Counsyl

RESULTS RECIPIENT
**SEATTLE SPERM BANK**
**Attn:** Dr. Jeffrey Olliffe
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Seattle, WA 98105
**Phone:** (206) 588-1484
**Fax:** (206) 466-4696
**NPI:** 1306838271
**Report Date:** 01/30/2017

MALE
**DONOR 10116**
**DOB:**
**Ethnicity:** South Asian
**Sample Type:** EDTA Blood
**Date of Collection:** 01/13/2017
**Date Received:** 01/15/2017
**Date Tested:** 01/30/2017
**Barcode:** 11004212022548
**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 10116 | Partner |
|---|---|---|
| Panel Information | Family Prep Screen 2.0<br>Universal Panel Minus X-Linked<br>**(102 conditions tested)** | N/A |
| **POSITIVE: CARRIER**<br>Primary Carnitine Deficiency<br>**Reproductive Risk: 1 in 2,000**<br>**Inheritance: Autosomal Recessive** | **CARRIER***<br>NM_003060.3(SLC22A5):c.248G>T (R83L) 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 6.

## 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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MALE
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**DOB:**
**Ethnicity:** South Asian
**Barcode:** 11004212022548

FEMALE
N/A

**POSITIVE: CARRIER**

# Primary Carnitine Deficiency

**Reproductive risk: 1 in 2,000**
Risk before testing: < 1 in 1,000,000

**Gene:** SLC22A5 | **Inheritance Pattern:** Autosomal Recessive

| Patient | DONOR 10116 | No partner tested |
|---|---|---|
| Result | ⊕ Carrier | N/A |
| Variant(s) | NM_003060.3(SLC22A5):c.248G>T(R83L) heterozygote † | N/A |
| Methodology | Sequencing | N/A |
| Interpretation | This individual is a carrier of primary carnitine deficiency. Carriers generally do not experience symptoms. | N/A |
| Detection rate | >99% | N/A |
| Exons tested | NM_003060:1-10. | N/A |

†Likely to have a negative impact on gene function.

## What is Primary Carnitine Deficiency?

Primary carnitine deficiency is a condition in which the body cannot properly process fats into energy. It is caused by a defect in the protein that transports carnitine, a natural substance derived from an amino acid. The condition is typically treatable by the daily use of L-carnitine supplements. However without early detection and treatment, the condition can cause permanent brain damage and may even prove fatal.

If left untreated, primary carnitine deficiency causes a weakening of the heart muscles, leading to a diminished ability to pump blood around the body (cardiomyopathy). Both the heart and liver may become enlarged. It also causes a weakness in skeletal muscles and dangerously low blood sugar (hypoglycemia) that can lead to brain damage. While this brain damage can cause irreversible learning problems or even mental retardation, the remaining symptoms tend to disappear once the person begins taking L-carnitine supplements.

Without supplements, a person with primary carnitine deficiency is particularly vulnerable to "metabolic crisis"-sleepiness, irritability, fever, nausea, vomiting, low blood sugar-when they go long periods without eating or are ill. If the crises are not treated, the child may experience seizures, swelling of the brain, and other life-threatening symptoms.

## How common is Primary Carnitine Deficiency?

Primary carnitine deficiency affects approximately 1 in 100,000 newborns and is known to be more common-1 in 40,000-in Japan.

## How is Primary Carnitine Deficiency treated?

People with primary carnitine deficiency will need to take supplements of L-carnitine for their entire lives. If these children have begun to experience heart problems or muscle weakness, they can typically reverse those symptoms by taking L-carnitine. A physician may also recommend that people with primary carnitine deficiency eat more frequently, even if they don't feel hungry. This is particularly important when they are young and/or sick.

## What is the prognosis for a person with Primary Carnitine Deficiency?

With regular treatment begun at birth, the prognosis for a person with primary carnitine deficiency is very good. They can typically live normal lives. If treatment is not begun soon enough, these children can experience permanent brain damage, leading to learning difficulties or even mental retardation. Without any treatment, the disease causes numerous serious health problems and would likely be fatal.

# Methods and Limitations

**DONOR 10116** [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:** South Asian 88%.

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

**Achromatopsia** - **Gene:** CNGB3. Autosomal Recessive. Sequencing. **Exons:** NM_019098:1-18. **Detection Rate:** South Asian >99%.

**Alkaptonuria** - **Gene:** HGD. Autosomal Recessive. Sequencing. **Exons:** NM_000187:1-14. **Detection Rate:** South Asian >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:** South Asian 90%.

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

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

**Alpha-Sarcoglycanopathy** - **Gene:** SGCA. Autosomal Recessive. Sequencing. **Exons:** NM_000023:1-9. **Detection Rate:** South Asian 99%.

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

**ARSACS** - **Gene:** SACS. Autosomal Recessive. Sequencing. **Exons:** NM_014363:2-10. **Detection Rate:** South Asian 97%.

**Aspartylglycosaminuria** - **Gene:** AGA. Autosomal Recessive. Sequencing. **Exons:** NM_000027:1-9. **Detection Rate:** South Asian >99%.

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

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

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

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

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

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

**Bloom Syndrome** - **Gene:** BLM. Autosomal Recessive. Sequencing. **Exons:** NM_000057:2-22. **Detection Rate:** South Asian 96%.

**Canavan Disease** - **Gene:** ASPA. Autosomal Recessive. Sequencing. **Exons:** NM_000049:1-6. **Detection Rate:** South Asian 94%.

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

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

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

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

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

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

**Cohen Syndrome** - **Gene:** VPS13B. Autosomal Recessive. Sequencing. **Exons:** NM_017890:2-62. **Detection Rate:** South Asian 83%.

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

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

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

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

**Cystinosis** - **Gene:** CTNS. Autosomal Recessive. Sequencing. **Exons:** NM_004937:3-12. **Detection Rate:** South Asian >99%.

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

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

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

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

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

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

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

**Galactosemia** - **Gene:** GALT. Autosomal Recessive. Sequencing. **Exons:** NM_000155:1-11. **Detection Rate:** South Asian >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:** South Asian 60%.

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

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

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

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

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

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

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

**HADHA-related Disorders** - **Gene:** HADHA. Autosomal Recessive. Sequencing. **Exons:** NM_000182:1-20. **Detection Rate:** South Asian >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:** South Asian 91%.

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

**Herlitz Junctional Epidermolysis Bullosa, LAMA3-related** - **Gene:** LAMA3. Autosomal Recessive. Sequencing. **Exons:** NM_000227:1-16,18-38. **Detection Rate:** South Asian >99%.

**Herlitz Junctional Epidermolysis Bullosa, LAMB3-related** - **Gene:** LAMB3. Autosomal Recessive. Sequencing. **Exons:** NM_000228:2-23. **Detection Rate:** South Asian >99%.

**Herlitz Junctional Epidermolysis Bullosa, LAMC2-related** - **Gene:** LAMC2. Autosomal Recessive. Sequencing. **Exons:** NM_005562:1-23. **Detection Rate:** South Asian >99%.

**Hexosaminidase A Deficiency (Including Tay-Sachs Disease)** - **Gene:** HEXA. Autosomal Recessive. Sequencing. **Exons:** NM_000520:1-14. **Detection Rate:** South Asian >99%.

**Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency** - **Gene:** CBS. Autosomal Recessive. Sequencing. **Exons:** NM_000071:3-17. **Detection Rate:** South Asian >99%.

**Hypophosphatasia, Autosomal Recessive** - **Gene:** ALPL. Autosomal Recessive. Sequencing. **Exons:** NM_000478:2-12. **Detection Rate:** South Asian >99%.

**Inclusion Body Myopathy 2** - **Gene:** GNE. Autosomal Recessive. Sequencing. **Exons:** NM_001128227:3-12. **Detection Rate:** South Asian >99%.

**Isovaleric Acidemia - Gene:** IVD. Autosomal Recessive. Sequencing. **Exons:** NM_002225:1-12. **Detection Rate:** South Asian >99%.
**Joubert Syndrome 2 - Gene:** TMEM216. Autosomal Recessive. Sequencing. **Exons:** NM_001173990:1-5. **Detection Rate:** South Asian >99%.
**Krabbe Disease - Gene:** GALC. Autosomal Recessive. Sequencing. **Exons:** NM_000153:1-17. **Detection Rate:** South Asian >99%.
**Lipoamide Dehydrogenase Deficiency - Gene:** DLD. Autosomal Recessive. Sequencing. **Exons:** NM_000108:1-14. **Detection Rate:** South Asian >99%.
**Maple Syrup Urine Disease Type 1B - Gene:** BCKDHB. Autosomal Recessive. Sequencing. **Exons:** NM_183050:1-10. **Detection Rate:** South Asian >99%.
**Medium Chain Acyl-CoA Dehydrogenase Deficiency - Gene:** ACADM. Autosomal Recessive. Sequencing. **Exons:** NM_000016:1-12. **Detection Rate:** South Asian >99%.
**Megalencephalic Leukoencephalopathy With Subcortical Cysts - Gene:** MLC1. Autosomal Recessive. Sequencing. **Exons:** NM_015166:2-12. **Detection Rate:** South Asian >99%.
**Metachromatic Leukodystrophy - Gene:** ARSA. Autosomal Recessive. Sequencing. **Exons:** NM_000487:1-8. **Detection Rate:** South Asian >99%.
**Mucolipidosis IV - Gene:** MCOLN1. Autosomal Recessive. Sequencing. **Exons:** NM_020533:1-14. **Detection Rate:** South Asian >99%.
**Mucopolysaccharidosis Type I - Gene:** IDUA. Autosomal Recessive. Targeted Genotyping. **Variants (2):** Q70*, W402*. **Detection Rate:** South Asian 67%.
**Muscle-Eye-Brain Disease - Gene:** POMGNT1. Autosomal Recessive. Sequencing. **Exons:** NM_017739:2-22. **Detection Rate:** South Asian 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:** South Asian 97%.
**Niemann-Pick Disease Type C - Gene:** NPC1. Autosomal Recessive. Sequencing. **Exons:** NM_000271:1-25. **Detection Rate:** South Asian 96%.
**Niemann-Pick Disease, SMPD1-associated - Gene:** SMPD1. Autosomal Recessive. Sequencing. **Exons:** NM_000543:1-6. **Detection Rate:** South Asian >99%.
**Nijmegen Breakage Syndrome - Gene:** NBN. Autosomal Recessive. Sequencing. **Exons:** NM_002485:1-16. **Detection Rate:** South Asian >99%.
**Northern Epilepsy - Gene:** CLN8. Autosomal Recessive. Sequencing. **Exons:** NM_018941:2-3. **Detection Rate:** South Asian >99%.
**PCDH15-related Disorders - Gene:** PCDH15. Autosomal Recessive. Sequencing. **Exons:** NM_033056:2-33. **Detection Rate:** South Asian 85%.
**Pendred Syndrome - Gene:** SLC26A4. Autosomal Recessive. Sequencing. **Exons:** NM_000441:2-21. **Detection Rate:** South Asian >99%.
**PEX1-related Zellweger Syndrome Spectrum - Gene:** PEX1. Autosomal Recessive. Sequencing. **Exons:** NM_000466:1-24. **Detection Rate:** South Asian >99%.
**Phenylalanine Hydroxylase Deficiency - Gene:** PAH. Autosomal Recessive. Sequencing. **Exons:** NM_000277:1-13. **Detection Rate:** South Asian >99%.
**PKHD1-related Autosomal Recessive Polycystic Kidney Disease - Gene:** PKHD1. Autosomal Recessive. Sequencing. **Exons:** NM_138694:2-67. **Detection Rate:** South Asian 98%.
**Polyglandular Autoimmune Syndrome Type 1 - Gene:** AIRE. Autosomal Recessive. Sequencing. **Exons:** NM_000383:1-14. **Detection Rate:** South Asian >99%.
**Pompe Disease - Gene:** GAA. Autosomal Recessive. Sequencing. **Exons:** NM_000152:2-20. **Detection Rate:** South Asian >99%.
**PPT1-related Neuronal Ceroid Lipofuscinosis - Gene:** PPT1. Autosomal Recessive. Sequencing. **Exons:** NM_000310:1-9. **Detection Rate:** South Asian >99%.
**Primary Carnitine Deficiency - Gene:** SLC22A5. Autosomal Recessive. Sequencing. **Exons:** NM_003060:1-10. **Detection Rate:** South Asian >99%.
**Primary Hyperoxaluria Type 1 - Gene:** AGXT. Autosomal Recessive. Sequencing. **Exons:** NM_000030:1-11. **Detection Rate:** South Asian >99%.
**Primary Hyperoxaluria Type 2 - Gene:** GRHPR. Autosomal Recessive. Sequencing. **Exons:** NM_012203:1-9. **Detection Rate:** South Asian >99%.
**PROP1-related Combined Pituitary Hormone Deficiency - Gene:** PROP1. Autosomal Recessive. Sequencing. **Exons:** NM_006261:1-3. **Detection Rate:** South Asian >99%.
**Pseudocholinesterase Deficiency - Gene:** BCHE. Autosomal Recessive. Sequencing. **Exons:** NM_000055:2-4. **Detection Rate:** South Asian >99%.
**Pycnodysostosis - Gene:** CTSK. Autosomal Recessive. Sequencing. **Exons:** NM_000396:2-8. **Detection Rate:** South Asian >99%.
**Rhizomelic Chondrodysplasia Punctata Type 1 - Gene:** PEX7. Autosomal Recessive. Sequencing. **Exons:** NM_000288:1-10. **Detection Rate:** South Asian >99%.
**Salla Disease - Gene:** SLC17A5. Autosomal Recessive. Sequencing. **Exons:** NM_012434:1-11. **Detection Rate:** South Asian 93%.
**Segawa Syndrome - Gene:** TH. Autosomal Recessive. Sequencing. **Exons:** NM_000360:1-13. **Detection Rate:** South Asian 96%.
**Short Chain Acyl-CoA Dehydrogenase Deficiency - Gene:** ACADS. Autosomal Recessive. Sequencing. **Exons:** NM_000017:1-10. **Detection Rate:** South Asian >99%.
**Sjogren-Larsson Syndrome - Gene:** ALDH3A2. Autosomal Recessive. Sequencing. **Exons:** NM_000382:1-10. **Detection Rate:** South Asian 92%.
**Smith-Lemli-Opitz Syndrome - Gene:** DHCR7. Autosomal Recessive. Sequencing. **Exons:** NM_001360:3-9. **Detection Rate:** South Asian >99%.
**Spinal Muscular Atrophy - Gene:** SMN1. Autosomal Recessive. Copy Number Analysis. **Variant (1):** SMN1 copy number. **Detection Rate:** South Asian 89%.
**Steroid-Resistant Nephrotic Syndrome - Gene:** NPHS2. Autosomal Recessive. Sequencing. **Exons:** NM_014625:1-8. **Detection Rate:** South Asian >99%.
**Sulfate Transporter-Related Osteochondrodysplasia - Gene:** SLC26A2. Autosomal Recessive. Sequencing. **Exons:** NM_000112:2-3. **Detection Rate:** South Asian >99%.
**TPP1-related Neuronal Ceroid Lipofuscinosis - Gene:** TPP1. Autosomal Recessive. Sequencing. **Exons:** NM_000391:1-13. **Detection Rate:** South Asian >99%.
**Tyrosinemia Type I - Gene:** FAH. Autosomal Recessive. Sequencing. **Exons:** NM_000137:1-14. **Detection Rate:** South Asian >99%.
**Usher Syndrome Type 3 - Gene:** CLRN1. Autosomal Recessive. Sequencing. **Exons:** NM_174878:1-3. **Detection Rate:** South Asian >99%.
**Very Long Chain Acyl-CoA Dehydrogenase Deficiency - Gene:** ACADVL. Autosomal Recessive. Sequencing. **Exons:** NM_000018:1-20. **Detection Rate:** South Asian >99%.
**Wilson Disease - Gene:** ATP7B. Autosomal Recessive. Sequencing. **Exons:** NM_000053:1-21. **Detection Rate:** South Asian >99%.

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RESULTS RECIPIENT
**SEATTLE SPERM BANK**
**Attn:** Dr. Jeffrey Olliffe
**NPI:** 1306838271
**Report Date:** 01/30/2017

MALE
**DONOR 10116**
**DOB:**
**Ethnicity:** South Asian
**Barcode:** 11004212022548

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 10116 Residual Risk | Reproductive Risk |
|---|---|---|
| **21-Hydroxylase-Deficient Congenital Adrenal Hyperplasia** | 1 in 360 | 1 in 60,000 |
| **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 12,000 | < 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 8,600 | < 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 50,000 | < 1 in 1,000,000 |
| **Gaucher Disease** | 1 in 280 | 1 in 120,000 |
| **GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness** | 1 in 10,000 | < 1 in 1,000,000 |
| **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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**DOB:**
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FEMALE
N/A

| Disease | DONOR 10116 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 470 | 1 in 85,000 |
| 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 35,000 | < 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 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 16,000 | < 1 in 1,000,000 |
| PPT1-related Neuronal Ceroid Lipofuscinosis | < 1 in 50,000 | < 1 in 1,000,000 |
| Primary Carnitine Deficiency | NM_003060.3(SLC22A5):c.248G>T(R83L) heterozygote † | 1 in 2,000 |
| 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 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 7,500 | < 1 in 1,000,000 |
| Segawa Syndrome | < 1 in 13,000 | < 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 3,100 | < 1 in 1,000,000 |
| Smith-Lemli-Opitz Syndrome | < 1 in 50,000 | < 1 in 1,000,000 |
| Spinal Muscular Atrophy | SMN1: 2 copies<br>1 in 380 | 1 in 76,000 |
| 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 |