VCGS Leaders in Genetic Health

the partumpost

Are you getting the most from your NIPT? Volume 1 Issue 6 December 2017

Evolution of percept™ NIPT

The first commercial NIPT tests became available in the USA in 2011 (1-3). Since that time there have been significant advances in our understanding of the biology of cell-free DNA (cfDNA) screening, together with on-going improvements in cfDNA screening protocols.

In this edition of the partum**post** we highlight developments in the evolution of the *percept* NIPT offered by VCGS, now Australia's most advanced cfDNA screening option (4-7). Discover what makes *percept* unique and see whether you're getting the most from your NIPT.

Analysis of all 24 chromosomes:

percept NIPT includes an analysis of all 24 chromosomes rather than the 3-5 chromosomes analysed using standard NIPT (5). Our recent collaborative study published in *Science Translational Medicine* highlights the benefits of this approach by identifying pregnancies at increased risk for a wide range of complications including miscarriage, rare trisomy mosaicism, uniparental disomy and fetal growth restriction associated with confined placental mosaicism (8).

High test sensitivity at low fetal fractions:

percept enables high sensitivity (detection rates) for trisomy from just 2.5% fetal fraction (4). Observed sensitivities for trisomies 21, 18 and 13 using *percept* NIPT are >99%, 96% and >99% respectively, based on over 400 trisomies identified from 30,000 pregnancies.

Recollection rates are below 1% and failed NIPT due to persistently low fetal fraction (<2.5%) occurs in less than 2 in every 1,000 referrals.

Trisomic fraction and whole chromosome analysis:

Trisomic fraction (TF) is the proportion of trisomic cfDNA found in affected pregnancies. This measurement is unique to *percept* NIPT. Each trisomic result is confirmed by physically plotting the increase in sequence counts across the length of the affected chromosome.

The amount of trisomic cfDNA in the sample is then calculated and compared with the fetal fraction. This helps identify pregnancies affected by placental mosaicism and increases the likelihood of diagnostic confirmation (positive predictive value; PPV) in those pregnancies without obvious mosaicism.

Identification of mosaicism:

The fetal component of cfDNA is derived from the placenta (fetal fraction) while the majority of the cfDNA originates from the mother (4). Chromosome abnormalities confined to the placenta are one of the most common causes of false positive NIPT results.

Every high risk result identified by *percept* NIPT is analysed for evidence of mosaicism. If mosaicism is suspected this finding is included in the patient report to help guide pregnancy management. This analysis is also unique to *percept*.

CVS or amniocentesis:

VCGS provides accurate and contemporary advice on the choice of invasive diagnostic procedure based on trisomy outcome data from more than 30,000 pregnancies.

By using fetal fraction, trisomic fraction and whole chromosome analysis to predict non-mosaic trisomy, positive predictive values (PPVs) in this group exceed 95% for trisomies 21 and 18 and 90% for trisomy 13 (VCGS data on file).

Our patient reports have been updated recently to reflect these improved PPVs. NIPT results that indicate mosaicism are more likely to be associated with confined placental mosaicism and normal amniocentesis results (VCGS data on file).

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Other pathogenic findings:

A significant advantage of *percept's* whole genome approach is our ability to detect unbalanced chromosome conditions during routine screening for aneuploidy. Clinically significant findings reported since our move to 'all chromosome' screening include de novo deletions, duplications, unbalanced translocations and isochromosomes (VCGS data on file).

Despite these advantages, *percept* is **not a substitute** for prenatal diagnosis using CVS or amniocentesis. *percept* will report on clinically significant chromosomal imbalances when detected, but a negative result does not remove the possibility of an unbalanced chromosome condition in the pregnancy. *percept* NIPT is an excellent screening option for women who want information on a wider range of chromosome conditions.

Translocation analysis:

Carriers of balanced reciprocal translocations now have a non-invasive option for prenatal screening by using *percept* NIPT (7). Demand for this NATA accredited service has been high as awareness grows, with enquiries coming from throughout Australia and New Zealand.

Once eligibility is established, blood can be collected anytime from 11 weeks of gestation. A prior ultrasound scan is required to confirm dates, confirm singleton viable pregnancy and to exclude evidence of recent co-twin demise.

Triplet pregnancies and complications of co-twin demise:

percept now provides a screening option for women carrying triplets. Our very low limit of detection combined with several independent measures of fetal fraction provides women with additional reassurance to compliment ultrasound assessment of the pregnancy (6).

Our service also provides screening advice in the event of co-twin demise. Please contact us to determine the most appropriate gestation for *percept* NIPT when there is evidence for co-twin demise.

The 'go-to' NIPT when you need answers:

percept® cell-free DNA prenatal test

An advanced NIPT

Not every cfDNA screening test during pregnancy is straightforward. VCGS regularly receives repeat samples from within Australia and abroad where other NIPT tests have failed to produce a result. We often find causes for unusual test findings and find specific biological reasons for test failures. We offer solutions and provide answers where others just can't.

As a complete NIPT screening service we gather cytogenetic and pregnancy outcome data in real time. This means you can always have confidence in receiving the most comprehensive NIPT advice available.

So...are you getting the most from your NIPT?

See our website for more information about *percept™ : vcgs.org.au/perceptNIPT*

Please email vcgs@vcgs.org.au for any questions, topic suggestions or to subscribe to the partum**post**.

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