

|                               |             |                                |             |                       |                                  |
|-------------------------------|-------------|--------------------------------|-------------|-----------------------|----------------------------------|
| <b>Patient name:</b>          | DONOR 16032 | <b>Sample type:</b>            | Blood       | <b>Report date:</b>   | 21-OCT-2024                      |
| <b>DOB:</b>                   | ██████████  | <b>Sample collection date:</b> | 22-FEB-2023 | <b>Invitae #:</b>     | RQ4726574-1                      |
| <b>Sex assigned at birth:</b> | Male        | <b>Sample accession date:</b>  | 23-FEB-2023 | <b>Clinical team:</b> | Sarah O'Brien<br>Jeffrey Olliffe |
| <b>Gender:</b>                |             |                                |             |                       |                                  |
| <b>Patient ID (MRN):</b>      |             |                                |             |                       |                                  |

**Reason for testing**

Gamete donor

**Test performed**

Invitae Carrier Screen

## ADDENDED REPORT

This report supersedes RQ4726574 (03-MAR-2023) and updates the interpretation of the variant(s) in the table below. See bullet(s) below for a complete list of the report updates.

- The change in variant classification was made as a result of re-review of the evidence in light of new variant interpretation guidelines and/or new information. Updating variant classification may result in variant(s) being added to, removed from, or moved to a different section of the report.

### Updated Interpretations

| GENE   | VARIANT                  | ZYGOSITY     | PRIOR VARIANT CLASSIFICATION | NEW VARIANT CLASSIFICATION |
|--------|--------------------------|--------------|------------------------------|----------------------------|
| COL7A1 | c.5086C>T (p.Arg1696Cys) | heterozygous | Uncertain Significance       | PATHOGENIC                 |



## RESULT: POSITIVE

This carrier test evaluated 514 gene(s) for genetic changes (variants) that are associated with an increased risk of having a child with a genetic condition. Knowledge of carrier status for one of these conditions may provide information that can be used to assist with family planning and/or preparation. Carrier screening is not intended for diagnostic purposes. To identify a potential genetic basis for a condition in the individual being tested, diagnostic testing for the gene(s) of interest is recommended.

This test shows the presence of clinically significant genetic change(s) in this individual in the gene(s) indicated below. No other clinically significant changes were identified in the remaining genes evaluated with this test.

| RESULTS                                          | GENE   | VARIANT(S)                     | INHERITANCE         | PARTNER TESTING RECOMMENDED |
|--------------------------------------------------|--------|--------------------------------|---------------------|-----------------------------|
| <b>Carrier:</b> CC2D2A-related conditions        | CC2D2A | c.4303_4314+1del (Splice site) | Autosomal recessive | Yes                         |
| <b>Carrier:</b> Dystrophic epidermolysis bullosa | COL7A1 | c.5086C>T (p.Arg1696Cys)       | Autosomal recessive | Yes                         |
| <b>Carrier:</b> Glutaric acidemia type IIA       | ETFA   | c.667C>T (p.Arg223*)           | Autosomal recessive | Yes                         |



Patient name: DONOR 16032 DOB: [REDACTED]

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## Next steps

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- See the table above for recommendations regarding testing of this individual's reproductive partner.
- Even for genes that have a negative test result, there is always a small risk that an individual could still be a carrier. This is called “residual risk.” See the Carrier detection rates and residual risks document.
- Discussion with a physician and/or genetic counselor is recommended to further review the implications of this test result and to understand these results in the context of any family history of a genetic condition.
- All patients, regardless of result, may wish to consider additional screening for hemoglobinopathies by complete blood count (CBC) and hemoglobin electrophoresis, if this has not already been completed.
- Individuals can register their tests at <https://www.invitae.com/patients/> to access online results, educational resources, and next steps.

## Clinical summary



### RESULT: CARRIER

#### CC2D2A-related conditions

A single Likely Pathogenic variant, c.4303\_4314+1del (Splice site), was identified in CC2D2A.

##### What are CC2D2A-related conditions?

CC2D2A-related conditions include Joubert syndrome and related disorders (JSRD) and isolated retinal dystrophy. JSRD is part of a spectrum of disorders called ciliopathies, which involve defects in the microscopic, finger-like projections (cilia) that are located on the surface of cells and that are involved in cell movement and signaling. Ciliopathies affect many parts of the body. Isolated retinal dystrophy is a class of inherited eye conditions characterized by degeneration of the rods and cones (photoreceptors) which are the cells in the retina that respond to light. Both conditions can be caused by changes in several different genes.

Historically, Joubert syndrome is characterized by specific brain malformations called the “molar tooth sign,” low muscle tone (hypotonia), and developmental delay. Affected newborns can also have abnormally rapid breathing (tachypnea), temporary pauses in breathing (apnea), and difficulties controlling voluntary eye movement, particularly horizontal eye movement (oculomotor apraxia). Over time, breathing difficulties and visual acuity may improve. Individuals may develop difficulty coordinating movements (ataxia) and developmental delay during childhood. Many individuals have moderate intellectual disability. Other features include distinct facial appearance, extra fingers and toes (polydactyly), difficulty producing speech (speech apraxia), and seizures.

Joubert syndrome, Meckel syndrome, COACH syndrome, and orofacioidigital syndrome are part of the spectrum of conditions called JSRD. The term JSRD has been applied to individuals with characteristic Joubert syndrome features, in addition to other anomalies. This includes, but is not limited to, retinal dystrophy, kidney disease, liver disease, neural tube defects, and congenital malformations affecting the skull and face (craniofacial malformations).

Symptoms and severity can vary, even between family members with the same genetic change. Prognosis depends on the severity of symptoms.

Individuals with isolated retinal dystrophy typically do not have features of Joubert syndrome. Symptoms of isolated retinal dystrophy can present at any age. The earliest feature is typically involuntary eye movements (nystagmus) that can present during infancy. Retinal dystrophies can cause reduced visual acuity, loss of side (peripheral) and/or central vision, impaired color vision, increased sensitivity to light (photophobia), and night blindness. Symptoms, severity, and progression of disease are highly variable.

Follow-up depends on each affected individual's specific situation, and discussion with a healthcare provider should be considered.

## Next steps

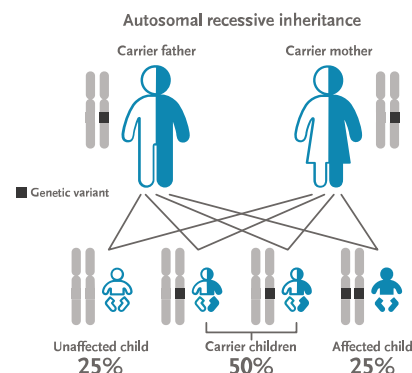
Carrier testing for the reproductive partner is recommended.

### + If your partner tests positive:

In autosomal recessive inheritance, an individual must have disease-causing genetic changes in each copy of the CC2D2A gene to be affected. Carriers, who have a disease-causing genetic change in only one copy of the gene, typically do not have symptoms. When both reproductive partners are carriers of an autosomal recessive condition, there is a 25% chance for each child to have the condition.

### - If your partner tests negative:

A negative carrier test result reduces, but does not eliminate, the chance that a person may be a carrier. The risk that a person could still be a carrier, even after a negative test result, is called a residual risk. See the table below for your partner's hypothetical residual risk after testing negative for CC2D2A-related conditions. These values are provided only as a guide, are based on the detection rate for the condition as tested at Invitae, and assume a negative family history, the absence of symptoms, and vary based on the ethnic background of an individual. For genes associated with both dominant and recessive inheritance, the numbers provided apply to the recessive condition(s) associated with the gene.



| DISORDER (INHERITANCE)                           | GENE   | ETHNICITY  | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|--------------------------------------------------|--------|------------|------------------------------------|---------------------------------------------|
| CC2D2A-related conditions (AR)<br>NM_001080522.2 | CC2D2A | Pan-ethnic | 1 in 426                           | 1 in 42500                                  |


**RESULT: CARRIER**

## Dystrophic epidermolysis bullosa

A single Pathogenic variant, c.5086C>T (p.Arg1696Cys), was identified in COL7A1.

### What is dystrophic epidermolysis bullosa?

Dystrophic epidermolysis bullosa is a condition that can be inherited in an autosomal recessive or autosomal dominant manner. To understand which condition a genetic change is associated with, a review of the entire report, including the variant details section, is recommended.

Please note that the COL7A1 variant identified in this individual is expected to be associated with autosomal recessive dystrophic epidermolysis bullosa.

Epidermolysis bullosa (EB) is a group of conditions that affect the skin. EB is caused by a defect in collagen, the protein that gives skin its strength and holds it together. Defects in collagen cause extremely fragile skin. Dystrophic epidermolysis bullosa (DEB) is a form of EB, and is primarily characterized by blistering and scarring of skin and mucous membranes following minor trauma. Symptoms and severity are quite variable. Individuals with autosomal recessive DEB (RDEB) typically have more severe symptoms compared to individuals with autosomal dominant DEB (DDEB). Infants are often born with blisters and areas of missing skin over much of the body. Blisters in the mouth and digestive tract make feeding difficult, which leads to chronic malnutrition and poor growth (failure to thrive). As the blisters heal, this causes extensive scarring of the arms, legs, hands and feet, leading to joint deformities that restrict movement (contractures) and the fusion of fingers or toes (pseudosyndactyly). Affected individuals also have high risk for an aggressive form of skin cancer called squamous cell carcinoma, as well as vision loss due to scarring of the clear covering at the front of the eye (cornea); non-skin-related findings are also possible. The constellation of symptoms of RDEB can be life-threatening. Prognosis depends on the severity of symptoms. Follow-up depends on each affected individual's specific situation, and discussion with a healthcare provider should be considered.

## Next steps

Carrier testing for the reproductive partner is recommended.



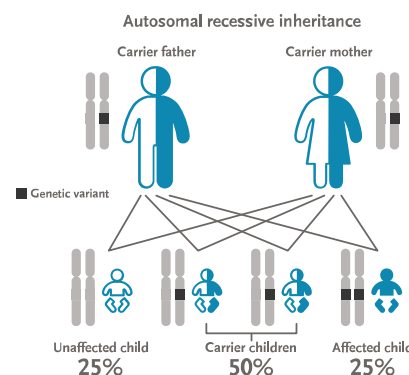
### If your partner tests positive:

In autosomal recessive inheritance, an individual must have disease-causing genetic changes in each copy of the COL7A1 gene to be affected. Carriers, who have a disease-causing genetic change in only one copy of the gene, typically do not have symptoms. When both reproductive partners are carriers of an autosomal recessive condition, there is a 25% chance for each child to have the condition.



### If your partner tests negative:

A negative carrier test result reduces, but does not eliminate, the chance that a person may be a carrier. The risk that a person could still be a carrier, even after a negative test result, is called a residual risk. See the table below for your partner's hypothetical residual risk after testing negative for dystrophic epidermolysis bullosa. These values are provided only as a guide, are based on the detection rate for the condition as tested at Invitae, and assume a negative family history, the absence of symptoms, and vary based on the ethnic background of an individual. For genes associated with both dominant and recessive inheritance, the numbers provided apply to the recessive condition(s) associated with the gene.



| DISORDER (INHERITANCE)                               | GENE   | ETHNICITY  | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|------------------------------------------------------|--------|------------|------------------------------------|---------------------------------------------|
| Dystrophic epidermolysis bullosa (AR)<br>NM_000094.3 | COL7A1 | Pan-ethnic | 1 in 370                           | 1 in 12300                                  |


**RESULT: CARRIER**

## Glutaric acidemia type IIA

A single Pathogenic variant, c.667C>T (p.Arg223\*), was identified in ETFA.

### What is glutaric acidemia type IIA?

Glutaric acidemia type II (GA II), also called multiple acyl-CoA dehydrogenase deficiency (MADD), is a group of conditions in which the body cannot properly break down proteins and fats. These proteins and fats build up in the body and cause the blood and tissues to become too acidic (metabolic acidosis). Symptoms and age of onset of GA IIA can vary. There are three commonly recognized forms of GA II. Most individuals present with symptoms within a few days of birth, either with or without birth defects. Symptoms of both early-onset forms typically include metabolic acidosis, low blood sugar (hypoglycemia), low muscle tone (hypotonia), weakened heart muscle (cardiomyopathy), and feeding problems. Symptoms are often triggered by illness. In the more severe form, infants may have unusual facial features (dysmorphism) as well as abnormalities of the brain, kidney, liver, abdomen, and/or external genitalia. Many individuals with either of the early-onset forms of GA II die during infancy. Children who survive may have learning and other health problems. The late-onset form of GA II typically presents in adolescence or adulthood. Symptoms are milder than in the early-onset forms, and usually involve muscle weakness. However, individuals with metabolic crises as well as individuals who do not have any signs or symptoms of the condition (asymptomatic) have been reported. Early initiation of treatment, including dietary management and, in some cases, riboflavin (vitamin B2) supplementation, may reduce the severity of symptoms. Follow-up depends on each affected individual's specific situation, and discussion with a healthcare provider should be considered.

## Next steps

Carrier testing for the reproductive partner is recommended.



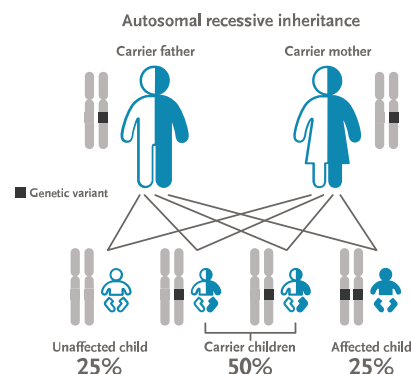
### If your partner tests positive:

In autosomal recessive inheritance, an individual must have disease-causing genetic changes in each copy of the ETFA gene to be affected. Carriers, who have a disease-causing genetic change in only one copy of the gene, typically do not have symptoms. When both reproductive partners are carriers of an autosomal recessive condition, there is a 25% chance for each child to have the condition.



### If your partner tests negative:

A negative carrier test result reduces, but does not eliminate, the chance that a person may be a carrier. The risk that a person could still be a carrier, even after a negative test result, is called a residual risk. See the table below for your partner's hypothetical residual risk after testing negative for glutaric acidemia type IIA. These values are provided only as a guide, are based on the detection rate for the condition as tested at Invitae, and assume a negative family history, the absence of symptoms, and vary based on the ethnic background of an individual. For genes associated with both dominant and recessive inheritance, the numbers provided apply to the recessive condition(s) associated with the gene.



| DISORDER (INHERITANCE)                         | GENE  | ETHNICITY  | CARRIER FREQUENCY BEFORE SCREENING | CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT |
|------------------------------------------------|-------|------------|------------------------------------|---------------------------------------------|
| Glutaric acidemia type IIA (AR)<br>NM_000126.3 | ETF A | Pan-ethnic | ≤1 in 500                          | Reduced                                     |

## Results to note

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### GALT

- c.-119\_-116del (Non-coding) was identified in the GALT gene.
- This benign variant is not known to cause disease and does not impact this individual's risk to be a carrier for galactosemia (GALT-related). Carrier testing for the reproductive partner is not indicated based on this result. See Variant details for more information.

### NPHS2

- c.686G>A (p.Arg229Gln) , was identified in NPHS2. This variant may be pathogenic when in combination with certain NPHS2 variants, and therefore its clinical significance is currently uncertain.
- Please note that the c.686G>A (p.Arg229Gln) variant may be pathogenic when on the opposite chromosome (in trans) from certain other NPHS2 variants. The c.686G>A (p.Arg229Gln) variant is unlikely to be associated with nephrotic syndrome when homozygous (two copies).

If identified, pathogenic NPHS2 variant(s) would be included in the Clinical summary section. Additionally, when the combination of a pathogenic NPHS2 variant and c.686G>A (p.Arg229Gln) has been reported to be clinically significant, this would be described in the Variant details for the pathogenic variant.

Congenital nephrotic syndrome type 2 (NPHS2), also called steroid-resistant nephrotic syndrome, is a condition in which the kidneys are unable to properly filter waste products from the blood and remove them in the urine. The combination of c.686G>A (p.Arg229Gln) and certain other NPHS2 variants is associated with a form of the condition which has later onset and slower disease progression.

Carrier testing for the reproductive partner may be considered, since c.686G>A (p.Arg229Gln) may be pathogenic when on the opposite chromosome from certain other NPHS2 variants.

### SMN1

- Negative result. SMN1: 2 copies; c.\*3+80T>G not detected.

### Pseudodeficiency allele(s)

- Benign changes, c.1685T>C (p.Ile562Thr), known to be pseudodeficiency alleles, identified in the GALT gene. Pseudodeficiency alleles are not known to be associated with disease, including Krabbe disease.
- The presence of a pseudodeficiency allele does not impact this individual's risk to be a carrier. Individuals with pseudodeficiency alleles may exhibit false positive results on related biochemical tests, including newborn screening. However, pseudodeficiency alleles are not known to cause disease, even when there are two copies of the variant (homozygous) or when in combination with another disease-causing variant (compound heterozygous). Carrier testing for the reproductive partner is not indicated based on this result.

## Variant details

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### CC2D2A, Exon 34, c.4303\_4314+1del (Splice site), heterozygous, Likely Pathogenic

- This variant results in the deletion of part of exon 34 (c.4303\_4314+1del) of the CC2D2A gene. It is expected to disrupt RNA splicing. Variants that disrupt the donor or acceptor splice site typically lead to a loss of protein function (PMID: 16199547), and loss-of-function variants in CC2D2A are known to be pathogenic (PMID: 19777577).
- This variant is not present in population databases (gnomAD no frequency).
- This variant has not been reported in the literature in individuals affected with CC2D2A-related conditions.

- In summary, the currently available evidence indicates that the variant is pathogenic, but additional data are needed to prove that conclusively. Therefore, this variant has been classified as Likely Pathogenic.

**COL7A1, Exon 55, c.5086C>T (p.Arg1696Cys), heterozygous, PATHOGENIC**

- This sequence change replaces arginine, which is basic and polar, with cysteine, which is neutral and slightly polar, at codon 1696 of the COL7A1 protein (p.Arg1696Cys).
- This variant is present in population databases (rs2229820, gnomAD 0.03%).
- This missense change has been observed in individual(s) with autosomal recessive dystrophic epidermolysis bullosa (PMID: 27899325).
- ClinVar contains an entry for this variant (Variation ID: 899655).
- Invitae Evidence Modeling of protein sequence and biophysical properties (such as structural, functional, and spatial information, amino acid conservation, physicochemical variation, residue mobility, and thermodynamic stability) indicates that this missense variant is expected to disrupt COL7A1 protein function with a positive predictive value of 95%.
- For these reasons, this variant has been classified as Pathogenic.

**ETFA, Exon 8, c.667C>T (p.Arg223\*), heterozygous, PATHOGENIC**

- This sequence change creates a premature translational stop signal (p.Arg223\*) in the ETFA gene. It is expected to result in an absent or disrupted protein product. Loss-of-function variants in ETFA are known to be pathogenic (PMID: 16510302, 23785301).
- This variant is present in population databases (rs769976586, gnomAD 0.006%).
- This premature translational stop signal has been observed in individual(s) with bilateral renal dysplasia and multiple renal cysts (PMID: 29096039).
- ClinVar contains an entry for this variant (Variation ID: 429752).
- For these reasons, this variant has been classified as Pathogenic.

**GALT, Exon 1, c.-119\_-116del (Non-coding), heterozygous, Benign (reportable variant)**

- This variant occurs in a non-coding region of the GALT gene. It does not change the encoded amino acid sequence of the GALT protein. This variant is unique to the D2 allele and is also known as the Duarte variant.
- This variant is present in population databases (rs142496102, gnomAD 8%), including at least one homozygous and/or hemizygous individual. The c.-119\_-116del variant is the most common galactosemia variant (PMID: 19904210).
- Compound heterozygosity for the Duarte allele and a pathogenic galactosemia variant (termed Duarte variant Galactosemia, DG) results in approximately 14-25% of normal GALT enzyme activity (PMID: 25473725, 25681083) and causes elevations of the metabolites found in galactosemia. DG may trigger a positive galactosemia newborn screening or abnormal biochemical test results but does not require dietary intervention (PMID: 30593450, 30593448) and does not cause the significant clinical consequences of classic galactosemia (PMID: 30593450, 31160755). A homozygous c.-119\_-116del variant alone (DD) can have mildly reduced GALT enzyme activity but is insufficient to cause metabolite accumulation and is considered clinically benign (PMID: 24718839, 25473725).
- ClinVar contains two entries for this variant (Variation ID: 140570, 25111).
- Algorithms developed to predict the effect of variants on gene product structure and function are not available or were not evaluated for this variant.
- Experimental studies have shown that this variant affects GALT enzyme activity (PMID: 11286503, 11479743, 19224951).
- For these reasons, this variant has been classified as a Benign reportable variant.

## Residual risk

No carrier test can detect 100% of carriers. There still remains a small risk of being a carrier after a negative test (residual risk). Residual risk values assume a negative family history and are inferred from published carrier frequencies and estimated detection rates based on testing technologies used at Invitae. You can view Invitae's complete Carrier detection rates and residual risks document (containing all carrier genes) online at <https://www.invitae.com/carrier-residual-risks/>. Additionally, the order-specific information for this report is available to download in the portal (under this order's documents) or can be requested by contacting Invitae Client Services. The complete Carrier detection rates and residual risks document will not be



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applicable for any genes with specimen-specific limitations in sequencing and/or deletion/duplication coverage. Please see the final bullet point in the Limitations section of this report to view if this specimen had any gene-specific coverage gaps.

## Genes analyzed

This table represents a complete list of genes analyzed for this individual, including the relevant gene transcript(s). If more than one transcript is listed for a single gene, variants were reported using the first transcript listed unless otherwise indicated in the report. An asterisk (\*) indicates that this gene has a limitation. Please see the Limitations section for details. Results are negative, unless otherwise indicated in the report.

| GENE     | TRANSCRIPT  | GENE     | TRANSCRIPT              | GENE     | TRANSCRIPT     |
|----------|-------------|----------|-------------------------|----------|----------------|
| AAAS     | NM_015665.5 | AP1S1    | NM_001283.3             | CBS      | NM_000071.2    |
| ABCA12   | NM_173076.2 | AQP2     | NM_000486.5             | CC2D1A   | NM_017721.5    |
| ABCA3    | NM_001089.2 | ARG1     | NM_000045.3             | CC2D2A   | NM_001080522.2 |
| ABCA4    | NM_000350.2 | ARL6     | NM_177976.2             | CCDC103  | NM_213607.2    |
| ABCB11   | NM_003742.2 | ARSA     | NM_000487.5             | CCDC39   | NM_181426.1    |
| ABCB4    | NM_000443.3 | ARSB     | NM_000046.3             | CCDC88C  | NM_001080414.3 |
| ABCC2*   | NM_000392.4 | ASL      | NM_000048.3             | CD3D     | NM_000732.4    |
| ABCC8    | NM_000352.4 | ASNS     | NM_133436.3             | CD3E     | NM_000733.3    |
| ACAD9    | NM_014049.4 | ASPA     | NM_000049.2             | CD40     | NM_001250.5    |
| ACADM    | NM_000016.5 | ASS1     | NM_000050.4             | CD59     | NM_203330.2    |
| ACADVL   | NM_000018.3 | ATM*     | NM_000051.3             | CDH23    | NM_022124.5    |
| ACAT1    | NM_000019.3 | ATP6V1B1 | NM_001692.3             | CEP152   | NM_014985.3    |
| ACOX1    | NM_004035.6 | ATP7B    | NM_000053.3             | CEP290   | NM_025114.3    |
| ACSF3    | NM_174917.4 | ATP8B1*  | NM_005603.4             | CERKL    | NM_001030311.2 |
| ADA      | NM_000022.2 | BBS1     | NM_024649.4             | CFTR*    | NM_000492.3    |
| ADAMTS2  | NM_014244.4 | BBS10    | NM_024685.3             | CHAT     | NM_020549.4    |
| ADAMTSL4 | NM_019032.5 | BBS12    | NM_152618.2             | CHRNE    | NM_000080.3    |
| ADGRG1   | NM_005682.6 | BBS2     | NM_031885.3             | CHRNA    | NM_005199.4    |
| ADGRV1   | NM_032119.3 | BBS4     | NM_033028.4             | CIITA    | NM_000246.3    |
| AGA      | NM_000027.3 | BBS5     | NM_152384.2             | CLCN1    | NM_000083.2    |
| AGL      | NM_000642.2 | BBS7     | NM_176824.2             | CLN3     | NM_001042432.1 |
| AGPS     | NM_003659.3 | BBS9*    | NM_198428.2             | CLN5     | NM_006493.2    |
| AGXT     | NM_000030.2 | BCKDHA   | NM_000709.3             | CLN6     | NM_017882.2    |
| AHI1     | NM_017651.4 | BCKDHB   | NM_183050.2             | CLN8     | NM_018941.3    |
| AIPL1*   | NM_014336.4 | BCS1L    | NM_004328.4             | CLRN1    | NM_174878.2    |
| AIRE     | NM_000383.3 | BLM      | NM_000057.3             | CNGB3    | NM_019098.4    |
| ALDH3A2  | NM_000382.2 | BLOC1S3  | NM_212550.4             | COL11A2* | NM_080680.2    |
| ALDH7A1  | NM_001182.4 | BLOC1S6  | NM_012388.3             | COL17A1  | NM_000494.3    |
| ALDOB    | NM_000035.3 | BMP1     | NM_006129.4;NM_001199.3 | COL27A1  | NM_032888.3    |
| ALG1     | NM_019109.4 | BRIP1    | NM_032043.2             | COL4A3   | NM_000091.4    |
| ALG6     | NM_013339.3 | BSND     | NM_057176.2             | COL4A4   | NM_000092.4    |
| ALMS1    | NM_015120.4 | BTD      | NM_000060.3             | COL7A1   | NM_000094.3    |
| ALPL     | NM_000478.5 | CAD      | NM_004341.4             | COX15    | NM_004376.6    |
| AMN*     | NM_030943.3 | CANT1    | NM_138793.3             | CPS1     | NM_001875.4    |
| AMT      | NM_000481.3 | CAPN3    | NM_000070.2             | CPT1A    | NM_001876.3    |
| ANO10*   | NM_018075.3 | CASQ2    | NM_001232.3             | CPT2     | NM_000098.2    |


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| GENE     | TRANSCRIPT     |
|----------|----------------|
| CRB1     | NM_201253.2    |
| CRTAP    | NM_006371.4    |
| CTNS     | NM_004937.2    |
| CTSA     | NM_000308.3    |
| CTSC     | NM_001814.5    |
| CTSD     | NM_001909.4    |
| CTSK     | NM_000396.3    |
| CYBA     | NM_000101.3    |
| CYP11A1  | NM_000781.2    |
| CYP11B1  | NM_000497.3    |
| CYP11B2  | NM_000498.3    |
| CYP17A1  | NM_000102.3    |
| CYP19A1  | NM_031226.2    |
| CYP1B1   | NM_000104.3    |
| CYP21A2* | NM_000500.7    |
| CYP27A1  | NM_000784.3    |
| CYP27B1  | NM_000785.3    |
| CYP7B1   | NM_004820.3    |
| DBT      | NM_001918.3    |
| DCAF17   | NM_025000.3    |
| DCLRE1C  | NM_001033855.2 |
| DDX11*   | NM_030653.3    |
| DFNB59   | NM_001042702.3 |
| DGAT1    | NM_012079.5    |
| DGUOK    | NM_080916.2    |
| DHCR7    | NM_001360.2    |
| DHDDS    | NM_024887.3    |
| DLD      | NM_000108.4    |
| DLL3     | NM_016941.3    |
| DNAH11   | NM_001277115.1 |
| DNAH5    | NM_001369.2    |
| DNAI1    | NM_012144.3    |
| DNAI2    | NM_023036.4    |
| DNMT3B   | NM_006892.3    |
| DOK7     | NM_173660.4    |
| DUOX2*   | NM_014080.4    |
| DYNC2H1  | NM_001080463.1 |
| DYSF     | NM_003494.3    |
| EIF2AK3  | NM_004836.6    |

| GENE    | TRANSCRIPT     |
|---------|----------------|
| EIF2B1  | NM_001414.3    |
| EIF2B2  | NM_014239.3    |
| EIF2B3  | NM_020365.4    |
| EIF2B4  | NM_015636.3    |
| EIF2B5  | NM_003907.2    |
| ELP1    | NM_003640.3    |
| EPG5    | NM_020964.2    |
| ERCC2   | NM_000400.3    |
| ERCC6   | NM_000124.3    |
| ERCC8   | NM_000082.3    |
| ESCO2   | NM_001017420.2 |
| ETFA    | NM_000126.3    |
| ETFB    | NM_001985.2    |
| ETFDH   | NM_004453.3    |
| ETHE1   | NM_014297.3    |
| EVC     | NM_153717.2    |
| EVC2    | NM_147127.4    |
| EXOSC3  | NM_016042.3    |
| EYS*    | NM_001142800.1 |
| FAH*    | NM_000137.2    |
| FAM161A | NM_001201543.1 |
| FANCA   | NM_000135.2    |
| FANCC   | NM_000136.2    |
| FANCD2* | NM_033084.3    |
| FANCE   | NM_021922.2    |
| FANCG   | NM_004629.1    |
| FANCI   | NM_001113378.1 |
| FANCL*  | NM_018062.3    |
| FBP1    | NM_000507.3    |
| FBXO7   | NM_012179.3    |
| FH*     | NM_000143.3    |
| FKBP10  | NM_021939.3    |
| FKRP    | NM_024301.4    |
| FKTN    | NM_001079802.1 |
| FMO3    | NM_006894.6    |
| FOXN1   | NM_003593.2    |
| FOXRED1 | NM_017547.3    |
| FRAS1   | NM_025074.6    |
| FREM2   | NM_207361.5    |

| GENE   | TRANSCRIPT     |
|--------|----------------|
| FUCA1  | NM_000147.4    |
| G6PC   | NM_000151.3    |
| G6PC3  | NM_138387.3    |
| GAA    | NM_000152.3    |
| GALC*  | NM_000153.3    |
| GALE*  | NM_000403.3    |
| GALK1  | NM_000154.1    |
| GALNS  | NM_000512.4    |
| GALNT3 | NM_004482.3    |
| GALT   | NM_000155.3    |
| GAMT   | NM_000156.5    |
| GATM   | NM_001482.2    |
| GBA*   | NM_001005741.2 |
| GBE1   | NM_000158.3    |
| GCDH   | NM_000159.3    |
| GCH1   | NM_000161.2    |
| GDF5   | NM_000557.4    |
| GFM1   | NM_024996.5    |
| GHR*   | NM_000163.4    |
| GJB2   | NM_004004.5    |
| GLB1   | NM_000404.2    |
| GLDC   | NM_000170.2    |
| GLE1   | NM_001003722.1 |
| GNE*   | NM_001128227.2 |
| GNPAT  | NM_014236.3    |
| GNPTAB | NM_024312.4    |
| GNPTG  | NM_032520.4    |
| GNS    | NM_002076.3    |
| GORAB  | NM_152281.2    |
| GRHPR  | NM_012203.1    |
| GRIP1  | NM_021150.3    |
| GSS    | NM_000178.2    |
| GUCY2D | NM_000180.3    |
| GUSB   | NM_000181.3    |
| HADH   | NM_005327.4    |
| HADHA  | NM_000182.4    |
| HADHB  | NM_000183.2    |
| HAMP   | NM_021175.2    |
| HAX1   | NM_006118.3    |


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| GENE    | TRANSCRIPT     |
|---------|----------------|
| HBA1*   | NM_000558.4    |
| HBA2    | NM_000517.4    |
| HBB     | NM_000518.4    |
| HEXA    | NM_000520.4    |
| HEXB    | NM_000521.3    |
| HGSNAT  | NM_152419.2    |
| HJV     | NM_213653.3    |
| HLCS    | NM_000411.6    |
| HMGCL   | NM_000191.2    |
| HMOX1   | NM_002133.2    |
| HOGA1   | NM_138413.3    |
| HPD     | NM_002150.2    |
| HPS1    | NM_000195.4    |
| HPS3    | NM_032383.4    |
| HPS4    | NM_022081.5    |
| HPS5    | NM_181507.1    |
| HPS6    | NM_024747.5    |
| HSD17B3 | NM_000197.1    |
| HSD17B4 | NM_000414.3    |
| HSD3B2  | NM_000198.3    |
| HYAL1   | NM_153281.1    |
| HYLS1   | NM_145014.2    |
| IDUA    | NM_000203.4    |
| IGHMBP2 | NM_002180.2    |
| IKBBK   | NM_001556.2    |
| IL7R    | NM_002185.3    |
| INVS    | NM_014425.3    |
| ITGA6   | NM_000210.3    |
| ITGB3   | NM_000212.2    |
| ITGB4   | NM_001005731.2 |
| IVD     | NM_002225.3    |
| JAK3    | NM_000215.3    |
| KCNJ1   | NM_000220.4    |
| KCNJ11  | NM_000525.3    |
| LAMA2   | NM_000426.3    |
| LAMA3   | NM_000227.4    |
| LAMB3   | NM_000228.2    |
| LAMC2   | NM_005562.2    |
| LARGE1  | NM_004737.4    |

| GENE    | TRANSCRIPT     |
|---------|----------------|
| LCA5    | NM_181714.3    |
| LDLR    | NM_000527.4    |
| LDLRAP1 | NM_015627.2    |
| LHX3    | NM_014564.4    |
| LIFR*   | NM_002310.5    |
| LIG4    | NM_002312.3    |
| LIPA    | NM_000235.3    |
| LMBRD1  | NM_018368.3    |
| LOXHD1  | NM_144612.6    |
| LPL     | NM_000237.2    |
| LRAT    | NM_004744.4    |
| LRP2    | NM_004525.2    |
| LRPPRC  | NM_133259.3    |
| LYST    | NM_000081.3    |
| MAK     | NM_001242957.2 |
| MAN2B1  | NM_000528.3    |
| MANBA   | NM_005908.3    |
| MCEE    | NM_032601.3    |
| MCOLN1  | NM_020533.2    |
| MCPH1   | NM_024596.4    |
| MECR    | NM_016011.3    |
| MED17   | NM_004268.4    |
| MESP2   | NM_001039958.1 |
| MFSD8   | NM_152778.2    |
| MKKS    | NM_018848.3    |
| MKS1    | NM_017777.3    |
| MLC1*   | NM_015166.3    |
| MLYCD   | NM_012213.2    |
| MMAA    | NM_172250.2    |
| MMAB    | NM_052845.3    |
| MMACHC  | NM_015506.2    |
| MMADHC  | NM_015702.2    |
| MOCS1   | NM_001358530.2 |
| MOCS2A  | NM_176806.3    |
| MOCS2B  | NM_004531.4    |
| MPI     | NM_002435.2    |
| MPL     | NM_005373.2    |
| MPV17   | NM_002437.4    |
| MRE11   | NM_005591.3    |

| GENE    | TRANSCRIPT              |
|---------|-------------------------|
| MTHFR*  | NM_005957.4             |
| MTR     | NM_000254.2             |
| MTRR    | NM_002454.2             |
| MTTP    | NM_000253.3             |
| MUSK    | NM_005592.3             |
| MUT     | NM_000255.3             |
| MVK     | NM_000431.3             |
| MYO15A  | NM_016239.3             |
| MYO7A   | NM_000260.3             |
| NAGA    | NM_000262.2             |
| NAGLU   | NM_000263.3             |
| NAGS    | NM_153006.2             |
| NBN     | NM_002485.4             |
| NCF2    | NM_000433.3             |
| NDRG1   | NM_006096.3             |
| NDUFAF2 | NM_174889.4             |
| NDUFAF5 | NM_024120.4             |
| NDUFS4  | NM_002495.3             |
| NDUFS6  | NM_004553.4             |
| NDUFS7  | NM_024407.4             |
| NDUFV1  | NM_007103.3             |
| NEB*    | NM_001271208.1          |
| NEU1    | NM_000434.3             |
| NGLY1   | NM_018297.3             |
| NPC1    | NM_000271.4             |
| NPC2    | NM_006432.3             |
| NPHP1   | NM_000272.3             |
| NPHS1   | NM_004646.3             |
| NPHS2   | NM_014625.3             |
| NR2E3   | NM_014249.3             |
| NSMCE3  | NM_138704.3             |
| NTRK1   | NM_001012331.1          |
| OAT*    | NM_000274.3             |
| OCA2    | NM_000275.2             |
| OPA3    | NM_025136.3             |
| OSTM1   | NM_014028.3             |
| OTOA*   | NM_144672.3             |
| OTOF    | NM_194248.2;NM_194323.2 |
| P3H1    | NM_022356.3             |


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| GENE    | TRANSCRIPT                  |
|---------|-----------------------------|
| PAH     | NM_000277.1                 |
| PANK2   | NM_153638.2                 |
| PC      | NM_000920.3                 |
| PCBD1   | NM_000281.3                 |
| PCCA    | NM_000282.3                 |
| PCCB    | NM_000532.4                 |
| PCDH15  | NM_033056.3                 |
| PCNT    | NM_006031.5                 |
| PDHB    | NM_000925.3                 |
| PEPD    | NM_000285.3                 |
| PET100  | NM_001171155.1              |
| PEX1*   | NM_000466.2                 |
| PEX10   | NM_153818.1                 |
| PEX12   | NM_000286.2                 |
| PEX13   | NM_002618.3                 |
| PEX16   | NM_004813.2                 |
| PEX2    | NM_000318.2                 |
| PEX26   | NM_017929.5                 |
| PEX5    | NM_001131025.1              |
| PEX6    | NM_000287.3                 |
| PEX7    | NM_000288.3                 |
| PFKM    | NM_000289.5                 |
| PGM3    | NM_001199917.1              |
| PHGDH   | NM_006623.3                 |
| PHKB    | NM_000293.2;NM_00103183.5.2 |
| PHKG2   | NM_000294.2                 |
| PHYH    | NM_006214.3                 |
| PIGN    | NM_176787.4                 |
| PKHD1*  | NM_138694.3                 |
| PLA2G6  | NM_003560.2                 |
| PLEKHG5 | NM_020631.4                 |
| PLOD1   | NM_000302.3                 |
| PMM2    | NM_000303.2                 |
| PNPO    | NM_018129.3                 |
| POLG    | NM_002693.2                 |
| POLH    | NM_006502.2                 |
| POMGNT1 | NM_017739.3                 |
| POMT1   | NM_007171.3                 |
| POMT2   | NM_013382.5                 |

| GENE     | TRANSCRIPT     |
|----------|----------------|
| POR      | NM_000941.2    |
| POU1F1   | NM_000306.3    |
| PPT1     | NM_000310.3    |
| PRCD     | NM_001077620.2 |
| PRDM5    | NM_018699.3    |
| PRF1     | NM_001083116.1 |
| PROP1    | NM_006261.4    |
| PSAP     | NM_002778.3    |
| PTPRC*   | NM_002838.4    |
| PTS      | NM_000317.2    |
| PUS1     | NM_025215.5    |
| PYGM     | NM_005609.3    |
| QDPR     | NM_000320.2    |
| RAB23    | NM_183227.2    |
| RAG1     | NM_000448.2    |
| RAG2     | NM_000536.3    |
| RAPSN    | NM_005055.4    |
| RARS2    | NM_020320.3    |
| RDH12    | NM_152443.2    |
| RLBP1    | NM_000326.4    |
| RMRP     | NR_003051.3    |
| RNASEH2A | NM_006397.2    |
| RNASEH2B | NM_024570.3    |
| RNASEH2C | NM_032193.3    |
| RPE65    | NM_000329.2    |
| RPGRIP1L | NM_015272.2    |
| RTEL1    | NM_001283009.1 |
| RXYLT1   | NM_014254.2    |
| RYR1     | NM_000540.2    |
| SACS     | NM_014363.5    |
| SAMD9    | NM_017654.3    |
| SAMHD1   | NM_015474.3    |
| SCO2     | NM_005138.2    |
| SEC23B   | NM_006363.4    |
| SEPSECS  | NM_016955.3    |
| SGCA     | NM_000023.2    |
| SGCB     | NM_000232.4    |
| SGCD     | NM_000337.5    |
| SGCG     | NM_000231.2    |

| GENE     | TRANSCRIPT     |
|----------|----------------|
| SGSH     | NM_000199.3    |
| SKIV2L   | NM_006929.4    |
| SLC12A1  | NM_000338.2    |
| SLC12A3  | NM_000339.2    |
| SLC12A6  | NM_133647.1    |
| SLC17A5  | NM_012434.4    |
| SLC19A2  | NM_006996.2    |
| SLC19A3  | NM_025243.3    |
| SLC1A4   | NM_003038.4    |
| SLC22A5  | NM_003060.3    |
| SLC25A13 | NM_014251.2    |
| SLC25A15 | NM_014252.3    |
| SLC25A20 | NM_000387.5    |
| SLC26A2  | NM_000112.3    |
| SLC26A3  | NM_000111.2    |
| SLC26A4  | NM_000441.1    |
| SLC27A4  | NM_005094.3    |
| SLC35A3  | NM_012243.2    |
| SLC37A4  | NM_001164277.1 |
| SLC38A8  | NM_001080442.2 |
| SLC39A4  | NM_130849.3    |
| SLC45A2  | NM_016180.4    |
| SLC4A11  | NM_032034.3    |
| SLC5A5   | NM_000453.2    |
| SLC7A7   | NM_001126106.2 |
| SMARCA1  | NM_014140.3    |
| SMN1*    | NM_000344.3    |
| SMPD1    | NM_000543.4    |
| SNAP29   | NM_004782.3    |
| SPG11    | NM_025137.3    |
| SPR      | NM_003124.4    |
| SRD5A2   | NM_000348.3    |
| ST3GAL5  | NM_003896.3    |
| STAR     | NM_000349.2    |
| STX11    | NM_003764.3    |
| STXBP2   | NM_006949.3    |
| SUMF1    | NM_182760.3    |
| SUOX     | NM_000456.2    |
| SURF1    | NM_003172.3    |


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| GENE    | TRANSCRIPT     |
|---------|----------------|
| SYNE4   | NM_001039876.2 |
| TANGO2  | NM_152906.6    |
| TAT     | NM_000353.2    |
| TBCD    | NM_005993.4    |
| TBCE*   | NM_003193.4    |
| TCIRG1  | NM_006019.3    |
| TCN2    | NM_000355.3    |
| TECPR2  | NM_014844.3    |
| TERT    | NM_198253.2    |
| TF      | NM_001063.3    |
| TFR2    | NM_003227.3    |
| TG*     | NM_003235.4    |
| TGM1    | NM_000359.2    |
| TH      | NM_199292.2    |
| TK2     | NM_004614.4    |
| TMC1    | NM_138691.2    |
| TMEM216 | NM_001173990.2 |
| TMEM67  | NM_153704.5    |
| TMPRSS3 | NM_024022.2    |
| TPO     | NM_000547.5    |
| TPP1    | NM_000391.3    |
| TREX1   | NM_033629.4    |
| TRIM32  | NM_012210.3    |
| TRIM37  | NM_015294.4    |
| TRMU    | NM_018006.4    |
| TSEN54  | NM_207346.2    |
| TSFM*   | NM_001172696.1 |
| TSHB    | NM_000549.4    |
| TSHR    | NM_000369.2    |
| TTC37   | NM_014639.3    |
| TTPA    | NM_000370.3    |
| TULP1   | NM_003322.4    |
| TYMP    | NM_001953.4    |
| TYR*    | NM_000372.4    |
| TYRP1   | NM_000550.2    |
| UBR1    | NM_174916.2    |
| UNC13D  | NM_199242.2    |
| USH1C*  | NM_005709.3    |
| USH2A   | NM_206933.2    |

| GENE    | TRANSCRIPT     |
|---------|----------------|
| VDR     | NM_001017535.1 |
| VLDLR   | NM_003383.4    |
| VPS11   | NM_021729.5    |
| VPS13A* | NM_033305.2    |
| VPS13B  | NM_017890.4    |
| VPS45   | NM_007259.4    |
| VPS53*  | NM_001128159.2 |
| VRK1    | NM_003384.2    |
| VSX2    | NM_182894.2    |
| WISP3   | NM_003880.3    |
| WNT10A  | NM_025216.2    |
| WRN*    | NM_000553.4    |
| XPA     | NM_000380.3    |
| XPC     | NM_004628.4    |
| ZBTB24  | NM_014797.2    |
| ZFYVE26 | NM_015346.3    |
| ZNF469  | NM_001127464.2 |

## Methods

- Genomic DNA obtained from the submitted sample is enriched for targeted regions using a hybridization-based protocol, and sequenced using Illumina technology. Unless otherwise indicated, all targeted regions are sequenced with  $\geq 50\times$  depth or are supplemented with additional analysis. Reads are aligned to a reference sequence (GRCh37), and sequence changes are identified and interpreted in the context of a single clinically relevant transcript, indicated in the Genes analyzed section. Enrichment and analysis focus on the coding sequence of the indicated transcripts, 20bp of flanking intronic sequence, and other specific genomic regions demonstrated to be causative of disease at the time of assay design. Promoters, untranslated regions, and other non-coding regions are not otherwise interrogated. Exonic deletions and duplications are called using an in-house algorithm that determines copy number at each target by comparing the read depth for each target in the proband sequence with both mean read-depth and read-depth distribution, obtained from a set of clinical samples. Markers across the X and Y chromosomes are analyzed for quality control purposes and may detect deviations from the expected sex chromosome complement. Such deviations may be included in the report in accordance with internal guidelines. Invitae utilizes a classification methodology to identify next-generation sequencing (NGS)-detected variants that require orthogonal confirmation (Lincoln, et al. J Mol Diagn. 2019 Mar;21(2):318-329.). Confirmation of the presence and location of reportable variants is performed based on stringent criteria established by Invitae (1400 16th Street, San Francisco, CA 94103, #05D2040778), as needed, using one of several validated orthogonal approaches (PubMed ID 30610921). The following analyses are performed if relevant to the requisition. For GBA the reference genome has been modified to mask the sites of polymorphic paralog sequence variants (PSVs) in both the gene and pseudogene. For CYP21A2 and GBA, if one or more reportable variants, gene conversion, or fusion event is identified via our NGS pipeline (see Limitations), these variants are confirmed by PacBio sequencing of an amplicon generated by long-range PCR and subsequent short-range PCR. In some cases, it may not be possible to disambiguate between the gene and pseudogene. For GJB2, the reportable range includes large upstream deletions overlapping GJB6. For HBA1/2, the reference genome has been modified to force some sequencing reads derived from HBA1 to align to HBA2, and variant calling algorithms are modified to support an expectation of 4 alleles in these regions. HBA1/2 copy number calling is performed by a custom hypothesis testing algorithm which generates diplotype calls. If sequence data for a sample does not support a unique high confidence match from among hypotheses tested, that sample is flagged for manual review. Copy number variation is only reported for coding sequence of HBA1 and HBA2 and the HS-40 region. This assay does not distinguish among the  $\alpha 3.7$  subtypes, and all  $\alpha 3.7$  variants are called as HBA1 deletions. This assay may not detect overlapping copy gain and copy loss events when the breakpoints of those events are similar. For FMR1, triplet repeats are detected by PCR with fluorescently labeled primers followed by capillary electrophoresis. Reference ranges: Normal:  $<45$  CGG repeats, intermediate: 45-54 CGG repeats, premutation: 55-200 CGG repeats, full mutation:  $>200$  CGG repeats. For alleles with 55-90 triplet repeats, the region surrounding the FMR1 repeat is amplified by PCR. The PCR amplicons are then processed through PacBio SMRTbell library prep and sequenced using PacBio long read technology. The number of AGG interruptions within the 55-90 triplet repeat is read directly from the resulting DNA sequences. Technical component of confirmatory sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778).
- This report only includes variants that have a clinically significant association with the conditions tested as of the report date. Variants of uncertain significance, benign variants, and likely benign variants are not included in this report. However, if additional evidence becomes available to indicate that the clinical significance of a variant has changed, Invitae may update this report and provide notification.
- A PMID is a unique identifier referring to a published, scientific paper. Search by PMID at <http://www.ncbi.nlm.nih.gov/pubmed>.
- An rsID is a unique identifier referring to a single genomic position, and is used to associate population frequency information with sequence changes at that position. Reported population frequencies are derived from a number of public sites that aggregate data from large-scale population sequencing projects, including ExAC (<http://exac.broadinstitute.org>), gnomAD (<http://gnomad.broadinstitute.org>), and dbSNP (<http://ncbi.nlm.nih.gov/SNP>).

## Disclaimer

DNA studies do not constitute a definitive test for the selected condition(s) in all individuals. It should be realized that there are possible sources of error. Errors can result from trace contamination, rare technical errors, rare genetic variants that interfere with analysis, recent scientific developments, and alternative classification systems. This test should be one of many aspects used by the healthcare provider to help with a diagnosis and treatment plan, but it is not a diagnosis itself. This test was developed and its performance characteristics determined by Invitae. It has not been cleared or approved by the FDA. The laboratory is regulated under the Clinical Laboratory Improvement Act (CLIA) as qualified to perform high-complexity clinical tests (CLIA ID: 05D2040778). This test is used for clinical purposes. It should not be regarded as investigational or for research.

## Limitations

- Based on validation study results, this assay achieves >99% analytical sensitivity and specificity for single nucleotide variants, insertions and deletions <15bp in length, and exon-level deletions and duplications. Invitae's methods also detect insertions and deletions larger than 15bp but smaller than a full exon but sensitivity for these may be marginally reduced. Invitae's deletion/duplication analysis determines copy number at a single exon resolution at virtually all targeted exons. However, in rare situations, single-exon copy number events may not be analyzed due to inherent sequence properties or isolated reduction in data quality. Certain types of variants, such as structural rearrangements (e.g. inversions, gene conversion events, translocations, etc.) or variants embedded in sequence with complex architecture (e.g. short tandem repeats or segmental duplications), may not be detected. Additionally, it may not be possible to fully resolve certain details about variants, such as mosaicism, phasing, or mapping ambiguity. Unless explicitly guaranteed, sequence changes in the promoter, non-coding exons, and other non-coding regions are not covered by this assay. Please consult the test definition on our website for details regarding regions or types of variants that are covered or excluded for this test. This report reflects the analysis of an extracted genomic DNA sample. While this test is intended to reflect the analysis of extracted genomic DNA from a referred patient, in very rare cases the analyzed DNA may not represent that individual's constitutional genome, such as in the case of a circulating hematolymphoid neoplasm, bone marrow transplant, blood transfusion, chimerism, culture artifact or maternal cell contamination.
- FANCL:** Sequencing analysis for exons 4, 10 includes only cds +/- 10 bp. **AIPL1:** Sequencing analysis for exons 2 includes only cds +/- 10 bp. **VPS53:** Sequencing analysis for exons 14 includes only cds +/- 5 bp. **FH:** Sequencing analysis for exons 9 includes only cds +/- 10 bp. **GALC:** Deletion/duplication analysis is not offered for exon 6. **GNE:** Sequencing analysis for exons 8 includes only cds +/- 10 bp. **TG:** Deletion/duplication analysis is not offered for exon 18. Sequencing analysis for exons 44 includes only cds +/- 0 bp. **EYS:** Sequencing analysis for exons 30 includes only cds +/- 0 bp. **HBA1/2:** This assay is designed to detect deletions and duplications of HBA1 and/or HBA2, resulting from the -alpha20.5, --MED, --SEA, --FIL/--THAI, -alpha3.7, -alpha4.2, anti3.7 and anti4.2. Sensitivity to detect other copy number variants may be reduced. Detection of overlapping deletion and duplication events will be limited to combinations of events with significantly differing boundaries. In addition, deletion of the enhancer element HS-40 and the sequence variant, Constant Spring (NM\_000517.4:c.427T>C), can be identified by this assay. **GHR:** Deletion/duplication and sequencing analysis is not offered for exon 3. **CYP21A2:** Analysis includes the most common variants (c.92C>T (p.Pro31Leu), c.293-13C>G (intronic), c.332\_339delGAGACTAC (p.Gly111Valfs\*21), c.518T>A (p.Ile173Asn), c.710T>A (p.Ile237Asn), c.713T>A (p.Val238Glu), c.719T>A (p.Met240Lys), c.844G>T (p.Val282Leu), c.923dupT (p.Leu308Phefs\*6), c.955C>T (p.Gln319\*), c.1069C>T (p.Arg357Trp), c.1360C>T (p.Pro454Ser) and the 30Kb deletion) as well as select rare HGMD variants only (list available upon request). Full gene duplications are reported only in the presence of a pathogenic variant(s). When a duplication and a pathogenic variant(s) is identified, phase (cis/trans) cannot be determined. Full gene deletion analysis is not offered. Sensitivity to detect these variants, if they result from complex gene conversion/fusion events, may be reduced. **ABCC2:** Deletion/duplication analysis is not offered for exons 24-25. **LIFR:** Sequencing analysis for exons 3 includes only cds +/- 5 bp. **MLC1:** Sequencing analysis for exons 11 includes only cds +/- 10 bp. **MTHFR:** The NM\_005957.4:c.665C>T (p.Ala222Val) (aka 677C>T) and c.1286A>C (p.Glu429Ala) (aka 1298A>C) variants are not reported in our primary report. **NEB:** Deletion/duplication analysis is not offered for exons 82-105. NEB variants in this region with no evidence towards pathogenicity are not included in this report, but are available upon request. **PEX1:** Sequencing analysis for exons 16 includes only cds +/- 0 bp. **PKHD1:** Deletion/duplication analysis is not offered for exon 13. **FAH:** Deletion/duplication analysis is not offered for exon 14. **USH1C:** Deletion/duplication analysis is not offered for exons 5-6. **OTOA:** Deletion/duplication and sequencing analysis is not offered for exons 20-28. **DUOX2:** Deletion/duplication and sequencing analysis is not offered for exons 6-7. **FANCD2:** Deletion/duplication analysis is not offered for exons 14-17, 22 and sequencing analysis is not offered for exons 15-17. Sequencing analysis for exons 6, 14, 18, 20, 23, 25, 34 includes only cds +/- 10 bp. **ATP8B1:** Sequencing analysis for exons 19 includes only cds +/- 10 bp. **ATM:** Sequencing analysis for exons 6, 24, 43 includes only cds +/- 10 bp. **WRN:** Deletion/duplication analysis is not offered for exons 10-11. Sequencing analysis for exons 8, 10-11 includes only cds +/- 10 bp. **GALE:** Sequencing analysis for exons 10 includes only cds +/- 5 bp. **BBS9:** Deletion/duplication analysis is not offered for exon 4. **TSFM:** Sequencing analysis is not offered for exon 5. **VPS13A:** Deletion/duplication analysis is not offered for exons 2-3, 27-28. **ANO10:** Sequencing analysis for exons 8 includes only cds +/- 0 bp. **DDX11:** NM\_030653.3:c.1763-1G>C variant only. **TYR:** Deletion/duplication and sequencing analysis is not offered for exon 5. **PTPRC:** Sequencing analysis is not offered for exons 3, 15. **TBCE:** Sequencing analysis for exons 2 includes only cds +/- 10 bp. **COL11A2:** Deletion/duplication analysis is not offered for exon 36. **SMN1:** Systematic exon numbering is used for all genes, including SMN1, and for this reason the exon typically referred to as exon 7 in the literature (PMID: 8838816) is referred to as exon 8 in this report. This assay unambiguously detects SMN1 exon 8 copy number. The presence of the g.27134T>G variant (also known as c.\*3+80T>G) is reported if SMN1 copy number = 2. SMN1 or SMN2: NM\_000344.3:c.\*3+80T>G variant only. **AMN:** Deletion/duplication analysis is not offered for exon 1. **CFTR:** Sequencing analysis for exons 7 includes only cds +/- 10 bp. **GBA:** c.84dupG (p.Leu29Alafs\*18), c.115+1G>A (Splice donor), c.222\_224delTAC (p.Thr75del), c.475C>T (p.Arg159Trp), c.595\_596delCT (p.Leu199Aspfs\*62), c.680A>G (p.Asn227Ser), c.721G>A (p.Gly241Arg), c.754T>A (p.Phe252Ile), c.1226A>G (p.Asn409Ser), c.1246G>A (p.Gly416Ser), c.1263\_1317del (p.Leu422Profs\*4), c.1297G>T (p.Val433Leu), c.1342G>C (p.Asp448His), c.1343A>T (p.Asp448Val), c.1448T>C (p.Leu483Pro), c.1504C>T (p.Arg502Cys), c.1505G>A (p.Arg502His), c.1603C>T (p.Arg535Cys), c.1604G>A



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(p.Arg535His) variants only. Rarely, sensitivity to detect these variants may be reduced. When sensitivity is reduced, zygosity may be reported as "unknown". OAT: Deletion/duplication analysis is not offered for exon 2.

- For Added, Amended, Corrected and Reanalysis reports, orthogonal confirmation may not have been performed on variants that would have otherwise met criteria for confirmation at the time of the original analysis.

### This report has been reviewed and approved by:



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Clinical Molecular Geneticist, Clinical Biochemical Geneticist  
ch\_2a51\_pr

This table displays residual risks after a negative result for each of the genes and corresponding disorders. The values provided assume a negative family history and the absence of symptoms for each disorder. For genes associated with both dominant and recessive inheritance, the numbers in this table apply to the recessive condition(s) associated with the gene, unless otherwise noted. Residual risk values are provided for disorders when carrier frequency is greater than 1 in 500. For disorders with carrier frequency equal to, or less than, 1 in 500, residual risk is considered to be reduced substantially. When provided, residual risk values are inferred from published carrier frequencies, and estimated detection rates are based on testing technologies used at Invitae. Residual risks are provided only as a guide for assessing approximate risk given a negative result; values may vary based on the ethnic background(s) of an individual. For any genes marked with an asterisk\*, refer to the Limitations section of the patient report for detailed coverage information. In the case of a sample-specific limitation, "N/A" indicates that a residual risk value could not be calculated. AR = autosomal recessive, XL = X-linked, AD = autosomal dominant.

| DISORDER (INHERITANCE)                                                                                                                                                                                                                       | GENE            | ETHNICITY        | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|------------------|-------------------|----------------|--------------------------------------------|
| 3-hydroxy-3-methylglutaryl-CoA lyase deficiency (AR)<br>NM_000191.2                                                                                                                                                                          | HMGCL           | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| 17-beta hydroxysteroid dehydrogenase 3 deficiency (AR)<br>NM_000197.1                                                                                                                                                                        | HSD17B3         | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| ABCA3-related conditions (AR)<br>NM_001089.2                                                                                                                                                                                                 | ABCA3           | Pan-ethnic       | 1 in 277          | 99%            | 1 in 27600                                 |
| ABCA4-related conditions (AR)<br>NM_000350.2                                                                                                                                                                                                 | ABCA4           | Pan-ethnic       | 1 in 45           | 90%            | 1 in 441                                   |
| ABCB4-related conditions (AR)<br>NM_000443.3                                                                                                                                                                                                 | ABCB4           | Pan-ethnic       | 1 in 204          | 99%            | 1 in 20300                                 |
| ABCB11-related conditions (AR)<br>NM_003742.2                                                                                                                                                                                                | ABCB11          | Pan-ethnic       | 1 in 100          | 99%            | 1 in 9900                                  |
| ABCC8-related conditions (AR)<br>NM_000352.4<br>When the mother is a noncarrier, but the father is a carrier, there is a residual risk for focal disease (1 in 540 for the Ashkenazi Jewish population; undetermined in other ethnic groups) | ABCC8           | Pan-ethnic       | 1 in 177          | 99%            | 1 in 17600                                 |
| Abetalipoproteinemia (AR)<br>NM_000253.3                                                                                                                                                                                                     | MTTP            | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Achromatopsia (CNGB3-related) (AR)<br>NM_019098.4                                                                                                                                                                                            | CNGB3           | Pan-ethnic       | 1 in 93           | 99%            | 1 in 9200                                  |
| ACOX1-related conditions (AR)<br>NM_004035.6                                                                                                                                                                                                 | ACOX1           | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Acrodermatitis enteropathica (AR)<br>NM_130849.3                                                                                                                                                                                             | SLC39A4         | Pan-ethnic       | 1 in 354          | 99%            | 1 in 35300                                 |
| Adenosine deaminase deficiency (AR)<br>NM_000022.2                                                                                                                                                                                           | ADA             | Pan-ethnic       | 1 in 224          | 92%            | 1 in 2788                                  |
| ADGRV1-related conditions (AR)<br>NM_032119.3                                                                                                                                                                                                | ADGRV1          | Pan-ethnic       | 1 in 223          | 99%            | 1 in 22200                                 |
| AHI1-related conditions (AR)<br>NM_017651.4                                                                                                                                                                                                  | AHI1            | Pan-ethnic       | 1 in 447          | 99%            | 1 in 44600                                 |
| Aicardi-Goutieres syndrome 2 (AR)<br>NM_024570.3                                                                                                                                                                                             | RNASEH2B        | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Aicardi-Goutieres syndrome 3 (AR)<br>NM_032193.3                                                                                                                                                                                             | RNASEH2C        | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Aicardi-Goutieres syndrome 4 (AR)<br>NM_006397.2                                                                                                                                                                                             | RNASEH2A        | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Aicardi-Goutieres syndrome 5 (AR)<br>NM_015474.3                                                                                                                                                                                             | SAMHD1          | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| AIPL1-related conditions (AR)<br>NM_014336.4                                                                                                                                                                                                 | AIPL1 *         | Pan-ethnic       | 1 in 408          | 99%            | 1 in 40700                                 |
| Aldosterone synthase deficiency (AR)<br>NM_000498.3                                                                                                                                                                                          | CYP11B2         | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Alpha-mannosidosis (AR)<br>NM_000528.3                                                                                                                                                                                                       | MAN2B1          | Pan-ethnic       | 1 in 354          | 99%            | 1 in 35300                                 |
| Alpha-N-acetylgalactosaminidase deficiency (AR)<br>NM_000262.2                                                                                                                                                                               | NAGA            | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Alpha-thalassemia (AR)<br>NM_000558.4, NM_000517.4                                                                                                                                                                                           | HBA1/<br>HBA2 * | African-American | 1 in 30           | 90%            | 1 in 291                                   |
|                                                                                                                                                                                                                                              |                 | Asian            | 1 in 20           | 90%            | 1 in 191                                   |
|                                                                                                                                                                                                                                              |                 | Caucasian        | ≤1 in 500         | 90%            | Reduced                                    |

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| DISORDER (INHERITANCE)                                                                         | GENE     | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|------------------------------------------------------------------------------------------------|----------|------------|-------------------|----------------|--------------------------------------------|
|                                                                                                |          | Pan-ethnic | 1 in 25           | 90%            | 1 in 241                                   |
| Alport syndrome (COL4A3-related) (AR)<br>NM_000091.4                                           | COL4A3   | Pan-ethnic | 1 in 354          | 99%            | 1 in 35300                                 |
| Alport syndrome (COL4A4-related) (AR)<br>NM_000092.4                                           | COL4A4   | Pan-ethnic | 1 in 353          | 99%            | 1 in 35200                                 |
| Alström syndrome (AR)<br>NM_015120.4                                                           | ALMS1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Arginase deficiency (AR)<br>NM_000045.3                                                        | ARG1     | Pan-ethnic | 1 in 274          | 99%            | 1 in 27300                                 |
| Argininosuccinate lyase deficiency (AR)<br>NM_000048.3                                         | ASL      | Pan-ethnic | 1 in 133          | 90%            | 1 in 1321                                  |
| ARL6-related conditions (AR)<br>NM_177976.2                                                    | ARL6     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Aromatase deficiency (AR)<br>NM_031226.2                                                       | CYP19A1  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Asparagine synthetase deficiency (AR)<br>NM_133436.3                                           | ASNS     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Aspartylglucosaminuria (AR)<br>NM_000027.3                                                     | AGA      | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Ataxia with vitamin E deficiency (AR)<br>NM_000370.3                                           | TTPA     | Pan-ethnic | ≤1 in 500         | 90%            | Reduced                                    |
| Ataxia-telangiectasia-like disorder (AR)<br>NM_005591.3                                        | MRE11    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| ATM-related conditions (AR)<br>NM_000051.3                                                     | ATM *    | Pan-ethnic | 1 in 100          | 99%            | 1 in 9900                                  |
| ATP8B1-related conditions (AR)<br>NM_005603.4                                                  | ATP8B1 * | Pan-ethnic | 1 in 112          | 99%            | 1 in 11100                                 |
| Atransferrinemia (AR)<br>NM_001063.3                                                           | TF       | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Autoimmune polyendocrinopathy with candidiasis and<br>ectodermal dysplasia (AR)<br>NM_000383.3 | AIRE     | Pan-ethnic | 1 in 150          | 99%            | 1 in 14900                                 |
| Autosomal recessive congenital ichthyosis<br>(ABCA12-related) (AR)<br>NM_173076.2              | ABCA12   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Autosomal recessive congenital ichthyosis (TGM1-related)<br>(AR)<br>NM_000359.2                | TGM1     | Pan-ethnic | 1 in 224          | 95%            | 1 in 4460                                  |
| Autosomal recessive spastic ataxia of Charlevoix-Saguenay<br>(AR)<br>NM_014363.5               | SACS     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Bardet-Biedl syndrome (BBS7-related) (AR)<br>NM_176824.2                                       | BBS7     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Bardet-Biedl syndrome (BBS9-related) (AR)<br>NM_198428.2                                       | BBS9 *   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Bardet-Biedl syndrome (BBS10-related) (AR)<br>NM_024685.3                                      | BBS10    | Pan-ethnic | 1 in 354          | 99%            | 1 in 35300                                 |
| Bardet-Biedl syndrome (BBS12-related) (AR)<br>NM_152618.2                                      | BBS12    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Bartter syndrome type 1 (AR)<br>NM_000338.2                                                    | SLC12A1  | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |
| Bartter syndrome type 2 (AR)<br>NM_000220.4                                                    | KCNJ1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| BBS1-related conditions (AR)<br>NM_024649.4                                                    | BBS1     | Pan-ethnic | 1 in 330          | 99%            | 1 in 32900                                 |
| BBS2-related conditions (AR)<br>NM_031885.3                                                    | BBS2     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| BBS4-related conditions (AR)<br>NM_033028.4                                                    | BBS4     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| BBS5-related conditions (AR)<br>NM_152384.2                                                    | BBS5     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| BCS1L-related conditions (AR)<br>NM_004328.4                                                   | BCS1L    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |

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| DISORDER (INHERITANCE)                                                                        | GENE     | ETHNICITY               | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|-----------------------------------------------------------------------------------------------|----------|-------------------------|-------------------|----------------|--------------------------------------------|
| Beta-ketothiolase deficiency (AR)<br>NM_000019.3                                              | ACAT1    | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Beta-mannosidosis (AR)<br>NM_005908.3                                                         | MANBA    | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Biopterin-deficient hyperphenylalaninemia (PCBD1-related) (AR)<br>NM_000281.3                 | PCBD1    | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Biopterin-deficient hyperphenylalaninemia (PTS-related) (AR)<br>NM_000317.2                   | PTS      | Pan-ethnic              | 1 in 433          | 99%            | 1 in 43200                                 |
| Biopterin-deficient hyperphenylalaninemia (QDPR-related) (AR)<br>NM_000320.2                  | QDPR     | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Biotin-responsive basal ganglia disease (AR)<br>NM_025243.3                                   | SLC19A3  | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Biotinidase deficiency (AR)<br>NM_000060.3                                                    | BTD      | Pan-ethnic              | 1 in 125          | 99%            | 1 in 12400                                 |
| Bloom syndrome (AR)<br>NM_000057.3                                                            | BLM      | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| BRIP1-related conditions (AR)<br>NM_032043.2                                                  | BRIP1    | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Brittle cornea syndrome (PRDM5-related) (AR)<br>NM_018699.3                                   | PRDM5    | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Brittle cornea syndrome (ZNF469-related) (AR)<br>NM_001127464.2                               | ZNF469   | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| BSND-related conditions (AR)<br>NM_057176.2                                                   | BSND     | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Canavan disease (AR)<br>NM_000049.2                                                           | ASPA     | Pan-ethnic              | 1 in 159          | 99%            | 1 in 15800                                 |
| Carbamoyl phosphate synthetase I deficiency (AR)<br>NM_001875.4                               | CPS1     | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Cardioencephalomyopathy (AR)<br>NM_005138.2                                                   | SCO2     | Pan-ethnic              | 1 in 387          | 99%            | 1 in 38600                                 |
| Carnitine palmitoyltransferase I deficiency (AR)<br>NM_001876.3                               | CPT1A    | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Carnitine palmitoyltransferase II deficiency (AR)<br>NM_000098.2                              | CPT2     | Pan-ethnic              | 1 in 182          | 99%            | 1 in 18100                                 |
| Carnitine-acylcarnitine translocase deficiency (AR)<br>NM_000387.5                            | SLC25A20 | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Carpenter syndrome (RAB23-related) (AR)<br>NM_183227.2                                        | RAB23    | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Cartilage-hair hypoplasia-anauxetic dysplasia spectrum disorders (AR)<br>NR_003051.3          | RMRP     | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Catecholaminergic polymorphic ventricular tachycardia (CASQ2-related) (AR)<br>NM_001232.3     | CASQ2    | Pan-ethnic              | 1 in 224          | 99%            | 1 in 22300                                 |
| CDH23-related conditions (AR)<br>NM_022124.5                                                  | CDH23    | Pan-ethnic              | 1 in 202          | 95%            | 1 in 4020                                  |
| CEP290-related conditions (AR)<br>NM_025114.3                                                 | CEP290   | Pan-ethnic              | 1 in 185          | 99%            | 1 in 18400                                 |
| Cerebellar ataxia, intellectual disability, and dysequilibrium syndrome 1 (AR)<br>NM_003383.4 | VLDLR    | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Cerebral dysgenesis, neuropathy, ichthyosis, and keratoderma (AR)<br>NM_004782.3              | SNAP29   | Pan-ethnic              | ≤1 in 500         | 99%            | Reduced                                    |
| Cerebrotendinous xanthomatosis (AR)<br>NM_000784.3                                            | CYP27A1  | Pan-ethnic              | 1 in 112          | 98%            | 1 in 5550                                  |
| CERKL-related conditions (AR)<br>NM_001030311.2                                               | CERKL    | Pan-ethnic              | 1 in 137          | 99%            | 1 in 13600                                 |
| CFTR-related conditions (AR)<br>NM_000492.3                                                   | CFTR *   | Pan-ethnic - classic CF | 1 in 45           | 99%            | 1 in 4400                                  |

| DISORDER (INHERITANCE)                                                                                   | GENE      | ETHNICITY                                          | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|----------------------------------------------------------------------------------------------------------|-----------|----------------------------------------------------|-------------------|----------------|--------------------------------------------|
|                                                                                                          |           | Pan-ethnic - classic CF and CFTR-related disorders | 1 in 9            | 99%            | 1 in 800                                   |
| Charcot-Marie-Tooth disease type 4D (AR)<br>NM_006096.3                                                  | NDRG1     | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Chediak-Higashi syndrome (AR)<br>NM_000081.3                                                             | LYST      | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Childhood-onset dystonia with optic atrophy and basal ganglia abnormalities (AR)<br>NM_016011.3          | MECR      | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Chorea-acanthocytosis (AR)<br>NM_033305.2                                                                | VPS13A *  | Pan-ethnic                                         | ≤1 in 500         | 97%            | Reduced                                    |
| Chronic granulomatous disease (CYBA-related) (AR)<br>NM_000101.3                                         | CYBA      | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Chronic granulomatous disease (NCF2-related) (AR)<br>NM_000433.3                                         | NCF2      | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Citrin deficiency (AR)<br>NM_014251.2                                                                    | SLC25A13  | Pan-ethnic                                         | 1 in 313          | 99%            | 1 in 31200                                 |
| Citrullinemia type 1 (AR)<br>NM_000050.4                                                                 | ASS1      | Pan-ethnic                                         | 1 in 120          | 96%            | 1 in 2975                                  |
| CLN3-related conditions (AR)<br>NM_001042432.1                                                           | CLN3      | Pan-ethnic                                         | 1 in 230          | 99%            | 1 in 22900                                 |
| CLRN1-related conditions (AR)<br>NM_174878.2                                                             | CLRN1     | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Cobalamin C deficiency (AR)<br>NM_015506.2                                                               | MMACHC    | Pan-ethnic                                         | 1 in 123          | 99%            | 1 in 12200                                 |
| Cobalamin D deficiency (AR)<br>NM_015702.2                                                               | MMADHC    | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Cobalamin F deficiency (AR)<br>NM_018368.3                                                               | LMBRD1    | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Cockayne syndrome A (AR)<br>NM_000082.3                                                                  | ERCC8     | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Cockayne syndrome B (AR)<br>NM_000124.3                                                                  | ERCC6     | Pan-ethnic                                         | 1 in 377          | 99%            | 1 in 37600                                 |
| Cohen syndrome (AR)<br>NM_017890.4                                                                       | VPS13B    | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| COL11A2-related conditions (AR)<br>NM_080680.2                                                           | COL11A2 * | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| COL17A1-related conditions (AR)<br>NM_000494.3                                                           | COL17A1   | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Combined malonic and methylmalonic aciduria (AR)<br>NM_174917.4                                          | ACSF3     | Pan-ethnic                                         | 1 in 87           | 99%            | 1 in 8600                                  |
| Combined oxidative phosphorylation deficiency 1 (AR)<br>NM_024996.5                                      | GFM1      | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Combined oxidative phosphorylation deficiency 3 (AR)<br>NM_001172696.1                                   | TSFM *    | Pan-ethnic                                         | ≤1 in 500         | 93%            | Reduced                                    |
| Combined pituitary hormone deficiency (LHX3-related) (AR)<br>NM_014564.4                                 | LHX3      | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Combined pituitary hormone deficiency (POU1F1-related) (AR)<br>NM_000306.3                               | POU1F1    | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Combined pituitary hormone deficiency (PROP1-related) (AR)<br>NM_006261.4                                | PROP1     | Pan-ethnic                                         | 1 in 45           | 98%            | 1 in 2200                                  |
| Congenital adrenal hyperplasia due to 3-beta-hydroxysteroid dehydrogenase deficiency (AR)<br>NM_000198.3 | HSD3B2    | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital adrenal hyperplasia due to 21-hydroxylase deficiency (AR)<br>NM_000500.7                      | CYP21A2 * | Pan-ethnic                                         | 1 in 61           | 92%            | 1 in 751                                   |
| Congenital adrenal insufficiency (AR)<br>NM_000781.2                                                     | CYP11A1   | Pan-ethnic                                         | ≤1 in 500         | 99%            | Reduced                                    |

This table is relevant to patient report RQ4726574-1  
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| DISORDER (INHERITANCE)                                                       | GENE    | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|------------------------------------------------------------------------------|---------|------------|-------------------|----------------|--------------------------------------------|
| Congenital chronic diarrhea (DGAT1-related) (AR)<br>NM_012079.5              | DGAT1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital disorder of glycosylation (SLC35A3-related) (AR)<br>NM_012243.2   | SLC35A3 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital disorder of glycosylation type Ia (AR)<br>NM_000303.2             | PMM2    | Pan-ethnic | 1 in 190          | 99%            | 1 in 18900                                 |
| Congenital disorder of glycosylation type Ib (AR)<br>NM_002435.2             | MPI     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital disorder of glycosylation type Ic (AR)<br>NM_013339.3             | ALG6    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital disorder of glycosylation type Ik (AR)<br>NM_019109.4             | ALG1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital disorder of glycosylation type Iv (AR)<br>NM_018297.3             | NGLY1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital dyserythropoietic anemia type II (AR)<br>NM_006363.4              | SEC23B  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital hydrocephalus-1 (AR)<br>NM_001080414.3                            | CCDC88C | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital hypothyroidism (TSHB-related) (AR)<br>NM_000549.4                 | TSHB    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital insensitivity to pain with anhidrosis (AR)<br>NM_001012331.1      | NTRK1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital myasthenic syndrome (CHAT-related) (AR)<br>NM_020549.4            | CHAT    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital myasthenic syndrome (CHRNE-related) (AR)<br>NM_000080.3           | CHRNE   | Pan-ethnic | 1 in 200          | 99%            | 1 in 19900                                 |
| Congenital nephrotic syndrome type 1 (AR)<br>NM_004646.3                     | NPHS1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital nephrotic syndrome type 2 (AR)<br>NM_014625.3                     | NPHS2   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Congenital secretory chloride diarrhea (AR)<br>NM_000111.2                   | SLC26A3 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Corneal dystrophy and perceptive deafness (AR)<br>NM_032034.3                | SLC4A11 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| CRB1-related conditions (AR)<br>NM_201253.2                                  | CRB1    | Pan-ethnic | 1 in 112          | 99%            | 1 in 11100                                 |
| CTSC-related conditions (AR)<br>NM_001814.5                                  | CTSC    | Pan-ethnic | 1 in 250          | 99%            | 1 in 24900                                 |
| CYP1B1-related conditions (AR)<br>NM_000104.3                                | CYP1B1  | Pan-ethnic | 1 in 79           | 99%            | 1 in 7800                                  |
| CYP7B1-related conditions (AR)<br>NM_004820.3                                | CYP7B1  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| CYP11B1-related conditions (AR)<br>NM_000497.3                               | CYP11B1 | Pan-ethnic | 1 in 194          | 99%            | 1 in 19300                                 |
| CYP17A1-related conditions (AR)<br>NM_000102.3                               | CYP17A1 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Cystinosis (AR)<br>NM_004937.2                                               | CTNS    | Pan-ethnic | 1 in 158          | 99%            | 1 in 15700                                 |
| Cytochrome P450 oxidoreductase deficiency (AR)<br>NM_000941.2                | POR     | Pan-ethnic | 1 in 158          | 99%            | 1 in 15700                                 |
| Desbuquois dysplasia type 1 (AR)<br>NM_138793.3                              | CANT1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Developmental and epileptic encephalopathy (CAD-related) (AR)<br>NM_004341.4 | CAD     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| DGUOK-related conditions (AR)<br>NM_080916.2                                 | DGUOK   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| DHDDS-related conditions (AR)<br>NM_024887.3                                 | DHDDS   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Dihydrolipoamide dehydrogenase deficiency (AR)<br>NM_000108.4                | DLD     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |

| DISORDER (INHERITANCE)                                                             | GENE     | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|------------------------------------------------------------------------------------|----------|------------|-------------------|----------------|--------------------------------------------|
| Distal renal tubular acidosis with deafness (ATP6V1B1-related) (AR)<br>NM_001692.3 | ATP6V1B1 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| DOK7-related conditions (AR)<br>NM_173660.4                                        | DOK7     | Pan-ethnic | 1 in 115          | 99%            | 1 in 11400                                 |
| Donnai-Barrow syndrome (AR)<br>NM_004525.2                                         | LRP2     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Dubin-Johnson syndrome (AR)<br>NM_000392.4                                         | ABCC2 *  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| DUOX2-related conditions (AR)<br>NM_014080.4                                       | DUOX2 *  | Pan-ethnic | 1 in 58           | 91%            | 1 in 634                                   |
| DYNC2H1-related conditions (AR)<br>NM_001080463.1                                  | DYNC2H1  | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |
| DYSF-related conditions (AR)<br>NM_003494.3                                        | DYSF     | Pan-ethnic | 1 in 311          | 99%            | 1 in 31000                                 |
| Dyskeratosis congenita spectrum disorders (RTEL1-related) (AR)<br>NM_001283009.1   | RTEL1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Dyskeratosis congenita spectrum disorders (TERT-related) (AR)<br>NM_198253.2       | TERT     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Ehlers-Danlos syndrome, dermatosparaxis type (AR)<br>NM_014244.4                   | ADAMTS2  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Ehlers-Danlos syndrome, kyphoscoliotic type (AR)<br>NM_000302.3                    | PLOD1    | Pan-ethnic | 1 in 150          | 99%            | 1 in 14900                                 |
| Ellis-van Creveld syndrome (EVC-related) (AR)<br>NM_153717.2                       | EVC      | Pan-ethnic | 1 in 220          | 99%            | 1 in 21900                                 |
| Epidermolysis bullosa with pyloric atresia (ITGB4-related) (AR)<br>NM_001005731.2  | ITGB4    | Pan-ethnic | 1 in 393          | 99%            | 1 in 39200                                 |
| Epimerase deficiency galactosemia (AR)<br>NM_000403.3                              | GALE *   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| ERCC2-related conditions (AR)<br>NM_000400.3                                       | ERCC2    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Ethylmalonic encephalopathy (AR)<br>NM_014297.3                                    | ETHE1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| EVC2-related conditions (AR)<br>NM_147127.4                                        | EVC2     | Pan-ethnic | 1 in 199          | 99%            | 1 in 19800                                 |
| Familial chylomicronemia syndrome (AR)<br>NM_000237.2                              | LPL      | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Familial dysautonomia (AR)<br>NM_003640.3                                          | ELP1     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Familial hemophagocytic lymphohistiocytosis type 2 (AR)<br>NM_001083116.1          | PRF1     | Pan-ethnic | 1 in 177          | 99%            | 1 in 17600                                 |
| Familial hemophagocytic lymphohistiocytosis type 3 (AR)<br>NM_199242.2             | UNC13D   | Pan-ethnic | 1 in 177          | 93%            | 1 in 2515                                  |
| Familial hemophagocytic lymphohistiocytosis type 4 (AR)<br>NM_003764.3             | STX11    | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |
| Familial hemophagocytic lymphohistiocytosis type 5 (AR)<br>NM_006949.3             | STXB2    | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |
| Familial hypercholesterolemia (LDLR-related) (AD)<br>NM_000527.4                   | LDLR     | Pan-ethnic | 1 in 250          | 99%            | 1 in 24900                                 |
| Familial hypercholesterolemia (LDLRAP1-related) (AR)<br>NM_015627.2                | LDLRAP1  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Fanconi anemia type A (AR)<br>NM_000135.2                                          | FANCA    | Pan-ethnic | 1 in 345          | 99%            | 1 in 34400                                 |
| Fanconi anemia type C (AR)<br>NM_000136.2                                          | FANCC    | Pan-ethnic | 1 in 417          | 99%            | 1 in 41600                                 |
| Fanconi anemia type D2 (AR)<br>NM_033084.3                                         | FANCD2 * | Pan-ethnic | ≤1 in 500         | 94%            | Reduced                                    |
| Fanconi anemia type E (AR)<br>NM_021922.2                                          | FANCE    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |

| DISORDER (INHERITANCE)                                                  | GENE    | ETHNICITY        | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|-------------------------------------------------------------------------|---------|------------------|-------------------|----------------|--------------------------------------------|
| Fanconi anemia type G (AR)<br>NM_004629.1                               | FANCG   | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Fanconi anemia type I (AR)<br>NM_001113378.1                            | FANCI   | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Fanconi anemia type L (AR)<br>NM_018062.3                               | FANCL * | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| FH-related conditions (AR)<br>NM_000143.3                               | FH *    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| FKBP10-related conditions (AR)<br>NM_021939.3                           | FKBP10  | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Foveal hypoplasia (SLC38A8-related) (AR)<br>NM_001080442.2              | SLC38A8 | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| FOXN1-related conditions (AR)<br>NM_003593.2                            | FOXN1   | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Fraser syndrome (FRAS1-related) (AR)<br>NM_025074.6                     | FRAS1   | Pan-ethnic       | 1 in 316          | 99%            | 1 in 31500                                 |
| Fraser syndrome (FREM2-related) (AR)<br>NM_207361.5                     | FREM2   | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Fraser syndrome (GRIP1-related) (AR)<br>NM_021150.3                     | GRIP1   | Pan-ethnic       | 1 in 447          | 99%            | 1 in 44600                                 |
| Fructose-1,6-bisphosphatase deficiency (AR)<br>NM_000507.3              | FBP1    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Fucosidosis (AR)<br>NM_000147.4                                         | FUCA1   | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Galactokinase deficiency galactosemia (AR)<br>NM_000154.1               | GALK1   | Pan-ethnic       | 1 in 122          | 99%            | 1 in 12100                                 |
| Galactosemia (GALT-related) (AR)<br>NM_000155.3                         | GALT    | Pan-ethnic       | 1 in 100          | 99%            | 1 in 9900                                  |
| Galactosialidosis (AR)<br>NM_000308.3                                   | CTSA    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| GATM-related conditions (AR)<br>NM_001482.2                             | GATM    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| GBA-related conditions including Gaucher disease (AR)<br>NM_001005741.2 | GBA *   | Ashkenazi Jewish | 1 in 15           | 94%            | 1 in 234                                   |
|                                                                         |         | Pan-ethnic       | 1 in 158          | 72%            | 1 in 561                                   |
| GBE1-related conditions (AR)<br>NM_000158.3                             | GBE1    | Pan-ethnic       | 1 in 387          | 99%            | 1 in 38600                                 |
| GCH1-related conditions (AR)<br>NM_000161.2                             | GCH1    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| GDF5-related conditions (AR)<br>NM_000557.4                             | GDF5    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Geroderma osteodysplastica (AR)<br>NM_152281.2                          | GORAB   | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| GHR-related conditions (AR)<br>NM_000163.4                              | GHR *   | Pan-ethnic       | ≤1 in 500         | 98%            | Reduced                                    |
| Gitelman syndrome (AR)<br>NM_000339.2                                   | SLC12A3 | Pan-ethnic       | 1 in 100          | 99%            | 1 in 9900                                  |
| GJB2-related conditions (AR)<br>NM_004004.5                             | GJB2    | Pan-ethnic       | 1 in 50           | 99%            | 1 in 4900                                  |
| GLB1-related conditions (AR)<br>NM_000404.2                             | GLB1    | Pan-ethnic       | 1 in 158          | 99%            | 1 in 15700                                 |
| GLE1-related conditions (AR)<br>NM_001003722.1                          | GLE1    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Glutaric acidemia type I (AR)<br>NM_000159.3                            | GCDH    | Pan-ethnic       | 1 in 87           | 99%            | 1 in 8600                                  |
| Glutaric acidemia type IIB (AR)<br>NM_001985.2                          | ETFB    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Glutaric acidemia type IIC (AR)<br>NM_004453.3                          | ETFDH   | Pan-ethnic       | 1 in 250          | 99%            | 1 in 24900                                 |
| Glutathione synthetase deficiency (AR)<br>NM_000178.2                   | GSS     | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Glycine encephalopathy (AMT-related) (AR)<br>NM_000481.3                | AMT     | Pan-ethnic       | 1 in 325          | 99%            | 1 in 32400                                 |

| DISORDER (INHERITANCE)                                               | GENE    | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|----------------------------------------------------------------------|---------|------------|-------------------|----------------|--------------------------------------------|
| Glycine encephalopathy (GLDC-related) (AR)<br>NM_000170.2            | GLDC    | Pan-ethnic | 1 in 165          | 99%            | 1 in 16400                                 |
| Glycogen storage disease type Ia (AR)<br>NM_000151.3                 | G6PC    | Pan-ethnic | 1 in 177          | 95%            | 1 in 3520                                  |
| Glycogen storage disease type II (Pompe disease) (AR)<br>NM_000152.3 | GAA     | Pan-ethnic | 1 in 100          | 99%            | 1 in 9900                                  |
| Glycogen storage disease type III (AR)<br>NM_000642.2                | AGL     | Pan-ethnic | 1 in 159          | 95%            | 1 in 3160                                  |
| Glycogen storage disease type IXb (AR)<br>NM_000293.2                | PHKB    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Glycogen storage disease type IXc (AR)<br>NM_000294.2                | PHKG2   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Glycogen storage disease type V (AR)<br>NM_005609.3                  | PYGM    | Pan-ethnic | 1 in 171          | 99%            | 1 in 17000                                 |
| Glycogen storage disease type VII (AR)<br>NM_000289.5                | PFKM    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| GM3 synthase deficiency (AR)<br>NM_003896.3                          | ST3GAL5 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| GNE-related conditions (AR)<br>NM_001128227.2                        | GNE *   | Pan-ethnic | 1 in 179          | 99%            | 1 in 17800                                 |
| GNPTAB-related conditions (AR)<br>NM_024312.4                        | GNPTAB  | Pan-ethnic | 1 in 200          | 99%            | 1 in 19900                                 |
| Guanidinoacetate methyltransferase deficiency (AR)<br>NM_000156.5    | GAMT    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| GUCY2D-related conditions (AR)<br>NM_000180.3                        | GUCY2D  | Pan-ethnic | 1 in 204          | 99%            | 1 in 20300                                 |
| Gyrate atrophy of the choroid and retina (AR)<br>NM_000274.3         | OAT *   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| HADHA-related conditions (AR)<br>NM_000182.4                         | HADHA   | Pan-ethnic | 1 in 350          | 99%            | 1 in 34900                                 |
| HBB-related hemoglobinopathies (AR)<br>NM_000518.4                   | HBB     | Pan-ethnic | 1 in 49           | 99%            | 1 in 4800                                  |
| Heme oxygenase 1 deficiency (AR)<br>NM_002133.2                      | HMOX1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hemolytic anemia, CD59-mediated (AR)<br>NM_203330.2                  | CD59    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hereditary fructose intolerance (AR)<br>NM_000035.3                  | ALDOB   | Pan-ethnic | 1 in 122          | 99%            | 1 in 12100                                 |
| Hereditary hemochromatosis type 2 (HAMP-related) (AR)<br>NM_021175.2 | HAMP    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hereditary hemochromatosis type 2 (HJV-related) (AR)<br>NM_213653.3  | HJV     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hereditary hemochromatosis type 3 (AR)<br>NM_003227.3                | TFR2    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hermansky-Pudlak syndrome type 1 (AR)<br>NM_000195.4                 | HPS1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hermansky-Pudlak syndrome type 3 (AR)<br>NM_032383.4                 | HPS3    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hermansky-Pudlak syndrome type 4 (AR)<br>NM_022081.5                 | HPS4    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hermansky-Pudlak syndrome type 5 (AR)<br>NM_181507.1                 | HPS5    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hermansky-Pudlak syndrome type 6 (AR)<br>NM_024747.5                 | HPS6    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hermansky-Pudlak syndrome type 8 (AR)<br>NM_212550.4                 | BLOC1S3 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hermansky-Pudlak syndrome type 9 (AR)<br>NM_012388.3                 | BLOC1S6 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| HGSNAT-related conditions (AR)<br>NM_152419.2                        | HGSNAT  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Holocarboxylase synthetase deficiency (AR)<br>NM_000411.6            | HLCS    | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |

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| DISORDER (INHERITANCE)                                                                    | GENE     | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|-------------------------------------------------------------------------------------------|----------|------------|-------------------|----------------|--------------------------------------------|
| Homocystinuria due to cobalamin E deficiency (AR)<br>NM_002454.2                          | MTRR     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Homocystinuria due to cobalamin G deficiency (AR)<br>NM_000254.2                          | MTR      | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Homocystinuria due to cystathionine beta-synthase deficiency (AR)<br>NM_000071.2          | CBS      | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |
| Homocystinuria due to MTHFR deficiency (AR)<br>NM_005957.4                                | MTHFR *  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| HSD17B4-related conditions (AR)<br>NM_000414.3                                            | HSD17B4  | Pan-ethnic | 1 in 158          | 99%            | 1 in 15700                                 |
| Hydrolethalus syndrome type 1 (AR)<br>NM_145014.2                                         | HYLS1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hyper-IgM immunodeficiency (CD40-related) (AR)<br>NM_001250.5                             | CD40     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hyperornithinemia-hyperammonemia-homocitrullinuria syndrome (AR)<br>NM_014252.3           | SLC25A15 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hyperphosphatemic familial tumoral calcinosis (GALNT3-related) (AR)<br>NM_004482.3        | GALNT3   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hypomyelinating leukodystrophy-12 (AR)<br>NM_021729.5                                     | VPS11    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Hypophosphatasia (AR)<br>NM_000478.5                                                      | ALPL     | Pan-ethnic | 1 in 150          | 95%            | 1 in 2980                                  |
| Ichthyosis prematurity syndrome (AR)<br>NM_005094.3                                       | SLC27A4  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| IGHMBP2-related conditions (AR)<br>NM_002180.2                                            | IGHMBP2  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| IKBKB-related conditions (AR)<br>NM_001556.2                                              | IKBKB    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Imerslund-Gräsbeck syndrome (AR)<br>NM_030943.3                                           | AMN *    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Immunodeficiency-centromeric instability-facial anomalies syndrome 1 (AR)<br>NM_006892.3  | DNMT3B   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Immunodeficiency-centromeric instability-facial anomalies syndrome 2 (AR)<br>NM_014797.2  | ZBTB24   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Isolated ectopia lentis (AR)<br>NM_019032.5                                               | ADAMTSL4 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Isovaleric acidemia (AR)<br>NM_002225.3                                                   | IVD      | Pan-ethnic | 1 in 250          | 99%            | 1 in 24900                                 |
| ITGB3-related conditions (AR)<br>NM_000212.2                                              | ITGB3    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Johanson-Blizzard syndrome (AR)<br>NM_174916.2                                            | UBR1     | Pan-ethnic | 1 in 250          | 99%            | 1 in 24900                                 |
| Joubert syndrome and related disorders (MKS1-related) (AR)<br>NM_017777.3                 | MKS1     | Pan-ethnic | 1 in 260          | 95%            | 1 in 5180                                  |
| Joubert syndrome and related disorders (RPGRIP1L-related) (AR)<br>NM_015272.2             | RPGRIP1L | Pan-ethnic | 1 in 259          | 95%            | 1 in 5160                                  |
| Joubert syndrome and related disorders (TMEM216-related) (AR)<br>NM_001173990.2           | TMEM216  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Junctional epidermolysis bullosa (LAMC2-related) (AR)<br>NM_005562.2                      | LAMC2    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Junctional epidermolysis bullosa with pyloric atresia (ITGA6-related) (AR)<br>NM_000210.3 | ITGA6    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| KCNJ11-related conditions (AR)<br>NM_000525.3                                             | KCNJ11   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |

| DISORDER (INHERITANCE)                                                                   | GENE   | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|------------------------------------------------------------------------------------------|--------|------------|-------------------|----------------|--------------------------------------------|
| Krabbe disease (AR)<br>NM_000153.3                                                       | GALC * | Pan-ethnic | 1 in 158          | 99%            | 1 in 15700                                 |
| LAMA2-related muscular dystrophy (AR)<br>NM_000426.3                                     | LAMA2  | Pan-ethnic | 1 in 87           | 99%            | 1 in 8600                                  |
| LAMA3-related conditions (AR)<br>NM_000227.4                                             | LAMA3  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| LAMB3-related conditions (AR)<br>NM_000228.2                                             | LAMB3  | Pan-ethnic | 1 in 317          | 99%            | 1 in 31600                                 |
| Leber congenital amaurosis 5 (AR)<br>NM_181714.3                                         | LCA5   | Pan-ethnic | ≤1 in 500         | 97%            | Reduced                                    |
| Leukoencephalopathy with vanishing white matter (EIF2B1-related) (AR)<br>NM_001414.3     | EIF2B1 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Leukoencephalopathy with vanishing white matter (EIF2B2-related) (AR)<br>NM_014239.3     | EIF2B2 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Leukoencephalopathy with vanishing white matter (EIF2B3-related) (AR)<br>NM_020365.4     | EIF2B3 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Leukoencephalopathy with vanishing white matter (EIF2B4-related) (AR)<br>NM_015636.3     | EIF2B4 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Leukoencephalopathy with vanishing white matter (EIF2B5-related) (AR)<br>NM_003907.2     | EIF2B5 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| LIG4 syndrome (AR)<br>NM_002312.3                                                        | LIG4   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Limb-girdle muscular dystrophy (CAPN3-related) (AR)<br>NM_000070.2                       | CAPN3  | Pan-ethnic | 1 in 134          | 99%            | 1 in 13300                                 |
| Limb-girdle muscular dystrophy type 2C (AR)<br>NM_000231.2                               | SGCG   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Limb-girdle muscular dystrophy type 2D (AR)<br>NM_000023.2                               | SGCA   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Limb-girdle muscular dystrophy type 2E (AR)<br>NM_000232.4                               | SGCB   | Pan-ethnic | ≤1 in 500         | 92%            | Reduced                                    |
| Limb-girdle muscular dystrophy type 2F (AR)<br>NM_000337.5                               | SGCD   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Lipoid congenital adrenal hyperplasia (AR)<br>NM_000349.2                                | STAR   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| LRAT-related conditions (AR)<br>NM_004744.4                                              | LRAT   | Pan-ethnic | 1 in 296          | 99%            | 1 in 29500                                 |
| Lysinuric protein intolerance (AR)<br>NM_001126106.2                                     | SLC7A7 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Lysosomal acid lipase deficiency (AR)<br>NM_000235.3                                     | LIPA   | Pan-ethnic | 1 in 359          | 94%            | 1 in 5967                                  |
| Major histocompatibility complex class II deficiency (CIITA-related) (AR)<br>NM_000246.3 | CIITA  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Malonyl-CoA decarboxylase deficiency (AR)<br>NM_012213.2                                 | MLYCD  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Maple syrup urine disease type 1A (AR)<br>NM_000709.3                                    | BCKDHA | Pan-ethnic | 1 in 373          | 99%            | 1 in 37200                                 |
| Maple syrup urine disease type 1B (AR)<br>NM_183050.2                                    | BCKDHB | Pan-ethnic | 1 in 346          | 99%            | 1 in 34500                                 |
| Maple syrup urine disease type 2 (AR)<br>NM_001918.3                                     | DBT    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Medium-chain acyl-CoA dehydrogenase deficiency (AR)<br>NM_000016.5                       | ACADM  | Pan-ethnic | 1 in 66           | 99%            | 1 in 6500                                  |
| Medium/short-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (AR)<br>NM_005327.4        | HADH   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| MEDNIK syndrome (AR)<br>NM_001283.3                                                      | AP1S1  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |

| DISORDER (INHERITANCE)                                                                              | GENE    | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|-----------------------------------------------------------------------------------------------------|---------|------------|-------------------|----------------|--------------------------------------------|
| Megalencephalic leukoencephalopathy with subcortical cysts 1 (AR)<br>NM_015166.3                    | MLC1 *  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Metabolic crises with rhabdomyolysis, cardiac arrhythmias and neurodegeneration (AR)<br>NM_152906.6 | TANGO2  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Metachromatic leukodystrophy (ARSA-related) (AR)<br>NM_000487.5                                     | ARSA    | Pan-ethnic | 1 in 100          | 95%            | 1 in 1980                                  |
| Methylmalonic acidemia (MCEE-related) (AR)<br>NM_032601.3                                           | MCEE    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Methylmalonic acidemia (MMAA-related) (AR)<br>NM_172250.2                                           | MMAA    | Pan-ethnic | 1 in 316          | 97%            | 1 in 10500                                 |
| Methylmalonic acidemia (MMAB-related) (AR)<br>NM_052845.3                                           | MMAB    | Pan-ethnic | 1 in 456          | 98%            | 1 in 22750                                 |
| Methylmalonic acidemia (MUT-related) (AR)<br>NM_000255.3                                            | MUT     | Pan-ethnic | 1 in 204          | 96%            | 1 in 5075                                  |
| MFSD8-related conditions (AR)<br>NM_152778.2                                                        | MFSD8   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Microcephalic osteodysplastic primordial dwarfism type II (AR)<br>NM_006031.5                       | PCNT    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Microcephaly, postnatal progressive, with seizures and brain atrophy (AR)<br>NM_004268.4            | MED17   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mitochondrial complex I deficiency 1 (AR)<br>NM_002495.3                                            | NDUFS4  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mitochondrial complex I deficiency 3 (AR)<br>NM_024407.4                                            | NDUFS7  | Pan-ethnic | 1 in 387          | 99%            | 1 in 38600                                 |
| Mitochondrial complex I deficiency 4 (AR)<br>NM_007103.3                                            | NDUFV1  | Pan-ethnic | 1 in 387          | 99%            | 1 in 38600                                 |
| Mitochondrial complex I deficiency 9 (AR)<br>NM_004553.4                                            | NDUFS6  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mitochondrial complex I deficiency 10 (AR)<br>NM_174889.4                                           | NDUFAF2 | Pan-ethnic | 1 in 387          | 99%            | 1 in 38600                                 |
| Mitochondrial complex I deficiency 16 (AR)<br>NM_024120.4                                           | NDUFAF5 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mitochondrial complex I deficiency 19 (AR)<br>NM_017547.3                                           | FOXRED1 | Pan-ethnic | 1 in 376          | 99%            | 1 in 37500                                 |
| Mitochondrial complex I deficiency 20/ACAD9 deficiency (AR)<br>NM_014049.4                          | ACAD9   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mitochondrial complex IV deficiency 6 (AR)<br>NM_004376.6                                           | COX15   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mitochondrial complex IV deficiency 12 (AR)<br>NM_001171155.1                                       | PET100  | Pan-ethnic | 1 in 387          | 99%            | 1 in 38600                                 |
| Mitochondrial complex IV deficiency / Leigh syndrome, French Canadian type (AR)<br>NM_133259.3      | LRPPRC  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mitochondrial DNA depletion syndrome-2 (AR)<br>NM_004614.4                                          | TK2     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mitochondrial neurogastrointestinal encephalomyopathy (AR)<br>NM_001953.4                           | TYMP    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mitochondrial trifunctional protein deficiency (HADHB-related) (AR)<br>NM_000183.2                  | HADHB   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| MKKS-related conditions (AR)<br>NM_018848.3                                                         | MKKS    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Molybdenum cofactor deficiency (MOCS1-related) (AR)<br>NM_001358530.2                               | MOCS1   | Pan-ethnic | 1 in 226          | 99%            | 1 in 22500                                 |
| Molybdenum cofactor deficiency (MOCS2-related) (AR)<br>NM_004531.4                                  | MOCS2B  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Molybdenum cofactor deficiency (MOCS2-related) (AR)<br>NM_176806.3                                  | MOCS2A  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |

| DISORDER (INHERITANCE)                                                      | GENE   | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|-----------------------------------------------------------------------------|--------|------------|-------------------|----------------|--------------------------------------------|
| MPL-related conditions (AR)<br>NM_005373.2                                  | MPL    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| MPV17-related conditions (AR)<br>NM_002437.4                                | MPV17  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mucopolidosis type III gamma (AR)<br>NM_032520.4                            | GNPTG  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mucopolidosis type IV (AR)<br>NM_020533.2                                   | MCOLN1 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mucopolysaccharidosis type I (AR)<br>NM_000203.4                            | IDUA   | Pan-ethnic | 1 in 148          | 97%            | 1 in 4900                                  |
| Mucopolysaccharidosis type IIIA (AR)<br>NM_000199.3                         | SGSH   | Pan-ethnic | 1 in 215          | 99%            | 1 in 21400                                 |
| Mucopolysaccharidosis type IIIB (AR)<br>NM_000263.3                         | NAGLU  | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |
| Mucopolysaccharidosis type IIID (AR)<br>NM_002076.3                         | GNS    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mucopolysaccharidosis type IVA (AR)<br>NM_000512.4                          | GALNS  | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |
| Mucopolysaccharidosis type IX (AR)<br>NM_153281.1                           | HYAL1  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Mucopolysaccharidosis type VI (AR)<br>NM_000046.3                           | ARSB   | Pan-ethnic | 1 in 250          | 99%            | 1 in 24900                                 |
| Mucopolysaccharidosis type VII (AR)<br>NM_000181.3                          | GUSB   | Pan-ethnic | 1 in 250          | 99%            | 1 in 24900                                 |
| Mulibrey nanism (AR)<br>NM_015294.4                                         | TRIM37 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Multiple pterygium syndrome (AR)<br>NM_005199.4                             | CHRNA  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Multiple sulfatase deficiency (AR)<br>NM_182760.3                           | SUMF1  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Muscular dystrophy-dystroglycanopathy (FKRP-related) (AR)<br>NM_024301.4    | FKRP   | Pan-ethnic | 1 in 158          | 99%            | 1 in 15700                                 |
| Muscular dystrophy-dystroglycanopathy (FKTN-related) (AR)<br>NM_001079802.1 | FKTN   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Muscular dystrophy-dystroglycanopathy (LARGE1-related) (AR)<br>NM_004737.4  | LARGE1 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Muscular dystrophy-dystroglycanopathy (POMT1-related) (AR)<br>NM_007171.3   | POMT1  | Pan-ethnic | 1 in 268          | 99%            | 1 in 26700                                 |
| Muscular dystrophy-dystroglycanopathy (POMT2-related) (AR)<br>NM_013382.5   | POMT2  | Pan-ethnic | 1 in 371          | 99%            | 1 in 37000                                 |
| Muscular dystrophy-dystroglycanopathy (RXYLT1-related) (AR)<br>NM_014254.2  | RXYLT1 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| MUSK-related conditions (AR)<br>NM_005592.3                                 | MUSK   | Pan-ethnic | 1 in 447          | 99%            | 1 in 44600                                 |
| MVK-related conditions (AR)<br>NM_000431.3                                  | MVK    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| MYO7A-related conditions (AR)<br>NM_000260.3                                | MYO7A  | Pan-ethnic | 1 in 200          | 95%            | 1 in 3980                                  |
| Myopathy, lactic acidosis, and sideroblastic anemia 1 (AR)<br>NM_025215.5   | PUS1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Myotonia congenita (AR)<br>NM_000083.2                                      | CLCN1  | Pan-ethnic | 1 in 112          | 99%            | 1 in 11100                                 |
| N-acetylglutamate synthase deficiency (AR)<br>NM_153006.2                   | NAGS   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Nemaline myopathy 2 (AR)<br>NM_001271208.1                                  | NEB *  | Pan-ethnic | 1 in 158          | 95%            | 1 in 3140                                  |

| DISORDER (INHERITANCE)                                                    | GENE    | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|---------------------------------------------------------------------------|---------|------------|-------------------|----------------|--------------------------------------------|
| Nephrogenic diabetes insipidus (AQP2-related) (AR)<br>NM_000486.5         | AQP2    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Nephronophthisis (INVS-related) (AR)<br>NM_014425.3                       | INVS    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Nephronophthisis (NPHP1-related) (AR)<br>NM_000272.3                      | NPHP1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Neuronal ceroid lipofuscinosis type 1 (AR)<br>NM_000310.3                 | PPT1    | Pan-ethnic | 1 in 199          | 98%            | 1 in 9900                                  |
| Neuronal ceroid lipofuscinosis type 2 (AR)<br>NM_000391.3                 | TPP1    | Pan-ethnic | 1 in 250          | 97%            | 1 in 8300                                  |
| Neuronal ceroid lipofuscinosis type 5 (AR)<br>NM_006493.2                 | CLN5    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Neuronal ceroid lipofuscinosis type 6 (AR)<br>NM_017882.2                 | CLN6    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Neuronal ceroid lipofuscinosis type 8 (AR)<br>NM_018941.3                 | CLN8    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Neuronal ceroid lipofuscinosis type 10 (AR)<br>NM_001909.4                | CTSD    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Niemann-Pick disease type C (NPC1-related) (AR)<br>NM_000271.4            | NPC1    | Pan-ethnic | 1 in 183          | 99%            | 1 in 18200                                 |
| Niemann-Pick disease type C (NPC2-related) (AR)<br>NM_006432.3            | NPC2    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Niemann-Pick disease types A and B (AR)<br>NM_000543.4                    | SMPD1   | Pan-ethnic | 1 in 250          | 95%            | 1 in 4980                                  |
| Nijmegen breakage syndrome (AR)<br>NM_002485.4                            | NBN     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Nonsyndromic deafness (LOXHD1-related) (AR)<br>NM_144612.6                | LOXHD1  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Nonsyndromic deafness (MYO15A-related) (AR)<br>NM_016239.3                | MYO15A  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Nonsyndromic deafness (OTOA-related) (AR)<br>NM_144672.3                  | OTOA *  | Pan-ethnic | ≤1 in 500         | 88%            | Reduced                                    |
| Nonsyndromic deafness (SYNE4-related) (AR)<br>NM_001039876.2              | SYNE4   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Nonsyndromic deafness (TMC1-related) (AR)<br>NM_138691.2                  | TMC1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Nonsyndromic deafness (TMPRSS3-related) (AR)<br>NM_024022.2               | TMPRSS3 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Nonsyndromic intellectual disability (CC2D1A-related) (AR)<br>NM_017721.5 | CC2D1A  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| NR2E3-related conditions (AR)<br>NM_014249.3                              | NR2E3   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| NSMCE3 deficiency (AR)<br>NM_138704.3                                     | NSMCE3  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Oculocutaneous albinism type 2 (AR)<br>NM_000275.2                        | OCA2    | Pan-ethnic | 1 in 95           | 99%            | 1 in 9400                                  |
| Oculocutaneous albinism type 3 (AR)<br>NM_000550.2                        | TYRP1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Oculocutaneous albinism type 4 (AR)<br>NM_016180.4                        | SLC45A2 | Pan-ethnic | 1 in 158          | 99%            | 1 in 15700                                 |
| Oculocutaneous albinism types 1A and 1B (AR)<br>NM_000372.4               | TYR *   | Pan-ethnic | 1 in 100          | 97%            | 1 in 3300                                  |
| OPA3-related conditions (AR)<br>NM_025136.3                               | OPA3    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Osteogenesis imperfecta (BMP1-related) (AR)<br>NM_006129.4                | BMP1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Osteogenesis imperfecta (CRTAP-related) (AR)<br>NM_006371.4               | CRTAP   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Osteogenesis imperfecta (P3H1-related) (AR)<br>NM_022356.3                | P3H1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| OSTM1 deficiency associated osteopetrosis (AR)<br>NM_014028.3             | OSTM1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |

This table is relevant to patient report RQ4726574-1  
Issue date: 10/21/2024

| DISORDER (INHERITANCE)                                               | GENE    | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|----------------------------------------------------------------------|---------|------------|-------------------|----------------|--------------------------------------------|
| OTOF-related conditions (AR)<br>NM_194248.2                          | OTOF    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Pantothenate kinase-associated neurodegeneration (AR)<br>NM_153638.2 | PANK2   | Pan-ethnic | 1 in 289          | 99%            | 1 in 28800                                 |
| Parkinson disease 15 (AR)<br>NM_012179.3                             | FBXO7   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| PCDH15-related conditions (AR)<br>NM_033056.3                        | PCDH15  | Pan-ethnic | 1 in 400          | 99%            | 1 in 39900                                 |
| PEX5-related conditions (AR)<br>NM_001131025.1                       | PEX5    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| PEX7-related conditions (AR)<br>NM_000288.3                          | PEX7    | Pan-ethnic | 1 in 157          | 99%            | 1 in 15600                                 |
| PGM3-congenital disorder of glycosylation (AR)<br>NM_001199917.1     | PGM3    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Phenylalanine hydroxylase deficiency (AR)<br>NM_000277.1             | PAH     | Pan-ethnic | 1 in 58           | 99%            | 1 in 5700                                  |
| Phosphoglycerate dehydrogenase deficiency (AR)<br>NM_006623.3        | PHGDH   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| PIGN-congenital disorder of glycosylation (AR)<br>NM_176787.4        | PIGN    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| PJVK-related conditions (AR)<br>NM_001042702.3                       | DFNB59  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| PLA2G6-related conditions (AR)<br>NM_003560.2                        | PLA2G6  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| PLEKHG5-related conditions (AR)<br>NM_020631.4                       | PLEKHG5 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| POLG-related conditions (AR)<br>NM_002693.2                          | POLG    | Pan-ethnic | 1 in 113          | 95%            | 1 in 2240                                  |
| Polycystic kidney disease (PKHD1-related) (AR)<br>NM_138694.3        | PKHD1 * | Pan-ethnic | 1 in 70           | 99%            | 1 in 6900                                  |
| Polymicrogyria (ADGRG1-related) (AR)<br>NM_005682.6                  | ADGRG1  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| POMGNT1-related conditions (AR)<br>NM_017739.3                       | POMGNT1 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Pontocerebellar hypoplasia (TSEN54-related) (AR)<br>NM_207346.2      | TSEN54  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Pontocerebellar hypoplasia type 1B (AR)<br>NM_016042.3               | EXOSC3  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Pontocerebellar hypoplasia type 2D (AR)<br>NM_016955.3               | SEPSECS | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Pontocerebellar hypoplasia type 6 (AR)<br>NM_020320.3                | RARS2   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Primary carnitine deficiency (AR)<br>NM_003060.3                     | SLC22A5 | Pan-ethnic | 1 in 71           | 99%            | 1 in 7000                                  |
| Primary ciliary dyskinesia (CCDC39-related) (AR)<br>NM_181426.1      | CCDC39  | Pan-ethnic | 1 in 211          | 99%            | 1 in 21000                                 |
| Primary ciliary dyskinesia (CCDC103-related) (AR)<br>NM_213607.2     | CCDC103 | Pan-ethnic | 1 in 316          | 99%            | 1 in 31500                                 |
| Primary ciliary dyskinesia (DNAH5-related) (AR)<br>NM_001369.2       | DNAH5   | Pan-ethnic | 1 in 109          | 99%            | 1 in 10800                                 |
| Primary ciliary dyskinesia (DNAH11-related) (AR)<br>NM_001277115.1   | DNAH11  | Pan-ethnic | 1 in 211          | 99%            | 1 in 21000                                 |
| Primary ciliary dyskinesia (DNAI1-related) (AR)<br>NM_012144.3       | DNAI1   | Pan-ethnic | 1 in 250          | 99%            | 1 in 24900                                 |
| Primary ciliary dyskinesia (DNAI2-related) (AR)<br>NM_023036.4       | DNAI2   | Pan-ethnic | 1 in 354          | 99%            | 1 in 35300                                 |
| Primary hyperoxaluria type 1 (AR)<br>NM_000030.2                     | AGXT    | Pan-ethnic | 1 in 135          | 99%            | 1 in 13400                                 |
| Primary hyperoxaluria type 2 (AR)<br>NM_012203.1                     | GRHPR   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Primary hyperoxaluria type 3 (AR)<br>NM_138413.3                     | HOGA1   | Pan-ethnic | 1 in 354          | 99%            | 1 in 35300                                 |

| DISORDER (INHERITANCE)                                                                                         | GENE     | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|----------------------------------------------------------------------------------------------------------------|----------|------------|-------------------|----------------|--------------------------------------------|
| Primary microcephaly (MCPH1-related) (AR)<br>NM_024596.4                                                       | MCPH1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Progressive early-onset encephalopathy with brain atrophy and thin corpus callosum (PEBAT) (AR)<br>NM_005993.4 | TBCD     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Progressive pseudorheumatoid dysplasia (AR)<br>NM_003880.3                                                     | WISP3    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Prolidase deficiency (AR)<br>NM_000285.3                                                                       | PEPD     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Propionic acidemia (PCCA-related) (AR)<br>NM_000282.3                                                          | PCCA     | Pan-ethnic | 1 in 224          | 96%            | 1 in 5575                                  |
| Propionic acidemia (PCCB-related) (AR)<br>NM_000532.4                                                          | PCCB     | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |
| PSAP-related conditions (AR)<br>NM_002778.3                                                                    | PSAP     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Pycnodysostosis (AR)<br>NM_000396.3                                                                            | CTSK     | Pan-ethnic | 1 in 438          | 99%            | 1 in 43700                                 |
| Pyridoxal 5'-phosphate-dependent epilepsy (AR)<br>NM_018129.3                                                  | PNPO     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Pyridoxine-dependent epilepsy (ALDH7A1-related) (AR)<br>NM_001182.4                                            | ALDH7A1  | Pan-ethnic | 1 in 127          | 99%            | 1 in 12600                                 |
| Pyruvate carboxylase deficiency (AR)<br>NM_000920.3                                                            | PC       | Pan-ethnic | 1 in 250          | 95%            | 1 in 4980                                  |
| Pyruvate dehydrogenase complex deficiency (PDHB-related) (AR)<br>NM_000925.3                                   | PDHB     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| RAPSN-related conditions (AR)<br>NM_005055.4                                                                   | RAPSN    | Pan-ethnic | 1 in 283          | 99%            | 1 in 28200                                 |
| RDH12-related conditions (AR)<br>NM_152443.2                                                                   | RDH12    | Pan-ethnic | 1 in 460          | 99%            | 1 in 45900                                 |
| Refsum disease (PHYH-related) (AR)<br>NM_006214.3                                                              | PHYH     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Retinitis pigmentosa 25 (AR)<br>NM_001142800.1                                                                 | EYS *    | Pan-ethnic | 1 in 129          | 99%            | 1 in 12800                                 |
| Retinitis pigmentosa 28 (AR)<br>NM_001201543.1                                                                 | FAM161A  | Pan-ethnic | 1 in 289          | 99%            | 1 in 28800                                 |
| Retinitis pigmentosa 36 (AR)<br>NM_001077620.2                                                                 | PRCD     | Pan-ethnic | 1 in 296          | 99%            | 1 in 29500                                 |
| Retinitis pigmentosa 62 (AR)<br>NM_001242957.2                                                                 | MAK      | Pan-ethnic | 1 in 274          | 99%            | 1 in 27300                                 |
| Rhizomelic chondrodysplasia punctata type 2 (AR)<br>NM_014236.3                                                | GNPAT    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Rhizomelic chondrodysplasia punctata type 3 (AR)<br>NM_003659.3                                                | AGPS     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| RLBP1-related conditions (AR)<br>NM_000326.4                                                                   | RLBP1    | Pan-ethnic | 1 in 296          | 99%            | 1 in 29500                                 |
| Roberts syndrome (AR)<br>NM_001017420.2                                                                        | ESCO2    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| RPE65-related conditions (AR)<br>NM_000329.2                                                                   | RPE65    | Pan-ethnic | 1 in 228          | 99%            | 1 in 22700                                 |
| RYR1-related conditions (AR)<br>NM_000540.2                                                                    | RYR1     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| SAMD9-related conditions (AR)<br>NM_017654.3                                                                   | SAMD9    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Sandhoff disease (AR)<br>NM_000521.3                                                                           | HEXB     | Pan-ethnic | 1 in 180          | 99%            | 1 in 17900                                 |
| Schimke immuno-osseous dysplasia (AR)<br>NM_014140.3                                                           | SMARCAL1 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Seckel syndrome (CEP152-related) (AR)<br>NM_014985.3                                                           | CEP152   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Sepiapterin reductase deficiency (AR)<br>NM_003124.4                                                           | SPR      | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |

| DISORDER (INHERITANCE)                                                                                                                                                    | GENE    | ETHNICITY        | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|------------------|-------------------|----------------|--------------------------------------------|
| Severe combined immunodeficiency due to CD3-delta deficiency (AR)<br>NM_000732.4                                                                                          | CD3D    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Severe combined immunodeficiency due to CD3-epsilon deficiency (AR)<br>NM_000733.3                                                                                        | CD3E    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Severe combined immunodeficiency due to CD45 deficiency (AR)<br>NM_002838.4                                                                                               | PTPRC * | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Severe combined immunodeficiency due to DCLRE1C (Artemis) deficiency (AR)<br>NM_001033855.2                                                                               | DCLRE1C | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Severe combined immunodeficiency due to IL7R-alpha deficiency (AR)<br>NM_002185.3                                                                                         | IL7R    | Pan-ethnic       | 1 in 348          | 99%            | 1 in 34700                                 |
| Severe combined immunodeficiency due to JAK3 deficiency (AR)<br>NM_000215.3                                                                                               | JAK3    | Pan-ethnic       | 1 in 455          | 99%            | 1 in 45400                                 |
| Severe combined immunodeficiency due to RAG1 deficiency (AR)<br>NM_000448.2                                                                                               | RAG1    | Pan-ethnic       | 1 in 301          | 99%            | 1 in 30000                                 |
| Severe combined immunodeficiency due to RAG2 deficiency (AR)<br>NM_000536.3                                                                                               | RAG2    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Severe congenital neutropenia due to G6PC3 deficiency (AR)<br>NM_138387.3                                                                                                 | G6PC3   | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Severe congenital neutropenia due to HAX1 deficiency (AR)<br>NM_006118.3                                                                                                  | HAX1    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Severe congenital neutropenia due to VPS45 deficiency (AR)<br>NM_007259.4                                                                                                 | VPS45   | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Sialic acid storage diseases (AR)<br>NM_012434.4                                                                                                                          | SLC17A5 | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Sialidosis (AR)<br>NM_000434.3                                                                                                                                            | NEU1    | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Sjögren-Larsson syndrome (AR)<br>NM_000382.2                                                                                                                              | ALDH3A2 | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| SLC12A6-related conditions (AR)<br>NM_133647.1                                                                                                                            | SLC12A6 | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| SLC26A2-related conditions (AR)<br>NM_000112.3                                                                                                                            | SLC26A2 | Pan-ethnic       | 1 in 158          | 95%            | 1 in 3140                                  |
| SLC26A4-related conditions (AR)<br>NM_000441.1                                                                                                                            | SLC26A4 | Pan-ethnic       | 1 in 80           | 99%            | 1 in 7900                                  |
| SLC37A4-related conditions (AR)<br>NM_001164277.1                                                                                                                         | SLC37A4 | Pan-ethnic       | 1 in 354          | 95%            | 1 in 7060                                  |
| Smith-Lemli-Opitz syndrome (AR)<br>NM_001360.2                                                                                                                            | DHCR7   | Pan-ethnic       | 1 in 71           | 99%            | 1 in 7000                                  |
| Spastic paraplegia type 15 (AR)<br>NM_015346.3                                                                                                                            | ZFYVE26 | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Spastic paraplegia type 49 (AR)<br>NM_014844.3                                                                                                                            | TECPR2  | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| Spastic tetraplegia, thin corpus callosum, and progressive microcephaly (AR)<br>NM_003038.4                                                                               | SLC1A4  | Pan-ethnic       | ≤1 in 500         | 99%            | Reduced                                    |
| SPG11-related conditions (AR)<br>NM_025137.3                                                                                                                              | SPG11   | Pan-ethnic       | 1 in 141          | 99%            | 1 in 14000                                 |
| Spinal muscular atrophy (AR)<br>NM_000344.3<br>Carrier residual risks listed are for 2 copy SMN1 results.<br>Carrier residual risk for >2 copies are 5- to 10-fold lower. | SMN1 *  | African-American | 1 in 59           | 83%            | 1 in 342                                   |
|                                                                                                                                                                           |         | Ashkenazi Jewish | 1 in 62           | 94%            | 1 in 1017                                  |
|                                                                                                                                                                           |         | Asian            | 1 in 50           | 93%            | 1 in 701                                   |
|                                                                                                                                                                           |         | Caucasian        | 1 in 45           | 95%            | 1 in 880                                   |
|                                                                                                                                                                           |         | Hispanic         | 1 in 48           | 94%            | 1 in 784                                   |
|                                                                                                                                                                           |         | Pan-ethnic       | 1 in 49           | 94%            | 1 in 800                                   |

| DISORDER (INHERITANCE)                                            | GENE    | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|-------------------------------------------------------------------|---------|------------|-------------------|----------------|--------------------------------------------|
| Spinocerebellar ataxia (ANO10-related) (AR)<br>NM_018075.3        | ANO10 * | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Spondylocostal dysostosis (DLL3-related) (AR)<br>NM_016941.3      | DLL3    | Pan-ethnic | 1 in 350          | 99%            | 1 in 34900                                 |
| Spondylocostal dysostosis (MESP2-related) (AR)<br>NM_001039958.1  | MESP2   | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |
| Steel syndrome (AR)<br>NM_032888.3                                | COL27A1 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Steroid 5-alpha-reductase deficiency (AR)<br>NM_000348.3          | SRD5A2  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Stüve-Wiedemann syndrome (AR)<br>NM_002310.5                      | LIFR *  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Sulfite oxidase deficiency (AR)<br>NM_000456.2                    | SUOX    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| SURF1-related conditions (AR)<br>NM_003172.3                      | SURF1   | Pan-ethnic | 1 in 128          | 99%            | 1 in 12700                                 |
| Tay-Sachs disease (AR)<br>NM_000520.4                             | HEXA    | Pan-ethnic | 1 in 250          | 99%            | 1 in 24900                                 |
| TBCE-related conditions (AR)<br>NM_003193.4                       | TBCE *  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| TCIRG1-related conditions (AR)<br>NM_006019.3                     | TCIRG1  | Pan-ethnic | 1 in 317          | 99%            | 1 in 31600                                 |
| Thiamine-responsive megaloblastic anemia (AR)<br>NM_006996.2      | SLC19A2 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Thyroid dysharmonogenesis (SLC5A5-related) (AR)<br>NM_000453.2    | SLC5A5  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Thyroid dysharmonogenesis (TG-related) (AR)<br>NM_003235.4        | TG *    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Thyroid dysharmonogenesis (TPO-related) (AR)<br>NM_000547.5       | TPO     | Pan-ethnic | 1 in 129          | 99%            | 1 in 12800                                 |
| TMEM67-related conditions (AR)<br>NM_153704.5                     | TMEM67  | Pan-ethnic | 1 in 316          | 99%            | 1 in 31500                                 |
| Transcobalamin II deficiency (AR)<br>NM_000355.3                  | TCN2    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Transient infantile liver failure (AR)<br>NM_018006.4             | TRMU    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| TREX1-related conditions (AR)<br>NM_033629.4                      | TREX1   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Trichohepatoenteric syndrome (SKIV2L-related) (AR)<br>NM_006929.4 | SKIV2L  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Trichohepatoenteric syndrome (TTC37-related) (AR)<br>NM_014639.3  | TTC37   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| TRIM32-related conditions (AR)<br>NM_012210.3                     | TRIM32  | Pan-ethnic | 1 in 408          | 99%            | 1 in 40700                                 |
| Trimethylaminuria (AR)<br>NM_006894.6                             | FMO3    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Triple A syndrome (AR)<br>NM_015665.5                             | AAAS    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| TSHR-related conditions (AR)<br>NM_000369.2                       | TSHR    | Pan-ethnic | 1 in 158          | 99%            | 1 in 15700                                 |
| TULP1-related conditions (AR)<br>NM_003322.4                      | TULP1   | Pan-ethnic | 1 in 296          | 99%            | 1 in 29500                                 |
| Tyrosine hydroxylase deficiency (AR)<br>NM_199292.2               | TH      | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Tyrosinemia type I (AR)<br>NM_000137.2                            | FAH *   | Pan-ethnic | 1 in 125          | 95%            | 1 in 2480                                  |
| Tyrosinemia type II (AR)<br>NM_000353.2                           | TAT     | Pan-ethnic | 1 in 250          | 99%            | 1 in 24900                                 |
| Tyrosinemia type III (AR)<br>NM_002150.2                          | HPD     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| USH1C-related conditions (AR)<br>NM_005709.3                      | USH1C * | Pan-ethnic | 1 in 353          | 90%            | 1 in 3521                                  |

This table is relevant to patient report RQ4726574-1  
Issue date: 10/21/2024

| DISORDER (INHERITANCE)                                                | GENE    | ETHNICITY  | CARRIER FREQUENCY | DETECTION RATE | RISK TO BE A CARRIER AFTER NEGATIVE RESULT |
|-----------------------------------------------------------------------|---------|------------|-------------------|----------------|--------------------------------------------|
| USH2A-related conditions (AR)<br>NM_206933.2                          | USH2A   | Pan-ethnic | 1 in 112          | 99%            | 1 in 11100                                 |
| Very long-chain acyl-CoA dehydrogenase deficiency (AR)<br>NM_000018.3 | ACADVL  | Pan-ethnic | 1 in 100          | 99%            | 1 in 9900                                  |
| Vici syndrome (AR)<br>NM_020964.2                                     | EPG5    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Vitamin D-dependent rickets type 1A (AR)<br>NM_000785.3               | CYP27B1 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Vitamin D-dependent rickets type 2A (AR)<br>NM_001017535.1            | VDR     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| VPS53-related conditions (AR)<br>NM_001128159.2                       | VPS53 * | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| VRK1-related conditions (AR)<br>NM_003384.2                           | VRK1    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| VSX2-related conditions (AR)<br>NM_182894.2                           | VSX2    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Warsaw syndrome (AR)<br>NM_030653.3                                   | DDX11 * | Pan-ethnic | ≤1 in 500         | 15%            | Reduced                                    |
| Werner syndrome (AR)<br>NM_000553.4                                   | WRN *   | Pan-ethnic | 1 in 224          | 99%            | 1 in 22300                                 |
| Wilson disease (AR)<br>NM_000053.3                                    | ATP7B   | Pan-ethnic | 1 in 90           | 98%            | 1 in 4450                                  |
| WNT10A-related conditions (AR)<br>NM_025216.2                         | WNT10A  | Pan-ethnic | 1 in 305          | 99%            | 1 in 30400                                 |
| Wolcott-Rallison syndrome (AR)<br>NM_004836.6                         | EIF2AK3 | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Woodhouse-Sakati syndrome (AR)<br>NM_025000.3                         | DCAF17  | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Xeroderma pigmentosum complementation group A (AR)<br>NM_000380.3     | XPA     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Xeroderma pigmentosum complementation group C (AR)<br>NM_004628.4     | XPC     | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Xeroderma pigmentosum, variant type (AR)<br>NM_006502.2               | POLH    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Zellweger spectrum disorder (PEX1-related) (AR)<br>NM_000466.2        | PEX1 *  | Pan-ethnic | 1 in 144          | 99%            | 1 in 14300                                 |
| Zellweger spectrum disorder (PEX2-related) (AR)<br>NM_000318.2        | PEX2    | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Zellweger spectrum disorder (PEX6-related) (AR)<br>NM_000287.3        | PEX6    | Pan-ethnic | 1 in 294          | 99%            | 1 in 29300                                 |
| Zellweger spectrum disorder (PEX10-related) (AR)<br>NM_153818.1       | PEX10   | Pan-ethnic | ≤1 in 500         | 94%            | Reduced                                    |
| Zellweger spectrum disorder (PEX12-related) (AR)<br>NM_000286.2       | PEX12   | Pan-ethnic | 1 in 409          | 99%            | 1 in 40800                                 |
| Zellweger spectrum disorder (PEX13-related) (AR)<br>NM_002618.3       | PEX13   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Zellweger spectrum disorder (PEX16-related) (AR)<br>NM_004813.2       | PEX16   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |
| Zellweger spectrum disorder (PEX26-related) (AR)<br>NM_017929.5       | PEX26   | Pan-ethnic | ≤1 in 500         | 99%            | Reduced                                    |



| Patient Information                                                                                                                          | Specimen Information                                                                                                                             | Client Information                                                                                                            |
|----------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|
| <b>16032, DONOR</b><br><br><b>DOB:</b> [REDACTED] <b>AGE:</b> [REDACTED]<br>Gender: M Fasting: U<br>Phone: 206.466.4696<br>Patient ID: 16032 | Specimen: OW940798U<br>Requisition: 0000490<br><br>Collected: 02/22/2023<br>Received: 02/23/2023 / 00:27 PST<br>Reported: 03/01/2023 / 12:42 PST | Client #: 98105026 VNLZR00<br>OLLIFFE, JEFFREY F<br>SEATTLE SPERM BANK<br>4915 25TH AVE NE STE 204W<br>SEATTLE, WA 98105-5668 |

**COMMENTS:** FASTING:UNKNOWN

## Cytogenetic Report

### CHROMOSOME ANALYSIS, BLOOD - 14596

**Lab:EZ**

#### CHROMOSOME ANALYSIS, BLOOD

Order ID: 23-82984  
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: 450  
Cells Analyzed: 6  
Cells Karyotyped: 6

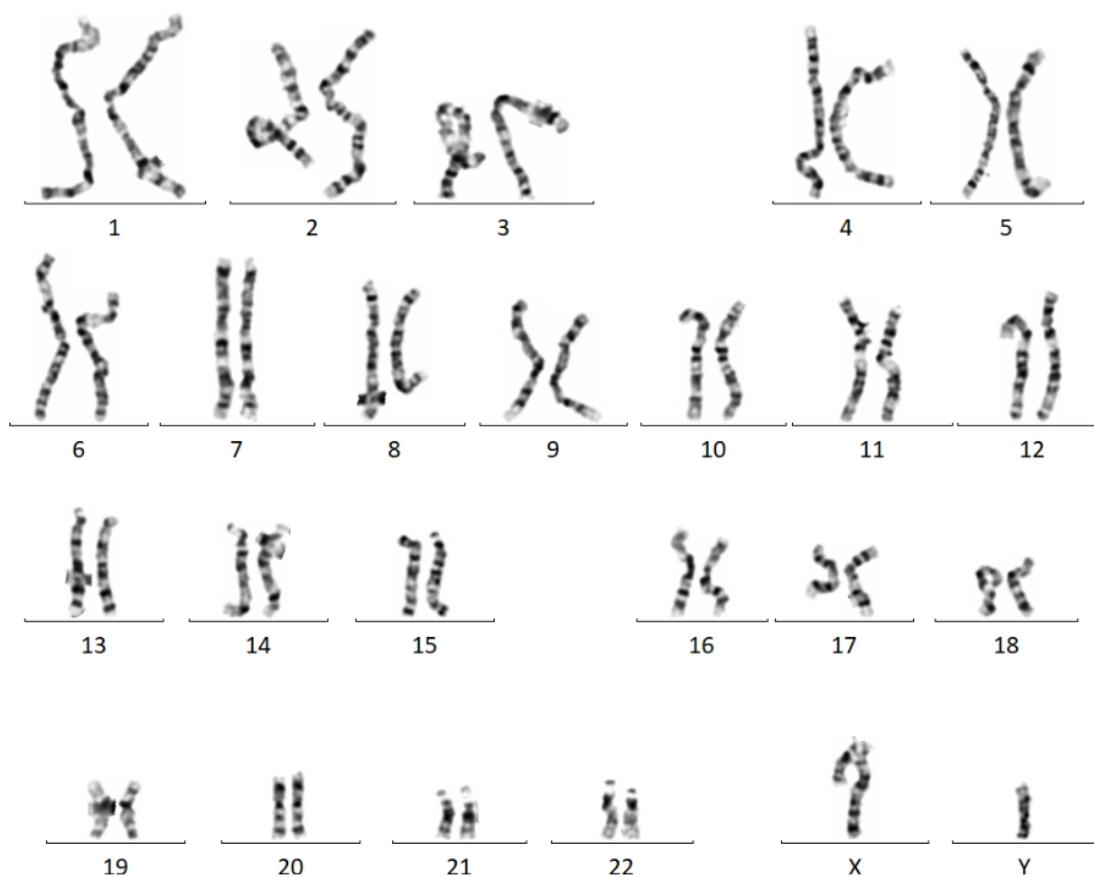
This test does not address genetic disorders that cannot be detected by standard cytogenetic methods or rare events such as low level mosaicism or subtle rearrangements.

Lauren Walters-Sen, PhD, FACMG (800) NICHOLS-4307

Electronic Signature: 3/1/2023 2:57 PM



| Patient Information                                                                                           | Specimen Information                                                                                                 | Client Information                       |
|---------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| <b>16032, DONOR</b><br><br><b>DOB:</b> ██████ <b>AGE:</b> ██████<br>Gender: M Fasting: U<br>Patient ID: 16032 | Specimen: OW940798U<br>Collected: 02/22/2023<br>Received: 02/23/2023 / 00:27 PST<br>Reported: 03/01/2023 / 12:42 PST | Client #: 98105026<br>OLLIFFE, JEFFREY F |



**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

Date Collected: 02/22/2023

Date Received: 02/22/2023

Date Reported: 02/27/2023

Fasting: Not Given

Ordered Items: LP+12AC+CBC/D/Plt+UA+Rh+ABO...

General Comments & Additional Information

A courtesy copy of this report has been sent to 2064664696.

Date Collected: 02/22/2023

LP+12AC+CBC/D/Plt+UA+Rh+ABO...

| Test                                       | Current Result and Flag |      | Previous Result and Date | Units       | Reference Interval |
|--------------------------------------------|-------------------------|------|--------------------------|-------------|--------------------|
| Glucose <sup>01</sup>                      | 86                      |      |                          | mg/dL       | 70-99              |
| Uric Acid <sup>01</sup>                    | 5.4                     |      |                          | mg/dL       | 3.8-8.4            |
| Therapeutic target for gout patients: <6.0 |                         |      |                          |             |                    |
| BUN <sup>01</sup>                          | 13                      |      |                          | mg/dL       | 6-20               |
| ▼ Creatinine <sup>01</sup>                 | 0.74                    | Low  |                          | mg/dL       | 0.76-1.27          |
| eGFR                                       | 122                     |      |                          | mL/min/1.73 | >59                |
| Calcium <sup>01</sup>                      | 9.7                     |      |                          | mg/dL       | 8.7-10.2           |
| Protein, Total <sup>01</sup>               | 7.0                     |      |                          | g/dL        | 6.0-8.5            |
| Albumin <sup>01</sup>                      | 4.8                     |      |                          | g/dL        | 4.0-5.0            |
| Bilirubin, Total <sup>01</sup>             | 0.4                     |      |                          | mg/dL       | 0.0-1.2            |
| ▼ Alkaline Phosphatase <sup>01</sup>       | 39                      | Low  |                          | IU/L        | 44-121             |
| LDH <sup>01</sup>                          | 147                     |      |                          | IU/L        | 121-224            |
| AST (SGOT) <sup>01</sup>                   | 23                      |      |                          | IU/L        | 0-40               |
| ALT (SGPT) <sup>01</sup>                   | 13                      |      |                          | IU/L        | 0-44               |
| ▲ Cholesterol, Total <sup>01</sup>         | 215                     | High |                          | mg/dL       | 100-199            |
| Triglycerides <sup>01</sup>                | 41                      |      |                          | mg/dL       | 0-149              |
| HDL Cholesterol <sup>01</sup>              | 77                      |      |                          | mg/dL       | >39                |
| ▲ LDL Chol Calc (NIH)                      | 131                     | High |                          | mg/dL       | 0-99               |
| LDL/HDL Ratio                              | 1.7                     |      |                          | ratio       | 0.0-3.6            |
| Please Note: <sup>01</sup>                 |                         |      |                          |             |                    |

| LDL/HDL Ratio |  |     |       |
|---------------|--|-----|-------|
|               |  | Men | Women |
| 1/2 Avg.Risk  |  | 1.0 | 1.5   |
| Avg.Risk      |  | 3.6 | 3.2   |
| 2X Avg.Risk   |  | 6.2 | 5.0   |
| 3X Avg.Risk   |  | 8.0 | 6.1   |

|                                        |      |  |   |           |
|----------------------------------------|------|--|---|-----------|
| Hgb Fractionation by CE: <sup>02</sup> |      |  |   |           |
| Hgb F <sup>02</sup>                    | 0.0  |  | % | 0.0-2.0   |
| Hgb A <sup>02</sup>                    | 97.7 |  | % | 96.4-98.8 |
| Hgb A2 <sup>02</sup>                   | 2.3  |  | % | 1.8-3.2   |
| Hgb S <sup>02</sup>                    | 0.0  |  | % | 0.0       |

Interpretation:<sup>02</sup>

Normal hemoglobin present; no hemoglobin variant or beta thalassemia identified.

Note: Alpha thalassemia may not be detected by the Hgb Fractionation Cascade panel. If alpha thalassemia is suspected, Labcorp offers

Date Collected: 02/22/2023

LP+12AC+CBC/D/Plt+UA+Rh+ABO... (Cont.)

Alpha-Thalassemia DNA Analysis (#511172).

|                                          |                                                                                                            |          |                |
|------------------------------------------|------------------------------------------------------------------------------------------------------------|----------|----------------|
| ABO Grouping <sup>01</sup>               | A                                                                                                          |          |                |
| Rh Factor <sup>01</sup>                  | Negative                                                                                                   |          |                |
|                                          | Please note: Prior records for this patient's ABO / Rh type are not available for additional verification. |          |                |
| . <sup>01</sup>                          |                                                                                                            |          |                |
| CBC, Platelet Ct, and Diff <sup>01</sup> |                                                                                                            |          |                |
| WBC <sup>01</sup>                        | 4.0                                                                                                        | x10E3/uL | 3.4-10.8       |
| RBC <sup>01</sup>                        | 4.48                                                                                                       | x10E6/uL | 4.14-5.80      |
| Hemoglobin <sup>01</sup>                 | 14.3                                                                                                       | g/dL     | 13.0-17.7      |
| Hematocrit <sup>01</sup>                 | 39.8                                                                                                       | %        | 37.5-51.0      |
| MCV <sup>01</sup>                        | 89                                                                                                         | fL       | 79-97          |
| MCH <sup>01</sup>                        | 31.9                                                                                                       | pg       | 26.6-33.0      |
| ▲ MCHC <sup>01</sup>                     | 35.9                                                                                                       | High     | g/dL 31.5-35.7 |
| RDW <sup>01</sup>                        | 12.2                                                                                                       | %        | 11.6-15.4      |
| Platelets <sup>01</sup>                  | 214                                                                                                        | x10E3/uL | 150-450        |
| Neutrophils <sup>01</sup>                | 59                                                                                                         | %        | Not Estab.     |
| Lymphs <sup>01</sup>                     | 31                                                                                                         | %        | Not Estab.     |
| Monocytes <sup>01</sup>                  | 7                                                                                                          | %        | Not Estab.     |
| Eos <sup>01</sup>                        | 2                                                                                                          | %        | Not Estab.     |
| Basos <sup>01</sup>                      | 1                                                                                                          | %        | Not Estab.     |
| Neutrophils (Absolute) <sup>01</sup>     | 2.4                                                                                                        | x10E3/uL | 1.4-7.0        |
| Lymphs (Absolute) <sup>01</sup>          | 1.3                                                                                                        | x10E3/uL | 0.7-3.1        |
| Monocytes(Absolute) <sup>01</sup>        | 0.3                                                                                                        | x10E3/uL | 0.1-0.9        |
| Eos (Absolute) <sup>01</sup>             | 0.1                                                                                                        | x10E3/uL | 0.0-0.4        |
| Baso (Absolute) <sup>01</sup>            | 0.0                                                                                                        | x10E3/uL | 0.0-0.2        |
| Immature Granulocytes <sup>01</sup>      | 0                                                                                                          | %        | Not Estab.     |
| Immature Grans (Abs) <sup>01</sup>       | 0.0                                                                                                        | x10E3/uL | 0.0-0.1        |
| . <sup>01</sup>                          |                                                                                                            |          |                |
| Urinalysis Gross Exam <sup>01</sup>      |                                                                                                            |          |                |
| Specific Gravity <sup>01</sup>           | 1.012                                                                                                      |          | 1.005-1.030    |
| pH <sup>01</sup>                         | 7.5                                                                                                        |          | 5.0-7.5        |
| Urine-Color <sup>01</sup>                | Yellow                                                                                                     |          | Yellow         |
| Appearance <sup>01</sup>                 | Clear                                                                                                      |          | Clear          |
| WBC Esterase <sup>01</sup>               | Negative                                                                                                   |          | Negative       |
| Protein <sup>01</sup>                    | Negative                                                                                                   |          | Negative/Trace |
| Glucose <sup>01</sup>                    | Negative                                                                                                   |          | Negative       |
| Ketones <sup>01</sup>                    | Negative                                                                                                   |          | Negative       |
| Occult Blood <sup>01</sup>               | Negative                                                                                                   |          | Negative       |
| Bilirubin <sup>01</sup>                  | Negative                                                                                                   |          | Negative       |
| Urobilinogen,Semi-Qn <sup>01</sup>       | 0.2                                                                                                        | mg/dL    | 0.2-1.0        |
| Nitrite, Urine <sup>01</sup>             | Negative                                                                                                   |          | Negative       |
| Microscopic Examination <sup>01</sup>    | Microscopic not indicated and not performed.                                                               |          |                |

**16032, Donor**

Patient ID:  
Specimen ID: **053-129-0558-0**

DOB: [REDACTED]  
Age: [REDACTED]  
Sex: **Male**

**Patient Report**

Account Number: [REDACTED]  
Ordering Physician: **J OLLIFFE**



**Disclaimer**

The Previous Result is listed for the most recent test performed by Labcorp in the past 5 years where there is sufficient patient demographic data to match the result to the patient. Results from certain tests are excluded from the Previous Result display.

**Icon Legend**

▲ Out of Reference Range ■ Critical or Alert

**Performing Labs**

01: SE - Labcorp Seattle 550 17th Avenue Ste 300, Seattle, WA, 98122-5789 Dir: Daniel Toweill, MD  
02: BN - Labcorp Burlington 1447 York Court, Burlington, NC, 27215-3361 Dir: Sanjai Nagendra, MD  
For Inquiries, the physician may contact Branch: 206-861-7000 Lab: 206-861-7000

**Patient Details**  
**16032, Donor**

Phone:  
Date of Birth: [REDACTED]  
Age: [REDACTED]  
Sex: **Male**  
Patient ID:  
Alternate Patient ID:

**Physician Details**  
**J OLLIFFE**  
**Seattle Sperm Bank**  
**4915 25th Ave Ne Ste 204, SEATTLE, WA, 98105**

Phone: **206-588-1484**  
Account Number: [REDACTED]  
Physician ID:  
NPI: **1306838271**

**Specimen Details**  
Specimen ID: **053-129-0558-0**  
Control ID: **L2301182791**  
Alternate Control Number: **L2301182791**  
Date Collected: **02/22/2023 1159 Local**  
Date Received: **02/22/2023 0000 ET**  
Date Entered: **02/22/2023 1905 ET**  
Date Reported: **02/27/2023 1007 ET**