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POWERED BY Billion To One

PATIENT		SAMPLE		PROVIDER	
First Name	Jane	**Sample Type**	Blood	**Name**	Dr. Jane Smith
Last Name	Doe	**Date Collected**	05/01/2021	**Address 1**	1234 Street Name
DOB	10/20/1990	**Date Received**	05/02/2021	**Address 2**	Suite 120
Gender	Female	**Sample ID**	123-123-123	**City**	San Francisco
Ethnicity	Caucasian	**Requisition ID**	11223344	**State Zip**	CA, 94102
Gestational Age	12W	**Date Reported**	05/10/2021	**Phone**	555-555-5555
Medical Record #	12344321			**Fax**	555-555-5555

UNITY™ **Five Gene Carrier** Screen

NEGATIVE CARRIER

CONDITIONS SCREENED	CARRIER STATUS
Alpha-Thalassemia ***(HBA1, HBA2)***	**Negative**
Sickle Cell Disease / Beta-Thalassemia / Hemoglobinopathies ***(HBB)***	**Negative**
Cystic Fibrosis ***(CFTR)***	**Negative**
Spinal Muscular Atrophy ***(SMN1)***	**Negative**

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.

Interpretation *next page* ›

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	10/20/1990	Gestational Age	12W	Medical Record #	12341234

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**
Sickle Cell Disease/Beta-Thalassemia/Hemoglobinopathy *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 both before and after screening vary by ethnicity and assume no personal or family history of the condition. See Pre- and Post-Test Carrier Frequencies tables on the last page of the report.

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 a Custom Amplicon Panel PCR that utilized Spikein DNA technology to detect both small nucleotide variants and large copy number changes. The DNA was sequenced by synthesis on an Illumina NextSeq. Results were aligned and examined on a custom bioinformatics pipeline and compared to the published human genome build GRCh37/hg19 reference sequence. NGS performance was confirmed via 10x validation of small nucleotide variants (SNV) in each gene via Sanger sequencing. In addition, SNVs were confirmed using Sanger Sequencing for any variants with sequencing coverage less than 100x. Large copy number variants were confirmed using digital Multiplex Ligation Probe Amplification (digitalMLPA). Pathogenic and likely pathogenic variants were reported.

Test limitations: A negative result significantly reduces but does not eliminate the chance of being a carrier. Additional carrier screening may be indicated for individuals of Ashkenazi Jewish, French Canadian, or Cajun descent, as these patients are at higher risk of diseases that we do not test in our panel.

Test sensitivity and mutation spectrum: UNITY™ is designed to maximize detection of pathogenic alleles for cystic fibrosis, spinal muscular atrophy, and hemoglobinopathies (alpha-thalassemia, beta-thalassemia, and sickle cell disease). We sequence all exons, exon-intron junctions and select intronic regions of *CFTR*, *HBA1*, *HBA2*, and *HBB*. Copy number analysis is performed on *CFTR*, *SMN1*, *HBA1*, *HBA2*, and *HBB*. This includes all *CFTR* variants recommended by the American College of Medical Genetics (ACMG), all common *HBB* 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 (rs143838139) 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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UNITY™ CARRIER SCREEN: CARRIER FREQUENCIES

Disease	Gene	Ethnicity	Carrier Frequency *Before* Testing	Detection Rate	Carrier Risk *After* Negative Testing
Alpha-Thalassemia Alpha thalassemia silent carrier includes the single allele deletion and trans double allele deletion. Double deletion includes cis double deletion only. CS means Constant Spring mutation	*HBA1, HBA2*	African American	aa/a-: 1 in 3 aa/--: 1 in 5,000 aa/aa^{CS}: 1 in 10,000	>95%	aa/a-: <1 in 60 aa/--: <1 in 100,000 aa/aa^{CS}: <1 in 200,000
		Asian	aa/a-: 1 in 16 aa/--: 1 in 93 aa/aa^{CS}: 1 in 93	>95%	aa/a-: <1 in 320 aa/--: <1 in 1860 aa/aa^{CS}: <1 in 1860
		Northern European	aa/a-: 1 in 44 aa/--: 1 in 3807 aa/aa^{CS}: 1in 10,000	>95%	aa/a-: <1 in 880 aa/--: <1 in 76,140 aa/aa^{CS}: <1 in 200,000
		General Population	aa/a-: 1 in 16 aa/--: 1 in 570 aa/aa^{CS}: 1 in 10,000	>95%	aa/a-: <1 in 320 aa/--: <1 in 11,400 aa/aa^{CS}: <1 in 200,000
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)