SULLIVAN NICOLAIDES PATHOLOGY

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Reproductive carrier screening – making it work in your practice

- With reproductive carrier screening (RCS) now recommended by RANZCOG for women considering pregnancy, its adoption into routine practice presents challenges for the busy clinician.
- Selecting a screening test from an evolving and increasing range of options, from three-gene tests to expanded panels inclusive of hundreds of genes, requires knowledge and resources.
- What should be considered, and what guidelines do we have available?

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) recommends that any practitioner providing reproductive care should offer information about carrier screening to women who are planning a pregnancy or who are in early pregnancy.

What are the criteria for conditions covered by carrier screening?

In identifying couples at high risk of having a child with a severe autosomal recessive (AR) or X-linked (XL) disorder, it is generally accepted that RCS **must** cover conditions that are **sufficiently severe** that they would be expected to impact pregnancy decision-making or for which early diagnosis would be beneficial in other ways, such as informing management in the neonatal period.

What are the available guidelines and recommendations?

Guidelines play an important role in providing evidence-based information and advice. Globally, the American College of Medical Genetics and Genomics (ACMG) has set the standard with a four-tier-based practice resource, recommending that a tier 3 gene list, encompassing 113 AR/XL conditions, be offered to all women during pregnancy or prior to conception.

However, the relevance of the ACMG tier 3 gene list to the Australian population remains uncertain. While there are no comparable guidelines in Australia, it is expected that local experience and the comprehensive work performed by the national RCS study Mackenzie's Mission (MM), will inform the development of any future guidelines.

Learnings from an extensive review of our expanded gene panel

In 2022, we performed a thorough review of the genes tested in our Sonic Genetics custom screen, Beacon, to optimise the inclusion of conditions that met the criteria identified for RCS.

Data from 1,624 females and 1,100 males was analysed to determine whether the ACMG-recommended approach would have identified all at-risk couples. We next compared our panel to both the ACMG and MM gene lists to determine if any improvements could be made to the gene selection in our panel.

Our analysis showed that inclusion of genes beyond the ACMG-recommended tier 3 gene list increased the yield of actionable high-risk results and was therefore warranted in the Australian population. (See Table 1, which outlines examples of conditions that would have been missed by the ACMG approach.)

The comparative analysis with the MM-recommended gene list brought to light several conditions screened by the Sonic Genetics expanded panel that were not included in the MM gene list. Reasons included technical limitations inherent in the MM testing method (such as inability to detect deletional variants in the HBA1/2 or DMD genes that cause alpha thalassaemia and Duchenne muscular dystrophy respectively) or MM's approach to exclude certain phenotypes such as deafness.

Our detailed review resulted in the new iteration of our gene list, **Sonic Beacon v 2.0.**

Gene and condition	Description
Gene: COL4A4 **AR/XL:** AR **MIM #:** 203780 **Condition:** Alport syndrome	Early onset progressive disorder, characterised by failure to thrive, sensorineural deafness, ocular and renal manifestation and, in some cases, progression to end-stage renal failure.
Gene: FANCA **AR/XL:** AR **MIM #:** 227650 **Condition:** Fanconi anaemia	Heterogeneous multisystem disorder that causes genomic instability. Characteristic clinical features include developmental abnormalities in major organ systems, early-onset bone marrow failure, and increased predisposition to cancer.
Gene: CHM **AR/XL:** XL **MIM #:** 303100 **Condition:** Choroideremia	Associated with degeneration of the choriocapillaris, the retinal pigment epithelium, and the photoreceptor of the eye, resulting in progressive vision loss.
Gene: EMD **AR/XL:** XL **MIM #:** 310300 **Condition:** Emery-Dreifuss muscular dystrophy	Early onset degenerative myopathy characterised by weakness and atrophy of muscle, as well as signs of cardiac involvement and mental retardation.

Table 1. High-risk carriers of severe, early onset AR and XL conditions that would have been missed by the ACMG approach alone, but were identified by the Beacon panel.

Our commitment to responsible provision of RCS

We recognise that laboratories offering RCS must be prepared to critically appraise available literature and their own panel, and we have an ongoing commitment to this dynamic process and the clinically responsible provision of RCS.

Furthermore, we have several resources to assist patients and referrers, including:

- free genetic counselling for high-risk results
- clinician consultations with Sonic Genetics pathologists
- online reproductive carrier screening course for patients

To read more about reproductive carrier screening, visit the Sonic Genetics website: sonicgenetics.com.au/rcs/beacon

If you have any questions or feedback regarding this article, please email our genetic pathologist, Dr James Harraway, at **james_harraway@snp.com.au**

Online course for patients

Sonic Genetics has developed an online educational course about reproductive carrier screening for women and their partners. The free online course is designed to assist with and support clinician-patient discussions surrounding RCS.

To register or log in, visit **patientedu.sonicpathology.com.au**

For more information regarding the online course, please contact your Medical Liaison Manager.

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Pathologist profile

Dr Nicholas Roetger MBBS IB FRCPA

Dr Nicholas Roetger is an anatomical pathologist at SNP Toowoomba where he reports a broad range of histopathology cases, with special interests in dermatopathology, gastrointestinal pathology and uropathology.

Dr Roetger graduated in Medicine from Bond University in 2015 and undertook clinical internship and residency at Gold Coast University Hospital. He went on to train in anatomical pathology in public and private laboratories in Queensland. These included Princess Alexandra, Townsville, The Royal Brisbane and Women's and Sunshine Coast Hospitals, as well as SNP's Toowoomba laboratory.

Dr Roetger was awarded Fellowship of the Royal College of Pathologists of Australasia in 2023 and joined SNP as a consultant pathologist soon after. He has an active interest in research and is widely published. He has also presented at multiple international conferences.

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We are pleased to announce the launch of **Sonic Edu**, our centralised app for handbooks and guides, on a brand new platform.

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Sonic Healthcare Pathology Handbook – second edition

Hard copies of the Sonic Healthcare Pathology Handbook – second edition are available on request from your Medical Liaison Manager.

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Sustainability at SNP

As a healthcare provider, SNP recognises the importance of operating sustainably while we deliver our important and vital services. We continue to take proactive steps to implement initiatives and processes to support sustainable healthcare.

We are committed to operating in a sustainable, ethical and responsible manner across all facets of our operations: medical, financial, social and environmental.

Our aim is to support sustainable healthcare while maintaining our high levels of service.

From our collection centres and courier fleet, to our laboratories and support services, sustainability is front-of-mind across our entire practice. Some of our key focus areas are summarised below:

Going digital

- Building on digital resource libraries for both patients and clinicians.
- Using more targeted and timely electronic communications, with critical service updates delivered straight to your inbox.

Sourcing responsibly

- Using sustainable and ethical suppliers who adhere to, and advocate modern slavery guidelines.
- Being more conscious of consumables and the impacts of the material life cycle on the environment.
- Finding new and innovative ways to reduce, reuse and recycle, where and when available.

Many of our innovative programs and processes are driven by people in our organisation who are passionate about all things sustainability.

We will share some of these stories and case studies in upcoming issues of Syzygy to inspire readers with just some of the ways we can all try to adopt more sustainable practices in a healthcare setting.

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Please reach out if you wish to receive Syzygy and our service updates via email. We welcome requests to change your preferences so we can communicate with you, your way.

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Our sustainable practices reflect environmental, social and governance business standards.

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