cryobio

Genetic Testing Summary

Enclosed are the genetic testing results for

CB 461

No amount of genetic testing can guarantee that a child will not be affected with a genetic condition. Genetic testing can inform you of the likelihood of passing on the genetic conditions that are tested for, but it cannot eliminate the risk of passing on any genetic condition.

The genetic conditions Cryobio tests for are inherited in an autosomal recessive manner. This means that the child would have to inherit a genetic mutation from both the sperm source and the egg source to be affected with the condition. When both the sperm source and the egg source have undergone genetic carrier screening and the test results are negative, the risk of a child being affected with the conditions tested for is significantly reduced, but it cannot be completely eliminated.

All recipients should discuss both or their own risk for passing on genetic conditions and whether would benefit from genetic counseling and testing with their health care provider. Before using a donor that is a carrier for a specific recessive genetic condition or conditions, we strongly recommend that the recipient (or egg source, if different) consider genetic counseling and testing to determine if they are a carrier for the same genetic condition or conditions as the donor.

Screening and testing have changed dramatically over the years, and so the screening and testing done on each donor may very depending on the testing that was in place when he was actively in Cryobio's donor program. Earlier donors may not have had as extensive testing as later donors. Screening and testing may change again in the future, so please review the results each time before ordering as both the testing done and the results may change.

BCM
Baylor College of Medicine

MEDICAL GENETICS LABORATORIES
2450 Holcombe Blvd - Houston, TX 77021 - 1-800-411-4363
Fax: 713-798-6584 - www.bcmgeneticlabs.org - genetictest@bcm.edu

KLEBERG CYTOGENETICS LABORATORY

Name: DONOR CB461

Sample Type: BLOOD

Date of birth:		Date collected:
Hospital #:	Sendouts	Date received:
Accession #:	Cryobiology	Report date:
KCL Lab #:	4830-D Knightsbridge Blvd	Telephone: 614-451-4375
Family #:	Columbus, OH 43214	Fax No: 614-451-5284
Indication: Sperm Donor		

CHROMOSOME ANALYSIS

METHOD OF ANALYSIS:
GTG-Banding

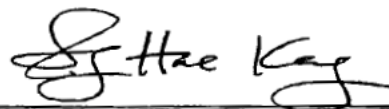|			
Cultures:	2	*No. of images:*	12
Cells counted:	30	*Cells karyotyped:*	3
Cells analyzed:	5	*Band resolution:*	575
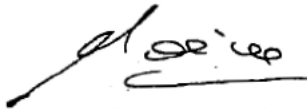
RESULTS
46,XY

INTERPRETATION
Normal male chromosome analysis. Analysis of 30 cells rules out 10% mosaicism at the 95% confidence level.

Carlos A. Bacino, M.D., FACMG
ABMG Certified Cytogeneticist and Molecular Geneticist
Medical Director

Sung-Hae Kang, Ph.D.
ABMG Certified Clinical Cytogeneticist
Assistant Laboratory Director

genzyme

Cystic Fibrosis Mutation Analysis

Patient Name: CB, 461
Referring Physician: David Prescott, MD
Specimen #: ▮
Patient ID: ▮

Client #: ▮
Case #: ▮

Cryobiology, Inc.
4830-D Knightsbridge Boulevard
Columbus OH 43214

DOB: ▮
Sex: M
SSN:

Date Collected: ▮
Date Received: ▮
Lab ID:
Hospital ID:
Specimen Type: ▮

Ethnicity: Caucasian

Indication: Carrier test / Gamete donor

RESULTS: Negative for the 97 mutations analyzed

INTERPRETATION

This individual's risk to be a carrier is reduced from 1/25 (4%) to 1/343 (0.3%), based on these results and a negative family history.

COMMENTS:

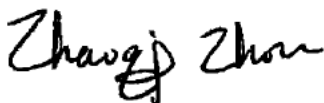| Mutation Detection Rates among Ethnic Groups	Detection rates are based on mutation frequencies in patients affected with cystic fibrosis. Among individuals with an atypical or mild presentation (e.g. congenital absence of the vas deferens, pancreatitis) detection rates may vary from those provided here.		
Ethnicity	**Carrier risk reduction when no family history**	**Detection rate**	**References**
African American	1/65 to 1/338	81%	Genet in Med 3:168, 2001
Ashkenazi Jewish	1/26 to 1/834	97%	Am J Hum Genet 51:951, 1994
Asian		Not Provided	Insufficient data
Caucasian	1/25 to 1/343	93%	Genet in Med 3:168, 2001; Genet in Med 4:90, 2002
Hispanic	1/46 to 1/205	78%	Genet in Med 3:168, 2001;www.dhs.ca.gov/pcfh/gdb/html/PDE/CFStudy.htm
Jewish, non-Ashkenazi		Varies by country of origin	Genet Testing 5:47, 2001, Genet Testing, 1:35, 1997
Other or Mixed Ethnicity		Not Provided	Detection rate not determined and varies with ethnicity

This interpretation is based on the clinical and family relationship information provided and the current understanding of the molecular genetics of this condition.

METHOD

DNA is isolated from the sample and tested for the 97 CF mutations listed. Regions of the *CFTR* gene are amplified enzymatically and subjected to a solution-phase multiplex allele-specific primer extension with subsequent hybridization to a bead array and fluorescent detection. The assay discriminates between ΔF508 and the following polymorphisms: F508C, I506V and I507V. In some cases, specific allele identification requires enzymatic amplification followed by hybridization to oligonucleotide probes.

Under the direction of:

Zhaoqing Zhou

Zhaoqing Zhou, Ph.D.

Date: ▮

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Testing Performed At Genzyme Genetics 3400 Computer Drive Westborough, MA 01581 1-800-255-7357

genzyme

SMN1 Copy Number Analysis

Patient Name: 461 CB
  DOB: ▮
  Age ▮
  SSN #: ▮
  Gender: Male

Genzyme Specimen # ▮
  Case #: ▮
  Patient ID # ▮
  Date Collected: ▮
  Date Received ▮

Cryobiology, Inc.
4830-D Knightsbridge Boulevard
Columbus, OH 43214

Referring Physician: David Prescott
Genetic Counselor:

Client Lab ID #:
Hospital ID #:
Specimen ID #:

Specimen Type: Peripheral Blood

Specimen(s) Received: 1 - Lavender 7 ml round bottom tube(s)

Clinical Data: Carrier Test/Gamete donor

Ethnicity: Caucasian

RESULTS: SMN1 copy number: 2 (Reduced Carrier Risk)

INTERPRETATION:
This individual has an SMN1 copy number of two. This result reduces but does not eliminate the risk to be a carrier of SMA. Ethnic specific risk reductions based on a negative family history and an SMN1 copy number of two are provided in the Comments section of this report.

COMMENT:
Spinal muscular atrophy (SMA) is an autosomal recessive disease of variable age of onset and severity caused by mutations (most often deletions or gene conversions) in the survival motor neuron (SMN1) gene. Molecular testing assesses the number of copies of the SMN1 gene. Individuals with one copy of the SMN1 gene are predicted to be carriers of SMA. Individuals with two or more copies have a reduced risk to be carriers. (Affected individuals have 0 copies of the SMN1 gene.)

This copy number analysis cannot detect individuals who are carriers of SMA as a result of either 2 (or very rarely 3) copies of the SMN1 gene on one chromosome and the absence of the SMN1 gene on the other chromosome or small intragenic mutations within the SMN1 gene. This analysis also will not detect germline mosaicism or mutations in genes other than SMN1. Additionally, de novo mutations have been reported in approximately 2% of SMA patients.

Carrier Frequency and Risk Reductions for Individuals with No Family History of SMA				
Ethnicity	**Detection Rate[1]**	**A priori Carrier Risk[1]**	**Reduced Carrier Risk for 2 copy result**	**Reduced Carrier Risk for 3 copy result**
Caucasian	94.9%	1:35	1:632	1:3,500
Ashkenazi Jewish	90.2%	1:41	1:350	1:4,000
Asian	92.6%	1:53	1:628	1:5,000
Hispanic	90.6%	1:117	1:1061	1:11,000
African American	71.1%	1:66	1:121	1:3,000
Mixed Ethnicities	For counseling purposes, consider using the ethnic background with the most conservative risk estimates.			

METHOD/LIMITATIONS:
Specimen DNA is isolated and amplified by real-time polymerase chain reaction (PCR) for exon 7 of the SMN1 gene and two reference genes. A mathematical algorithm is used to calculate the number of copies of SMN1. Sequencing of the primer and probe binding sites for the SMN1 real-time PCR reaction is performed on all fetal samples, and on samples from individuals with 1 copy of SMN on carrier testing, to rule out the presence of sequence variants which could interfere with analysis and interpretation. False positive or negative results may occur for reasons that include genetic variants, blood transfusions, bone marrow transplantation, erroneous representation of family relationships or contamination of a fetal sample with maternal cells.

REFERENCES:
1. Carrier frequency and detection rate are calculated based on analysis of allele frequencies among > 1000 individuals from each ethnic group noted (Genzyme Genetics, data submitted for publication). 2. Online review of SMA: http://www.genereviews.org/profiles/sma

The test was developed and its performance characteristics have been determined by Genzyme. The laboratory is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical testing. This test must be used in conjunction with clinical assessment, when available.

Electronically Signed by: Hui Zhu, Ph.D. FACMG, or ▮
Reported by: /

sema4

Patient Information

Name: 461 Cb

Date of Birth: ▉▉▉▉▉

Sema4 ID: ▉▉▉▉▉

Client ID: ▉▉▉▉▉

Indication: Carrier Screening

Specimen Information

Specimen Type: Saliva

Date Collected: ▉▉▉▉▉

Date Received: ▉▉▉▉▉

Final Report: ▉▉▉▉▉

Referring Provider

David Prescott, M.D.

Cryobiology, Inc.

4845 Knightsbridge Blvd. Suite 200

Columbus, OH, 43214

Fax: 614-451-5284

Expanded Carrier Screen (502 genes)
with Personalized Residual Risk

SUMMARY OF RESULTS AND RECOMMENDATIONS

⊕ Positive	⊖ Negative
Carrier of Homocystinuria (*CBS*-Related) (AR) Associated gene(s): *CBS* Variant(s) Detected: c.919G>A, p.G307S, Pathogenic, Heterozygous (one copy) **Carrier of Mucopolysaccharidosis Type IVa (AR)** Associated gene(s): *GALNS* Variant(s) Detected: c.1156C>T, p.R386C, Pathogenic, Heterozygous (one copy) **Carrier of Schimke Immunoosseous Dysplasia (AR)** Associated gene(s): *SMARCAL1* Variant(s) Detected: c 2114C>T, p.T705I, 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

Special Notes

Please note that it is not possible to perform Tay-Sachs enzyme analysis on saliva samples, and therefore this test does not include enzyme analysis for Tay-Sachs disease.

Recommendations

- Testing the partner for the above positive disorder(s) and genetic counseling are recommended.
- 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.

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Interpretation of positive results

Homocystinuria (*CBS*-Related) (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.919G>A, p.G307S, was detected in the *CBS* gene (NM_000071 2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for homocystinuria (*CBS*-related). Therefore, this individual is expected to be at least a carrier for homocystinuria (*CBS*-related). Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Homocystinuria (*CBS*-Related)?

Homocystinuria (*CBS*-related) is an autosomal recessive disorder caused by pathogenic variants in the gene *CBS* , and while it is considered to be a pan-ethnic disorder, it is most commonly seen among those of Qatari and Caucasian ancestry. Symptoms include intellectual disability, dislocated lenses of the eye, blood clots, brittle bones, and other skeletal abnormalities. The severity of the symptoms varies significantly. Some individuals with the more severe disease, known as the B6-non-responsive type, develop symptoms during infancy, while others with the milder B6-responsive disease may not clinically develop symptoms until childhood or early adulthood. The majority of affected individuals have a shortened lifespan due to the lack of effective treatment. Affected infants must be on a methionine-restricted diet in order to reduce the reduce symptoms and possibility of seizures. Several specific variants have been associated with milder or more severe disease phenotypes, and therefore the disease severity may be predicted in some individuals based on the variants inherited.

Mucopolysaccharidosis Type IVa (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.1156C>T, p.R386C, was detected in the *GALNS* gene (NM_000512.4). When this variant is present in trans with a pathogenic variant, it is considered to be causative for mucopolysaccharidosis type IVa. Therefore, this individual is expected to be at least a carrier for mucopolysaccharidosis type IVa. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Mucopolysaccharidosis Type IVa?

Mucopolysaccharidosis type IVa (MPS IVA), also known as Morquio syndrome A, is an autosomal recessive disorder caused by pathogenic variants in the gene *GALNS*. MPS IVA has a variable age of onset and rate of progression. It is generally diagnosed during the second year of life and is associated with joint laxity, ulnar deviation of the wrist, and inguinal hernia, but can also present with kyphoscoliosis, knock-knee, and pectus carinatum, which can lead to short stature, pain, and arthritis. Effects on other organ systems may include respiratory compromise, obstructive sleep apnea, valvular heart disease, hearing impairment, visual impairment, dental abnormalities, and hepatomegaly. Life expectancy for these patients varies depending on the severity of the disorder and the quality of care. Generally, patients with the severe form of the disorder do not survive beyond the third decade of life, while patients with an attenuated form may survive past 70 years of age.

Schimke Immunoosseous Dysplasia (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.2114C>T, p.T705I, was detected in the *SMARCAL1* gene (NM_014140.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for Schimke immunoosseous dysplasia. Therefore, this individual is expected to be at least a carrier for Schimke immunoosseous dysplasia. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Schimke Immunoosseous Dysplasia?

Schimke immunoosseous dysplasia is a pan-ethnic, autosomal recessive disease that is caused by pathogenic variants in the *SMARCAL1* gene. The condition is characterized by short stature, facial dysmorphism, discolored skin patches, skeletal abnormalities, and T-cell deficiency. Most individuals with this condition have proteinuria, which can develop into end stage renal disease. Although age of onset does not directly predict life expectancy, the severe form of the disease that presents in infancy usually results in reduced life expectancy. Individuals with the mild presentation typically survive into adulthood if renal complications are treated. Although pathogenic *SMARCAL1* variants that result in complete loss of protein function may cause a more severe form of the disease, no direct genotype-phenotype correlations have been reported.

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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.

Christie Buchovecky, Ph.D., Assistant Director, Reproductive Genomic
Laboratory Medical Consultant: George A. Diaz, M.D., Ph.D

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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				
Homocystinuria (*CBS*-Related)	CBS	AR	Carrier	c.919G>A, p.G307S, Pathogenic, Heterozygous (one copy)
Mucopolysaccharidosis Type IVa	GALNS	AR	Carrier	c.1156C>T, p.R386C, Pathogenic, Heterozygous (one copy)
Schimke Immunoosseous Dysplasia	SMARCAL1	AR	Carrier	c.2114C>T, p.T705I, Pathogenic, Heterozygous (one copy)
⊖ Negative				
2-Methylbutyrylglycinuria	ACADSB	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,800
3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency	HSD3B2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,300
3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC1*-Related)	MCCC1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,400
3-Methylcrotonyl-CoA Carboxylase Deficiency (*MCCC2*-Related)	MCCC2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,200
3-Methylglutaconic Aciduria, Type III	OPA3	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 50,000
3-Phosphoglycerate Dehydrogenase Deficiency	PHGDH	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 63,000
6-Pyruvoyl-Tetrahydropterin Synthase Deficiency	PTS	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,800
CD59-Mediated Hemolytic Anemia	CD59	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 415,000
Abetalipoproteinemia	MTTP	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,200
Achalasia-Addisonianism-Alacrimia Syndrome	AAAS	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,500
Achromatopsia (*CNGA3*-Related)	CNGA3	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 830
Achromatopsia (*CNGB3*-related)	CNGB3	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,600
Acrodermatitis Enteropathica	SLC39A4	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 12,000
Acute Infantile Liver Failure	TRMU	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 9,400
Acyl-CoA Oxidase I Deficiency	ACOX1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 39,000
Adams-Oliver Syndrome 4	EOGT	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 44,000
Adenosine Deaminase Deficiency	ADA	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,100
Adrenocorticotropic Hormone Deficiency	TBX19	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 35,000
Adrenoleukodystrophy, X-Linked	ABCD1	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 19,000
Agammaglobulinemia	BTK	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 250,000
Agenesis of the Corpus Callosum	FRMD4A	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,393,000
Aicardi-Goutieres Syndrome (*RNASEH2C*-Related)	RNASEH2C	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 11,000
Aicardi-Goutieres Syndrome (*SAMHD1*-Related)	SAMHD1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 10,000
Aicardi-Goutieres Syndrome (*TREX1*-Related)	TREX1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,200
Albinism, Oculocutaneous, Type III	TYRP1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,500
Alkaptonuria	HGD	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,100
Alpha-Mannosidosis	MAN2B1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,200

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Alpha-Thalassemia	HBA1/HBA2	AR	Reduced Risk	*HBA1* Copy Number: 2 *HBA2* Copy Number: 2 No pathogenic copy number variants detected *HBA1/ HBA2* Sequencing: Negative **Personalized Residual Risk:** 1 in 10,000
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 1,800
Alport Syndrome (*COL4A4*-Related)	COL4A4	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
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 3,800
Andermann Syndrome	SLC12A6	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 151,000
Antley-Bixler Syndrome (*POR*-Related)	POR	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Argininemia	ARG1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,500
Argininosuccinic Aciduria	ASL	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Aromatase Deficiency	CYP19A1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,400
Arthrogryposis, Mental Retardation, and Seizures	SLC35A3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 454,000
Asparagine Synthetase Deficiency	ASNS	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 202,000
Aspartylglycosaminuria	AGA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
Ataxia With Isolated Vitamin E Deficiency	TTPA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 61,000
Ataxia-Telangiectasia	ATM	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Ataxia-Telangiectasia-Like Disorder 1	MRE11	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,500
Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay	SACS	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
BH4-Deficient Hyperphenylalaninemia C	QDPR	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,100
BH4-Deficient Hyperphenylalaninemia D	PCBD1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,000
Bardet-Biedl Syndrome (*ARL6*-Related)	ARL6	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 29,000
Bardet-Biedl Syndrome (*BBS10*-Related)	BBS10	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
Bardet-Biedl Syndrome (*BBS12*-Related)	BBS12	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,900
Bardet-Biedl Syndrome (*BBS1*-Related)	BBS1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,400
Bardet-Biedl Syndrome (*BBS2*-Related)	BBS2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Bardet-Biedl Syndrome (*BBS4*-Related)	BBS4	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 22,000
Bare Lymphocyte Syndrome, Type II	CIITA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 35,000
Barth Syndrome	TAZ	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 183,000
Bartter Syndrome, Type 3	CLCNKB	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 740
Bartter Syndrome, Type 4A	BSND	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 91,000
Bernard-Soulier Syndrome, Type A1	GP1BA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 42,000
Bernard-Soulier Syndrome, Type C	GP9	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,300
Beta-Globin-Related Hemoglobinopathies	HBB	AR	Reduced Risk	**Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies):** 1 in 2,000 **Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbS Variant):** 1 in 790,000 **Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant):** 1 in 2,107,000
Beta-Ketothiolase Deficiency	ACAT1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,400
Beta-Mannosidosis	MANBA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,100
Bilateral Frontoparietal Polymicrogyria	GPR56	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 203,000
Biotinidase Deficiency	BTD	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 500
Bloom Syndrome	BLM	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,400
Canavan Disease	ASPA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Carbamoylphosphate Synthetase I Deficiency	CPS1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100

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Carnitine Acylcarnitine Translocase Deficiency	*SLC25A20*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,100
Carnitine Palmitoyltransferase IA Deficiency	*CPT1A*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 24,000
Carnitine Palmitoyltransferase II Deficiency	*CPT2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 670
Carpenter Syndrome	*RAB23*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 21,000
Cartilage-Hair Hypoplasia	*RMRP*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 960
Catecholaminergic Polymorphic Ventricular Tachycardia	*CASQ2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,900
Central Hypothyroidism and Testicular Enlargement	*IGSF1*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 781,000
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 2,100
Cerebral Creatine Deficiency Syndrome 3	*GATM*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 7,900
Cerebral Dysgenesis, Neuropathy, Ichthyosis, and Palmoplantar Keratoderma Syndrome	*SNAP29*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,730,000
Cerebrotendinous Xanthomatosis	*CYP27A1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,900
Charcot-Marie-Tooth Disease, Type 4D	*NDRG1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 730,000
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
Chediak-Higashi Syndrome	*LYST*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 7,100
Chondrodysplasia Punctata	*ARSE*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 862,000
Choreoacanthocytosis	*VPS13A*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 13,000
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 5,000
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 12,000
Citrullinemia, Type 1	*ASS1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,500
Cockayne Syndrome, Type A	*ERCC8*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,900
Cockayne Syndrome, Type B and other *ERCC6*-Related Disorders	*ERCC6*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,100
Cohen Syndrome	*VPS13B*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,400
Combined Factor V and VIII Deficiency	*LMAN1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 102,000
Combined Malonic and Methylmalonic Aciduria	*ACSF3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,400
Combined Oxidative Phosphorylation Deficiency 1	*GFM1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 13,000
Combined Oxidative Phosphorylation Deficiency 3	*TSFM*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 27,000
Combined Pituitary Hormone Deficiency 1	*POU1F1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,900
Combined Pituitary Hormone Deficiency 2	*PROP1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,800
Combined Pituitary Hormone Deficiency 3	*LHX3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 140,000
Combined SAP Deficiency	*PSAP*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 44,000
Cone-Rod Dystrophy 6 / Leber Congenital Amaurosis 1	*GUCY2D*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,200
Congenital Adrenal Hyperplasia due to 11-Beta-Hydroxylase Deficiency	*CYP11B1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 520
Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency	*CYP17A1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,800
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 200 **Personalized Residual Risk (Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency (Classic))**: 1 in 1,300
Congenital Adrenal Hypoplasia (*NR0B1* Related)	*NR0B1*	XL	Reduced Risk	**Personalized Residual Risk** 1 in 353,000
Congenital Adrenal Insufficiency (*CYP11A1*-Related)	*CYP11A1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,100

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Congenital Amegakaryocytic Thrombocytopenia	MPL	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,100
Congenital Bile Acid Synthesis Defect (*AKR1D1*-Related)	AKR1D1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,900
Congenital Bile Acid Synthesis Defect (*HSD3B7*-Related)	HSD3B7	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,900
Congenital Disorder of Deglycosylation	NGLY1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 14,000
Congenital Disorder of Glycosylation, Type Ia	PMM2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 540
Congenital Disorder of Glycosylation, Type Ib	MPI	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,600
Congenital Disorder of Glycosylation, Type Ic	ALG6	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Congenital Disorder of Glycosylation, Type Im	DOLK	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 134,000
Congenital Dyserythropoietic Anemia Type 2	SEC23B	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Congenital Dyserythropoietic Anemia, Type Ia	CDAN1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 470
Congenital Ichthyosis 4A and 4B	ABCA12	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,100
Congenital Insensitivity to Pain with Anhidrosis	NTRK1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,700
Congenital Muscular Dystrophy (*LAMA2*-Related)	LAMA2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 640
Congenital Myasthenic Syndrome (*CHAT*-Related)	CHAT	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,100
Congenital Myasthenic Syndrome (*CHRNE*-Related)	CHRNE	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,100
Congenital Myasthenic Syndrome (*DOK7*-Related)	DOK7	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Congenital Myasthenic Syndrome (*RAPSN*-Related)	RAPSN	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,900
Congenital Neutropenia (*HAX1*-Related)	HAX1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 82,000
Congenital Neutropenia (*VPS45*-Related)	VPS45	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 163,000
Congenital Nongoitrous Hypothyroidism 1	TSHR	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Congenital Nongoitrous Hypothyroidism 4	TSHB	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 118,000
Congenital Secretory Chloride Diarrhea 1	SLC26A3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,400
Corneal Dystrophy and Perceptive Deafness	SLC4A11	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,600
Corticosterone Methyloxidase Deficiency	CYP11B2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Cystic Fibrosis	CFTR	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 440
Cystinosis	CTNS	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,700
Cystinuria (*SLC3A1*-Related)	SLC3A1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 590
Cytochrome C Oxidase Deficiency / Leigh Syndrome (*COX15*-Related)	COX15	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,300
D-Bifunctional Protein Deficiency	HSD17B4	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,000
Deafness, Autosomal Recessive 3	MYO15A	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 240
Deafness, Autosomal Recessive 59	PJVK	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 57,000
Deafness, Autosomal Recessive 7	TMC1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Deafness, Autosomal Recessive 76	SYNE4	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 43,000
Deafness, Autosomal Recessive 77	LOXHD1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,700
Deafness, Autosomal Recessive 8/10	TMPRSS3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 510
Deafness, Autosomal Recessive 9	OTOF	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Desbuquois Dysplasia 1	CANT1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 24,000
Desmosterolosis	DHCR24	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 27,000
Diaphanospondylodysostosis	BMPER	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 18,000
Distal Renal Tubular Acidosis and other *SLC4A1*-related Disorders	SLC4A1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
Duchenne Muscular Dystrophy / Becker Muscular Dystrophy	DMD	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Dyskeratosis Congenita (*DKC1*-related)	DKC1	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 9,259,000
Dyskeratosis Congenita (*RTEL1*-Related)	RTEL1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,800
Dystrophic Epidermolysis Bullosa	COL7A1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 900

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Ehlers-Danlos Syndrome, Type VI	PLOD1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Ehlers-Danlos Syndrome, Type VIIC	ADAMTS2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 243,000
Ellis-Van Creveld Syndrome (*EVC2*-Related)	EVC2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,300
Ellis-van Creveld Syndrome (*EVC*-Related)	EVC	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
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 1,600
Ethylmalonic Encephalopathy	ETHE1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,400
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 VII Deficiency	F7	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 450
Factor XI Deficiency	F11	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,500
Familial Autosomal Recessive Hypercholesterolemia	LDLRAP1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 136,000
Familial Dysautonomia	IKBKAP	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 51,000
Familial Hypercholesterolemia	LDLR	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 280
Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	HADH	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,200
Familial Hyperinsulinism (*ABCC8*-Related)	ABCC8	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 450
Familial Hyperinsulinism (*KCNJ11*-Related)	KCNJ11	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,300
Familial Hyperphosphatemic Tumoral Calcinosis	GALNT3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,800
Familial Mediterranean Fever	MEFV	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Fanconi Anemia, Group A	FANCA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Fanconi Anemia, Group C	FANCC	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Fanconi Anemia, Group G	FANCG	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 28,000
Fanconi-Bickel Syndrome	SLC2A2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,000
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 19,000
Fructose-1,6-Bisphosphatase Deficiency	FBP1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,600
Fucosidosis	FUCA1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,200
Fumarase Deficiency	FH	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,500
Fundus Albipunctatus	RDH5	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
GRACILE Syndrome and Other *BCS1L*-Related Disorders	BCS1L	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,900
Galactokinase Deficiency	GALK1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
Galactose Epimerase Deficiency	GALE	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,600
Galactosemia	GALT	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
Galactosialidosis	CTSA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,900
Gaucher Disease	GBA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Generalized Thyrotropin-Releasing Hormone Resistance	TRHR	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 104,000
Geroderma Osteodysplasticum	GORAB	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 70,000
Gitelman Syndrome	SLC12A3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 290
Glanzmann Thrombasthenia (*ITGA2B*-Related)	ITGA2B	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Glanzmann Thrombasthenia (*ITGB3*-Related)	ITGB3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Glutaric Acidemia, Type I	GCDH	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
Glutaric Acidemia, Type IIa	ETFA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,700
Glutaric Acidemia, Type IIb	ETFB	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Glutaric Acidemia, Type IIc	ETFDH	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Glutathione Synthetase Deficiency	GSS	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,500

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Glycine Encephalopathy (*AMT*-Related)	AMT	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,700
Glycine Encephalopathy (*GLDC*-Related)	GLDC	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 760
Glycogen Storage Disease, Type 0	GYS2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,200
Glycogen Storage Disease, Type II	GAA	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 520
Glycogen Storage Disease, Type III	AGL	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,600
Glycogen Storage Disease, Type IV / Adult Polyglucosan Body Disease	GBE1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,400
Glycogen Storage Disease, Type IXb	PHKB	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,600
Glycogen Storage Disease, Type Ia	G6PC	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,300
Glycogen Storage Disease, Type Ib	SLC37A4	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 7,300
Glycogen Storage Disease, Type V	PYGM	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,200
Glycogen Storage Disease, Type VI	PYGL	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,600
Glycogen Storage Disease, Type VII	PFKM	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,300
Gray Platelet Syndrome	NBEAL2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,800
Growth Hormone Deficiency, Type IB	GHRHR	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,900
HMG-CoA Lyase Deficiency	HMGCL	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,700
Hemochromatosis, Type 2A	HFE2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 12,000
Hemochromatosis, Type 3	TFR2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 11,000
Hereditary Fructose Intolerance	ALDOB	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,900
Hereditary Spastic Paraparesis 49	TECPR2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 116,000
Hermansky-Pudlak Syndrome, Type 1	HPS1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,500
Hermansky-Pudlak Syndrome, Type 3	HPS3	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 49,000
Hermansky-Pudlak Syndrome, Type 4	HPS4	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 35,000
Hermansky-Pudlak Syndrome, Type 6	HPS6	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 87,000
Hmg-CoA Synthase 2 Deficiency	HMGCS2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,000
Holocarboxylase Synthetase Deficiency	HLCS	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,500
Homocystinuria due to *MTHFR* Deficiency	MTHFR	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,300
Homocystinuria, cblE Type	MTRR	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 9,600
Homocystinuria-Megaloblastic Anemia, Cobalamin G Type	MTR	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,100
Hydrocephalus	L1CAM	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 40,000
Hydrolethalus Syndrome	HYLS1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 52,000
Hyper-Igm Syndrome	CD40LG	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 1,167,000
Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome	SLC25A15	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,700
Hyperuricemia, Pulmonary Hypertension, Renal Failure, and Alkalosis	SARS2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 23,000
Hypohidrotic Ectodermal Dysplasia 1	EDA	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 22,000
Hypomagnesemia 1	TRPM6	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 11,000
Hypomyelinating Leukodystrophy 3	AIMP1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 341,000
Hypomyelinating Leukodystrophy 12	VPS11	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 72,000
Hypoparathyroidism-Retardation-Dysmorphic Syndrome	TBCE	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 21,000
Hypophosphatasia	ALPL	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 790
Hypophosphatemic Rickets with Hypercalciuria	SLC34A3	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,200
Hypotrichosis 8 / Autosomal Recessive Woolly Hair 1	LPAR6	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 27,000
Immunodeficiency 18	CD3E	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 73,000
Immunodeficiency 19	CD3D	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 46,000
Inclusion Body Myopathy 2	GNE	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,000
Infantile Cerebral and Cerebellar Atrophy	MED17	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 129,000
Infantile Neuroaxonal Dystrophy 1 and other *PLA2G6*-Related Disorders	PLA2G6	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 690

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Intrahepatic Cholestasis	ATP8B1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,400
Isovaleric Acidemia	IVD	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,000
Joubert Syndrome 2	TMEM216	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 152,000
Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronophthisis 1	NPHP1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 21,000
Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome	RPGRIP1L	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 32,000
Junctional Epidermolysis Bullosa (*COL17A1*-Related)	COL17A1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 25,000
Junctional Epidermolysis Bullosa (*ITGA6*-Related)	ITGA6	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 125,000
Junctional Epidermolysis Bullosa (*ITGB4*-Related)	ITGB4	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,400
Junctional Epidermolysis Bullosa (*LAMA3*-Related)	LAMA3	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 21,000
Junctional Epidermolysis Bullosa (*LAMB3*-Related)	LAMB3	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,900
Junctional Epidermolysis Bullosa (*LAMC2*-Related)	LAMC2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 77,000
Kohlschutter-Tonz Syndrome	ROGDI	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,300
Krabbe Disease	GALC	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 860
Lamellar Ichthyosis, Type 1	TGM1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,500
Laron Dwarfism	GHR	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,700
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 5,500
Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14	TULP1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,800
Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20	RPE65	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,500
Leber Congenital Amaurosis 4	AIPL1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,100
Leber Congenital Amaurosis 5	LCA5	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 14,000
Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy	CRB1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 990
Leigh Syndrome (*NDUFS7*-Related)	NDUFS7	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 26,000
Leigh Syndrome (*SURF1*-Related)	SURF1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,400
Leigh Syndrome, French-Canadian Type	LRPPRC	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 32,000
Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogryposis with Anterior Horn Cell Disease	GLE1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 10,000
Lethal Congenital Contracture Syndrome 2	ERBB3	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 96,000
Lethal Congenital Contracture Syndrome 3	PIP5K1C	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 318,000
Leukoencephalopathy with Vanishing White Matter	EIF2B5	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,300
Limb-Girdle Muscular Dystrophy, Type 2A	CAPN3	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 960
Limb-Girdle Muscular Dystrophy, Type 2B	DYSF	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,100
Limb-Girdle Muscular Dystrophy, Type 2C	SGCG	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,900
Limb-Girdle Muscular Dystrophy, Type 2D	SGCA	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,500
Limb-Girdle Muscular Dystrophy, Type 2E	SGCB	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 31,000
Limb-Girdle Muscular Dystrophy, Type 2F	SGCD	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 52,000
Limb-Girdle Muscular Dystrophy, Type 2H	TRIM32	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 10,000
Limb-Girdle Muscular Dystrophy, Type 2I	FKRP	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,400
Limb-Girdle Muscular Dystrophy, Type 2L	ANO5	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 660
Lipoamide Dehydrogenase Deficiency	DLD	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 14,000
Lipoid Adrenal Hyperplasia	STAR	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,600
Lipoprotein Lipase Deficiency	LPL	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,400

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Long-Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency	HADHA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Lowe Syndrome	OCRL	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 1,375,000
Lysinuric Protein Intolerance	SLC7A7	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
MEDNIK Syndrome	AP1S1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 211,000
Malonyl-CoA Decarboxylase Deficiency	MLYCD	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,800
Maple Syrup Urine Disease, Type 1a	BCKDHA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,100
Maple Syrup Urine Disease, Type 1b	BCKDHB	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Maple Syrup Urine Disease, Type 2	DBT	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,600
Meckel Syndrome 1 / Bardet-Biedl Syndrome 13	MKS1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Medium Chain Acyl-CoA Dehydrogenase Deficiency	ACADM	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Megalencephalic Leukoencephalopathy with Subcortical Cysts	MLC1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,300
Megaloblastic Anemia 1	AMN	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,300
Menkes Disease	ATP7A	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 172,000
Mental Retardation, Autosomal Recessive 3	CC2D1A	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 220,000
Metachromatic Leukodystrophy	ARSA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Methionine Adenosyltransferase I/III Deficiency	MAT1A	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,900
Methylmalonic Acidemia (*MMAA*-Related)	MMAA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 15,000
Methylmalonic Acidemia (*MMAB*-Related)	MMAB	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Methylmalonic Acidemia (*MUT*-Related)	MUT	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Methylmalonic Aciduria and Homocystinuria, Cobalamin C Type	MMACHC	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,800
Methylmalonic Aciduria and Homocystinuria, Cobalamin D Type	MMADHC	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 219,000
Methylmalonic Aciduria and Homocystinuria, Cobalamin F Type	LMBRD1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
Methylmalonyl-CoA Epimerase Deficiency	MCEE	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 98,000
Microphthalmia / Anophthalmia	VSX2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 40,000
Mitochondrial Complex I Deficiency (*ACAD9*-Related)	ACAD9	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Mitochondrial Complex I Deficiency (*NDUFA11*-Related)	NDUFA11	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 414,000
Mitochondrial Complex I Deficiency (*NDUFAF5*-Related)	NDUFAF5	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 98,000
Mitochondrial Complex I Deficiency (*NDUFS6*-Related)	NDUFS6	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 353,000
Mitochondrial Complex I Deficiency (*NDUFV1*-Related)	NDUFV1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 870
Mitochondrial Complex I Deficiency / Leigh Syndrome (*FOXRED1*-Related)	FOXRED1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (*NDUFAF2*-Related)	NDUFAF2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 168,000
Mitochondrial Complex I Deficiency / Leigh Syndrome (*NDUFS4*-Related)	NDUFS4	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 41,000
Mitochondrial Complex IV Deficiency (*COX20*-related)	COX20	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 42,000
Mitochondrial Complex IV Deficiency (*COX6B1*-related)	COX6B1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,116,000
Mitochondrial Complex IV Deficiency (*APOPT1*-Related)	APOPT1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,200
Mitochondrial Complex IV Deficiency (*PET100*-Related)	PET100	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 469,000
Mitochondrial Complex IV Deficiency (*SCO1*-related)	SCO1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
Mitochondrial Complex IV Deficiency / Leigh Syndrome (*COX10*-Related)	COX10	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,200
Mitochondrial DNA Depletion Syndrome 2	TK2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,900
Mitochondrial DNA Depletion Syndrome 3	DGUOK	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,200

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Disease	Gene	Inheritance	Risk	Residual Risk
Mitochondrial DNA Depletion Syndrome 4A and 4B and other *POLG*-Related Disorders	POLG	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 320
Mitochondrial DNA Depletion Syndrome 5	SUCLA2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 78,000
Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy	MPV17	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,400
Mitochondrial Myopathy and Sideroblastic Anemia 1	PUS1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 449,000
Mitochondrial Trifunctional Protein Deficiency (*HADHB*-Related)	HADHB	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,000
Molybdenum Cofactor Deficiency A	MOCS1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,700
Mucolipidosis II / IIIA	GNPTAB	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,100
Mucolipidosis III Gamma	GNPTG	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 68,000
Mucolipidosis IV	MCOLN1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 9,400
Mucopolysaccharidosis Type I	IDUA	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,300
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 2,700
Mucopolysaccharidosis Type IIIB	NAGLU	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 950
Mucopolysaccharidosis Type IIIC	HGSNAT	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,200
Mucopolysaccharidosis Type IIID	GNS	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 137,000
Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis	GLB1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,700
Mucopolysaccharidosis VII	GUSB	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,600
Mucopolysaccharidosis type IX	HYAL1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 149,000
Mucopolysaccharidosis type VI	ARSB	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,300
Mulibrey Nanism	TRIM37	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 31,000
Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1	PIGN	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,800
Multiple Pterygium Syndrome	CHRNG	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 9,900
Multiple Sulfatase Deficiency	SUMF1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 69,000
Muscle-Eye-Brain Disease and Other *POMGNT1*-Related Congenital Muscular Dystrophy-Dystroglycanopathies	POMGNT1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,200
Myoneurogastrointestinal Encephalopathy	TYMP	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,100
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 3,200
Nemaline Myopathy 2	NEB	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,400
Nephrogenic Diabetes Insipidus, Type II	AQP2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,400
Nephrogenic Diabetes insipidus (*AVPR2*-related) / Nephrogenic Syndrome of Inappropriate Antidiuresis	AVPR2	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 471,000
Nephronophthisis 2	INVS	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 56,000
Nephrotic Syndrome (*NPHS1*-Related) / Congenital Finnish Nephrosis	NPHS1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 920
Nephrotic Syndrome (*NPHS2*-Related) / Steroid-Resistant Nephrotic Syndrome	NPHS2	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 780
Neurodegeneration due to Cerebral Folate Transport Deficiency	FOLR1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,300
Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies	PLAA	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 229,000
Neuronal Ceroid-Lipofuscinosis (*CLN3*-Related)	CLN3	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 9,200
Neuronal Ceroid-Lipofuscinosis (*CLN5*-Related)	CLN5	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,300
Neuronal Ceroid-Lipofuscinosis (*CLN6*-Related)	CLN6	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,600
Neuronal Ceroid-Lipofuscinosis (*CLN8*-Related)	CLN8	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 3,100
Neuronal Ceroid-Lipofuscinosis (*MFSD8*-Related)	MFSD8	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,200
Neuronal Ceroid-Lipofuscinosis (*PPT1*-Related)	PPT1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 7,500
Neuronal Ceroid-Lipofuscinosis (*TPP1*-Related)	TPP1	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,300

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Niemann-Pick Disease (*SMPD1*-Related)	*SMPD1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,800
Niemann-Pick Disease, Type C (*NPC1*-Related)	*NPC1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 690
Niemann-Pick Disease, Type C (*NPC2*-Related)	*NPC2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,600
Nijmegen Breakage Syndrome	*NBN*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 14,000
Non-Syndromic Hearing Loss (*GJB2*-Related)	*GJB2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 600
Oculocutaneous Albinism, Type IA / IB	*TYR*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 240
Oculocutaneous Albinism, Type IV	*SLC45A2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 830
Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome	*WNT10A*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,900
Omenn Syndrome (*RAG2*-Related)	*RAG2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 17,000
Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type	*DCLRE1C*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,500
Omenn Syndrome and other *RAG1*-Related Disorders	*RAG1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 850
Ornithine Aminotransferase Deficiency	*OAT*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,400
Ornithine Transcarbamylase Deficiency	*OTC*	XL	Reduced Risk	**Personalized Residual Risk**: 1 in 103,000
Osteogenesis Imperfecta, Type XI	*FKBP10*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 9,500
Osteopetrosis 1	*TCIRG1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,700
Osteopetrosis 8	*SNX10*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 16,000
Otospondylomegaepiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2	*COL11A2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,700
Papillon-Lefevre Syndrome	*CTSC*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,000
Pendred Syndrome	*SLC26A4*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 390
Peroxisome Biogenesis Disorder 3A and 3B	*PEX12*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 30,000
Peroxisome Biogenesis Disorder 7A and 7B	*PEX26*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 70,000
Phenylalanine Hydroxylase Deficiency	*PAH*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 340
Polycystic Kidney Disease, Autosomal Recessive	*PKHD1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 450
Polyglandular Autoimmune Syndrome, Type 1	*AIRE*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,300
Pontocerebellar Hypoplasia, Type 1A	*VRK1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 25,000
Pontocerebellar Hypoplasia, Type 1B	*EXOSC3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 10,000
Pontocerebellar Hypoplasia, Type 2A and Type 4	*TSEN54*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 4,700
Pontocerebellar Hypoplasia, Type 2E	*VPS53*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 139,000
Pontocerebellar Hypoplasia, Type 6	*RARS2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 8,600
Primary Carnitine Deficiency	*SLC22A5*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,500
Primary Ciliary Dyskinesia (*CCDC103*-Related)	*CCDC103*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 27,000
Primary Ciliary Dyskinesia (*CCDC151*-Related)	*CCDC151*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 59,000
Primary Ciliary Dyskinesia (*CCDC39*-Related)	*CCDC39*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 12,000
Primary Ciliary Dyskinesia (*DNAH5*-Related)	*DNAH5*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,500
Primary Ciliary Dyskinesia (*DNAI1*-Related)	*DNAI1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,000
Primary Ciliary Dyskinesia (*DNAI2*-Related)	*DNAI2*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 76,000
Primary Ciliary Dyskinesia (*RSPH9*-Related)	*RSPH9*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 253,000
Primary Coenzyme Q10 Deficiency 7	*COQ4*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 12,000
Primary Congenital Glaucoma 3A	*CYP1B1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 880
Primary Hyperoxaluria, Type 1	*AGXT*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 1,900
Primary Hyperoxaluria, Type 2	*GRHPR*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 11,000
Primary Hyperoxaluria, Type 3	*HOGA1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 2,400
Progressive Cerebello-Cerebral Atrophy	*SEPSECS*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 6,400
Progressive Familial Intrahepatic Cholestasis, Type 2	*ABCB11*	AR	Reduced Risk	**Personalized Carized Residual Risk**: 1 in 950
Progressive Myoclonic Epilepsy, Type 1B	*PRICKLE1*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 98,000
Progressive Pseudorheumatoid Dysplasia	*WISP3*	AR	Reduced Risk	**Personalized Residual Risk**: 1 in 5,600

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Prolidase Deficiency	PEPD	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 30,000
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 12,000
Pulmonary Surfactant Dysfunction	ABCA3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Pycnodysostosis	CTSK	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,100
Pyridoxamine 5'-Phosphate Oxidase Deficiency	PNPO	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Pyridoxine-Dependent Epilepsy	ALDH7A1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,100
Pyruvate Carboxylase Deficiency	PC	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,000
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 15,000
Renal Tubular Acidosis and Deafness	ATP6V1B1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,600
Retinitis Pigmentosa 25	EYS	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Retinitis Pigmentosa 26	CERKL	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 13,000
Retinitis Pigmentosa 28	FAM161A	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 34,000
Retinitis Pigmentosa 36	PRCD	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 304,000
Retinitis Pigmentosa 59	DHDDS	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 601,000
Retinitis Pigmentosa 64 / Bardet-Biedl Syndrome 21 / Cone-Rod Dystrophy 16	C8ORF37	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 168,000
Rh Deficiency Syndrome	RHAG	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 46,000
Rhizomelic Chondrodysplasia Punctata, Type 1	PEX7	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Rhizomelic Chondrodysplasia Punctata, Type 3	AGPS	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 620,000
Roberts Syndrome	ESCO2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 139,000
Salla Disease	SLC17A5	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,400
Salt and Pepper Developmental Regression Syndrome	ST3GAL5	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 25,000
Sandhoff Disease	HEXB	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Seckel Syndrome 5 / Microcephaly 9	CEP152	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Segawa Syndrome	TH	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,100
Sepiapterin Reductase Deficiency	SPR	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 35,000
Severe Combined Immunodeficiency (*IL7R*-Related)	IL7R	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 20,000
Severe Combined Immunodeficiency (*JAK3*-Related)	JAK3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,100
Severe Combined Immunodeficiency (*PTPRC*-Related)	PTPRC	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 8,500
Severe Congenital Neutropenia 4	G6PC3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 10,000
Severe Neonatal Hyperparathyroidism	CASR	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,700
Short Stature, Onychodysplasia, Facial Dysmorphism, and Hypotrichosis	POC1A	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 108,000
Short-Chain Acyl-CoA Dehydrogenase Deficiency	ACADS	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 660
Shwachman-Diamond Syndrome	SBDS	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,700
Sialidosis, Type I and Type II	NEU1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Sjogren-Larsson Syndrome	ALDH3A2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,500
Smith-Lemli-Opitz Syndrome	DHCR7	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 750
Spastic Paraplegia 15	ZFYVE26	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 46,000
Spastic Tetraplegia, Thin Corpus Callosum, and Progressive Microcephaly	SLC1A4	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 855,000
Spherocytosis, Type 5	EPB42	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
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 1,107

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Disease	Gene	Inheritance	Result	Risk
Spinal Muscular Atrophy with Respiratory Distress 1 / Charcot-Marie-Tooth Disease, Type 2S	IGHMBP2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,200
Spinocerebellar Ataxia with Axonal Neuropathy 3	COA7	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Spondylocostal Dysostosis 1	DLL3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,200
Spondylometaepiphyseal Dysplasia (*DDR2*-Related)	DDR2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 236,000
Spondylothoracic Dysostosis	MESP2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 382,000
Steel Syndrome	COL27A1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 93,000
Stuve-Wiedemann Syndrome	LIFR	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,000
Sulfate Transporter-Related Osteochondrodysplasia	SLC26A2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Tay-Sachs Disease	HEXA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Thiamine-Responsive Megaloblastic Anemia Syndrome	SLC19A2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Thyroid Dyshormonogenesis 1	SLC5A5	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 45,000
Thyroid Dyshormonogenesis 2A	TPO	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 910
Thyroid Dyshormonogenesis 3	TG	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 850
Thyroid Dyshormonogenesis 4	IYD	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,800
Thyroid Dyshormonogenesis 5	DUOXA2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 29,000
Thyroid Dyshormonogenesis 6	DUOX2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 190
Trichohepatoenteric Syndrome 1	TTC37	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 14,000
Tyrosinemia, Type I	FAH	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,900
Tyrosinemia, Type II	TAT	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,800
Tyrosinemia, Type III	HPD	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 266,000
Usher Syndrome, Type IB	MYO7A	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,000
Usher Syndrome, Type IC	USH1C	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600
Usher Syndrome, Type ID	CDH23	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,400
Usher Syndrome, Type IF	PCDH15	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,800
Usher Syndrome, Type IIA	USH2A	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 290
Usher Syndrome, Type III	CLRN1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,300
Very Long Chain Acyl-CoA Dehydrogenase Deficiency	ACADVL	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 920
Vitamin D-Dependent Rickets, Type I	CYP27B1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 7,900
Vitamin D-Resistant Rickets, Type IIA	VDR	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 17,000
Walker-Warburg Syndrome and Other *FKTN*-Related Dystrophies	FKTN	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 4,200
Werner Syndrome	WRN	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 9,200
Wilson Disease	ATP7B	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 350
Wiskott-Aldrich Syndrome (*WAS*-Related)	WAS	XL	Reduced Risk	**Personalized Residual Risk:** 1 in 1,203,000
Wolcott-Rallison Syndrome	EIF2AK3	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 22,000
Wolman Disease / Cholesteryl Ester Storage Disease	LIPA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,200
Woodhouse-Sakati Syndrome	DCAF17	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 81,000
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
Xeroderma Pigmentosum (*POLH*-Related)	POLH	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 5,900
Xeroderma Pigmentosum, Group A	XPA	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 11,000
Xeroderma Pigmentosum, Group C	XPC	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 12,000
Xeroderma Pigmentosum, Group G	ERCC5	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 3,000
Zellweger Syndrome Spectrum (*PEX10*-Related)	PEX10	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 6,300
Zellweger Syndrome Spectrum (*PEX1*-Related)	PEX1	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 2,000
Zellweger Syndrome Spectrum (*PEX2*-Related)	PEX2	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 77,000

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Zellweger Syndrome Spectrum (*PEX6*-Related)	*PEX6*	AR	Reduced Risk	**Personalized Residual Risk:** 1 in 1,600

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 2+0 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.*3+80T>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.*3+80T>G is likely indicative of a silent (2+0) carrier. In individuals with two copies of *SMN1* with African American, Hispanic or Caucasian ancestry, the presence or absence of c.*3+80T>G significantly increases or decreases, respectively, the likelihood of being a silent 2+0 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.

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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.

Exceptions: ABCD1 (NM_000033.3) exons 8 and 9; *ACADSB* (NM_ 001609.3) chr10:124,810,695-124,810,707 (partial exon 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); *ALDH7A1* (NM_001182.4) chr5:125,911,150-125,911,163 (partial exon 7) and chr5:125,896,807-125,896,821 (partial exon 10); *ALMS1* (NM_015120.4) chr2:73,612,990-73,613,041 (partial exon 1); *APOPT1* (NM_ 032374.4) chr14:104,040,437-104,040,455 (partial exon 3); *CDAN1* (NM_138477.2) exon 2; *CEP152* (NM_014985.3) chr15:49,061,146-49,061,165 (partial exon 14) and exon 22; *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); *COX10* (NM_001303.3) exon 6; *CYP11B1* (NM_000497.3) exons 3-7; *CYP11B2* (NM_000498.3) exons 3-7; *DNAI2* (NM_023036 4) chr17:72,308,136-72,308,147 (partial exon 12); *DOK7* (NM_173660.4) chr4:3,465,131-3,465,161 (partial exon 1) and exon 2; *DUOX2* (NM_014080.4) exons 6-8; *EIF2AK3* (NM_004836.5 exon 8; *EVC* (NM_1537172) 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; *GHR* (NM_000163 4) exon 3; *GYS2* (NM_021957.3) chr12 21,699,370-21,699,409 (partial exon 12); *HGSNAT* (NM_152419.2) exon 1; *IDS* (NM_000202.6 exon 3; *ITGB4* (NM_000213 4) chr17:73,749,976-73,750,060 (partial exon 33); *JAK3* (NM_000215.3) chr19:17,950,462-17,950,483 (partial exon 10); *LIFR* (NM_002310.5 exon 19; *LMBRD1* (NM_018368.3) chr6:70,459,226-70,459,257 (partial exon 5), chr6:70,447,828-70,447,836 (partial exon 7) and exon 12; *LYST* (NM_000081.3) chr1 235,944,158-235,944,176 (partial exon 16) and chr1 235,875,350-235,875,362 (partial exon 43); *MLYCD* (NM_012213.2) chr16:83,933,242-83,933,282 (partial exon 1); *MTR* (NM_000254 2) chr1 237,024,418-237,024,439 (partial exon 20) and chr1 237,038,019-237,038,029 (partial exon 24); *NBEAL2* (NM_015175 2) chr3 47,021,385-47,021,407 (partial exon 1); *NEB* (NM_001271208.1 exons 82-105; *NPC1* (NM_000271 4) chr18 21,123,519-21,123,538 (partial exon 14); *NPHP1* (NM_000272.3) chr2:110,937,251-110,937,263 (partial exon 3); *OCRL* (NM_000276.3) chrX:128,674,450-128,674,460 (partial exon 1); *PHKB* (NM_000293.2) exon 1 and chr16:47,732,498-47,732,504 (partial exon 30); *PIGN* (NM_176787.4) chr18:59,815,547-59,815,576 (partial exon 8); *PIP5K1C* (NM_012398.2) exon 1 and chr19:3637602-3637616 (partial exon 17); *POU1F1* (NM_000306.3) exon 5; *PTPRC* (NM_002838 4) exons 11 and 23; *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; *ST3GAL5* (NM_003896.3) exon 1; *SURF1* (NM_003172.3) chr9:136,223,269-136,223,307 (partial exon 1); *TRPM6* (NM_017662 4) chr9:77,362,800-77,362,811 (partial exon 31); *TSEN54* (NM_207346.2) exon 1; *TYR* (NM_000372.4) exon 5; *VWF* (NM_000552.3) exons 24-26, chr12:6,125,675-6,125,684 (partial exon 30), chr12:6,121,244-6,121,265 (partial exon 33), and exon 34.

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%)

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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%)

Th 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 $\Delta\Delta$Ct 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 (cis/trans 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™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.

Tay-Sachs Disease (TSD) Enzyme Analysis (Analytical Detection Rate ≥98%)

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Hexosaminidase activity and Hex A% activity were measured by a standard heat-inactivation, fluorometric method using artificial 4-MU-β-N-acetyl glucosaminide (4-MUG) substrate. This assay is highly sensitive and accurate in detecting Tay-Sachs carriers and individuals affected with TSD. Normal ranges of Hex A% activity are 55.0-72.0 for white blood cells and 58.0-72.0 for plasma. It is estimated that less than 0.5% of Tay-Sachs carriers have non-carrier levels of percent Hex A activity, and therefore may not be identified by this assay. In addition, this assay may detect individuals that are carriers of or are affected with Sandhoff disease. False positive results may occur if benign variants, such as pseudodeficiency alleles, interfere with the enzymatic assay. False negative results may occur if both *HEXA* and *HEXB* pathogenic or pseudodeficiency variants are present in the same individual.

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.

SELECTED REFERENCES

Carrier Screening

Grody W et al. ACMG position statement on prenatal/preconception expanded carrier screening. *Genet Med.* 2013 15:482-3.

Fragile X syndrome:

Chen L et al. An information-rich CGG repeat primed PCR that detects the full range of Fragile X expanded alleles and minimizes the need for Southern blot analysis. *J Mol Diag* 2010 12:589-600.

Spinal Muscular Atrophy:

Luo M et al. An Ashkenazi Jewish SMN1 haplotype specific to duplication alleles improves pan-ethnic carrier screening for spinal muscular atrophy. *Genet Med.* 2014 16:149-56.

Ashkenazi Jewish Disorders:

Scott SA et al. Experience with carrier screening and prenatal diagnosis for sixteen Ashkenazi Jewish Genetic Diseases. *Hum. Mutat.* 2010 31:1-11.

Duchenne Muscular Dystrophy:

Flanigan KM et al. Mutational spectrum of DMD mutations in dystrophinopathy patients: application of modern diagnostic techniques to a large cohort. *Hum Mutat.* 2009 30:1657-66.

Variant Classification:

Richards S et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med.* 2015 May;17(5):405-24

Additional disease-specific references available upon request.

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