MaterniT™ GENOME Lab Report

Sequenom Laboratories
3595 John Hopkins Court, San Diego, CA 92121
CLIA #: 05D2015356 CAP #: 7527138
Tel: 877.821.7266

FINAL REPORT

Ordering Provider:		Patient:	
Provider Location:	**Pronto Diagnostics LTD**	DOB:	
Provider Phone:	**972-73-2126155**	Patient ID:	
Date Ordered:	**09/01/2016**	Specimen:	
Date Collected:	**08/31/2016**	Referral Clinician:	
Date Received:	**09/02/2016**	Lab Director:	**Phillip Cacheris, MD, PhD**
Order ID:	**ORD16245-01019**	Date Reported:	**9/10/2016 3:07 PM PT**

Test Result

Negative

Fetal sex consistent with male

Lab Director's Comments

Genome-wide analysis of this specimen did not detect gains or losses of chromosomal material suggestive of whole chromosome aneuploidies, subchromosomal duplications or deletions >=7 Mb, or select microdeletions ranging in size below 7Mb. A negative result does not ensure an unaffected pregnancy. Please refer to the "Performance" and "Limitations of the Test" sections of this laboratory report for additional information.

Fetal Fraction: 16%

Result Table

Content	Result
AUTOSOMAL ANEUPLOIDIES	
Trisomy 21 (Down syndrome)	Negative
Trisomy 18 (Edwards syndrome)	Negative
Trisomy 13 (Patau syndrome)	Negative
Other autosomal aneuploidies	Negative
SEX CHROMOSOME ANEUPLOIDIES	
Fetal Sex	Consistent with male
Monosomy X (Turner syndrome)	Negative
XYY (Jacobs syndrome)	Negative
XXY (Klinefelter syndrome)	Negative
XXX (Triple X syndrome)	Negative
GENOME-WIDE COPY NUMBER VARIANTS ≥ 7Mb	
Gains/Losses ≥ 7 Mb	Negative
SELECT MICRODELETIONS	
22q11 deletion (associated with DiGeorge syndrome)	Negative
15q11 deletion (associated with Prader-Willi / Angelman syndrome)	Negative
11q23 deletion (associated with Jacobsen syndrome)	Negative
8q24 deletion (associated with Langer-Giedion syndrome)	Negative
5p15 deletion (associated with Cri-du-chat syndrome)	Negative
4p16 deletion (associated with Wolf-Hirschhorn syndrome)	Negative
1p36 deletion syndrome	Negative

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About the Test

The MaterniT™ GENOME laboratory-developed test analyzes the relative amount of chromosomal material across the genome in circulating cell-free DNA from a maternal blood sample. The test is indicated for use in pregnant women with singleton pregnancies at risk of fetal chromosomal and/or subchromosomal abnormalities.

Test Method

Circulating cell-free DNA was purified from the plasma component of anti-coagulated maternal whole blood. A genomic DNA library was prepared to determine chromosomal representation by massively parallel sequencing.[1] Gain or loss of chromosomal material ≥7 Mb was evaluated across the entire genome. Select chromosomal regions (1p, 4p, 5p, 8q, 11q, 15q, and 22q) associated with known syndromes were also evaluated. Fetal sex was assessed by Y chromosome representation.

Performance

The MaterniT™ GENOME test utilizes the same proprietary technology as the MaterniT21® PLUS test, with deeper sequencing. In a clinical study using 448 patient samples to evaluate concordance, the MaterniT™ GENOME test was equivalent in performance for the analysis of trisomy 21, trisomy 18, trisomy 13, sex chromosome aneuploidies and fetal sex classification, to the MaterniT21® PLUS test.[2] The MaterniT21® PLUS test performance has previously been validated and published extensively.[1, 3–6]

The MaterniT™ GENOME test performance characteristics for the detection of genome-wide gain or loss events ≥7 Mb, and select microdeletions below 7 Mb were established using *in silico* analytic methods, and validated using test samples comprised of genomic DNA mixed with plasma from non-pregnant females.[2] Sensitivity for genome-wide events greater than or equal to 7 Mb was determined to be 95.9%. Sensitivities for select microdeletions varied by size of the event and fetal fraction. Specificity for genome-wide events and select microdeletions was established using 1060 maternal plasma DNA samples and was determined to be >99.9%.

Additional details can be found in the table below, and at http://sequenom.com/genome/performance.

Performance Characteristics

Region (associated syndrome)	Size Range (Mb)*	Median Size (Mb)*	Reportable Fetal Fraction	Estimated Sensitivity**	Estimated Specificity
Genome-wide	NA	NA	≥ 4%	96% (61–> 99%)	> 99.9%
22q11.2 (DiGeorge)	0.8–3.6	2.6	≥ 4%	> 74% (17–94%)	> 99.9%
15q11.2 (Prader-Willi & Angelman)	1.2–15.8	5.1	≥ 4%	> 59% (16–74%)	> 99.9%
11q23 (Jacobsen)	1.3–15.7	9	≥ 4%	> 87% (57–> 99%)	> 99.9%
8q24.11-q24.13 (Langer-Giedion)	7.6–8.8	7.9	≥ 4%	> 97% (80–> 99%)	> 99.9%
5p15.3 (Cri du Chat)	1.5–17.8	6	≥ 4%	> 83% (48–96%)	> 99.9%
4p16.3 (Wolf-Hirschhorn)	1.1–17.3	4.2	≥ 4%	> 73% (37–91%)	> 99.9%
1p36 (1p36 deletion syndrome)	1.6–13.3	3.8	≥ 4%	> 51% (13–81%)	> 99.9%

* As reported in ISCA database nstd37 [http://dbsearch.clinicalgenome.org/search/]

** Sensitivity estimated across the observed size distribution of each syndrome [per ISCA database nstd37] and across the range of fetal fractions observed in routine clinical NIPT. Figures in parentheses indicate upper and lower estimates for sensitivity at the lowest reportable fetal fraction (4%) and at fetal fraction ≥20%, respectively. Actual sensitivity can also be influenced by other factors such as the size of the event, total sequence counts, amplification bias, or sequence bias.

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Limitations of the Test

While the results of the MateriniT™ GENOME test are highly accurate, discordant results, including inaccurate fetal sex prediction, may occur due to placental, maternal, or fetal mosaicism, or other causes. Cell-free DNA (cfDNA) testing does not replace the accuracy and precision of prenatal diagnosis with CVS or amniocentesis. A patient with a positive MateriniT™ GENOME test result should be referred for genetic counseling and offered invasive prenatal diagnosis for confirmation of test results. A negative MateriniT21® PLUS test result does not ensure an unaffected pregnancy. An uninformative result may be reported, the causes of which may include, but are not limited to, insufficient sequencing coverage, sequencing noise or artifacts, amplification bias, or insufficient fetal fraction. The MateriniT™ GENOME test is not intended to identify pregnancies at risk for neural tube defects or ventral wall defects. cfDNA testing for whole chromosome abnormalities (including sex chromosomes) and for subchromosomal abnormalities could lead to the potential discovery of both fetal and maternal genomic abnormalities that could have minor, or no, clinical significance. Evaluating the significance of a positive or a non-reportable test result may involve both invasive testing and additional studies on the pregnant woman. Such studies may lead to a diagnosis of whole or partial chromosomal abnormalities in the pregnant woman, which on occasion could be associated with benign or malignant neoplasms. cfDNA testing may not accurately identify fetal triploidy, balanced rearrangements, or the precise location of subchromosomal duplications or deletions; these may be detected by prenatal diagnosis with CVS or amniocentesis. The ability to report results may be impacted by maternal BMI, maternal weight, or maternal systemic lupus erythematosus (SLE). The results of this testing, including the benefits and limitations, should be discussed with a qualified health care provider. Management decisions, including termination of the pregnancy, should not be based on the results of this test alone.

Note

This laboratory-developed test was developed and its performance characteristics determined by Sequenom Laboratories. It has not been cleared or approved by the U.S. FDA. This test is used for clinical purposes. It should not be regarded as investigational or for research. Although laboratory-developed tests to date have not been subject to U.S. FDA regulation, certification of the laboratory is required under the Clinical Laboratory Improvement Amendments (CLIA) to ensure the quality and validity of the tests. This laboratory is certified under CLIA to perform high complexity clinical laboratory testing and accredited by the College of American Pathologists (CAP).

References

1. Palomaki GE, et al. Genet Med. 2011;13(11):913-920.
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3. Palomaki GE, et al. Genet Med. 2012;14(3):296-305.
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5. Mazloom AR, et al. American Society of Human Genetics. November 2012.
6. Zhao C, et al. Clin Chem. 2015 Apr;61(4):608-616.

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09/10/2016