

Patient name: Jane Doe	Sample type: Blood	Report date: 07/10/2018
DOB:	Sample collection date: 06/15/2018	Invitae #: RQ123456
Sex: Female	Sample accession date: 06/25/2018	Clinical team: Michael Henderson Zoe Holzberger
MRN:	Estimated due date: 08/24/2019	
Pregnancy type: Singleton	Gestational age: 12 weeks	

Reason for testing

Advanced maternal age

Test performed

- Invitae NIPS for Singleton Pregnancies (chromosomes 13, 18, 21)
 - Add-on for Sex Chromosomes (will report predicted fetal sex)
 - Add-on for Select Microdeletions (1p36, 4p16.3, 5p15.2, 15q11.2, 22q11.2)

+
RESULT: ANEUPLOIDY DETECTED
Fetal fraction: 10%

CHROMOSOME	RESULTS	PPV (%)
Chromosome 21	POSITIVE: ANEUPLOIDY DETECTED Results consistent with pregnancy at increased risk for trisomy 21	82%
Chromosome 18	NEGATIVE: NO ANEUPLOIDY DETECTED Results consistent with two copies of chromosome 18	
Chromosome 13	NEGATIVE: NO ANEUPLOIDY DETECTED Results consistent with two copies of chromosome 13	
Sex chromosome	POSITIVE: ANEUPLOIDY DETECTED Results consistent with pregnancy at increased risk for XYY	N/A**
Microdeletions (1p36, 4p16.3, 5p15.2, 15q11.2, 22q11.2)	POSITIVE: ANEUPLOIDY DETECTED Results consistent with a microdeletion in the 22q11.2 region NEGATIVE: NO ANEUPLOIDY DETECTED Results consistent with no microdeletions detected in the regions of 1p36, 4p16.3, 5p15.2, 15q11.2	N/A**

Clinical summary

This is a screening test; therefore, false positive and false negative results can occur. Results may be reflective of fetal, placental, or maternal conditions. No irreversible clinical decisions should be made based on these screening results alone. Clinical correlation is indicated. If definitive diagnosis is desired, chorionic villus sampling or amniocentesis would be necessary. Genetic counseling is recommended. The fetal fraction (FF) is estimated to be 10%. FF estimation is one component of the Invitae non-invasive prenatal screening algorithm and is combined with other quality metrics to determine the confidence in the results. The FF estimate is not used in isolation to exclude samples.

Positive predictive value (PPV) is calculated based on stated performance, maternal and gestational age as provided on the Test Requisition Form (TRF). Other factors may impact the patient specific PPV.

*Performance data for sex chromosome aneuploidy is limited, precluding accurate calculation of PPV.

**Performance data for microdeletion analysis is limited, precluding accurate calculation of PPV.

Next steps

A positive non-invasive prenatal screen (NIPS) result indicates that the pregnancy is at increased risk of a specific chromosome disorder.

It is important to note that this is a screening test; therefore even after a positive result, it is always possible that the pregnancy is not affected by a chromosome disorder. The actual chance the pregnancy is affected depends on many factors, including the patient's clinical and family history.

- No irreversible clinical decisions should be made based on these screening results alone.
 - The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine state, "All women with a positive cell-free DNA (also known as NIPS) test result should have further detailed counseling and testing and should have a diagnostic procedure before any irreversible action is taken."¹
 - Diagnostic testing using either chorionic villus sampling (CVS) or amniocentesis is required for a definitive prenatal diagnosis.
 - Confirmation prior to birth can also help with pregnancy and neonatal management.
 - For information about chorionic villus sampling (CVS) or amniocentesis please visit:
 - Amniocentesis: <https://www.marchofdimes.org/pregnancy/amniocentesis.aspx>
 - CVS: <https://www.marchofdimes.org/pregnancy/chorionic-villus-sampling.aspx>
 - To learn more about prenatal diagnostic testing with Invitae please visit www.invitae.com/prenatal-diagnosis.
 - Genetic counseling is recommended to further explain the implications of this test result.
 - Your doctor can also refer you to a local genetic counselor. Please visit <https://www.findageneticcounselor.com>
 - You can also speak with an Invitae genetic counselor. Please visit www.invitae.com/counseling

1. American College of Obstetricians and Gynecologists. Screening for fetal aneuploidy. Practice Bulletin No. 163. Obstet Gynecol. 2016;127:e123-e137

Performance Metrics

CHROMOSOME	N	SENSITIVITY	95% CI	SPECIFICITY	95% CI	ACCURACY	95% CI
21	500	99.9% (90/90)	96.0-100.0	99.8% (409/410)	98.7 - 100.00	-	-
18	501	97.4% (37/38)	86.2-99.9	99.6% (461/463)	98.5 - 100.00	-	-
13	501	87.5% (14/16)	61.7-98.5	99.9% (485/485)	99.2 - 100.00	-	-
Monosomy X	508	95% (19/20)	75.1-99.9	99.0% (483/488)	97.6 - 99.7	-	-
XX	508	97.6% (243/249)	94.8-99.1	99.2% (257/259)	97.2 - 99.9	98.40%	96.9-99.3
XY	508	99.1% (227/229)	96.9-99.9	98.9% (276/279)	96.9 - 99.8	99.00%	97.7-99.7
XXX/XXY/XYX	Other sex aneuploidies will be reported if detected. (Limited data of these more rare aneuploidies preclude performance calculations)						
Microdeletions & other autosomal aneuploidies	Microdeletions and other autosomal aneuploidies if requested and detected will be reported. (Limited data of these more rare aneuploidies preclude performance calculations)						

†Data on file at Illumina, Inc. regarding Performance and Method Comparison studies

Methods

Nucleic Acid extraction, DNA sequencing, and analysis of sequencing results to determine fetal aneuploidy.

Disclaimer

The manner in which this information is used to guide patient care is the responsibility of the health care provider, including advising for the need for genetic counseling or diagnostic testing. Any test should be interpreted in the context of all available clinical findings.

Limitations

The Invitae non-invasive prenatal screen is validated for aneuploidy of any chromosome, including 21, 13, 18, X, and Y and for specific deletions in chromosomal regions 1p36, 4p16.3, 5p15.2, 15q11.2, 22q11.2, in singleton pregnancies, with gestational age of at least 10 weeks 0 days. This is a screening test that looks only for specific chromosomal abnormalities. A normal result does not eliminate the possibility that the pregnancy is associated with other chromosomal or subchromosomal abnormalities, birth defects, genetic conditions, or other conditions, such as open neural tube defects or autism. There is a small possibility that the test results might not reflect the chromosomes of the fetus, but may reflect chromosomal changes of the placenta (confined placental mosaicism, CPM) or of you (maternal chromosomal abnormalities). Examples include maternal XXX, sex chromosome status, or benign and malignant maternal neoplasm. CPM may be associated with a higher chance for pregnancy complications or for uniparental disomy (UPD), which may affect the growth and development of the fetus. Some of these rare chromosomal aneuploidies may only occur in mosaic form. Clinical consequences depend on the chromosome involved and can not be predicted prenatally. This test, like many tests, have limitations, including false negative and false positive results. A negative test result does not eliminate the possibility of chromosomal abnormalities for the tested chromosomes or microdeletions. See performance metrics for test performance.

Disclosure

The Invitae non-invasive prenatal screen was developed by, and its performance characteristics were determined by Verinata Health, Inc. a wholly owned subsidiary of Illumina, Inc. The VHI laboratory is CAP-accredited and certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. The Invitae non-invasive prenatal screen has not been cleared or approved by the U.S. Food and Drug Administration.