TYKS Laboratory

PATIENT INFORMATION FOR NON-INVASIVE PRENATAL TESTING (NIPT)

WHAT IS A NIPT TEST?

Most of the pregnancies go to term uneventfully, but sometimes specific changes are detected in the fetal development that may indicate abnormality in the fetal genetic material. Some of these abnormalities are numerical chromosomal changes, where fetuses have an extra chromosome compared to normal chromosomal number. For example, in the most common chromosomal abnormality syndrome, Down syndrome, the fetus has three copies (trisomy) of chromosome 21 instead of the normal two copies. Other common chromosome abnormality syndromes are trisomy 18, where the fetus has three copies of chromosome 18, and trisomy 13, where the fetus has three copies of chromosome 13. Turner syndrome and Klinefelter syndrome are the most common sex chromosome abnormality syndromes, where the fetus has only one X chromosome instead of two (X0, Turner) or two X chromosome instead of one (XXY, Klinefelter).

Abnormalities in the other chromosomes are very rare. Numerical changes can affect any chromosome, and in addition, smaller changes that do not change the number of chromosomes but change the structure of the chromosome (copy number changes) can be present in any chromosome. These rare abnormalities may affect the fetal growth or placental function, or sometimes cause congenital anomalies in the fetus. Sometimes these abnormalities are restricted only to the placenta, or they are mosaics, meaning that the change can be detected only in a small fraction of cells of the fetus.

NIPT test is a non-invasive **screening test** that can be used to predict the risk of chromosomal changes in the fetus. NIPT test cannot be used as a diagnostic test.

HOW IS NIPT TEST PERFORMED?

NIPT test is based on the cell free fetal DNA (cffDNA), which is released from the placenta into the maternal bloodstream. The amount of cffDNA in maternal blood is sufficient for the analysis starting from the pregnancy week 10 onwards, and after that, testing is possible at any time until term. One tube of venous blood is drawn from the mother for the test, and at the same appointment information regarding the test and meaning of the results are explained in sufficient detail. The test request form is filled. If the expanded test is selected (see test content below), the informed consent is signed. The blood sample is then analyzed in the Genomics laboratory of Turku University Hospital. Sometimes the results may be delayed due to technical reasons, or sometimes a new sample is needed because the amount of cffDNA is too low for the analysis in the original sample. Health care professionals always interpret the test results.

TEST CONTENT OPTIONS

The basic test (B-NIPTtri 6373) screens for the most common chromosomal abnormality syndromes: the changes in the numbers of chromosomes 13, 18, 21, X and Y. If requested, fetal sex is reported. However, if a sex chromosome abnormality is detected, it will be reported even if the fetal sex is not requested.

The expanded test (B-NIPTdel 6374) screens for numerical chromosome abnormalities in all chromosomes and, in addition, chromosomal structural changes (copy number changes) that are larger than 7 Mb. Such large changes usually have clinical relevance. If requested, fetal sex is reported. However, if a sex chromosome abnormality is detected, it will be reported even if the fetal sex is not requested.

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INFORMED CONSENT

For the expanded NIPT test, a signed informed consent is mandatory. Expanded test may reveal findings that are not related to the initial referral reason (incidental findings). By signing the consent the mother agrees the reporting of these findings. It is important that the occurrence and relevance of incidental findings are comprehensively discussed before ordering the expanded test.

BENEFITS OF THE TEST

As the name of the test indicates, NIPT is a non-invasive test, which means that the screening of the fetal genetic abnormalities can be performed from a maternal blood sample. With non-invasive test the small risk of miscarriage due to the invasive procedure is avoided. The NIPT test can be performed from the pregnancy week 10 onwards, and the results are provided in a short time. NIPT test can also be performed in twin pregnancies and in pregnancies resulting from donor eggs or embryos.

LIMITATIONS OF THE TEST

NIPT test is not a diagnostic test but a **screening test, which provides a computational risk of the chromosome abnormality for the fetus. Also, fetal gender is a prediction.** Screening test means that there is always a small risk for false positive and false negative result. As a result, it is extremely important to confirm abnormal NIPT test results with invasive test, preferably with amniotic fluid testing. Normal result does not exclude the possibility that the fetus has a genetic abnormality that the NIPT test is not intended to detect. Other factors that may affect the results of the test are maternal obesity, certain medications and organ transplantations. If the pregnancy has started as a twin pregnancy but the other twin has demised, it is not recommended to take NIPT test.

Sensitivity of the fetal sex determination is ~99.5%, meaning that in some cases the result of the NIPT test does not reflect the gender of the fetus. For example, sometimes a low level chromosome X monosomy is detected, but it originates from the mother instead of the fetus. Also, sometimes low level chromosome Y material can be detected although the fetus is female. In this case the most common reason in vanishing twin or the placenta has both XX and XY cells. If the mother has received a donor transplantation or a blood transfusion from a male donor, this can also sometimes be seen as Y chromosome material in the test.

If a chromosomal abnormality is detected in twin pregnancy, it is not possible to conclude which fetus is affected, and therefore the results should be confirmed with amniotic fluid testing. If the sex of the fetuses is requested in twin pregnancy, the results state if the Y chromosome is present or not in the analyzed sample. If the Y chromosome is not present, it means that both fetuses are females. If the Y chromosome is present, it means that either one or both fetuses are males, but the genders cannot be exclusively determined.

In rare occasions, an abnormality of maternal origin is detected instead of fetal origin (incidental findings). These are for example maternal congenital chromosome aneuploidies or maternal malignancies. If these incidental finding are detected, the mother should be offered targeted counselling and monitoring to clarify the significance of the finding.

RESEARCH USE

Leftover samples and results may be used in the internal research, development and validation of the laboratory processes in relation to NIPT testing. Disposal of the leftover sample and results can be requested at any time from the laboratory by a written request. Results of the testing may be presented anonymously in the scientific congresses and/or publications. Personal identification data will never be published.