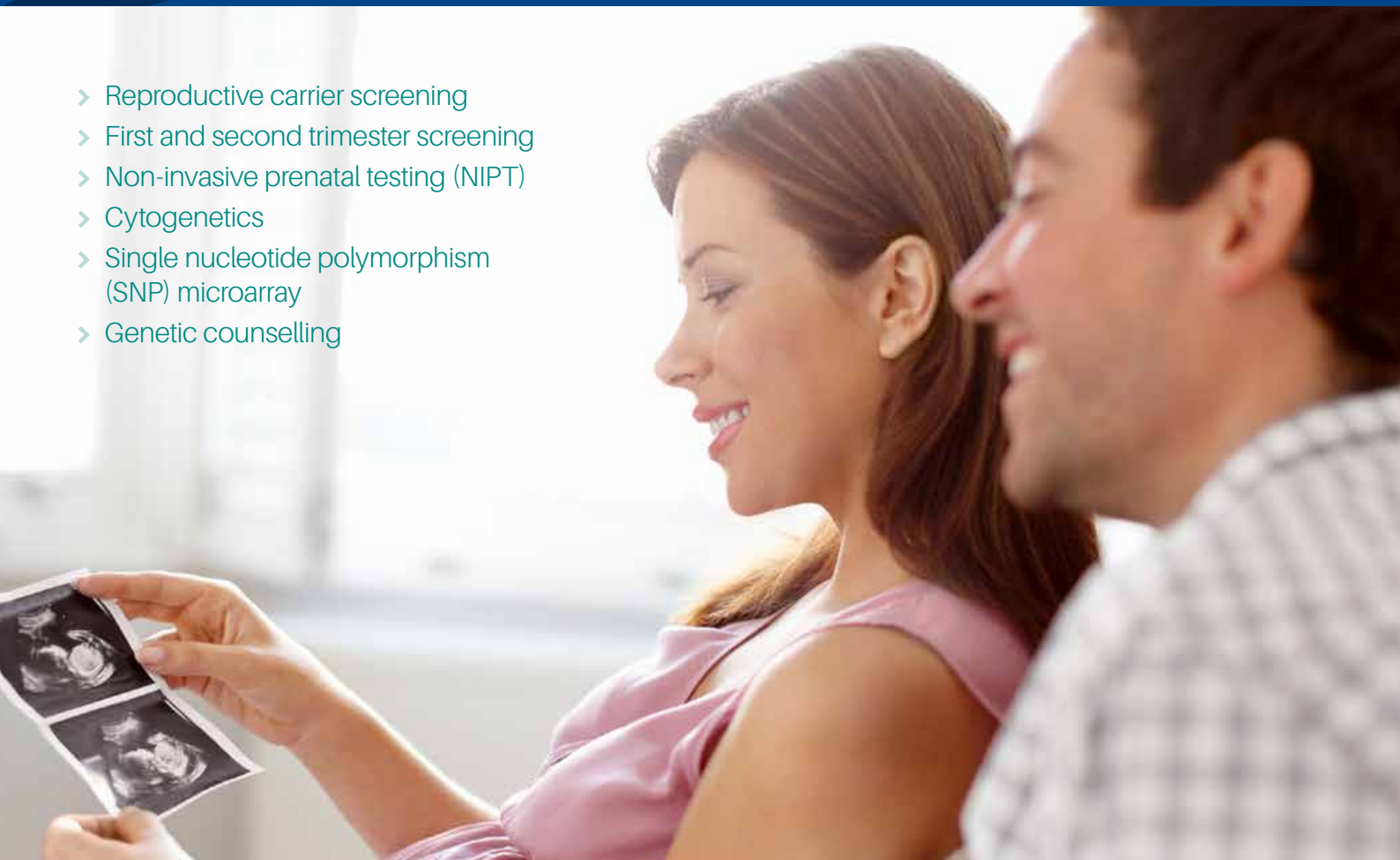
Sonic Genetics

Douglass Hanly Moir Pathology

Genetic testing: Preconception to pregnancy

Information for Doctors

- Reproductive carrier screening
- First and second trimester screening
- Non-invasive prenatal testing (NIPT)
- Cytogenetics
- Single nucleotide polymorphism (SNP) microarray
- Genetic counselling



Sonic Genetics provides a comprehensive range of preconception and pregnancy genetic testing services throughout Australia. Our genetic pathologists and medical scientists have established national and international reputations in genomic testing.

Our Genetic Pathologists

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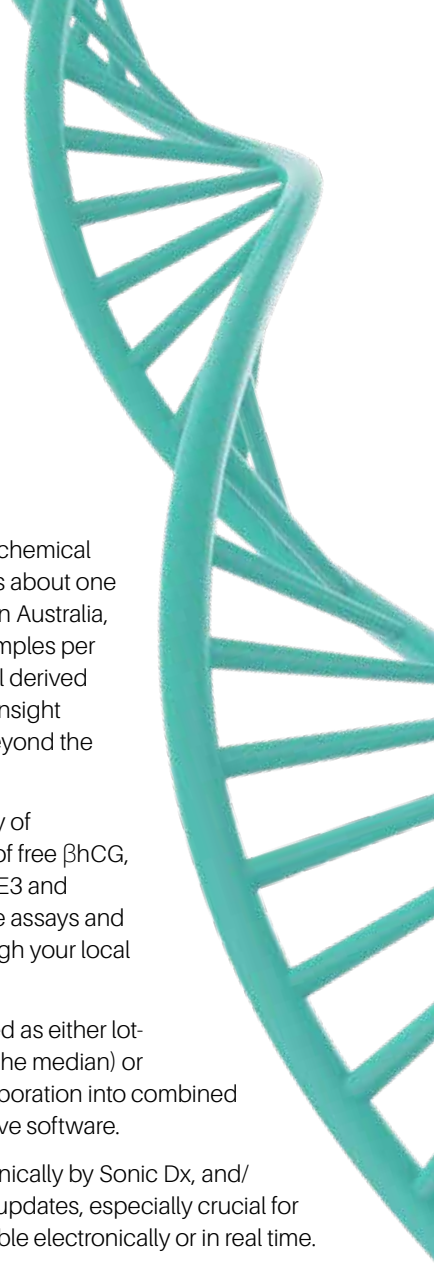
Sonic Genetics preconception to pregnancy testing services



Reproductive carrier screening

RANZCOG now recommends* that information about reproductive carrier screening for common disorders be offered to every woman either prior to conception (preferred) or in early pregnancy.

Whilst recognising the clinical and medico-legal significance of reviewing family histories, the reality is that most children with a familial genetic disorder do not have a family history of that disorder. The presence of a family history of a disorder is an important clue; the absence of such a history provides little information. A test to screen for genetic carriers can provide information about the risk of a familial disorder that is not evident from reviewing the family history.

There are two types of reproductive carrier screening provided by Sonic Genetics:

- A three-gene panel that looks for mutations responsible for three common genetic disorders: cystic fibrosis, spinal muscular atrophy and Fragile X syndrome. Approximately 6% of people in Australia will be identified as carriers for one or more of these disorders, and one in 160 couples will be found to be at risk of having an affected child.
- The Beacon expanded carrier screen is a screening test that looks for mutations in 299 autosomal recessive genes and 28 X-linked genes which cause serious disorders affecting babies and children. Approximately 70% of people in Australia will be identified as carriers for one or more of these disorders, and one in 30 couples will be found to be at risk of having an affected child.

First and second trimester screening

Sonic Healthcare's prenatal biochemical screening service annually tests about one quarter of all pregnant women in Australia, analysing more than 75,000 samples per year. Our panel of feto-placental derived biochemical markers provides insight into feto-maternal wellbeing, beyond the major trisomies.

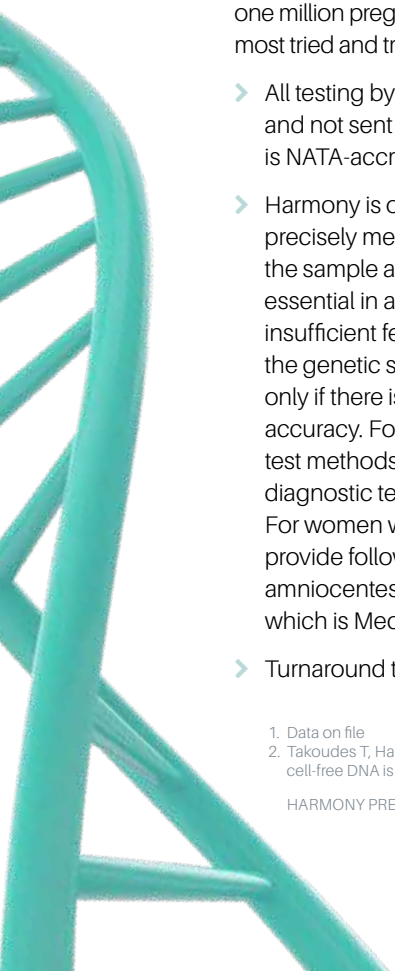
- Our laboratories use a variety of platforms to provide assays of free βhCG, PAPP-A, αFP, unconjugated E3 and PLGF. Combinations of these assays and platforms are available through your local Sonic Healthcare laboratory.
- Analytical results are provided as either lot-specific MoMs (multiples of the median) or concentration units for incorporation into combined risk assessment by interpretive software.
- Reports are available electronically by Sonic Dx, and/or by fax. Amendments and updates, especially crucial for MoM calculations, are available electronically or in real time.
- Turnaround time is typically one working day after specimen receipt.

*Prenatal screening and diagnosis of chromosomal and genetic conditions in the fetus in pregnancy (C-Obs59), RANZCOG College Statements and Guidelines

Non-invasive prenatal testing (Harmony®)

Non-invasive prenatal testing (NIPT) is a cell-free DNA-based blood test that screens for trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome), trisomy 13 (Patau syndrome) and 22q11.2 deletion (DiGeorge syndrome), with greater accuracy than conventional first trimester screening. NIPT can also screen for abnormalities in sex chromosomes and report gender. NIPT can be incorporated with biochemical screening (sometimes known as contingent screening). Many peer-reviewed studies have documented the clinical utility of the Harmony Prenatal Test. It has been used in more than one million pregnancies internationally,[1] and is one of the most tried and trusted forms of NIPT worldwide.

- All testing by Sonic Genetics is performed in Australia and not sent overseas. Sullivan Nicolaides Pathology is NATA-accredited to perform this test.
- Harmony is one of the few NIPTs globally that precisely measures the amount of fetal DNA in the sample and reports this to the clinician. This is essential in achieving an accurate result. If there is insufficient fetal DNA, the result may merely reflect the genetic status of the mother.[2] We report a result only if there is sufficient fetal DNA to be confident of accuracy. For patients with low fetal DNA, alternative test methods, such as serum screening or invasive diagnostic testing, may be more appropriate.
  For women who have a high-risk NIPT result, we provide follow-up cytogenetic testing on CVS or amniocentesis (rapid FISH test plus full karyotype) which is Medicare rebatable.
- Turnaround time is typically 5–8 days.



1. Data on file
2. Takoudes T, Hamar B. Performance of non-invasive prenatal testing when fetal cell-free DNA is absent. *Ultrasound Obstet Gynecol.* 2015 Jan; 45(1): 112.

Cytogenetics

Sonic Genetics is Australia's largest provider of cytogenetics testing, with reference laboratories in Melbourne (Melbourne Pathology) and Brisbane (Sullivan Nicolaides Pathology). They provide a comprehensive range of investigations including prenatal diagnosis, analysis of products of conception and preconception screening for couples experiencing recurrent miscarriages.

- The karyotype can be determined by cytogenetic analysis (light microscopy) or microarray. If a woman is at increased risk of having a chromosomally abnormal fetus (for example, fetal malformations on ultrasound), the fetal karyotype can be assessed by microarray (recommended) or cytogenetic analysis of CVS or amniocytes. Following a high-risk NIPT result, we recommend the fetal karyotype be assessed by cytogenetic analysis (microarray could miss the rare instance of trisomy due to a heritable translocation). Rapid testing for common trisomies is also available with a 24-hour turnaround.
- Most miscarriages are due to chromosome abnormalities that arise during the formation of the sperm or egg during early embryogenesis. They are not inherited and hence do not constitute a hazard in subsequent pregnancies. Many clinicians and couples wish to confirm this. The analysis can be done by microarray (recommended) or cytogenetic analysis of the products of conception.
- About 4% of couples with recurrent miscarriages have a balanced chromosome translocation in one or both parents that can cause miscarriages or congenital malformations in future pregnancies. If a potential parent is found to have a balanced translocation, we recommend genetic counselling. Preconception testing for a parental translocation should be done by cytogenetic analysis, not by microarray.

Single nucleotide polymorphism (SNP) microarray

Chromosomal microarray is a whole-genome screening test that can detect losses and gains of chromosomal material. With its high resolution, it has a better diagnostic yield than conventional cytogenetic testing in the prenatal setting. For example, where a fetal abnormality has been detected by ultrasonography, microarrays detect an abnormality in an additional 5-7% of cases.

- Microarray testing is now recommended for use in prenatal diagnosis in fetuses with one or more structural abnormalities identified on ultrasound. This test replaces the need for fetal cytogenetics. It is also recommended for the analysis of products of conception, as it does not depend on the presence of viable cells.
- Microarray testing is not recommended when testing for a parental translocation as it cannot detect a balanced rearrangement, that is, where there is no net gain or loss of chromosomal material. Similarly, it is not recommended when testing CVS or amniocytes for autosomal trisomy. It can identify the trisomy but may not detect the rare instance of trisomy due to a familial translocation.

Genetic counselling

Sonic Genetics actively encourages pre- and post- test genetic counselling where clinically applicable. To help you support your patients, we provide a link to a national list of general genetics clinics on our website at www.sonicgenetics.com.au/counsellingservices. We can also direct patients to private genetic counselling services in their region.

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For further information, please refer to our website, www.sonicgenetics.com.au or call us on 1800 010 447

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