

A scientist and entrepreneur



YEN MENG JIN

Nailing the gut-busting *Helicobacter pylori* bagged Barry Marshall the Nobel Prize for medicine last year. ANNA TEO finds out the scientist is completely computer-savvy, is into surveillance technology, and now wants to be a serial entrepreneur

THERE'S no question about the role and place of *Helicobacter pylori* in Barry Marshall's life. Not when the number plate on his eight-year old BMW spells PYLORI, his wife once declared the microbe to be "like our fifth child", and when a lifetime of work on the gut-busting bug finally clinched him (and fellow Australian researcher Robin Warren) the 2005 Nobel Prize for medicine.

Based in Perth, Professor Marshall, 55, still runs a *Helicobacter pylori* research laboratory at the University of Western Australia. He is also — following a public feting for the Stockholm honours — "trying to organise the new job", as a Nobel laureate, of being "promotional person" for science and biotech.

But the soft-spoken doctor with a quirky sense of humour has now also set his sights on being an entrepreneur — and a particularly successful one, no less — and being involved in dozens of biotech projects. He has, for a start, two small firms. Tri-Med in Western Australia develops and distributes diagnostic kits for *Helicobacter pylori* (or *H pylori*) — the bacterium that Professors Warren and Marshall discovered, back in 1982, and proved, against prevailing dogma, to be the cause of stomach ulcers.

Prof Marshall's newer company is Ondek, which is seeking investors to fund its work of developing a new vaccine and drug delivery system using a genetically modified *H pylori* bacterium. Depending on the financing, Ondek hopes to produce vaccines against influenza (including the avian flu virus), hepatitis C and HIV.

The archetypal poor country lad made good perhaps — he grew up in a tough mining town near Perth — he now has the "personal resources" for such ventures, he tells BT during a visit here last month.

"Enough to start these things off myself, but not really to continue them on past the initial stage," he says, "so I still need investors who are, basically, interested in taking big risks and who might be a bit excited about the project, and excited about the prospect that they could possibly make a big win down the end".

But it is a big risk at the front, he concedes, "so those people are not as easy to find as you might think by listening to the news... only the ones who are successful make the news".

Indeed, he's not sure that the average investor is "in tune" with investing in biotechnology, and the way governments "support" high-risk investments does not help, he says.

"The big projects that attract venture capital do see lots of interest and they're like big numbers — hundreds of millions or fifty millions (of dollars) — but I'm not sure that the average investor is really in tune with investing into biotech, which is very high risk, and may be a bit too complicated. And I'm not sure that governments are supporting high-risk investments the right way."

Perhaps biotechnology is still too new a field, compared with investing in iron or gold mines, he surmises. Besides, developing a vaccine or a new technology typically takes many years, with no assurance of success until the final stages.

"So, not only is it risky, but part of the risk is because of the fact that it'll be a long time before you make profits," he says.

There is also the issue of competing technology. "It could be across the road secretly in someone else's lab or it could be on the other side of the world — someone has got another idea to do it. And then both technologies arrive at the same time or one might beat the other, and one might be more expensive or less expensive, so that you end up with a business issue ultimately.

"But one of the risks is that a technology that looks very good today might not be as important five years down the track when you're trying to make a business out of it. Whereas I suppose if you invest in a gold mine, you can say — if I can find some gold in there, I don't have to worry that five years from now gold might not be worth anything, because you know it will be. So that probably is a risk in technology which is not really appreciated. Many investors do appreciate it, but the people who, say, provide tax deductions or tax incentives for biotechnology haven't properly assessed the amount of risks, and so the incentives are not great enough yet to make private investors go out."

Prof Marshall adds: "I have seen people start the investment and not have enough capital invested initially to actually do the work programme that they need to get to the next step and scale it up. So there are many reasons why long-term investments are a little risky, I think."

He cites another example of a risky — but popular, at least in Australia — investment: "tree farms", or commercial woodland.

"Because paper pulp needs to use wood, and people don't like cutting down old forests, so they like to use tree farms, where it takes 12 years or so for your trees to grow. And any year you could have a bush fire which completely burns up your whole farm, and which you have trouble getting insurance for. If you insure for that bush fire, in fact that whole investment is not profitable any more. So you got to sit there, in this nervous state, for eight, nine, 10, 11, 12 years, until your trees are finally harvested and you make a success of the investment. And I suppose a biotech investment in some ways is like that."

That said, Prof Marshall believes that the "few successful entrepreneurs who originally made their money in biotech" will, in 10 years, be reinvesting in lots of little biotech firms.

"So if my company is successful now, in 10 years' time I'd like to be the entrepreneur-investor whom other people come to, and I'd say — yes, here's your seed money for that project — and maybe have 10 or 20 projects that I could be involved with. So that's what I'd like

to be — a successful entrepreneur at this stage, so I can do that when I'm semi-retired. And that would be just as much fun."

For now, while nursing entrepreneurial aspirations, he is quite occupied fulfilling Laureate obligations as a science and biotech spokesman.

"To some degree, I was already doing that, because there were always enough *Helicobacter* scientists and activities to require that role, and I'd been lecturing around the world for quite a number of years, based at University of Western Australia. So that's just a little more organised and formal at the moment. I'll do a couple of lecture tours this year, probably one in Asia, one in Europe, one in America."

He reckons about 30 per cent of his year would be on the lecture travel circuit. "But part of the process is to attract the resources and recruit the people, so that the things that I'd normally do back in the lab I can have somebody else doing. These days I can actually find somebody who's better than me at certain parts of it. It might be best for me to try and develop the business plan and fund-raising, see how the progress is going, the licensing and things like that, for the big picture. It's wasteful for me to be spending 10 days in the lab doing my own PCR on a hundred test tube samples when I can get an honours or PhD student who is happy to do that and publish a paper. So that's the way it develops." PCR, or polymerase chain reaction, is a laboratory procedure to amplify the amount of DNA present in a sample.

Is there time in his schedule for anything else? "We have a little farm which my wife started up, we have about an acre of grapevines and fruit trees, and so I'm interested in

studying the many many insect pests which are attracted to the grapevines, and I think there should be a biotechnology solution to these things," he deadpans.

But he used to build his own computers — his first paper on *H pylori* was written on a homemade word processor — "I still have that as a hobby, I guess", he says. And he is interested in surveillance and optical image processing, "for various reasons", he adds.

He has roaming cameras around his farmhouse "so that if I want to — here, I can probably log into it — I can see if there are any kangaroos eating my grass." And so, while seated in an office at the Biopolis in Singapore, he is

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— Barry Marshall

receiving images of his property in Australia, about 100km north of Perth.

"I'm interested in the technology, and Internet service, all that kind of stuff. I was actually planning to take a sabbatical for a year this year and going to reschool myself, but it turns out that I'm going to be too busy to do that." The *H pylori*, in truth, still takes centre stage.

Since the breakthrough discovery by Profs Marshall and Warren, an entire *H pylori* "industry" has been born, with some 2,000 scientists around the world working on the bug, initially just "trying to kill it". Much knowledge has been collected on the microbe.

"For instance, the genome is available now. And so it's possible to actually utilise parts of *Helicobacter* in different ways, for instance, to deliver vaccine by putting vaccine genes into it. So we can remove the harmful genes, put in the genes that we want to have some biological effect — maybe a drug delivery system or maybe a vaccine delivery. All those things can probably be delivered with *Helicobacter* and it solves a problem which people have been trying to solve for many years — how do you vaccinate people just by giving them something to drink?"

But, using *Helicobacter*, "we think we'll be able to vaccinate you against practically anything... so that would be the future, maybe 10 years down the track".

Now, for all the work worldwide on *H pylori*, he estimates they are only about "10 per cent of the way" there.

"We know where we want to be, we know where we're going, over the next five years. It requires a lot of PhDs, and scientists and laboratory effort to develop the product that we're trying to create. It's a new thing, so you can't promise with 100 per cent certainty that it's going to be a success."

It takes many years to develop a vaccine, he points out. "Of course you can make one in a test tube, but until you can give it to some people and see what happens, you can't be sure that it's going to work."

So, will Prof Marshall — who famously drank a solution of the *H pylori* in 1984 to prove to a sceptical medical world that the bug

causes peptic ulcer diseases — do another self-experiment? "Ahhh, I don't make any promises," he laughs. "I may or may not."

Has he done any since? "Not drinking bacteria! I only did that once. But I test myself every now and again with an endoscopy or some diagnostic test, just to make sure that I'm clear, in case I'm using my own blood sample for an experiment."

But, he adds: "I think nowadays we could plan a careful self-experiment, we could look

for some volunteers, and I could be one of the volunteers". In any case, there are two international laboratories — one in the US, the other in Europe — that infect people with the *H pylori* "just to see what happens, and they're learning a lot". But not all the findings and data have been released, he notes.

Looking back, he says the pioneering work of Prof Warren and himself on *H pylori* is "a perfect example" of how "an apparently small, focused research can ultimately develop into something that's very dramatic and benefit millions of people".

He says: "It was just an incredibly large discovery because half the world turned out to be infected with *Helicobacter*, which we didn't really understand. So, just numerically, everybody has a stake in this discovery." But one thing to take away from it is — "practically any scientist in any little lab anywhere could make a fundamental discovery of world-shattering importance", he says.

Many major scientific discoveries and breakthroughs today involved big scaled-up projects that, it would seem, can't quite emerge from a small lab.

But there is still the "initial idea" about "a couple of little basic experiments... often done with quite minimal resources, by somebody who's just an original thinker", he maintains. "So you want to encourage anybody that that's possible, and you could say — What are the really, really big medical problems facing Western health? And obviously Alzheimer's disease is one, it's already right up there in importance.

"High blood pressure and cholesterol — it seems to me, particularly blood pressure, I haven't really figured out the fundamental problem: Why do people have to have high blood pressure? Doesn't seem to have any useful purpose; it could be a virus or something that nobody's thought of.

"And then diabetes — the actual fundamental trigger for diabetes. Next one, rheumatoid arthritis and various chronic forms of arthritis — it could be an unusual infection or just something that people are exposed to that nobody's thought of.

"So, any one of these billion-dollar problems could potentially be solved by some very small operation doing original research in some lab somewhere."

Stressed? It's boredom that kills

IRRELEVANT and useless.

That's what Barry Marshall thinks of the popular notion that stress causes illness. Indeed, he pooh-poohs any theory that links emotion and disease.

If stress causes gastric ulcer, then there could be no cure for ulcers, he reckons, since stress cannot be completely eliminated.

"I am one of the people who works better under stress," he declares. I think stress is far better than boredom."

Stress "was the final diagnosis when every other test — medical test — failed", he notes. "So if you came in with any disease (and it's still the same) no matter what you had wrong with you, if I could not actually make a diagnosis I would say: 'Well, you know, you're under a lot of stress. Obviously, you're a hardworking person and, you know, there's bad traffic, and people are calling you on your cellphone, so that's the cause of your illness.'

"So many of these diseases then have this vocal audience built around them. Particularly gastroenterology diseases, and ulcer was the main one. And things like colitis and irritable bowel — we don't know what causes them, so this vocal... then develops, and then these practitioners who practise on the basis of stress and holistic medicine and naturo-pathic therapy, natural healing, all that kind of stuff, then develops around it and creates an industry in itself.

"But the fundamental problem is that we don't know the cause of irritable bowel."

And so it becomes "open" for everybody to theorise, hypothesise, conjecture, on the causes — and point to stress, "and develop some kind of stress-related treatment for it".

Says the good doctor: "They blame it on stress. Some of the patients like to hear that, but most people don't. It's useless to know that."

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