SAMPLE REPORT

Non-Invasive Prenatal Test Report

Personal Information		Specimen Information		Test Information	
Patient Name	Jane Doe	**Sample ID**	20200101-123-4567	**Test reported**	2020-01-08
Date of Birth	1990-01-01	**GCG No**	G20NIPT999-99	**Ordering physician**	Dr. John
Sex	Female	**Date collected**	2020-01-01	**Institution**	GC hospital

PREGNANCY INFORMATION					QUALITY CONTROL		
Gest.Age/Weight	**Ultrasound Feature**	**Multiple Marker Screening Test**	**In-vitro Fertilization**	**No. of Fetus**	**DNA Quality**	**NGS Data Quality**	**QC Quality**
11w+0d / 50kg	None	Low Risk	None	Single	Pass	Pass	Pass

FETAL FRACTION	9.1%	FETAL SEX	Male

TEST RESULT	LOW RISK		
Chromocomal Abnormality	**Result**	**Negative Predictive Value (NPV) [1]**	**Positive Predictive Value (PPV) [2]**
Trisomy 21	LOW RISK	> 99.99%	99.14%
Trisomy 18	LOW RISK	> 99.99%	92.16%
Trisomy 13	LOW RISK	> 99.99%	71.43%
Sex Chromosome Aneuploidies (XO, XXX, XXY, XYY)	LOW RISK	> 99.99%	68.75%
Trisomy 9	LOW RISK	N/A [3]	
Trisomy 16	LOW RISK		
Trisomy 22	LOW RISK		

Deletion Syndrome	Result
1p36	LOW RISK
2q33.1	LOW RISK
5p15 (Cri-du-chat)	LOW RISK
11qter (Jacobsen)	LOW RISK
*** Other Microdeletions**	Not Detected

1. Negative Predictive Value (NPV): The probability that the subject with negative G-NIPT test result has negative result in the confirmation test.
2. Positive Predictive Value (PPV): The probability that the subject with positive G-NIPT test result has positive result in the confirmation test.
3. In case of trisomy 9, 16, 22, PPV and NPV were not determined due to low incidence.

* >7Mb deletion tested

Tested by : Kim,MinJeong M.T(37668) Confirmed by : Sae-Mi, Lee M.D(1067) Cho,EunHae M.D(690) [1/4]

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ADDITIONAL TEST RESULT

Chromosomal Abnormality	Result	Chromosomal Abnormality	Result
Trisomy 1	LOW RISK	**Trisomy 10**	LOW RISK
Trisomy 2	LOW RISK	**Trisomy 11**	LOW RISK
Trisomy 3	LOW RISK	**Trisomy 12**	LOW RISK
Trisomy 4	LOW RISK	**Trisomy 14**	LOW RISK
Trisomy 5	LOW RISK	**Trisomy 15**	LOW RISK
Trisomy 6	LOW RISK	**Trisomy 17**	LOW RISK
Trisomy 7	LOW RISK	**Trisomy 19**	LOW RISK
Trisomy 8	LOW RISK	**Trisomy 20**	LOW RISK

- The clinical sensitivity was not determined due to low incidence.

INTERPRETATION

As the G-NIPT result, any fetal chromosomal abnormalities in the autosomes and sex chromosomes did not detected. However, we cannot completely rule out the possibility of false negative result due to maternal chromosomal microdeletion/duplication, confined placental mosaicism (CPM), low fetal fraction and low level fetal mosaicism. It is recommended to perform a high resolution cytogenetic testing if any fetal abnormalities are found on untrasonography regardless of G-NIPT result.

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TEST INFORMATION

- Test Method: Next Generation Sequencing (NGS)
- Test Subject: Fetal Trisomy (Chromosome 21, 18, 13, 9, 16, 22), Sex Chromosome Aneuploidy, Microdeletion Syndrome (>7Mb)
- Specimen Type: cfDNA tube WB 10mL
- Bioinformatics Pipeline: NIPT.v1.2

TEST PERFORMANCE

Test Item	Sensitivity	Specificity	NPV	PPV
Trisomy 21	> 99.99%	99.99%	> 99.99%	99.14%
Trisomy 18	> 99.99%	99.99%	> 99.99%	92.16%
Trisomy 13	> 99.99%	99.98%	> 99.99%	71.43%
Sex Chromosome Aneuploidies (XO, XXX, XXY, XYY)	> 99.99%	99.92%	> 99.99%	68.75%
Other Chromosomes	The clinical sensitivity was not determined due to low incidence.			
Microdeletion Syndrome	The clinical sensitivity was not determined due to low incidence, and the sensitivity may be significantly affected by factors such as fetal DNA fraction and microdeletion size.			

METHOD and LIMITATIONS

- The purpose of this test is for risk assessment of common fetal trisomies 21, 18, 13 and sex chromosome aneuploidies. This test is performed by massively parallel sequencing for whole-genome using circulating cell-free fetal DNA in maternal plasma and it is possible to detect abnormalities in all chromosomes as well as chromosome 21, 18 and 13. NIPT performance is superior to the existing prenatal multiple marker screening tests.
- This test cannot identify neural tube defects and polyploidy such as trioploidy and tetraploidy.
- This test does not report monosomy. Fetal sex is not reported for twins.
- In case of trisomy 9, 16, 22 and microdeletion syndrome, the clinical sensitivity was not determined due to low incidence, and the sensitivity may be significantly affected by factors such as fetal DNA fraction and microdeletion size.
- This test is not to verify fetal karyotypes but is to determine the risk of fetal aneuploidies. If the result is positive, confirmatory test such as fetal karyotyping should be performed. Moreover, this is not a diagnostic test which does not rule out probability of false positive or false negative results.
- The factors affecting accuracy of this test are as follows: low fetal DNA fraction (early gestational weeks and high maternal BMI), undetermined maternal chromosomal abnormalities, confined placental mosaicism, fetal chromosomal mosaicism, multiple gestation, arithmetic error of calculating fetal DNA fraction, and maternal status (cancer, blood transfusion, transplantation, chemotherapy, stem cell treatment, or autoimmune disease), etc.

REFERENCE

- Placenta. 2014 Feb;35 Suppl(Suppl):S64-8. Review: cell-free fetal DNA in the maternal circulation as an indication of placental health and disease
- PLoS One. 2016 Jan 15;11(1):e0146794. False Negative NIPT Results: Risk Figures for Chromosomes 13, 18 and 21 Based on Chorionic Villi Results in 5967 Cases and Literature Review
- JAMA. 2015 Jul 14;314(2):162-9. Noninvasive Prenatal Testing and Incidental Detection of Occult Maternal Malignancies
- N Engl J Med. 2015 Apr 23;372(17):1639-45. Copy-number variation and false positive prenatal aneuploidy screening results
- Clin Genet. 2016 May;89(5):523-30. Clinical implementation of NIPT - technical and biological challenges

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Fetal Fraction may be Insufficient in following cases

Significance of Fetal Fraction

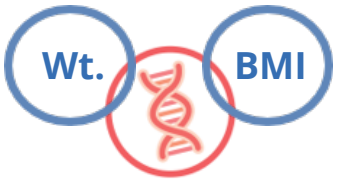
The G-NIPT test isolates trace amounts of fetal-derived DNA present in maternal blood and screens for fetal chromosomal abnormalities. Fetal derived DNA from placental cells flow into maternal blood and can be detected in the maternal blood from fourth week of pregnancy. As the gestational period increase, the amount of fetal DNA is maternal blood also increase. The average fetal fraction is known to be 11-13.4% at the gestational week of 10 -22 weeks. But this can vary significantly from person to person.

At least 4% fetal fraction is required for accurate analysis of chromosomal abnormality in NIPT tests. G-NIPT test can analyze autosomal chromosome abnormalities in 3-4% fetal fractions. If fetal fraction is less than 3%, all chromosomal abnormalities cannot be analyzed and are reported as “no result”.

*** G-NIPT Test Scope**

Fetal Fraction	Autosomal Chromosome	Sex Chromosome
>4%	Reported	Reported
3-4%	Reported	No Result
<3%	No Result	

Cause of Insufficient Fetal Fraction



1. The main causes of low fetal fraction are gestational weeks and mother’s weight (BMI). When the gestational week is short, the fetal fraction is normally low. If the mother’s weight and BMI are high, the maternal blood volume increase and the fetal fraction is diluted. In addition, the maternal derived DNA from the mother’s fat cells increase, so the fetal fraction is relatively reduced.

2. Other than the maternal weight and gestational week, low fetal fraction is also known to be highly associated with chromosomal abnormalities in the fetus. The G-NIPT test also showed that in 11.4% of the mothers with low fetal fraction, amniocentesis revealed chromosomal abnormalities.

Guidelines

American College of Medical Genetics and Genomics recommendations for when the fetal fraction is found insufficient are as below

- If fetal fraction is low, even with adequate gestational weeks, this may indicate a high risk of chromosomal abnormalities. Hence, conformational test such as amniocentesis is recommended rather than blood redraw.
- In case of severe obesity, fetal fraction is likely to be too low for Non-invasive prenatal test (NIPT), so screening with another prenatal testing option is recommended.

If the fetal fraction is found insufficient in the result, blood redraw or amniocentesis should be referred taking into account the mother’s gestational age, weight and other risks.

* References

- Wang E et al., Gestational age and maternal weight effects on fetal cell-free DNA in maternal plasma, Prenat Diagn 2013;33:662-6.
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