INVITAE

INVITAE NON-INVASIVE PRENATAL SCREENING

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	**Clincial 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: NO ANEUPLOIDY DETECTED

Fetal fraction: 10%

CHROMOSOME	RESULTS	PPV (%)
Chromosome 21	**NEGATIVE: NO ANEUPLOIDY DETECTED** Results consistent with two copies of chromosome 21	
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	**NEGATIVE: NO ANEUPLOIDY DETECTED** Results consistent with two sex chromosomes (XX), predicted fetal sex is female	**N/A***
Microdeletions (1p36, 4p16.3, 5p15.2, 15q11.2, 22q11.2)	**NEGATIVE: NO ABNORMALITY DETECTED** Results consistent with no microdeletions detected in the regions of 1p36, 4p16.3, 5p15.2, 15q11.2, 22q11.2	**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.

This prenatal test is performed by Verinata Health, Inc., a wholly owned subsidiary of Illumina, Inc.
Illumina, Inc., 200 Lincoln Centre Dr, Foster City, CA 94404 1-855-266-6563
CAP, CLIA, CA Laboratory Director: Sue Beruti, MD, MHA **CAP:** 7519312 **CLIA:** 05D2013691 **California License #:** CLF00340177
State of New York Laboratory Directors: Maria L. Cremona, PhD, FACMG, Eileen De Feo, PhD

Next steps

A negative result on a non-invasive prenatal screen (NIPS) indicates that the pregnancy is not at an increased risk of one of the specific chromosome disorders analyzed. If the test included sex chromosome analysis, the report will include the predicted fetal sex.

It is important to note that this is a screening test; therefore even after a negative result, there is always a small chance that the pregnancy could still be affected with a chromosome disorder. NIPS does not screen for all possible genetic conditions or other birth defects, please follow the recommended prenatal screening guidelines for these other conditions.

- These results should be considered in the clinical context of the pregnancy including abnormal ultrasound findings, other positive prenatal screening results, and personal or family history.
- If you have questions about these results, ask your doctor about a referral for genetic counseling. A genetic counselor can further explain the implications of this test result and assess personal family health history, which may identify health information that merits additional consideration.
  - 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

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/XYY	Other sex aneuploidies will be reported if detected. (Limited data of these more rare aneuploidies preclude performance calculations)						
Microdeletions & other autosomal aneuplodies	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.