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: 12/16/2016

MALE
DONOR 12145
DOB: [redacted]
Ethnicity: African or African American
Sample Type: EDTA Blood
Date of Collection: 12/01/2016
Date Received: 12/02/2016
Date Tested: 12/16/2016
Barcode: 11004211673015
Indication: Egg or sperm donor

FEMALE
N/A

Family Prep Screen

POSITIVE: CARRIER

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 12145	Partner
Panel Information	Family Prep Screen 2.0 Universal Panel Minus X-Linked (102 conditions tested)	N/A
POSITIVE: CARRIER GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness Reproductive Risk: 1 in 190 Inheritance: Autosomal Recessive	CARRIER* NM_004004.5(GJB2):c.427C>T (R143W) 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".
POSITIVE: CARRIER Short Chain Acyl-CoA Dehydrogenase Deficiency Reproductive Risk: 1 in 630 Inheritance: Autosomal Recessive	CARRIER* NM_000017.2(ACADS):c.529T>C (W177R) 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".

†Likely to have a negative impact on gene function.
*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 8.

CLINICAL NOTES

- None

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.

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FEMALE
N/A

POSITIVE: CARRIER

GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness

Reproductive risk: 1 in 190
Risk before testing: 1 in 9,000

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

Patient	DONOR 12145	No partner tested
Result	✚ Carrier	N/A
Variant(s)	NM_004004.5(GJB2):c.427C>T(R143W) heterozygote †	N/A
Methodology	Sequencing	N/A
Interpretation	This individual is a carrier of GJB2-related DFNB1 nonsyndromic hearing loss and deafness. Carriers generally do not experience symptoms.	N/A
Detection rate	>99%	N/A
Exons tested	NM_004004:1-2.	N/A

†Likely to have a negative impact on gene function.

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.

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FEMALE
N/A

POSITIVE: CARRIER

Short Chain Acyl-CoA Dehydrogenase Deficiency

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

Reproductive risk: 1 in 630
Risk before testing: 1 in 100,000

Patient	DONOR 12145	No partner tested
Result	✚ Carrier	N/A
Variant(s)	NM_000017.2(ACADS):c.529T>C(W177R) heterozygote †	N/A
Methodology	Sequencing	N/A
Interpretation	This individual is a carrier of short chain acyl-CoA dehydrogenase deficiency. Carriers generally do not experience symptoms.	N/A
Detection rate	>99%	N/A
Exons tested	NM_000017:1-10.	N/A

†Likely to have a negative impact on gene function.

What is Short Chain Acyl-CoA Dehydrogenase Deficiency?

Short-chain acyl-CoA dehydrogenase (SCAD) deficiency is an inherited disease in which the body cannot turn certain fats (known as short-chain fatty acids) into energy due to a deficient enzyme. Its symptoms can be triggered by illness or long periods without food.

Infants affected by the disease may display episodes of vomiting, low blood sugar, and fatigue. These episodes can be fatal. Affected infants may have difficulty feeding and fail to grow at the expected rate. Some show poor muscle tone, seizures, and small head size. If the disease is untreated, the child may show developmental delays and permanent learning difficulties.

Some people with SCAD deficiency do not display any symptoms until adulthood. In these cases, the main symptom is chronic muscle weakness. Some may experience periods of pain, nausea, and shortness of breath. It is thought that many cases are so mild that they are never diagnosed.

SCAD deficiency belongs to a group of diseases known as fatty acid oxidation disorders.

How common is Short Chain Acyl-CoA Dehydrogenase Deficiency?

SCAD deficiency affects 1 in every 40,000 to 100,000 newborns. Researchers have hypothesized that this disease may be more common because some people with the disease are asymptomatic or have mild symptoms.

How is Short Chain Acyl-CoA Dehydrogenase Deficiency treated?

It is critical that people with SCAD deficiency avoid going long periods of time without food. Infants and children with SCAD deficiency may require feedings at regular intervals throughout the night. A cornstarch paste is often recommended to provide a sustained release of energy between meals. Foods high in carbohydrates and low in fat are also recommended. During times of illness, dietary rules must be very carefully followed. If the child cannot eat food for any reason, intravenous glucose must be administered promptly.

Some physicians recommend carnitine supplements for people with SCAD deficiency.

What is the prognosis for a person with Short Chain Acyl-CoA Dehydrogenase Deficiency?

The prognosis for a person with SCAD deficiency varies widely and depends upon the severity of his or her symptoms. In some cases, infants with the disease can die early in life. The prognosis for those who live into adolescence and adulthood and/or develop symptoms of muscle weakness later in life is not known. Some people with the mutations that cause this disease do not develop symptoms, or have mild undiagnosed symptoms.

Methods and Limitations

DONOR 12145 [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.

Detection rates are calculated by estimating from literature the fraction of disease alleles that the methodology is unable to detect.

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.

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 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. 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

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, G111VfsX21, I173N, L308FfsX6, P31L, Q319*, Q319*+CYP21A2dup, R357W, V281L, [I237N;V238E;M240K], c.293-13C>G. **Detection Rate:** African or African American 92%.

ABCC8-related Hyperinsulinism - **Gene:** ABCC8. Autosomal Recessive. Sequencing. **Exons:** NM_000352:1-39. **Detection Rate:** African or African American >99%.

Achromatopsia - **Gene:** CNGB3. Autosomal Recessive. Sequencing. **Exons:** NM_019098:1-18. **Detection Rate:** African or African American >99%.

Alkaptonuria - **Gene:** HGD. Autosomal Recessive. Sequencing. **Exons:** NM_000187:1-14. **Detection Rate:** African or African American >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:** African or African American 90%.

Alpha-1 Antitrypsin Deficiency - **Gene:** SERPINA1. Autosomal Recessive. Sequencing. **Exons:** NM_000295:2-5. **Detection Rate:** African or African American >99%.

Alpha-Mannosidosis - **Gene:** MAN2B1. Autosomal Recessive. Sequencing. **Exons:** NM_000528:1-15,17-24. **Detection Rate:** African or African American >99%.

Alpha-Sarcoglycanopathy - **Gene:** SGCA. Autosomal Recessive. Sequencing. **Exons:** NM_000023:1-9. **Detection Rate:** African or African American 99%.

Andermann Syndrome - **Gene:** SLC12A6. Autosomal Recessive. Sequencing. **Exons:** NM_133647:1-25. **Detection Rate:** African or African American >99%.

ARSACS - **Gene:** SACS. Autosomal Recessive. Sequencing. **Exons:** NM_014363:2-10. **Detection Rate:** African or African American 97%.

Aspartylglycosaminuria - **Gene:** AGA. Autosomal Recessive. Sequencing. **Exons:** NM_000027:1-9. **Detection Rate:** African or African American >99%.

Ataxia With Vitamin E Deficiency - **Gene:** TTPA. Autosomal Recessive. Sequencing. **Exons:** NM_000370:1-5. **Detection Rate:** African or African American >99%.

Ataxia-Telangiectasia - **Gene:** ATM. Autosomal Recessive. Sequencing. **Exons:** NM_000051:2-63. **Detection Rate:** African or African American >99%.

Bardet-Biedl Syndrome, BBS1-related - **Gene:** BBS1. Autosomal Recessive. Sequencing. **Exons:** NM_024649:1-17. **Detection Rate:** African or African American >99%.

Bardet-Biedl Syndrome, BBS10-related - **Gene:** BBS10. Autosomal Recessive. Sequencing. **Exons:** NM_024685:1-2. **Detection Rate:** African or African American >99%.

Beta-Sarcoglycanopathy - **Gene:** SGCB. Autosomal Recessive. Sequencing. **Exons:** NM_000232:1-6. **Detection Rate:** African or African American >99%.

Biotinidase Deficiency - **Gene:** BTD. Autosomal Recessive. Sequencing. **Exons:** NM_000060:1-4. **Detection Rate:** African or African American >99%.

Bloom Syndrome - **Gene:** BLM. Autosomal Recessive. Sequencing. **Exons:** NM_000057:2-22. **Detection Rate:** African or African American 96%.

Canavan Disease - **Gene:** ASPA. Autosomal Recessive. Sequencing. **Exons:** NM_000049:1-6. **Detection Rate:** African or African American 94%.

Carnitine Palmitoyltransferase IA Deficiency - **Gene:** CPT1A. Autosomal Recessive. Sequencing. **Exons:** NM_001876:2-19. **Detection Rate:** African or African American 98%.

Carnitine Palmitoyltransferase II Deficiency - **Gene:** CPT2. Autosomal Recessive. Sequencing. **Exons:** NM_000098:1-5. **Detection Rate:** African or African American >99%.

Cartilage-Hair Hypoplasia - **Gene:** RMRP. Autosomal Recessive. Sequencing. **Exon:** NR_003051:1. **Detection Rate:** African or African American >99%.

Citrullinemia Type 1 - **Gene:** ASS1. Autosomal Recessive. Sequencing. **Exons:** NM_000050:3-16. **Detection Rate:** African or African American >99%.

CLN3-related Neuronal Ceroid Lipofuscinosis - **Gene:** CLN3. Autosomal Recessive. Sequencing. **Exons:** NM_001042432:2-16. **Detection Rate:** African or African American >99%.

CLN5-related Neuronal Ceroid Lipofuscinosis - **Gene:** CLN5. Autosomal Recessive. Sequencing. **Exons:** NM_006493:1-4. **Detection Rate:** African or African American 98%.

Cohen Syndrome - **Gene:** VPS13B. Autosomal Recessive. Sequencing. **Exons:** NM_017890:2-62. **Detection Rate:** African or African American 83%.

Congenital Disorder of Glycosylation Type Ia - **Gene:** PMM2. Autosomal Recessive. Sequencing. **Exons:** NM_000303:1-8. **Detection Rate:** African or African American >99%.

Congenital Disorder of Glycosylation Type Ib - **Gene:** MPI. Autosomal Recessive. Sequencing. **Exons:** NM_002435:1-8. **Detection Rate:** African or African American >99%.

Congenital Finnish Nephrosis - **Gene:** NPHS1. Autosomal Recessive. Sequencing. **Exons:** NM_004646:2-23,26-27,29. **Detection Rate:** African or African American >99%.

Costeff Optic Atrophy Syndrome - **Gene:** OPA3. Autosomal Recessive. Sequencing. **Exons:** NM_025136:1-2. **Detection Rate:** African or African American >99%.

Cystic Fibrosis - **Gene:** CFTR. Autosomal Recessive. Sequencing. **Exons:** NM_000492:1-27. IVS8-5T allele analysis is only reported in the presence of the R117H mutation. **Detection Rate:** African or African American >99%.

Cystinosis - **Gene:** CTNS. Autosomal Recessive. Sequencing. **Exons:** NM_004937:3-12. **Detection Rate:** African or African American >99%.

D-Bifunctional Protein Deficiency - **Gene:** HSD17B4. Autosomal Recessive. Sequencing. **Exons:** NM_000414:1-24. **Detection Rate:** African or African American 94%.

Dihydropyrimidine Dehydrogenase Deficiency - **Gene:** DPYD. Autosomal Recessive. Sequencing. **Exons:** NM_000110:1-23. **Detection Rate:** African or African American 93%.

Factor XI Deficiency - **Gene:** F11. Autosomal Recessive. Sequencing. **Exons:** NM_000128:2-15. **Detection Rate:** African or African American >99%.

Familial Dysautonomia - **Gene:** IKBKAP. Autosomal Recessive. Sequencing. **Exons:** NM_003640:19-20,26. **Detection Rate:** African or African American >99%.

Familial Mediterranean Fever - **Gene:** MEFV. Autosomal Recessive. Sequencing. **Exons:** NM_000243:1-10. **Detection Rate:** African or African American >99%.

Fanconi Anemia Type C - **Gene:** FANCC. Autosomal Recessive. Sequencing. **Exons:** NM_000136:2-15. **Detection Rate:** African or African American >99%.

FKTN-related Disorders - **Gene:** FKTN. Autosomal Recessive. Sequencing. **Exons:** NM_001079802:3-11. **Detection Rate:** African or African American >99%.

Galactosemia - **Gene:** GALT. Autosomal Recessive. Sequencing. **Exons:** NM_000155:1-11. **Detection Rate:** African or African American >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:** African or African American 60%.

GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness - **Gene:** GJB2. Autosomal Recessive. Sequencing. **Exons:** NM_004004:1-2. **Detection Rate:** African or African American >99%.

Glutaric Acidemia Type 1 - **Gene:** GCDH. Autosomal Recessive. Sequencing. **Exons:** NM_000159:2-12. **Detection Rate:** African or African American >99%.

Glycogen Storage Disease Type Ia - **Gene:** G6PC. Autosomal Recessive. Sequencing. **Exons:** NM_000151:1-5. **Detection Rate:** African or African American >99%.

Glycogen Storage Disease Type Ib - **Gene:** SLC37A4. Autosomal Recessive. Sequencing. **Exons:** NM_001164277:3-11. **Detection Rate:** African or African American >99%.

Glycogen Storage Disease Type III - **Gene:** AGL. Autosomal Recessive. Sequencing. **Exons:** NM_000642:2-34. **Detection Rate:** African or African American >99%.

Glycogen Storage Disease Type V - **Gene:** PYGM. Autosomal Recessive. Sequencing. **Exons:** NM_005609:1-20. **Detection Rate:** African or African American >99%.

GRACILE Syndrome - **Gene:** BCS1L. Autosomal Recessive. Sequencing. **Exons:** NM_004328:3-9. **Detection Rate:** African or African American >99%.

HADHA-related Disorders - **Gene:** HADHA. Autosomal Recessive. Sequencing. **Exons:** NM_000182:1-20. **Detection Rate:** African or African American >99%.

Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease) - **Gene:** HBB. Autosomal Recessive. Sequencing. **Exons:** NM_000518:1-3. **Detection Rate:** African or African American >99%.

Hereditary Fructose Intolerance - **Gene:** ALDOB. Autosomal Recessive. Sequencing. **Exons:** NM_000035:2-9. **Detection Rate:** African or African American >99%.

Herlitz Junctional Epidermolysis Bullosa, LAMA3-related - **Gene:** LAMA3. Autosomal Recessive. Sequencing. **Exons:** NM_000227:1-16,18-38. **Detection Rate:** African or African American >99%.
Herlitz Junctional Epidermolysis Bullosa, LAMB3-related - **Gene:** LAMB3. Autosomal Recessive. Sequencing. **Exons:** NM_000228:2-23. **Detection Rate:** African or African American >99%.
Herlitz Junctional Epidermolysis Bullosa, LAMC2-related - **Gene:** LAMC2. Autosomal Recessive. Sequencing. **Exons:** NM_005562:1-23. **Detection Rate:** African or African American >99%.
Hexosaminidase A Deficiency (Including Tay-Sachs Disease) - **Gene:** HEXA. Autosomal Recessive. Sequencing. **Exons:** NM_000520:1-14. **Detection Rate:** African or African American >99%.
Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency - **Gene:** CBS. Autosomal Recessive. Sequencing. **Exons:** NM_000071:3-17. **Detection Rate:** African or African American >99%.
Hypophosphatasia, Autosomal Recessive - **Gene:** ALPL. Autosomal Recessive. Sequencing. **Exons:** NM_000478:2-12. **Detection Rate:** African or African American >99%.
Inclusion Body Myopathy 2 - **Gene:** GNE. Autosomal Recessive. Sequencing. **Exons:** NM_001128227:3-12. **Detection Rate:** African or African American >99%.
Isovaleric Acidemia - **Gene:** IVD. Autosomal Recessive. Sequencing. **Exons:** NM_002225:1-12. **Detection Rate:** African or African American >99%.
Joubert Syndrome 2 - **Gene:** TMEM216. Autosomal Recessive. Sequencing. **Exons:** NM_001173990:1-5. **Detection Rate:** African or African American >99%.
Krabbe Disease - **Gene:** GALC. Autosomal Recessive. Sequencing. **Exons:** NM_000153:1-17. **Detection Rate:** African or African American >99%.
Lipoamide Dehydrogenase Deficiency - **Gene:** DLD. Autosomal Recessive. Sequencing. **Exons:** NM_000108:1-14. **Detection Rate:** African or African American >99%.
Maple Syrup Urine Disease Type 1B - **Gene:** BCKDHB. Autosomal Recessive. Sequencing. **Exons:** NM_183050:1-10. **Detection Rate:** African or African American >99%.
Medium Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADM. Autosomal Recessive. Sequencing. **Exons:** NM_000016:1-12. **Detection Rate:** African or African American >99%.
Megalencephalic Leukoencephalopathy With Subcortical Cysts - **Gene:** MLC1. Autosomal Recessive. Sequencing. **Exons:** NM_015166:2-12. **Detection Rate:** African or African American >99%.
Metachromatic Leukodystrophy - **Gene:** ARSA. Autosomal Recessive. Sequencing. **Exons:** NM_000487:1-8. **Detection Rate:** African or African American >99%.
Mucolipidosis IV - **Gene:** MCOLN1. Autosomal Recessive. Sequencing. **Exons:** NM_020533:1-14. **Detection Rate:** African or African American >99%.
Mucopolysaccharidosis Type I - **Gene:** IDUA. Autosomal Recessive. Targeted Genotyping. **Variants (2):** Q70*, W402*. **Detection Rate:** African or African American 67%.
Muscle-Eye-Brain Disease - **Gene:** POMGNT1. Autosomal Recessive. Sequencing. **Exons:** NM_017739:2-22. **Detection Rate:** African or African American 90%.
NEB-related Nemaline Myopathy - **Gene:** NEB. Autosomal Recessive. Sequencing. **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:** African or African American 97%.
Niemann-Pick Disease Type C - **Gene:** NPC1. Autosomal Recessive. Sequencing. **Exons:** NM_000271:1-25. **Detection Rate:** African or African American 96%.
Niemann-Pick Disease, SMPD1-associated - **Gene:** SMPD1. Autosomal Recessive. Sequencing. **Exons:** NM_000543:1-6. **Detection Rate:** African or African American >99%.
Nijmegen Breakage Syndrome - **Gene:** NBN. Autosomal Recessive. Sequencing. **Exons:** NM_002485:1-16. **Detection Rate:** African or African American >99%.
Northern Epilepsy - **Gene:** CLN8. Autosomal Recessive. Sequencing. **Exons:** NM_018941:2-3. **Detection Rate:** African or African American >99%.
PCDH15-related Disorders - **Gene:** PCDH15. Autosomal Recessive. Sequencing. **Exons:** NM_033056:2-33. **Detection Rate:** African or African American 85%.
Pendred Syndrome - **Gene:** SLC26A4. Autosomal Recessive. Sequencing. **Exons:** NM_000441:2-21. **Detection Rate:** African or African American >99%.
PEX1-related Zellweger Syndrome Spectrum - **Gene:** PEX1. Autosomal Recessive. Sequencing. **Exons:** NM_000466:1-24. **Detection Rate:** African or African American >99%.
Phenylalanine Hydroxylase Deficiency - **Gene:** PAH. Autosomal Recessive. Sequencing. **Exons:** NM_000277:1-13. **Detection Rate:** African or African American >99%.
PKHD1-related Autosomal Recessive Polycystic Kidney Disease - **Gene:** PKHD1. Autosomal Recessive. Sequencing. **Exons:** NM_138694:2-67. **Detection Rate:** African or African American 98%.
Polyglandular Autoimmune Syndrome Type 1 - **Gene:** AIRE. Autosomal Recessive. Sequencing. **Exons:** NM_000383:1-14. **Detection Rate:** African or African American >99%.
Pompe Disease - **Gene:** GAA. Autosomal Recessive. Sequencing. **Exons:** NM_000152:2-20. **Detection Rate:** African or African American >99%.
PPT1-related Neuronal Ceroid Lipofuscinosis - **Gene:** PPT1. Autosomal Recessive. Sequencing. **Exons:** NM_000310:1-9. **Detection Rate:** African or African American >99%.
Primary Carnitine Deficiency - **Gene:** SLC22A5. Autosomal Recessive. Sequencing. **Exons:** NM_003060:1-10. **Detection Rate:** African or African American >99%.
Primary Hyperoxaluria Type 1 - **Gene:** AGXT. Autosomal Recessive. Sequencing. **Exons:** NM_000030:1-11. **Detection Rate:** African or African American >99%.
Primary Hyperoxaluria Type 2 - **Gene:** GRHPR. Autosomal Recessive. Sequencing. **Exons:** NM_012203:1-9. **Detection Rate:** African or African American >99%.
PROP1-related Combined Pituitary Hormone Deficiency - **Gene:** PROP1. Autosomal Recessive. Sequencing. **Exons:** NM_006261:1-3. **Detection Rate:** African or African American >99%.
Pseudocholinesterase Deficiency - **Gene:** BCHE. Autosomal Recessive. Sequencing. **Exons:** NM_000055:2-4. **Detection Rate:** African or African American >99%.
Pycnodysostosis - **Gene:** CTSK. Autosomal Recessive. Sequencing. **Exons:** NM_000396:2-8. **Detection Rate:** African or African American >99%.
Rhizomelic Chondrodysplasia Punctata Type 1 - **Gene:** PEX7. Autosomal Recessive. Sequencing. **Exons:** NM_000288:1-10. **Detection Rate:** African or African American >99%.
Salla Disease - **Gene:** SLC17A5. Autosomal Recessive. Sequencing. **Exons:** NM_012434:1-11. **Detection Rate:** African or African American 93%.
Segawa Syndrome - **Gene:** TH. Autosomal Recessive. Sequencing. **Exons:** NM_000360:1-13. **Detection Rate:** African or African American 96%.
Short Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADS. Autosomal Recessive. Sequencing. **Exons:** NM_000017:1-10. **Detection Rate:** African or African American >99%.
Sjogren-Larsson Syndrome - **Gene:** ALDH3A2. Autosomal Recessive. Sequencing. **Exons:** NM_000382:1-10. **Detection Rate:** African or African American 92%.
Smith-Lemli-Opitz Syndrome - **Gene:** DHCR7. Autosomal Recessive. Sequencing. **Exons:** NM_001360:3-9. **Detection Rate:** African or African American >99%.
Spinal Muscular Atrophy - **Gene:** SMN1. Autosomal Recessive. Copy Number Analysis. **Variant (1):** SMN1 copy number. **Detection Rate:** African or African American 71%.
Steroid-Resistant Nephrotic Syndrome - **Gene:** NPHS2. Autosomal Recessive. Sequencing. **Exons:** NM_014625:1-8. **Detection Rate:** African or African American >99%.
Sulfate Transporter-Related Osteochondrodysplasia - **Gene:** SLC26A2. Autosomal Recessive. Sequencing. **Exons:** NM_000112:2-3. **Detection Rate:** African or African American >99%.
TPP1-related Neuronal Ceroid Lipofuscinosis - **Gene:** TPP1. Autosomal Recessive. Sequencing. **Exons:** NM_000391:1-13. **Detection Rate:** African or African American >99%.
Tyrosinemia Type I - **Gene:** FAH. Autosomal Recessive. Sequencing. **Exons:** NM_000137:1-14. **Detection Rate:** African or African American >99%.
Usher Syndrome Type 3 - **Gene:** CLRN1. Autosomal Recessive. Sequencing. **Exons:** NM_174878:1-3. **Detection Rate:** African or African American >99%.
Very Long Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADVL. Autosomal Recessive. Sequencing. **Exons:** NM_000018:1-20. **Detection Rate:** African or African American >99%.
Wilson Disease - **Gene:** ATP7B. Autosomal Recessive. Sequencing. **Exons:** NM_000053:1-21. **Detection Rate:** African or African American >99%.

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RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
NPI: 1306838271
Report Date: 12/16/2016

MALE
DONOR 12145
DOB: [redacted]
Ethnicity: African or African American
Barcode: 11004211673015

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.

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

Disease	DONOR 12145 Residual Risk	Reproductive Risk
21-Hydroxylase-Deficient Congenital Adrenal Hyperplasia	1 in 1,400	1 in 660,000
ABCC8-related Hyperinsulinism	1 in 11,000	< 1 in 1,000,000
Achromatopsia	1 in 8,600	< 1 in 1,000,000
Alkaptonuria	< 1 in 50,000	< 1 in 1,000,000
Alpha Thalassemia	Alpha globin status: aa/aa.	Not calculated
Alpha-1 Antitrypsin Deficiency	1 in 10,000	< 1 in 1,000,000
Alpha-Mannosidosis	1 in 35,000	< 1 in 1,000,000
Alpha-Sarcoglycanopathy	1 in 31,000	< 1 in 1,000,000
Andermann Syndrome	< 1 in 50,000	< 1 in 1,000,000
ARSACS	< 1 in 18,000	< 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 16,000	< 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 12,000	< 1 in 1,000,000
Bloom Syndrome	< 1 in 12,000	< 1 in 1,000,000
Canavan Disease	< 1 in 7,700	< 1 in 1,000,000
Carnitine Palmitoyltransferase IA Deficiency	< 1 in 31,000	< 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 23,000	< 1 in 1,000,000
Cohen Syndrome	< 1 in 3,000	< 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 6,500	< 1 in 1,000,000
Cystinosis	1 in 22,000	< 1 in 1,000,000
D-Bifunctional Protein Deficiency	1 in 2,900	< 1 in 1,000,000
Dihydropyrimidine Dehydrogenase Deficiency	1 in 1,400	1 in 570,000
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.427C>T(R143W) heterozygote †	1 in 190
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

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RESULTS RECIPIENT
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Attn: Dr. Jeffrey Olliffe
NPI: 1306838271
Report Date: 12/16/2016

MALE
DONOR 12145
DOB: [redacted]
Ethnicity: African or African American
Barcode: 11004211673015

FEMALE
N/A

Disease	DONOR 12145 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 950	1 in 38,000
Hereditary Fructose Intolerance	< 1 in 50,000	< 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 11,000	< 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 480	1 in 300,000
Muscle-Eye-Brain Disease	< 1 in 5,000	< 1 in 1,000,000
NEB-related Nemaline Myopathy	< 1 in 18,000	< 1 in 1,000,000
Niemann-Pick Disease Type C	1 in 5,400	< 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 2,300	< 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 16,000	< 1 in 1,000,000
PKHD1-related Autosomal Recessive Polycystic Kidney Disease	< 1 in 33,000	< 1 in 1,000,000
Polyglandular Autoimmune Syndrome Type 1	< 1 in 50,000	< 1 in 1,000,000
Pompe Disease	1 in 5,900	< 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	1 in 2,700	< 1 in 1,000,000
Pycnodysostosis	< 1 in 50,000	1 in 300,000
Rhizomelic Chondrodysplasia Punctata Type 1	1 in 16,000	< 1 in 1,000,000
Salla Disease	< 1 in 7,500	< 1 in 1,000,000
Segawa Syndrome	< 1 in 13,000	< 1 in 1,000,000
Short Chain Acyl-CoA Dehydrogenase Deficiency	NM_000017.2(ACADS):c.529T>C(W177R) heterozygote †	1 in 630
Sjogren-Larsson Syndrome	1 in 3,100	< 1 in 1,000,000
Smith-Lemli-Opitz Syndrome	< 1 in 50,000	< 1 in 1,000,000
Spinal Muscular Atrophy	SMN1: 3+ copies	
Steroid-Resistant Nephrotic Syndrome	1 in 4,300	< 1 in 1,000,000
Sulfate Transporter-Related Osteochondrodysplasia	1 in 40,000	< 1 in 1,000,000
TPP1-related Neuronal Ceroid Lipofuscinosis	1 in 11,000	< 1 in 1,000,000
Tyrosinemia Type I	1 in 30,000	< 1 in 1,000,000
Usher Syndrome Type 3	1 in 17,000	< 1 in 1,000,000
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	< 1 in 50,000	< 1 in 1,000,000
Wilson Disease	1 in 8,800	< 1 in 1,000,000
	1 in 8,600	< 1 in 1,000,000

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) 466-4696 WAB-55

LCLS Specimen Number: **336-129-0487-0**
Patient Name: **12145, DONOR**
Date of Birth: [redacted]
Gender: M
Patient ID:
Lab Number: (J16-4675 L

Account Number: [redacted]
Ordering Physician: **J OLLIFFE**
Specimen Type: **BLOOD**
Client Reference: 0051535368
Date Collected: 12/01/2016
Date Received: 12/02/2016

Indications: DONOR

Date Reported: **12/14/2016**

Test: **Chromosome, Blood, Routine**

Cells Counted: 15
Cells Analyzed: 5

Cells Karyotyped: 2
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.

Chromosome analysis performed by Dianon Pathology CLIA 07D0644713. 1 Forest Parkway Shelton CT, 06484. Laboratory Director, James B Amberson, MD.

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Hiba Risheg, PhD., FACMG
Board Certified Cytogeneticist

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

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