TDL GENETICS

Information for healthcare professionals

Non-invasive prenatal testing

Genetic testing during pregnancy

Performed in the UK

Targeted screening for specific common chromosome disorders

Our NIPT assay is designed to screen for:

- Trisomy 21 (Down syndrome), which is associated with moderate to severe intellectual disability, congenital heart defects and other malformations;
- Trisomy 18 (Edwards syndrome) and trisomy 13 (Patau syndrome), which are associated with severe brain and cardiac malformations. There is a high risk of stillbirth or death during infancy; and
- Sex chromosome aneuploidy (abnormalities in the number of X or Y chromosomes), which can be associated with malformations and infertility, Turner syndrome (45,X) and Klinefelter syndrome (47,XXY). Triple X syndrome and XYY syndrome can also be detected. This screen is optional (no additional cost).

In addition, NIPT can also assess fetal sex. This is optional (no additional cost).

NIPT does not screen for non-chromosome disorders, familial mutations, malformations, fetal growth or fetal viability.

Non-invasive prenatal testing (NIPT) screens for the presence of specific chromosome disorders in the developing fetus. The test analyses fragments of cell-free DNA in maternal plasma that have been released from both maternal and placental cells.

By analysing the proportions of cell-free DNA fragments derived from different chromosomes or chromosome regions, NIPT can screen for the presence or absence of specific chromosome disorders.

NIPT is more accurate than first trimester maternal serum screening and ultrasound in identifying pregnancies with or without these disorders.

TDL Genetics uses the NIPT assay VeriSeq NIPT Solution v2, which is manufactured by Illumina and is processed at our laboratory in London.

Accuracy of NIPT

NIPT provides fewer false-positive and false-negative results than combined first trimester screening for trisomy 21, 18 and 13.

It is important to note that NIPT is a screening test and does not provide a definitive genetic diagnosis, as NIPT cannot differentiate potential chromosome differences between the placenta and fetus. A definitive genetic diagnosis of the fetus requires cytogenetic analysis of either amniotic fluid or chorionic villus sampling (CVS).

Accuracy (T21, T18, T13)	Sensitivity*	False-positive rate#
Combined first trimester screening	82%	1 in 26
NIPT	>99%	<1 in 1,000

* Proportion of fetuses with trisomy correctly identified by the test as high probability of disorder.

\# Proportion of normal fetuses incorrectly identified by the test as high probability of disorder.

NIPT Performance data in a general screening population

	Detection rate/sensitivity	Specificity
Trisomy 21	>99.9% (95% CI:97.1%)	>99.90% (95% CI:99.63%)
Trisomy 18	>99.9% (95% CI:91.4%)	>99.90% (95% CI:99.64%)
Trisomy 13	>99.9% (95% CI:91.4%)	>99.90% (95% CI:99.64%)

When to perform NIPT

NIPT should not be performed before a gestational age of 10 weeks. However, it is suitable at any time after that, preferably while there is sufficient time for further investigation or decision-making (should this be required). An ultrasound scan is required prior to NIPT to confirm dates and fetal viability, and to check for twins. Performing first trimester screening before NIPT may provide supplementary information regarding the status of the fetus.

Who is eligible for NIPT?

Eligible patients:

- Women who are at least ten weeks pregnant
- Women with twin pregnancies
- Women with IVF pregnancies

NIPT is not suitable for patients with:

- Recent maternal blood transfusion
- Maternal mosaicism
- Maternal prior organ transplant/stem cell transplant
- Maternal copy number variations
- Maternal autoimmune disease
- Fetoplacental mosaicism/confined placental mosaicism
- Maternal neoplasms (benign and malignant)
- Pregnancies with fetal demise/vanishing twin

Patients with a twin pregnancy are not eligible for the sex chromosome aneuploidy component of the screen.

Reporting results

Results will be ready within 3–5 business days upon receipt of sample in the laboratory.

TDL first checks that there is sufficient cell-free fetal DNA in the maternal sample and quality data to provide an accurate assessment. A re-collection may be recommended if the sample is not suitable or an assessment may not be feasible.

The report then summarises the screening assessment for each disorder specified by the requesting doctor (see example below).

Example report

Chromosome	Result	Recommendation
Trisomy 21	**HIGH PROBABILITY**	Genetic counselling and additional testing
Trisomy 18	Low probability	Review result with patient
Trisomy 13	Low probability	Review result with patient
Sex chromosome aneuploidy	Not requested	--
Fetal sex	Male	Review result with patient

A HIGH PROBABILITY NIPT result should always be confirmed by amniocentesis or CVS before making any decision regarding subsequent management of the pregnancy.

Limitations of NIPT

The VeriSeq NIPT Solution v2 is not validated for use in pregnancies with more than two fetuses, fetal demise, mosaicism, partial chromosome aneuploidy, triploidy, translocations, maternal aneuploidy, transplant or malignancy. VeriSeq NIPT Solution v2 does not detect neural tube defects. Certain rare biological conditions may also affect the accuracy of the test.

For twin pregnancies, HIGH PROBABILITY test results apply to at least one fetus; male test results apply to one or both fetuses; female test results apply to both fetuses. Due to the limitations of the test, inaccurate results are possible.

A LOW PROBABILITY result does not guarantee that a fetus is unaffected by a chromosomal or genetic condition. Some non-aneuploid fetuses may have HIGH PROBABILITY results. In cases of HIGH PROBABILITY results and/or other clinical indications of a chromosomal condition, confirmatory testing is necessary for diagnosis.

If an assessment cannot be provided

On rare occasions, NIPT is unable to provide an assessment of the probability of specific chromosome disorders. This usually reflects the complex biology of genetics and pregnancy, and is not due to a failing in the laboratory.

If NIPT cannot provide a specific assessment, it is not worth repeating the NIPT (unless advised by the laboratory). A decision about other tests (maternal serum screening, detailed ultrasound, amniocentesis or CVS) should be based on the doctor's assessment of all risk factors identified,and may require specialist consultation.

Further information

- TDL Genetics website: www.tdlpathology.com/tdlgenetics
- Borth H, et al. Analysis of cell-free DNA in a consecutive series of 13,607 routine cases for the detection of fetal chromosomal aneuploidies in a single center in Germany. Arch Gynecol Obstet. 2021 Jun;303(6):1407-1414.

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