

Client/Sending Facility:
Phoenix Sperm Bank

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

LCLS Specimen Number: 204-944-3232-0

Patient Name: 10065, DONOR

Date of Birth: [REDACTED]

Gender: M

Patient ID:

Lab Number: YU16-58206 L

Indications: NOT GIVEN

Account Number: [REDACTED]

Ordering Physician: J OLLIFFE

Specimen Type: BLOOD

Client Reference:

Date Collected: 07/22/2016

Date Received: 07/24/2016

Date Reported: 08/03/2016

Test: Chromosome, Blood, Routine

Cells Counted: 20

Cells Analyzed: 20

Cells Karyotyped: 2

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.

Chromosome analysis performed by LabCorp, CLIA 45D0674994. 3701 Kirby Dr. Suite 528, Houston, TX 77098. Laboratory Director, Venkateswara R Potluri PhD.

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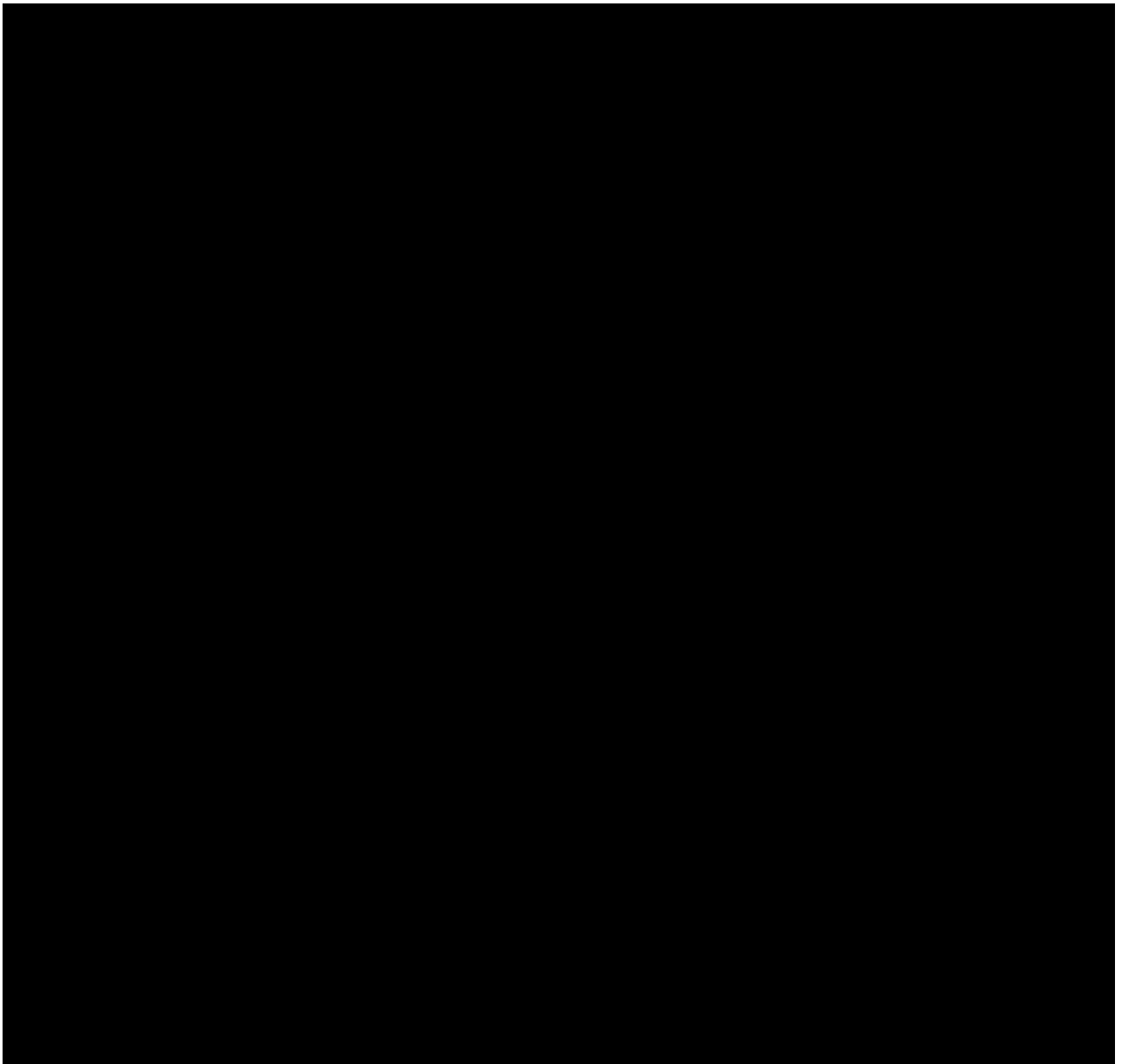
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John E. Wiley, Ph.D., FACMG.
Board Certified Cytogeneticist

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

Technical component performed by Laboratory Corporation of America Holdings,
1904 TW Alexander Drive, RTP, NC, 27709-0153 (800) 345-4363

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.**



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: 08/02/2016

MALE
DONOR 10065
DOB: [REDACTED]
Ethnicity: African or African American
Sample Type: EDTA Blood
Date of Collection: 07/22/2016
Date Received: 07/23/2016
Date Tested: 08/02/2016
Barcode: 11200059738920
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 10065	Partner
Panel Information	Family Prep Screen 2.0 Universal Panel Minus X-Linked (102 conditions tested)	N/A
POSITIVE: CARRIER Alpha Thalassemia Reproductive Risk: Not Calculated Inheritance: Autosomal Recessive	+ CARRIER* chr16:g.(?_226678)_(227520_?)del (aka -alpha3.7) heterozygote Alpha globin status: -a/aa.	Reproductive risk can be more accurately assessed after carrier screening of the partner. 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 7.

CLINICAL NOTES

- None

NEXT STEPS

- Carrier testing should be considered for the diseases specified above for the patient's partner, as both parents must be carriers before a child is at high risk of developing the disease.
- Genetic counseling is recommended and patients may wish to discuss any positive results with blood relatives, as there is an increased chance that they are also carriers.



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FEMALE
N/A

POSITIVE: CARRIER

Alpha Thalassemia

Genes: HBA1, HBA2 | Inheritance Pattern: Autosomal Recessive

Patient	DONOR 10065	No partner tested
Result	⊕ Carrier	N/A
Variant(s)	chr16:g.(?_226678)_(227520_?)del(aka -alpha3.7) heterozygote	N/A
Methodology	Analysis of homologous regions	N/A
Interpretation	This individual is a carrier of alpha thalassemia. Carriers do not experience symptoms, but may have hematologic abnormalities. -alpha3.7 is classified as an alpha+ mutation. Based on this result, the patient's alpha globin status is -a/aa (carrier), where "-" indicates a deleted or nonfunctional alpha globin gene.	N/A
Detection rate	90%	N/A
Variants tested	-(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.	N/A

REPRODUCTIVE RISK SUMMARY

Reproductive risk can be more accurately assessed after carrier screening of the partner. Genetic counseling is recommended to review results and risks in further detail.

What is Alpha Thalassemia?

Alpha thalassemia is a blood disorder that affects hemoglobin, a major component of red blood cells that carries oxygen in the body. Hemoglobin is a protein complex made up of two different chains. There are many forms of hemoglobin, but the primary type is made up of alpha chains and beta chains. Alpha thalassemia is caused by mutations involving the genes, *HBA1* and *HBA2*, that code for the alpha chains.

Most individuals have two functional pairs or four functional copies of the alpha globin genes (one copy each of *HBA1* and *HBA2* on both chromosomes).

Carriers generally have either two or three functional alpha globin genes and do not have any symptoms.



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- **Three functional alpha globin genes, silent carrier:** These individuals are typically known as silent carriers, because they do not have any symptoms or abnormalities on a complete blood count. This status results from the presence of an alpha+ mutation (mutation that eliminates the function/presence of one copy of an alpha globin gene).
- **Two functional alpha globin genes, carrier:** These carriers generally have mild anemia characterized by hypochromic (pale) and microcytic (small) red blood cells, which can be measured on a complete blood count. However, they usually do not have any symptoms of the disease (note exception below). Carrier status may result from the presence of two alpha+ mutations (eliminates function/presence of one copy of an alpha globin gene on each chromosome) or an alpha0 mutation (eliminates function/presence of both copies of the alpha globin genes on one chromosome).

Exception: There have been reports of individuals with two copies of certain types of point mutations who have a diagnosis of hemoglobin H disease with variable symptoms. One example of this is when individuals have two copies of the hemoglobin Constant Spring mutation, which is common in the Southeast Asian population.

Disease symptoms most typically occur if an individual has one or zero functional alpha globin genes.

- **One functional alpha globin gene, hemoglobin H disease:** This form of alpha thalassemia is very variable. Disease severity ranges from asymptomatic to moderate microcytic/hypochromic anemia with the possibility of jaundice (yellowing of the skin or eyes), enlarged spleen, bone deformities, fatigue, and other minor complications.
- **Zero functional alpha globin genes, hemoglobin Bart syndrome:** Individuals who have no functional copies or are missing all four copies of the associated genes almost always have this fatal form of alpha thalassemia. Hb Bart syndrome is generally associated with death *in utero* due to the buildup of excess fluid in the body and tissues (hydrops fetalis). Signs and symptoms in the newborn period can include severe anemia, hepatosplenomegaly (enlarged liver and spleen), and birth defects of the heart, urinary system, and genitalia. Most babies with this condition are stillborn or die soon after birth.

How common is Alpha Thalassemia?

The carrier frequency and incidence of alpha thalassemia vary by the type and population. Carrier frequency of this condition is reported to be the highest in individuals of Southeast Asian, African, West Indian, and Mediterranean descent. In 2010, the estimated number of worldwide annual births of patients with Hb H disease was 9,568 and with Hb Bart syndrome was 5,183. Therefore, the worldwide birth prevalence of Hb H disease and Hb Bart's hydrops is estimated at ~1/14500 and ~1/27000, respectively; however, for Hb Bart's hydrops, this is likely to be an underestimate because most at-risk couples are not currently identified.

How is Alpha Thalassemia treated?

Alpha thalassemia carrier status does not necessitate treatment. Treatment for hemoglobin H disease varies based on the severity of the symptoms. For many individuals, blood transfusions are given during crises, which are episodic and usually precipitated by environmental stressors, like oxidant medications or fever. Individuals with more severe symptoms may require regular blood transfusions, folic acid supplementation, prophylactic antibiotics, iron chelation therapy (removal of excess iron from the body), and possible hemoglobin F-enhancing agents and splenectomy.

Extremely rare cases of survivors with hemoglobin Bart syndrome have been reported when fetal blood transfusions were given, followed by regular treatments similar to those who have hemoglobin H disease. Treatments or surgical correction of potential birth defects may also be available. However, there is a high risk for intellectual and physical disability in these rare survivors. These individuals may be candidates for hematopoietic stem cell transplantation.



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N/A

What is the prognosis for a person with Alpha Thalassemia?

Because hemoglobin H disease can be variable, prognosis ultimately depends on the severity of the disease. Mild disease may be manageable with little effect on daily life. However, more severe disease will necessitate frequent and regular therapy, and may be associated with a shortened lifespan. Untreated, the prognosis is poor with a shortened lifespan of up to age 5 years. However, when treated, individuals with hemoglobin H disease have a lifespan that approaches normal.

Hemoglobin Bart syndrome is the most severe clinical condition related to alpha thalassemia, and death may occur *in utero* or in the newborn period. Of note, there may also be maternal complications during pregnancy if the fetus has hemoglobin Bart syndrome. These complications include preeclampsia (high blood pressure, fluid build-up/swelling, protein in the urine), polyhydramnios (excessive amniotic fluid) or oligohydramnios (reduced amniotic fluid), hemorrhage, and premature delivery.

Methods and Limitations

DONOR 10065 [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**.

LAB DIRECTORS

Hyunseok Kang

H. Peter Kang, MD, MS, FCAP

Rebecca Mar-Heyming

Rebecca Mar-Heyming, PhD, DABMG

Conditions Tested

21-Hydroxylase-Deficient Congenital Adrenal Hyperplasia - Gene: CYP21A2. Autosomal Recessive. Analysis of Homologous Regions. **Variants (13):** CYP21A2 deletion, CYP21A2 duplication, CYP21A2 triplication, G111VfsX21, I173N, L308FfsX6, P31L, Q319*, Q319*+CYP21A2dup, R357W, V281L, [I237N;V238E;M240K], c.293-13C>G. **Detection Rate:** African or African American 92%.

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

Achromatopsia - Gene: CNGB3. Autosomal Recessive. Sequencing. **Exons:** NM_019098:1-18. **Detection Rate:** African or African American > 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:** African or African American 90%.

Alpha-1 Antitrypsin Deficiency - Gene: SERPINA1. Autosomal Recessive. Sequencing. **Exons:** NM_000295:2-5. **Detection Rate:** African or African American > 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:** African or African American > 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:** African or African American > 10%.

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

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

Biotinidase Deficiency - Gene: BTBD. Autosomal Recessive. Sequencing. **Exons:** NM_000060:1-4. **Detection Rate:** African or African American > 45%.

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

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

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

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

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

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

CLN3-related Neuronal Ceroid Lipofuscinosis - Gene: CLN3. Autosomal Recessive. Sequencing. **Exons:** NM_001042432:2-16. **Detection Rate:** African or African American > 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:** African or African American > 78%.

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:** African or African American > 35%.

Factor XI Deficiency - Gene: F11. Autosomal Recessive. Sequencing. **Exons:** NM_000128:2-15. **Detection Rate:** African or African American > 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: MEV. 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:** African or African American > 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:** African or African American 60%.

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

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

Glycogen Storage Disease Type Ia - Gene: G6PC. Autosomal Recessive. Sequencing. **Exons:** NM_000151:1-5. **Detection Rate:** African or African American > 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:** African or African American > 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:** African or African American > 78%.

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:** African or African American > 10%.

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

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

Hurler Syndrome - Gene: IDUA. Autosomal Recessive. Targeted Genotyping. **Variants (2):** Q70*, W402*. **Detection Rate:** African or African American 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:** African or African American > 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:** African or African American > 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:** African or African American > 13%.

Metachromatic Leukodystrophy - Gene: ARSA. Autosomal Recessive. Sequencing. Exons: NM_000487:1-8. **Detection Rate:** Unknown due to rarity of disease.

Mucopolidosis IV - Gene: MCOLN1. Autosomal Recessive. Sequencing. Exons: NM_020533:1-14. **Detection Rate:** African or African American > 10%.

Muscle-Eye-Brain Disease - Gene: POMGNT1. Autosomal Recessive. Sequencing. Exons: NM_017739:2-22. **Detection Rate:** African or African American > 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:** African or African American > 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:** African or African American > 68%.

Phenylalanine Hydroxylase Deficiency - Gene: PAH. Autosomal Recessive. Sequencing. Exons: NM_000277:1-13. **Detection Rate:** African or African American > 43%.

Polyglandular Autoimmune Syndrome Type 1 - Gene: AIRE. Autosomal Recessive. Sequencing. Exons: NM_000383:1-14. **Detection Rate:** African or African American > 65%.

Pompe Disease - Gene: GAA. Autosomal Recessive. Sequencing. Exons: NM_000152:2-20. **Detection Rate:** African or African American > 55%.

PPT1-related Neuronal Ceroid Lipofuscinosis - Gene: PPT1. Autosomal Recessive. Sequencing. Exons: NM_000310:1-9. **Detection Rate:** African or African American > 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:** African or African American > 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:** African or African American > 55%.

Pseudocholinesterase Deficiency - Gene: BCHE. Autosomal Recessive. Sequencing. Exons: NM_000055:2-4. **Detection Rate:** African or African American > 83%.

Pycnodysostosis - Gene: CTSK. Autosomal Recessive. Sequencing. Exons: NM_000396:2-8. **Detection Rate:** African or African American > 10%.

Rhizomelic Chondrodysplasia Punctata Type 1 - Gene: PEX7. Autosomal Recessive. Sequencing. Exons: NM_000288:1-10. **Detection Rate:** African or African American > 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:** African or African American > 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:** African or African American > 69%.

Spinal Muscular Atrophy - Gene: SMN1. Autosomal Recessive. Copy Number Analysis. **Variant (1):** SMN1 copy number. **Detection Rate:** African or African American 71%.

Steroid-Resistant Nephrotic Syndrome - Gene: NPHS2. Autosomal Recessive. Sequencing. Exons: NM_014625:1-8. **Detection Rate:** Unknown due to rarity of disease.

Sulfate Transporter-Related Osteochondrodysplasia - Gene: SLC26A2. Autosomal Recessive. Sequencing. Exons: NM_000112:2-3. **Detection Rate:** African or African American > 75%.

TPP1-related Neuronal Ceroid Lipofuscinosis - Gene: TPP1. Autosomal Recessive. Sequencing. Exons: NM_000391:1-13. **Detection Rate:** African or African American > 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:** African or African American > 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.



RESULTS RECIPIENT
SEATTLE SPERM BANK
Attn: Dr. Jeffrey Olliffe
NPI: 1306838271
Report Date: 08/02/2016

MALE
DONOR 10065
DOB: [REDACTED]
Ethnicity: African or African
American
Barcode: 11200059738920

FEMALE
N/A

Risk Calculations

Below are the risk calculations for all conditions tested. Since negative results do not completely rule out the possibility of being a carrier, the **residual risk** represents the patient's post-test likelihood of being a carrier and the **reproductive risk** represents the likelihood the patient's future children could inherit each disease. These risks are inherent to all carrier screening tests, may vary by ethnicity, are predicated on a negative family history and are present even after a negative test result. Inaccurate reporting of ethnicity may cause errors in risk calculation. The reproductive risk presented is based on a hypothetical pairing with a partner of the same ethnic group.

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

Disease	DONOR 10065 Residual Risk	Reproductive Risk
21-Hydroxylase-Deficient Congenital Adrenal Hyperplasia	1 in 1,400	1 in 660,000
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	chr16:g.(?_226678)_(227520_?)del(aka -alpha3.7) heterozygote † Alpha globin status: -a/aa.	Not calculated
Alpha-1 Antitrypsin Deficiency	< 1 in 2,000	< 1 in 820,000
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 290	< 1 in 77,000
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 430	< 1 in 150,000
Gaucher Disease	1 in 280	1 in 120,000
GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness	< 1 in 48	< 1 in 9,000
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



RESULTS RECIPIENT
SEATTLE SPERM BANK
 Attn: Dr. Jeffrey Olliffe
 NPI: 1306838271
 Report Date: 08/02/2016

MALE
DONOR 10065
DOB: [REDACTED]
 Ethnicity: African or African
 American
 Barcode: 11200059738920

FEMALE
 N/A

Disease	DONOR 10065 Residual Risk	Reproductive Risk
Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease)	< 1 in 43	< 1 in 1,700
Hereditary Fructose Intolerance	< 1 in 500	< 1 in 1,000,000
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
Mucopolidosis 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 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 350	< 1 in 160,000
Phenylalanine Hydroxylase Deficiency	< 1 in 280	< 1 in 180,000
Polyglandular Autoimmune Syndrome Type 1	< 1 in 500	< 1 in 1,000,000
Pompe Disease	< 1 in 130	< 1 in 31,000
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: 3+ copies 1 in 4,300	< 1 in 1,000,000
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