Counsyl

RESULTS RECIPIENT
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Report Date: 07/20/2016

MALE
DONOR 12083
DOB: [redacted]
Ethnicity: Northern European
Sample Type: EDTA Blood
Date of Collection: 06/30/2016
Date Received: 07/01/2016
Date Tested: 07/11/2016
Barcode: 11200059695491
Indication: Egg or sperm donor

FEMALE
N/A

This is an **amended report**, from the 07/18/2016 original. Panel change requested.

Family Prep Screen

POSITIVE: CARRIER AT RISK FOR SYMPTOMS

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 12083	Partner
Panel Information	Family Prep Screen 2.0 Universal Panel **(104 conditions tested)**	N/A
POSITIVE: CARRIER AT RISK FOR SYMPTOMS Hereditary Thymine-Uraciluria **Reproductive Risk: 1 in 400** **Inheritance: Autosomal Recessive**	**CARRIER AT RISK FOR SYMPTOMS** NM_000110.3(DPYD):c.2846A>T (D949V) 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.

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.

POSITIVE: CARRIER AT RISK FOR SYMPTOMS

Hereditary Thymine-Uraciluria

Reproductive risk: 1 in 400
Risk before testing: 1 in 40,000

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

Patient	DONOR 12083	No partner tested
Result	⊕ Carrier At Risk for Symptoms	N/A
Variant(s)	NM_000110.3(DPYD):c.2846A>T(D949V) heterozygote †	N/A
Methodology	Sequencing	N/A
Interpretation	This individual is a carrier of hereditary thymine-uraciluria. Carriers are at risk for toxicity following treatment with certain types of chemotherapy.	N/A
Detection rate	> 52%	N/A
Exons tested	NM_000110:1-23.	N/A

†Likely to have a negative impact on gene function.

What is Hereditary Thymine-Uraciluria?

Hereditary thymine-uraciluria is an inherited disease that can cause serious mental and physical delays in children. For reasons that are not understood, most people with the genetic mutations that cause hereditary thymine-uraciluria have no symptoms at any time in their lives, while others are severely affected in infancy or childhood.

Among those who are affected, about 50% have neurological symptoms including seizures, mental disability, and a delay in motor skills. Less common symptoms include autism, a small head, a delay in physical growth, eye abnormalities, and speech difficulties. These symptoms typically appear in infancy or childhood.

All people with hereditary thymine-uraciluria, regardless of the presence or absence of symptoms, cannot properly break down the common chemotherapy drug 5-fluorouracil. If given this drug, they will have a severe toxic reaction that could be life-threatening. Signs of this reaction include diarrhea, swelling, digestive problems, muscle weakness, and an inability to coordinate muscle movement. Carriers of a mutation in the gene that causes this disease are also at risk for toxicity following 5-fluorouracil treatment.

Hereditary thymine-uraciluria is caused by the absence of an enzyme called dihydropyrimidine dehydrogenase which is needed for breaking down the molecules thymine and uracil, and also 5-fluorouracil when it is present in the body.

How common is Hereditary Thymine-Uraciluria?

Studies have shown that about 1% of Caucasians are carriers for a particular mutation that causes hereditary thymine-uraciluria. This mutation is common among people in the Netherlands, Finland, and Taiwan. Due to this mutation and other mutations in the same gene, an estimated 3% of Caucasians and 8% of African Americans are at risk for 5-fluorouracil toxicity.

How is Hereditary Thymine-Uraciluria treated?

There is no cure for hereditary thymine-uraciluria. Its symptoms can only be addressed as they arise (i.e. medication to prevent seizures). People with this disease must not take the drug 5-fluorouracil in order to avoid a toxic reaction.

What is the prognosis for a person with Hereditary Thymine-Uraciluria?

For those who are asymptomatic, the prognosis is very good. Their lifespan should be unaffected by the disease. For those with more severe symptoms, it is unknown how these symptoms affect lifespan.

Methods and Limitations

DONOR 12083 [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.

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

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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:** Northern European 96%.

ABCC8-related Hyperinsulinism - **Gene:** ABCC8. Autosomal Recessive. Sequencing. **Exons:** NM_000352:1-39. **Detection Rate:** Unknown due to rarity of disease.

Achromatopsia - **Gene:** CNGB3. Autosomal Recessive. Sequencing. **Exons:** NM_019098:1-18. **Detection Rate:** Northern European > 62%.

Alkaptonuria - **Gene:** HGD. Autosomal Recessive. Sequencing. **Exons:** NM_000187:1-14. **Detection Rate:** Northern European > 80%.

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

Alpha-1 Antitrypsin Deficiency - **Gene:** SERPINA1. Autosomal Recessive. Sequencing. **Exons:** NM_000295:2-5. **Detection Rate:** Northern European > 95%.

Alpha-Mannosidosis - **Gene:** MAN2B1. Autosomal Recessive. Sequencing. **Exons:** NM_000528:1-15,17-24. **Detection Rate:** Northern European > 32%.

Andermann Syndrome - **Gene:** SLC12A6. Autosomal Recessive. Sequencing. **Exons:** NM_133647:1-25. **Detection Rate:** Unknown due to rarity of disease.

ARSACS - **Gene:** SACS. Autosomal Recessive. Sequencing. **Exons:** NM_014363:2-10. **Detection Rate:** Unknown due to rarity of disease.

Aspartylglycosaminuria - **Gene:** AGA. Autosomal Recessive. Sequencing. **Exons:** NM_000027:1-9. **Detection Rate:** Unknown due to rarity of disease.

Ataxia With Vitamin E Deficiency - **Gene:** TTPA. Autosomal Recessive. Sequencing. **Exons:** NM_000370:1-5. **Detection Rate:** Northern European > 10%.

Ataxia-Telangiectasia - **Gene:** ATM. Autosomal Recessive. Sequencing. **Exons:** NM_000051:2-63. **Detection Rate:** Northern European > 65%.

Autosomal Recessive Polycystic Kidney Disease - **Gene:** PKHD1. Autosomal Recessive. Sequencing. **Exons:** NM_138694:2-67. **Detection Rate:** Northern European > 18%.

Bardet-Biedl Syndrome, BBS1-related - **Gene:** BBS1. Autosomal Recessive. Sequencing. **Exons:** NM_024649:1-17. **Detection Rate:** Northern European > 79%.

Bardet-Biedl Syndrome, BBS10-related - **Gene:** BBS10. Autosomal Recessive. Sequencing. **Exons:** NM_024685:1-2. **Detection Rate:** Northern European > 46%.

Biotinidase Deficiency - **Gene:** BTD. Autosomal Recessive. Sequencing. **Exons:** NM_000060:1-4. **Detection Rate:** Northern European > 45%.

Bloom Syndrome - **Gene:** BLM. Autosomal Recessive. Sequencing. **Exons:** NM_000057:2-22. **Detection Rate:** Northern European > 10%.

Canavan Disease - **Gene:** ASPA. Autosomal Recessive. Sequencing. **Exons:** NM_000049:1-6. **Detection Rate:** Northern European > 53%.

Carnitine Palmitoyltransferase IA Deficiency - **Gene:** CPT1A. Autosomal Recessive. Sequencing. **Exons:** NM_001876:2-19. **Detection Rate:** Northern European > 10%.

Carnitine Palmitoyltransferase II Deficiency - **Gene:** CPT2. Autosomal Recessive. Sequencing. **Exons:** NM_000098:1-5. **Detection Rate:** Northern European > 80%.

Cartilage-Hair Hypoplasia - **Gene:** RMRP. Autosomal Recessive. Sequencing. **Exon:** NR_003051:1. **Detection Rate:** Northern European > 48%.

Choroideremia - **Gene:** CHM. X-linked Recessive. Sequencing. **Exons:** NM_000390:1-15. **Detection Rate:** Unknown due to rarity of disease.

Citrullinemia Type 1 - **Gene:** ASS1. Autosomal Recessive. Sequencing. **Exons:** NM_000050:3-16. **Detection Rate:** Northern European > 20%.

CLN3-related Neuronal Ceroid Lipofuscinosis - **Gene:** CLN3. Autosomal Recessive. Sequencing. **Exons:** NM_001042432:2-16. **Detection Rate:** Northern European > 96%.

CLN5-related Neuronal Ceroid Lipofuscinosis - **Gene:** CLN5. Autosomal Recessive. Sequencing. **Exons:** NM_006493:1-4. **Detection Rate:** Unknown due to rarity of disease.

Cohen Syndrome - **Gene:** VPS13B. Autosomal Recessive. Sequencing. **Exons:** NM_017890:2-62. **Detection Rate:** Unknown due to rarity of disease.

Congenital Disorder of Glycosylation Type Ia - **Gene:** PMM2. Autosomal Recessive. Sequencing. **Exons:** NM_000303:1-8. **Detection Rate:** Northern European > 72%.

Congenital Disorder of Glycosylation Type Ib - **Gene:** MPI. Autosomal Recessive. Sequencing. **Exons:** NM_002435:1-8. **Detection Rate:** Unknown due to rarity of disease.

Congenital Finnish Nephrosis - **Gene:** NPHS1. Autosomal Recessive. Sequencing. **Exons:** NM_004646:2-23,26-27,29. **Detection Rate:** Unknown due to rarity of disease.

Costeff Optic Atrophy Syndrome - **Gene:** OPA3. Autosomal Recessive. Sequencing. **Exons:** NM_025136:1-2. **Detection Rate:** Unknown due to rarity of disease.

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:** Northern European > 91%.

Cystinosis - **Gene:** CTNS. Autosomal Recessive. Sequencing. **Exons:** NM_004937:3-12. **Detection Rate:** Northern European > 67%.

D-Bifunctional Protein Deficiency - **Gene:** HSD17B4. Autosomal Recessive. Sequencing. **Exons:** NM_000414:1-24. **Detection Rate:** Northern European > 35%.

Factor XI Deficiency - **Gene:** F11. Autosomal Recessive. Sequencing. **Exons:** NM_000128:2-15. **Detection Rate:** Northern European > 10%.

Familial Dysautonomia - **Gene:** IKBKAP. Autosomal Recessive. Sequencing. **Exons:** NM_003640:19-20,26. **Detection Rate:** Unknown due to rarity of disease.

Familial Mediterranean Fever - **Gene:** MEFV. Autosomal Recessive. Sequencing. **Exons:** NM_000243:1-10. **Detection Rate:** Unknown due to rarity of disease.

Fanconi Anemia Type C - **Gene:** FANCC. Autosomal Recessive. Sequencing. **Exons:** NM_000136:2-15. **Detection Rate:** Northern European > 54%.

Galactosemia - **Gene:** GALT. Autosomal Recessive. Sequencing. **Exons:** NM_000155:1-11. **Detection Rate:** Northern European > 80%.

Gaucher Disease - **Gene:** GBA. Autosomal Recessive. Targeted Genotyping. **Variants (10):** D409V, D448H, IVS2+1G>A, L444P, N370S, R463C, R463H, R496H, V394L, p.L29Afs*18. **Detection Rate:** Northern European 60%.

GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness - **Gene:** GJB2. Autosomal Recessive. Sequencing. **Exons:** NM_004004:1-2. **Detection Rate:** Northern European > 79%.

Glutaric Acidemia Type 1 - **Gene:** GCDH. Autosomal Recessive. Sequencing. **Exons:** NM_000159:2-12. **Detection Rate:** Northern European > 40%.

Glycogen Storage Disease Type Ia - **Gene:** G6PC. Autosomal Recessive. Sequencing. **Exons:** NM_000151:1-5. **Detection Rate:** Northern European > 61%.

Glycogen Storage Disease Type Ib - **Gene:** SLC37A4. Autosomal Recessive. Sequencing. **Exons:** NM_001164277:3-11. **Detection Rate:** Northern European > 46%.

Glycogen Storage Disease Type III - **Gene:** AGL. Autosomal Recessive. Sequencing. **Exons:** NM_000642:2-34. **Detection Rate:** Northern European > 45%.

Glycogen Storage Disease Type V - **Gene:** PYGM. Autosomal Recessive. Sequencing. **Exons:** NM_005609:1-20. **Detection Rate:** Northern European > 80%.

GRACILE Syndrome - **Gene:** BCS1L. Autosomal Recessive. Sequencing. **Exons:** NM_004328:3-9. **Detection Rate:** Unknown due to rarity of disease.

Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease) - **Gene:** HBB. Autosomal Recessive. Sequencing. **Exons:** NM_000518:1-3. **Detection Rate:** Northern European > 83%.

Hereditary Fructose Intolerance - **Gene:** ALDOB. Autosomal Recessive. Sequencing. **Exons:** NM_000035:2-9. **Detection Rate:** Northern European > 75%.

Hereditary Thymine-Uraciluria - **Gene:** DPYD. Autosomal Recessive. Sequencing. **Exons:** NM_000110:1-23. **Detection Rate:** Northern European > 52%.

Herlitz Junctional Epidermolysis Bullosa, LAMA3-related - **Gene:** LAMA3. Autosomal Recessive. Sequencing. **Exons:** NM_000227:1-16,18-38. **Detection Rate:** Northern European > 10%.

Herlitz Junctional Epidermolysis Bullosa, LAMB3-related - **Gene:** LAMB3. Autosomal Recessive. Sequencing. **Exons:** NM_000228:2-23. **Detection Rate:** Northern European > 48%.

Herlitz Junctional Epidermolysis Bullosa, LAMC2-related - **Gene:** LAMC2. Autosomal Recessive. Sequencing. **Exons:** NM_005562:1-23. **Detection Rate:** Unknown due to rarity of disease.

Hexosaminidase A Deficiency (Including Tay-Sachs Disease) - **Gene:** HEXA. Autosomal Recessive. Sequencing. **Exons:** NM_000520:1-14. **Detection Rate:** Northern European > 23%.

Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency - **Gene:** CBS. Autosomal Recessive. Sequencing. **Exons:** NM_000071:3-17. **Detection Rate:** Northern European > 14%.
Hurler Syndrome - **Gene:** IDUA. Autosomal Recessive. Targeted Genotyping. **Variants (2):** Q70*, W402*. **Detection Rate:** Northern European 67%.
Hypophosphatasia, Autosomal Recessive - **Gene:** ALPL. Autosomal Recessive. Sequencing. **Exons:** NM_000478:2-12. **Detection Rate:** Northern European > 30%.
Inclusion Body Myopathy 2 - **Gene:** GNE. Autosomal Recessive. Sequencing. **Exons:** NM_001128227:3-12. **Detection Rate:** Unknown due to rarity of disease.
Isovaleric Acidemia - **Gene:** IVD. Autosomal Recessive. Sequencing. **Exons:** NM_002225:1-12. **Detection Rate:** Northern European > 47%.
Joubert Syndrome 2 - **Gene:** TMEM216. Autosomal Recessive. Sequencing. **Exons:** NM_001173990:1-5. **Detection Rate:** Unknown due to rarity of disease.
Krabbe Disease - **Gene:** GALC. Autosomal Recessive. Sequencing. **Exons:** NM_000153:1-17. **Detection Rate:** Northern European > 58%.
Limb-Girdle Muscular Dystrophy Type 2D - **Gene:** SGCA. Autosomal Recessive. Sequencing. **Exons:** NM_000023:1-9. **Detection Rate:** Northern European > 32%.
Limb-Girdle Muscular Dystrophy Type 2E - **Gene:** SGCB. Autosomal Recessive. Sequencing. **Exons:** NM_000232:1-6. **Detection Rate:** Northern European > 12%.
Lipoamide Dehydrogenase Deficiency - **Gene:** DLD. Autosomal Recessive. Sequencing. **Exons:** NM_000108:1-14. **Detection Rate:** Unknown due to rarity of disease.
Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency - **Gene:** HADHA. Autosomal Recessive. Sequencing. **Exons:** NM_000182:1-20. **Detection Rate:** Northern European > 87%.
Maple Syrup Urine Disease Type 1B - **Gene:** BCKDHB. Autosomal Recessive. Sequencing. **Exons:** NM_183050:1-10. **Detection Rate:** Unknown due to rarity of disease.
Medium Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADM. Autosomal Recessive. Sequencing. **Exons:** NM_000016:1-12. **Detection Rate:** Northern European > 78%.
Megalencephalic Leukoencephalopathy With Subcortical Cysts - **Gene:** MLC1. Autosomal Recessive. Sequencing. **Exons:** NM_015166:2-12. **Detection Rate:** Northern European > 13%.
Metachromatic Leukodystrophy - **Gene:** ARSA. Autosomal Recessive. Sequencing. **Exons:** NM_000487:1-8. **Detection Rate:** Northern European > 53%.
Mucolipidosis IV - **Gene:** MCOLN1. Autosomal Recessive. Sequencing. **Exons:** NM_020533:1-14. **Detection Rate:** Northern European > 10%.
Muscle-Eye-Brain Disease - **Gene:** POMGNT1. Autosomal Recessive. Sequencing. **Exons:** NM_017739:2-22. **Detection Rate:** Northern European > 75%.
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:** Unknown due to rarity of disease.
Niemann-Pick Disease Type C - **Gene:** NPC1. Autosomal Recessive. Sequencing. **Exons:** NM_000271:1-25. **Detection Rate:** Northern European > 17%.
Niemann-Pick Disease, SMPD1-associated - **Gene:** SMPD1. Autosomal Recessive. Sequencing. **Exons:** NM_000543:1-6. **Detection Rate:** Northern European > 38%.
Nijmegen Breakage Syndrome - **Gene:** NBN. Autosomal Recessive. Sequencing. **Exons:** NM_002485:1-16. **Detection Rate:** Northern European > 78%.
Northern Epilepsy - **Gene:** CLN8. Autosomal Recessive. Sequencing. **Exons:** NM_018941:2-3. **Detection Rate:** Unknown due to rarity of disease.
Pendred Syndrome - **Gene:** SLC26A4. Autosomal Recessive. Sequencing. **Exons:** NM_000441:2-21. **Detection Rate:** Northern European > 69%.
PEX1-related Zellweger Syndrome Spectrum - **Gene:** PEX1. Autosomal Recessive. Sequencing. **Exons:** NM_000466:1-24. **Detection Rate:** Northern European > 68%.
Phenylalanine Hydroxylase Deficiency - **Gene:** PAH. Autosomal Recessive. Sequencing. **Exons:** NM_000277:1-13. **Detection Rate:** Northern European > 43%.
Polyglandular Autoimmune Syndrome Type 1 - **Gene:** AIRE. Autosomal Recessive. Sequencing. **Exons:** NM_000383:1-14. **Detection Rate:** Northern European > 65%.
Pompe Disease - **Gene:** GAA. Autosomal Recessive. Sequencing. **Exons:** NM_000152:2-20. **Detection Rate:** Northern European > 67%.
PPT1-related Neuronal Ceroid Lipofuscinosis - **Gene:** PPT1. Autosomal Recessive. Sequencing. **Exons:** NM_000310:1-9. **Detection Rate:** Northern European > 53%.
Primary Carnitine Deficiency - **Gene:** SLC22A5. Autosomal Recessive. Sequencing. **Exons:** NM_003060:1-10. **Detection Rate:** Unknown due to rarity of disease.
Primary Hyperoxaluria Type 1 - **Gene:** AGXT. Autosomal Recessive. Sequencing. **Exons:** NM_000030:1-11. **Detection Rate:** Northern European > 42%.
Primary Hyperoxaluria Type 2 - **Gene:** GRHPR. Autosomal Recessive. Sequencing. **Exons:** NM_012203:1-9. **Detection Rate:** Northern European > 37%.
PROP1-related Combined Pituitary Hormone Deficiency - **Gene:** PROP1. Autosomal Recessive. Sequencing. **Exons:** NM_006261:1-3. **Detection Rate:** Northern European > 55%.
Pseudocholinesterase Deficiency - **Gene:** BCHE. Autosomal Recessive. Sequencing. **Exons:** NM_000055:2-4. **Detection Rate:** Northern European > 83%.
Pycnodysostosis - **Gene:** CTSK. Autosomal Recessive. Sequencing. **Exons:** NM_000396:2-8. **Detection Rate:** Northern European > 10%.
Rhizomelic Chondrodysplasia Punctata Type 1 - **Gene:** PEX7. Autosomal Recessive. Sequencing. **Exons:** NM_000288:1-10. **Detection Rate:** Northern European > 70%.
Salla Disease - **Gene:** SLC17A5. Autosomal Recessive. Sequencing. **Exons:** NM_012434:1-11. **Detection Rate:** Unknown due to rarity of disease.
Segawa Syndrome - **Gene:** TH. Autosomal Recessive. Sequencing. **Exons:** NM_000360:1-13. **Detection Rate:** Northern European > 10%.
Short Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADS. Autosomal Recessive. Sequencing. **Exons:** NM_000017:1-10. **Detection Rate:** Unknown due to rarity of disease.
Sjogren-Larsson Syndrome - **Gene:** ALDH3A2. Autosomal Recessive. Sequencing. **Exons:** NM_000382:1-10. **Detection Rate:** Northern European > 24%.
Smith-Lemli-Opitz Syndrome - **Gene:** DHCR7. Autosomal Recessive. Sequencing. **Exons:** NM_001360:3-9. **Detection Rate:** Northern European > 69%.
Spinal Muscular Atrophy - **Gene:** SMN1. Autosomal Recessive. Copy Number Analysis. **Variant (1):** SMN1 copy number. **Detection Rate:** Northern European 95%.
Steroid-Resistant Nephrotic Syndrome - **Gene:** NPHS2. Autosomal Recessive. Sequencing. **Exons:** NM_014625:1-8. **Detection Rate:** Northern European > 33%.
Sulfate Transporter-Related Osteochondrodysplasia - **Gene:** SLC26A2. Autosomal Recessive. Sequencing. **Exons:** NM_000112:2-3. **Detection Rate:** Northern European > 75%.
TPP1-related Neuronal Ceroid Lipofuscinosis - **Gene:** TPP1. Autosomal Recessive. Sequencing. **Exons:** NM_000391:1-13. **Detection Rate:** Northern European > 60%.
Tyrosinemia Type I - **Gene:** FAH. Autosomal Recessive. Sequencing. **Exons:** NM_000137:1-14. **Detection Rate:** Northern European > 50%.
Usher Syndrome Type 1F - **Gene:** PCDH15. Autosomal Recessive. Sequencing. **Exons:** NM_033056:2-33. **Detection Rate:** Unknown due to rarity of disease.
Usher Syndrome Type 3 - **Gene:** CLRN1. Autosomal Recessive. Sequencing. **Exons:** NM_174878:1-3. **Detection Rate:** Unknown due to rarity of disease.
Very Long Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADVL. Autosomal Recessive. Sequencing. **Exons:** NM_000018:1-20. **Detection Rate:** Northern European > 20%.
Walker-Warburg Syndrome - **Gene:** FKTN. Autosomal Recessive. Sequencing. **Exons:** NM_001079802:3-11. **Detection Rate:** Unknown due to rarity of disease.
Wilson Disease - **Gene:** ATP7B. Autosomal Recessive. Sequencing. **Exons:** NM_000053:1-21. **Detection Rate:** Northern European > 40%.
X-Linked Juvenile Retinoschisis - **Gene:** RS1. X-linked Recessive. Sequencing. **Exons:** NM_000330:1-6. **Detection Rate:** Northern European > 20%.

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 12083 Residual Risk	Reproductive Risk
21-Hydroxylase-Deficient Congenital Adrenal Hyperplasia	1 in 1,400	1 in 310,000
ABCC8-related Hyperinsulinism	< 1 in 110	< 1 in 50,000
Achromatopsia	< 1 in 230	< 1 in 79,000
Alkaptonuria	< 1 in 500	< 1 in 1,000,000
Alpha Thalassemia	Alpha globin status: aa/aa.	Not calculated
Alpha-1 Antitrypsin Deficiency	< 1 in 680	< 1 in 93,000
Alpha-Mannosidosis	< 1 in 520	< 1 in 730,000
Andermann Syndrome	< 1 in 500	< 1 in 1,000,000
ARSACS	< 1 in 500	< 1 in 1,000,000
Aspartylglycosaminuria	< 1 in 500	< 1 in 1,000,000
Ataxia With Vitamin E Deficiency	< 1 in 500	< 1 in 1,000,000
Ataxia-Telangiectasia	< 1 in 450	< 1 in 290,000
Autosomal Recessive Polycystic Kidney Disease	< 1 in 75	< 1 in 18,000
Bardet-Biedl Syndrome, BBS1-related	< 1 in 750	< 1 in 480,000
Bardet-Biedl Syndrome, BBS10-related	< 1 in 290	< 1 in 180,000
Biotinidase Deficiency	< 1 in 220	< 1 in 110,000
Bloom Syndrome	< 1 in 500	< 1 in 1,000,000
Canavan Disease	< 1 in 500	< 1 in 1,000,000
Carnitine Palmitoyltransferase IA Deficiency	< 1 in 500	< 1 in 1,000,000
Carnitine Palmitoyltransferase II Deficiency	< 1 in 500	< 1 in 1,000,000
Cartilage-Hair Hypoplasia	< 1 in 500	< 1 in 1,000,000
Choroideremia	< 1 in 500	< 1 in 100,000
Citrullinemia Type 1	< 1 in 150	< 1 in 70,000
CLN3-related Neuronal Ceroid Lipofuscinosis	< 1 in 5,600	< 1 in 1,000,000
CLN5-related Neuronal Ceroid Lipofuscinosis	< 1 in 500	< 1 in 1,000,000
Cohen Syndrome	< 1 in 500	< 1 in 1,000,000
Congenital Disorder of Glycosylation Type Ia	< 1 in 560	< 1 in 360,000
Congenital Disorder of Glycosylation Type Ib	< 1 in 500	< 1 in 1,000,000
Congenital Finnish Nephrosis	< 1 in 500	< 1 in 1,000,000
Costeff Optic Atrophy Syndrome	< 1 in 500	< 1 in 1,000,000
Cystic Fibrosis	< 1 in 300	< 1 in 33,000
Cystinosis	< 1 in 670	< 1 in 600,000
D-Bifunctional Protein Deficiency	< 1 in 500	< 1 in 1,000,000
Factor XI Deficiency	< 1 in 500	< 1 in 1,000,000
Familial Dysautonomia	< 1 in 500	< 1 in 1,000,000
Familial Mediterranean Fever	< 1 in 500	< 1 in 1,000,000
Fanconi Anemia Type C	< 1 in 340	< 1 in 220,000
Galactosemia	< 1 in 430	< 1 in 150,000
Gaucher Disease	1 in 280	1 in 120,000
GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness	< 1 in 160	< 1 in 20,000
Glutaric Acidemia Type 1	< 1 in 170	< 1 in 67,000
Glycogen Storage Disease Type Ia	< 1 in 450	< 1 in 320,000
Glycogen Storage Disease Type Ib	< 1 in 660	< 1 in 930,000
Glycogen Storage Disease Type III	< 1 in 290	< 1 in 180,000
Glycogen Storage Disease Type V	< 1 in 790	< 1 in 500,000
GRACILE Syndrome	< 1 in 500	< 1 in 1,000,000
Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease)	< 1 in 290	< 1 in 58,000

Disease	DONOR 12083 Residual Risk	Reproductive Risk
Hereditary Fructose Intolerance	< 1 in 320	< 1 in 100,000
Hereditary Thymine-Uraciluria	NM_000110.3(DPYD):c.2846A>T(D949V) heterozygote †	1 in 400
Herlitz Junctional Epidermolysis Bullosa, LAMA3-related	< 1 in 500	< 1 in 1,000,000
Herlitz Junctional Epidermolysis Bullosa, LAMB3-related	< 1 in 500	< 1 in 1,000,000
Herlitz Junctional Epidermolysis Bullosa, LAMC2-related	< 1 in 500	< 1 in 1,000,000
Hexosaminidase A Deficiency (Including Tay-Sachs Disease)	< 1 in 390	< 1 in 470,000
Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency	< 1 in 290	< 1 in 290,000
Hurler Syndrome	1 in 480	1 in 300,000
Hypophosphatasia, Autosomal Recessive	< 1 in 230	< 1 in 140,000
Inclusion Body Myopathy 2	< 1 in 500	< 1 in 1,000,000
Isovaleric Acidemia	< 1 in 470	< 1 in 470,000
Joubert Syndrome 2	< 1 in 500	< 1 in 1,000,000
Krabbe Disease	< 1 in 360	< 1 in 210,000
Limb-Girdle Muscular Dystrophy Type 2D	< 1 in 660	< 1 in 1,000,000
Limb-Girdle Muscular Dystrophy Type 2E	< 1 in 500	< 1 in 1,000,000
Lipoamide Dehydrogenase Deficiency	< 1 in 500	< 1 in 1,000,000
Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	< 1 in 1,200	< 1 in 690,000
Maple Syrup Urine Disease Type 1B	< 1 in 250	< 1 in 250,000
Medium Chain Acyl-CoA Dehydrogenase Deficiency	< 1 in 270	< 1 in 63,000
Megalencephalic Leukoencephalopathy With Subcortical Cysts	< 1 in 500	< 1 in 1,000,000
Metachromatic Leukodystrophy	< 1 in 430	< 1 in 340,000
Mucolipidosis IV	< 1 in 500	< 1 in 1,000,000
Muscle-Eye-Brain Disease	< 1 in 500	< 1 in 1,000,000
NEB-related Nemaline Myopathy	< 1 in 500	< 1 in 1,000,000
Niemann-Pick Disease Type C	< 1 in 230	< 1 in 180,000
Niemann-Pick Disease, SMPD1-associated	< 1 in 400	< 1 in 400,000
Nijmegen Breakage Syndrome	< 1 in 720	< 1 in 450,000
Northern Epilepsy	< 1 in 500	< 1 in 1,000,000
Pendred Syndrome	< 1 in 220	< 1 in 63,000
PEX1-related Zellweger Syndrome Spectrum	< 1 in 350	< 1 in 160,000
Phenylalanine Hydroxylase Deficiency	< 1 in 88	< 1 in 17,000
Polyglandular Autoimmune Syndrome Type 1	< 1 in 400	< 1 in 230,000
Pompe Disease	< 1 in 480	< 1 in 300,000
PPT1-related Neuronal Ceroid Lipofuscinosis	< 1 in 500	< 1 in 1,000,000
Primary Carnitine Deficiency	< 1 in 500	< 1 in 1,000,000
Primary Hyperoxaluria Type 1	< 1 in 600	< 1 in 850,000
Primary Hyperoxaluria Type 2	< 1 in 500	< 1 in 1,000,000
PROP1-related Combined Pituitary Hormone Deficiency	< 1 in 250	< 1 in 110,000
Pseudocholinesterase Deficiency	< 1 in 160	< 1 in 18,000
Pycnodysostosis	< 1 in 500	< 1 in 1,000,000
Rhizomelic Chondrodysplasia Punctata Type 1	< 1 in 530	< 1 in 330,000
Salla Disease	< 1 in 500	< 1 in 1,000,000
Segawa Syndrome	< 1 in 500	< 1 in 1,000,000
Short Chain Acyl-CoA Dehydrogenase Deficiency	< 1 in 160	< 1 in 100,000
Sjogren-Larsson Syndrome	< 1 in 330	< 1 in 330,000
Smith-Lemli-Opitz Syndrome	< 1 in 160	< 1 in 32,000
Spinal Muscular Atrophy	SMN1: 2 copies 1 in 610	1 in 84,000
Steroid-Resistant Nephrotic Syndrome	< 1 in 600	< 1 in 950,000
Sulfate Transporter-Related Osteochondrodysplasia	< 1 in 420	< 1 in 180,000
TPP1-related Neuronal Ceroid Lipofuscinosis	< 1 in 740	< 1 in 870,000
Tyrosinemia Type I	< 1 in 350	< 1 in 240,000
Usher Syndrome Type 1F	< 1 in 190	< 1 in 150,000
Usher Syndrome Type 3	< 1 in 500	< 1 in 1,000,000
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	< 1 in 110	< 1 in 39,000
Walker-Warburg Syndrome	< 1 in 500	< 1 in 1,000,000
Wilson Disease	< 1 in 140	< 1 in 50,000
X-Linked Juvenile Retinoschisis	< 1 in 500	< 1 in 50,000