CENTOGENE
THE RARE DISEASE COMPANY

CENTOGENE GmbH • Am Strande 7 • 18055 Rostock • Germany

XXX

Order no.: xxx
Order received: xxx
Sample type / Sample collection date:
blood, Cell-Free DNA BCT® / xxx
Report date: xxx
Report type: Final Report

Patient no.: **xxx**, First Name: **xxx**, Last Name: **xxx**
DOB: **xxx**, Sex: **female**, Your ref.: **xxx**
NIPT BCT tube no.: **NI000xxxxxx,** Gestational age at sample collection (week): **12**

Additional report recipient(s): XXX

Test(s) requested: Non-invasive prenatal testing CentoNIPT® Singleton

CLINICAL INFORMATION

Normal pregnancy

POSITIVE RESULT
Aneuploidy identified

INTERPRETATION

The analysis indicates a high risk for trisomy 21 (Down syndrome).

Since NIPT is a screening test, validation by an independent invasive method is recommended (e.g. karyotyping or chromosomal microarray). Genetic counselling and clinical correlation are also advised.

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RESULT SUMMARY

	Aneuploidy (Yes/No)
Chromosome 21	**YES (trisomy)**
Chromosome 18	No
Chromosome 13	No
Gonosomal chromosomes	No
Fetal Fraction	6%
Fetal gender	male

METHODS

CentoNIPT® is based on the in vitro diagnostic test Illumina VeriSeq™ NIPT Solution and its performance has been validated by CENTOGENE. This noninvasive IVD test utilizes whole-genome sequencing of cfDNA fragments derived from maternal peripheral whole blood samples. The included workflow consists of automated sample preparation, library batching in 48- or 96-sample volumes and next generation whole genome sequencing. Paired-end sequencing data is analyzed by the Illumina VeriSeq™ NIPT Assay Software to combine chromosome read numbers and fetal fraction, and a report is generated.

LIMITATIONS

This NIP-test is only designed to analyze full chromosome aneuploidies of the fetus after 10 weeks of gestation. Reported are overrepresentations of chromosomes 21, 18 and 13, as well as the sex chromosome aneuploidies X0, XXX, XXY and XYY. Fetal gender mismatch is a potential rare occurrence due to biological or statistical reasons, as an algorithm is used to predict gender. However, it does not influence the overall test performance for autosomal aneuploidies. Chromosome aneuploidies in general for a twin gestation can be detected by this test but cannot be attributed to individual twin fetuses and sensitivity and specificity for detection of aneuploidies in twin gestations are limited. In case of twin gestations, the detection of chromosome Y indicates that at least one of the fetus is male; however, the fetal gender of each individual twin cannot be determined by the test.

Results might not reflect the chromosomes of the baby, but instead reflect chromosomal changes to the placenta (confined placental mosaicism), or in the mother (chromosomal mosaicism). Test results can be confounded by maternal and /or fetal factors like recent maternal blood transfusion, maternal malignancy, and stem cell therapy. Especially in case of organ transplantation from a male donor for the mother, sex chromosome status for the fetus cannot be determined by this test.

Negative results (reported as "No Aneuploidy Detected") do not eliminate the possibility of chromosomal abnormalities of the tested chromosomes. A negative result does not eliminate the possibility that the pregnancy has other chromosomal abnormalities (for example microdeletions), genetic conditions or birth defects, for example open neural tube defects or others. Noninvasive prenatal testing (NIPT) based on cell-free DNA analysis from maternal blood is a screening test; it is not diagnostic. Test results must not be used as the sole basis for diagnosis. Further confirmatory testing is necessary prior to making any irreversible pregnancy decision.

SENSITIVITY AND SPECIFICITY FOR TRISOMIES 21, 18 AND 13

	TRISOMY 21	**TRISOMY 18**	**TRISOMY 13**
Sensitivity	>99.9% (130/130)	>99.9% (41/41)	>99.9% (26/26)
2-sided 95% CI	(97.1%, 100%)	(91.4%, 100%)	(87.1%, 100%)
Specificity	99.9% (1982/1984)	99.9% (1995/1997)	99.9% (2000/2002)
2-sided 95% CI	(99.63%, 99.97%)	(99.64%, 99.97%)	(99.63%, 99.97%)

Numbers in brackets next to sensitivity/specificity depict analyzed cases. VeriSeq™ NIPT Solution v2, Illumina, Inc. 2019

CONCORDANCE FOR GONOSOMAL ANEUPLOIDIES AND FETAL GENDER

	XX	**XY**	**X0**	**XXX**	**XXY**	**XYY**
Percent Concordant	100% (21/21)	100% (15/15)	90.5% (19/21)	100% (17/17)	100% (23/23)	91.7% (11/12)

Concordance compared to clinical reference standard outcome and cytogenetic results; numbers in brackets depict analyzed cases. VeriSeq™ NIPT Solution v2, Illumina, Inc. 2019

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ADDITIONAL INFORMATION

Please note that under the German Genetic Diagnostics Act the responsible physician is only allowed to report the gender after the 12th week of the pregnancy.
Due to legal restrictions - even if requested - fetal gender will not be included and/or disclosed in the report in selected countries (particularly China and India).
To exclude mistaken identity in your clinic, several guidelines recommend testing a second sample that is independently obtained from the proband. Please note that any further analysis will result in additional costs.

DISCLAIMER

Samples for NIP-testing can only be accepted if provided to CENTOGENE within the CentoNIPT Streck tube. Due to technical limitations and depending on certain circumstances, the collection of further sampling may be requested by CENTOGENE for a small percentage of tests in order to be able to provide adequate testing results. Any preparation and processing of a sample from patient material provided to CENTOGENE by a physician, clinical institute or a laboratory (by a "Partner") and the requested genetic testing itself is based on the highest and most current scientific and analytical standards. However, in very few cases genetic tests may not show the correct result, e.g. because of the quality of the material provided by a Partner to CENTOGENE or in cases where any test provided by CENTOGENE fails for unforeseeable or unknown reasons that cannot be influenced by CENTOGENE in advance. In such cases, CENTOGENE shall not be responsible and/or liable for the incomplete, potentially misleading or even wrong result of any testing if such issue could not be recognized by CENTOGENE in advance.

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