

FINAL REPORT

Ordering Provider:
 Provider Location:
 Provider Phone:
 Date Ordered:
 Date Collected:
 Date Received:
 Order ID:

Patient:
 DOB:
 Patient ID:
 Specimen:
 External Accession:
 Referral Clinician:
 Date Reported:

Test Result

Positive
Trisomy 20

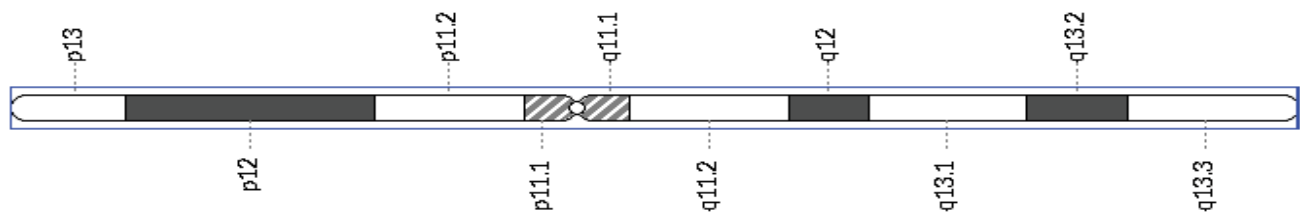
Lab Director's Comments

Fetal Fraction: 6%

This specimen showed an increased representation of chromosome 20, suggestive of trisomy 20. In placental testing, trisomy 20 can be mosaic, an occasional finding that is usually confined to the placenta (CPM), Grati et al, 2014. Chromosome 20 is possibly imprinted. Therefore, subsequent trisomy rescue in fetal tissue may carry a residual risk for uniparental disomy (UPD). Clinical correlation is recommended.

Chr20

Trisomy



A whole chromosome trisomy was observed for chromosome 20.

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Result Table

Content	Result
AUTOSOMAL ANEUPLOIDIES	
Trisomy 21 (Down syndrome)	Negative
Trisomy 18 (Edwards syndrome)	Negative
Trisomy 13 (Patau syndrome)	Negative
Other autosomal aneuploidies	Positive
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 ≥ 7 Mb	
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 (LDT) 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 MaterniT[®] 21 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 MaterniT[®] 21 PLUS test.[2] The MaterniT[®] 21 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.

Performance Characteristics

Region (associated syndrome)	Size Range (Mb)*	Median Size (Mb)*	Estimated Sensitivity**	Estimated Specificity
Genome-wide	NA	NA	96% (61->99%)	$>99.9\%$
22q11 deletion (associated with DiGeorge syndrome)	0.8-3.6	2.6	$>74\%$ (17-94%)	$>99.9\%$
15q11 deletion (associated with Prader-Willi / Angelman syndrome)	1.2-15.8	5.1	$>59\%$ (16-74%)	$>99.9\%$
11q23 deletion (associated with Jacobsen syndrome)	1.3-15.7	9	$>87\%$ (57->99%)	$>99.9\%$
8q24 deletion (associated with Langer-Giedion syndrome)	7.6-8.8	7.9	$>97\%$ (80->99%)	$>99.9\%$
5p15 deletion (associated with Cri-du-chat syndrome)	1.5-17.8	6	$>83\%$ (48-96%)	$>99.9\%$
4p16 deletion (associated with Wolf-Hirschhorn syndrome)	1.1-17.3	4.2	$>73\%$ (37-91%)	$>99.9\%$
1p36 deletion syndrome	1.6-13.3	3.8	$>51\%$ (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. 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 these tests are highly accurate, discordant results, including inaccurate fetal sex prediction, may occur due to placental, maternal, or fetal mosaicism or neoplasm; vanishing twin; prior maternal organ transplant; or other causes. Sex chromosomal aneuploidies are not reportable for known multiple gestations. These tests are screening tests and not diagnostic; they do not replace the accuracy and precision of prenatal diagnosis with CVS or amniocentesis. A patient with a positive test result should be referred for genetic counseling and offered invasive prenatal diagnosis for confirmation of test results.[7] A negative result does not ensure an unaffected pregnancy nor does it exclude the possibility of other chromosomal abnormalities or birth defects which are not a part of these tests. An uninformative result may be reported, the causes of which may include, but are not limited to, insufficient sequencing coverage, noise or artifacts in the region, amplification or sequencing bias, or insufficient fetal fraction. These tests are not intended to identify pregnancies at risk for neural tube defects or ventral wall defects. 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 major, minor, or no, clinical significance. Evaluating the significance of a positive or a non-reportable result may involve both invasive testing and additional studies on the mother. Such investigations may lead to a diagnosis of maternal chromosomal or subchromosomal abnormalities, which on occasion may be associated with benign or malignant maternal neoplasms. These tests 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, maternal systemic lupus erythematosus (SLE) and/or by certain pharmaceutical agents such as low molecular weight heparin (for example: Lovenox[®], Xaparin[®], Clexane[®] and Fragmin[®]). The results of this testing, including the benefits and limitations, should be discussed with a qualified healthcare provider. Pregnancy management decisions, including termination of the pregnancy, should not be based on the results of these tests alone. The healthcare provider is responsible for the use of this information in the management of their patient.

Note

This test was developed and its performance characteristics determined by LabCorp. It has not been cleared or approved by the Food and Drug Administration. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified 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.
2. Tynan J, et al. International Society of Prenatal Diagnosis Annual Meeting. Jul 2015
3. Palomaki GE, et al. *Genet Med*. 2012;14(3):296-305.
4. Mazloom AR, et al. *Prenat Diag*. 2013;33(6):591-597.
5. Mazloom AR, et al. *American Society of Human Genetics*. Nov 2012.
6. Zhao C, et al. *Clin Chem*. 2015 Apr;61(4):608-616.
7. ACOG/SMFM Joint Committee Opinion No. 545, Dec 2012.

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