Fetal Aneuploidy Screening with Microdeletions

ARUP LABORATORIES

Patient: [redacted] DOB: [redacted] Age: 20 Sex: F **Patient Identifiers:** [redacted] **Visit Number (FIN):** [redacted]	Client: [redacted] Physician: [redacted]	ARUP Test Code: 3004781 Collection Date: 08/25/2022 Received in lab: 08/29/2022 Completion Date: 09/05/2022

Test Information

Method

DNA isolated from the maternal blood, which contains placental DNA, is amplified at specific loci using a targeted PCR assay, and sequenced using a high-throughput sequencer. Sequencing data is analyzed using Natera's proprietary algorithm to determine the fetal copy number for chromosomes 13, 18, 21, X, and Y, thereby identifying whole chromosome abnormalities at these locations, and if ordered, the microdeletion panel will identify microdeletions at the specified loci only. If sample fails to meet the quality threshold, no result will be reported for the specified chromosome(s). The test requires sufficient fetal fraction to produce a result.

Patient Report

Patient's genetic report from Natera continues on following pages.

ARUP LABORATORIES | 800-522-2787 | aruplab.com
500 Chipeta Way, Salt Lake City, UT 84108-1221
Jonathan R. Genzen, MD, PhD, Laboratory Director

Chart continues on following page(s)

Patient Information

Patient Name:	[redacted]
Date of Birth:	[redacted]
Maternal Age at EDD:	21
Gestational Age:	12 weeks/1 days
Maternal Weight:	97 lbs
Patient ID:	[redacted]
Collection Kit:	22614821-2-N
Accessioning ID:	22238402552
Case File ID:	[redacted]

Test Information

Ordering Physician:	[redacted]
Clinic Information:	ARUP Laboratories
Additional Reports:	N/A
Report Date:	09/04/2022
Samples Collected:	08/25/2022
Samples Received:	08/31/2022
	Mother Blood

panorama® natera prenatal screen

ABOUT THIS SCREEN: Panorama™ is a screening test, not diagnostic. It evaluates genetic information in the maternal blood, which is a mixture of maternal and placental DNA, to determine the chance for specific chromosome abnormalities. The test does NOT tell with certainty if a fetus is affected, and only tests for the conditions ordered by the healthcare provider. A low risk result does not guarantee an unaffected fetus.

FINAL RESULTS SUMMARY

Result	*Fetal Sex*	*Fetal Fraction*
LOW RISK	Male	12.1%

RESULT DETAILS: ANEUPLOIDIES

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Risk After Test*[3]
Trisomy 21	Low Risk	1/1,068	<1/10,000
Trisomy 18	Low Risk	1/2,484	<1/10,000
Trisomy 13	Low Risk	1/7,826	<1/10,000
Monosomy X	Low Risk	1/255	<1/10,000
Triploidy	Low Risk		

RESULT DETAILS: MICRODELETIONS

Condition tested[1]	*Result*	*Risk Before Test*[2]	*Risk After Test*[4]
22q11.2 deletion syndrome	Low Risk	1/2,000	1/12,000
1p36 deletion syndrome	Low Risk	1/5,000	1/12,400
Angelman syndrome	Low Risk	1/12,000	1/16,600
Cri-du-chat syndrome	Low Risk	1/20,000	1/57,100
Prader-Willi syndrome	Low Risk	1/10,000	1/13,800

1. Excludes cases with evidence of fetal and/or placental mosaicism. 2. Based on maternal age, gestational age, and/or general population, as applicable. References available upon request. 3. Risk after test for aneuploidy incorporates results from the Panorama algorithm and data from a published population study of over 1 million women [DiNonno et al.J.Clin.Med.2019.Aug 26; 8(9):1311.doi:10.3390/jcm8091311] and are reported as PPVs (high risk) and NPVs (low risk). Maternal age and fetal fraction are utilized in this calculation; however, the "risk after test" may not reflect the actual PPVs for this patient, as additional risk factors, including but not limited to: results of other screening, ultrasound findings, and personal/family history, are not included in the risk assessment. 4. Risk after test for microdeletion(s) incorporates results from the Panorama algorithm and data from multiple studies [Dar P et al. Cell-free DNA screening for prenatal detection of 22q11.2 deletion syndrome. American Journal of Obstetrics and Gynecology (2022). https://doi.org/10.1016/j.ajog.2022.01.002; Martin et al. Clin Genetics. 2017 Jul 11, Wapner R J et al. Am J Obstst Gynecol. 2015 Mar;212 (3):332 .e1-9] and are reported as PPVs (high risk) and NPVs (low risk). Risks for microdeletions are independent of maternal age and fetal fraction is utilized in this calculation; however, the "risk after test" may not reflect the actual PPV for this patient, as additional risk factors, including but not limited to: results of other screening, ultrasound findings, personal/family history, are not included in the risk assessment.

Reviewed By: [redacted]

CLIA Laboratory Director: J. Dianne Keen-Kim, Ph.D., FACMG

IF THE ORDERING PROVIDER HAS QUESTIONS OR WISHES TO DISCUSS THE RESULTS, PLEASE CONTACT US AT 650-249-9090 #3. Ask for the NIPT genetic counselor on call.

CLIA ID#05D1082992; Rev DEV
Natera, Inc., 1-855-866-NIPT (6478)

Report ID7177104-136893736
201 Industrial Road Suite 410, San Carlos, CA 94070

natera Conceive. Deliver. Thrive.

Patient Information	
Patient Name:	[redacted]
Date of Birth:	[redacted]
Maternal Age at EDD:	21
Gestational Age:	12 weeks/1 days
Maternal Weight:	97 lbs
Patient ID:	[redacted]
Collection Kit:	22614821-2-N
Accessioning ID:	22238402552
Case File ID:	[redacted]

Test Information	
Ordering Physician:	[redacted]
Clinic Information:	ARUP Laboratories
Additional Reports:	N/A
Report Date:	09/04/2022
Samples Collected:	08/25/2022
Samples Received:	08/31/2022
	Mother Blood

panorama® natera prenatal screen

ABOUT THIS SCREEN: Panorama™ is a screening test, not diagnostic. It evaluates genetic information in the maternal blood, which is a mixture of maternal and placental DNA, to determine the chance for specific chromosome abnormalities. The test does NOT tell with certainty if a fetus is affected, and only tests for the conditions ordered by the healthcare provider. A low risk result does not guarantee an unaffected fetus.

OVERALL TEST SPECIFICATIONS FOR PANORAMA

The information in the table below relates to the general performance of the test.

Sensitivity is the ability to correctly identify a truly high risk case as high risk. For example, in a group of Trisomy 21 cases, Panorama will correctly identify more than 99% of those cases.

Specificity is the ability to correctly identify an unaffected case as low risk.

Positive Predictive Value (PPV) is the likelihood the result says high-risk and the fetus is actually affected. For example, when Panorama shows a high-risk result for Trisomy 21, there is a 95% chance that the fetus is affected by Trisomy 21. In other words, 5% of the time, you may get a high-risk result when the fetus is not affected by Trisomy 21.

Negative Predictive Value (NPV) is the likelihood the result says low-risk and the fetus is truly not affected.

Condition	*Sensitivity (95% CI)*	*Specificity (95% CI)*	*PPV*	*NPV*
Trisomy 21 [1,2]	99.0% (CI 97.1-100)	>99% (CI 99.93-99.99)	95%	>99.99%*
Trisomy 18 [1,2]	94.1% (CI 82.9-100)	>99% (CI 99.96-100)	91%	>99.99%*
Trisomy 13 [1,2]	>99% (CI 73.5-100)	>99% (CI 99.96-100)	68%	>99.99%*
Monosomy X [1,2]	94.7% (CI 74.0-99.9)	>99% (CI 99.7-100)	78%	>99.99%*
Triploidy [3,4]	>99% (CI 66.4-100)	>99% (CI 99.5-100)	5.3%	>99.99%*
XXX, XXY, XYY [5] **	73.1% (CI 61.0-85.1)	99.9% (CI 99.90-99.99)	86.4%	99.87%
22q11.2 deletion syndrome [6]	83.3% (CI 51.6-97.9)	>99% (CI 99.91-99.98)	53%***	99.9% (CI 99.9-100)****
1p36 deletion syndrome [7,8]	>99% (CI 2.5-100)	>99% (CI 99.1-100)	7-17%****	99.98-99.99%****
Angelman syndrome [7,8]	95.5% (CI 77.2-99.9)	>99% (CI 99.1-100)	10% ***	>99.99%
Cri-du-chat syndrome [7,8]	>99% (CI 85.8-100)	>99% (CI 99.1-100)	2-5%****	>99.99%
Prader-Willi syndrome [7,8]	93.8% (CI 69.8-99.8)	>99% (CI 99.1-100)	5%	>99.99%
Female	>99.9% (CI 99.4-100)	>99.9% (CI 99.5-100)		
Male	>99.9% (CI 99.5-100)	>99.9% (CI 99.4-100)		

1. Dar P et al. Am J Obstet Gynecol. 2022. doi: https://doi.org/10.1016/j.ajog.2022.01.019
2. DiNonno W et al. J Clin Med. 2019. 26;8(9):1311. doi: https://doi.org/10.3390/jcm8091311
3. Nicolaides KH et al. Fetal Diagn Ther. 2014. 35;(3):212-7. doi: https://doi.org/10.1159/000355655
4. Curnow KJ et al. Am J Obstet Gynecol. 2015. 212(1):79.e1-9. doi: https://doi.org/10.1016/j.ajog.2014.10.012
5. Martin K et al. ISPD 25th International Conference: June, 2021
6. Dar P et al. Am J Obstet Gynecol. 2022. doi: https://doi.org/10.1016/j.ajog.2022.01.002
7. Martin K et al. Clin Genet. 2018. 93(2):293-300. doi: https://doi.org/10.1111/cge.13098
8. Wapner RJ et al. Am J Obstet Gynecol. 2015. 212(3):332.e1-9. doi: https://doi.org/10.1016/j.ajog.2014.11.041

* Ongoing clinical follow-up is performed to ensure the NPV does not fall below the quoted value but follow up is not obtained for all low risk calls.

** Sex chromosome abnormalities are only reported when identified.

*** PPV for 22q11.2 deletion syndrome and Angelman syndrome in published studies was 53% and 10% respectively when no ultrasound anomalies were seen and was up to 100% when ultrasound anomalies were seen prior to testing.

**** Dependent upon fetal fraction. For 22q11.2 deletion syndrome, only the paternal allele is evaluated at FF ≤ 6.5%. For 1p36 deletion syndrome and Cri-du-chat syndrome, only the paternal allele is evaluated at FF < 7%. For Angelman syndrome, no risk assessment is reported at FF < 7%. For Prader-Willi syndrome, no risk assessment is reported at FF ≤ 2.8%.

Test specifications above are applicable to singleton and monozygotic twin pregnancies only. For additional information, please visit: ***www.natera.com/panorama-test/test-specs***

Testing Methodology: DNA isolated from the maternal blood, which contains placental DNA, is amplified at specific loci using a targeted PCR assay and is sequenced using a high-throughput sequencer. Fetal fraction is determined using a proprietary algorithm incorporating data from single nucleotide polymorphism-based (SNP-based) next-generation sequencing [Pergament E et al. Obstet Gynecol. 2014 Aug;124(2 Pt 1):210-8]. If the estimated fetal fraction is ≥2.8%, sequencing data is analyzed using a proprietary SNP-based algorithm to determine the fetal copy number for chromosomes 13, 18, 21, X and Y [Ryan A et al. Am J Obstet Gynecol. 2014 Nov;211(5):527.e1-527.e17]. If ordered, specific microdeletions will be evaluated using similar methodology [Wapner RJ et al. Am J Obstet Gynecol. 2015 Mar;212(3):332.e1-9]. If a sample fails to meet the quality threshold, or the fetal fraction is insufficient, an additional algorithm is utilized to determine whether there is an increased risk for triploidy, trisomy 18 and trisomy 13 [McKanna et al. The European Human Genetics Conference. Copenhagen, Denmark. May 27-30, 2017]. However, some samples will not produce a result due to failure to meet the necessary quality thresholds.

This test has been validated on women with a singleton, twin or egg donor pregnancy of at least nine weeks gestation. A result will not be available for higher order multiples and multiple gestation pregnancies with an egg donor or surrogate, or bone marrow transplant recipients. Complete test panel is not available for twin gestations and pregnancies achieved with an egg donor or surrogate. For twin pregnancies with a fetal fraction value below the threshold for analysis, a sum of the fetal fractions for both twins will be reported. Findings of unknown significance will not be reported. As this assay is a screening test and not diagnostic, false positives and false negatives can occur. High risk test results need diagnostic confirmation by alternative testing methods. Low risk results do not fully exclude the diagnosis of any of the syndromes nor do they exclude the possibility of other chromosomal abnormalities or birth defects, which are not a part of this test. Potential sources of inaccurate results include, but are not limited to, mosaicism, low fetal fraction, limitations of current diagnostic techniques, or misidentification of samples. This test will not identify all deletions associated with each microdeletion syndrome. This test has been validated on full region deletions only and may be unable to detect smaller deletions. Microdeletion risk score is dependent upon fetal fraction, as deletions on the maternally inherited copy are difficult to identify at lower fetal fractions. Test results should always be interpreted by a clinician in the context of clinical and familial data with the availability of genetic counseling when appropriate.