Fairfax Cryobank
The Trusted Choice for Donor Sperm

Donor 6814

Genetic Testing Summary

Fairfax Cryobank recommends reviewing this genetic testing summary with your healthcare provider to determine suitability.

Last Updated: 12/30/22

Donor Reported Ancestry: Chinese Jewish Ancestry: No

Genetic Test*	**Result**	**Comments/Donor's Residual Risk****
Chromosome analysis (karyotype)	Normal male karyotype	No evidence of clinically significant chromosome abnormalities
Hemoglobin evaluation	Normal hemoglobin fractionation and MCV/MCH results	Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies
Cystic Fibrosis (CF) carrier screening	Negative by gene sequencing in the CFTR gene	1/1400
Spinal Muscular Atrophy (SMA) carrier screening	Negative for deletions of exon 7 and gene sequencing in the SMN1 gene	1/1115
Expanded Genetic Disease Carrier Screening Panel attached- 283 diseases by gene sequencing	Variant Detected for Alpha-Thalassemia (HBA1/HBA2) aaa/aa One copy of the alpha 4.2 duplication Carrier: Leber Congenital Amaurosis 5 (LCA5) Carrier: Segawa Syndrome (TH) Carrier: Usher Syndrome, Type IIA (USH2A) Carrier: Wilson Disease (ATP7B) Negative for other genes sequenced	Partner testing recommended for HBB before using this donor. Partner testing recommended before using this donor.

*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy.**Donor residual risk is the chance the donor is still a carrier after testing negative.

Patient Information
Name: Donor 6814
Date of Birth: [redacted]
Sema4 ID: [redacted]
Client ID: [redacted]
Indication: Carrier Screening

Specimen Information
Specimen Type: Blood
Date Collected: 10/08/2021
Date Received: 10/09/2021
Final Report: 10/28/2021

Referring Provider
[redacted]
Fairfax Cryobank, Inc.
[redacted]
[redacted]
[redacted]

Expanded Carrier Screen Minus TSE (283 genes)

with Personalized Residual Risk

SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
Variant Detected for Alpha-Thalassemia (AR) Associated gene(s): *HBA1/HBA2* Variant(s) Detected: One copy of the alpha 4.2 duplication **Carrier of Leber Congenital Amaurosis 5 (AR)** Associated gene(s): *LCA5* Variant(s) Detected: c.1758delA, p.K586NfsX7, Likely Pathogenic, Heterozygous (one copy) **Carrier of Segawa Syndrome (AR)** Associated gene(s): *TH* Variant(s) Detected: c.1228C>T, p.R410W, Likely Pathogenic, Heterozygous (one copy) **Carrier of Usher Syndrome, Type IIA (AR)** Associated gene(s): *USH2A* Variant(s) Detected: c.5608C>T, p.R1870W, Likely Pathogenic, Heterozygous (one copy) **Carrier of Wilson Disease (AR)** Associated gene(s): *ATP7B* Variant(s) Detected: c.3800A>T, p.D1267V, Likely Pathogenic, Heterozygous (one copy)	**Negative for all other genes tested** To view a full list of genes and diseases tested please see Table 1 in this report

AR=Autosomal recessive; XL=X-linked

Recommendations

- Testing the partner for the above positive disorder(s) and genetic counseling are recommended.
- An alpha-thalassemia duplication allele is generally considered to be a benign polymorphism. Testing the partner for both alpha-thalassemia and beta-thalassemia are recommended to assess the likelihood that the patients offspring may be affected with thalassemia intermedia.
- Please note that for female carriers of X-linked diseases, follow-up testing of a male partner is not indicated.
- CGG repeat analysis of *FMR1* for fragile X syndrome is not performed on males as repeat expansion of premutation alleles is not expected in the male germline.
- Individuals of Asian, African, Hispanic and Mediterranean ancestry should also be screened for hemoglobinopathies by CBC and hemoglobin electrophoresis.
- Consideration of residual risk by ethnicity after a negative carrier screen is recommended for the other diseases on the panel, especially in the case of a positive family history for a specific disorder.

Interpretation of positive results

Alpha-Thalassemia (AR)

Results and Interpretation

HBA1 Copy Number: 2
HBA2 Copy Number: 3
One copy of the alpha 4.2 duplication detected
HBA1/ HBA2 Sequencing: Negative

Gene(s) analyzed: *HBA1* (NM_000558.4) and *HBA2* (NM_000517.4)

Inheritance: Autosomal Recessive

This patient carries an alpha 4.2 duplication allele, resulting in a total of five copies of the alpha-globin gene (aaa/aa). This duplication allele is considered to be a benign polymorphism and therefore the chance that this patient is an alpha-thalassemia carrier is decreased. However, testing the partner for beta-thalassemia is recommended in order to rule out the possibility of being a thalassemia intermedia carrier couple. The literature indicates that co-inheritance of a *beta*--thalassemia pathogenic variant with additional copies of the *HBA* genes (more than 4) can lead to a thalassaemia intermedia phenotype with a variable clinical presentation. No pathogenic or likely pathogenic variants were identified by sequence analysis.

Typically, individuals have four functional alpha-globin genes: 2 copies of *HBA1* and 2 copies of *HBA2*, whose expression is regulated by a cis-acting regulatory element HS-40. Alpha-thalassemia carriers have three (silent carrier) or two (carrier of the alpha-thalassemia trait) functional alpha-globin genes with or without a mild phenotype. Individuals with only one functional alpha-globin gene have HbH disease with microcytic, hypochromic hemolytic anemia and hepatosplenomegaly. Loss of all four alpha-globin genes results in Hb Barts syndrome with the accumulation of Hb Barts in red blood cells and hydrops fetalis, which is fatal in utero or shortly after birth.

Leber Congenital Amaurosis 5 (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic frameshift variant, c.1758delA, p.K586NfsX7, was detected in the *LCA5* gene (NM_181714.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for Leber congenital amaurosis 5. Therefore, this individual is expected to be at least a carrier for Leber congenital amaurosis 5. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Leber Congenital Amaurosis 5?

Leber congenital amaurosis 5 is an autosomal recessive, pan-ethnic disease that is caused by pathogenic variants in the gene *LCA5* . Clinical features include uncontrollable eye movements and loss of vision that begins during infancy. Patients develop a profound loss of vision at an early age. Life expectancy is not decreased, and no genotype-phenotype correlation has been noted.

Segawa Syndrome (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic missense variant, c.1228C>T, p.R410W, was detected in the *TH* gene (NM_000360.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for Segawa syndrome. Therefore, this individual is expected to be at least a carrier for Segawa syndrome. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Segawa Syndrome?

Segawa syndrome is an autosomal recessive disease that is caused by pathogenic variants in the *TH* gene. The condition has been identified in individuals of multiple ethnicities, but may have a higher prevalence in Caucasians. Onset of this neurologic disorder is typically within the first few years of life and presents with generalized dystonia. Other symptoms may include progressive lack of coordination, tremors, or abnormal eye movements. There is an earlier onset form of this disease that presents as infantile Parkinsonism and can include low muscle tone, tremors, delayed motor milestones, and abnormal functions of the brain. A more severe form of the disease also exists that presents in infancy and results in progressive infantile encephalopathy. Life expectancy of individuals with the more severe form of the disorder is variable but prognosis is good for patients with the less severe form. Several specific variants have been reported to be associated with a milder form of the disease.

Usher Syndrome, Type IIA (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic missense variant, c.5608C>T, p.R1870W, was detected in the *USH2A* gene (NM_206933.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for Usher syndrome type IIA. Therefore, this individual is expected to be at least a carrier for Usher syndrome type IIA. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Usher Syndrome, Type IIA?

Usher syndrome type IIA is an autosomal recessive disease caused by pathogenic variants in the gene *USH2A* . While it is a pan-ethnic disease, due to the presence of a founder mutation it is found more frequently in Sephardic Jewish individuals from Iraq and Iran. The disease is characterized by congenital moderate to severe hearing loss, and patients may benefit from the use of hearing aids. Progressive loss of vision due to retinitis pigmentosa begins in late childhood or adolescence. Retinitis pigmentosa first presents with night blindness, but progresses to tunnel vision and eventually blindness. Several specific variants have been associated with a milder form of the disease, and therefore disease severity may be predicted in some patients.

Wilson Disease (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic missense variant, c.3800A>T, p.D1267V, was detected in the *ATP7B* gene (NM_000053.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for Wilson disease. Therefore, this individual is expected to be at least a carrier for Wilson disease. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Wilson Disease?

Wilson disease is an autosomal recessive disease caused by pathogenic variants in the gene *ATP7B* . While it is a pan-ethnic disease, it is found more frequently in individuals of Sephardic and Ashkenazi Jewish descent, as well as individuals from the Canary Islands and from Sardinia. As the protein encoded by *ATP7B* plays a role in copper transport, pathogenic variants in this gene result in the toxic accumulation of copper in different tissues in the body, particularly the liver, nervous system and eyes. Liver disease includes cirrhosis caused by chronic hepatitis, leading to liver failure. Copper depositions in the nervous system can cause neurologic symptoms including changes in behavior, parkinsonism, ataxia and dystonia, and psychiatric symptoms including anxiety, depression and psychosis. While the presence of two null variants is often associated with a more severe disease phenotype, the severity of the disease can vary within families, thereby making it difficult to predict disease severity based on genotype. Without treatment, life expectancy is estimated to be 40 years, but with prompt and efficient treatment, patients may have a normal lifespan.

Test description

This patient was tested for a panel of diseases using a combination of sequencing, targeted genotyping and copy number analysis. Please note that negative results reduce but do not eliminate the possibility that this individual is a carrier for one or more of the disorders tested. Please see Table 1 for a list of genes and diseases tested with the patient's personalized residual risk. If personalized residual risk is not provided, please see the complete residual risk table at **go.sema4.com/residualrisk**. Only variants determined to be pathogenic or likely pathogenic are reported in this carrier screening test.

Wei Kelly, M.D., Ph.D., Assistant Director
Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D

Genes and diseases tested

The personalized residual risks listed below are specific to this individual. The complete residual risk table is available at **go.sema4.com/residualrisk**

Table 1: List of genes and diseases tested with detailed results

	Disease	Gene	Inheritance Pattern	Status	Detailed Summary
⊕	**Positive**				
	Alpha-Thalassemia	*HBA1/HBA2*	AR	Reduced Risk (Duplication Detected)	*HBA1* Copy Number: 2 *HBA2* Copy Number: 3 One copy of the alpha 4.2 duplication detected *HBA1/HBA2* Sequencing: Negative **Personalized Residual Risk:** 1 in 380 As additional gene copies are present, the patient's residual risk is expected to be lower than displayed
	Leber Congenital Amaurosis 5	*LCA5*	AR	Carrier	c.1758delA, p.K586NfsX7, Likely Pathogenic, Heterozygous (one copy)
	Segawa Syndrome	*TH*	AR	Carrier	c.1228C>T, p.R410W, Likely Pathogenic, Heterozygous (one copy)
	Usher Syndrome, Type IIA	*USH2A*	AR	Carrier	c.5608C>T, p.R1870W, Likely Pathogenic, Heterozygous (one copy)
	Wilson Disease	*ATP7B*	AR	Carrier	c.3800A>T, p.D1267V, Likely Pathogenic, Heterozygous (one copy)
⊖	**Negative**				
	3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	*HSD3B2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 181,000
	3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC1*-Related)	*MCCC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 930
	3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC2*-Related)	*MCCC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 500
	3-Methylglutaconic Aciduria, Type III	*OPA3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 29,000
	3-Phosphoglycerate Dehydrogenase Deficiency	*PHGDH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 123,000
	6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	*PTS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
	Abetalipoproteinemia	*MTTP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,500
	Achromatopsia (*CNGB3*-related)	*CNGB3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 21,000
	Acrodermatitis Enteropathica	*SLC39A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 62,000
	Acute Infantile Liver Failure	*TRMU*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 55,000
	Acyl-CoA Oxidase I Deficiency	*ACOX1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 59,000
	Adenosine Deaminase Deficiency	*ADA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 127,000
	Adrenoleukodystrophy, X-Linked	*ABCD1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 19,000
	Aicardi-Goutieres Syndrome (*SAMHD1*-Related)	*SAMHD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
	Alpha-Mannosidosis	*MAN2B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,000
	Alpha-Thalassemia Intellectual Disability Syndrome	*ATRX*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 48,000
	Alport Syndrome (*COL4A3*-Related)	*COL4A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
	Alport Syndrome (*COL4A4*-Related)	*COL4A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 510
	Alport Syndrome (*COL4A5*-Related)	*COL4A5*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 150,000
	Alstrom Syndrome	*ALMS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,100
	Andermann Syndrome	*SLC12A6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 287,000
	Argininosuccinic Aciduria	*ASL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
	Aromatase Deficiency	*CYP19A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200

Arthrogryposis, Mental Retardation, and Seizures	*SLC35A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 240,000
Asparagine Synthetase Deficiency	*ASNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 178,000
Aspartylglycosaminuria	*AGA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Ataxia With Isolated Vitamin E Deficiency	*TTPA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Ataxia-Telangiectasia	*ATM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 540
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	*SACS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Bardet-Biedl Syndrome (*BBS10*-Related)	*BBS10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Bardet-Biedl Syndrome (*BBS12*-Related)	*BBS12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 287,000
Bardet-Biedl Syndrome (*BBS1*-Related)	*BBS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Bardet-Biedl Syndrome (*BBS2*-Related)	*BBS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,400
Bare Lymphocyte Syndrome, Type II	*CIITA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 129,000
Bartter Syndrome, Type 4A	*BSND*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 69,000
Bernard-Soulier Syndrome, Type A1	*GP1BA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Bernard-Soulier Syndrome, Type C	*GP9*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Beta-Globin-Related Hemoglobinopathies	*HBB*	AR	Reduced Risk	**Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies):** 1 in 1,200 **Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant):** 1 in 11,000 **Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant):** 1 in 42,000
Beta-Ketothiolase Deficiency	*ACAT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,800
Bilateral Frontoparietal Polymicrogyria	*GPR56*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 143,000
Biotinidase Deficiency	*BTD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,800
Bloom Syndrome	*BLM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 34,000
Canavan Disease	*ASPA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,200
Carbamoylphosphate Synthetase I Deficiency	*CPS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 690
Carnitine Palmitoyltransferase IA Deficiency	*CPT1A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 143,000
Carnitine Palmitoyltransferase II Deficiency	*CPT2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 930
Carpenter Syndrome	*RAB23*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 28,000
Cartilage-Hair Hypoplasia	*RMRP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 450
Cerebral Creatine Deficiency Syndrome 1	*SLC6A8*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 208,000
Cerebral Creatine Deficiency Syndrome 2	*GAMT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,300
Cerebrotendinous Xanthomatosis	*CYP27A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 750
Charcot-Marie-Tooth Disease, Type 4D	*NDRG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 225,000
Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome	*PRPS1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 114,000
Charcot-Marie-Tooth Disease, X-Linked	*GJB1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Choreoacanthocytosis	*VPS13A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,700
Choroideremia	*CHM*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 125,000
Chronic Granulomatous Disease (*CYBA*-Related)	*CYBA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,700
Chronic Granulomatous Disease (*CYBB*-Related)	*CYBB*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 294,000
Citrin Deficiency	*SLC25A13*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,200
Citrullinemia, Type 1	*ASS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 81,000
Cohen Syndrome	*VPS13B*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
Combined Malonic and Methylmalonic Aciduria	*ACSF3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 23,000
Combined Oxidative Phosphorylation Deficiency 1	*GFM1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,100
Combined Oxidative Phosphorylation Deficiency 3	*TSFM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 21,000
Combined Pituitary Hormone Deficiency 2	*PROP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,300

Combined Pituitary Hormone Deficiency 3	*LHX3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 121,000
Combined SAP Deficiency	*PSAP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 78,000
Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency	*CYP17A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 840
Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency	*CYP21A2*	AR	Reduced Risk	*CYP21A2* copy number: 2 *CYP21A2* sequencing: Negative **Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Non-Classic)):** 1 in 300 **Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic)):** 1 in 1,200
Congenital Amegakaryocytic Thrombocytopenia	*MPL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 68,000
Congenital Disorder of Glycosylation, Type Ia	*PMM2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 550
Congenital Disorder of Glycosylation, Type Ib	*MPI*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Congenital Disorder of Glycosylation, Type Ic	*ALG6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,300
Congenital Insensitivity to Pain with Anhidrosis	*NTRK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Congenital Myasthenic Syndrome (*CHRNE*-Related)	*CHRNE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 30,000
Congenital Myasthenic Syndrome (*RAPSN*-Related)	*RAPSN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 47,000
Congenital Neutropenia (*HAX1*-Related)	*HAX1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 126,000
Congenital Neutropenia (*VPS45*-Related)	*VPS45*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 110,000
Corneal Dystrophy and Perceptive Deafness	*SLC4A11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,200
Corticosterone Methyloxidase Deficiency	*CYP11B2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Cystic Fibrosis	*CFTR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Cystinosis	*CTNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,100
D-Bifunctional Protein Deficiency	*HSD17B4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
Deafness, Autosomal Recessive 77	*LOXHD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
Duchenne Muscular Dystrophy / Becker Muscular Dystrophy	*DMD*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Dyskeratosis Congenita (*RTEL1*-Related)	*RTEL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,900
Dystrophic Epidermolysis Bullosa	*COL7A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Ehlers-Danlos Syndrome, Type VIIC	*ADAMTS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 63,000
Ellis-van Creveld Syndrome (*EVC*-Related)	*EVC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Emery-Dreifuss Myopathy 1	*EMD*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 833,000
Enhanced S-Cone Syndrome	*NR2E3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Ethylmalonic Encephalopathy	*ETHE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
Fabry Disease	*GLA*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 7,700
Factor IX Deficiency	*F9*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 5,100
Factor XI Deficiency	*F11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 440
Familial Autosomal Recessive Hypercholesterolemia	*LDLRAP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 171,000
Familial Dysautonomia	*IKBKAP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 78,000
Familial Hypercholesterolemia	*LDLR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 260
Familial Hyperinsulinism (*ABCC8*-Related)	*ABCC8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 240
Familial Hyperinsulinism (*KCNJ11*-Related)	*KCNJ11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Familial Mediterranean Fever	*MEFV*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,400
Fanconi Anemia, Group A	*FANCA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Fanconi Anemia, Group C	*FANCC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 34,000
Fanconi Anemia, Group G	*FANCG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200

Fragile X Syndrome	*FMR1*	XL	Reduced Risk	*FMR1* CGG repeat sizes: Not Performed *FMR1* Sequencing: Negative Fragile X CGG triplet repeat expansion testing was not performed at this time, as the patient has either been previously tested or is a male. **Personalized Residual Risk:** 1 in 222,000
Fumarase Deficiency	*FH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,900
GRACILE Syndrome and Other *BCS1L*-Related Disorders	*BCS1L*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Galactokinase Deficiency	*GALK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Galactosemia	*GALT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 390
Gaucher Disease	*GBA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Gitelman Syndrome	*SLC12A3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 230
Glutaric Acidemia, Type I	*GCDH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Glutaric Acidemia, Type IIa	*ETFA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Glutaric Acidemia, Type IIc	*ETFDH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 260
Glycine Encephalopathy (*AMT*-Related)	*AMT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 144,000
Glycine Encephalopathy (*GLDC*-Related)	*GLDC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 240
Glycogen Storage Disease, Type II	*GAA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 280
Glycogen Storage Disease, Type III	*AGL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 55,000
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	*GBE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 64,000
Glycogen Storage Disease, Type Ia	*G6PC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 410
Glycogen Storage Disease, Type Ib	*SLC37A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,900
Glycogen Storage Disease, Type V	*PYGM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Glycogen Storage Disease, Type VII	*PFKM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,900
HMG-CoA Lyase Deficiency	*HMGCL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 113,000
Hemochromatosis, Type 2A	*HFE2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 740
Hemochromatosis, Type 3	*TFR2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 275,000
Hereditary Fructose Intolerance	*ALDOB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 35,000
Hereditary Spastic Paraparesis 49	*TECPR2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 166,000
Hermansky-Pudlak Syndrome, Type 1	*HPS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 286,000
Hermansky-Pudlak Syndrome, Type 3	*HPS3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 22,000
Holocarboxylase Synthetase Deficiency	*HLCS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,900
Homocystinuria (*CBS*-Related)	*CBS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,200
Homocystinuria due to *MTHFR* Deficiency	*MTHFR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,000
Homocystinuria, cblE Type	*MTRR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 16,000
Hydrolethalus Syndrome	*HYLS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 296,000
Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome	*SLC25A15*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 30,000
Hypohidrotic Ectodermal Dysplasia 1	*EDA*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 22,000
Hypophosphatasia	*ALPL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,200
Inclusion Body Myopathy 2	*GNE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
Infantile Cerebral and Cerebellar Atrophy	*MED17*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 130,000
Isovaleric Acidemia	*IVD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
Joubert Syndrome 2	*TMEM216*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 133,000
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	*RPGRIP1L*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Junctional Epidermolysis Bullosa (*LAMA3*-Related)	*LAMA3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 49,000
Junctional Epidermolysis Bullosa (*LAMB3*-Related)	*LAMB3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,600
Junctional Epidermolysis Bullosa (*LAMC2*-Related)	*LAMC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 28,000
Krabbe Disease	*GALC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 340

Lamellar Ichthyosis, Type 1	*TGM1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies	*CEP290*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Leber Congenital Amaurosis 13	*RDH12*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 88,000
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	*RPE65*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	*CRB1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 960
Leigh Syndrome, French-Canadian Type	*LRPPRC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 22,000
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease	*GLE1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Leukoencephalopathy with Vanishing White Matter	*EIF2B5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,200
Limb-Girdle Muscular Dystrophy, Type 2A	*CAPN3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
Limb-Girdle Muscular Dystrophy, Type 2B	*DYSF*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Limb-Girdle Muscular Dystrophy, Type 2C	*SGCG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,000
Limb-Girdle Muscular Dystrophy, Type 2D	*SGCA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,400
Limb-Girdle Muscular Dystrophy, Type 2E	*SGCB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 72,000
Limb-Girdle Muscular Dystrophy, Type 2I	*FKRP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 460
Lipoamide Dehydrogenase Deficiency	*DLD*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 225,000
Lipoid Adrenal Hyperplasia	*STAR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 36,000
Lipoprotein Lipase Deficiency	*LPL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 800
Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	*HADHA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,500
Lysinuric Protein Intolerance	*SLC7A7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 72,000
Maple Syrup Urine Disease, Type 1a	*BCKDHA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Maple Syrup Urine Disease, Type 1b	*BCKDHB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	*MKS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 28,000
Medium Chain Acyl-CoA Dehydrogenase Deficiency	*ACADM*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Megalencephalic Leukoencephalopathy with Subcortical Cysts	*MLC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 171,000
Menkes Disease	*ATP7A*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Metachromatic Leukodystrophy	*ARSA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
Methylmalonic Acidemia (*MMAA*-Related)	*MMAA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 216,000
Methylmalonic Acidemia (*MMAB*-Related)	*MMAB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,700
Methylmalonic Acidemia (*MUT*-Related)	*MUT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 830
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	*MMACHC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	*MMADHC*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Microphthalmia / Anophthalmia	*VSX2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 83,000
Mitochondrial Complex I Deficiency (*ACAD9*-Related)	*ACAD9*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,100
Mitochondrial Complex I Deficiency (*NDUFAF5*-Related)	*NDUFAF5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 770
Mitochondrial Complex I Deficiency (*NDUFS6*-Related)	*NDUFS6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 211,000
Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	*MPV17*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,400
Mitochondrial Myopathy and Sideroblastic Anemia 1	*PUS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 333,000
Mucolipidosis II / IIIA	*GNPTAB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Mucolipidosis III Gamma	*GNPTG*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 213,000
Mucolipidosis IV	*MCOLN1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,500
Mucopolysaccharidosis Type I	*IDUA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 630

Mucopolysaccharidosis Type II	*IDS*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 76,000
Mucopolysaccharidosis Type IIIA	*SGSH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 700
Mucopolysaccharidosis Type IIIB	*NAGLU*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 900
Mucopolysaccharidosis Type IIIC	*HGSNAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 42,000
Mucopolysaccharidosis Type IIID	*GNS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 201,000
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	*GLB1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Mucopolysaccharidosis type IX	*HYAL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 63,000
Mucopolysaccharidosis type VI	*ARSB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 144,000
Multiple Sulfatase Deficiency	*SUMF1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 144,000
Muscle-Eye-Brain Disease and Other *POMGNT1*-Related Congenital Muscular Dystrophy-Dystroglycanopathies	*POMGNT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,100
Myoneurogastrointestinal Encephalopathy	*TYMP*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,400
Myotubular Myopathy 1	*MTM1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 192,000
N-Acetylglutamate Synthase Deficiency	*NAGS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,700
Nemaline Myopathy 2	*NEB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 300
Nephrogenic Diabetes Insipidus, Type II	*AQP2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,700
Nephrotic Syndrome (*NPHS1*-Related) / Congenital Finnish Nephrosis	*NPHS1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 980
Nephrotic Syndrome (*NPHS2*-Related) / Steroid-Resistant Nephrotic Syndrome	*NPHS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Neuronal Ceroid-Lipofuscinosis (*CLN3*-Related)	*CLN3*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 59,000
Neuronal Ceroid-Lipofuscinosis (*CLN5*-Related)	*CLN5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 75,000
Neuronal Ceroid-Lipofuscinosis (*CLN6*-Related)	*CLN6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 91,000
Neuronal Ceroid-Lipofuscinosis (*CLN8*-Related)	*CLN8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Neuronal Ceroid-Lipofuscinosis (*MFSD8*-Related)	*MFSD8*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 87,000
Neuronal Ceroid-Lipofuscinosis (*PPT1*-Related)	*PPT1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,300
Neuronal Ceroid-Lipofuscinosis (*TPP1*-Related)	*TPP1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Niemann-Pick Disease (*SMPD1*-Related)	*SMPD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Niemann-Pick Disease, Type C (*NPC1*-Related)	*NPC1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
Niemann-Pick Disease, Type C (*NPC2*-Related)	*NPC2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Nijmegen Breakage Syndrome	*NBN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 214,000
Non-Syndromic Hearing Loss (*GJB2*-Related)	*GJB2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 280
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	*WNT10A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 900
Omenn Syndrome (*RAG2*-Related)	*RAG2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 32,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	*DCLRE1C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 48,000
Ornithine Aminotransferase Deficiency	*OAT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,900
Ornithine Transcarbamylase Deficiency	*OTC*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 103,000
Osteopetrosis 1	*TCIRG1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,700
Pendred Syndrome	*SLC26A4*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 72
Phenylalanine Hydroxylase Deficiency	*PAH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 150
Polycystic Kidney Disease, Autosomal Recessive	*PKHD1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 350
Polyglandular Autoimmune Syndrome, Type 1	*AIRE*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Pontocerebellar Hypoplasia, Type 1A	*VRK1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 215,000
Pontocerebellar Hypoplasia, Type 6	*RARS2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 52,000
Primary Carnitine Deficiency	*SLC22A5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 600
Primary Ciliary Dyskinesia (*DNAH5*-Related)	*DNAH5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 19,000
Primary Ciliary Dyskinesia (*DNAI1*-Related)	*DNAI1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,300
Primary Ciliary Dyskinesia (*DNAI2*-Related)	*DNAI2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 144,000

Primary Hyperoxaluria, Type 1	*AGXT*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Primary Hyperoxaluria, Type 2	*GRHPR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 68,000
Primary Hyperoxaluria, Type 3	*HOGA1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Progressive Cerebello-Cerebral Atrophy	*SEPSECS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 247,000
Progressive Familial Intrahepatic Cholestasis, Type 2	*ABCB11*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 390
Propionic Acidemia (*PCCA*-Related)	*PCCA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
Propionic Acidemia (*PCCB*-Related)	*PCCB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 920
Pycnodysostosis	*CTSK*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,200
Pyruvate Dehydrogenase E1-Alpha Deficiency	*PDHA1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 139,000
Pyruvate Dehydrogenase E1-Beta Deficiency	*PDHB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,300
Renal Tubular Acidosis and Deafness	*ATP6V1B1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,800
Retinitis Pigmentosa 25	*EYS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 580
Retinitis Pigmentosa 26	*CERKL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Retinitis Pigmentosa 28	*FAM161A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 145,000
Retinitis Pigmentosa 59	*DHDDS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 201,000
Rhizomelic Chondrodysplasia Punctata, Type 1	*PEX7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 55,000
Rhizomelic Chondrodysplasia Punctata, Type 3	*AGPS*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,024,000
Roberts Syndrome	*ESCO2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 95,000
Salla Disease	*SLC17A5*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Sandhoff Disease	*HEXB*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 680
Schimke Immunoosseous Dysplasia	*SMARCAL1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 56,000
Sjogren-Larsson Syndrome	*ALDH3A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Smith-Lemli-Opitz Syndrome	*DHCR7*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,800
Spinal Muscular Atrophy	*SMN1*	AR	Reduced Risk	*SMN1* copy number: 2 *SMN2* copy number: 2 c.*3+80T>G: Negative *SMN1* Sequencing: Negative **Personalized Residual Risk:** 1 in 1,115
Spondylothoracic Dysostosis	*MESP2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 53,000
Steel Syndrome	*COL27A1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 275,000
Stuve-Wiedemann Syndrome	*LIFR*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Sulfate Transporter-Related Osteochondrodysplasia	*SLC26A2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Tay-Sachs Disease	*HEXA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
Tyrosinemia, Type I	*FAH*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,900
Usher Syndrome, Type IB	*MYO7A*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 180
Usher Syndrome, Type IC	*USH1C*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 400
Usher Syndrome, Type ID	*CDH23*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 880
Usher Syndrome, Type IF	*PCDH15*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Usher Syndrome, Type III	*CLRN1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	*ACADVL*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 380
Walker-Warburg Syndrome and Other *FKTN*-Related Dystrophies	*FKTN*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 390
Wolman Disease / Cholesteryl Ester Storage Disease	*LIPA*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 32,000
X-Linked Juvenile Retinoschisis	*RS1*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 40,000
X-Linked Severe Combined Immunodeficiency	*IL2RG*	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 250,000
Zellweger Syndrome Spectrum (*PEX10*-Related)	*PEX10*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 218,000
Zellweger Syndrome Spectrum (*PEX1*-Related)	*PEX1*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 740
Zellweger Syndrome Spectrum (*PEX2*-Related)	*PEX2*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 108,000
Zellweger Syndrome Spectrum (*PEX6*-Related)	*PEX6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500

AR=Autosomal recessive; XL=X-linked

Test methods and comments

Genomic DNA isolated from this patient was analyzed by one or more of the following methodologies, as applicable:

Fragile X CGG Repeat Analysis (Analytical Detection Rate >99%)

PCR amplification using Asuragen, Inc. AmplideX® *FMR1* PCR reagents followed by capillary electrophoresis for allele sizing was performed. Samples positive for *FMR1* CGG repeats in the premutation and full mutation size range were further analyzed by Southern blot analysis to assess the size and methylation status of the *FMR1* CGG repeat.

Genotyping (Analytical Detection Rate >99%)

Multiplex PCR amplification and allele specific primer extension analyses using the MassARRAY® System were used to identify certain recurrent variants that are complex in nature or are present in low copy repeats. Rare sequence variants may interfere with assay performance.

Multiplex Ligation-Dependent Probe Amplification (MLPA) (Analytical Detection Rate >99%)

MLPA® probe sets and reagents from MRC-Holland were used for copy number analysis of specific targets versus known control samples. False positive or negative results may occur due to rare sequence variants in target regions detected by MLPA probes. Analytical sensitivity and specificity of the MLPA method are both 99%.

For alpha thalassemia, the copy numbers of the *HBA1* and *HBA2* genes were analyzed. Alpha-globin gene deletions, triplications, and the Constant Spring (CS) mutation are assessed. This test is expected to detect approximately 90% of all alpha-thalassemia mutations, varying by ethnicity. carriers of alpha-thalassemia with three or more *HBA* copies on one chromosome, and one or no copies on the other chromosome, may not be detected. With the exception of triplications, other benign alpha-globin gene polymorphisms will not be reported. Analyses of *HBA1* and *HBA2* are performed in association with long-range PCR of the coding regions followed by short-read sequencing.

For Duchenne muscular dystrophy, the copy numbers of all *DMD* exons were analyzed. Potentially pathogenic single exon deletions and duplications are confirmed by a second method. Analysis of *DMD* is performed in association with sequencing of the coding regions.

For congenital adrenal hyperplasia, the copy number of the *CYP21A2* gene was analyzed. This analysis can detect large deletions typically due to unequal meiotic crossing-over between *CYP21A2* and the pseudogene *CYP21A1P*. Classic 30-kb deletions make up approximately 20% of *CYP21A2* pathogenic alleles. This test may also identify certain point mutations in *CYP21A2* caused by gene conversion events between *CYP21A2* and *CYP21A1P*. Some carriers may not be identified by dosage sensitive methods as this testing cannot detect individuals with two copies (duplication) of the *CYP21A2* gene on one chromosome and loss of *CYP21A2* (deletion) on the other chromosome. Analysis of *CYP21A2* is performed in association with long-range PCR of the coding regions followed by short-read sequencing.

For spinal muscular atrophy (SMA), the copy numbers of the *SMN1* and *SMN2* genes were analyzed. The individual dosage of exons 7 and 8 as well as the combined dosage of exons 1, 4, 6 and 8 of *SMN1* and *SMN2* were assessed. Copy number gains and losses can be detected with this assay. Depending on ethnicity, 6 - 29 % of carriers will not be identified by dosage sensitive methods as this testing cannot detect individuals with two copies (duplication) of the *SMN1* gene on one chromosome and loss of *SMN1* (deletion) on the other chromosome (silent 20 carrier) or individuals that carry an intragenic mutation in *SMN1*. Please also note that 2% of individuals diagnosed with SMA have a causative *SMN1* variant that occurred *de novo*, and therefore cannot be picked up by carrier screening in the parents. Analysis of *SMN1* is performed in association with short-read sequencing of exons 2a-7, followed by confirmation using long-range PCR (described below).

The presence of the c.*380T>G (chr5:70,247,901T>G) variant allele in an individual with Ashkenazi Jewish or Asian ancestry is typically indicative of a duplication of *SMN1*. When present in an Ashkenazi Jewish or Asian individual with two copies of *SMN1*, c.*380T>G is likely indicative of a silent (20) carrier. In individuals with two copies of *SMN1* with African American, Hispanic or Caucasian ancestry, the presence or absence of c.*380T>G significantly increases or decreases, respectively, the likelihood of being a silent 20 silent carrier.

MLPA for Gaucher disease (*GBA*), cystic fibrosis (*CFTR*), and non-syndromic hearing loss (*GJB2/GJB6*) will only be performed if indicated for confirmation of detected CNVs. If *GBA* analysis was performed, the copy numbers of exons 1, 3, 4, and 6 - 10 of the *GBA* gene (of 11 exons total) were analyzed. If *CFTR* analysis was performed, the copy numbers of all 27 *CFTR* exons were analyzed. If *GJB2/GJB6* analysis was performed, the copy number of the two *GJB2* exons were analyzed, as well as the presence or absence of the two upstream deletions of the *GJB2* regulatory region, del(*GJB6*-D13S1830) and del(*GJB6*-D13S1854).

Next Generation Sequencing (NGS) (Analytical Detection Rate >95%)

NGS was performed on a panel of genes for the purpose of identifying pathogenic or likely pathogenic variants.

Agilent SureSelect^{TM}XT Low Input technology was used with a custom capture library to target the exonic regions and intron/exon splice junctions of the relevant genes, as well as a number of UTR, intronic or promoter regions that contain previously reported mutations. Libraries were pooled and sequenced on the Illumina NovaSeq 9000 platform, using paired-end 100 bp reads. The sequencing data was analyzed using a custom bioinformatics algorithm designed and validated in house.

The coding exons and splice junctions of the known protein-coding RefSeq genes were assessed for the average depth of coverage (minimum of 20X) and data quality threshold values. Most exons not meeting a minimum of >20X read depth across the exon are further analyzed by Sanger sequencing. Please note that several genomic regions present difficulties in mapping or obtaining read depth >20X. These regions, which are described below, will not be reflexed to Sanger sequencing if the mapping quality or coverage is poor. Any variants identified during testing in these regions are confirmed by a second method and reported if determined to be pathogenic or likely pathogenic. However, as there is a possibility of false negative results within these regions, detection rates and residual risks for these genes have been calculated with the presumption that variants in these exons will not be detected, unless included in the MassARRAY® genotyping platform.

This test will detect variants within the exons and the intron-exon boundaries of the target regions. Variants outside these regions may not be detected, including, but not limited to, UTRs, promoters, and deep intronic areas, or regions that fall into the Exceptions mentioned above. This technology may not detect all small insertion/deletions and is not diagnostic for repeat expansions and structural genomic variation. In addition, a mutation(s) in a gene not included on the panel could be present in this patient.

Variant interpretation and classification was performed based on the American College of Medical Genetics Standards and Guidelines for the Interpretation of Sequence Variants (Richards et al, 2015). All potentially pathogenic variants may be confirmed by either a specific genotyping assay or Sanger sequencing, if indicated. Any benign variants, likely benign variants or variants of uncertain significance identified during this analysis will not be reported.

Next Generation Sequencing for SMN1

Exonic regions and intron/exon splice junctions of *SMN1* and *SMN2* were captured, sequenced, and analyzed as described above. Any variants located within exons 2a-7 and classified as pathogenic or likely pathogenic were confirmed to be in either *SMN1* or *SMN2* using gene-specific long-range PCR analysis followed by Sanger sequencing. Variants located in exon 1 cannot be accurately assigned to either *SMN1* or *SMN2* using our current methodology, and so these variants are considered to be of uncertain significance and are not reported.

Copy Number Variant Analysis (Analytical Detection Rate >95%)

Large duplications and deletions were called from the relative read depths on an exon-by-exon basis using a custom exome hidden Markov model (XHMM) algorithm. Deletions or duplications determined to be pathogenic or likely pathogenic were confirmed by either a custom arrayCGH platform, quantitative PCR, or MLPA (depending on CNV size and gene content). While this algorithm is designed to pick up deletions and duplications of 2 or more exons in length, potentially pathogenic single-exon CNVs will be confirmed and reported, if detected.

Exon Array (Confirmation method) (Accuracy >99%)

The customized oligonucleotide microarray (Oxford Gene Technology) is a highly-targeted exon-focused array capable of detecting medically relevant microdeletions and microduplications at a much higher resolution than traditional aCGH methods. Each array matrix has approximately 180,000 60-mer oligonucleotide probes that cover the entire genome. This platform is designed based on human genome NCBI Build 37 (hg19) and the CGH probes are enriched to target the exonic regions of the genes in this panel.

Quantitative PCR (Confirmation method) (Accuracy >99%)

The relative quantification PCR is utilized on a Roche Universal Library Probe (UPL) system, which relates the PCR signal of the target region in one group to another. To test for genomic imbalances, both sample DNA and reference DNA is amplified with primer/probe sets that specific to the target region and a control region with known genomic copy number. Relative genomic copy numbers are calculated based on the standard ΔΔCt formula.

Long-Range PCR (Analytical Detection Rate >99%)

Long-range PCR was performed to generate locus-specific amplicons for *CYP21A2*, *HBA1* and *HBA2* and *GBA*. The PCR products were then prepared for short-read NGS sequencing and sequenced. Sequenced reads were mapped back to the original genomic locus and run through the bioinformatics pipeline. If indicated, copy number from MLPA was correlated with the sequencing output to analyze the results. For *CYP21A2*, a certain percentage of healthy individuals carry a duplication of the *CYP21A2* gene, which has no clinical consequences. In cases where two copies of a gene are located on the same chromosome in tandem, only the second copy will be amplified and assessed for potentially pathogenic variants, due to size limitations of the PCR reaction. However, because these alleles contain at least two copies of the *CYP21A2* gene in tandem, it is expected that this patient has at least one functional gene in the tandem allele and this patient is therefore less likely to be a carrier. When an individual carries both a duplication allele and a pathogenic variant, or multiple pathogenic variants, the current analysis may not be able to determine the phase (cisrans configuration) of the *CYP21A2* alleles identified. Family studies may be required in certain scenarios where phasing is required to determine the carrier status.

Residual Risk Calculations

Carrier frequencies and detection rates for each ethnicity were calculated through the combination of internal curations of >30,000 variants and genomic frequency data from >138,000 individuals across seven ethnic groups in the gnomAD database. Additional variants in HGMD and novel deleterious variants were also incorporated into the calculation. Residual risk values are calculated using a Bayesian analysis combining the *a priori* risk of being a pathogenic mutation carrier (carrier frequency) and the detection rate. They are provided only as a guide for assessing approximate risk given a negative result, and values will vary based on the exact ethnic background of an individual. This report does not represent medical advice but should be interpreted by a genetic counselor, medical geneticist or physician skilled in genetic result interpretation and the relevant medical literature.

Personalized Residual Risk Calculations

Agilent SureSelect^{TM}XT Low-Input technology was utilized in order to create whole-genome libraries for each patient sample. Libraries were then pooled and sequenced on the Illumina NovaSeq platform. Each sequencing lane was multiplexed to achieve 0.4-2x genome coverage, using paired-end 100 bp reads. The sequencing data underwent ancestral analysis using a customized, licensed bioinformatics algorithm that was validated in house. Identified sub-ethnic groupings were binned into one of 7 continental-level groups (African, East Asian, South Asian, Non-Finnish European, Finnish, Native American, and Ashkenazi Jewish) or, for those ethnicities that matched poorly to the continental-level groups, an 8th "unassigned" group, which were then used to select residual risk values for each gene. For individuals belonging to multiple high-level ethnic groupings, a weighting strategy was used to select the most appropriate residual risk. For genes that had insufficient data to calculate ethnic-specific residual risk values, or for sub-ethnic groupings that fell into the "unassigned" group, a "worldwide" residual risk was used. This "worldwide" residual risk was calculated using data from all available continental-level groups.

Sanger Sequencing (Confirmation method) (Accuracy >99%)

Sanger sequencing, as indicated, was performed using BigDye Terminator chemistry with the ABI 3730 DNA analyzer with target specific amplicons. It also may be used to supplement specific guaranteed target regions that fail NGS sequencing due to poor quality or low depth of coverage (<20 reads) or as a confirmatory method for NGS positive results. False negative results may occur if rare variants interfere with amplification or annealing.

Please note these tests were developed and their performance characteristics were determined by Mount Sinai Genomics, Inc. They have not been cleared or approved by the FDA. These analyses generally provide highly accurate information regarding the patient's carrier or affected status. Despite this high level of accuracy, it should be kept in mind that there are many potential sources of diagnostic error, including misidentification of samples, polymorphisms, or other rare genetic variants that interfere with analysis. Families should understand that rare diagnostic errors may occur for these reasons.

Exceptions:

Gene	Transcript	Exceptions
ABCD1	NM_000033.3	Exons 8 and 9
ADA	NM_000022.2	Exon 1
ADAMTS2	NM_014244.4	Exon 1
AGPS	NM_003659.3	chr2:178,257,512 - 178,257,649 (partial exon 1)
ALMS1	NM_015120.4	chr2:73,612,990 - 73,613,041 (partial exon 1)
CEP290	NM_025114.3	Exon 5, exon 7, chr12:88,519,017 - 88,519,039 (partial exon 13), chr12:88,514,049 - 88,514,058 (partial exon 15), chr12:88,502,837 - 88,502,841 (partial exon 23), chr12:88,481,551 - 88,481,589 (partial exon 32), chr12:88,471,605 - 88,471,700 (partial exon 40)
CFTR	NM_000492.3	Exon 10
COL4A4	NM_000092.4	chr2:227,942,604 - 227,942,619 (partial exon 25)
CYP11B2	NM_000498.3	Exons 3 - 7
DNAI2	NM_023036.4	chr17:72,308,136 - 72,308,147 (partial exon 12)
EVC	NM_153717.2	Exon 1
FH	NM_000143.3	Exon 1
GAMT	NM_000156.5	Exon 1
GLDC	NM_000170.2	Exon 1
GNPTAB	NM_024312.4	chr17:4,837,000 - 4,837,400 (partial exon 2)
GNPTG	NM_032520.4	Exon 1
HGSNAT	NM_152419.2	Exon 1
IDS	NM_000202.6	Exon 3
LIFR	NM_002310.5	Exon 19
NEB	NM_001271208	Exons 82 - 105

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NPC1	NM_000271.4	chr18:21,123,519 - 21,123,538 (partial exon 14)
PUS1	NM_025215.5	chr12:132,414,446 - 132,414,532 (partial exon 2)
RPGRIP1L	NM_015272.2	Exon 23
SGSH	NM_000199.3	chr17:78,194,022 - 78,194,072 (partial exon 1)
SLC6A8	NM_005629.3	Exons 3 and 4

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Additional disease-specific references available upon request.