Navigating the minefield of **genomics**

Dr Sarah Taylor
Medico-legal Adviser, MDA National

The National Health Genomics Policy Framework defines the term 'genomics' to refer to both the study of single genes (genetics) and the study of an individual's entire genetic makeup (genome) and how it interacts with environmental or non-genetic factors.

Genomics is a rapidly advancing area of medicine with increasing clinical application. While some tests are standard practice (e.g. offering preconception carrier screening) others are not (e.g. screening low-risk patients for cancer-causing genes). Many tests lack concrete clinical application; can produce results of unknown significance; and can cause unnecessary stress and uncertainty for the patient.

There can be unexpected consequences including barriers to obtaining insurance, implications for other family members, and psychological harm. Patients may need to think carefully about irreversible decisions (such as surgical resections) based on the findings of a genetic test; not to mention the potential for increased interventions for the 'worried well'.[1]

A good example of the unexpected fallout from genomic testing is Australian actor Chris Hemsworth who became aware of his increased risk of developing Alzheimer's disease after he was found to be carrying two copies of the gene APOE e4 during filming of the National Geographic documentary series, Limitless. Hemsworth chose to not edit the unexpected finding from the program, but he has instead focused on preventative measures he can take now to reduce his overall risk of developing Alzheimer's disease.

Consent

Pre-test consent must be approached very carefully, and doctors have a duty to ensure the patient has capacity to consent and an understanding of the complex issues that might arise once the results are provided.

The patient should be encouraged to ask themselves:

- *What will I do with this result?*
- *What could be the consequences of having this information?*

The patient should be aware of the risks of receiving unexpected findings, or of information where medicine does not yet fully understand the implications of the results.

More information on gaining appropriate consent for different types of genomic testing and with different patient populations can be found in the NHMRC publication: *Medical genetic testing: information for health professionals.*[2]

What genomic tests are available?

The utility of genomic testing is broad, and examples include:

- preconception carrier screening – a standard test looking for SMA, CF and Fragile X (now Medicare-funded). An extended screen is also available;
- antenatal Non-invasive Prenatal Testing;
- preimplantation genetic diagnosis testing as part of assisted reproductive treatment;
- paternity testing;
- cancer genetics – looking at genes that increase the risk of developing particular cancers (e.g. BRCA) and also testing existing cancers to tailor treatments or determine prognosis;
- risk testing (as part of a diagnostic workup) for specific medical conditions including familial hypercholesterolemia, coeliac disease and haemochromatosis; and
- diagnosis of rare and inherited diseases.

Other areas with emerging clinical application include:

- pharmacogenomics[3] – which describes how common gene variants influence drug metabolism and clinical response.[4] Theoretically, this can assist in minimising adverse effects, choosing efficacious medications, and informing speed of dose titrations. There are only two items on the Medicare Benefits Schedule that inform individualised prescribing: tests for abacavir hypersensitivity and one to guide dosing with thiopurines. Other testing is 'user pays' and has variable supportive evidence – some medications have higher level evidence than others; and
- nutrigenomics, ancestry, risk/susceptibility testing for a wide range of diseases using polygenic risk scores.

References available on request.

CASE STUDY

Carolyn is a fit and well 55-year-old woman. She doesn't like seeing doctors, but she has heard about a test she can get to see if she will develop cancer in the future. She has no medical diagnoses, but smokes 15 cigarettes a day and her BP is elevated at 148/92.

She hands over a pamphlet from a local pathology company and points to the test she wants – which tests for genes for breast, ovarian, colorectal and pancreatic cancer. Her mother had breast cancer in her 50s, and she has no other family history.

What do you do?

You have a long discussion with Carolyn about the limitations of the test and explain that sometimes the results can be unclear or provide no benefit in terms of clinical significance. You explain this could result in a lot of uncertainty and may end up making her more concerned about her risk of cancer than providing the reassurance she is seeking. You advise her that her family history did not put her at high risk for an obvious genetic risk of cancer.

You speak about genetics being only one risk factor for the development of cancer, and that there are other more reliable risk factors to consider – such as smoking, regular exercise, and alcohol use. You explain the importance of screening tests like mammograms and the cervical screening test (CST), and that she could now self-collect her CST as a first step.

Carolyn is grateful for the thorough explanation, and she realises there was a lot more to genetic cancer tests than she had initially thought. She agrees to go away and think about it, and that in the meantime she would self-collect her CST, monitor her blood pressure, and do some baseline blood tests. She acknowledges that she should give up smoking, and this was something she would also think about. ■