

Printed July 30, 2008 09:06am AEST

A price on your genes

Adam Cresswell | July 30, 2008

WHEN cancer came calling on Jacinta Green for the second time, it did so indirectly and in the most unexpected way.

Green's family has had several brushes with cancer. Green, a 38-year-old PhD student, had cancer of the thyroid 15 years ago, but it was caught early enough to be cut out without any need for radiation or chemotherapy.

But then, four years ago, another close family member found a breast lump that turned out to be malignant. That person was her father. He underwent a mastectomy and the nearby lymph nodes were also dug out.

Green's father, a man with four adult daughters, decided to be tested to see if he had a genetic mutation that dramatically increased the risk of developing breast cancer. Although this would make no difference to his own prognosis, it would help his daughters find out whether they might be at increased risk.

Green's father tested positive for a mutation of the BRCA2 gene, one of the two genes (the other being BRCA1) where mutations are strongly linked to breast cancer.

"He rang us all up and said: 'I've been tested, it's genetic and this is what you should do,'" Green recalls. "I went to my local doctor and got referred for the test ... it took several weeks and came back that I did have (the mutation). "It sucked, really, I've got to say; it wasn't what I wanted to hear."

Australian women face a one in 11 chance they will develop breast cancer by age 75. Green was told her inherited BRCA2 mutation meant she faced a 40 per cent to 50 per cent chance of contracting breast cancer.

Worse, she faced a 90 per cent chance of developing ovarian cancer, which the BRCA1 and BRCA2 genes also affect, once she reached 40.

"I was a bit gobsmacked for a while," she says. "Several doctors suggested I needed to have my ovaries removed in the next two years and several also suggested I have my breasts removed. I sat down and discussed with my partner what the best options were. It was all rather distressing at the time."

But Green insists the test -- the \$2500 cost of which was picked up by the NSW public hospital system -- allowed her to take preventive steps to reduce her risk. She takes tamoxifen, normally given to women after they are diagnosed with breast cancer, as a preventive measure. Every six months she also has a mammogram, which usually is not needed until a woman reaches 50.

"There's no way I could have afforded the test (privately)," Green says. "I couldn't have afforded \$40."

Cancer experts have raised an alarm over the decision by a Melbourne-based company to enforce its patent rights over the test, which is available through eight public laboratories. For several years the Australian Securities Exchange-listed Genetic Technologies (GTG) has held a local licence for the patent owned by Myriad Genetics, based in Utah in the US.

Although in May 2003 GTG described its patent rights as a "gift to the Australian people", it recently wrote to all eight other labs, asking for their written agreement to refer all such testing in future to GTG.

The move has sent a shudder down the collective spine of Australia's genetic research and testing community for several reasons. One is the fear, held by the Cancer Council of Australia, among others, that allowing GTG a monopoly in time will allow GTG to jack up prices, which are covered by state governments.

Cancer Council Australia chief executive Ian Olver says prices rocketed two to three-fold in Canada when a different company took similar steps several years ago to enforce its own patent rights over the same test.

GTG strenuously denies similar action will be taken here and dismisses the concerns as misconceptions. Chief executive Michael Ohanessian says he does not expect prices -- about \$2000 to \$2500 -- to change dramatically and that in any case Australia is "doing very well" as the test here costs about half the \$4000 or so charged in the US.

Other concerns relate to the effect on research. Olver says if applied broadly, the patent could stifle innovation by potentially restricting access to the testing techniques and by encouraging a drift of expertise away from the public laboratories conducting the testing.

The company insists this concern, too, has no foundation. Ohanessian insists GTG's patent rights "relate to diagnostics ... we have no interest in preventing researchers studying breast cancer". Ohanessian instead suggests there will be benefits for patients, saying GTG's four-week turnaround time is significantly faster than the time taken by some public laboratories.

Olver says his qualms remain.

Debate continues over who will be proven right. In the meantime, the case has also ignited more far-reaching concerns. Is the patent system, which has allowed companies to recoup the costs of medical and pharmaceutical innovation for more than 100 years, the best way to protect the fruits of genetic research? Does the identification and location of a gene, and the means to test for it, meet patent criteria: namely that it comprises an invention, is novel and has an industrial application? Finally, and perhaps most important, should it be possible to patent parts of the human genome at all?

Many warn that it shouldn't and they have been uttering similar warnings for some time, to little response from government or regulators. Five years ago, a paper in the Medical Journal of Australia singled out the business model of Myriad Genetics and its Australian commercial partner GTG, as being "of particular concern" to the healthcare industry.

"The Myriad patents and business model have major implications for other genetic diseases with commercial significance," the MJA paper said. "If other companies follow the Myriad precedent, then negotiating licences and implementing gene tests within the scope of those licences will pose an overwhelming logistical impediment to the maintenance of integrated, publicly funded, functional laboratory and clinical services."

Oncologist Gillian Mitchell, director of the familial cancer centre at the Peter MacCallum Cancer Centre in Melbourne, speaks for many when she asks if it should be possible to own the patent for a genetic sequence.

"All you are doing is discovering something that's in existence," Mitchell says. "If you discover an orchid in the South American rainforest, does that make it yours?"

Myriad's patent application in respect of the BRCA2 gene, lodged with the Australian Patent Office in January 2001, listed 47 separate claims defining its invention. Although some of these individual claims related to methods for detecting a mutation, at least a dozen defined the invention as being bits of nucleic acid, or DNA.

In 2005, a paper in Science noted critics had attacked the growth of gene sequence patents as "an intellectual property 'land grab' over a finite number of human genes".

David Bowtell, director of research at the Peter Mac, as the centre is known, shares Olver's concerns about what effect GTG's move will have on cost and accessibility in future. "We were very surprised by GTG's position," he says.

He is concerned that the move could hamper the work of the Peter Mac in two specific areas.

One is the progress it's making to develop a test that would detect the BRCA1 and BRCA2 mutations in tissue from a dead body.

This would be useful, for example, if a woman died from breast cancer and her surviving female relatives wanted to know if it was caused by a genetic trait they might have inherited.

The other area relates to ovarian cancer. Bowtell's institute has just been awarded a US grant to test 1000 Australian ovarian cancer patients to see if they have the BRCA mutations after a Canadian study 18 months ago suggested the changes were present much more frequently in ovarian cancer cases than had been thought.

"If that's true, this will change the guidelines for who is offered genetic testing for women and their families with ovarian cancer, possibly suggesting that any woman with malignant ovarian cancer should be offered testing for these genes," Bowtell says.

He says GTG's recent position had already set back the ovarian cancer research study by months.

Like Mitchell, Bowtell says personalised medicine -- where medication and treatment can be tailored to a specific genetic profile for maximum effect -- is "really taking off".

"What you want is a playing field where there's a lot of opportunity for people to research and innovate and develop effective tests," he says. "I think the present patent situation is acting as a real brake on that."

Solutions have certainly been proposed. In 2004 the Australian Law Reform Commission published the 700-page report of its inquiry into genes and genetic patents.

The inquiry found that given the large number of patents already granted over gene sequences, the horse had effectively already bolted, and "if there had been a time to recommend that gene sequences should not be patentable, that time had long since passed". Instead, it recommended various measures to improve the system, including a statutory exemption from patent infringement for "experimental use" to protect researchers. The report also recommended improving training for patent examiners and beefing up the role of the Australian Competition and Consumer Commission.

That report sat on the shelf under the Howard government and it remains unclear whether it will be dusted off by Labor.

However, the final determination on the validity of a patent is not made by a patent office when the patent is issued. Instead, such decisions are made by the courts, if and when a patent is challenged.

Already some legal experts think a legal challenge to Myriad's patents would stand a good chance of success.

Biotechnology patent expert Luigi Palombi, a law lecturer at the Australian National University, believes the Myriad patents -- because they seek to cover the genetic material itself rather than just the testing technology -- are invalid and should be revoked.

"One of the problems with the patent system is that there's no government body with oversight, so it's left to private individuals to do the scrutiny," Palombi says.

Likewise, ANU law lecturer Matthew Rimmer says while a court challenge is one option, other avenues could be explored. These include the existing legal power of compulsory licence, which if granted by a court would compel GTG to allow others access to the patented material in return for compensation.

Meanwhile, patients such as Green continue to hope the patent fights do not restrict access to tests. Green plans to have her ovaries removed as a preventive measure. Last month, two breast lumps were found on her latest six-monthly mammogram.

Unlike the outlook for gene testing, the lumps were benign.

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