Counsyl

RESULTS RECIPIENT
UNIVERSITY MEDICAL CENTER 245
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Report Date: 02/18/2014

FEMALE
JANE MILLER
DOB: 11/11/1977
Ethnicity: Northern European
Sample Type: EDTA Blood
Date of Collection: 02/06/2014
Date Received: 02/16/2014
Date Tested: 02/16/2014
Barcode: 11200002829153
Accession ID: FAKERQPEOCLD
Indication: Screening for genetic disease carrier status

MALE
JOHN MILLER
DOB: 11/23/1969
Ethnicity: Northern European
Sample Type: EDTA Blood
Date of Collection: 02/06/2014
Date Received: 02/16/2014
Date Tested: 02/16/2014
Barcode: 11200026329007
Accession ID: FAKERQPEOCLD
Indication: Screening for genetic disease carrier status

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	JANE MILLER	JOHN MILLER
Panel Information	Family Prep Screen 2.0 Universal Panel With Fragile X Syndrome **(105 conditions tested)**	Family Prep Screen 2.0 Universal Panel With Fragile X Syndrome **(105 conditions tested)**
POSITIVE: CARRIER Smith-Lemli-Opitz Syndrome **Reproductive Risk: 1 in 20,000** **Inheritance: Autosomal Recessive**	**CARRIER*** NM_001360.2(DHCR7):c.964-1G>C (aka IVS8-1G>C) heterozygote	**NEGATIVE** No disease-causing mutations detected.

*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

- 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

Smith-Lemli-Opitz Syndrome

Reproductive risk: 1 in 20,000
Risk before testing: 1 in 9,800

Gene: DHCR7 | **Inheritance Pattern:** Autosomal Recessive

Patient	JANE MILLER	JOHN MILLER
Result	⊕ Carrier	⊖ Negative
Variant(s)	NM_001360.2(DHCR7):c.964-1G>C(aka IVS8-1G>C) heterozygote	No disease-causing mutations detected.
Methodology	Sequencing	Sequencing
Interpretation	This individual is a carrier of Smith-Lemli-Opitz syndrome. Carriers generally do not experience symptoms. The c.964-1G>C mutation is associated with the severe form of this disease.	This does not rule out the possibility of being a carrier. The post-test risk of being a carrier, assuming a negative family history, is 1 in 4,900.
Detection rate	>99%	>99%
Exons tested	NM_001360:3-9.	NM_001360:3-9.

What is Smith-Lemli-Opitz Syndrome?

Smith-Lemli-Opitz syndrome, or SLO syndrome, is an inherited disorder in which the body's ability to make cholesterol is impaired due to a deficient enzyme. Cholesterol is critical for the structure of cells, and is necessary for normal fetal development. It also plays an important role in the production of hormones and digestive acids. In addition to low cholesterol levels, SLO syndrome also causes toxic byproducts of cholesterol production to build up throughout the body, further disrupting growth and development.

In children with little or no ability to make cholesterol, symptoms are severe. These infants are commonly born with an abnormally small head, cleft palate, and weak muscle tone. They often have difficulty feeding because they lack the sucking reflex or have an abnormally small stomach that causes persistent vomiting. Some have extra fingers or toes as well as the typical fused second and third toes on both feet. Male infants may have deformed or underdeveloped genitalia.

Infants with the severe form of SLO syndrome grow slowly and 90% have moderate to severe mental disability. Severely affected infants may also have heart defects and problems with their kidneys, causing death in the first months of life.

Some children are born with a milder form of the condition in which the body can produce some cholesterol. Symptoms may include developmental delays, feet with the second and third toes fused together, slow growth, and short stature. These children generally learn to walk and talk and can acquire other skills, although they can rarely live independently as adults. Adults with the disease often show aggressive behavior.

Symptoms of the disease can vary from person to person. Some affected people have only minor symptoms of the condition.

How common is Smith-Lemli-Opitz Syndrome?

Smith-Lemli-Opitz syndrome affects an estimated 1 in 20,000 to 60,000 people. This disease is more common in those of European ancestry, particularly those in Slovakia and the Czech Republic. It is very rare among people of African and Asian descent.

How is Smith-Lemli-Opitz Syndrome treated?

There is no cure for SLO syndrome, but its symptoms can be addressed. The primary treatment is to supplement the person's diet with large amounts of dietary cholesterol, either in the form of purified cholesterol or in foods such as egg yolks and cream. This has been shown to improve symptoms. Early intervention and therapy helps with speech and physical disabilities. Medication may treat symptoms such as vomiting, constipation, and gastroesophageal reflux. Surgery and orthotics can help muscle spasms and improve mobility.

Because the condition can cause extreme sun sensitivity, people with SLO syndrome should always wear sunblock, sunglasses, and appropriate clothing when they go outdoors.

What is the prognosis for a person with Smith-Lemli-Opitz Syndrome?

Although serious internal malformations can lead to early death, with good nutrition and medical care many people with SLO syndrome can have a normal lifespan. Mental disability typically prevents people with this disease from living independently.

Methods and Limitations

JANE MILLER [Family Prep Screen 2.0]: sequencing, targeted genotyping, triplet repeat detection, copy number analysis, and analysis of homologous regions.
JOHN MILLER [Family Prep Screen 2.0]: sequencing, targeted genotyping, triplet repeat detection, 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. The test is not validated for detection of homozygous mutations, and although rare, asymptomatic individuals affected by the disease may not be genotyped accurately.

Triplet repeat detection

PCR is used to size the CGG repeat in the 5' UTR of *FMR1* (NM_002024.4: c.1-131CGG[1_n]). PCR products generated from fluorescently labeled primers are detected by capillary electrophoresis. Reported sizes are accurate to +/- 1 repeat for up to 200 repeats. Alleles above 200 CGG repeats (full mutations), while identified, are not sized. Nearby mutations may interfere with detection of CGG expansions. Deletion of the CGG repeat and other *FMR1* mutations may not be detectable. Methylation will not be detected. Small degrees of size mosaicism, including gonadal mosaicism, will not be detected as the test has been calibrated to yield results that are equivalent to the results from Southern blot.

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

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, V282L, [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:** Northern European >99%.

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

Alkaptonuria - **Gene:** HGD. Autosomal Recessive. Sequencing. **Exons:** NM_000187:1-14. **Detection Rate:** Northern European >99%.

Alpha Thalassemia - **Genes:** HBA1, HBA2. Autosomal Recessive. Analysis of Homologous Regions. **Variants (13):** -(alpha)20.5, --BRIT, --MEDI, --MEDII, --SEA, --THAI/--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 >99%.

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

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

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

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

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

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

Ataxia-Telangiectasia - **Gene:** ATM. Autosomal Recessive. Sequencing. **Exons:** NM_000051:2-63. **Detection Rate:** Northern European 92%.

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

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

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

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

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

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

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

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

Choroideremia - **Gene:** CHM. X-linked Recessive. Sequencing. **Exons:** NM_000390:1-15. **Detection Rate:** Northern European 87%.

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

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

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

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

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

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

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

Costeff Optic Atrophy Syndrome - **Gene:** OPA3. Autosomal Recessive. Sequencing. **Exons:** NM_025136:1-2. **Detection Rate:** Northern European >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:** Northern European 97%.

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

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

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

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

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

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

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

Fragile X Syndrome - **Gene:** FMR1. X-linked Dominant. Triplet Repeat Detection. **Variant (1):** FMR1 CGG repeat number. **Detection Rate:** Northern European >99%.

Galactosemia - **Gene:** GALT. Autosomal Recessive. Sequencing. **Exons:** NM_000155:1-11. **Detection Rate:** Northern European >99%.

Gaucher Disease - **Gene:** GBA. Autosomal Recessive. Targeted Genotyping. **Variants (10):** D448H, D448V, L483P, N409S, R502C, R502H, R535H, V433L, c.115+1G>A, c.84dupG. **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 98%.

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

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

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

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

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

GRACILE Syndrome - **Gene:** BCS1L. Autosomal Recessive. Sequencing. **Exons:** NM_004328:3-9. **Detection Rate:** Northern European >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:** Northern European 96%.

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

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

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

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

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

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

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 >99%.
Inclusion Body Myopathy 2 - **Gene:** GNE. Autosomal Recessive. Sequencing. **Exons:** NM_001128227:3-12. **Detection Rate:** Northern European >99%.
Isovaleric Acidemia - **Gene:** IVD. Autosomal Recessive. Sequencing. **Exons:** NM_002225:1-12. **Detection Rate:** Northern European >99%.
Joubert Syndrome 2 - **Gene:** TMEM216. Autosomal Recessive. Sequencing. **Exons:** NM_001173990:1-5. **Detection Rate:** Northern European >99%.
Krabbe Disease - **Gene:** GALC. Autosomal Recessive. Sequencing. **Exons:** NM_000153:1-17. **Detection Rate:** Northern European >99%.
Limb-Girdle Muscular Dystrophy Type 2E - **Gene:** SGCB. Autosomal Recessive. Sequencing. **Exons:** NM_000232:1-6. **Detection Rate:** Northern European >99%.
Lipoamide Dehydrogenase Deficiency - **Gene:** DLD. Autosomal Recessive. Sequencing. **Exons:** NM_000108:1-14. **Detection Rate:** Northern European >99%.
Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency - **Gene:** HADHA. Autosomal Recessive. Sequencing. **Exons:** NM_000182:1-20. **Detection Rate:** Northern European >99%.
Maple Syrup Urine Disease Type 1B - **Gene:** BCKDHB. Autosomal Recessive. Sequencing. **Exons:** NM_183050:1-10. **Detection Rate:** Northern European >99%.
Medium Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADM. Autosomal Recessive. Sequencing. **Exons:** NM_000016:1-12. **Detection Rate:** Northern European >99%.
Megalencephalic Leukoencephalopathy With Subcortical Cysts - **Gene:** MLC1. Autosomal Recessive. Sequencing. **Exons:** NM_015166:2-12. **Detection Rate:** Northern European >99%.
Metachromatic Leukodystrophy - **Gene:** ARSA. Autosomal Recessive. Sequencing. **Exons:** NM_000487:1-8. **Detection Rate:** Northern European >99%.
Mucolipidosis IV - **Gene:** MCOLN1. Autosomal Recessive. Sequencing. **Exons:** NM_020533:1-14. **Detection Rate:** Northern European >99%.
Muscle-Eye-Brain Disease - **Gene:** POMGNT1. Autosomal Recessive. Sequencing. **Exons:** NM_017739:2-22. **Detection Rate:** Northern European 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:** Northern European 96%.
Niemann-Pick Disease Type C - **Gene:** NPC1. Autosomal Recessive. Sequencing. **Exons:** NM_000271:1-25. **Detection Rate:** Northern European 96%.
Niemann-Pick Disease, SMPD1-associated - **Gene:** SMPD1. Autosomal Recessive. Sequencing. **Exons:** NM_000543:1-6. **Detection Rate:** Northern European >99%.
Nijmegen Breakage Syndrome - **Gene:** NBN. Autosomal Recessive. Sequencing. **Exons:** NM_002485:1-16. **Detection Rate:** Northern European >99%.
Northern Epilepsy - **Gene:** CLN8. Autosomal Recessive. Sequencing. **Exons:** NM_018941:2-3. **Detection Rate:** Northern European >99%.
PCDH15-related Disorders - **Gene:** PCDH15. Autosomal Recessive. Sequencing. **Exons:** NM_033056:2-33. **Detection Rate:** Northern European 85%.
Pendred Syndrome - **Gene:** SLC26A4. Autosomal Recessive. Sequencing. **Exons:** NM_000441:2-21. **Detection Rate:** Northern European >99%.
PEX1-related Zellweger Syndrome Spectrum - **Gene:** PEX1. Autosomal Recessive. Sequencing. **Exons:** NM_000466:1-24. **Detection Rate:** Northern European >99%.
Phenylalanine Hydroxylase Deficiency - **Gene:** PAH. Autosomal Recessive. Sequencing. **Exons:** NM_000277:1-13. **Detection Rate:** Northern European 98%.
PKHD1-related Autosomal Recessive Polycystic Kidney Disease - **Gene:** PKHD1. Autosomal Recessive. Sequencing. **Exons:** NM_138694:2-67. **Detection Rate:** Northern European 98%.
Polyglandular Autoimmune Syndrome Type 1 - **Gene:** AIRE. Autosomal Recessive. Sequencing. **Exons:** NM_000383:1-14. **Detection Rate:** Northern European >99%.
Pompe Disease - **Gene:** GAA. Autosomal Recessive. Sequencing. **Exons:** NM_000152:2-20. **Detection Rate:** Northern European 90%.
PPT1-related Neuronal Ceroid Lipofuscinosis - **Gene:** PPT1. Autosomal Recessive. Sequencing. **Exons:** NM_000310:1-9. **Detection Rate:** Northern European >99%.
Primary Carnitine Deficiency - **Gene:** SLC22A5. Autosomal Recessive. Sequencing. **Exons:** NM_003060:1-10. **Detection Rate:** Northern European >99%.
Primary Hyperoxaluria Type 1 - **Gene:** AGXT. Autosomal Recessive. Sequencing. **Exons:** NM_000030:1-11. **Detection Rate:** Northern European >99%.
Primary Hyperoxaluria Type 2 - **Gene:** GRHPR. Autosomal Recessive. Sequencing. **Exons:** NM_012203:1-9. **Detection Rate:** Northern European >99%.
PROP1-related Combined Pituitary Hormone Deficiency - **Gene:** PROP1. Autosomal Recessive. Sequencing. **Exons:** NM_006261:1-3. **Detection Rate:** Northern European >99%.
Pseudocholinesterase Deficiency - **Gene:** BCHE. Autosomal Recessive. Sequencing. **Exons:** NM_000055:2-4. **Detection Rate:** Northern European >99%.
Pycnodysostosis - **Gene:** CTSK. Autosomal Recessive. Sequencing. **Exons:** NM_000396:2-8. **Detection Rate:** Northern European >99%.
Rhizomelic Chondrodysplasia Punctata Type 1 - **Gene:** PEX7. Autosomal Recessive. Sequencing. **Exons:** NM_000288:1-10. **Detection Rate:** Northern European >99%.
Salla Disease - **Gene:** SLC17A5. Autosomal Recessive. Sequencing. **Exons:** NM_012434:1-11. **Detection Rate:** Northern European 93%.
Segawa Syndrome - **Gene:** TH. Autosomal Recessive. Sequencing. **Exons:** NM_000360:1-13. **Detection Rate:** Northern European 96%.
Short Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADS. Autosomal Recessive. Sequencing. **Exons:** NM_000017:1-10. **Detection Rate:** Northern European >99%.
Sjogren-Larsson Syndrome - **Gene:** ALDH3A2. Autosomal Recessive. Sequencing. **Exons:** NM_000382:1-10. **Detection Rate:** Northern European 92%.
Smith-Lemli-Opitz Syndrome - **Gene:** DHCR7. Autosomal Recessive. Sequencing. **Exons:** NM_001360:3-9. **Detection Rate:** Northern European >99%.
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 >99%.
Sulfate Transporter-Related Osteochondrodysplasia - **Gene:** SLC26A2. Autosomal Recessive. Sequencing. **Exons:** NM_000112:2-3. **Detection Rate:** Northern European >99%.
TPP1-related Neuronal Ceroid Lipofuscinosis - **Gene:** TPP1. Autosomal Recessive. Sequencing. **Exons:** NM_000391:1-13. **Detection Rate:** Northern European >99%.
Tyrosinemia Type I - **Gene:** FAH. Autosomal Recessive. Sequencing. **Exons:** NM_000137:1-14. **Detection Rate:** Northern European >99%.
Usher Syndrome Type 3 - **Gene:** CLRN1. Autosomal Recessive. Sequencing. **Exons:** NM_174878:1-3. **Detection Rate:** Northern European >99%.
Very Long Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADVL. Autosomal Recessive. Sequencing. **Exons:** NM_000018:1-20. **Detection Rate:** Northern European >99%.
Walker-Warburg Syndrome - **Gene:** FKTN. Autosomal Recessive. Sequencing. **Exons:** NM_001079802:3-11. **Detection Rate:** Northern European >99%.
Wilson Disease - **Gene:** ATP7B. Autosomal Recessive. Sequencing. **Exons:** NM_000053:1-21. **Detection Rate:** Northern European >99%.
X-Linked Juvenile Retinoschisis - **Gene:** RS1. X-linked Recessive. Sequencing. **Exons:** NM_000330:1-6. **Detection Rate:** Northern European 94%.

Risk Calculations

Below are the risk calculations for all conditions tested. Since negative results do not completely rule out the possibility of being a carrier, the **residual risk** represents each patients' post-test likelihood of being a carrier and the **reproductive risk** represents the likelihood the patients' 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.

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

Disease	JANE MILLER Residual Risk	JOHN MILLER Residual Risk	Reproductive Risk
21-Hydroxylase-Deficient Congenital Adrenal Hyperplasia	1 in 1,400	1 in 1,400	< 1 in 1,000,000
ABCC8-related Hyperinsulinism	1 in 11,000	1 in 11,000	< 1 in 1,000,000
Achromatopsia	1 in 8,600	1 in 8,600	< 1 in 1,000,000
Alkaptonuria	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Alpha Thalassemia	Alpha globin status: aa/aa.	Alpha globin status: aa/aa.	Low
Alpha-1 Antitrypsin Deficiency	1 in 3,400	1 in 3,400	< 1 in 1,000,000
Alpha-Mannosidosis	1 in 35,000	1 in 35,000	< 1 in 1,000,000
Alpha-Sarcoglycanopathy	1 in 31,000	1 in 31,000	< 1 in 1,000,000
Andermann Syndrome	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
ARSACS	< 1 in 18,000	< 1 in 18,000	< 1 in 1,000,000
Aspartylglycosaminuria	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Ataxia With Vitamin E Deficiency	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Ataxia-Telangiectasia	1 in 2,100	1 in 2,100	< 1 in 1,000,000
Bardet-Biedl Syndrome, BBS1-related	1 in 16,000	1 in 16,000	< 1 in 1,000,000
Bardet-Biedl Syndrome, BBS10-related	1 in 16,000	1 in 16,000	< 1 in 1,000,000
Biotinidase Deficiency	1 in 12,000	1 in 12,000	< 1 in 1,000,000
Bloom Syndrome	< 1 in 12,000	< 1 in 12,000	< 1 in 1,000,000
Canavan Disease	< 1 in 7,700	< 1 in 7,700	< 1 in 1,000,000
Carnitine Palmitoyltransferase IA Deficiency	< 1 in 31,000	< 1 in 31,000	< 1 in 1,000,000
Carnitine Palmitoyltransferase II Deficiency	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Cartilage-Hair Hypoplasia	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Choroideremia	1 in 190,000	< 1 in 1,000,000	1 in 780,000
Citrullinemia Type 1	1 in 12,000	1 in 12,000	< 1 in 1,000,000
CLN3-related Neuronal Ceroid Lipofuscinosis	1 in 22,000	1 in 22,000	< 1 in 1,000,000
CLN5-related Neuronal Ceroid Lipofuscinosis	< 1 in 23,000	< 1 in 23,000	< 1 in 1,000,000
Cohen Syndrome	< 1 in 3,000	< 1 in 3,000	< 1 in 1,000,000
Congenital Disorder of Glycosylation Type Ia	1 in 16,000	1 in 16,000	< 1 in 1,000,000
Congenital Disorder of Glycosylation Type Ib	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Congenital Finnish Nephrosis	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Costeff Optic Atrophy Syndrome	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Cystic Fibrosis	1 in 910	1 in 910	< 1 in 1,000,000
Cystinosis	1 in 22,000	1 in 22,000	< 1 in 1,000,000
D-Bifunctional Protein Deficiency	1 in 2,900	1 in 2,900	< 1 in 1,000,000
Dihydropyrimidine Dehydrogenase Deficiency	1 in 1,400	1 in 1,400	< 1 in 1,000,000
Factor XI Deficiency	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Familial Dysautonomia	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Familial Mediterranean Fever	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Fanconi Anemia Type C	1 in 16,000	1 in 16,000	< 1 in 1,000,000
Fragile X Syndrome	Normal: 29 and 31 repeats	Normal: 29 repeats	Not calculated
Galactosemia	1 in 8,600	1 in 8,600	< 1 in 1,000,000
Gaucher Disease	1 in 280	1 in 280	1 in 310,000
GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness	1 in 1,700	1 in 1,700	< 1 in 1,000,000
Glutaric Acidemia Type 1	1 in 10,000	1 in 10,000	< 1 in 1,000,000
Glycogen Storage Disease Type Ia	1 in 18,000	1 in 18,000	< 1 in 1,000,000
Glycogen Storage Disease Type Ib	1 in 35,000	1 in 35,000	< 1 in 1,000,000
Glycogen Storage Disease Type III	1 in 16,000	1 in 16,000	< 1 in 1,000,000
Glycogen Storage Disease Type V	1 in 16,000	1 in 16,000	< 1 in 1,000,000
GRACILE Syndrome	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000

Counsyl

RESULTS RECIPIENT
UNIVERSITY MEDICAL CENTER 245
Attn: Dr. Paul Smith
NPI: 3652760645
Report Date: 02/18/2014

FEMALE
JANE MILLER
DOB: 11/11/1977
Ethnicity: Northern European
Barcode: 11200002829153

MALE
JOHN MILLER
DOB: 11/23/1969
Ethnicity: Northern European
Barcode: 11200026329007

Disease	JANE MILLER Residual Risk	JOHN MILLER Residual Risk	Reproductive Risk
Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease)	1 in 1,200	1 in 1,200	< 1 in 1,000,000
Hereditary Fructose Intolerance	1 in 8,000	1 in 8,000	< 1 in 1,000,000
Herlitz Junctional Epidermolysis Bullosa, LAMA3-related	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Herlitz Junctional Epidermolysis Bullosa, LAMB3-related	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Herlitz Junctional Epidermolysis Bullosa, LAMC2-related	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Hexosaminidase A Deficiency (Including Tay-Sachs Disease)	1 in 30,000	1 in 30,000	< 1 in 1,000,000
Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency	1 in 25,000	1 in 25,000	< 1 in 1,000,000
Hurler Syndrome	1 in 480	1 in 480	1 in 910,000
Hypophosphatasia, Autosomal Recessive	1 in 16,000	1 in 16,000	< 1 in 1,000,000
Inclusion Body Myopathy 2	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Isovaleric Acidemia	1 in 25,000	1 in 25,000	< 1 in 1,000,000
Joubert Syndrome 2	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Krabbe Disease	1 in 15,000	1 in 15,000	< 1 in 1,000,000
Limb-Girdle Muscular Dystrophy Type 2E	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Lipoamide Dehydrogenase Deficiency	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	1 in 15,000	1 in 15,000	< 1 in 1,000,000
Maple Syrup Urine Disease Type 1B	1 in 25,000	1 in 25,000	< 1 in 1,000,000
Medium Chain Acyl-CoA Dehydrogenase Deficiency	1 in 5,900	1 in 5,900	< 1 in 1,000,000
Megalencephalic Leukoencephalopathy With Subcortical Cysts	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Metachromatic Leukodystrophy	1 in 20,000	1 in 20,000	< 1 in 1,000,000
Mucolipidosis IV	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Muscle-Eye-Brain Disease	< 1 in 5,000	< 1 in 5,000	< 1 in 1,000,000
NEB-related Nemaline Myopathy	< 1 in 12,000	< 1 in 12,000	< 1 in 1,000,000
Niemann-Pick Disease Type C	1 in 5,400	1 in 5,400	< 1 in 1,000,000
Niemann-Pick Disease, SMPD1-associated	1 in 25,000	1 in 25,000	< 1 in 1,000,000
Nijmegen Breakage Syndrome	1 in 16,000	1 in 16,000	< 1 in 1,000,000
Northern Epilepsy	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
PCDH15-related Disorders	1 in 2,300	1 in 2,300	< 1 in 1,000,000
Pendred Syndrome	1 in 7,000	1 in 7,000	< 1 in 1,000,000
PEX1-related Zellweger Syndrome Spectrum	1 in 11,000	1 in 11,000	< 1 in 1,000,000
Phenylalanine Hydroxylase Deficiency	1 in 3,000	1 in 3,000	< 1 in 1,000,000
PKHD1-related Autosomal Recessive Polycystic Kidney Disease	1 in 4,100	1 in 4,100	< 1 in 1,000,000
Polyglandular Autoimmune Syndrome Type 1	1 in 14,000	1 in 14,000	< 1 in 1,000,000
Pompe Disease	1 in 1,600	1 in 1,600	< 1 in 1,000,000
PPT1-related Neuronal Ceroid Lipofuscinosis	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Primary Carnitine Deficiency	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Primary Hyperoxaluria Type 1	1 in 35,000	1 in 35,000	< 1 in 1,000,000
Primary Hyperoxaluria Type 2	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
PROP1-related Combined Pituitary Hormone Deficiency	1 in 11,000	1 in 11,000	< 1 in 1,000,000
Pseudocholinesterase Deficiency	1 in 2,700	1 in 2,700	< 1 in 1,000,000
Pycnodysostosis	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Rhizomelic Chondrodysplasia Punctata Type 1	1 in 16,000	1 in 16,000	< 1 in 1,000,000
Salla Disease	< 1 in 7,500	< 1 in 7,500	< 1 in 1,000,000
Segawa Syndrome	< 1 in 13,000	< 1 in 13,000	< 1 in 1,000,000
Short Chain Acyl-CoA Dehydrogenase Deficiency	1 in 16,000	1 in 16,000	< 1 in 1,000,000
Sjogren-Larsson Syndrome	1 in 3,100	1 in 3,100	< 1 in 1,000,000
Smith-Lemli-Opitz Syndrome	c.964-1G>C heterozygote †	1 in 4,900	1 in 20,000
Spinal Muscular Atrophy	SMN1: 2 copies 1 in 610	SMN1: 2 copies 1 in 610	< 1 in 1,000,000
Steroid-Resistant Nephrotic Syndrome	1 in 40,000	1 in 40,000	< 1 in 1,000,000
Sulfate Transporter-Related Osteochondrodysplasia	1 in 11,000	1 in 11,000	< 1 in 1,000,000
TPP1-related Neuronal Ceroid Lipofuscinosis	1 in 30,000	1 in 30,000	< 1 in 1,000,000
Tyrosinemia Type I	1 in 17,000	1 in 17,000	< 1 in 1,000,000
Usher Syndrome Type 3	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	1 in 8,800	1 in 8,800	< 1 in 1,000,000
Walker-Warburg Syndrome	< 1 in 50,000	< 1 in 50,000	< 1 in 1,000,000
Wilson Disease	1 in 8,600	1 in 8,600	< 1 in 1,000,000
X-Linked Juvenile Retinoschisis	1 in 210,000	< 1 in 1,000,000	1 in 840,000