



Donor 7003

Genetic Testing Summary

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

Last Updated: 06/27/23

Donor Reported Ancestry: Irish, English

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 |
| Expanded Genetic Disease Carrier Screening Panel attached- 502 diseases by gene sequencing. Personalized residual risk by gene is in the attached report. | <p>Carrier: BH4-Deficient Hyperphenylalaninemia D (PCBD1)</p> <p>Carrier: Congenital Disorder of Glycosylation, Type Ia (PMM2)</p> <p>Carrier: Shwachman-Diamond Syndrome (SBDS)</p> <p>Negative for other genes sequenced.</p> | Partner testing recommended before using this donor. |
| Special Testing | | |
| Gene: CLPANE1 | Negative by gene sequencing | |

*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: 7003 Donor
 Date of Birth: [REDACTED]
 Sema4 ID: [REDACTED]
 Client ID: [REDACTED]
 Indication: Carrier Screening

Specimen Information

Specimen Type: Blood
 Date Collected: 02/08/2022
 Date Received: 02/09/2022
 Final Report: 02/27/2022

Referring Provider

[REDACTED]
 Fairfax Cryobank, Inc.
 [REDACTED]
 [REDACTED]

Expanded Carrier Screen Minus TSE (502 genes)
 with Personalized Residual Risk

SUMMARY OF RESULTS AND RECOMMENDATIONS

| ⊕ Positive | ⊖ Negative |
|---|---|
| <p>Carrier of BH4-Deficient Hyperphenylalaninemia D (AR) Associated gene(s): <i>PCBD1</i> Variant(s) Detected: c.292C>T, p.Q98X, Likely Pathogenic, Heterozygous (one copy)</p> <p>Carrier of Congenital Disorder of Glycosylation, Type Ia (AR) Associated gene(s): <i>PMM2</i> Variant(s) Detected: c.422G>A, p.R141H, Pathogenic, Heterozygous (one copy)</p> <p>Carrier of Shwachman-Diamond Syndrome (AR) Associated gene(s): <i>SBDS</i> Variant(s) Detected: c.258+2T>C, Pathogenic, Heterozygous (one copy)</p> | <p>Negative for all other genes tested To view a full list of genes and diseases tested please see Table 1 in this report</p> |

AR=Autosomal recessive; XL=X-linked

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.

Interpretation of positive results

BH4-Deficient Hyperphenylalaninemia D (AR)

Results and Interpretation

A heterozygous (one copy) likely pathogenic premature stop codon, c.292C>T, p.Q98X, was detected in the *PCBD1* gene (NM_000281.3). When this variant is present in trans with a pathogenic variant, it is considered to be causative for BH4-deficient hyperphenylalaninemia D. Therefore, this individual is expected to be at least a carrier for BH4-deficient hyperphenylalaninemia D. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is BH4-Deficient Hyperphenylalaninemia D?

BH4-deficient hyperphenylalaninemia D is an autosomal recessive disorder caused by pathogenic variants in the gene *PCBD1*. Affected individuals may present with intellectual disability, progressive developmental problems, movement disorders, difficulty swallowing, seizures, behavioral problems, and abnormal body temperature regulation, as well as hypomagnesemia and non-autoimmune diabetes mellitus that can present during puberty. The life expectancy for this disorder is normal with proper management.

Congenital Disorder of Glycosylation, Type Ia (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic missense variant, c.422G>A, p.R141H, was detected in the *PMM2* gene (NM_000303.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for congenital disorder of glycosylation, type Ia. Therefore, this individual is expected to be at least a carrier for congenital disorder of glycosylation, type Ia. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Congenital Disorder of Glycosylation, Type Ia?

Congenital disorder of glycosylation, type Ia is an autosomal recessive syndrome caused by pathogenic variants in the gene *PMM2*. While patients have been reported from multiple ethnicities, this disease is more common in the Ashkenazi Jewish and Caucasian populations. This disease may present in infancy, childhood or adolescence, and the clinical manifestations are highly variable. In infants, the disease may present as failure to thrive as a result of feeding problems; later, the disease may manifest as encephalopathy, hypotonia, delayed language and motor development, intellectual disability, stroke-like episodes, and retinitis pigmentosa. Severely affected individuals may die in early childhood, but more mildly affected individuals may survive into adulthood with variable intellectual disability, spinal abnormalities, endocrine dysfunction and coagulopathy. Several specific variants have been associated with milder or more severe disease, and therefore the disease severity may be predicted in some patients.

Shwachman-Diamond Syndrome (AR)

Results and Interpretation

A heterozygous (one copy) pathogenic splice site variant, c.258+2T>C, was detected in the *SBDS* gene (NM_016038.2). When this variant is present in trans with a pathogenic variant, it is considered to be causative for Shwachman-Diamond syndrome. Therefore, this individual is expected to be at least a carrier for Shwachman-Diamond syndrome. Heterozygous carriers are not expected to exhibit symptoms of this disease.

What is Shwachman-Diamond Syndrome?

Shwachman-Diamond syndrome is an autosomal recessive disorder caused by pathogenic variants in the gene *SBDS*. The age of onset of this disorder is infancy or early childhood. Clinical manifestations include bone marrow dysfunction with cytopenias, pancreatic insufficiency, and skeletal abnormalities. Affected individuals may have recurrent infections due to the cytopenias as well as increased susceptibility of myelodysplastic syndrome and acute myeloid leukemia. Pancreatic insufficiency causes poor food digestion and absorption, resulting in foul smelling stools and growth delays. Skeletal abnormalities include low bone density, narrow rib cage and ribs, and short stature. Life expectancy is possibly reduced. No clear genotype-phenotype correlation has been established.

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.

A handwritten signature in black ink, appearing to read "Lisa Edelman".

Lisa Edelman, Ph.D., FACMG, Laboratory 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 | | | | |
| BH4-Deficient Hyperphenylalaninemia D | <i>PCBD1</i> | AR | Carrier | c.292C>T, p.Q98X, Likely Pathogenic, Heterozygous (one copy) |
| Congenital Disorder of Glycosylation, Type Ia | <i>PMM2</i> | AR | Carrier | c.422G>A, p.R141H, Pathogenic, Heterozygous (one copy) |
| Shwachman-Diamond Syndrome | <i>SBDS</i> | AR | Carrier | c.258>T>C, Pathogenic, Heterozygous (one copy) |
| Negative | | | | |
| 2-Methylbutyrylglycinuria | <i>ACADSB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,800 |
| 3-Beta-Hydroxysteroid Dehydrogenase Type II Deficiency | <i>HSD3B2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,300 |
| 3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC1-Related) | <i>MCCC1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,400 |
| 3-Methylcrotonyl-CoA Carboxylase Deficiency (MCCC2-Related) | <i>MCCC2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,200 |
| 3-Methylglutaconic Aciduria, Type III | <i>OPA3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 50,000 |
| 3-Phosphoglycerate Dehydrogenase Deficiency | <i>PHGDH</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 63,000 |
| 6-Pyruvoyl-Tetrahydropterin Synthase Deficiency | <i>PTS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,800 |
| CD59-Mediated Hemolytic Anemia | <i>CD59</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 415,000 |
| Abetalipoproteinemia | <i>MTTP</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,200 |
| Achalasia-Addisonianism-Alacrimia Syndrome | <i>AAAS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,500 |
| Achromatopsia (CNGA3-Related) | <i>CNGA3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 830 |
| Achromatopsia (CNGB3-related) | <i>CNGB3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 8,600 |
| Acrodermatitis Enteropathica | <i>SLC39A4</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 12,000 |
| Acute Infantile Liver Failure | <i>TRMU</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,400 |
| Acyl-CoA Oxidase I Deficiency | <i>ACOX1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 39,000 |
| Adams-Oliver Syndrome 4 | <i>EOGT</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 44,000 |
| Adenosine Deaminase Deficiency | <i>ADA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,100 |
| Adrenocorticotrophic Hormone Deficiency | <i>TBX19</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 35,000 |
| Adrenoleukodystrophy, X-Linked | <i>ABCD1</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 19,000 |
| Agammaglobulinemia | <i>BTK</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 250,000 |
| Agenesis of the Corpus Callosum | <i>FRMD4A</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,393,000 |
| Aicardi-Goutieres Syndrome (RNASEH2C-Related) | <i>RNASEH2C</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 11,000 |
| Aicardi-Goutieres Syndrome (SAMHD1-Related) | <i>SAMHD1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 10,000 |
| Aicardi-Goutieres Syndrome (TREX1-Related) | <i>TREX1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,200 |
| Albinism, Oculocutaneous, Type III | <i>TYRP1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,500 |
| Alkaptonuria | <i>HGD</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,100 |
| Alpha-Mannosidosis | <i>MAN2B1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,200 |

| | | | | |
|---|------------------|----|--------------|--|
| Alpha-Thalassemia | <i>HBA1/HBA2</i> | AR | Reduced Risk | <i>HBA1</i> Copy Number: 2 <i>HBA2</i> Copy Number: 2 No pathogenic copy number variants detected <i>HBA1/HBA2</i> Sequencing: Negative Personalized Residual Risk: 1 in 490 |
| Alpha-Thalassemia Intellectual Disability Syndrome | <i>ATRX</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 48,000 |
| Alport Syndrome (<i>COL4A3</i> -Related) | <i>COL4A3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,800 |
| Alport Syndrome (<i>COL4A4</i> -Related) | <i>COL4A4</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,800 |
| Alport Syndrome (<i>COL4A5</i> -Related) | <i>COL4A5</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 150,000 |
| Alstrom Syndrome | <i>ALMS1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,800 |
| Andermann Syndrome | <i>SLC12A6</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 151,000 |
| Antley-Bixler Syndrome (<i>POR</i> -Related) | <i>POR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,000 |
| Argininemia | <i>ARG1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,500 |
| Argininosuccinic Aciduria | <i>ASL</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,200 |
| Aromatase Deficiency | <i>CYP19A1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,400 |
| Arthrogryposis, Intellectual Disability, and Seizures | <i>SLC35A3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 454,000 |
| Asparagine Synthetase Deficiency | <i>ASNS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 202,000 |
| Aspartylglycosaminuria | <i>AGA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 13,000 |
| Ataxia With Isolated Vitamin E Deficiency | <i>TTPA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 61,000 |
| Ataxia-Telangiectasia | <i>ATM</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,300 |
| Ataxia-Telangiectasia-Like Disorder 1 | <i>MRE11</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,500 |
| Autosomal Recessive Spastic Ataxia of Charlevoix-Saguenay | <i>SACS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,600 |
| BH4-Deficient Hyperphenylalaninemia C | <i>QDPR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,100 |
| Bardet-Biedl Syndrome (<i>ARL6</i> -Related) | <i>ARL6</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 29,000 |
| Bardet-Biedl Syndrome (<i>BBS10</i> -Related) | <i>BBS10</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,700 |
| Bardet-Biedl Syndrome (<i>BBS12</i> -Related) | <i>BBS12</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,900 |
| Bardet-Biedl Syndrome (<i>BBS1</i> -Related) | <i>BBS1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,400 |
| Bardet-Biedl Syndrome (<i>BBS2</i> -Related) | <i>BBS2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,200 |
| Bardet-Biedl Syndrome (<i>BBS4</i> -Related) | <i>BBS4</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 22,000 |
| Bare Lymphocyte Syndrome, Type II | <i>CIITA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 35,000 |
| Barth Syndrome | <i>TAZ</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 183,000 |
| Bartter Syndrome, Type 3 | <i>CLCNKB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 740 |
| Bartter Syndrome, Type 4A | <i>BSND</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 91,000 |
| Bernard-Soulier Syndrome, Type A1 | <i>GP1BA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 42,000 |
| Bernard-Soulier Syndrome, Type C | <i>GP9</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,300 |
| Beta-Globin-Related Hemoglobinopathies | <i>HBB</i> | 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 11,000 Personalized Residual Risk (Beta-Globin-Related Hemoglobinopathies: HbC Variant): 1 in 42,000 |
| Beta-Ketothiolase Deficiency | <i>ACAT1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,400 |
| Beta-Mannosidosis | <i>MANBA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,100 |
| Bilateral Frontoparietal Polymicrogyria | <i>GPR56</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 203,000 |
| Biotinidase Deficiency | <i>BTBD</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 500 |
| Bloom Syndrome | <i>BLM</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 7,400 |
| Canavan Disease | <i>ASPA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,000 |
| Carbamoylphosphate Synthetase I Deficiency | <i>CPS1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,100 |
| Carnitine Acylcarnitine Translocase Deficiency | <i>SLC25A20</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,100 |

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|--|-----------------|----|--------------|--|
| Carnitine Palmitoyltransferase IA Deficiency | <i>CPT1A</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 24,000 |
| Carnitine Palmitoyltransferase II Deficiency | <i>CPT2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 670 |
| Carpenter Syndrome | <i>RAB23</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 21,000 |
| Cartilage-Hair Hypoplasia | <i>RMRP</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 960 |
| Catecholaminergic Polymorphic Ventricular Tachycardia | <i>CASQ2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,900 |
| Central Hypothyroidism and Testicular Enlargement | <i>IGSF1</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 781,000 |
| Cerebral Creatine Deficiency Syndrome 1 | <i>SLC6A8</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 208,000 |
| Cerebral Creatine Deficiency Syndrome 2 | <i>GAMT</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,100 |
| Cerebral Creatine Deficiency Syndrome 3 | <i>GATM</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 7,900 |
| Cerebral Dysgenesis, Neuropathy, Ichthyosis, and Palmoplantar Keratoderma Syndrome | <i>SNAP29</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,730,000 |
| Cerebrotendinous Xanthomatosis | <i>CYP27A1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,900 |
| Charcot-Marie-Tooth Disease, Type 4D | <i>NDRG1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 730,000 |
| Charcot-Marie-Tooth Disease, Type 5 / Arts Syndrome | <i>PRPS1</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 114,000 |
| Charcot-Marie-Tooth Disease, X-Linked | <i>GJB1</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 11,000 |
| Chediak-Higashi Syndrome | <i>LYST</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 7,100 |
| Chondrodysplasia Punctata | <i>ARSE</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 862,000 |
| Choreoacanthocytosis | <i>VPS13A</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 13,000 |
| Choroideremia | <i>CHM</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 125,000 |
| Chronic Granulomatous Disease (CYBA-Related) | <i>CYBA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,000 |
| Chronic Granulomatous Disease (CYBB-Related) | <i>CYBB</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 294,000 |
| Citrin Deficiency | <i>SLC25A13</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 12,000 |
| Citrullinemia, Type 1 | <i>ASS1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,500 |
| Cockayne Syndrome, Type A | <i>ERCC8</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 8,900 |
| Cockayne Syndrome, Type B and other ERCC6-Related Disorders | <i>ERCC6</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 8,100 |
| Cohen Syndrome | <i>VPS13B</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,400 |
| Combined Factor V and VIII Deficiency | <i>LMAN1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 102,000 |
| Combined Malonic and Methylmalonic Aciduria | <i>ACSF3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,400 |
| Combined Oxidative Phosphorylation Deficiency 1 | <i>GFM1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 13,000 |
| Combined Oxidative Phosphorylation Deficiency 3 | <i>TSMF</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 27,000 |
| Combined Pituitary Hormone Deficiency 1 | <i>POU1F1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,900 |
| Combined Pituitary Hormone Deficiency 2 | <i>PROP1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,800 |
| Combined Pituitary Hormone Deficiency 3 | <i>LHX3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 140,000 |
| Combined SAP Deficiency | <i>PSAP</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 44,000 |
| Cone-Rod Dystrophy 6 / Leber Congenital Amaurosis 1 | <i>GUCY2D</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,200 |
| Congenital Adrenal Hyperplasia due to 11-Beta-Hydroxylase Deficiency | <i>CYP11B1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 520 |
| Congenital Adrenal Hyperplasia due to 17-Alpha-Hydroxylase Deficiency | <i>CYP17A1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,800 |
| Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency | <i>CYP21A2</i> | 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) | <i>NR0B1</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 353,000 |
| Congenital Adrenal Insufficiency (CYP11A1-Related) | <i>CYP11A1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,100 |

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|---|----------------|----|--------------|---|
| Congenital Amegakaryocytic Thrombocytopenia | <i>MPL</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,100 |
| Congenital Bile Acid Synthesis Defect (AKR1D1-Related) | <i>AKR1D1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,900 |
| Congenital Bile Acid Synthesis Defect (HSD3B7-Related) | <i>HSD3B7</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 8,900 |
| Congenital Disorder of Deglycosylation | <i>NGLY1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 14,000 |
| Congenital Disorder of Glycosylation, Type Ib | <i>MPI</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,600 |
| Congenital Disorder of Glycosylation, Type Ic | <i>ALG6</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,100 |
| Congenital Disorder of Glycosylation, Type Im | <i>DOLK</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 134,000 |
| Congenital Dyserythropoietic Anemia Type 2 | <i>SEC23B</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,000 |
| Congenital Dyserythropoietic Anemia, Type Ia | <i>CDAN1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 470 |
| Congenital Ichthyosis 4A and 4B | <i>ABCA12</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,100 |
| Congenital Insensitivity to Pain with Anhidrosis | <i>NTRK1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,700 |
| Congenital Muscular Dystrophy (LAMA2-Related) | <i>LAMA2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 640 |
| Congenital Myasthenic Syndrome (CHAT-Related) | <i>CHAT</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,100 |
| Congenital Myasthenic Syndrome (CHRNE-Related) | <i>CHRNE</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,100 |
| Congenital Myasthenic Syndrome (DOK7-Related) | <i>DOK7</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,200 |
| Congenital Myasthenic Syndrome (RAPSN-Related) | <i>RAPSN</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,900 |
| Congenital Neutropenia (HAX1-Related) | <i>HAX1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 82,000 |
| Congenital Neutropenia (VPS45-Related) | <i>VPS45</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,500 |
| Congenital Nongoitrous Hypothyroidism 1 | <i>TSHR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,000 |
| Congenital Nongoitrous Hypothyroidism 4 | <i>TSHB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 118,000 |
| Congenital Secretory Chloride Diarrhea 1 | <i>SLC26A3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,400 |
| Corneal Dystrophy and Perceptive Deafness | <i>SLC4A11</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,600 |
| Corticosterone Methyloxidase Deficiency | <i>CYP11B2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,500 |
| Cystic Fibrosis | <i>CFTR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 440 |
| Cystinosis | <i>CTNS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 7,700 |
| Cystinuria (SLC3A1-Related) | <i>SLC3A1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 590 |
| Cytochrome C Oxidase Deficiency / Leigh Syndrome (COX15-Related) | <i>COX15</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,300 |
| D-Bifunctional Protein Deficiency | <i>HSD17B4</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,000 |
| Deafness, Autosomal Recessive 3 | <i>MYO15A</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 240 |
| Deafness, Autosomal Recessive 59 | <i>PJVK</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 57,000 |
| Deafness, Autosomal Recessive 7 | <i>TMC1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,200 |
| Deafness, Autosomal Recessive 76 | <i>SYNE4</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 43,000 |
| Deafness, Autosomal Recessive 77 | <i>LOXHD1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,700 |
| Deafness, Autosomal Recessive 8/10 | <i>TMPPSS3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 510 |
| Deafness, Autosomal Recessive 9 | <i>OTOF</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,400 |
| Desbuquois Dysplasia 1 | <i>CANT1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 24,000 |
| Desmosterolosis | <i>DHCR24</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 27,000 |
| Diaphanospondylodysostosis | <i>BMPER</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 18,000 |
| Distal Renal Tubular Acidosis and other SLC4A1-related Disorders | <i>SLC4A1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,000 |
| Duchenne Muscular Dystrophy / Becker Muscular Dystrophy | <i>DMD</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 10,000 |
| Dyskeratosis Congenita (DKC1-related) | <i>DKC1</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 9,259,000 |
| Dyskeratosis Congenita (RTEL1-Related) | <i>RTEL1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,800 |
| Dystrophic Epidermolysis Bullosa | <i>COL7A1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 900 |
| Ehlers-Danlos Syndrome, Type VI | <i>PLOD1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 20,000 |

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|---|----------------|----|--------------|--|
| Ehlers-Danlos Syndrome, Type VIIC | <i>ADAMTS2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 243,000 |
| Ellis-Van Creveld Syndrome (<i>EVC2</i> -Related) | <i>EVC2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,300 |
| Ellis-van Creveld Syndrome (<i>EVC</i> -Related) | <i>EVC</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,200 |
| Emery-Dreifuss Myopathy 1 | <i>EMD</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 833,000 |
| Enhanced S-Cone Syndrome | <i>NR2E3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,600 |
| Ethylmalonic Encephalopathy | <i>ETHE1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,400 |
| Fabry Disease | <i>GLA</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 7,700 |
| Factor IX Deficiency | <i>F9</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 5,100 |
| Factor VII Deficiency | <i>F7</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 450 |
| Factor XI Deficiency | <i>F11</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,500 |
| Familial Autosomal Recessive Hypercholesterolemia | <i>LDLRAP1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 136,000 |
| Familial Dysautonomia | <i>IKBKAP</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 51,000 |
| Familial Hypercholesterolemia | <i>LDLR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 280 |
| Familial Hyperinsulinemic Hypoglycemia 4 / 3-Hydroxyacyl-CoA Dehydrogenase Deficiency | <i>HADH</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,200 |
| Familial Hyperinsulinism (<i>ABCC8</i> -Related) | <i>ABCC8</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 450 |
| Familial Hyperinsulinism (<i>KCNJ11</i> -Related) | <i>KCNJ11</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,300 |
| Familial Hyperphosphatemic Tumoral Calcinosis | <i>GALNT3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 7,800 |
| Familial Mediterranean Fever | <i>MEFV</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,200 |
| Fanconi Anemia, Group A | <i>FANCA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,100 |
| Fanconi Anemia, Group C | <i>FANCC</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 12,000 |
| Fanconi Anemia, Group G | <i>FANCG</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 28,000 |
| Fanconi-Bickel Syndrome | <i>SLC2A2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,000 |
| Fragile X Syndrome | <i>FMR1</i> | XL | Reduced Risk | <i>FMR1</i> CGG repeat sizes: Not Performed <i>FMR1</i> 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 | <i>FBP1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,600 |
| Fucosidosis | <i>FUCA1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,200 |
| Fumarase Deficiency | <i>FH</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,500 |
| Fundus Albipunctatus | <i>RDH5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,000 |
| GRACILE Syndrome and Other <i>BCS1L</i> -Related Disorders | <i>BCS1L</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,900 |
| Galactokinase Deficiency | <i>GALK1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,700 |
| Galactose Epimerase Deficiency | <i>GALE</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,600 |
| Galactosemia | <i>GALT</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,200 |
| Galactosialidosis | <i>CTSA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 7,900 |
| Gaucher Disease | <i>GBA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,300 |
| Generalized Thyrotropin-Releasing Hormone Resistance | <i>TRHR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 104,000 |
| Geroderma Osteodysplasticum | <i>GORAB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 70,000 |
| Gitelman Syndrome | <i>SLC12A3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 290 |
| Glanzmann Thrombasthenia (<i>ITGA2B</i> -Related) | <i>ITGA2B</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,800 |
| Glanzmann Thrombasthenia (<i>ITGB3</i> -Related) | <i>ITGB3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,600 |
| Glutaric Acidemia, Type I | <i>GCDH</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,700 |
| Glutaric Acidemia, Type IIa | <i>ETFA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,700 |
| Glutaric Acidemia, Type IIb | <i>ETFB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,900 |
| Glutaric Acidemia, Type IIc | <i>ETFDH</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,700 |
| Glutathione Synthetase Deficiency | <i>GSS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,500 |
| Glycine Encephalopathy (<i>AMT</i> -Related) | <i>AMT</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,700 |

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| 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 (CBS-Related) | CBS | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,400 |
| 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 |
| Hydrolethals 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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|---|-----------------|----|--------------|---|
| Intellectual Disability, Autosomal Recessive 3 | <i>CC2D1A</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 220,000 |
| Intrahepatic Cholestasis | <i>ATP8B1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,400 |
| Isovaleric Acidemia | <i>IVD</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,000 |
| Joubert Syndrome 2 | <i>TMEM216</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 152,000 |
| Joubert Syndrome 4 / Senior-Loken Syndrome 1 / Juvenile Nephronophthisis 1 | <i>NPHP1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 21,000 |
| Joubert Syndrome 7 / Meckel Syndrome 5 / COACH Syndrome | <i>RPGRIP1L</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 32,000 |
| Junctional Epidermolysis Bullosa (<i>COL17A1</i> -Related) | <i>COL17A1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 25,000 |
| Junctional Epidermolysis Bullosa (<i>ITGA6</i> -Related) | <i>ITGA6</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 125,000 |
| Junctional Epidermolysis Bullosa (<i>ITGB4</i> -Related) | <i>ITGB4</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,400 |
| Junctional Epidermolysis Bullosa (<i>LAMA3</i> -Related) | <i>LAMA3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,200 |
| Junctional Epidermolysis Bullosa (<i>LAMB3</i> -Related) | <i>LAMB3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,900 |
| Junctional Epidermolysis Bullosa (<i>LAMC2</i> -Related) | <i>LAMC2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 77,000 |
| Kohlschutter-Tonz Syndrome | <i>ROGDI</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,300 |
| Krabbe Disease | <i>GALC</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 860 |
| Lamellar Ichthyosis, Type 1 | <i>TGM1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,500 |
| Laron Dwarfism | <i>GHR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,700 |
| Leber Congenital Amaurosis 10 and Other CEP290-Related Ciliopathies | <i>CEP290</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,100 |
| Leber Congenital Amaurosis 13 | <i>RDH12</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,500 |
| Leber Congenital Amaurosis 15 / Retinitis Pigmentosa 14 | <i>TULP1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,800 |
| Leber Congenital Amaurosis 2 / Retinitis Pigmentosa 20 | <i>RPE65</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,500 |
| Leber Congenital Amaurosis 4 | <i>AIPL1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,100 |
| Leber Congenital Amaurosis 5 | <i>LCA5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 14,000 |
| Leber Congenital Amaurosis 8 / Retinitis Pigmentosa 12 / Pigmented Paravenous Chorioretinal Atrophy | <i>CRB1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 990 |
| Leigh Syndrome (<i>NDUFS7</i> -Related) | <i>NDUFS7</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 26,000 |
| Leigh Syndrome (<i>SURF1</i> -Related) | <i>SURF1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,400 |
| Leigh Syndrome, French-Canadian Type | <i>LRPPRC</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 32,000 |
| Lethal Congenital Contracture Syndrome 1 / Lethal Arthrogyposis with Anterior Horn Cell Disease | <i>GLE1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 10,000 |
| Lethal Congenital Contracture Syndrome 2 | <i>ERBB3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 96,000 |
| Lethal Congenital Contracture Syndrome 3 | <i>PIP5K1C</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 318,000 |
| Leukoencephalopathy with Vanishing White Matter | <i>EIF2B5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,300 |
| Limb-Girdle Muscular Dystrophy, Type 2A | <i>CAPN3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 960 |
| Limb-Girdle Muscular Dystrophy, Type 2B | <i>DYSF</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,100 |
| Limb-Girdle Muscular Dystrophy, Type 2C | <i>SGCG</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,900 |
| Limb-Girdle Muscular Dystrophy, Type 2D | <i>SGCA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,500 |
| Limb-Girdle Muscular Dystrophy, Type 2E | <i>SGCB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 31,000 |
| Limb-Girdle Muscular Dystrophy, Type 2F | <i>SGCD</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 52,000 |
| Limb-Girdle Muscular Dystrophy, Type 2H | <i>TRIM32</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 10,000 |
| Limb-Girdle Muscular Dystrophy, Type 2I | <i>FKRP</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,400 |
| Limb-Girdle Muscular Dystrophy, Type 2L | <i>ANO5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 660 |
| Lipoamide Dehydrogenase Deficiency | <i>DLD</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 14,000 |
| Lipoid Adrenal Hyperplasia | <i>STAR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,600 |
| Lipoprotein Lipase Deficiency | <i>LPL</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,400 |

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

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| Mitochondrial DNA Depletion Syndrome 4A and 4B and other <i>POLG</i> -Related Disorders | <i>POLG</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 320 |
| Mitochondrial DNA Depletion Syndrome 5 | <i>SUCLA2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 78,000 |
| Mitochondrial DNA Depletion Syndrome 6 / Navajo Neurohepatopathy | <i>MPV17</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,400 |
| Mitochondrial Myopathy and Sideroblastic Anemia 1 | <i>PUS1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 449,000 |
| Mitochondrial Trifunctional Protein Deficiency (<i>HADHB</i> -Related) | <i>HADHB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,000 |
| Molybdenum Cofactor Deficiency A | <i>MOCS1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,700 |
| Mucopolipidosis II / IIIA | <i>GNPTAB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,100 |
| Mucopolipidosis III Gamma | <i>GNPTG</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 68,000 |
| Mucopolipidosis IV | <i>MCOLN1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,400 |
| Mucopolysaccharidosis Type I | <i>IDUA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,300 |
| Mucopolysaccharidosis Type II | <i>IDS</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 76,000 |
| Mucopolysaccharidosis Type IIIA | <i>SGSH</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,700 |
| Mucopolysaccharidosis Type IIIB | <i>NAGLU</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 950 |
| Mucopolysaccharidosis Type IIIC | <i>HGSNAT</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,200 |
| Mucopolysaccharidosis Type IIID | <i>GNS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 137,000 |
| Mucopolysaccharidosis Type IVa | <i>GALNS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 690 |
| Mucopolysaccharidosis Type IVb / GM1 Gangliosidosis | <i>GLB1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,700 |
| Mucopolysaccharidosis VII | <i>GUSB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,600 |
| Mucopolysaccharidosis type IX | <i>HYAL1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 149,000 |
| Mucopolysaccharidosis type VI | <i>ARSB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,300 |
| Mulibrey Nanism | <i>TRIM37</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 31,000 |
| Multiple Congenital Anomalies-Hypotonia-Seizures Syndrome 1 | <i>PIGN</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,800 |
| Multiple Pterygium Syndrome | <i>CHRNA3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,900 |
| Multiple Sulfatase Deficiency | <i>SUMF1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 69,000 |
| Muscle-Eye-Brain Disease and Other <i>POMGNT1</i> -Related Congenital Muscular Dystrophy-Dystroglycanopathies | <i>POMGNT1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,200 |
| Myoneurogastrointestinal Encephalopathy | <i>TYMP</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,100 |
| Myotubular Myopathy 1 | <i>MTM1</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 192,000 |
| N-Acetylglutamate Synthase Deficiency | <i>NAGS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,200 |
| Nemaline Myopathy 2 | <i>NEB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,400 |
| Nephrogenic Diabetes Insipidus, Type II | <i>AQP2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,400 |
| Nephrogenic Diabetes insipidus (<i>AVPR2</i> -related)/ Nephrogenic Syndrome of Inappropriate Antidiuresis | <i>AVPR2</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 471,000 |
| Nephronophthisis 2 | <i>INVS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 56,000 |
| Nephrotic Syndrome (<i>NPHS1</i> -Related) / Congenital Finnish Nephrosis | <i>NPHS1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 920 |
| Nephrotic Syndrome (<i>NPHS2</i> -Related) / Steroid-Resistant Nephrotic Syndrome | <i>NPHS2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 780 |
| Neurodegeneration due to Cerebral Folate Transport Deficiency | <i>FOLR1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,300 |
| Neurodevelopmental Disorder with Progressive Microcephaly, Spasticity, and Brain Anomalies | <i>PLAA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 229,000 |
| Neuronal Ceroid-Lipofuscinosis (<i>CLN3</i> -Related) | <i>CLN3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,200 |
| Neuronal Ceroid-Lipofuscinosis (<i>CLN5</i> -Related) | <i>CLN5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,300 |
| Neuronal Ceroid-Lipofuscinosis (<i>CLN6</i> -Related) | <i>CLN6</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 8,600 |
| Neuronal Ceroid-Lipofuscinosis (<i>CLN8</i> -Related) | <i>CLN8</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,100 |
| Neuronal Ceroid-Lipofuscinosis (<i>MFSD8</i> -Related) | <i>MFSD8</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,200 |
| Neuronal Ceroid-Lipofuscinosis (<i>PPT1</i> -Related) | <i>PPT1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 7,500 |

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| Neuronal Ceroid-Lipofuscinosis (TPP1-Related) | <i>TPP1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,300 |
| Niemann-Pick Disease (SMPD1-Related) | <i>SMPD1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,800 |
| Niemann-Pick Disease, Type C (NPC1-Related) | <i>NPC1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 690 |
| Niemann-Pick Disease, Type C (NPC2-Related) | <i>NPC2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,600 |
| Nijmegen Breakage Syndrome | <i>NBN</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 14,000 |
| Non-Syndromic Hearing Loss (GJB2-Related) | <i>GJB2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 600 |
| Oculocutaneous Albinism, Type IA / IB | <i>TYR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 240 |
| Oculocutaneous Albinism, Type IV | <i>SLC45A2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 830 |
| Odonto-Onycho-Dermal Dysplasia / Schopf-Schulz-Passarge Syndrome | <i>WNT10A</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,900 |
| Omenn Syndrome (RAG2-Related) | <i>RAG2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 17,000 |
| Omenn Syndrome / Severe Combined Immunodeficiency, Athabaskan-Type | <i>DCLRE1C</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,500 |
| Omenn Syndrome and other RAG1-Related Disorders | <i>RAG1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 850 |
| Ornithine Aminotransferase Deficiency | <i>OAT</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,400 |
| Ornithine Transcarbamylase Deficiency | <i>OTC</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 103,000 |
| Osteogenesis Imperfecta, Type XI | <i>FKBP10</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,500 |
| Osteopetrosis 1 | <i>TCIRG1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,700 |
| Osteopetrosis 8 | <i>SNX10</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 16,000 |
| Otospondylomegaepiphyseal Dysplasia / Deafness / Fibrochondrogenesis 2 | <i>COL11A2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,700 |
| Papillon-Lefevre Syndrome | <i>CTSC</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,000 |
| Pendred Syndrome | <i>SLC26A4</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 390 |
| Peroxisome Biogenesis Disorder 3A and 3B | <i>PEX12</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 30,000 |
| Peroxisome Biogenesis Disorder 7A and 7B | <i>PEX26</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 70,000 |
| Phenylalanine Hydroxylase Deficiency | <i>PAH</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 340 |
| Polycystic Kidney Disease, Autosomal Recessive | <i>PKHD1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 450 |
| Polyglandular Autoimmune Syndrome, Type 1 | <i>AIRE</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,300 |
| Pontocerebellar Hypoplasia, Type 1A | <i>VRK1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 25,000 |
| Pontocerebellar Hypoplasia, Type 1B | <i>EXOSC3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 10,000 |
| Pontocerebellar Hypoplasia, Type 2A and Type 4 | <i>TSEN54</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,700 |
| Pontocerebellar Hypoplasia, Type 2E | <i>VPS53</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 139,000 |
| Pontocerebellar Hypoplasia, Type 6 | <i>RARS2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 8,600 |
| Primary Carnitine Deficiency | <i>SLC22A5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,500 |
| Primary Ciliary Dyskinesia (CCDC103-Related) | <i>CCDC103</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 27,000 |
| Primary Ciliary Dyskinesia (CCDC151-Related) | <i>CCDC151</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 59,000 |
| Primary Ciliary Dyskinesia (CCDC39-Related) | <i>CCDC39</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 12,000 |
| Primary Ciliary Dyskinesia (DNAH5-Related) | <i>DNAH5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,500 |
| Primary Ciliary Dyskinesia (DNAI1-Related) | <i>DNAI1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,000 |
| Primary Ciliary Dyskinesia (DNAI2-Related) | <i>DNAI2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 76,000 |
| Primary Ciliary Dyskinesia (RSPH9-Related) | <i>RSPH9</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 253,000 |
| Primary Coenzyme Q10 Deficiency 7 | <i>COQ4</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 12,000 |
| Primary Congenital Glaucoma 3A | <i>CYP1B1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 880 |
| Primary Hyperoxaluria, Type 1 | <i>AGXT</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,900 |
| Primary Hyperoxaluria, Type 2 | <i>GRHPR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 11,000 |
| Primary Hyperoxaluria, Type 3 | <i>HOGA1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,400 |
| Progressive Cerebello-Cerebral Atrophy | <i>SEPSECS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,400 |
| Progressive Familial Intrahepatic Cholestasis, Type 2 | <i>ABCB11</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 950 |
| Progressive Myoclonic Epilepsy, Type 1B | <i>PRICKLE1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 98,000 |

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| Progressive Pseudorheumatoid Dysplasia | <i>WISP3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,600 |
| Prolidase Deficiency | <i>PEPD</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 30,000 |
| Propionic Acidemia (<i>PCCA</i> -Related) | <i>PCCA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,600 |
| Propionic Acidemia (<i>PCCB</i> -Related) | <i>PCCB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 12,000 |
| Pulmonary Surfactant Dysfunction | <i>ABCA3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,200 |
| Pycnodysostosis | <i>CTSK</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,100 |
| Pyridoxamine 5'-Phosphate Oxidase Deficiency | <i>PNPO</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 10,000 |
| Pyridoxine-Dependent Epilepsy | <i>ALDH7A1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,100 |
| Pyruvate Carboxylase Deficiency | <i>PC</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 8,000 |
| Pyruvate Dehydrogenase E1-Alpha Deficiency | <i>PDHA1</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 139,000 |
| Pyruvate Dehydrogenase E1-Beta Deficiency | <i>PDHB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 15,000 |
| Renal Tubular Acidosis and Deafness | <i>ATP6V1B1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,600 |
| Retinitis Pigmentosa 25 | <i>EYS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,800 |
| Retinitis Pigmentosa 26 | <i>CERKL</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 13,000 |
| Retinitis Pigmentosa 28 | <i>FAM161A</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 34,000 |
| Retinitis Pigmentosa 36 | <i>PRCD</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 304,000 |
| Retinitis Pigmentosa 59 | <i>DHDDS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 601,000 |
| Retinitis Pigmentosa 64 / Bardet-Biedl Syndrome 21 / Cone-Rod Dystrophy 16 | <i>C8ORF37</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 168,000 |
| Rh Deficiency Syndrome | <i>RHAG</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 46,000 |
| Rhizomelic Chondrodysplasia Punctata, Type 1 | <i>PEX7</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 10,000 |
| Rhizomelic Chondrodysplasia Punctata, Type 3 | <i>AGPS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 620,000 |
| Roberts Syndrome | <i>ESCO2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 139,000 |
| Salla Disease | <i>SLC17A5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 8,400 |
| Salt and Pepper Developmental Regression Syndrome | <i>ST3GAL5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 25,000 |
| Sandhoff Disease | <i>HEXB</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,800 |
| Schimke Immunoosseous Dysplasia | <i>SMARCAL1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,800 |
| Seckel Syndrome 5 / Microcephaly 9 | <i>CEP152</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,700 |
| Segawa Syndrome | <i>TH</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,100 |
| Sepiapterin Reductase Deficiency | <i>SPR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 35,000 |
| Severe Combined Immunodeficiency (<i>IL7R</i> -Related) | <i>IL7R</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 20,000 |
| Severe Combined Immunodeficiency (<i>JAK3</i> -Related) | <i>JAK3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,100 |
| Severe Combined Immunodeficiency (<i>PTPRC</i> -Related) | <i>PTPRC</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 8,500 |
| Severe Congenital Neutropenia 4 | <i>G6PC3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 10,000 |
| Severe Neonatal Hyperparathyroidism | <i>CASR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,700 |
| Short Stature, Onychodysplasia, Facial Dysmorphism, and Hypotrichosis | <i>POC1A</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 108,000 |
| Short-Chain Acyl-CoA Dehydrogenase Deficiency | <i>ACADS</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 660 |
| Sialidosis, Type I and Type II | <i>NEU1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,000 |
| Sjogren-Larsson Syndrome | <i>ALDH3A2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,500 |
| Smith-Lemli-Opitz Syndrome | <i>DHCR7</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 750 |
| Spastic Paraplegia 15 | <i>ZFYVE26</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 46,000 |
| Spastic Tetraplegia, Thin Corpus Callosum, and Progressive Microcephaly | <i>SLC1A4</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 855,000 |
| Spherocytosis, Type 5 | <i>EPB42</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,200 |
| Spinal Muscular Atrophy | <i>SMN1</i> | 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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| Spinal Muscular Atrophy with Respiratory Distress 1 / Charcot-Marie-Tooth Disease, Type 2S | <i>IGHMBP2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,200 |
| Spinocerebellar Ataxia with Axonal Neuropathy 3 | <i>COA7</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 12,000 |
| Spondylocostal Dysostosis 1 | <i>DLL3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 7,200 |
| Spondylometaphyseal Dysplasia (DDR2-Related) | <i>DDR2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 236,000 |
| Spondylothoracic Dysostosis | <i>MESP2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 382,000 |
| Steel Syndrome | <i>COL27A1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 93,000 |
| Stuve-Wiedemann Syndrome | <i>LIFR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,000 |
| Sulfate Transporter-Related Osteochondrodysplasia | <i>SLC26A2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,800 |
| Tay-Sachs Disease | <i>HEXA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,400 |
| Thiamine-Responsive Megaloblastic Anemia Syndrome | <i>SLC19A2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 11,000 |
| Thyroid Dysmorphogenesis 1 | <i>SLC5A5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 45,000 |
| Thyroid Dysmorphogenesis 2A | <i>TPO</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 910 |
| Thyroid Dysmorphogenesis 3 | <i>TG</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 850 |
| Thyroid Dysmorphogenesis 4 | <i>IYD</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,800 |
| Thyroid Dysmorphogenesis 5 | <i>DUOXA2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 29,000 |
| Thyroid Dysmorphogenesis 6 | <i>DUOX2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 190 |
| Trichohepatoenteric Syndrome 1 | <i>TTC37</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 14,000 |
| Tyrosinemia, Type I | <i>FAH</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,900 |
| Tyrosinemia, Type II | <i>TAT</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,800 |
| Tyrosinemia, Type III | <i>HPD</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 15,000 |
| Usher Syndrome, Type IB | <i>MYO7A</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,000 |
| Usher Syndrome, Type IC | <i>USH1C</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,600 |
| Usher Syndrome, Type ID | <i>CDH23</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,400 |
| Usher Syndrome, Type IF | <i>PCDH15</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,800 |
| Usher Syndrome, Type IIA | <i>USH2A</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 290 |
| Usher Syndrome, Type III | <i>CLRN1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 1,300 |
| Very Long Chain Acyl-CoA Dehydrogenase Deficiency | <i>ACADVL</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 920 |
| Vitamin D-Dependent Rickets, Type I | <i>CYP27B1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 7,900 |
| Vitamin D-Resistant Rickets, Type IIA | <i>VDR</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 17,000 |
| Walker-Warburg Syndrome and Other FKTN-Related Dystrophies | <i>FKTN</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 4,200 |
| Werner Syndrome | <i>WRN</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 9,200 |
| Wilson Disease | <i>ATP7B</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 350 |
| Wiskott-Aldrich Syndrome (WAS-Related) | <i>WAS</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 1,203,000 |
| Wolcott-Rallison Syndrome | <i>EIF2AK3</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 22,000 |
| Wolman Disease / Cholesteryl Ester Storage Disease | <i>LIPA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,200 |
| Woodhouse-Sakati Syndrome | <i>DCAF17</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 81,000 |
| X-Linked Juvenile Retinoschisis | <i>RS1</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 40,000 |
| X-Linked Severe Combined Immunodeficiency | <i>IL2RG</i> | XL | Reduced Risk | Personalized Residual Risk: 1 in 250,000 |
| Xeroderma Pigmentosum (POLH-Related) | <i>POLH</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 5,900 |
| Xeroderma Pigmentosum, Group A | <i>XPA</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 11,000 |
| Xeroderma Pigmentosum, Group C | <i>XPC</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 12,000 |
| Xeroderma Pigmentosum, Group G | <i>ERCC5</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 3,000 |
| Zellweger Syndrome Spectrum (PEX10-Related) | <i>PEX10</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 6,300 |
| Zellweger Syndrome Spectrum (PEX1-Related) | <i>PEX1</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 2,000 |
| Zellweger Syndrome Spectrum (PEX2-Related) | <i>PEX2</i> | AR | Reduced Risk | Personalized Residual Risk: 1 in 77,000 |

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. AmpliX[®] *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.

Agilent SureSelect™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_153717.2) exon 1; *F5* (NM_000130.4) chr1:169,551,662-169,551,679 (partial exon 2); *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%)

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 $\Delta\Delta C_t$ 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 SureSelectTMXT 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 Sema4 Opco, 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.



| Patient Information | Specimen Information | Client Information |
|---|---|--|
| DONOR, 7003 DOB: [REDACTED] AGE: [REDACTED] Gender: M Phone: NG Patient ID: [REDACTED] | Specimen: [REDACTED] Requisition: [REDACTED] Lab Ref #: [REDACTED] Collected: 02/08/2022 Received: 02/10/2022 / 21:21 EST Reported: 02/18/2022 / 18:51 EST | Client #: 48041578 NYNJMAIL GENOMICS, SEMA4 SEMA4 62 SOUTHFIELD AVE STAMFORD, CT 06902-7229 |

| |
|------------------|
| Ward: FFXCB |
|------------------|

Cytogenetic Report

CHROMOSOME ANALYSIS, BLOOD - 14596 **Lab:EZ**

CHROMOSOME ANALYSIS, BLOOD

Order ID: [REDACTED]
 Specimen Type: Blood
 Clinical Indication: RULE OUT CHROMOSOME ABNORMALITY

RESULT:
 NORMAL MALE KARYOTYPE

INTERPRETATION:
 Chromosome analysis revealed normal G-band patterns within the limits of standard cytogenetic analysis.

Please expect the results of any other concurrent study in a separate report.

NOMENCLATURE:
 46,XY

ASSAY INFORMATION:

Method: G-Band (Digital Analysis: MetaSyst)
 Cells Counted: 20
 Band Level: 500
 Cells Analyzed: 5
 Cells Karyotyped: 5

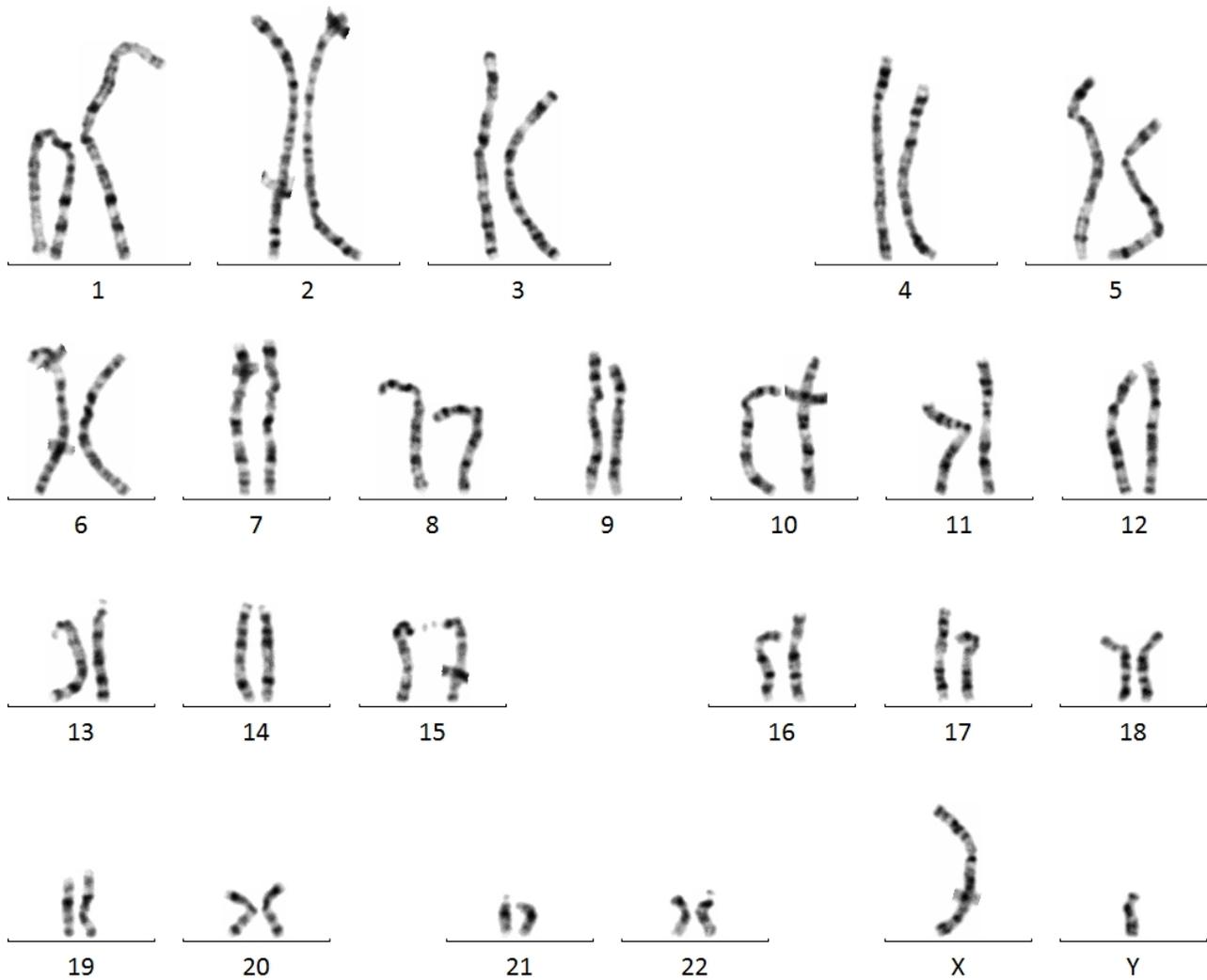
This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements.

Mark A. Micale, PhD, FACMG

Electronic Signature: 2/18/2022 5:53 PM



| Patient Information | Specimen Information | Client Information |
|--|---|---------------------------------------|
| DONOR, 7003 DOB: [REDACTED] AGE: [REDACTED] Gender: M Patient ID: [REDACTED] | Specimen: [REDACTED] Collected: 02/08/2022 Received: 02/10/2022 / 21:21 EST Reported: 02/18/2022 / 18:51 EST | Client #: 48041578 GENOMICS, SEMA4 |



PERFORMING SITE:

EZ QUEST DIAGNOSTICS/NICHOLS SJ, 33608 ORTEGA HWY, SAN JUAN CAPISTRANO, CA 92675-2042 Laboratory Director: IRINA MARAMICA, MD, PHD, MBA, CLIA: 05D0643352



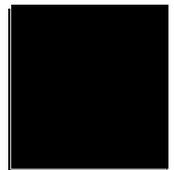
| Patient Information | Specimen Information | Client Information |
|---|---|---|
| DONOR, 7003 DOB: [REDACTED] AGE: [REDACTED] Gender: M Phone: NG Patient ID: [REDACTED] | Specimen: [REDACTED] Requisition: [REDACTED] Lab Ref #: [REDACTED] Collected: 02/08/2022 Received: 02/10/2022 / 21:57 EST Reported: 02/14/2022 / 07:43 EST | Client #: 48041578 NYNJMAIL GENOMICS, SEMA4 SEMA4 62 SOUTHFIELD AVE STAMFORD, CT 06902-7229 |

Ward: FFXCB

| Test Name | In Range | Out Of Range | Reference Range | Lab |
|-----------------------------|----------|--------------|----------------------|-----|
| HEMOGLOBINOPATHY EVALUATION | | | | |
| RED BLOOD CELL COUNT | 4.56 | | 4.20-5.80 Million/uL | Z99 |
| HEMOGLOBIN | 14.1 | | 13.2-17.1 g/dL | |
| HEMATOCRIT | 41.4 | | 38.5-50.0 % | |
| MCV | 90.8 | | 80.0-100.0 fL | |
| MCH | 30.9 | | 27.0-33.0 pg | |
| RDW | 11.9 | | 11.0-15.0 % | |
| HEMOGLOBIN A | 97.1 | | >96.0 % | Z99 |
| HEMOGLOBIN F | <1.0 | | <2.0 % | |
| HEMOGLOBIN A2 (QUANT) | 2.9 | | 2.2-3.2 % | |
| INTERPRETATION | * | | | |
| Normal phenotype. | | | | |

PERFORMING SITE:

Z99 QUEST DIAGNOSTICS CLIFTON, 1 INSIGHTS DRIVE, CLIFTON, NJ 07012-2355 Laboratory Director: SHELLA K MONGIA,MD, CLIA: 31D0696246



Patient Information:

7003, Donor

DOB: [REDACTED]

Sex: M

MR#: 7003

Patient#: [REDACTED]

Accession:

[REDACTED]

Test#: [REDACTED]

Order#: [REDACTED]

Ext Test#: [REDACTED]

Ext Order#: [REDACTED]

Specimen Type: DNA

Collected: Not provided

Received Date: May 12,2023

Authorized Date: May 20,2023

Physician:

Seitz, Suzanne

ATTN: Seitz, Suzanne

Fairfax Cryobank

3015 Williams Drive

Fairfax, VA 22031

Phone:

Fax:

Laboratory:

Fulgent Genetics

CAP#: 8042697

CLIA#: 05D2043189

Laboratory Director:

Dr. Hanlin (Harry) Gao

Report Date: Jun 09,2023

Final Report

TEST PERFORMED

CPLANE1 Single Gene

(1 Gene Panel: *CPLANE1*; gene sequencing with deletion and duplication analysis; deletion and duplication analysis failed)

RESULTS:

No clinically significant sequence variants were identified in the submitted specimen.

A negative result does not rule out the possibility of a genetic predisposition nor does it rule out any pathogenic mutations of the sort not queried by this test or in areas not reliably assessed by this test.

Deletion and duplication analysis failed. See Notes and Recommendations .

INTERPRETATION:

Notes and Recommendations:

- **The present analysis failed to generate data of sufficient quality for analysis of copy number variants. Deletions and duplications were not evaluated. A new sample is required to repeat this test.**
- As requested, this report only includes variants classified as Pathogenic, Likely Pathogenic, or Risk Allele at the time of analysis. If detected, this report does not include variants classified as of uncertain significance.
- Gene specific notes and limitations may be present. See below.
- These results should be interpreted in the context of this individual's clinical findings, biochemical profile, and family history.
- Genetic counseling is recommended. Available genetic counselors and additional resources can be found at the National Society of Genetic Counselors (NSGC; <https://www.nsgc.org>)
- Guide to Interpreting Genomic Reports: A Genomics Toolkit (CSER Consortium; February 2017) (<https://www.genome.gov/For-Health-Professionals/Provider-Genomics-Education-Resources#hep>)

GENES TESTED:

CPLANE1 Single Gene

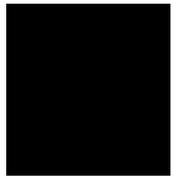
1 genes tested (100.00% at >20x).

CPLANE1

Gene Specific Notes and Limitations

Patient: 7003, Donor; Sex: M;
DOB: [REDACTED] MR#: 7003

Accession#: [REDACTED] Patient#: [REDACTED]
DocID: [REDACTED]; PAGE 1 of 3



No gene specific limitations apply to the genes on the tested panel.

METHODS:

Genomic DNA was isolated from the submitted specimen indicated above (if cellular material was submitted). DNA was barcoded, and enriched for the coding exons of targeted genes using hybrid capture technology. Prepared DNA libraries were then sequenced using a Next Generation Sequencing technology. Following alignment to the human genome reference sequence (assembly GRCh37), variants were detected in regions of at least 10x coverage. For this specimen, 100.00% and 100.00% of coding regions and splicing junctions of genes listed had been sequenced with coverage of at least 10x and 20x, respectively, by NGS or by Sanger sequencing. The remaining regions did not have 10x coverage, and were not evaluated. Variants were interpreted manually using locus specific databases, literature searches, and other molecular biological principles. To minimize false positive results, any variants that do not meet internal quality standards are confirmed by Sanger sequencing. Variants classified as pathogenic, likely pathogenic, or risk allele which are located in the coding regions and nearby intronic regions (+/- 20bp) of the genes listed above are reported. Variants outside these intervals may be reported but are typically not guaranteed. When a single pathogenic or likely pathogenic variant is identified in a clinically relevant gene with autosomal recessive inheritance, the laboratory will attempt to ensure 100% coverage of coding sequences either through NGS or Sanger sequencing technologies ("fill-in"). Deletion/duplication analysis has not been performed. New York patients: diagnostic findings are confirmed by Sanger, MLPA, or qPCR; exception SNV variants in genes for which confirmation of NGS results has been performed ≥ 10 times may not be confirmed if identified with high quality by NGS. Bioinformatics: The Fulgent Germline v2019.2 pipeline was used to analyze this specimen.

LIMITATIONS:

These test results and variant interpretation are based on the proper identification of the submitted specimen, accuracy of any stated familial relationships, and use of the correct human reference sequences at the queried loci. In very rare instances, errors may result due to mix-up or co-mingling of specimens. Positive results do not imply that there are no other contributors, genetic or otherwise, to this individual's phenotype, and negative results do not rule out a genetic cause for the indication for testing. Official gene names change over time. Fulgent uses the most up to date gene names based on HUGO Gene Nomenclature Committee (<https://www.genenames.org>) recommendations. If the gene name on report does not match that of ordered gene, please contact the laboratory and details can be provided. Result interpretation is based on the available clinical and family history information for this individual, collected published information, and Alamut annotation available at the time of reporting. This assay is designed and validated for detection of germline variants only. It is not designed or validated for the detection of low-level mosaicism or somatic mutations. This assay will not detect certain types of genomic aberrations such as translocations, inversions, or repeat expansions (eg. trinucleotide or hexanucleotide repeat expansion). DNA alterations in regulatory regions or deep intronic regions (greater than 20bp from an exon) may not be detected by this test. Unless otherwise indicated, no additional assays have been performed to evaluate genetic changes in this specimen. There are technical limitations on the ability of DNA sequencing to detect small insertions and deletions. Our laboratory uses a sensitive detection algorithm, however these types of alterations are not detected as reliably as single nucleotide variants. Rarely, due to systematic chemical, computational, or human error, DNA variants may be missed. Although next generation sequencing technologies and our bioinformatics analysis significantly reduce the confounding contribution of pseudogene sequences or other highly-homologous sequences, sometimes these may still interfere with the technical ability of the assay to identify pathogenic alterations in both sequencing and deletion/duplication analyses. Deletion/duplication analysis can identify alterations of genomic regions which are two or more contiguous exons in size; single exon deletions or duplications may occasionally be identified, but are not routinely detected by this test. When novel DNA duplications are identified, it is not possible to discern the genomic location or orientation of the duplicated segment, hence the effect of the duplication cannot be predicted. Where deletions are detected, it is not always possible to determine whether the predicted product will remain in-frame or not. Unless otherwise indicated, deletion/duplication analysis has not been performed in regions that have been sequenced by Sanger.

SIGNATURE:



Zhenbin Chen, Ph.D., CGMB, FACMG on 6/9/2023 08:45 AM PDT
Electronically signed



DISCLAIMER:

This test was developed and its performance characteristics determined by **Fulgent Genetics**. It has not been cleared or approved by the FDA. The laboratory is regulated under CLIA as qualified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research. Since genetic variation, as well as systematic and technical factors, can affect the accuracy of testing, the results of testing should always be interpreted in the context of clinical and familial data. For assistance with interpretation of these results, healthcare professionals may contact us directly at **(626) 350-0537** or **info@fulgentgenetics.com**. It is recommended that patients receive appropriate genetic counseling to explain the implications of the test result, including its residual risks, uncertainties and reproductive or medical options.