# Donor 7359

# Genetic Testing Summary

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

Last Updated: 08/09/24

Donor Reported Ancestry: Nicaraguan, Spanish (from Spain), Afro-Venezuelan, Italian, French, German
Jewish Ancestry: No

| Genetic Test* | Result | Comments/Donor's Residual Risk** |
|---|---|---|
| Chromosome analysis (karyotype) | Normal male karyotype | No evidence of clinically significant chromosome abnormalities |
| Hemoglobin evaluation | Normal hemoglobin fractionation and MCV/MCH results | Reduced risk to be a carrier for sickle cell anemia, beta thalassemia, alpha thalassemia trait (aa/-- and a-/a-) and other hemoglobinopathies |
| Expanded Genetic Disease Carrier Screening Panel attached- 514 diseases by gene sequencing. | Carrier: GJB2-related conditions (GJB2)<br><br>Carrier: Glycogen storage disease type IXb (PHKB)<br><br>Carrier: Wilson disease (ATP7B)<br><br>Increased Carrier Risk: Spinal muscular atrophy (SMN1). Carrier risk is 1/34<br><br>Duplication carrier for Alpha thalassemia (HBA1/HBA2) aaa/aa<br>See Results to note on pages 6 and 7.<br>Partner testing for **HBB** is indicated.<br><br>Negative for other genes sequenced. | Partner testing is recommended before using this donor.<br><br>Residual risks for negative results can be seen here:<br><br>https://fairfaxcryobank.com/invitae-residual-risk-table |

*No single test can screen for all genetic disorders. A negative screening result significantly reduces, but cannot eliminate, the risk for these conditions in a pregnancy.

**Donor residual risk is the chance the donor is still a carrier after testing negative.

INVITAE

# INVITAE CARRIER SCREEN RESULTS

| | | | | | |
|---|---|---|---|---|---|
| **Patient name:** | Donor 7359 | **Sample type:** | Blood | **Report date:** | 11-MAR-2024 |
| **DOB:** | [redacted] | **Sample collection date:** | 01-MAR-2024 | **Invitae #:** | [redacted] |
| **Sex assigned at birth:** | Male | **Sample accession date:** | 02-MAR-2024 | **Clinical team:** | [redacted] |
| **Gender:** | | | | | |
| **Patient ID (MRN):** | 7359-[redacted] | | | | |

**Reason for testing**

Gamete donor

**Test performed**

Invitae Carrier Screen

## 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 |
|---|---|---|---|---|
| **Carrier:** GJB2-related conditions | GJB2 | c.109G>A (p.Val37Ile) § | Autosomal recessive | Yes |
| **Carrier:** Glycogen storage disease type IXb | PHKB | c.2014C>T (p.Arg672*) | Autosomal recessive | Yes |
| **Carrier:** Wilson disease | ATP7B | c.2605G>A (p.Gly869Arg) | Autosomal recessive | Yes |
| **Increased Carrier Risk:** Spinal muscular atrophy | SMN1 | c.*3+80T>G (also known as g.27134T>G) | Autosomal recessive | Yes |

§ This variant is known to have low penetrance. See Clinical summary and/or Variant details on following pages for more information.

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## Next steps

- 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

## GJB2-related conditions

A single Pathogenic (low penetrance) variant, c.109G>A (p.Val37Ile), was identified in GJB2.

### What are GJB2-related conditions?

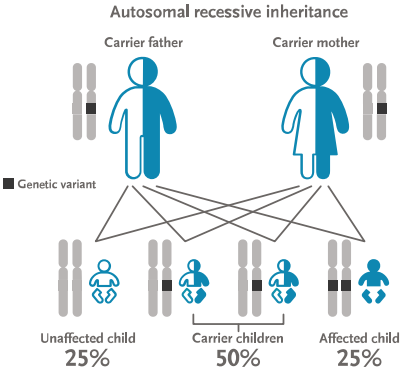
The GJB2 gene is associated with multiple conditions that can have both distinct and overlapping symptoms, as well as different inheritance patterns. GJB2-related conditions include autosomal recessive nonsyndromic deafness (DFNB1), as well as autosomal dominant nonsyndromic deafness (DFNA3) and several conditions involving deafness and skin findings. 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 GJB2 variant identified in this individual is expected to be associated with autosomal recessive nonsyndromic deafness (DFNB1).

Nonsyndromic deafness is a condition that affects an individual's ability to hear. It can be caused by changes in several different genes. Nonsyndromic deafness does not affect any other part of the body. Affected individuals are born with mild to profound deafness that typically does not worsen over time. Severity of deafness may vary, even among members of the same family. Intellect and life span are not impacted. Fewer than 1% of individuals with GJB2-related nonsyndromic deafness have been reported to have a variant in GJB2 on one chromosome and a deletion that includes both a region upstream of the GJB2 gene and a portion of GJB6, an adjacent gene, on the opposite chromosome. 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 GJB2 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 GJB2-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 |
|---|---|---|---|---|
| GJB2-related conditions (AR) NM_004004.5 | GJB2 | Pan-ethnic | 1 in 50 | 1 in 4900 |

## RESULT: CARRIER

# Glycogen storage disease type IXb

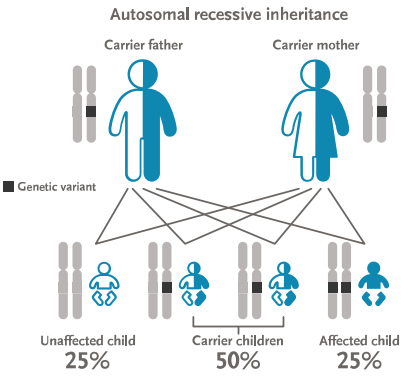
A single Pathogenic variant, c.2014C>T (p.Arg672*), was identified in PHKB.

### What is glycogen storage disease type IXb?

Glycogen storage disease (GSD) is a group of conditions in which individuals have difficulty breaking down a complex sugar called glycogen. A buildup of glycogen impairs the function of certain organs and tissues. There are different forms of GSD type IX (GSD IX) that affect the liver, muscles, or both the liver and muscles, and each form is caused by changes in different genes. GSD IXb affects both the liver and muscles. Symptoms are variable, typically begin in childhood, and include slow growth, short stature, an enlarged liver (hepatomegaly), liver dysfunction, low muscle tone (hypotonia), low blood sugar (hypoglycemia) associated with fasting and strenuous exercise, and an accumulation of byproducts from fat breakdown (ketosis) associated with fasting. 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 PHKB 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 glycogen storage disease type IXb. 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 |
|---|---|---|---|---|
| Glycogen storage disease type IXb (AR) NM_000293.2 | PHKB | Pan-ethnic | ≤1 in 500 | Reduced |

## RESULT: CARRIER

# Wilson disease

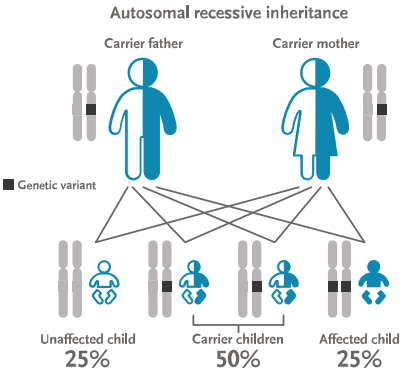
A single Pathogenic variant, c.2605G>A (p.Gly869Arg), was identified in ATP7B.

### What is Wilson disease?

Wilson disease is a condition that causes an accumulation of copper in the organs, particularly in the liver, brain, and eyes. The age of onset and severity of symptoms in Wilson disease are variable. Initial symptoms typically develop during the teenage years but may occur at any time between childhood and middle age. Symptoms include liver dysfunction, which ranges in severity from a yellowing of the skin and whites of the eyes (jaundice) to liver damage due to the formation of scar tissue (cirrhosis) and liver failure. In a majority of affected individuals, copper deposits in the eye form a brownish-yellow ring around the iris, known as a Kayser-Fleischer ring. Other symptoms may include kidney disease, heart disease, weakening of the bones, difficulty walking or speaking, the premature breakdown of red blood cells, causing them to be destroyed faster than the body can replace them (hemolytic anemia), and psychiatric concerns such as personality changes, anxiety and depression. Lifelong treatment, including medication that causes excretion of copper from the body (chelation therapy), may prevent or reduce symptoms of Wilson disease.

## 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 ATP7B 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 Wilson disease. 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 |
|---|---|---|---|---|
| Wilson disease (AR)<br>NM_000053.3 | ATP7B | Pan-ethnic | 1 in 90 | 1 in 4450 |

### Increased carrier risk: Spinal muscular atrophy

- This individual has two copies of SMN1 and carries the c.*3+80T>G variant, also known as g.27134T>G. The presence of this variant increases the likelihood that this individual is a carrier of spinal muscular atrophy (SMA) with two copies of SMN1 on the same chromosome and a deletion of SMN1 on the opposite chromosome. This test cannot determine whether this individual's two copies of SMN1 are on the same chromosome or opposite chromosomes.

  The risk to be an SMA carrier with this type of result varies by ethnicity. See the table below for additional information.

- This test cannot determine whether this individual has one copy of SMN1 on each chromosome or if both copies are on the same chromosome. Individuals with two copies of SMN1 on the same chromosome and a deletion (zero copies of SMN1) on the opposite chromosome (2+0) are sometimes referred to as 'silent' carriers of SMA.

  Consider parental testing, which may help clarify carrier status.

  Testing of the reproductive partner may be considered.

  Spinal muscular atrophy (SMA) is a condition that affects the neuromuscular system. SMA is characterized by loss of the nerves within the spinal cord that control voluntary muscle movement (motor neurons), resulting in progressive muscle weakness and wasting (atrophy). This leads to difficulty with activities such as crawling, sitting up, and walking. Other features of SMA may include involuntary muscle twitching (fasciculations), tremor, swallowing problems leading to feeding difficulties and poor weight gain, sleeping difficulties, respiratory problems due to weakness of the muscles used for breathing, pneumonia, side-to-side curvature of the spine (scoliosis), joint deformities that restrict movement (contractures), and congenital heart disease. Five clinical SMA subtypes have been described based on age of onset and milestones achieved: SMA type 0 (with prenatal onset), severe infantile acute SMA type I (also referred to as Werdnig-Hoffman disease), infantile chronic SMA type II, juvenile SMA type III (also referred to as Kugelberg-Welander disease), and adult-onset SMA type IV. Prognosis depends on the severity of symptoms, and life expectancy is often reduced in the severe subtypes of the condition. However, age of onset, symptoms, severity, and life expectancy are highly variable. Targeted therapy treatments may delay onset of symptoms and extend life expectancy. Follow-up depends on each affected individual's specific situation, and discussion with a healthcare provider should be considered.

  Spinal muscular atrophy is inherited in an autosomal recessive fashion. In autosomal recessive inheritance, an individual must have disease-causing genetic changes in each copy of the SMN1 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.

| ETHNICITY | CARRIER FREQUENCY | RESIDUAL RISK WITH C.*3+80T>G PRESENT |
|---|---|---|
| Ashkenazi Jewish | 1 in 62 | 1 in 7 |
| Asian | 1 in 50 | 1 in 32 |
| African-American | 1 in 59 | 1 in 35 |
| Caucasian | 1 in 45 | 1 in 34 |
| Hispanic | 1 in 48 | 1 in 42 |
| Pan-ethnic | 1 in 49 | 1 in 33 |

## Results to note

### HBA1/HBA2

- Additional copy(ies) detected (HBA1 copy number=3). Result not associated with alpha-thalassemia.
- Additional copy(ies) of the alpha-globin gene (HBA1/HBA2) do not impact alpha-thalassemia risk, however, co-inheritance of this genetic change with beta-thalassemia may worsen the clinical and hematological features of the latter condition. There is also a possibility for hematological changes or clinical symptoms in beta-thalassemia carriers when this alpha-globin gene change is present. Carrier testing of the reproductive partner for beta-thalassemia (HBB) may be considered.

**Pseudodeficiency allele(s)**

- Benign changes, c.550C>T (p.Arg184Cys) and c.1685T>C (p.Ile562Thr), known to be pseudodeficiency alleles, identified in the GALC 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

ATP7B, Exon 11, c.2605G>A (p.Gly869Arg), heterozygous, PATHOGENIC

- This sequence change replaces glycine, which is neutral and non-polar, with arginine, which is basic and polar, at codon 869 of the ATP7B protein (p.Gly869Arg).
- This variant is present in population databases (rs191312027, gnomAD 0.1%), and has an allele count higher than expected for a pathogenic variant.
- This missense change has been observed in individual(s) with Wilson disease (PMID: 11093740, 15952988, 23843956, 27398169, 30702195).
- ClinVar contains an entry for this variant (Variation ID: 157939).
- Advanced modeling of protein sequence and biophysical properties (such as structural, functional, and spatial information, amino acid conservation, physicochemical variation, residue mobility, and thermodynamic stability) performed at Invitae indicates that this missense variant is expected to disrupt ATP7B protein function with a positive predictive value of 80%.
- For these reasons, this variant has been classified as Pathogenic.

GJB2, Exon 2, c.109G>A (p.Val37Ile), heterozygous, Pathogenic (low penetrance)

- This sequence change replaces valine, which is neutral and non-polar, with isoleucine, which is neutral and non-polar, at codon 37 of the GJB2 protein (p.Val37Ile).
- This variant is present in population databases (rs72474224, gnomAD 8%), and has an allele count higher than expected for a pathogenic variant.
- This variant has been reported in the literature in a large meta-analysis involving several thousand cases and controls (PMID: 28489599). This variant has been reported frequently in individuals affected with mild to moderate deafness particularly among populations in eastern Asia (PMID: 23637863, 26885124, 26061099, 17036313, 16952406, 21488715). It has been shown to segregate with autosomal recessive deafness in families (PMID: 28489599, 24945352, 26088551). Although this variant is more common in the population than expected for a pathogenic variant, the penetrance of this variant is estimated to be less than 20% of other disease-causing variants in GJB2 (PMID: 17935238, 24654934).
- ClinVar contains an entry for this variant (Variation ID: 17023).
- Advanced modeling of protein sequence and biophysical properties (such as structural, functional, and spatial information, amino acid conservation, physicochemical variation, residue mobility, and thermodynamic stability) has been performed at Invitae for this missense variant, however the output from this modeling did not meet the statistical confidence thresholds required to predict the impact of this variant on GJB2 protein function.
- Experimental studies have shown that this missense change disrupts the formation of homotypic junctional channels in vitro (PMID: 12505163). Furthermore in vivo knock-in and knock-out mouse models recapitulate the deafness phenotype observed in humans (PMID: 27623246).
- In summary, this variant is reported to cause sensorineural deafness. However, as this variant is associated with a lower penetrance than other pathogenic alleles in the GJB2 gene, it has been classified as Pathogenic (low penetrance).

PHKB, Exon 21, c.2014C>T (p.Arg672*), heterozygous, PATHOGENIC

- This sequence change creates a premature translational stop signal (p.Arg672*) in the PHKB gene. It is expected to result in an absent or disrupted protein product. Loss-of-function variants in PHKB are known to be pathogenic (PMID: 9215682, 9326319).
- This variant is present in population databases (no rsID available, gnomAD 0.02%).
- This variant has not been reported in the literature in individuals affected with PHKB-related conditions.
- ClinVar contains an entry for this variant (Variation ID: 523816).
- For these reasons, this variant has been classified as Pathogenic.

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

| 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 |

| 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 |
| IKBKB | 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 |

| 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_001031835.2 |
| 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 |
| SMARCAL1 | 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 |

| 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 ≥50x 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 table. 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. Variants are reported according to the Human Genome Variation Society (HGVS) guidelines. Confirmation of the presence and location of reportable variants is performed as needed based on stringent criteria, using one of several validated orthogonal approaches (PubMed ID 30610921). Sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778). Confirmatory sequencing is performed by Invitae Corporation (1400 16th Street, San Francisco, CA 94103, #05D2040778).

  The following additional 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 -α3.7 subtypes, and all -α3.7 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, cytosine-guanine-guanine (CGG) triplet repeats in the 5' untranslated region (5' UTR) of the FMR1 gene are detected by triplet repeat-primed PCR (RP-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.

- 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. Interpretations are made on the assumption that any clinical information provided, including specimen identity, is accurate.
- ANO10: Sequencing analysis for exons 8 includes only cds +/- 0 bp. ATP8B1: Sequencing analysis for exons 19 includes only cds +/- 10 bp. AIPL1: Sequencing analysis for exons 2 includes only cds +/- 10 bp. GHR: Deletion/duplication and sequencing analysis is not offered for exon 3. TBCE: Sequencing analysis for exons 2 includes only cds +/- 10 bp. 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. TYR: Deletion/duplication and sequencing analysis is not offered for exon 5. PTPRC: Sequencing analysis is not offered for exons 3, 15. ABCC2: Deletion/duplication analysis is not offered for exons 24-25. 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. TG: Deletion/duplication analysis is not offered for exon 18. Sequencing analysis for exons 44 includes only cds +/- 0 bp. 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. FANCL: Sequencing analysis for exons 4, 10 includes only cds +/- 10 bp. ATM: Sequencing analysis for exons 6, 24, 43 includes only cds +/- 10 bp. CFTR: Sequencing analysis for exons 7 includes only cds +/- 10 bp. EYS: Sequencing analysis for exons 30 includes only cds +/- 0 bp. FAH: Deletion/duplication analysis is not offered for exon 14. FH: Sequencing analysis for exons 9 includes only cds +/- 10 bp. GALC: Deletion/duplication analysis is not offered for exon 6. 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 (p.Arg535His) variants only. Rarely, sensitivity to detect these variants may be reduced. When sensitivity is reduced, zygosity may be reported as "unknown". GNE: Sequencing analysis for exons 8 includes only cds +/- 10 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. HBA2: Sequencing analysis is not offered for exons 1-2. 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. OAT: Deletion/duplication analysis is not offered for exon 2. PEX1: Sequencing analysis for exons 16 includes only cds +/- 0 bp. PKHD1: Deletion/duplication analysis is not offered for exon 13. 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. TSFM: Sequencing analysis is not offered for exon 5. USH1C: Deletion/duplication analysis is not offered for exons 5-6. VPS13A: Deletion/duplication analysis is not offered for exons 2-3, 27-28. VPS53: Sequencing analysis for exons 14 includes only cds +/- 5 bp. AMN: Deletion/duplication analysis is not offered for exon 1. GALE: Sequencing analysis for exons 10 includes only cds +/- 5 bp. DDX11: NM_030653.3:c.1763-1G>C variant only. BBS9: Deletion/duplication analysis is not offered for exon 4. COL11A2: Deletion/duplication analysis is not offered for exon 36. WRN: Deletion/duplication analysis is not offered for exons 10-11. Sequencing analysis for exons 8, 10-11 includes only cds +/- 10 bp.

## This report has been reviewed and approved by:

Fatimah Nahhas-Alwan, PhD, FACMG
Clinical Molecular Geneticist

fn_017b_pr

QuestQuantum

# 7359,DONOR ⚠

DOB: [redacted]
Sex: M
Phone:
Patient ID: 7359[redacted]

Age: [redacted]
Fasting:

Specimen: [redacted]
Requisition: [redacted]
Lab Reference ID: [redacted]
Report Status: FINAL / SEE REPORT

Collected: 03/01/2024 00:00
Received: 03/02/2024 13:17
Reported: 03/07/2024 19:41

Client #: [redacted]

## ⚠ CBC (includes Differential and Platelets) FINAL

Lab: AMD

| Analyte | Value | | |
|---|---|---|---|
| White Blood Cell Count | 7.0 | Reference Range: 3.8-10.8 Thous/uL | FINAL |
| Red Blood Cell Count | 4.56 | Reference Range: 4.20-5.80 Mill/uL | FINAL |
| HEMOGLOBIN | 13.7 | Reference Range: 13.2-17.1 g/dL | FINAL |
| Hematocrit | 43.6 | Reference Range: 38.5-50.0 % | FINAL |
| MCV | 95.6 | Reference Range: 80.0-100.0 fL | FINAL |
| MCH | 30.0 | Reference Range: 27.0-33.0 pg | FINAL |
| ⚠ MCHC | 31.4 L | Reference Range: 32.0-36.0 g/dL | FINAL |
| RDW | 13.3 | Reference Range: 11.0-15.0 % | FINAL |
| PLATELET COUNT | 293 | Reference Range: 140-400 Thous/uL | FINAL |
| MPV | 11.5 | Reference Range: 7.5-12.5 fl | FINAL |
| Absolute Neutrophils | 4536 | Reference Range: 1500-7800 cells/uL | FINAL |
| Absolute Lymphocytes | 1680 | Reference Range: 850-3900 cells/uL | FINAL |
| Absolute Monocytes | 539 | Reference Range: 200-950 cells/uL | FINAL |
| Absolute Eosinophils | 168 | Reference Range: 15-500 cells/uL | FINAL |
| Absolute Basophils | 77 | Reference Range: 0-200 cells/uL | FINAL |
| Neutrophils | 64.8 | % | FINAL |
| Lymphocytes | 24.0 | % | FINAL |
| Monocytes | 7.70 | % | FINAL |
| Eosinophils | 2.4 | % | FINAL |
| Basophils | 1.10 | % | FINAL |
| Nucleated RBC | 0.00 | Reference Range: 0 /100 WBC | FINAL |

## Hemoglobinopathy Evaluation FINAL

Lab: AMD

| Analyte | Value | | |
|---|---|---|---|
| Hemoglobinopathy Evaluation | | | FINAL |
| Red Blood Cell Count | 4.56 | Reference Range: 4.20-5.80 Mill/uL | FINAL |
| HEMOGLOBIN | 13.7 | Reference Range: 13.2-17.1 g/dL | FINAL |
| Hematocrit | | | FINAL |
| Hematocrit | 43.6 | Reference Range: 38.5-50.0 % | FINAL |
| MCV | 95.6 | Reference Range: 80.0-100.0 fL | FINAL |
| MCH | 30.0 | Reference Range: 27.0-33.0 pg | FINAL |

| | | | |
|---|---|---|---|
| **RDW** | **13.3** | Reference Range: 11.0-15.0 % | FINAL |
| **Hemoglobinopathy Evaluation** | | | FINAL |
| **Hemoglobin A** | **97.5** | Reference Range: >96.0 % | FINAL |
| **Hemoglobin F** | **0.0** | Reference Range: <2.0 % | FINAL |
| **Hemoglobin A2 (Quant)** | **2.5** | Reference Range: 2.2-3.2 % | FINAL |

**Interpretation** FINAL

NORMAL PATTERN

There is a normal pattern of hemoglobins and
normal levels of Hb A2 and Hb F are present.
No variant hemoglobins are observed. This is
consistent with A/A phenotype.
If iron deficiency coexists with a mild/silent beta
thalassemia trait Hb A2 may be in the normal range.
Rare variant hemoglobins have no separation from
hemoglobin A by capillary zone electrophoresis (CZE) or
high-performance liquid chromatography (HPLC).
If clinically indicated, Thalassemia and
Hemoglobinopathy Comprehensive (TC 17365) should be
considered.

## Chromosome Analysis, Blood FINAL

Lab: AMD

| Analyte | Value |
|---|---|
| **Chromosome Analysis, Blood** | FINAL |

Order ID: [redacted]

Specimen Type: Blood

Clinical Indication: Donor screening, 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: MetaSystems/Ikaros)
Cells Counted: 20
Band Level: 550
Cells Analyzed: 5
Cells Karyotyped: 5

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

A portion of the testing was performed at AMD11.

Steven A. Schonberg, Ph.D., FACMG, Technical Director, Cytogenetics and Genomics, 703-802-7156

Electronic Signature: 3/7/2024 6:57 PM

For additional information, please refer to
http://education.questdiagnostics.com/faq/chromsblood
(This link is being provided for informational/
educational purposes only).

**Performing Sites**

AMD Quest Diagnostics Nichols Institute, 14225 Newbrook Drive, Chantilly, VA 20151 Laboratory Director: Patrick W Mason, MD PhD

**Key**

Priority Out of Range | Out of Range | (PEND) Pending Result | (PRE) Preliminary Result | (FINAL) Final Result | (RE) Reissued Result