1 in 1,000,000
Bardet-Biedl Syndrome, BBS1-related	1 in 16,000	< 1 in 1,000,000
Bardet-Biedl Syndrome, BBS10-related	1 in 16,000	< 1 in 1,000,000
Beta-sarcoglycanopathy	< 1 in 50,000	< 1 in 1,000,000
Biotinidase Deficiency	1 in 13,000	1 in 670,000
Bloom Syndrome	< 1 in 50,000	< 1 in 1,000,000
Canavan Disease	< 1 in 31,000	< 1 in 1,000,000
Carnitine Palmitoyltransferase IA Deficiency	< 1 in 50,000	< 1 in 1,000,000
Carnitine Palmitoyltransferase II Deficiency	< 1 in 50,000	< 1 in 1,000,000
Cartilage-hair Hypoplasia	< 1 in 50,000	< 1 in 1,000,000
Citrullinemia Type 1	1 in 12,000	< 1 in 1,000,000
CLN3-related Neuronal Ceroid Lipofuscinosis	1 in 22,000	< 1 in 1,000,000
CLN5-related Neuronal Ceroid Lipofuscinosis	< 1 in 50,000	< 1 in 1,000,000
CNGB3-related Achromatopsia	1 in 11,000	< 1 in 1,000,000
Cohen Syndrome	< 1 in 15,000	< 1 in 1,000,000
Congenital Disorder of Glycosylation Type Ia	1 in 16,000	< 1 in 1,000,000
Congenital Disorder of Glycosylation Type Ib	< 1 in 50,000	< 1 in 1,000,000
Congenital Finnish Nephrosis	< 1 in 50,000	< 1 in 1,000,000
Costeff Optic Atrophy Syndrome	< 1 in 50,000	< 1 in 1,000,000
Cystic Fibrosis	1 in 2,700	1 in 290,000
Cystinosis	1 in 22,000	< 1 in 1,000,000
D-bifunctional Protein Deficiency	1 in 9,000	< 1 in 1,000,000
Dihydropyrimidine Dehydrogenase Deficiency	< 1 in 29,000	< 1 in 1,000,000
Factor XI Deficiency	< 1 in 50,000	< 1 in 1,000,000
Familial Dysautonomia	< 1 in 50,000	< 1 in 1,000,000
Familial Mediterranean Fever	< 1 in 50,000	< 1 in 1,000,000
Fanconi Anemia Type C	1 in 16,000	< 1 in 1,000,000
FKTN-related Disorders	< 1 in 50,000	< 1 in 1,000,000
Galactosemia	1 in 8,600	< 1 in 1,000,000
Gaucher Disease	1 in 280	1 in 120,000
GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness	NM_004004.5(GJB2):c.101T>C(M34T) heterozygote †	1 in 130
Glutaric Acidemia Type 1	1 in 10,000	< 1 in 1,000,000
Glycogen Storage Disease Type Ia	1 in 18,000	< 1 in 1,000,000
Glycogen Storage Disease Type Ib	1 in 35,000	< 1 in 1,000,000
Glycogen Storage Disease Type III	1 in 16,000	< 1 in 1,000,000
Glycogen Storage Disease Type V	1 in 16,000	< 1 in 1,000,000
GRACILE Syndrome	< 1 in 50,000	< 1 in 1,000,000

Disease	DONOR 9854 Residual Risk	Reproductive Risk
HADHA-related Disorders	1 in 15,000	< 1 in 1,000,000
Hb Beta Chain-related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease)	1 in 5,000	1 in 990,000
Hereditary Fructose Intolerance	1 in 8,000	< 1 in 1,000,000
Herlitz Junctional Epidermolysis Bullosa, LAMA3-related	< 1 in 50,000	< 1 in 1,000,000
Herlitz Junctional Epidermolysis Bullosa, LAMB3-related	< 1 in 50,000	< 1 in 1,000,000
Herlitz Junctional Epidermolysis Bullosa, LAMC2-related	< 1 in 50,000	< 1 in 1,000,000
Hexosaminidase A Deficiency (Including Tay-Sachs Disease)	1 in 30,000	< 1 in 1,000,000
Homocystinuria Caused by Cystathionine Beta-synthase Deficiency	1 in 25,000	< 1 in 1,000,000
Hypophosphatasia, Autosomal Recessive	1 in 16,000	< 1 in 1,000,000
Inclusion Body Myopathy 2	< 1 in 50,000	< 1 in 1,000,000
Isovaleric Acidemia	1 in 25,000	< 1 in 1,000,000
Joubert Syndrome 2	< 1 in 50,000	< 1 in 1,000,000
Krabbe Disease	1 in 15,000	< 1 in 1,000,000
Lipoamide Dehydrogenase Deficiency	< 1 in 50,000	< 1 in 1,000,000
Maple Syrup Urine Disease Type 1B	1 in 25,000	< 1 in 1,000,000
Medium Chain Acyl-CoA Dehydrogenase Deficiency	1 in 5,900	< 1 in 1,000,000
Megalencephalic Leukoencephalopathy with Subcortical Cysts	< 1 in 50,000	< 1 in 1,000,000
Metachromatic Leukodystrophy	1 in 20,000	< 1 in 1,000,000
Mucolipidosis IV	< 1 in 50,000	< 1 in 1,000,000
Mucopolysaccharidosis Type I	1 in 16,000	< 1 in 1,000,000
Muscle-eye-brain Disease	< 1 in 12,000	< 1 in 1,000,000
NEB-related Nemaline Myopathy	< 1 in 6,700	< 1 in 1,000,000
Niemann-Pick Disease Type C	1 in 19,000	< 1 in 1,000,000
Niemann-Pick Disease, SMPD1-associated	1 in 25,000	< 1 in 1,000,000
Nijmegen Breakage Syndrome	1 in 16,000	< 1 in 1,000,000
Northern Epilepsy	< 1 in 50,000	< 1 in 1,000,000
PCDH15-related Disorders	1 in 5,300	< 1 in 1,000,000
Pendred Syndrome	1 in 7,000	< 1 in 1,000,000
PEX1-related Zellweger Syndrome Spectrum	1 in 11,000	< 1 in 1,000,000
Phenylalanine Hydroxylase Deficiency	1 in 5,000	1 in 990,000
PKHD1-related Autosomal Recessive Polycystic Kidney Disease	1 in 6,100	< 1 in 1,000,000
Polyglandular Autoimmune Syndrome Type 1	1 in 14,000	< 1 in 1,000,000
Pompe Disease	1 in 6,300	< 1 in 1,000,000
PPT1-related Neuronal Ceroid Lipofuscinosis	< 1 in 50,000	< 1 in 1,000,000
Primary Carnitine Deficiency	< 1 in 50,000	< 1 in 1,000,000
Primary Hyperoxaluria Type 1	1 in 35,000	< 1 in 1,000,000
Primary Hyperoxaluria Type 2	< 1 in 50,000	< 1 in 1,000,000
PROP1-related Combined Pituitary Hormone Deficiency	1 in 11,000	< 1 in 1,000,000
Pseudocholinesterase Deficiency (Mild Condition)	1 in 2,700	1 in 300,000
Pycnodysostosis	< 1 in 50,000	< 1 in 1,000,000
Rhizomelic Chondrodysplasia Punctata Type 1	1 in 16,000	< 1 in 1,000,000
Salla Disease	< 1 in 30,000	< 1 in 1,000,000
Segawa Syndrome	< 1 in 50,000	< 1 in 1,000,000
Short Chain Acyl-CoA Dehydrogenase Deficiency	1 in 16,000	< 1 in 1,000,000
Sjogren-Larsson Syndrome	1 in 9,100	< 1 in 1,000,000
Smith-Lemli-Opitz Syndrome	1 in 4,900	1 in 970,000
Spinal Muscular Atrophy	Negative for g.27134T>G SNP SMN1: 2 copies 1 in 770	1 in 110,000
Steroid-resistant Nephrotic Syndrome	1 in 40,000	< 1 in 1,000,000
Sulfate Transporter-related Osteochondrodysplasia	1 in 11,000	< 1 in 1,000,000
TPP1-related Neuronal Ceroid Lipofuscinosis	1 in 30,000	< 1 in 1,000,000
Tyrosinemia Type I	1 in 17,000	< 1 in 1,000,000
Usher Syndrome Type 3	< 1 in 50,000	< 1 in 1,000,000
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	1 in 8,800	< 1 in 1,000,000
Wilson Disease	1 in 8,600	< 1 in 1,000,000

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: 08/13/2018

MALE
DONOR 9854
DOB: [redacted]
Ethnicity: Mixed or Other Caucasian
Sample Type: EDTA Blood
Date of Collection: 07/31/2018
Date Received: 08/01/2018
Date Tested: 08/13/2018
Barcode: 11004212276671
Accession ID: CSLYA2KGMLNR2WG
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 9854	Partner
Panel Information	Foresight Carrier Screen USH2A-related Disorders 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.

Methods and Limitations

DONOR 9854 [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**.

LABORATORY DIRECTOR

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

Report content approved by Bethany Buckley, PhD, FACMG on Aug 13, 2018

Conditions Tested

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

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 9854 Residual Risk	Reproductive Risk
USH2A-related Disorders	1 in 2,200	< 1 in 1,000,000

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) 588-1484
NPI: 1306838271
Report Date: 01/23/2016

MALE
DONOR 9854
DOB: [redacted]
Ethnicity: Mixed or Other Caucasian
Sample Type: OG-510 Saliva
Date of Collection: 01/12/2016
Date Received: 01/18/2016
Date Tested: 01/23/2016
Barcode: 55101505040527
Indication: Screening for genetic disease carrier status

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

Steroid-Resistant Nephrotic Syndrome Panel **(1 condition tested)**

VERSION

DONOR 9854 **(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 3.

CLINICAL NOTES

- None

NEXT STEPS

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

Methods and Limitations

DONOR 9854 [Family Prep Screen 2.0]: sequencing and targeted genotyping.

Sequencing: High-throughput sequencing is used to analyze 8 exons in 1 gene, 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 2 variants associated with 1 disease. The test is not validated for detection of homozygous mutations, and although rare, asymptomatic individuals affected by the disease may not be genotyped accurately.

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.

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

Conditions Tested

Autosomal Recessive Disorders

SEQUENCING AND TARGETED GENOTYPING

Steroid-Resistant Nephrotic Syndrome - **Gene:** NPHS2. **Variants (2):** R138*, R138Q. **Exons:** NM_014625:1-8. **Detection rate**: Mixed or Other Caucasian > 33%.

Counsyl

RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
NPI: 1306838271
Report Date: 01/23/2016

MALE
DONOR 9854
DOB: [redacted]
Ethnicity: Mixed or Other Caucasian
Barcode: 55101505040527

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 9854 Residual Risk	Reproductive Risk
Steroid-Resistant Nephrotic Syndrome	< 1 in 600	< 1 in 950,000