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POWERED BY Billion To One

PATIENT		SAMPLE		PROVIDER	
First Name	JANE	Sample Type	BLOOD	Name	NA
Last Name	DOE	Date Collected	5/1/2019	Address 1	NA
DOB	NA	Date Received	5/16/2019	Address 2	NA
Gender	FEMALE	Sample #	NA	City	NA
Ethnicity	NA	Case ID	NA	State, Zip	NA
Pregnant	NA	Date Reported	5/22/2019	Phone	NA
Gestational Age	NA			Fax	NA
Medical Record #	NA			Email	NA

UNITY™ Five Gene Carrier Screen

NEGATIVE

SUMMARY OF RESULTS

NEGATIVE

Carrier screening on DNA from the patient's blood was performed and concluded there are **NO reportable variants**.

Alpha-Thalassemia *HBA1/HBA2*	**Negative**
Beta-Thalassemia/Hemoglobinopathies *HBB*	**Negative**
Cystic Fibrosis *CFTR*	**Negative**
Spinal Muscular Atrophy *SMN1*	**Negative**
• SMN1 Copy Number	• **2 copies** (most common)
• SMA Region Informative SNP (rs143838139)	• **Not Present** (most common haplotype)

This result significantly reduces the probability of being a carrier; it does not eliminate the risk. See *Post-Test Carrier Frequencies* on page 4.

RECOMMENDED FOLLOW-UP

NO ADDITIONAL TESTING is recommended.

No additional testing for cystic fibrosis (*CFTR*), hemoglobinopathies (*HBB, HBA1* and *HBA2*), and spinal muscular atrophy (*SMN1*) is recommended based on the patient's UNITY™ carrier screening results.

The patient may contact BillionToOne at (650) 460-2551 to schedule an appointment for a complimentary telephone genetic consultation to review these results. A genetic counselor can also be found at www.nsgc.org.

The ACOG Committee on Genetics (co486 and co691) recommends cystic fibrosis, hemoglobinopathy, and spinal muscular atrophy carrier screening for all patients who are planning a pregnancy or seeking prenatal care. UNITY™ carrier screening evaluates for cystic fibrosis (CFTR), hemoglobinopathies (HBB, HBA1 and HBA2), and spinal muscular atrophy (SMN1). Reflex NIPT is performed to evaluate fetal risk when a pregnant patient is identified as a carrier.

Patient Name	**JANE** DOE	DOB	**1/1/1985**	Gestational Age	**NA**	Medical Records #	**NA**

INTERPRETATION

UNITY™ Five Gene Carrier Screen

Carrier screening on DNA from the patient's blood was performed and concluded there are no reportable variants.

Alpha-Thalassemia *HBA1* (NM_000558.5), *HBA2* (NM_000517.6)	**Negative**
Beta-Thalassemia/Hemoglobinopathies *HBB* (NM_000518.5)	**Negative**
Cystic Fibrosis *CFTR* (NM_000492.3)	**Negative**
Spinal Muscular Atrophy *SMN1* (NM_000344.3) • SMN1 Copy Number • SMA Region Informative SNP (rs143838139)	**Negative** • **2 copies** (most common) • **Not Present** (most common haplotype)

Carrier frequencies vary by ethnicity and assume no personal or family history of the condition. See *Pre- and Post-Test Carrier Frequencies* on page 4.

Comprehensive genetic counseling is recommended for a patient with a family history of a genetic disorder so that carrier risks can be accurately discussed, as well as potential reproductive risks and additional testing options that may be available.

Carrier screening does not evaluate for all genetic conditions. In addition, carrier screening is not able to identify all possible variants in the genes analyzed. As a result, a negative result significantly reduces the probability of being a carrier; it does not eliminate the risk.

METHODS AND LIMITATIONS

UNITY™ Five Gene Carrier Screen

DNA was extracted and purified from leukocyte enriched peripheral blood. The resulting DNA was subjected to two separate Laboratory Developed Procedures, digital Multiplex Ligation Probe Amplification (digitalMLPA) and a Custom Amplicon Panel PCR, that was sequenced by synthesis on an Illumina MiSeq. Results were aligned and examined on a custom bioinformatics pipeline and compared to the published human genome build GRCh37/hg19 reference sequence. Small nucleotide variants were confirmed using Sanger Sequencing and pathogenic and likely pathogenic variants were reported.

Test limitations: No test is perfect. While results of BillionToOne's Five Gene Carrier Screen test are highly accurate, a negative result significantly reduces but does not eliminate the chance of being a carrier. This test result assumes that the patient is not Ashkenazi Jewish, French Canadian or Cajun as these patients are at higher risk of diseases that we do not test in our panel.

Test sensitivity and mutation spectrum: The carrier screen panel is designed to detect the majority of pathogenic alleles for cystic fibrosis, sickle cell disease, alpha-thalassemia, beta-thalassemia, and spinal muscular atrophy. The test has sensitivity of >99% for cystic fibrosis, >99% for sickle cell disease and beta-thalassemia, >95% for alpha thalassemia and >90% for spinal muscular atrophy. All exons, exon-intron junctions and select intronic regions of *CFTR, HBB, HBA1* and *HBA2* are sequenced. Copy number analysis is performed on *SMN1, HBA1, HBA2, HBB* and *CFTR*. The carrier screen covers all 23 variants recommended by ACMG, all common *HBB* pathogenic variants including HbS, HbC, HbE, IVS1-1, and 41/42-TTCT, the *HBA2* Constant Spring variant and the *SMN1* silent carrier linked SNP g.27134T>G when two copies of *SMN1* are present. The alpha thalassemia carrier screen also reports single and double gene deletions including alpha3.7, alpha4.2, SEA, MED-I, SA, 20.5, BRIT, FIL or THAI.

This five gene carrier screen and NIPT was developed and its performance characteristics determined by the BillionToOne laboratory. It has not been cleared or approved by the U.S. Food and Drug Administration. The BillionToOne laboratory is regulated under CLIA. This test is used for clinical purposes. It should not be regarded as investigational or for research.

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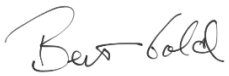

Bert Gold, PhD, FACMGG, CGMB
Laboratory Director
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UNITY™ CARRIER SCREEN: CARRIER FREQUENCIES

Disease	Gene	Ethnicity	Carrier Frequency *Before* Testing	Detection Rate	Carrier Risk *After* Negative Testing
Alpha-Thalassemia	*HBA1, HBA2*	African American	1 in 30	>95%	<1 in 600
		Asian	1 in 20	>95%	<1 in 400
		Northern European	1 in 500	>95%	<1 in 1000
		General Population	1 in 25	>95%	<1 in 500
Beta-Thalassemia, Hemoglobinopathies	*HBB*	African American	1 in 8	>99%	<1 in 800
		Ashkenazi Jewish	1 in 49	>99%	<1 in 4900
		Asian	1 in 54	>99%	<1 in 5400
		Northern European	1 in 373	>99%	<1 in 37300
		Hispanic	1 in 17	>99%	<1 in 1700
		Mediterranean	1 in 28	>99%	<1 in 2800
		General Population	1 in 49	>99%	<1 in 4900
Cystic Fibrosis	*CFTR*	African American	1 in 61	>99%	<1 in 6100
		Ashkenazi Jewish	1 in 24	>99%	<1 in 2400
		Asian	1 in 94	>99%	<1 in 9400
		Northern European	1 in 25	>99%	<1 in 2500
		Hispanic	1 in 58	>99%	<1 in 5800
		General Population	1 in 45	>99%	<1 in 4500
Spinal Muscular Atrophy	*SMN1*	African American	1 in 72	>90.3%	< in 375 (2 copies, SNP absent) <1 in 4200 (3+ copies)
		Ashkenazi Jewish	1 in 67	>92.8%	<1 in 900 (2 copies, SNP absent) <1 in 5400 (3+ copies)
		Asian	1 in 59	>93.6%	<1 in 900 (2 copies, SNP absent) <1 in 5600 (3+ copies)
		Northern European	1 in 47	>95%	<1 in 900 (2 copies, SNP absent) <1 in 5600 (3+ copies)
		Hispanic	1 in 68	>92.6%	<1 in 900 (2 copies, SNP absent) <1 in 5400 (3+ copies)
		General Population	1 in 54	>91.2%	<1 in 525 (2 copies, SNP absent) <1 in 5400 (3+ copies)