Counsyl

RESULTS RECIPIENT
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Report Date: 09/22/2016

MALE
DONOR 4125
DOB: 01/01/1901
Ethnicity: Northern European
Sample Type: EDTA Blood
Date of Collection: 09/08/2016
Date Received: 09/09/2016
Date Tested: 09/22/2016
Barcode: 11004211590583
Indication: Egg or sperm donor

FEMALE
N/A

Family Prep Screen

POSITIVE: CARRIER

ABOUT THIS TEST

The Counsyl Family Prep Screen (version 1.0) tests known mutations to help you learn about your chance to have a child with a genetic disease.

RESULTS SUMMARY

Risk Details	DONOR 4125	Partner
Panel Information	Family Prep Screen 1.0 Universal Plus **(106 conditions tested)**	N/A
POSITIVE: CARRIER TPP1-related Neuronal Ceroid Lipofuscinosis **Reproductive Risk: 1 in 1,200** **Inheritance: Autosomal Recessive**	**CARRIER*** NM_000391.3(TPP1):c.622C>T (R208*) 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".
POSITIVE: MILD CONDITION HFE-associated Hereditary Hemochromatosis **Reproductive Risk: Not Calculated** **Inheritance: Autosomal Recessive**	**MILD CONDITION** NM_000410.3(HFE):c.187C>G(H63D) heterozygote	Reproductive risk is not assessed for mild conditions.
POSITIVE: MILD CONDITION MTHFR Deficiency **Reproductive Risk: Not Calculated** **Inheritance: Autosomal Recessive**	**MILD CONDITION** NM_005957.4(MTHFR):c.1286A>C (E429A) heterozygote	Reproductive risk is not assessed for mild conditions.

*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 10.

CLINICAL NOTES

- None

NEXT STEPS

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

POSITIVE: CARRIER

TPP1-related Neuronal Ceroid Lipofuscinosis

Reproductive risk: 1 in 1,200
Risk before testing: 1 in 350,000

Gene: TPP1 | **Inheritance Pattern:** Autosomal Recessive

Patient	DONOR 4125	No partner tested
Result	✚ Carrier	N/A
Variant(s)	NM_000391.3(TPP1):c.622C>T(R208*) heterozygote	N/A
Methodology	Targeted genotyping	N/A
Interpretation	This individual is a carrier of TPP1-related neuronal ceroid lipofuscinosis. Carriers generally do not experience symptoms. The R208* mutation is associated with the late-infantile form of this disease.	N/A
Detection rate	60%	N/A
Variants tested	G284V, IVS5-1G>C, R208*.	N/A

What is TPP1-related Neuronal Ceroid Lipofuscinosis?

TPP1-related neuronal ceroid lipofuscinosis (NCL) is an inherited disease that causes degeneration of the brain leading to a progressive loss of mental and motor skills. It can also cause blindness and typically leads to an early death. In the final stages of the disease, an affected person will be in a vegetative state.

There are several forms of NCL, largely differentiated by the gene that carries the mutation and the age at which symptoms begin. Mutations in the TPP1 gene typically result in the classic late infantile form or juvenile form of NCL.

CLASSIC LATE INFANTILE FORM (LINCL)

The symptoms of classic LINCL typically begin between the ages of 2 and 4. Seizures are often the first sign, followed by a loss of the physical and mental milestones already achieved. Dementia soon follows along with a loss of motor coordination. Children with classic LINCL become blind between the ages of 4 and 6. They are often bedridden after the age of 6 and are unable to take care of themselves. Their life expectancy ranges from 6 to 40, with many succumbing to the disease by their 20s.

JUVENILE FORM (JNCL)

The symptoms of JNCL, also called Batten disease, often begin between the ages of 4 and 10. These children rapidly lose their vision, becoming completely blind within two to four years. People with JNCL often develop periodic seizures between the ages of 5 and 18.

Between the ages of 8 and 14, mental functions typically decline. Children may have difficulty with speech and show behavioral problems. Some people with JNCL also develop psychiatric problems including disturbed thoughts, attention problems, and aggression. These problems can eventually progress to dementia.

People with JNCL also show a decline in motor function and may have difficulty controlling their own movement.

How common is TPP1-related Neuronal Ceroid Lipofuscinosis?

Approximately 1 in 25,000 people globally are affected by some form of NCL. These diseases are most common in Scandinavian countries, but occur elsewhere as well. In the United States, it is estimated that 25,000 families are affected by some form of NCL.

Worldwide, 0.46 per 100,000 infants are born with TPP1-related NCL.

Mutations that cause TPP1-related NCL are more common in Iceland, Germany, and Finland than in other nations.

How is TPP1-related Neuronal Ceroid Lipofuscinosis treated?

There is no treatment for the underlying cause of TPP1-related NCL. Treatments can only address the symptoms as they arise. Various medications can be useful for treating seizures, poor muscle tone, sleep disorders, mood disorders, excessive drooling, and digestion. In some people, a feeding tube is also helpful.

What is the prognosis for a person with TPP1-related Neuronal Ceroid Lipofuscinosis?

The prognosis for people with TPP1-related NCL is generally poor. They will become blind and have severe mental deterioration. They will enter a vegetative state in childhood and become totally dependent on others to care for them. Death can occur between the ages of 6 and 40.

POSITIVE: MILD CONDITION

HFE-associated Hereditary Hemochromatosis

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

Patient	DONOR 4125	No partner tested
Result	Mild Condition	N/A
Variant(s)	NM_000410.3(HFE):c.187C>G(H63D) heterozygote	N/A
Methodology	Targeted genotyping	N/A
Interpretation	This individual is a carrier of HFE-associated hereditary hemochromatosis. Carriers generally do not experience symptoms. H63D is only associated with clinical hemochromatosis in the presence of some other genetic variant or condition that affects iron metabolism such as the C282Y variant or liver disease.	N/A
Variants tested	C282Y, H63D.	N/A

What is HFE-associated Hereditary Hemochromatosis?

HFE-associated hereditary hemochromatosis (HFE-HHC) is a common and treatable inherited disease in which the body absorbs and stores too much iron, potentially damaging organs such as the liver, heart, and pancreas. If the disease is diagnosed and treated before symptoms develop, people with HFE-HHC typically have a normal lifespan. If the disease is untreated, however, it can lead to fatal liver and heart failure.

For reasons not well understood, the majority of people with the genetic mutations that cause HFE-HHC do not develop symptoms of the disease at any point in their lives. For these people, simple blood tests can determine whether or not the body is storing too much iron. If it is, beginning treatment early can leave a person virtually symptom-free for life.

Depending on the specific mutation(s) a person has, he or she can be more or less likely to develop the iron overload symptoms of HFE-HHC.

People who have two copies of the C282Y mutation are most likely to have dangerously elevated levels of iron in their blood. Studies have found that among those with the C282Y/C282Y combination, men are more likely to develop symptoms of iron overload than women, perhaps because women's menstrual cycles lower their iron levels on a regular basis. Do keep in mind, however, that the majority of people with two copies of the C282Y mutation do not develop any symptoms of HFE-HHC.

Those who have C282Y in combination with another HFE-HHC mutation are much less likely to develop symptoms of the disease. Only 0.5% to 2% of people with C282Y in combination with another mutation are thought to have clinical signs of the disease. People with this genetic combination who have another disease of the liver may be more likely to develop HFE-HHC symptoms.

Among people who have two copies of any other HFE-HHC mutation, including a very common mutation known as H63D, the likelihood of developing symptoms is extremely low. In the absence of another liver disease, two copies of any HFE-HHC mutation other than C282Y is unlikely to cause any health problems.

In men who have not been treated for HFE-HHC, the first symptoms of the disease typically begin between the ages of 30 to 50; for untreated women, symptoms usually begin later, after menopause.

Early symptoms often include weakness, abdominal pain, joint pain, weight loss, loss of interest in sex, chest pain, and a progressive gray or bronze pigmentation to the skin. Liver disease (either fibrosis or the more serious cirrhosis) is a common problem associated with HFE-HHC. Cirrhosis can lead to fatal liver failure and/or an increased likelihood of developing cancer of the liver.

The heart can also be affected by HFE-HHC, seen as an irregular heartbeat and/or congestive heart failure. Other problems caused by HFE-HHC can include diabetes, arthritis, impotence (in men), early menopause (in women), thyroid problems, and adrenal gland problems.

How common is HFE-associated Hereditary Hemochromatosis?

HFE-HHC mutations are extremely common, particularly among Caucasians. Roughly one-third (33%) of Caucasians are carriers of the condition, most commonly the H63D mutation. The H63D mutation is almost always associated with asymptomatic cases unless paired with the C282Y mutation. In the general population, 1 in 200 to 400 has two copies of the C282Y genetic mutation, the combination of mutations which is most likely to cause symptoms of HFE-HHC.

Please bear in mind that most people who have these genetic mutations do not develop the disease.

The disease is less common among Hispanics, African Americans, Asians, and Native Americans. Roughly 13% of Hispanics, 8.5% of Asians, and 6% of African Americans is a carrier for the mild mutation, H63D. An additional 3% of Hispanics, 2.3% of African Americans are carriers of the potentially disease-causing C282Y mutation.

How is HFE-associated Hereditary Hemochromatosis treated?

Ideally HFE-HHC is treated before the organs of the body are damaged. However, not everyone who has the mutations that cause HFE-HHC develops symptoms or requires treatment. A simple blood test of iron levels in the blood—physicians specifically look at serum ferritin concentration and transferrin-iron saturation levels—can determine whether the body is absorbing too much. When iron reaches a certain threshold, treatment is recommended. If iron levels have not reached that threshold, no treatment is necessary. Blood tests must be repeated periodically to check these iron levels.

If a person has a high level of iron, treatment involves removing a certain quantity of blood at regular intervals. This is known as phlebotomy. Typically phlebotomy is performed frequently—perhaps weekly or twice weekly—until certain iron levels are reached, and then performed less frequently—often 2 to 4 times a year—on an indefinite basis. This treatment is simple, inexpensive, and safe.

If a person is already suffering from symptoms of HFE-HHC, treatment can lessen or relieve some of the symptoms. Cirrhosis is unlikely to improve with treatment, although treatment may slow its progression. If liver disease has reached severe levels, liver transplantation may be an option. Those who have any amount of liver damage are advised to avoid alcohol.

All people with symptoms of HFE-HHC are advised to eat only moderate amounts of iron-rich foods, avoid taking iron supplements or excess vitamin C, and refrain from eating uncooked seafood, as they are highly susceptible to a particular kind of bacterial infection.

What is the prognosis for a person with HFE-associated Hereditary Hemochromatosis?

The prognosis for a person with the genetic mutations that cause HFE-HHC is generally good, as the majority of people in that situation do not develop symptoms of the disease. Most will not have dangerously elevated levels of iron in their blood, and therefore will not have any iron-overload problems.

For those that do have dangerously high iron levels in their blood, beginning treatment before symptoms appear is a critical part of ensuring a long, healthy life. Nearly all symptoms of the disease can be prevented with early and ongoing treatment. If a person with HFE-HHC is treated before he or she develops cirrhosis of the liver, he or she can expect a normal lifespan. Among people who already have cirrhosis associated with HFE-HHC, 72% will survive at least 5 more years and 62% will survive at least 10 more years. People who already have cirrhosis are at an increased risk for developing a type of liver cancer.

POSITIVE: MILD CONDITION

MTHFR Deficiency

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

Patient	DONOR 4125	No partner tested
Result	✚ Mild Condition	N/A
Variant(s)	NM_005957.4(MTHFR):c.1286A>C(E429A) heterozygote	N/A
Methodology	Targeted genotyping	N/A
Interpretation	This individual is a carrier of MTHFR deficiency. Carriers generally do not experience symptoms.	N/A
Variants tested	A222V, E429A.	N/A

What is MTHFR Deficiency?

MTHFR deficiency is a mild condition associated with a slightly higher risk of neural tube defects and pregnancy loss. Roughly 40% of Americans are carriers of MTHFR deficiency, while 10% have the condition. For the vast majority, it causes no problems with their health or the health of their children. The mild MTHFR deficiency for which Counsyl tests should not be confused with severe MTHFR deficiency.

The MTHFR enzyme is involved in the conversion of the amino acid homocysteine to another amino acid, methionine. People with mild MTHFR deficiency have a decreased ability to perform this conversion, and as a result they have higher levels of homocysteine in their body and lower levels of the vitamin folate.

There are two common mutations found in the MTHFR gene, A222V and E429A (also known as C677T and A1298C respectively). Having one copy of either mutation (being a carrier) is not thought to have any impact on one's health or that of one's children.

The following gene combinations may be significant. Note that they are only significant if they raise the level of homocysteine in the blood, and this does not happen in everyone:

A222V/A222V

For women, two copies of the A222V mutation has been associated with a 2 to 3-fold higher risk of having a child with severe neural tube defects such as spina bifida. This type of birth defect normally affects 1 in 1,000 births, so women with two A222V mutations would face a 2 to 3 in 1,000 risk, which is still low.

Taking folate supplements has been shown to reduce neural tube defects by 75% and may be doing so by normalizing levels of homocysteine in the body.

Some studies have shown that mild MTHFR deficiency may be beneficial in lowering the risks for colorectal cancer or boosting immunity to certain pathogens. These findings are tentative, however.

A222V/E429A

This mutation pairing is thought to share the same risks as described above for the A222V/A222V mutation pairing.

E429A/E429A

This mutation pairing is NOT associated with any elevated risks for health problems.

How common is MTHFR Deficiency?

Mild MTHFR deficiency is very common. The table below shows the results of numerous studies conducted worldwide looking at the A222V mutation. The first number represents the percentage of the population who is a carrier and the second number represents the percentage of the population thought to be affected.

Ethnic Group	Carrier Rate	Affected Rate
Hispanic American	48%	15%
Caucasian American	45%	12%
Japanese	45%	12%
German	37%	6%
Asian	29%	3%
African American	24%	2%
Sub-Saharan African	12%	1%

The E429A mutation is less well-studied, but is also thought to be quite common. In three studies, the A222V/E429A mutation pairing was found in 17% of Americans, 15% of Canadians, and 20% of Dutch people.

How is MTHFR Deficiency treated?

Most people with mild MTHFR deficiency require no treatment. Because food in the United States is often fortified with vitamins, most people eat sufficient amounts of folate to compensate for higher levels of homocysteine.

Pregnant women with the condition—and all pregnant women—are advised to take folate supplements (folic acid) before and during pregnancy to reduce the risk of birth defects by as much as 75 to 85%. These vitamins are particularly important for women with MTHFR deficiency.

What is the prognosis for a person with MTHFR Deficiency?

Based on current scientific knowledge, most people with MTHFR deficiency will be totally unaffected by it. Women face a slightly elevated risk of having a child with neural tube defects, however the risk is still low.

Methods and Limitations

DONOR 4125 [Family Prep Screen 1.0]: targeted genotyping and copy number analysis.

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.

Limitations

In an unknown number of cases, nearby genetic variants may interfere with mutation detection. Other possible sources of diagnostic error include sample mix-up, trace contamination, bone marrow transplantation, blood transfusions and technical errors. If more than one variant is detected in a gene, additional studies may be necessary to determine if those variants lie on the same chromosome or different chromosomes. The Family Prep Screen does not fully address all inherited forms of intellectual disability, birth defects and genetic disease. A family history of any of these conditions may warrant additional evaluation. Furthermore, not all mutations will be identified in the genes analyzed and additional testing may be beneficial for some patients. For example, individuals of African, Southeast Asian, and Mediterranean ancestry are at increased risk for being carriers for hemoglobinopathies, which can be identified by CBC and hemoglobin electrophoresis or HPLC (*ACOG Practice Bulletin No. 78. Obstet.Gynecol. 2007;109:229-37*), and additional Tay-Sachs disease testing can be performed using a biochemical assay (*Gross et al. Genet. Med. 2008:10(1):54-56*).

This test was developed and its performance characteristics determined by Counsyl, Inc. It has not been cleared or approved by the US Food and Drug Administration (FDA). The FDA does not require this test to go through premarket review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high-complexity clinical testing. These results are adjunctive to the ordering physician's evaluation. CLIA Number: **#05D1102604**.

LAB DIRECTORS

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Conditions Tested

ABCC8-related Hyperinsulinism - **Gene:** ABCC8. Autosomal Recessive. Targeted Genotyping. **Variants (3):** 3992-9G>A, F1388del, V187D. **Detection Rate:** Unknown due to rarity of disease.
Achromatopsia - **Gene:** CNGB3. Autosomal Recessive. Targeted Genotyping. **Variants (3):** R274Vfs*13, R403Q, T383Ifs*13. **Detection Rate:** Northern European 62%.
Alkaptonuria - **Gene:** HGD. Autosomal Recessive. Targeted Genotyping. **Variants (11):** D153GfsX26, G161R, G270R, H371Pfs*4, M368V, P230S, S47L, S59Afs*52, V300G, c.16-1G>A, c.342+1G>A. **Detection Rate:** Northern European 80%.
Alpha-1 Antitrypsin Deficiency - **Gene:** SERPINA1. Autosomal Recessive. Targeted Genotyping. **Variant (1):** Z allele. **Detection Rate:** Northern European 95%.
Alpha-Mannosidosis - **Gene:** MAN2B1. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R750W. **Detection Rate:** Northern European 32%.
Andermann Syndrome - **Gene:** SLC12A6. Autosomal Recessive. Targeted Genotyping. **Variants (2):** R1011*, T813fs*813. **Detection Rate:** Unknown due to rarity of disease.
ARSACS - **Gene:** SACS. Autosomal Recessive. Targeted Genotyping. **Variants (2):** 6594delT, I2949Ffs*4, R2355*. **Detection Rate:** Unknown due to rarity of disease.
Aspartylglycosaminuria - **Gene:** AGA. Autosomal Recessive. Targeted Genotyping. **Variant (1):** AGU(Fin). **Detection Rate:** Unknown due to rarity of disease.
Ataxia With Vitamin E Deficiency - **Gene:** TTPA. Autosomal Recessive. Targeted Genotyping. **Variant (1):** E249Nfs*15. **Detection Rate:** Northern European <10%.
Ataxia-Telangiectasia - **Gene:** ATM. Autosomal Recessive. Targeted Genotyping. **Variants (8):** 5762ins137, 5762-1050A>G, E1978*, H1082Lfs*14, Q1970*, R2506Tfs*3, R35*, c.3576G>A, c.7638_7646del9. **Detection Rate:** Northern European 65%.
Autosomal Recessive Polycystic Kidney Disease - **Gene:** PKHD1. Autosomal Recessive. Targeted Genotyping. **Variants (4):** L1966Tfs*4, R496*, T36M, V3471G. **Detection Rate:** Northern European 18%.
Bardet-Biedl Syndrome, BBS1-related - **Gene:** BBS1. Autosomal Recessive. Targeted Genotyping. **Variant (1):** M390R. **Detection Rate:** Northern European 79%.
Bardet-Biedl Syndrome, BBS10-related - **Gene:** BBS10. Autosomal Recessive. Targeted Genotyping. **Variant (1):** C91Lfs*5. **Detection Rate:** Northern European 46%.
Biotinidase Deficiency - **Gene:** BTD. Autosomal Recessive. Targeted Genotyping. **Variants (4):** C33Ffs*36, D252G, Q456H, R538C. **Detection Rate:** Northern European 45%.
Bloom Syndrome - **Gene:** BLM. Autosomal Recessive. Targeted Genotyping. **Variant (1):** Y736Lfs*5. **Detection Rate:** Northern European <10%.
Canavan Disease - **Gene:** ASPA. Autosomal Recessive. Targeted Genotyping. **Variants (4):** A305E, E285A, IVS2-2A>G, Y231*. **Detection Rate:** Northern European 53%.
Carnitine Palmitoyltransferase IA Deficiency - **Gene:** CPT1A. Autosomal Recessive. Targeted Genotyping. **Variant (1):** G710E. **Detection Rate:** Northern European <10%.
Carnitine Palmitoyltransferase II Deficiency - **Gene:** CPT2. Autosomal Recessive. Targeted Genotyping. **Variants (3):** K414Tfs*7, R124*, S113L. **Detection Rate:** Northern European 80%.
Cartilage-Hair Hypoplasia - **Gene:** RMRP. Autosomal Recessive. Targeted Genotyping. **Variant (1):** c.71A>G. **Detection Rate:** Northern European 48%.
Choroideremia - **Gene:** CHM. X-linked Recessive. Targeted Genotyping. **Variant (1):** IVS13+2dupT. **Detection Rate:** Unknown due to rarity of disease.
Citrullinemia Type 1 - **Gene:** ASS1. Autosomal Recessive. Targeted Genotyping. **Variants (2):** G390R, c.421-2A>G. **Detection Rate:** Northern European 20%.
CLN3-related Neuronal Ceroid Lipofuscinosis - **Gene:** CLN3. Autosomal Recessive. Targeted Genotyping. **Variant (1):** 461_677del. **Detection Rate:** Northern European 96%.
CLN5-related Neuronal Ceroid Lipofuscinosis - **Gene:** CLN5. Autosomal Recessive. Targeted Genotyping. **Variant (1):** Y392*. **Detection Rate:** Unknown due to rarity of disease.
Cohen Syndrome - **Gene:** VPS13B. Autosomal Recessive. Targeted Genotyping. **Variant (1):** p.C1117Ffs*8. **Detection Rate:** Unknown due to rarity of disease.
Congenital Disorder of Glycosylation Type Ia - **Gene:** PMM2. Autosomal Recessive. Targeted Genotyping. **Variants (4):** F119L, P113L, R141H, V231M. **Detection Rate:** Northern European 72%.
Congenital Disorder of Glycosylation Type Ib - **Gene:** MPI. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R295H. **Detection Rate:** Unknown due to rarity of disease.
Congenital Finnish Nephrosis - **Gene:** NPHS1. Autosomal Recessive. Targeted Genotyping. **Variants (2):** Fin minor, L41Dfs*50, Fin major. **Detection Rate:** Unknown due to rarity of disease.
Costeff Optic Atrophy Syndrome - **Gene:** OPA3. Autosomal Recessive. Targeted Genotyping. **Variant (1):** c.143-1G>C. **Detection Rate:** Unknown due to rarity of disease.
Cystic Fibrosis - **Gene:** CFTR. Autosomal Recessive. Targeted Genotyping. **Variants (99):** 1078delT, 1288insTA, 1677delTA, 1717-1G>A, 1777A>C, 1812-1G>A, 1898+1G>A, 1898+1G>T, 1898+5G>T, 2043delG, 2055del9->A, 2108delA, 2143delT, 2183AA>G, 2184delA, 2184insA, 2307insA, 2789+5G>A, 2869insG, 296+12T>C, 3120+1G>A, 3120G>A, 3171delC, 3199del6, 3272-26A>G, 3659delC, 3667del4, 3791delC, 3849+10kbC>T, 3849+4A>G, 3876delA, 3905insT, 394delTT, 405+1 G>A, 405+3A>C, 406-1G>A, 444delA, 457TAT>G, 574delA, 621+1G>T, 663delT, 711+1G>T, 711+5G>A, 712-1G>T, 935delA, 936delTA, A455E, A559T, C524*, D1152H, E60*, E92*, F508del, G178R, G330*, G480C, G542*, G551D, G622D, G85E, I507del, K710*, L206W, M1101K, M607_Q643del, N1303K, P574H, Q1238*, Q493*, Q552*, Q890*, R1066C, R1158*, R1162*, R117C, R117H, R334W, R347H, R347P, R352Q, R553*, R560T, R709*, R75*, R764*, S1196*, S1251N, S1255*, S364P, S549N, S549R, T338I, V520F, W1089*, W1204*, W1282*, Y1092X, Y122*, c.1075_1079del5ins5. IVS8-5T allele analysis is only reported in the presence of the R117H mutation. **Detection Rate:** Northern European 91%.
Cystinosis - **Gene:** CTNS. Autosomal Recessive. Targeted Genotyping. **Variants (4):** 57 kb deletion, I67_P73del, L158P, W138*. **Detection Rate:** Northern European 67%.
D-Bifunctional Protein Deficiency - **Gene:** HSD17B4. Autosomal Recessive. Targeted Genotyping. **Variants (2):** G16S, N457Y. **Detection Rate:** Northern European 35%.
Factor V Leiden Thrombophilia - **Gene:** F5. Autosomal Recessive. Targeted Genotyping. **Variant (1):** c.1601G>A. **Detection Rate:** Unknown due to rarity of disease.
Factor XI Deficiency - **Gene:** F11. Autosomal Recessive. Targeted Genotyping. **Variants (4):** E117*, F283L, IVS14+1G>A, IVS14del14. **Detection Rate:** Northern European <10%.
Familial Dysautonomia - **Gene:** IKBKAP. Autosomal Recessive. Targeted Genotyping. **Variants (2):** R696P, c.2204+6T>C. **Detection Rate:** Unknown due to rarity of disease.
Familial Mediterranean Fever - **Gene:** MEFV. Autosomal Recessive. Targeted Genotyping. **Variants (4):** M680I, M694I, MED, V726A. **Detection Rate:** Unknown due to rarity of disease.
Fanconi Anemia Type C - **Gene:** FANCC. Autosomal Recessive. Targeted Genotyping. **Variants (3):** R548*, c.456+4A>T, c.67delG. **Detection Rate:** Northern European 54%.
Galactosemia - **Gene:** GALT. Autosomal Recessive. Targeted Genotyping. **Variants (8):** F171S, IVS2-2A>G, K285N, L195P, Q188R, S135L, T138M, Y209C. **Detection Rate:** Northern European 80%.
Gaucher Disease - **Gene:** GBA. Autosomal Recessive. Targeted Genotyping. **Variants (10):** D409V, D448H, IVS2+1G>A, L444P, N370S, R463C, R463H, R496H, V394L, p.L29Afs*18. **Detection Rate:** Northern European 60%.
GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness - **Gene:** GJB2. Autosomal Recessive. Targeted Genotyping. **Variants (7):** L79Cfs*3, L90P, W24*, W77R, c.358_360delGAG, p.G12Vfs*2, p.L56Rfs*26. **Detection Rate:** Northern European 79%.
Glucose-6-Phosphate Dehydrogenase Deficiency - **Gene:** G6PD. X-linked Recessive. Targeted Genotyping. **Variants (7):** A335T, Mahidol, R459L, R459P, S188F, V291M, V68M. **Detection Rate:** Unknown due to rarity of disease.
Glutaric Acidemia Type 1 - **Gene:** GCDH. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R402W. **Detection Rate:** Northern European 40%.
Glycogen Storage Disease Type Ia - **Gene:** G6PC. Autosomal Recessive. Targeted Genotyping. **Variants (7):** G188R, Q242*, Q347*, R83C, R83H, p.Q27Rfs*9, p.Y128Tfs*3. **Detection Rate:** Northern European 61%.

Glycogen Storage Disease Type Ib - **Gene:** SLC37A4. Autosomal Recessive. Targeted Genotyping. **Variants (2):** 1211delCT, G339C. **Detection Rate:** Northern European 46%.
Glycogen Storage Disease Type III - **Gene:** AGL. Autosomal Recessive. Targeted Genotyping. **Variants (3):** Q6*, Q6Hfs*20, S1486Pfs*18. **Detection Rate:** Northern European 45%.
Glycogen Storage Disease Type V - **Gene:** PYGM. Autosomal Recessive. Targeted Genotyping. **Variants (4):** G205S, R50*, V239del, W798R. **Detection Rate:** Northern European 80%.
GRACILE Syndrome - **Gene:** BCS1L. Autosomal Recessive. Targeted Genotyping. **Variant (1):** S78G. **Detection Rate:** Unknown due to rarity of disease.
Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease) - **Gene:** HBB. Autosomal Recessive. Targeted Genotyping. **Variants (28):** -28A>G, -29A>G, -87C>G, -88C>T, G25=, Hb C, Hb D-Punjab, Hb E, Hb O-Arab, Hb S, IVS-I-1, IVS-I-5, IVS-I-6T>C, IVS2-745C>G, K18Rfs*2, K9Vfs*14, Q40*, S10Vfs*14, W16*, c.315+1G>A, c.316-197C>T, c.316-2A>C, c.316-2A>G, c.93-21G>A, p.E7Gfs*13, p.F42Lfs*19, p.K18*, p.S73Kfs*2. **Detection Rate:** Northern European 83%.
Hereditary Fructose Intolerance - **Gene:** ALDOB. Autosomal Recessive. Targeted Genotyping. **Variants (3):** A150P, A175D, N335K. **Detection Rate:** Northern European 75%.
Hereditary Thymine-Uraciluria - **Gene:** DPYD. Autosomal Recessive. Targeted Genotyping. **Variant (1):** IVS14+1G>A. **Detection Rate:** Northern European 52%.
Herlitz Junctional Epidermolysis Bullosa, LAMA3-related - **Gene:** LAMA3. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R661*. **Detection Rate:** Northern European <10%.
Herlitz Junctional Epidermolysis Bullosa, LAMB3-related - **Gene:** LAMB3. Autosomal Recessive. Targeted Genotyping. **Variants (3):** Q243*, R42*, R635*. **Detection Rate:** Northern European 48%.
Herlitz Junctional Epidermolysis Bullosa, LAMC2-related - **Gene:** LAMC2. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R95*. **Detection Rate:** Unknown due to rarity of disease.
Hexosaminidase A Deficiency (Including Tay-Sachs Disease) - **Gene:** HEXA. Autosomal Recessive. Targeted Genotyping. **Variants (9):** 7.6kb del, G250D, G269S, IVS7+1G>A, IVS9+1G>A, R170W, R178H, Y427Ifs*5, c.1421+1G>C. **Detection Rate:** Northern European 23%.
HFE-associated Hereditary Hemochromatosis - **Gene:** HFE. Autosomal Recessive. Targeted Genotyping. **Variants (2):** C282Y, H63D. **Detection Rate:** Unknown due to rarity of disease.
Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency - **Gene:** CBS. Autosomal Recessive. Targeted Genotyping. **Variant (1):** G307S. **Detection Rate:** Northern European 14%.
Hurler Syndrome - **Gene:** IDUA. Autosomal Recessive. Targeted Genotyping. **Variants (2):** Q70*, W402*. **Detection Rate:** Northern European 67%.
Hypophosphatasia, Autosomal Recessive - **Gene:** ALPL. Autosomal Recessive. Targeted Genotyping. **Variants (4):** D361V, E174K, F310L, L520Rfs*86. **Detection Rate:** Northern European 30%.
Inclusion Body Myopathy 2 - **Gene:** GNE. Autosomal Recessive. Targeted Genotyping. **Variants (2):** M712T, V572L. **Detection Rate:** Unknown due to rarity of disease.
Isovaleric Acidemia - **Gene:** IVD. Autosomal Recessive. Targeted Genotyping. **Variant (1):** A311V. **Detection Rate:** Northern European 47%.
Joubert Syndrome 2 - **Gene:** TMEM216. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R73L. **Detection Rate:** Unknown due to rarity of disease.
Krabbe Disease - **Gene:** GALC. Autosomal Recessive. Targeted Genotyping. **Variants (2):** Ex11-17del, T513M. **Detection Rate:** Northern European 58%.
Limb-Girdle Muscular Dystrophy Type 2D - **Gene:** SGCA. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R77C. **Detection Rate:** Northern European 32%.
Limb-Girdle Muscular Dystrophy Type 2E - **Gene:** SGCB. Autosomal Recessive. Targeted Genotyping. **Variant (1):** S114F. **Detection Rate:** Northern European 12%.
Lipoamide Dehydrogenase Deficiency - **Gene:** DLD. Autosomal Recessive. Targeted Genotyping. **Variants (2):** G194C, Y35*. **Detection Rate:** Unknown due to rarity of disease.
Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency - **Gene:** HADHA. Autosomal Recessive. Targeted Genotyping. **Variant (1):** E474Q. **Detection Rate:** Northern European 87%.
Maple Syrup Urine Disease Type 1B - **Gene:** BCKDHB. Autosomal Recessive. Targeted Genotyping. **Variants (3):** E372*, G278S, R183P. **Detection Rate:** Unknown due to rarity of disease.
Medium Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADM. Autosomal Recessive. Targeted Genotyping. **Variants (2):** K304E, Y42H. **Detection Rate:** Northern European 78%.
Megalencephalic Leukoencephalopathy With Subcortical Cysts - **Gene:** MLC1. Autosomal Recessive. Targeted Genotyping. **Variants (4):** C46Lfs*34, G59E, IVS2-10T>A, S93L. **Detection Rate:** Northern European 13%.
Metachromatic Leukodystrophy - **Gene:** ARSA. Autosomal Recessive. Targeted Genotyping. **Variants (5):** I181S, IVS2+1G>A, P428L, T411I, c.1210+1G>A. **Detection Rate:** Northern European 53%.
MTHFR Deficiency - **Gene:** MTHFR. Autosomal Recessive. Targeted Genotyping. **Variants (2):** A222V, E429A. **Detection Rate:** Unknown due to rarity of disease.
Mucolipidosis IV - **Gene:** MCOLN1. Autosomal Recessive. Targeted Genotyping. **Variants (2):** 511_6944del, IVS3-2A>G. **Detection Rate:** Northern European <10%.
Muscle-Eye-Brain Disease - **Gene:** POMGNT1. Autosomal Recessive. Targeted Genotyping. **Variant (1):** c.1539+1G>A. **Detection Rate:** Northern European 75%.
NEB-related Nemaline Myopathy - **Gene:** NEB. Autosomal Recessive. Targeted Genotyping. **Variant (1):** c.(?_7431+1917)_(7536+373_?)del. **Detection Rate:** Unknown due to rarity of disease.
Niemann-Pick Disease Type C - **Gene:** NPC1. Autosomal Recessive. Targeted Genotyping. **Variant (1):** I1061T. **Detection Rate:** Northern European 17%.
Niemann-Pick Disease, SMPD1-associated - **Gene:** SMPD1. Autosomal Recessive. Targeted Genotyping. **Variants (4):** L302P, R496L, c.1829_1831delGCC, fsP330. **Detection Rate:** Northern European 38%.
Nijmegen Breakage Syndrome - **Gene:** NBN. Autosomal Recessive. Targeted Genotyping. **Variant (1):** K219Nfs*16. **Detection Rate:** Northern European 78%.
Northern Epilepsy - **Gene:** CLN8. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R24G. **Detection Rate:** Unknown due to rarity of disease.
Pendred Syndrome - **Gene:** SLC26A4. Autosomal Recessive. Targeted Genotyping. **Variants (5):** E384G, H723R, L236P, T416P, c.1001+1G>A. **Detection Rate:** Northern European 69%.
PEX1-related Zellweger Syndrome Spectrum - **Gene:** PEX1. Autosomal Recessive. Targeted Genotyping. **Variants (2):** G843D, I700Yfs*42. **Detection Rate:** Northern European 68%.
Phenylalanine Hydroxylase Deficiency - **Gene:** PAH. Autosomal Recessive. Targeted Genotyping. **Variants (13):** E280K, G272*, I65T, L48S, P281L, R158Q, R261Q, R408Q, R408W, S349P, Y414C, c.1066-11G>A, c.1315+1G>A. **Detection Rate:** Northern European 43%.
Polyglandular Autoimmune Syndrome Type 1 - **Gene:** AIRE. Autosomal Recessive. Targeted Genotyping. **Variants (2):** R257*, Y85C. **Detection Rate:** Northern European 65%.
Pompe Disease - **Gene:** GAA. Autosomal Recessive. Targeted Genotyping. **Variants (4):** D645E, E176Rfs*45, IVS1-13T>G, R854*. **Detection Rate:** Northern European 67%.
PPT1-related Neuronal Ceroid Lipofuscinosis - **Gene:** PPT1. Autosomal Recessive. Targeted Genotyping. **Variants (3):** R122W, R151*, T75P. **Detection Rate:** Northern European 53%.
Primary Carnitine Deficiency - **Gene:** SLC22A5. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R254*. **Detection Rate:** Unknown due to rarity of disease.
Primary Hyperoxaluria Type 1 - **Gene:** AGXT. Autosomal Recessive. Targeted Genotyping. **Variants (2):** G170R, I244T. **Detection Rate:** Northern European 42%.
Primary Hyperoxaluria Type 2 - **Gene:** GRHPR. Autosomal Recessive. Targeted Genotyping. **Variants (2):** D35Tfs*11, c.404+3_404+6delAAGT. **Detection Rate:** Northern European 37%.
PROP1-related Combined Pituitary Hormone Deficiency - **Gene:** PROP1. Autosomal Recessive. Targeted Genotyping. **Variant (1):** L102Cfs*8. **Detection Rate:** Northern European 55%.
Prothrombin Thrombophilia - **Gene:** F2. Autosomal Recessive. Targeted Genotyping. **Variant (1):** G20210A. **Detection Rate:** Unknown due to rarity of disease.
Pseudocholinesterase Deficiency - **Gene:** BCHE. Autosomal Recessive. Targeted Genotyping. **Variant (1):** D70G. **Detection Rate:** Northern European 83%.
Pycnodysostosis - **Gene:** CTSK. Autosomal Recessive. Targeted Genotyping. **Variant (1):** *330Wext*19. **Detection Rate:** Northern European <10%.
Rhizomelic Chondrodysplasia Punctata Type 1 - **Gene:** PEX7. Autosomal Recessive. Targeted Genotyping. **Variants (4):** A218V, G217R, IVS9+1G>C, L292*. **Detection Rate:** Northern European 70%.
Salla Disease - **Gene:** SLC17A5. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R39C. **Detection Rate:** Unknown due to rarity of disease.
Segawa Syndrome - **Gene:** TH. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R233H. **Detection Rate:** Northern European <10%.

Short Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADS. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R107C. **Detection Rate:** Unknown due to rarity of disease.
Sjogren-Larsson Syndrome - **Gene:** ALDH3A2. Autosomal Recessive. Targeted Genotyping. **Variant (1):** P315S. **Detection Rate:** Northern European 24%.
Smith-Lemli-Opitz Syndrome - **Gene:** DHCR7. Autosomal Recessive. Targeted Genotyping. **Variants (13):** E448K, F302L, G410S, IVS8-1G>C, R242C, R242H, R352Q, R352W, R404C, S169L, T93M, V326L, W151*. **Detection Rate:** Northern European 69%.
Spinal Muscular Atrophy - **Gene:** SMN1. Autosomal Recessive. Copy Number Analysis. **Variant (1):** SMN1 copy number. **Detection Rate:** Northern European 95%.
Steroid-Resistant Nephrotic Syndrome - **Gene:** NPHS2. Autosomal Recessive. Targeted Genotyping. **Variants (2):** R138*, R138Q. **Detection Rate:** Northern European 33%.
Sulfate Transporter-Related Osteochondrodysplasia - **Gene:** SLC26A2. Autosomal Recessive. Targeted Genotyping. **Variants (4):** C653S, IVS1+2T>C, R178*, R279W. **Detection Rate:** Northern European 75%.
TPP1-related Neuronal Ceroid Lipofuscinosis - **Gene:** TPP1. Autosomal Recessive. Targeted Genotyping. **Variants (3):** G284V, IVS5-1G>C, R208*. **Detection Rate:** Northern European 60%.
Tyrosinemia Type I - **Gene:** FAH. Autosomal Recessive. Targeted Genotyping. **Variants (6):** E357*, IVS6-1G>T, P261L, Q64H, W262*, c.1062+5G>A. **Detection Rate:** Northern European 50%.
Usher Syndrome Type 1F - **Gene:** PCDH15. Autosomal Recessive. Targeted Genotyping. **Variant (1):** R245*. **Detection Rate:** Unknown due to rarity of disease.
Usher Syndrome Type 3 - **Gene:** CLRN1. Autosomal Recessive. Targeted Genotyping. **Variant (1):** N48K. **Detection Rate:** Unknown due to rarity of disease.
Very Long Chain Acyl-CoA Dehydrogenase Deficiency - **Gene:** ACADVL. Autosomal Recessive. Targeted Genotyping. **Variant (1):** V243A. **Detection Rate:** Northern European 20%.
Wilson Disease - **Gene:** ATP7B. Autosomal Recessive. Targeted Genotyping. **Variants (2):** H1069Q, R778L. **Detection Rate:** Northern European 40%.
X-Linked Juvenile Retinoschisis - **Gene:** RS1. X-linked Recessive. Targeted Genotyping. **Variants (3):** E72K, G109R, G74V. **Detection Rate:** Northern European 20%.

Risk Calculations

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

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

Disease	DONOR 4125 Residual Risk	Reproductive Risk
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-1 Antitrypsin Deficiency	1 in 680	1 in 93,000
Alpha-Mannosidosis	1 in 520	1 in 730,000
Andermann Syndrome	< 1 in 500	< 1 in 1,000,000
ARSACS	< 1 in 500	< 1 in 1,000,000
Aspartylglycosaminuria	< 1 in 500	< 1 in 1,000,000
Ataxia With Vitamin E Deficiency	< 1 in 500	< 1 in 1,000,000
Ataxia-Telangiectasia	1 in 450	1 in 290,000
Autosomal Recessive Polycystic Kidney Disease	1 in 75	1 in 18,000
Bardet-Biedl Syndrome, BBS1-related	1 in 750	1 in 480,000
Bardet-Biedl Syndrome, BBS10-related	1 in 290	1 in 180,000
Biotinidase Deficiency	1 in 220	1 in 110,000
Bloom Syndrome	< 1 in 500	< 1 in 1,000,000
Canavan Disease	< 1 in 500	< 1 in 1,000,000
Carnitine Palmitoyltransferase IA Deficiency	< 1 in 500	< 1 in 1,000,000
Carnitine Palmitoyltransferase II Deficiency	< 1 in 500	< 1 in 1,000,000
Cartilage-Hair Hypoplasia	< 1 in 500	< 1 in 1,000,000
Choroideremia	< 1 in 500	1 in 100,000
Citrullinemia Type 1	1 in 150	1 in 70,000
CLN3-related Neuronal Ceroid Lipofuscinosis	1 in 5,600	< 1 in 1,000,000
CLN5-related Neuronal Ceroid Lipofuscinosis	< 1 in 500	< 1 in 1,000,000
Cohen Syndrome	< 1 in 500	< 1 in 1,000,000
Congenital Disorder of Glycosylation Type Ia	1 in 560	1 in 360,000
Congenital Disorder of Glycosylation Type Ib	< 1 in 500	< 1 in 1,000,000
Congenital Finnish Nephrosis	< 1 in 500	< 1 in 1,000,000
Costeff Optic Atrophy Syndrome	< 1 in 500	< 1 in 1,000,000
Cystic Fibrosis	1 in 300	1 in 33,000
Cystinosis	1 in 670	1 in 600,000
D-Bifunctional Protein Deficiency	< 1 in 500	< 1 in 1,000,000
Factor V Leiden Thrombophilia (Mild Condition)	Not calculated	Not calculated
Factor XI Deficiency	< 1 in 500	< 1 in 1,000,000
Familial Dysautonomia	< 1 in 500	< 1 in 1,000,000
Familial Mediterranean Fever	< 1 in 500	< 1 in 1,000,000
Fanconi Anemia Type C	1 in 340	1 in 220,000
Galactosemia	1 in 430	1 in 150,000
Gaucher Disease	1 in 280	1 in 120,000
GJB2-related DFNB1 Nonsyndromic Hearing Loss and Deafness	1 in 160	1 in 20,000
Glucose-6-Phosphate Dehydrogenase Deficiency (Mild Condition)	Not calculated	Not calculated
Glutaric Acidemia Type 1	1 in 170	1 in 67,000
Glycogen Storage Disease Type Ia	1 in 450	1 in 320,000
Glycogen Storage Disease Type Ib	1 in 660	1 in 930,000
Glycogen Storage Disease Type III	1 in 290	1 in 180,000
Glycogen Storage Disease Type V	1 in 790	1 in 500,000
GRACILE Syndrome	< 1 in 500	< 1 in 1,000,000
Hb Beta Chain-Related Hemoglobinopathy (Including Beta Thalassemia and Sickle Cell Disease)	1 in 290	1 in 58,000

Disease	DONOR 4125 Residual Risk	Reproductive Risk
Hereditary Fructose Intolerance	1 in 320	1 in 100,000
Hereditary Thymine-Uraciluria	1 in 210	1 in 83,000
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
HFE-associated Hereditary Hemochromatosis (Mild Condition)	H63D heterozygote †	Not calculated
Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency	1 in 290	1 in 290,000
Hurler Syndrome	1 in 480	1 in 300,000
Hypophosphatasia, Autosomal Recessive	1 in 230	1 in 140,000
Inclusion Body Myopathy 2	< 1 in 500	< 1 in 1,000,000
Isovaleric Acidemia	1 in 470	1 in 470,000
Joubert Syndrome 2	< 1 in 500	< 1 in 1,000,000
Krabbe Disease	1 in 360	1 in 210,000
Limb-Girdle Muscular Dystrophy Type 2D	1 in 660	< 1 in 1,000,000
Limb-Girdle Muscular Dystrophy Type 2E	< 1 in 500	< 1 in 1,000,000
Lipoamide Dehydrogenase Deficiency	< 1 in 500	< 1 in 1,000,000
Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	1 in 1,200	1 in 690,000
Maple Syrup Urine Disease Type 1B	1 in 250	1 in 250,000
Medium Chain Acyl-CoA Dehydrogenase Deficiency	1 in 270	1 in 63,000
Megalencephalic Leukoencephalopathy With Subcortical Cysts	< 1 in 500	< 1 in 1,000,000
Metachromatic Leukodystrophy	1 in 430	1 in 340,000
MTHFR Deficiency (Mild Condition)	E429A heterozygote †	Not calculated
Mucolipidosis IV	< 1 in 500	< 1 in 1,000,000
Muscle-Eye-Brain Disease	< 1 in 500	< 1 in 1,000,000
NEB-related Nemaline Myopathy	< 1 in 500	< 1 in 1,000,000
Niemann-Pick Disease Type C	1 in 230	1 in 180,000
Niemann-Pick Disease, SMPD1-associated	1 in 400	1 in 400,000
Nijmegen Breakage Syndrome	1 in 720	1 in 450,000
Northern Epilepsy	< 1 in 500	< 1 in 1,000,000
Pendred Syndrome	1 in 220	1 in 63,000
PEX1-related Zellweger Syndrome Spectrum	1 in 350	1 in 160,000
Phenylalanine Hydroxylase Deficiency	1 in 88	1 in 17,000
Polyglandular Autoimmune Syndrome Type 1	1 in 400	1 in 230,000
Pompe Disease	1 in 480	1 in 300,000
PPT1-related Neuronal Ceroid Lipofuscinosis	< 1 in 500	< 1 in 1,000,000
Primary Carnitine Deficiency	< 1 in 500	< 1 in 1,000,000
Primary Hyperoxaluria Type 1	1 in 600	1 in 850,000
Primary Hyperoxaluria Type 2	< 1 in 500	< 1 in 1,000,000
PROP1-related Combined Pituitary Hormone Deficiency	1 in 250	1 in 110,000
Prothrombin Thrombophilia (Mild Condition)	Not calculated	Not calculated
Pseudocholinesterase Deficiency	1 in 160	1 in 18,000
Pycnodysostosis	< 1 in 500	< 1 in 1,000,000
Rhizomelic Chondrodysplasia Punctata Type 1	1 in 530	1 in 330,000
Salla Disease	< 1 in 500	< 1 in 1,000,000
Segawa Syndrome	< 1 in 500	< 1 in 1,000,000
Short Chain Acyl-CoA Dehydrogenase Deficiency	1 in 160	1 in 100,000
Sjogren-Larsson Syndrome	1 in 330	1 in 330,000
Smith-Lemli-Opitz Syndrome	1 in 160	1 in 32,000
Spinal Muscular Atrophy	SMN1: 2 copies 1 in 610	1 in 84,000
Steroid-Resistant Nephrotic Syndrome	1 in 600	1 in 950,000
Sulfate Transporter-Related Osteochondrodysplasia	1 in 420	1 in 180,000
TPP1-related Neuronal Ceroid Lipofuscinosis	R208* heterozygote †	1 in 1,200
Tyrosinemia Type I	1 in 350	1 in 240,000
Usher Syndrome Type 1F	1 in 190	1 in 150,000
Usher Syndrome Type 3	< 1 in 500	< 1 in 1,000,000
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	1 in 110	1 in 39,000
Wilson Disease	1 in 140	1 in 50,000
X-Linked Juvenile Retinoschisis	< 1 in 500	1 in 50,000