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AMPATHCHAT

Ampath Genetics

Non-invasive prenatal testing (NIPT):Introducing the IONA® test

Non-invasive prenatal testing (NIPT)

NIPT is a safe and accurate prenatal screen to calculate the risk that a foetus has of being affected with a chromosomal condition, for example, Down Syndrome. NIPT makes use of cell-free DNA released from the placenta into the maternal bloodstream (Figure 1).

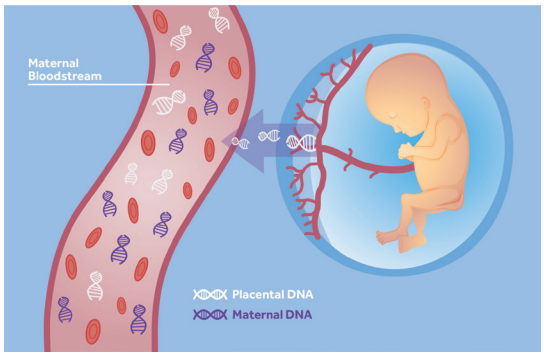

Figure 1: Cell-free DNA from the placenta is released into the maternal bloodstream during pregnancy.

Measuring the amount of cell-free DNA is now possible using a maternal blood sample. By calculating the ratio of DNA from the placenta, the risk of a foetus being affected with a chromosomal condition is calculated.

A trisomy occurs when a foetus inherits three copies of a chromosome instead of the usual two copies. Similarly, a monosomy occurs when one copy of a chromosome is inherited. Both trisomies and monosomies are referred to as aneuploidies, and are associated with adverse pregnancy outcomes (either miscarriage or a genetic condition).

The IONA® NIPT at Ampath

Ampath Genetics is pleased to announce the implementation of the IONA® non-invasive prenatal test at its National Reference Laboratory in Centurion, South Africa, as from November 2017.

The IONA® test uses the latest advances in genetic technology, allowing for fast and reliable results, while reducing the need for invasive testing and associated risks (such as procedure-related miscarriage).

The IONA® test estimates the probability that a foetus is affected with the following aneuploidies:

- Trisomy 21 (Down Syndrome)
- Trisomy 18 (Edwards Syndrome)
- Trisomy 13 (Patau Syndrome)

Testing for sex chromosome aneuploidies (Turner Syndrome, Klinefelter Syndrome, XYY Syndrome and XXX Syndrome) is also available for singleton pregnancies.

Key features of the IONA® test

- Reliable: CE-IVD (European Conformity In Vitro Diagnostic) NIPT performed at an accredited facility
- Fast: seven-day turnaround time
- Accurate: >99% detection rate
- Requires as little as 2% foetal fraction (see below)
- Available for singleton and twin pregnancies
- Can be performed on surrogate, donor and IVF pregnancies
- Blood can be taken from 10 weeks gestational age

How does the IONA® test work?

During pregnancy, cell-free foetal DNA from the apoptosing trophoblastic cells of the placenta enters the maternal bloodstream (Figure 1). Using a maternal blood sample, the IONA® test directly measures the cell-free DNA in the maternal plasma. The proportion of cell-free DNA that is attributed to the foetus is called the foetal fraction.

The IONA® test employs Next Generation Sequencing (NGS) technology to count chromosome copy numbers. By calculating the ratio of cell-free DNA from the placenta and the gestational carrier, the risk of a foetus being affected by Trisomy 21, 18, 13 or a sex chromosome abnormality is calculated.

IONA® test results

The IONA® test report gives a clear, easy-to-interpret result of high risk or low risk for each trisomy, as well as sex chromosome aneuploidies (Table 1). Foetal fraction and foetal sex (if requested) is also indicated.

Table 1: IONA® test results

Trisomy	Background risk	The IONA® test risk score	Clinical summary
Trisomy 21	1:171	> 95%	High-risk invasive test recommended
Trisomy 18	1:542	< 1:1,000,000 (< 0.0001%)	Low risk
Trisomy 13	1:1655	< 1:1,000,000 (< 0.0001%)	Low risk

Foetal fraction (%)	10%
Foetal sex	male

Benefits of the IONA® test

The IONA® test has a higher detection rate and lower false-positive rate than most conventional first and second trimester screening tests available at present, giving pregnant women, their families and their healthcare providers greater confidence in the result and reducing the need for unnecessary invasive and stressful tests, such as chorionic villus sampling or amniocentesis – both of which carry a small risk of miscarriage.

Clinical performance

Table 2: Clinical performance of the IONA® test

Aneuploidy	Detection rate	False positive rate	False negative rate
Trisomy 21	99%	0.02%	1.0%
Trisomy 18	91%	0.02%	8.6%
Trisomy 13	100%	0.01%	0.0%

Overall accuracy	>99.8%
Test failure rate	<0.5%

The clinical performance data of the IONA® test (Table 2) is based on >15 000 samples. The sensitivity for sex chromosome aneuploidies and sex determination are >93% and >99%, respectively.

Limitations of the IONA® test

Current NIPT technologies, including IONA®, cannot reliably perform aneuploidy testing of Chromosome 13, 18 and 21 on cell-free DNA derived from more than two foetuses.

When not to use the IONA® test

The IONA® test should not be used if the gestational carrier*:

- has cancer
- has had a recent blood transfusion
- is known to be chromosomally aneuploid for Trisomy 21
- is a known carrier of a mosaic cell line (such as XO)

As this test can also be used to test egg donor and surrogate pregnancies, the term gestational carrier is used, as the donor and surrogate are not the biological mother.

Caution must also be used if the gestational carrier has had an organ transplant (particularly from a male donor). This, in conjunction with the above, is of concern, as cell-free DNA from the gestational carrier is also present in the maternal bloodstream.

Thus, during pregnancy, both cell-free DNA from the gestational carrier and the foetus (placentally derived) are present in the maternal bloodstream. Aneuploidies or the presence of a Y-chromosome, derived from a male donor organ, which are maternally contributed to the cell-free DNA in the circulating bloodstream, can confound findings (as findings are ascribed to the foetus).

It is important to note that all non-invasive foetal tests performed on maternal blood are currently regarded as screening tests, and positive results should be followed up by an invasive diagnostic test (such as an amniocentesis). Furthermore, NIPT results should be interpreted in conjunction with any/all other antenatal tests.

Ampath Genetics offers diagnostic prenatal genetic test options, including karyotyping, to confirm high-risk results identified by NIPT. Even though further invasive testing is unnecessary for a negative IONA® test result, vigilance should still be maintained with regard to any foetal abnormalities, including those genetic disorders not screened for by the IONA® test.

Genetic counselling

Counselling from an HPCSA-registered genetic counsellor is available, upon professional referral, to do the following:

- discuss the merits and pitfalls with regard to all types of antenatal diagnostic options
- offer support to parents who experienced foetal loss and discuss laboratory testing to investigate possible causes
- counsel, explain recurrence risks, and guide parents and families with regard to reproductive options and laboratory testing in instances where a foetal abnormality has been identified

For genetic counselling, contact Sarah Walters at 012 678 1350/62 or walterss@ampath.co.za.

Queries

Please email nipt@ampath.co.za.

Alternatively, please contact:
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