Integrated
GENETICS
LabCorp Specialty Testing Group

**Client/Sending Facility:**
Phoenix Sperm Bank

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

| | | | |
|---|---|---|---|
| **LCLS Specimen Number:** | **226-944-0361-0** | Account Number: | [redacted] |
| Patient Name: | **10070, DONOR** | Ordering Physician: | **J OLLIFFE** |
| Date of Birth: | [redacted] | Specimen Type: | **BLOOD** |
| Gender: | M | Client Reference: | |
| Patient ID: | | Date Collected: | 08/13/2016 |
| Lab Number: | YU16-64330 L | Date Received: | 08/15/2016 |
| Indications: | NOT GIVEN | Date Reported: | **08/24/2016** |

Test: **Chromosome, Blood, Routine**

| | | | |
|---|---|---|---|
| Cells Counted: | 20 | Cells Karyotyped: | 2 |
| Cells Analyzed: | 20 | Band Resolution: | 500 |

**CYTOGENETIC RESULT: 46,XY**

**INTERPRETATION: NORMAL MALE KARYOTYPE**

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

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

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| Patient ID: | |
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| Ordering Physician: | **J OLLIFFE** |
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Justin Schleede

Justin Schleede, PhD, DABMG
Board Certified Cytogeneticist

Arundhati Chatterjee, MD
Medical Director
Peter Papenhausen, PhD
National Director of Cytogenetics

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Professional Component performed by LabCorp CLIA 34D1008914, 1904 TW Alexander Dr, Research Triangle Park, NC 27709. Medical Director, Arundhati Chatterjee, MD.
Integrated Genetics is a brand used by Esoterix Genetic Laboratories, LLC, a wholly-owned subsidiary of Laboratory Corporation of America Holdings.

This document contains private and confidential health information **protected by state and federal law.**

Counsyl

RESULTS RECIPIENT
**SEATTLE SPERM BANK**
**Attn:** Dr. Jeffrey Olliffe
4915 25th Ave NE, Suite 204W
Seattle, WA 98105
**Phone:** (206) 588-1484
**Fax:** (206) 588-1484
**NPI:** 1306838271
**Report Date:** 08/22/2016

MALE
**DONOR 10070**
**DOB:** [redacted]
**Ethnicity:** South Asian
**Sample Type:** EDTA Blood
**Date of Collection:** 08/13/2016
**Date Received:** 08/15/2016
**Date Tested:** 08/22/2016
**Barcode:** 11200059666839
**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 10070** | **Partner** |
|---|---|---|
| Panel Information | Family Prep Screen 2.0<br>Universal Panel Minus X-Linked<br>**(102 conditions tested)** | N/A |
| **POSITIVE: CARRIER**<br>Muscle-Eye-Brain Disease<br>**Reproductive Risk: 1 in 2,000**<br>**Inheritance: Autosomal Recessive** | ⊞ **CARRIER***<br>NM_017739.3(POMGNT1):c.<br>1539+1G>A 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". |

*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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**POSITIVE: CARRIER**

# Muscle-Eye-Brain Disease

**Gene:** POMGNT1 | **Inheritance Pattern:** Autosomal Recessive

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

| **Patient** | **DONOR 10070** | **No partner tested** |
|---|---|---|
| **Result** | ⊞ Carrier | N/A |
| **Variant(s)** | NM_017739.3(POMGNT1):c.1539+1G>A heterozygote | N/A |
| **Methodology** | Sequencing | N/A |
| **Interpretation** | This individual is a carrier of muscle-eye-brain disease. Carriers generally do not experience symptoms. | N/A |
| **Detection rate** | > 15% | N/A |
| **Exons tested** | NM_017739:2-22. | N/A |

## What is Muscle-Eye-Brain Disease?

Muscle-eye-brain disease (MEB) is an inherited condition causing a number of symptoms including muscle weakness, vision abnormalities, brain structure abnormalities, and severe mental disability.

MEB causes congenital muscular dystrophy, a form of muscle weakness that is present from birth or develops shortly after birth. It causes an infant to feel floppy in all of his or her muscles, including those of the face. He or she may also exhibit involuntary muscle jerks or twitches.

Eye problems associated with MEB include severe near-sightedness and glaucoma, among others.

Another hallmark of MEB is a brain abnormality known as cobblestone lissencephaly (or type II lissencephaly). The brain develops a bumpy "cobblestone" appearance and lacks the normal folding structure. Other structural changes in the brain are also present. Children with MEB may have a buildup of fluid around the brain that can create a dangerous amount of pressure.

The severity of symptoms can vary among people with MEB.

## How common is Muscle-Eye-Brain Disease?

MEB is very rare, although its exact prevalence is unknown.

## How is Muscle-Eye-Brain Disease treated?

There is no successful treatment or cure for MEB. Medical specialists can help treat specific symptoms, such as using medication to control seizures, physical and occupational therapy to aid in movement, and special eye glasses to help make the most of the child's vision.

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## What is the prognosis for a person with Muscle-Eye-Brain Disease?

The prognosis for a person with MEB varies depending on the severity of the symptoms, but is generally poor. Studies have shown people with MEB typically die between the ages of 6 and 16.

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# Methods and Limitations

**DONOR 10070 [Family Prep Screen 2.0]**: sequencing, targeted genotyping, copy number analysis, and analysis of homologous regions.

## Sequencing

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

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

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

## Targeted genotyping

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

## Copy number analysis

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

## Analysis of homologous regions

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

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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**.

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**LAB DIRECTORS**

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

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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:** South Asian 88%.

**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:** South Asian > 62%.

**Alkaptonuria** - **Gene:** HGD. Autosomal Recessive. Sequencing. **Exons:** NM_000187:1-14. **Detection Rate:** Unknown due to rarity of disease.

**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 > 95%.

**Alpha-Mannosidosis** - **Gene:** MAN2B1. Autosomal Recessive. Sequencing. **Exons:** NM_000528:1-15,17-24. **Detection Rate:** Unknown due to rarity of disease.

**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:** South Asian > 10%.

**Ataxia-Telangiectasia** - **Gene:** ATM. Autosomal Recessive. Sequencing. **Exons:** NM_000051:2-63. **Detection Rate:** Unknown due to rarity of disease.

**Autosomal Recessive Polycystic Kidney Disease** - **Gene:** PKHD1. Autosomal Recessive. Sequencing. **Exons:** NM_138694:2-67. **Detection Rate:** South Asian > 10%.

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

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

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

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

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

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

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

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

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

**CLN3-related Neuronal Ceroid Lipofuscinosis** - **Gene:** CLN3. Autosomal Recessive. Sequencing. **Exons:** NM_001042432:2-16. **Detection Rate:** South Asian > 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:** Unknown due to rarity of disease.

**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:** South Asian > 54%.

**Cystinosis** - **Gene:** CTNS. Autosomal Recessive. Sequencing. **Exons:** NM_004937:3-12. **Detection Rate:** Unknown due to rarity of disease.

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

**Factor XI Deficiency** - **Gene:** F11. Autosomal Recessive. Sequencing. **Exons:** NM_000128:2-15. **Detection Rate:** South Asian > 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:** Unknown due to rarity of disease.

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

**GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness** - **Gene:** GJB2. Autosomal Recessive. Sequencing. **Exons:** NM_004004:1-2. **Detection Rate:** Unknown due to rarity of disease.

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

**Glycogen Storage Disease Type Ia** - **Gene:** G6PC. Autosomal Recessive. Sequencing. **Exons:** NM_000151:1-5. **Detection Rate:** South Asian > 30%.

**Glycogen Storage Disease Type Ib** - **Gene:** SLC37A4. Autosomal Recessive. Sequencing. **Exons:** NM_001164277:3-11. **Detection Rate:** Unknown due to rarity of disease.

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

**Glycogen Storage Disease Type V** - **Gene:** PYGM. Autosomal Recessive. Sequencing. **Exons:** NM_005609:1-20. **Detection Rate:** Unknown due to rarity of disease.

**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:** South Asian > 86%.

**Hereditary Fructose Intolerance** - **Gene:** ALDOB. Autosomal Recessive. Sequencing. **Exons:** NM_000035:2-9. **Detection Rate:** Unknown due to rarity of disease.

**Hereditary Thymine-Uraciluria** - **Gene:** DPYD. Autosomal Recessive. Sequencing. **Exons:** NM_000110:1-23. **Detection Rate:** Unknown due to rarity of disease.

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

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

**Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency** - **Gene:** CBS. Autosomal Recessive. Sequencing. **Exons:** NM_000071:3-17. **Detection Rate:** South Asian > 14%.

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**Hurler Syndrome** - **Gene:** IDUA. Autosomal Recessive. Targeted Genotyping. **Variants (2):** Q70*, W402*. **Detection Rate:** South Asian 67%.
**Hypophosphatasia, Autosomal Recessive** - **Gene:** ALPL. Autosomal Recessive. Sequencing. **Exons:** NM_000478:2-12. **Detection Rate:** Unknown due to rarity of disease.
**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:** South Asian > 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:** Unknown due to rarity of disease.
**Limb-Girdle Muscular Dystrophy Type 2D** - **Gene:** SGCA. Autosomal Recessive. Sequencing. **Exons:** NM_000023:1-9. **Detection Rate:** Unknown due to rarity of disease.
**Limb-Girdle Muscular Dystrophy Type 2E** - **Gene:** SGCB. Autosomal Recessive. Sequencing. **Exons:** NM_000232:1-6. **Detection Rate:** South Asian > 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:** Unknown due to rarity of disease.
**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:** Unknown due to rarity of disease.
**Megalencephalic Leukoencephalopathy With Subcortical Cysts** - **Gene:** MLC1. Autosomal Recessive. Sequencing. **Exons:** NM_015166:2-12. **Detection Rate:** South Asian > 13%.
**Metachromatic Leukodystrophy** - **Gene:** ARSA. Autosomal Recessive. Sequencing. **Exons:** NM_000487:1-8. **Detection Rate:** Unknown due to rarity of disease.
**Mucolipidosis IV** - **Gene:** MCOLN1. Autosomal Recessive. Sequencing. **Exons:** NM_020533:1-14. **Detection Rate:** South Asian > 10%.
**Muscle-Eye-Brain Disease** - **Gene:** POMGNT1. Autosomal Recessive. Sequencing. **Exons:** NM_017739:2-22. **Detection Rate:** South Asian > 15%.
**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:** South Asian > 15%.
**Niemann-Pick Disease, SMPD1-associated** - **Gene:** SMPD1. Autosomal Recessive. Sequencing. **Exons:** NM_000543:1-6. **Detection Rate:** Unknown due to rarity of disease.
**Nijmegen Breakage Syndrome** - **Gene:** NBN. Autosomal Recessive. Sequencing. **Exons:** NM_002485:1-16. **Detection Rate:** Unknown due to rarity of disease.
**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:** Unknown due to rarity of disease.
**PEX1-related Zellweger Syndrome Spectrum** - **Gene:** PEX1. Autosomal Recessive. Sequencing. **Exons:** NM_000466:1-24. **Detection Rate:** South Asian > 68%.
**Phenylalanine Hydroxylase Deficiency** - **Gene:** PAH. Autosomal Recessive. Sequencing. **Exons:** NM_000277:1-13. **Detection Rate:** South Asian > 43%.
**Polyglandular Autoimmune Syndrome Type 1** - **Gene:** AIRE. Autosomal Recessive. Sequencing. **Exons:** NM_000383:1-14. **Detection Rate:** South Asian > 65%.
**Pompe Disease** - **Gene:** GAA. Autosomal Recessive. Sequencing. **Exons:** NM_000152:2-20. **Detection Rate:** South Asian > 10%.
**PPT1-related Neuronal Ceroid Lipofuscinosis** - **Gene:** PPT1. Autosomal Recessive. Sequencing. **Exons:** NM_000310:1-9. **Detection Rate:** South Asian > 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:** South Asian > 42%.
**Primary Hyperoxaluria Type 2** - **Gene:** GRHPR. Autosomal Recessive. Sequencing. **Exons:** NM_012203:1-9. **Detection Rate:** Unknown due to rarity of disease.
**PROP1-related Combined Pituitary Hormone Deficiency** - **Gene:** PROP1. Autosomal Recessive. Sequencing. **Exons:** NM_006261:1-3. **Detection Rate:** South Asian > 55%.
**Pseudocholinesterase Deficiency** - **Gene:** BCHE. Autosomal Recessive. Sequencing. **Exons:** NM_000055:2-4. **Detection Rate:** South Asian > 83%.
**Pycnodysostosis** - **Gene:** CTSK. Autosomal Recessive. Sequencing. **Exons:** NM_000396:2-8. **Detection Rate:** South Asian > 10%.
**Rhizomelic Chondrodysplasia Punctata Type 1** - **Gene:** PEX7. Autosomal Recessive. Sequencing. **Exons:** NM_000288:1-10. **Detection Rate:** South Asian > 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:** South Asian > 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:** Unknown due to rarity of disease.
**Smith-Lemli-Opitz Syndrome** - **Gene:** DHCR7. Autosomal Recessive. Sequencing. **Exons:** NM_001360:3-9. **Detection Rate:** South Asian > 69%.
**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:** Unknown due to rarity of disease.
**Sulfate Transporter-Related Osteochondrodysplasia** - **Gene:** SLC26A2. Autosomal Recessive. Sequencing. **Exons:** NM_000112:2-3. **Detection Rate:** South Asian > 75%.
**TPP1-related Neuronal Ceroid Lipofuscinosis** - **Gene:** TPP1. Autosomal Recessive. Sequencing. **Exons:** NM_000391:1-13. **Detection Rate:** South Asian > 60%.
**Tyrosinemia Type I** - **Gene:** FAH. Autosomal Recessive. Sequencing. **Exons:** NM_000137:1-14. **Detection Rate:** Unknown due to rarity of disease.
**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:** South Asian > 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:** Unknown due to rarity of disease.

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| RESULTS RECIPIENT | MALE | FEMALE |
|---|---|---|
| **SEATTLE SPERM BANK** | **DONOR 10070** | N/A |
| **Attn:** Dr. Jeffrey Olliffe | **DOB:** [redacted] | |
| **NPI:** 1306838271 | **Ethnicity:** South Asian | |
| **Report Date:** 08/22/2016 | **Barcode:** 11200059666839 | |

# 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 10070 Residual Risk | Reproductive Risk |
|---|---|---|
| **21-Hydroxylase-Deficient Congenital Adrenal Hyperplasia** | 1 in 360 | 1 in 60,000 |
| **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 2,500 | < 1 in 1,000,000 |
| **Alpha-Mannosidosis** | < 1 in 350 | < 1 in 500,000 |
| **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 160 | < 1 in 100,000 |
| **Autosomal Recessive Polycystic Kidney Disease** | < 1 in 500 | < 1 in 1,000,000 |
| **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 |
| **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 160 | < 1 in 100,000 |
| **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 190 | < 1 in 66,000 |
| **Cystinosis** | < 1 in 220 | < 1 in 200,000 |
| **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 160 | < 1 in 100,000 |
| **Galactosemia** | < 1 in 500 | < 1 in 1,000,000 |
| **Gaucher Disease** | 1 in 280 | 1 in 120,000 |
| **GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness** | < 1 in 100 | < 1 in 40,000 |
| **Glutaric Acidemia Type 1** | < 1 in 110 | < 1 in 46,000 |
| **Glycogen Storage Disease Type Ia** | < 1 in 250 | < 1 in 180,000 |
| **Glycogen Storage Disease Type Ib** | < 1 in 350 | < 1 in 500,000 |
| **Glycogen Storage Disease Type III** | < 1 in 290 | < 1 in 180,000 |
| **Glycogen Storage Disease Type V** | < 1 in 160 | < 1 in 100,000 |
| **GRACILE Syndrome** | < 1 in 500 | < 1 in 1,000,000 |
| **Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease)** | < 1 in 330 | < 1 in 58,000 |
| **Hereditary Fructose Intolerance** | < 1 in 500 | < 1 in 1,000,000 |

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RESULTS RECIPIENT
**SEATTLE SPERM BANK**
**Attn:** Dr. Jeffrey Olliffe
**NPI:** 1306838271
**Report Date:** 08/22/2016

MALE
**DONOR 10070**
**DOB:** [redacted]
**Ethnicity:** South Asian
**Barcode:** 11200059666839

FEMALE
N/A

| Disease | DONOR 10070 Residual Risk | Reproductive Risk |
|---|---|---|
| **Hereditary Thymine-Uraciluria** | < 1 in 100 | < 1 in 40,000 |
| **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 160 | < 1 in 100,000 |
| **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 150 | < 1 in 89,000 |
| **Limb-Girdle Muscular Dystrophy Type 2D** | < 1 in 450 | < 1 in 800,000 |
| **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 150 | < 1 in 90,000 |
| **Maple Syrup Urine Disease Type 1B** | < 1 in 250 | < 1 in 250,000 |
| **Medium Chain Acyl-CoA Dehydrogenase Deficiency** | < 1 in 110 | < 1 in 50,000 |
| **Megalencephalic Leukoencephalopathy With Subcortical Cysts** | < 1 in 500 | < 1 in 1,000,000 |
| **Metachromatic Leukodystrophy** | < 1 in 200 | < 1 in 160,000 |
| **Mucolipidosis IV** | < 1 in 500 | < 1 in 1,000,000 |
| **Muscle-Eye-Brain Disease** | c.1539+1G>A heterozygote † | 1 in 2,000 |
| **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 250 | < 1 in 250,000 |
| **Nijmegen Breakage Syndrome** | < 1 in 160 | < 1 in 100,000 |
| **Northern Epilepsy** | < 1 in 500 | < 1 in 1,000,000 |
| **Pendred Syndrome** | < 1 in 71 | < 1 in 20,000 |
| **PEX1-related Zellweger Syndrome Spectrum** | < 1 in 1,100 | < 1 in 1,000,000 |
| **Phenylalanine Hydroxylase Deficiency** | < 1 in 88 | < 1 in 17,000 |
| **Polyglandular Autoimmune Syndrome Type 1** | < 1 in 500 | < 1 in 1,000,000 |
| **Pompe Disease** | < 1 in 170 | < 1 in 110,000 |
| **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 250 | < 1 in 250,000 |
| **Smith-Lemli-Opitz Syndrome** | < 1 in 500 | < 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 400 | < 1 in 640,000 |
| **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 170 | < 1 in 120,000 |
| **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 87 | < 1 in 30,000 |

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