Acknowledgement of Positive Carrier Screening Results: Donor 6266

I, the undersigned recipient, understand that this donor has tested **POSITIVE** as a carrier for the following condition(s). More information regarding these conditions can be found in his Expanded Carrier Screening results.

- **BBS1-related conditions**
- **Glycogen storage disease type II (GAA)**

I intend to use sperm samples from this donor for insemination or other assisted conception procedure(s).

I acknowledge that The Sperm Bank of California (TSBC) has made the donor's genetic testing results available to me and my medical providers, and that I have reviewed these results. I understand that TSBC **strongly recommends** that I review these genetic testing results with a Genetic Counselor and my medical providers. I understand that TSBC can refer me to genetic counseling services if desired.

I understand that recipient testing is strongly recommended when a donor has positive carrier screening results and that such testing can reduce but not eliminate risks.

I acknowledge that I personally assume all risks associated with use of semen samples provided by a donor who has tested **POSITIVE as a carrier for BBS1-related conditions and Glycogen storage disease type II (GAA).**

On behalf of myself and my spouse, heirs, representatives, I hereby release and forever hold harmless TSBC and its current and former officers, directors, employees, attorneys, insurers, consultants, agents, and representatives (collectively "Releases") from any liability or responsibility whatsoever for any and all outcomes, and hereby release and forever discharge Releases from any and all actions, causes of action, demands, damages, losses, liabilities, suits, expenses, including attorneys' fees and costs, of whatever character, in law or in equity, whether currently known, suspected, unknown or unsuspected, matured or unmatured, arising out of my use of sperm donated by a donor who has tested **POSITIVE as a carrier for BBS1-related conditions and Glycogen storage disease type II (GAA). This release involves the waiver of all rights and benefits that I may have under California Civil Code section 1542, which states: "A general release does not extend to claims that the creditor or releasing party does not know or suspect to exist in his or her favor at the time of executing the release and that, if known by him or her, would have materially affected his or her settlement with the debtor or released party."**

Please select one of the following:

- ☐ I have been tested for the above named condition(s) and/or I plan to be tested prior to using the samples.

- ☐ I understand that TSBC **strongly recommends** that I discuss these results with a Genetic Counselor and my medical providers and consider testing for the above named condition(s). At this time I have **declined** testing and/or **do not anticipate being tested**.

I understand that if I transfer my vials (or embryos if applicable) to any other person, including my spouse, that TSBC requires that person (1) register with TSBC and (2) complete an **Acknowledgement of Positive Carrier Screening Results**.

I understand that any and all questions as to the legal interpretation, validity or any other aspect of this agreement shall be determined by the laws of the State of California, regardless of the location or residence of any of the parties.

_____   _____   _____
Recipient's signature   Recipient's printed name   Date

GENETIC TESTING: POSITIVE CARRIER STATUS

This donor tested **POSITIVE** as a carrier for one or more autosomal recessive conditions as described on the prior page and in the attached genetic testing results.

What does it mean to be a carrier?

All people carry genetic mutations in their DNA. Genetic testing can help to identify some, but not all, of these mutations. While this donor carries a mutation for one or more recessively inherited condition(s), **offspring from this donor are not expected to be at risk of developing these condition(s) unless the recipient (or egg provider if different from the recipient) also carries a genetic mutation for the same condition(s).** For this reason, we strongly encourage you to discuss carrier screening for yourself (or your egg provider) with your physician and a genetic counselor. Genetic testing can reduce but not eliminate risks.

What are my next steps?

1. **Download the genetic test results and review with your medical providers**
   We **strongly recommend** that you discuss this donor's genetic test results with your physician **PRIOR TO SCHEDULING A SHIPMENT OR PICK-UP**, to confirm the donor is suitable for your use. Vials retrieved from the building cannot be exchanged or refunded. The donor's genetic test results are available for free download on the donor's page at https://www.thespermbankofca.org/donor-catalog.

2. **We recommend scheduling a genetic counseling session.**
   A genetic counselor can explain the results in detail including the inheritance pattern, potential risks to your children, and the available testing options that you may want to consider for yourself (or your egg provider). Phone or in person consultations are available for a fee with TSBC's Genetic Counselors at San Francisco Genetic Counseling (https://www.sfgenetics.org/) or you can locate a genetic counselor at www.findageneticcounselor.com.

3. **Complete and return the Acknowledgement of Positive Carrier Screening Results**
   TSBC requires that all recipients selecting this donor complete this acknowledgement form **PRIOR TO SCHEDULING A SHIPMENT OR PICK-UP**. Completing this form documents that you have been informed about this donor's genetic test results and that you are aware of TSBC's recommendation to discuss the genetic test results with your medical providers as noted above.

Reproductive Technologies, Inc.

THE SPERM BANK OF CALIFORNIA

EXPANDED CARRIER SCREENING RESULTS DONOR 6266

Expanded carrier screening for 525 autosomal recessive conditions was completed by Invitae and reported on 2/07/2024.

The results were **POSITIVE** for **BBS1-related conditions and Glycogen storage disease type II (GAA)** . Donor 6266 is a carrier for these conditions.
It is strongly recommended that recipients who use this donor's sperm undergo carrier screening for these specific conditions.

Testing was negative for the remainder of genes screened.

Disease	Result	Residual risk to be a carrier (based on European ancestry)
BBS1-related conditions	POSITIVE	n/a
Glycogen storage disease type II (GAA)	POSITIVE	n/a
Cystic Fibrosis	Negative	1 in 4,400
Spinal Muscular Atrophy	Negative: 2 copies exon 7 c.*3+80T>G variant not detected	1 in 880
HBB Hemoglobinopathies & Thalassemia	Negative	1 in 4,800
Alpha Thalassemia	Negative	Reduced

Genetic screening tests can significantly reduce, but never completely eliminate, the chance that a person is a carrier for a particular disorder.

Please refer to the donor's Invitae expanded carrier test report for more information on the testing completed and the donor's results.

Please also see the Health Problems List for a summary of the information that this donor has provided to us regarding personal and family medical history.

Sincerely,
Janine Mash
LCGC Certified Genetic Counselor
San Francisco Genetic Counseling

INVITAE

Patient name:	6266 DONOR	**Sample type:**	Saliva	**Report date:**	07-FEB-2024
DOB:	**Sex**	**Sample collection date:**	26-JAN-2024	**Invitae #:**	RQ6130600
assigned at birth:	Male	**Sample accession date:**	31-JAN-2024	**Clinical team:**	Janine Gessner Mash
Gender:					Lorraine Bonner, MD
Patient ID (MRN):					

Reason for testing

Gamete donor

Test performed

Invitae Comprehensive Carrier Screen without X-linked Disorders

- ■ Primary Panel (CF, SMA)
- ■ Add-on Comprehensive Carrier Screen without X-linked Disorders genes

⊕ RESULT: POSITIVE

This carrier test evaluated 525 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: BBS1-related conditions	BBS1	c.871C>T (p.Gln291*)	Autosomal recessive	Yes
Carrier: Glycogen storage disease type II (Pompe disease)	GAA	c.2238G>C (p.Trp746Cys)	Autosomal recessive	Yes

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

BBS1-related conditions

A single Pathogenic variant, c.871C>T (p.Gln291*), was identified in BBS1.

What are BBS1-related conditions?

BBS1-related conditions include Bardet-Biedl syndrome (BBS) and nonsyndromic retinitis pigmentosa (RP). BBS is part of a spectrum of conditions 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. RP is a group of related conditions that affects the retina, which is the light-sensitive tissue that lines the back of the eye. BBS and RP can be caused by changes in many different genes.

Symptoms of BBS generally include rod-cone dystrophy, an eye condition characterized by degeneration of the rods and cones (photoreceptors) which are the cells in the retina that respond to light, leading to progressive vision loss, as well as potentially life-threatening kidney problems, intellectual disability, genital abnormalities, and infertility. Affected individuals are commonly obese and have extra fingers and toes (polydactyly). They may also have a mirror-image reversal of their internal organs (situs inversus totalis), in which, for example, the heart is on the right side of the body instead of on the left, or the organs in their chest and abdomen may not be arranged as expected (heterotaxy). The atypical position of the organs may lead to a variety of health complications. Symptoms of BBS can vary widely, even within the same family. Some affected individuals may not have obvious symptoms (reduced penetrance).

RP is characterized by progressive degeneration of the retina. The first symptom is often difficulty seeing in low light settings (night blindness), which usually occurs during childhood or adolescence. Vision loss continues over years or decades and typically progresses to a loss of side (peripheral) vision, causing tunnel vision. Ultimately, central vision loss occurs. Many individuals with RP are legally blind by adulthood, though the severity of symptoms and age of onset varies by individual. Intelligence and life expectancy are not typically affected.

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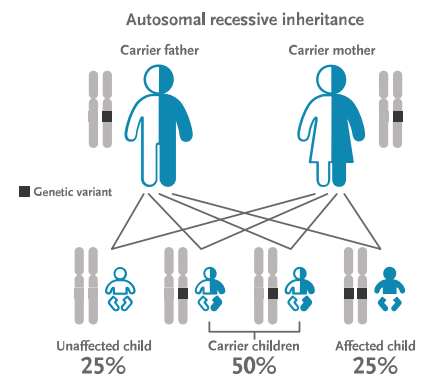
Next steps

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 BBS1 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 BBS1-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.

Autosomal recessive inheritance

Carrier father   Carrier mother

■ Genetic variant

Unaffected child **25%**   Carrier children **50%**   Affected child **25%**

DISORDER (INHERITANCE)	GENE	ETHNICITY	CARRIER FREQUENCY BEFORE SCREENING	CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT
BBS1-related conditions (AR) NM_024649.4	BBS1	Pan-ethnic	1 in 330	1 in 32900

◐ **RESULT: CARRIER**

Glycogen storage disease type II (Pompe disease)

A single Pathogenic variant, c.2238G>C (p.Trp746Cys), was identified in GAA.

What is glycogen storage disease type II (Pompe disease)?

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. The symptoms of glycogen storage disease type II (GSD II), also called Pompe disease, vary in age of onset and severity. Classical Pompe disease typically presents in infancy and is characterized by low muscle tone (hypotonia), poor growth (failure to thrive), muscle weakness (myopathy), an enlarged heart (cardiomegaly) and thickened heart muscle (hypertrophic cardiomyopathy). The condition is often fatal in infancy or early childhood due to heart or breathing problems. Non-classical forms of Pompe disease can present in infancy, childhood, adolescence, or adulthood, often with milder symptoms and slower disease progression. Symptoms may include weakness in the arm and leg muscles that are closest to the body (proximal myopathy) and breathing difficulties, with little to no heart muscle involvement. Enzyme replacement therapy is available and early initiation may delay the onset of the symptoms and reduce their severity. Follow-up depends on each affected individual's specific situation, and discussion with a healthcare provider should be considered.
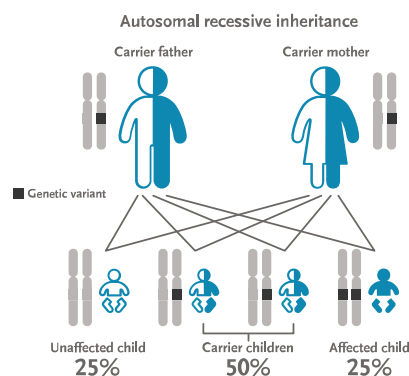
Next steps

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 GAA 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 II (Pompe 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.

Autosomal recessive inheritance

Carrier father — Carrier mother

■ Genetic variant

Unaffected child 25% — Carrier children 50% — Affected child 25%

DISORDER (INHERITANCE)	GENE	ETHNICITY	CARRIER FREQUENCY BEFORE SCREENING	CARRIER RESIDUAL RISK AFTER NEGATIVE RESULT
Glycogen storage disease type II (Pompe disease) (AR) NM_000152.3	GAA	Pan-ethnic	1 in 100	1 in 9900

Results to note

ABCA4

- c.5603A>T (p.Asn1868Ile) was identified in the ABCA4 gene.
- This benign variant is not known to cause disease and does not impact this individual's risk to be a carrier for ABCA4-related conditions. Carrier testing for the reproductive partner is not indicated based on this result. See Variant details for more information.

SMN1

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

Pseudodeficiency allele(s)

- Benign change, c.2065G>A (p.Glu689Lys), known to be a pseudodeficiency allele, identified in the GAA gene. Pseudodeficiency alleles are not known to be associated with disease, including glycogen storage disease type II (Pompe disease).
- Benign changes, c.742G>A (p.Asp248Asn) 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

ABCA4, Exon 40, c.5603A>T (p.Asn1868Ile), heterozygous, Benign (reportable variant)

- This sequence change replaces asparagine, which is neutral and polar, with isoleucine, which is neutral and non-polar, at codon 1868 of the ABCA4 protein (p.Asn1868Ile).
- This variant is present in population databases (rs1801466, gnomAD 7%), including several hundred presumably unaffected homozygous individuals.
- This missense change has been observed in individual(s) with late onset Stargardt disease with foveal sparing. However, the vast majority (estimated 95%) of homozygous and compound heterozygous individuals remain unaffected with penetrance ranging from 0.24% to 9.54% across published studies. This variant may modify disease severity and/or age of onset when it is present in combination with additional known pathogenic variants (e.g., when this variant is on the same chromosome as one or more deleterious variants, such as c.2588G>C, c.5461-10T>C, c.4496G>A, and/or c.2564G>A, and also on the opposite chromosome with a pathogenic variant). In other cases, disease progression is not impacted when this variant is one component of other complex alleles, such as with c.769-784C>T (PMID: 11328725, 28446513, 29971439, 30204727, 30480704, 30670881, 31614660, 31618761, 31884623, 32037395, 32307445, 32815999, 34440414, 34874912).
- ClinVar contains an entry for this variant (Variation ID: 99390).
- 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 ABCA4 protein function with a positive predictive value of 95%.
- Experimental studies are conflicting or provide insufficient evidence to determine the effect of this variant on ABCA4 function (PMID: 11017087, 32845050, 33375396).
- For these reasons, this variant has been classified as a Benign reportable variant.

BBS1, Exon 10, c.871C>T (p.Gln291*), heterozygous, PATHOGENIC

- This sequence change creates a premature translational stop signal (p.Gln291*) in the BBS1 gene. It is expected to result in an absent or disrupted protein product. Loss-of-function variants in BBS1 are known to be pathogenic (PMID: 12118255, 21520335, 27032803).
- This variant is not present in population databases (gnomAD no frequency).
- This premature translational stop signal has been observed in individual(s) with Bardet-Biedl syndrome (BBS) (PMID: 12677556, 25170860).
- ClinVar contains an entry for this variant (Variation ID: 371274).
- Algorithms developed to predict the effect of sequence changes on RNA splicing suggest that this variant may disrupt the consensus splice site.
- For these reasons, this variant has been classified as Pathogenic.

GAA, Exon 16, c.2238G>C (p.Trp746Cys), heterozygous, PATHOGENIC

- This sequence change replaces tryptophan, which is neutral and slightly polar, with cysteine, which is neutral and slightly polar, at codon 746 of the GAA protein (p.Trp746Cys).
- This variant is present in population databases (rs1800312, gnomAD 0.06%).
- This missense change has been observed in individual(s) with Pompe disease (PMID: 18458862, 21232767, 21757382, 23430493, 25093132, 25526786, 27099502). In at least one individual the data is consistent with being in trans (on the opposite chromosome) from a pathogenic variant.
- ClinVar contains an entry for this variant (Variation ID: 265160).
- 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 GAA protein function with a positive predictive value of 95%.
- Experimental studies have shown that this missense change affects GAA function (PMID: 7981676, 9535769, 21757382).
- 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	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	CHRNG	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

GENE	TRANSCRIPT	GENE	TRANSCRIPT	GENE	TRANSCRIPT
CRB1	NM_201253.2	EIF2B1	NM_001414.3	FOXRED1	NM_017547.3
CRTAP	NM_006371.4	EIF2B2	NM_014239.3	FRAS1	NM_025074.6
CTNS	NM_004937.2	EIF2B3	NM_020365.4	FREM2	NM_207361.5
CTSA	NM_000308.3	EIF2B4	NM_015636.3	FUCA1	NM_000147.4
CTSC	NM_001814.5	EIF2B5	NM_003907.2	G6PC	NM_000151.3
CTSD	NM_001909.4	ELP1	NM_003640.3	G6PC3	NM_138387.3
CTSK	NM_000396.3	EPG5	NM_020964.2	GAA	NM_000152.3
CYBA	NM_000101.3	ERCC2	NM_000400.3	GALC*	NM_000153.3
CYP11A1	NM_000781.2	ERCC6	NM_000124.3	GALE*	NM_000403.3
CYP11B1	NM_000497.3	ERCC8	NM_000082.3	GALK1	NM_000154.1
CYP11B2	NM_000498.3	ESCO2	NM_001017420.2	GALNS	NM_000512.4
CYP17A1	NM_000102.3	ETFA	NM_000126.3	GALNT3	NM_004482.3
CYP19A1	NM_031226.2	ETFB	NM_001985.2	GALT	NM_000155.3
CYP1B1	NM_000104.3	ETFDH	NM_004453.3	GAMT	NM_000156.5
CYP21A2*	NM_000500.7	ETHE1	NM_014297.3	GATM	NM_001482.2
CYP27A1	NM_000784.3	EVC	NM_153717.2	GBA*	NM_001005741.2
CYP27B1	NM_000785.3	EVC2	NM_147127.4	GBE1	NM_000158.3
CYP7B1	NM_004820.3	EXOSC3	NM_016042.3	GCDH	NM_000159.3
DBT	NM_001918.3	EYS*	NM_001142800.1	GCH1	NM_000161.2
DCAF17	NM_025000.3	F11	NM_000128.3	GDF5	NM_000557.4
DCLRE1C	NM_001033855.2	F2	NM_000506.3	GFM1	NM_024996.5
DDX11*	NM_030653.3	F5	NM_000130.4	GHR*	NM_000163.4
DFNB59	NM_001042702.3	FAH*	NM_000137.2	GJB2	NM_004004.5
DGAT1	NM_012079.5	FAM161A	NM_001201543.1	GLB1	NM_000404.2
DGUOK	NM_080916.2	FANCA	NM_000135.2	GLDC	NM_000170.2
DHCR7	NM_001360.2	FANCC	NM_000136.2	GLE1	NM_001003722.1
DHDDS	NM_024887.3	FANCD2*	NM_033084.3	GNE*	NM_001128227.2
DLD	NM_000108.4	FANCE	NM_021922.2	GNPAT	NM_014236.3
DLL3	NM_016941.3	FANCG	NM_004629.1	GNPTAB	NM_024312.4
DNAH11	NM_001277115.1	FANCI	NM_001113378.1	GNPTG	NM_032520.4
DNAH5	NM_001369.2	FANCL*	NM_018062.3	GNS	NM_002076.3
DNAI1	NM_012144.3	FBP1	NM_000507.3	GORAB	NM_152281.2
DNAI2	NM_023036.4	FBXO7	NM_012179.3	GP1BA*	NM_000173.6
DNMT3B	NM_006892.3	FH*	NM_000143.3	GP9	NM_000174.4
DOK7	NM_173660.4	FKBP10	NM_021939.3	GRHPR	NM_012203.1
DUOX2*	NM_014080.4	FKRP	NM_024301.4	GRIP1	NM_021150.3
DYNC2H1	NM_001080463.1	FKTN	NM_001079802.1	GSS	NM_000178.2
DYSF	NM_003494.3	FMO3	NM_006894.6	GUCY2D	NM_000180.3
EIF2AK3	NM_004836.6	FOXN1	NM_003593.2	GUSB	NM_000181.3

GENE	TRANSCRIPT	GENE	TRANSCRIPT	GENE	TRANSCRIPT
HADH	NM_005327.4	KCNJ1	NM_000220.4	MMAB	NM_052845.3
HADHA	NM_000182.4	KCNJ11	NM_000525.3	MMACHC	NM_015506.2
HADHB	NM_000183.2	LAMA2	NM_000426.3	MMADHC	NM_015702.2
HAMP	NM_021175.2	LAMA3	NM_000227.4	MOCS1	NM_001358530.2
HAX1	NM_006118.3	LAMB3	NM_000228.2	MOCS2A	NM_176806.3
HBA1*	NM_000558.4	LAMC2	NM_005562.2	MOCS2B	NM_004531.4
HBA2*	NM_000517.4	LARGE1	NM_004737.4	MPI	NM_002435.2
HBB	NM_000518.4	LCA5	NM_181714.3	MPL	NM_005373.2
HEXA	NM_000520.4	LDLR	NM_000527.4	MPV17	NM_002437.4
HEXB	NM_000521.3	LDLRAP1	NM_015627.2	MRE11	NM_005591.3
HFE	NM_000410.3	LHX3	NM_014564.4	MTHFR*	NM_005957.4
HGD	NM_000187.3	LIFR*	NM_002310.5	MTR	NM_000254.2
HGSNAT	NM_152419.2	LIG4	NM_002312.3	MTRR	NM_002454.2
HJV	NM_213653.3	LIPA	NM_000235.3	MTTP	NM_000253.3
HLCS	NM_000411.6	LMBRD1	NM_018368.3	MUSK	NM_005592.3
HMGCL	NM_000191.2	LOXHD1	NM_144612.6	MUT	NM_000255.3
HMOX1	NM_002133.2	LPL	NM_000237.2	MVK	NM_000431.3
HOGA1	NM_138413.3	LRAT	NM_004744.4	MYO15A	NM_016239.3
HPD	NM_002150.2	LRP2	NM_004525.2	MYO7A	NM_000260.3
HPS1	NM_000195.4	LRPPRC	NM_133259.3	NAGA	NM_000262.2
HPS3	NM_032383.4	LYST	NM_000081.3	NAGLU	NM_000263.3
HPS4	NM_022081.5	MAK	NM_001242957.2	NAGS	NM_153006.2
HPS5	NM_181507.1	MAN2B1	NM_000528.3	NBN	NM_002485.4
HPS6	NM_024747.5	MANBA	NM_005908.3	NCF2	NM_000433.3
HSD17B3	NM_000197.1	MCCC1	NM_020166.4	NDRG1	NM_006096.3
HSD17B4	NM_000414.3	MCCC2	NM_022132.4	NDUFAF2	NM_174889.4
HSD3B2	NM_000198.3	MCEE	NM_032601.3	NDUFAF5	NM_024120.4
HYAL1	NM_153281.1	MCOLN1	NM_020533.2	NDUFS4	NM_002495.3
HYLS1	NM_145014.2	MCPH1	NM_024596.4	NDUFS6	NM_004553.4
IDUA	NM_000203.4	MECR	NM_016011.3	NDUFS7	NM_024407.4
IGHMBP2	NM_002180.2	MED17	NM_004268.4	NDUFV1	NM_007103.3
IKBKB	NM_001556.2	MEFV	NM_000243.2	NEB*	NM_001271208.1
IL7R	NM_002185.3	MESP2	NM_001039958.1	NEU1	NM_000434.3
INVS	NM_014425.3	MFSD8	NM_152778.2	NGLY1	NM_018297.3
ITGA6	NM_000210.3	MKKS	NM_018848.3	NPC1	NM_000271.4
ITGB3	NM_000212.2	MKS1	NM_017777.3	NPC2	NM_006432.3
ITGB4	NM_001005731.2	MLC1*	NM_015166.3	NPHP1	NM_000272.3
IVD	NM_002225.3	MLYCD	NM_012213.2	NPHS1	NM_004646.3
JAK3	NM_000215.3	MMAA	NM_172250.2	NPHS2	NM_014625.3

GENE	TRANSCRIPT
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
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

GENE	TRANSCRIPT
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
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

GENE	TRANSCRIPT
SACS	NM_014363.5
SAMD9	NM_017654.3
SAMHD1	NM_015474.3
SCO2	NM_005138.2
SEC23B	NM_006363.4
SEPSECS	NM_016955.3
SERPINA1	NM_000295.4
SGCA	NM_000023.2
SGCB	NM_000232.4
SGCD	NM_000337.5
SGCG	NM_000231.2
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

GENE	TRANSCRIPT
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
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

GENE	TRANSCRIPT
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
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. GP1BA: c.104delA (p.Lys35Argfs*4), c.165_168delTGAG (p.Ser55Argfs*12), c.376A>G (p.Asn126Asp), c.434T>C (p.Leu145Pro), c.515C>T (p.Ala172Val), c.584_586delTCC (p.Leu195del), c.673T>A (p.Cys225Ser), c.1454dupT (p.Ser486Ilefs*12), c.1480delA (p.Thr494Profs*59), c.1601_1602delAT (p.Tyr534Cysfs*82), c.1620G>A (p.Trp540*) variants only. 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:

Matteo Vatta, Ph.D., FACMG
Clinical Molecular Geneticist

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