



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: 03/26/2016

MALE
DONOR 10031
DOB: [REDACTED]
Ethnicity: Mixed or Other
Caucasian
Sample Type: OG-510 Saliva
Date of Collection: 03/21/2016
Date Received: 03/22/2016
Date Tested: 03/26/2016
Barcode: 55101509201073
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 10031 (Family Prep Screen 2.0)

RESULTS SUMMARY

NEGATIVE

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

CLINICAL NOTES

- None

NEXT STEPS

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



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Methods and Limitations

DONOR 10031 [Family Prep Screen 2.0]: sequencing, targeted genotyping, copy number analysis, and analysis of homologous regions.

Sequencing

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

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

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

Targeted genotyping

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

Copy number analysis

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

Analysis of homologous regions

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



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

Limitations

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

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

LAB DIRECTORS

H. Peter Kang, MD, MS, FCAP

Rebecca Mar-Heyming, PhD, DABMG



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FEMALE
N/A

Conditions Tested

Autosomal Recessive Disorders

SEQUENCING AND TARGETED GENOTYPING

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

Bloom Syndrome - Gene: BLM. **Variants (1):** Y736Lfs*5. **Exons:** NM_000057:2-22. **Detection rate:** Mixed or Other Caucasian > 10%.

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

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

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

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

Glycogen Storage Disease Type Ia - Gene: G6PC. **Variants (7):** G188R, Q242*, Q347*, R83C, R83H, p.Q27Rfs*9, p.Y128Tfs*3. **Exons:** NM_000151:1-5. **Detection rate:** Mixed or Other Caucasian > 61%.

Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease) - Gene: HBB. **Variants (28):** -28A>G, -29A>G, -87C>G, -88C>T, G25=, Hb C, Hb D-Punjab, Hb E, Hb O-Arab, Hb S, IVS-I-1, IVS-I-5, IVS-I-6T>C,

IVS2-745C>G, K18Rfs*2, K9Vfs*14, Q40*, S10Vfs*14, W16*, c.315+1G>A, c.316-197C>T, c.316-2A>C, c.316-2A>G, c.93-21G>A, p.E7Gfs*13, p.F42Lfs*19, p.K18*, p.S73Kfs*2. **Exons:** NM_000518:1-3. **Detection rate:** Mixed or Other Caucasian > 83%.

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

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

Lipoamide Dehydrogenase Deficiency - Gene: DLD. **Variants (2):** G194C, Y35*. **Exons:** NM_000108:1-14. **Detection rate:** Unknown due to rarity of disease.

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

Mucopolipidosis IV - Gene: MCOLN1. **Variants (2):** 511_6944del, IVS3-2A>G. **Exons:** NM_020533:1-14. **Detection rate:** Mixed or Other Caucasian > 10%.

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

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

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

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

Walker-Warburg Syndrome - Gene: FKTN. **Variants (1):** p.F390Ifs*14. **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. **Variants (1):** SMN1 copy number. **Detection rate:** Mixed or Other Caucasian 95%.

TARGETED GENOTYPING

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



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Ethnicity: Mixed or Other
Caucasian
Barcode: 55101509201073

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 10031 Residual Risk	Reproductive Risk
ABCC8-related Hyperinsulinism	< 1 in 110	< 1 in 50,000
Alpha Thalassemia	Alpha globin status: aa/aa.	Not calculated
Bloom Syndrome	< 1 in 500	< 1 in 1,000,000
Canavan Disease	< 1 in 500	< 1 in 1,000,000
Cystic Fibrosis	< 1 in 300	< 1 in 33,000
Familial Dysautonomia	< 1 in 500	< 1 in 1,000,000
Fanconi Anemia Type C	< 1 in 340	< 1 in 220,000
Gaucher Disease	1 in 280	1 in 120,000
Glycogen Storage Disease Type Ia	< 1 in 450	< 1 in 320,000
Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease)	< 1 in 290	< 1 in 58,000
Hexosaminidase A Deficiency (Including Tay-Sachs Disease)	< 1 in 390	< 1 in 470,000
Joubert Syndrome 2	< 1 in 500	< 1 in 1,000,000
Lipoamide Dehydrogenase Deficiency	< 1 in 500	< 1 in 1,000,000
Maple Syrup Urine Disease Type 1B	< 1 in 250	< 1 in 250,000
Mucopolipidosis IV	< 1 in 500	< 1 in 1,000,000
NEB-related Nemaline Myopathy	< 1 in 500	< 1 in 1,000,000
Niemann-Pick Disease, SMPD1-associated	< 1 in 400	< 1 in 400,000
Spinal Muscular Atrophy	SMN1: 2 copies 1 in 610	1 in 84,000
Usher Syndrome Type 1F	< 1 in 190	< 1 in 150,000
Usher Syndrome Type 3	< 1 in 500	< 1 in 1,000,000
Walker-Warburg Syndrome	< 1 in 500	< 1 in 1,000,000



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Report Date: 04/06/2017

MALE
DONOR 10031
DOB: [REDACTED]
Ethnicity: Mixed or Other
Caucasian
Sample Type: EDTA Blood
Date of Collection:
Date Received: 03/22/2017
Date Tested: 04/05/2017
Barcode: 11004212111501
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.

RESULTS SUMMARY

Risk Details	DONOR 10031	Partner
Panel Information	Family Prep Screen 2.0 11004212111501 Custom Panel (3 conditions tested)	N/A
All conditions tested A complete list of all conditions tested can be found on page 3.	<input type="checkbox"/> 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.



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Caucasian
Barcode: 11004212111501

FEMALE
N/A

Methods and Limitations

DONOR 10031 [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

H. Peter Kang, MD, MS, FCAP



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Ethnicity: Mixed or Other
Caucasian
Barcode: 11004212111501

FEMALE
N/A

Conditions Tested

Herlitz Junctional Epidermolysis Bullosa, LAMA3-related - Gene: LAMA3. Autosomal Recessive. Sequencing with Copy Number Analysis. Exons: NM_000227:1-38. **Detection Rate:** Mixed or Other Caucasian >99%.
MYO7A-related Disorders - Gene: MYO7A. Autosomal Recessive. Sequencing with Copy Number Analysis. Exons: NM_000260:2-49. **Detection Rate:** Mixed or Other Caucasian >99%.

Steroid-resistant Nephrotic Syndrome - Gene: NPHS2. Autosomal Recessive. Sequencing with Copy Number Analysis. Exons: NM_014625:1-8. **Detection Rate:** Mixed or Other Caucasian >99%.



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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 10031 Residual Risk	Reproductive Risk
Herlitz Junctional Epidermolysis Bullosa, LAMA3-related	< 1 in 50,000	< 1 in 1,000,000
MYO7A-related Disorders	1 in 15,000	< 1 in 1,000,000
Steroid-resistant Nephrotic Syndrome	1 in 40,000	< 1 in 1,000,000



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Sample Type: EDTA Blood
Date of Collection: 02/07/2018
Date Received: 02/09/2018
Date Tested: 02/20/2018
Barcode: 11004212317689
Accession ID: CSLHJ4A4XH9PEWE
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 10031	Partner
Panel Information	Foresight Carrier Screen 11004212317689 Custom Panel (3 conditions tested)	N/A
All conditions tested A complete list of all conditions tested can be found on page 3.	<input type="checkbox"/> 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 10031 [Foresight Carrier Screen]: sequencing with copy number analysis.

Sequencing with copy number analysis

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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



H. Peter Kang, MD, MS, FCAP



RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
NPI: 1306838271
Report Date: 02/20/2018

MALE
DONOR 10031
DOB: [REDACTED]
Ethnicity: Mixed or Other
Caucasian
Barcode: 11004212317689

FEMALE
N/A

Conditions Tested

Biotinidase Deficiency - Gene: **BTD**. Autosomal Recessive. Sequencing with Copy Number Analysis. Exons: NM_000060:1-4. **Detection Rate:** Mixed or Other Caucasian >99%.
Dihydropyrimidine Dehydrogenase Deficiency - Gene: **DPYD**. Autosomal Recessive. Sequencing with Copy Number Analysis. Exons: NM_000110:1-23. **Detection Rate:** Mixed or Other Caucasian 98%.

Phenylalanine Hydroxylase Deficiency - Gene: **PAH**. Autosomal Recessive. Sequencing with Copy Number Analysis. Exons: NM_000277:1-13. **Detection Rate:** Mixed or Other Caucasian >99%.



RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
NPI: 1306838271
Report Date: 02/20/2018

MALE
DONOR 10031
DOB: [REDACTED]
Ethnicity: Mixed or Other
Caucasian
Barcode: 11004212317689

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 10031 Residual Risk	Reproductive Risk
Biotinidase Deficiency	1 in 13,000	1 in 650,000
Dihydropyrimidine Dehydrogenase Deficiency	< 1 in 29,000	< 1 in 1,000,000
Phenylalanine Hydroxylase Deficiency	1 in 5,000	1 in 990,000



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: 06/21/2018

MALE
DONOR 10031
 DOB: [REDACTED]
 Ethnicity: Mixed or Other
 Caucasian
 Sample Type: EDTA Blood
 Date of Collection: 06/13/2018
 Date Received: 06/15/2018
 Date Tested: 06/21/2018
 Barcode: 11004212409260
 Accession ID:
 CSLUXUPWWHKWUVG
 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 10031	Partner
Panel Information	Foresight Carrier Screen 21-hydroxylase-deficient Congenital Adrenal Hyperplasia Panel (1 condition tested)	N/A
All conditions tested A complete list of all conditions tested can be found on page 3.	<input checked="" type="checkbox"/> 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 10031 [Foresight Carrier Screen]: analysis of homologous regions.

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*).

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LABORATORY DIRECTOR



H. Peter Kang, MD, MS, FCAP

Report content approved by Rebecca Mar-Heyming, PhD, FACMG on Jun 21, 2018

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, L308Ffs*6, P31L, Q319*, Q319*+CYP21A2dup, R357W, V281L, [I237N;V238E;M240K], c.293-13C>G. **Detection Rate:** Mixed or Other Caucasian 96%.



RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
NPI: 1306838271
Report Date: 06/21/2018

MALE
DONOR 10031
DOB: [REDACTED]
Ethnicity: Mixed or Other
Caucasian
Barcode: 11004212409260

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 10031 Residual Risk	Reproductive Risk
21-hydroxylase-deficient Congenital Adrenal Hyperplasia	1 in 1,400	1 in 310,000

Client/Sending Facility:
Phoenix Sperm Bank

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

LCLS Specimen Number: 128-944-0112-0
Patient Name: 10031, DONOR
Date of Birth: [REDACTED]
Gender: M
Patient ID:
Lab Number: YU16-36654 L
Indications: NOT GIVEN

Account Number: [REDACTED]
Ordering Physician: J OLLIFFE
Specimen Type: BLOOD
Client Reference:
Date Collected: 05/07/2016
Date Received: 05/09/2016
Date Reported: 05/19/2016

Test: Chromosome, Blood, Routine

Cells Counted: 20
Cells Analyzed: 20

Cells Karyotyped: 2
Band Resolution: 500

CYTOGENETIC RESULT: 46,XY

INTERPRETATION: NORMAL MALE KARYOTYPE

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

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

Client/Sending Facility:
Phoenix Sperm Bank

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

LCLS Specimen Number: 128-944-0112-0
Patient Name: 10031, DONOR
Date of Birth: [REDACTED]
Gender: M
Patient ID:
Lab Number: YU16-36654 L

Account Number: [REDACTED]
Ordering Physician: J OLLIFFE
Specimen Type: BLOOD
Client Reference:
Date Collected: 05/07/2016
Date Received: 05/09/2016



Client/Sending Facility:
Phoenix Sperm Bank

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

LCLS Specimen Number: 128-944-0112-0

Patient Name: 10031, DONOR

Date of Birth: [REDACTED]

Gender: M

Patient ID:

Lab Number: YU16-36654 L

Account Number: [REDACTED]

Ordering Physician: J OLLIFFE

Specimen Type: BLOOD

Client Reference:

Date Collected: 05/07/2016

Date Received: 05/09/2016

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