Patient		Sample		Provider	
Name	**Jane Doe**	Specimen Type	**Blood**	Provider	**Jill Smith, MD**
Date of Birth	**01/01/1901**	Collection Date	**06/01/2025**	Clinic Address	**1035 O'Brien Dr., Suite 112 Menlo Park, CA 94025**
Sex Assigned at Birth	**Female**	Date Received	**06/02/2025**		
Gestational Age	**10w2d**	Accession ID	**1234567K1234**	Phone Number	**650-460-2551**
Medical Record #	**123456789**	Requisition ID	**1234567K1234-4**	Fax Number	**833-915-0146**
		Date Reported	**06/12/2025**		

SUMMARY OF RESULTS

POSITIVE Carrier

Low Risk Fetus

6.9% fetal fraction

Recommended Follow-Up

Genetic counseling is recommended to review the implications of this result. The patient may contact BillionToOne at **(650) 460-2551** to schedule an appointment for a complimentary telephone genetic consultation to review these results.

Unity Fetal Risk™ Screen: Carrier Screen + cfDNA Fetal Risk Assessment

CARRIER SCREEN		cfDNA FETAL RISK ASSESSMENT *(pregnant carriers only)*		
Conditions Screened	**Patient Carrier Status**	**Risk *Before* cfDNA**	**Fetal Risk *After* cfDNA**	
***Plus* Panel**				
Tay-Sachs Disease *HEXA*	**POSITIVE** c.459+5G>A	**1 in 112** (Ashkenazi Jewish paternal ethnicity) **1 in 772** (general population)	**< 1 in 10000** (Ashkenazi Jewish paternal ethnicity) **1 in 5900** (general population)	**Low Risk**

When applicable, fetal risk before and after cfDNA analysis assumes paternal carrier status is unknown (unless otherwise noted).
Condition carrier frequencies can be found at www.unityscreen.com/carrier-frequencies.

Patient Name Jane Jones **DOB** 11/27/1940 **Gestational Age** 10w2d **Medical Record #** 123456789

Unity Fetal Risk™ Screen: Carrier Screen + cfDNA Fetal Risk Assessment

CARRIER SCREEN		cfDNA FETAL RISK ASSESSMENT *(pregnant carriers only)*
Conditions Screened	**Patient Carrier Status**	**cfDNA Fetal Risk Status**
ACOG Guideline Panel		
Alpha-Thalassemia *HBA1, HBA2*	✓ Negative	N/A
Cystic Fibrosis *CFTR*	✓ Negative	N/A
Sickle Cell Disease / Beta-Thalassemia / Hemoglobinopathies *HBB*	✓ Negative	N/A
Spinal Muscular Atrophy *SMN1*	✓ Negative 2 *SMN1* copies, SNP not present	N/A
Fragile X Syndrome *FMR1*	✓ Negative 30 / 29 repeats	N/A
***Plus* Panel**		
Canavan Disease *ASPA*	✓ Negative	N/A
***DMD*-Associated Dystrophinopathies** *DMD*	✓ Negative	N/A
Familial Dysautonomia *ELP1*	✓ Negative	N/A
Medium-Chain Acyl-CoA Dehydrogenase Deficiency *ACADM*	✓ Negative	N/A
Phenylalanine Hydroxylase Deficiency *PAH*	✓ Negative	N/A
PMM2-Congenital Disorder of Glycosylation *PMM2*	✓ Negative	N/A
Smith-Lemli-Opitz Syndrome *DHCR7*	✓ Negative	N/A
Tay-Sachs Disease *HEXA*	⊕ POSITIVE	L Low Risk

Patient Name Jane Jones **DOB** 11/27/1940 **Gestational Age** 10w2d **Medical Record #** 123456789

Interpretation

Unity Fetal Risk Screen: Carrier Screen

UN-RPT-007-2606

This patient has the c.459+5G>A pathogenic variant in the *HEXA* gene (NM_000520.6) and is a CARRIER for Tay-Sachs disease.

Prior to a future pregnancy, carrier screening for Tay-Sachs disease for the patient's reproductive partner can be considered to clarify the risks for an affected child. If this patient's reproductive partner is a carrier, each pregnancy has a 25% risk for a child to inherit both the maternal and paternal *HEXA* variants and be affected with Tay-Sachs disease. If both variants are inherited, the phenotype would depend on the severity of the specific maternal and paternal variants inherited.

This patient's first-degree relatives each have a 50% chance to be a carrier for Tay-Sachs disease as well. We recommend these results be shared with blood relatives, especially those of reproductive age.

Unity Fetal Risk Screen: cfDNA Fetal Risk Assessment

The fetus is LOW RISK to be affected with Tay-Sachs disease.

cfDNA fetal risk assessment was performed to evaluate for fetal *HEXA* variants and concluded the fetus is LOW RISK to be affected with Tay-Sachs disease. No paternally inherited *HEXA* variants were detected in the cell-free DNA.

This result significantly reduces, but does not eliminate, the risk for Tay-Sachs disease in the fetus. The fetal risk after cfDNA analysis is based on the residual risk of the fetus being either homozygous for the maternal variant or compound heterozygous with a distinct paternal variant not assessed by this screen. The fetal risk after cfDNA analysis assumes paternal carrier status is unknown. If the father of the pregnancy is a known carrier, please contact BillionToOne at (650) 460-2551.

This cfDNA fetal risk assessment result is valid only for a singleton pregnancy achieved without egg donation or gestational carrier.

Prenatal diagnosis via chorionic villus sampling or amniocentesis can be considered if the patient desires additional information. UNITY Fetal Risk Screen is not diagnostic. No irreversible decisions regarding the pregnancy should be made without confirmatory invasive prenatal testing. Genetic testing can also be performed postnatally.

Patient Name Jane Jones **DOB** 11/27/1940 **Gestational Age** 10w2d **Medical Record #** 123456789

Interpretation

Unity Fetal Risk Screen: Carrier Screen

Negative Result Interpretation

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

Carrier frequencies both before and after screening vary by ethnicity and assume no personal or family history of the condition. Condition carrier frequencies can be found at www.unityscreen.com/carrier-frequencies.

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.

Patient Name Jane Jones **DOB** 11/27/1940 **Gestational Age** 10w2d **Medical Record #** 123456789

Methods and Limitations

Unity Fetal Risk Screen: Carrier Screen (ACOG Guideline Panel)

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 and was sequenced by next generation sequencing (NGS). Results were aligned and examined on a custom bioinformatics pipeline and compared to the published human genome build GRCh37/hg19 reference sequence and analyzed to identify single nucleotide variants (SNVs), insertion/deletion variants (indels), and copy number changes (CNVs). NGS SNVs and indels may be confirmed via Sanger sequencing. CNVs may be confirmed using digital Multiplex Ligation Probe Amplification (dMLPA). Pathogenic and likely pathogenic variants were reported. Variants classified as benign, likely benign, or having uncertain significance were not reported. Incidental findings may not be reported. Possible results include Positive (Carrier or May Be Affected), Negative, QC Fail, and No Call results. Variant classifications are determined by the information and data available at the time of reporting. Internal reanalysis of variants is performed at periodic intervals. A change in classification may occur over time as additional information becomes available.

Test limitations: A negative result significantly reduces but does not eliminate the chance of being a carrier. Condition carrier frequencies and residual risk can be found at www.unityscreen.com/carrier-frequencies (v1). Results from this test are highly accurate; however, discordant results may occur. Potential causes of discordant results include: laboratory-specific variant classifications, maternal bone marrow transplant, laboratory error, or other reasons. 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 variant spectrum: Unity Fetal Risk™ Screen: Carrier Screen is designed to maximize detection of pathogenic alleles for cystic fibrosis, spinal muscular atrophy, and hemoglobinopathies (alpha-thalassemia, beta-thalassemia, and sickle cell disease) and has analytical sensitivity and specificity of >99.9% for SNVs, indels, and CNVs. We sequence all exons (full exon coverage), exon-intron junctions, and select intronic regions of *CFTR* (NM_000492.4), *HBA1* (NM_000558.5), *HBA2* (NM_000517.6), and *HBB* (NM_000518.5), and include detection of SNVs and insertion/deletion variants of up to 25 bp. Copy number analysis is performed on *CFTR*, *SMN1* (NM_000344.4), *HBA1*, *HBA2*, and *HBB* and includes detection of single exon deletions and two or more exon duplications. This assay detects 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.

Unity Fetal Risk Screen: Carrier Screen (Fragile X Syndrome)

DNA was extracted and purified from leukocyte enriched peripheral blood. DNA was processed with restriction digestion followed by gene specific PCR. The number of CGG repeats was determined from fragment sizes measured by capillary electrophoresis. A negative result significantly reduces but does not eliminate the chance of being a carrier. The accuracy of the reported repeat sizes are expected to be +/- 2 repeats for alleles of repeat length 55 or shorter, +/- 5 for repeat lengths between 55-100, and +/- 10 repeats for alleles of repeat lengths 101-200. The repeat length of alleles greater than 200 repeats is reported as >200. *FMR1* repeat detection by PCR has inherent amplification bias for normal length alleles. This assay may not detect alleles of >940 repeats or mosaic alleles present at less than 5%. Repeat-length dependent amplification bias prevents the measurement of relative dosage for samples with multiple detected alleles and can also lead to the failure to detect expanded repeat alleles of low allele fractions. Possible results include: Negative (<45 repeats); Negative - Intermediate (45-54 repeats); Positive - Premutation (55-200 repeats); Positive - Full Mutation (>200 repeats), QC Fail, and No Call results. For premutation and full mutation carriers, the fetal risk will be reported as increased when the risk of the fetus inheriting a full mutation is <25%. The fetal risk will be reported as high when the risk of the fetus inheriting a full mutation is ≥25%.

For premutation alleles with 55-90 repeats, AGG interruption analysis will report both the number and sequence context of AGG sequences that interrupt the CGG repeat tract. *FMR1* genotype is determined via fragment analyses of allele-specific amplicons. The accuracy of this methodology is ±3 repeats. In certain circumstances, the genotype cannot be determined without ambiguity and will be reported as "indeterminate."

Patient Name Jane Jones **DOB** 11/27/1940 **Gestational Age** 10w2d **Medical Record #** 123456789

Methods and Limitations

Unity Fetal Risk Screen: Carrier Screen (*Plus* Panel)

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 and was sequenced by next generation sequencing (NGS). Results were aligned and examined on a custom bioinformatics pipeline and compared to the published human genome build GRCh37/hg19 reference sequence and analyzed to identify single nucleotide variants (SNVs), insertion/deletion variants (indels), and copy number changes (CNVs). NGS SNVs and indels may be confirmed via Sanger sequencing. CNVs may be confirmed using digital Multiplex Ligation Probe Amplification (dMLPA). Pathogenic and likely pathogenic variants were reported. Variants classified as benign, likely benign, or having uncertain significance were not reported. Incidental findings may not be reported. Possible results include Positive (Carrier or May Be Affected), Negative, QC Fail, and No Call results. Variant classifications are determined by the information and data available at the time of reporting. Internal reanalysis of variants is performed at periodic intervals. A change in classification may occur over time as additional information becomes available.

Test limitations: A negative result significantly reduces but does not eliminate the chance of being a carrier. Condition carrier frequencies and residual risk can be found at www.unityscreen.com/carrier-frequencies (v1). Results from this test are highly accurate; however, discordant results may occur. Potential causes of discordant results include: laboratory-specific variant classifications, maternal bone marrow transplant, laboratory error, or other reasons. 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 variant spectrum: Unity Fetal Risk™ Screen: Carrier Screen is designed to maximize detection of pathogenic alleles for Medium-Chain Acyl-CoA Dehydrogenase Deficiency, Canavan Disease, Smith-Lemli-Opitz Syndrome, Familial Dysautonomia, Tay-Sachs Disease, Phenylalanine Hydroxylase Deficiency, and PMM2-Congenital Disorder of Glycosylation, and DMD-Associated Dystrophinopathies for female patients. The assay has analytical sensitivity and specificity of >99% for SNVs, indels, and CNVs. We sequence all exons (full exon coverage), exon-intron junctions, and select intronic regions of *ACADM* (NM_000016.6), *ASPA* (NM_000049.4), *DHCR7* (NM_001360.3), *DMD* (NM_004006.3), *ELP1* (NM_003640.5), *HEXA* (NM_000520.6), *PAH* (NM_000277.3), and *PMM2* (NM_000303.3). Analysis includes detection of SNVs and insertion/deletion variants of up to 25 bp. Copy number analysis is performed on all genes and includes detection of single exon deletions and two or more exon duplications. Rarely single-exon deletions may not be detected or reported. This assay detects all common variants in these genes including the 7.6 kb deletion in the *HEXA* gene, and pseudodeficiency alleles will be reported in Additional Findings, but are considered clinically insignificant.

Unity Fetal Risk Screen: cfDNA for Recessive Conditions (*Plus* Panel)

Cell-free DNA (cfDNA) was isolated from 2-4mL of plasma from whole blood collected in a cell-free DNA tube. cfDNA for fetal risk assessment of relevant genes was performed as multiplex PCR & next-generation sequencing on (i) common single nucleotide variants (SNVs) to measure the fraction of cell-free DNA of fetal origin (i.e., fetal fraction), (ii) amplicons for *ACADM*, *ASPA*, *ELP1*, *DHCR7*, *HEXA*, *PAH*, *PMM2* exons and critical introns for paternal exclusion analysis of pathogenic alleles, and breakpoint PCR & sequencing for exclusion of the *HEXA* 7.6kb deletion, and (iii) selected variants of the 7 genes listed above for determining maternal inheritance by Relative Mutation Dosage and Quantitative Counting Templates™ (QCTs™) molecular counting technology, when indicated (i.e., maternal dosage analysis). Fetal fraction, paternal variant analysis, and maternal dosage analysis are combined in a statistical algorithm along with the prior risk to report a post-test fetal risk for each condition.

Test Limitations: cfDNA fetal risk assessment may not be reported when the amount of cell-free DNA in the blood sample is below the limit of detection. Results from this test are highly accurate; however, discordant results may occur. Potential causes of discordant results include: laboratory-specific variant classifications, low fetal fraction, vanishing twin, maternal bone marrow transplant, laboratory error, or other reasons. The cfDNA result is valid only for a singleton pregnancy achieved without egg donation or gestational carrier. This test is designed and optimized as a general population screening tool, and additional information regarding maternal and paternal variants should be supplied to the laboratory for appropriate risk adjustment in cases where the test is being used for high-risk couples where paternal carrier status is known. Relative Mutation Dosage analysis for the identification of homozygosity is not available for all variants. Therefore, while rare, it is possible that the cfDNA test result may not detect a homozygous affected fetus. While this limitation is accounted for in the post-test cfDNA fetal risk assessment for the specified populations, the reported post-test fetal risk assessment may not adequately represent the residual risk for consanguineous couples.

Test sensitivity and variant spectrum: Next generation sequencing of clinically relevant exons and introns in *ACADM*, *ASPA*, *ELP1*, *DHCR7*, *HEXA*, *PAH* and *PMM2* was performed. The cfDNA fetal risk assessment is designed to detect >90% of affected cases for these 7 genes. When performed on carriers of the *HEXA* 7.6kb deletion, the *HEXA* cfDNA fetal risk assessment detects or excludes paternal inheritance of an overlapping 7.6kb deletion.

This test 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. This test incorporates BillionToOne's patented technology (www.billiontoone.com/patents).

BillionToOne Inc.
3200 Whipple Road
Union City, CA 94587

Phone **(650) 460-2551**
Fax **(833) 915-0146**
Email support@unityscreen.com

John ten Bosch
New York Lab Director
New York License:
TENBJ1

Joseph Michael Anderson, MD
CLIA Lab Director
California License:
A 98379

Tay-Sachs Disease - Low Risk Fetus

What Is Tay-Sachs Disease?

Tay-Sachs disease is an inherited condition that affects the nervous system. It occurs when the body is unable to break down a specific type of fat, causing it to build up in the brain and nerve cells. Common symptoms of Tay-Sachs disease include muscle weakness that worsens over time, loss of motor skills, difficulty swallowing, and seizures.

There are three types of Tay-Sachs disease: infantile, juvenile, and late-onset. The range of symptoms can be broad. Genetic testing can sometimes predict which condition is more likely, however, it cannot always provide definitive answers. The infantile form is the most common and most severe type of Tay-Sachs disease, with symptoms typically appearing around six months of age. The disease progresses quickly and most children with the infantile form of Tay-Sachs disease do not live beyond four or five years of age. The juvenile form of Tay-Sachs disease usually appears in children between ages 2 and 10 and progresses more slowly but still leads to a shortened lifespan. The late-onset type is the mildest, with symptoms that can start in adolescence or adulthood and progress slowly, sometimes allowing for a typical lifespan.

Currently, there is no cure for Tay-Sachs disease, but treatments focus on managing symptoms and providing supportive care. This may include medications to help control seizures, physical therapy, and nutritional support to ensure proper feeding. UN-RPT-007-2606

What Causes Tay-Sachs Disease?

Everyone has two copies of the *HEXA* gene. Individuals with Tay-Sachs disease have two non-working copies of the *HEXA* gene, one from each of their parents. If someone has one non-working copy of the *HEXA* gene due to a genetic change (also called a variant), they are called a carrier. When both parents are carriers, there is a 25% (1 in 4) chance to have an affected child with each pregnancy.

Your Status: Carrier of Tay-Sachs Disease

You were identified to be a carrier of Tay-Sachs disease. Carriers of Tay-Sachs disease are typically healthy and do not have any symptoms. Carrier screening for Tay-Sachs disease for your reproductive partner is recommended to clarify the risk for an affected child. If your reproductive partner is a carrier for the same condition, each pregnancy may have a 25% risk to be affected with Tay-Sachs disease.

Your first-degree relatives (e.g., brothers, sisters, children, and parents) have a 50% chance to be a carrier of Tay-Sachs disease. More distant relatives also have a chance to be a carrier. We recommend that you share these results with blood relatives, especially those of reproductive age.

Tay-Sachs Disease - Low Risk Fetus

Your Baby's Risk: LOW RISK for Tay-Sachs Disease

The testing performed by Unity Fetal Risk Screen evaluated your baby's risk of having Tay-Sachs disease. The results show your baby's chance of being affected with Tay-Sachs disease is very low, but not zero. Please reference your report to review personalized risk estimates for this pregnancy.

Genetic counseling is available to discuss the implications of these results. You may contact BillionToOne at (650) 460-2551 to schedule an appointment for a complimentary telephone genetic consultation. A local genetic counselor can also be found at www.nsgc.org.

Resources

- National Organization of Rare Diseases: https://rarediseases.org/rare-diseases/tay-sachs-disease/
- Medline Plus: https://medlineplus.gov/genetics/condition/tay-sachs-disease/
- National Tay Sachs and Allied Diseases Association: https://ntsad.org/diseases/tay-sachs-disease