OILing the wheels of commercial success

In a global market increasingly driven by the need for innovative new products, Otago Innovation Ltd (OIL) guides Otago researchers through the commercialisation process, turning bright ideas into commercial realities.

YOU CAN FORGIVE HAMISH FINDLAY FOR LOOKING a bit jaded.

He's just returned from a whirlwind trip to San Francisco, Chicago and Frankfurt. And through those three different time zones, he's had one mission: meet with suppliers of components for a new gas-detecting laser machine developed by Otago's latest spin-off company, Photonic Innovations.

The brainchild of physics researcher Associate Professor Andrew Wilson, the technology has a wide range of applications that Findlay, a commercialisation manager at Otago Innovation Ltd (OIL), reckons is "really going to shake up the market" and could net the company hundreds of millions of dollars – US, that is.

"This is as exciting as it gets," he says. "After six months of running down blind alleys we finally cracked the market last year. We've had a lot of luck, but we've worked pretty hard for that luck."

Markets. Profits. Commercialisation. Spin-off companies. Venture capitalists. Why is the language of

There's a new law in town: patent or perish …

business describing the research of a brilliant physicist better known for exploring the rarefied realm of ultra-cold atoms?

Don't academics just concern themselves with esoteric pursuits? Surely it's the self-made men and women of society who get on with the truly "useful" stuff?

Indeed, an early 20th-century president of one of America's top medical universities, Johns Hopkins, once said that the word "useful" ought to be banned from the work of true scientists: they were to pursue the presumably loftier goals of knowledge for the sake of knowledge and share it with the world. Such are the tenets of "open science", the values upon which most of the world's finest universities were founded.

To a large degree academics' careers still rise and fall on the number of scholarly articles published in academic journals, and on sharing research findings at conferences. The decree "publish or perish" remains a dominant force within universities, but there's a new law in town: *patent* or perish.

So what's changed? Why have technology transfer offices sprung up on campuses all over the world? And what do they do?

Stanford and Cambridge led the way back in the late '60s and early '70s, being the first major research-intensive universities to promote successfully the concept of a "science park" – where university innovation could be further developed by spin-off companies with practical know-how and investment funding.

These universities were reacting to outside influences, including growing expectations that, in exchange for public dollars, tertiary institutions would do more to ensure their work directly benefited the economy and society at large.

"In the last few decades, the themes that have driven business have also changed," explains Otago Innovation's chief executive Colin Dawson. Companies, confronted by the pressures of a highly-competitive global economy, looked increasingly to innovative products that would differentiate them in the marketplace.

And universities, because they are involved in intellectual pursuits, are seen as "generators of innovation" in ways that companies cannot always be. This is particularly the case in New Zealand, he says, because industry's investment in research and development has been historically poor compared to other nations.

Individual university researchers had in the past sought patents for their inventions from time to time, but on an ad-hoc basis. Such was the case of Otago's legendary dental dean, Sir John Walsh, who patented his invention of the high-speed hand drill in 1949 without the benefit of a university technology transfer office. That invention, developed further by others, is now widely-acknowledged as having revolutionised dental practice.

But it wasn't until the mid-1990s with the arrival of industry-minded engineer Dr Ian Smith that Otago began to catch up with the leading UK and North American institutions.

At the time, New Zealand universities were feeling the funding squeeze and seeking other sources of income. And, like their UK and American counterparts, they were also responding to the new clarion call: innovation for the nation. That call was most clearly expressed in the 1992 Government reforms of the research science sector, which introduced

The silent treatment …

YOU HAVE A GREAT IDEA THAT COULD HELP SILENCE cancer-causing genes, your initial lab results are highly promising, but to go the next step you need a little expertise that can only come from one overseas company.

The trouble is, they aren't interested.

"It's like we're knocking on the door and no one is answering," says Professor Mike Eccles, head of Otago's ground-breaking Developmental Genetics Group in the Department of Pathology.

Eccles is experiencing the frustrating reality of trying to bring a highly-advanced technology to market from a small country, far away from the bio-tech expertise required to make things happen.

It's a situation that Otago Innovation commercialisation manager Dr Alexandra Tickle sympathises with. She's on the other end of the gene-silencing project, trying to get the attention of the Californian company, Isis Pharmaceuticals, whose expertise is required.

"If we were in California, I could go to their company office, sit there until I saw the man I need to see about this, or find out where he drinks his coffee and say, 'hey, here's this great idea – what about it?' But what can you do when you're on the other side of the world?"

In fact, she's already made one trip to the United States to do just that, but Isis has hundreds of projects under consideration, and Otago's idea "just isn't their priority", she says.

But perhaps it should be, because Eccles's idea just might hold the key to overcoming a problem that has plagued gene-therapy techniques for the past 15 years.

Eccles and his team are focusing on PAX genes, genes that are "the good guys when you are a fetus", allowing cells to grow, but "the bad guys" later on when, for some reason, their

the idea of contestable public funding and created Crown Research Institutes with a strong commercial focus.

As the Deputy Vice-Chancellor, Research and Enterprise, Smith – now CEO of the Australian Nuclear Science and Technology Organisation in Sydney – aimed to encourage greater co-operation between academia and the commercial sector, without which "it is not possible to deal with inventors who, by virtue of their academic freedom, can publish without disclosure".

While not the first in the game in New Zealand – Auckland had already set up a very large business venture, UniServices – Smith says Otago looked to the private sector for its model, ensuring that its commercial operations were clearly separated from its academic teaching and research pursuits.

Today, the University's commitment to entrepreneurialism is manifested by the Centre for Innovation, the impressive glass and steel structure situated on the corner of Castle and St David's Streets. Its "business incubator" area houses start-up companies such as BLIS Technologies, Pacific Edge Biotechnology Ltd and Iso-Trace NZ Ltd – three of the more well-known enterprises resulting from Otago innovations.

On the other side of the building is Otago Innovation Ltd, a small office with only six people: chief executive Dawson, three commercialisation managers, a financial officer and an office manager. This is one lean operation.

A wholly-owned subsidiary of the University, Otago Innovation Ltd is often confused with the similarly-named Innovate Otago, the University's in-house research and enterprise office, located next door. Their roles are similar, but different. Research and enterprise feeds Otago Innovation promising intellectual property ideas gleaned from various University departments, while Otago Innovation oversees the patenting and licensing process, and seeks private industry partnerships.

Once a month, the Otago Innovation team sits down with its R&E counterparts and ideas are assessed for commercial value – the more novel, the better. Those without impact are discarded, while the more promising ones are taken a step further.

In all, about half of the ideas that go through R&E and Otago Innovation make it through the initial assessment round. If found to be promising, a business strategy is drawn up considering a range of factors including market conditions, potential investors, competitors and the regulatory framework.

Laboratory "proof of concept" is then required to prove that the technology will, in fact, do what the researchers claim. Only about a quarter of innovations get past this stage. A decision must then be made about whether to sell the technology to industry, or to create a new spin-off company. If it's the latter, Otago Innovation can provide seed money, allowing the fledgling enterprise to grow.

"But we also talk to investment partners," says Findlay. "What are the big important things that people want to see to give investors more confidence that what they're investing in is something worthwhile?"

And when you are potentially talking about millions of dollars to develop a new drug, and 10 to 15 years of lab and human trials before finally bringing it to market, confidence in that product is critical to investors.

That's one of the reasons why Otago Innovation tries to get researchers in front of investors early on in the process, so that they can explain their innovation, and what it could do. But it's also an opportunity for researchers to "learn the ropes themselves", says Findlay.

off switch fails and cells can develop into cancerous tumours.

"If we could silence those genes, we could kill rogue cells causing the cancer, but hopefully leave the normal cells alone," he explains. "That's the $64 million question."

A multi-*billion* dollar question to be more precise; that's the potential global market for the technology Eccles has patented.

His cancer gene therapy application builds on another great Otago idea – TPP (triphenyl phosphonium), originally invented by Professor Rob Smith of Chemistry and former Otago researcher Dr Mike Murphy as a therapy against neurodegenerative diseases such as Parkinson's, and successfully developed by New Zealand company Antipodean Pharmaceuticals Ltd.

TPP acts like a truck, or a carrier, capable of delivering small molecules and synthetic nucleic acids called PNAs (peptide nucleic acid) directly through cell membranes to target genes within cells. PNA then silences, or blocks, the message of those genes. Isis Pharmaceuticals just happens to hold the patent to PNA.

But PNA has a problem: it cannot penetrate cell membranes. TPP overcomes this, but Eccles is looking at delivering PNA not to the mitochondria (implicated in neurodegenerative diseases), but to specific cancer-causing genes.

So far, Eccles and his research team have had promising results and have plans for further in vivo (rats and mice) lab trials. Toxicity tests are underway and have so far shown no harmful effects to the body.

"This is highly advanced both in terms of the technology and the risk reduction," explains Tickle. "We're the truck experts and the cancer experts, but we don't know enough about PNA to take it to the next step. We need a PNA expert to buddy up with."

If only the company would open the door …

Geography – New Zealand's relative isolation from the world's largest and most profitable markets – and a lack of existing biotech industry infrastructure "conspire" to make it "extra difficult" for Kiwi-based enterprises to succeed.

"It can take six months to a year to finalise a deal, sometimes longer, and that's just on the commercial side of it – never mind the research behind it."

Otago Innovation is also building up a global network of companies and private investors so that now companies come calling and "present us with their shopping list", says commercialisation manager Dr Alexandra Tickle. "And if something pops up, then you already know who would be interested."

But why the need to patent? Why can't researchers just publish and hope an investor will pick it up?

Dawson explains that once research gets published in, say, a scientific journal, it loses its commercial value.

"Most technological and scientific discoveries require significant investment and risk to get them to market. To get them to that point, most investors have to ask the question, 'What's in it for the company?'"

A patent allows a corporation to have unique ownership rights of a technology and, hence, income in exchange for revealing that technology to society.

"Otherwise, no one would bother taking the risk to develop it – they'd have done all the heavy lifting and received none of the profit," he says.

"Many well-meaning scientists want to benefit mankind, and it's counter-intuitive that to benefit humanity it would involve secrecy, but that's the way it is. Secrecy is absolutely paramount."

However, once patented, a discovery can be discussed openly, be it at conferences or in written publications. Subsequent publication can even be desirable in commercial terms, he says, because it promotes and strengthens the patent.

"So yes, you *can* publish, but it's a question of *when*."

Patently obvious

"IF YOU EVER FIND A NOVEL BRAIN REGULATOR, PATENT it – or it will never get out of the laboratory."

Those words of wisdom, spoken forcefully by a senior scientist to a young PhD student, were never forgotten.

That PhD student was Ian McLennan, now an associate professor in the University's Department of Anatomy and Structural Biology and head of the Neuromuscular Research Group.

These days McLennan straddles two worlds, that of basic research science where he is a much-respected figure in his field of neurodegenerative disorders, and that of applied science where McLennan and his research team have recently patented – you guessed it – a novel regulator in the brain.

The regulator is the protein MIS. Until recently, its only role was thought to be in the development of the reproductive anatomy of male embryos. But McLennan, his colleagues Dr Kyoko Koishi and PhD student Pei-Yu Wang – who this year was a co-winner of one of the prestigious MacDiarmid awards for young scientists – discovered that adult motor neurons of both sexes produce MIS, indicating that it helps regulate these vital brain cells, without which we would not be able to move or breathe.

The discovery that mature neurons respond to MIS raises the possibility that it can be used as a drug to treat some neurological conditions that are not now curable.

OIL has now filed a number of patents in areas relating to the discovery and is currently looking for industry partners.

Mentoring McLennan through the patenting process, hiring patent attorneys and developing a business strategy has been commercialisation manager Hamish Findlay, without whose help McLennan says his team "wouldn't have patented it, and we'd have lost various funding options.

"Frankly, the majority of us [research scientists] don't have a clear idea of what you can patent. There have been some real losses to human society – lots of potentially great drugs are sitting in the library," he says with a wry smile.

McLennan admits that he "almost mucked it up" himself when he naively agreed to a student giving a talk on the MIS discovery. He says that's an area that the University "needs to get sorted" – about what can and cannot be said, and at what point in the process.

However, patenting, he's since discovered, needn't be a barrier to publishing or sharing research knowledge with colleagues. The key is to get it patented first.

Neither does there need to be a great divide between basic and applied science, between "research for research's sake" and the requirements of companies investing millions of dollars into potentially helpful drugs or products. The two, he says, can be complementary. In fact, his team's breakthrough

The first step in the journey is gaining a provisional patent. Its $5,000 cost is covered by Otago Innovation and can be drafted and filed quickly – within two to four weeks. Filing a comprehensive international patent can cost up to $50,000, and is also paid by Otago Innovation on behalf of the researcher.

Ultimately, the intellectual property of any innovation developed by an Otago researcher is owned by the University. But, unlike research scientists working within corporations (who give up any right to their ideas), University researchers are entitled to a third of any ensuing dividends. The remainder is split between Otago Innovation on behalf of the University (to recoup patenting and other costs) and the inventor's department.

Sounds good. But what happens when there are no profits, at least not in the short-term? Has the University's entrepreneurial experiment really paid off?

Some critics say no, and point to the continued multi-million dollar losses of Otago spin-off companies such as BLIS Technologies Ltd, a highly promising bio-tech enterprise that has not yet made good on expectations of commercial pay-back.

Dawson isn't fazed by the prospect of initial lacklustre results. Indeed, the majority of start-up companies fail, he says.

The issue for him is not so much that bio-tech companies are risky, but that New Zealanders in particular do not understand "that this is part of creating a new industry and that it is not always possible to predict which companies will be winners".

Geography – New Zealand's relative isolation from the world's largest and most profitable markets – and a lack of existing biotech industry infrastructure "conspire", he says, to make it "extra difficult" for Kiwi-based enterprises to succeed.

But not impossible.

Associate Professor Ian McLennan, who's worked closely with Otago Innovation on his own patenting project [see story below], argues that the risk of failure and the fear of the unknown are no reason not to leap into the commercial world. For such are the foundation of future successes and are, in fact, an integral part of the scientific process itself.

"If you go back and look at Newton and Einstein," he says thoughtfully, "the majority of what they did has been found to be wrong. But we honour them for what they got right.

"Most of these commercial things *won't* work, but we're investing in a possibility. The money part is not the thing that's most important – it's the possibility of creating something useful."

Jill Rutherford

discovery, made while they were seeking a therapeutic application, has major implications for their basic research.

"We once thought that there was this big arrow that went straight from basic science to applied science, but it can actually go the other way around and work hand in hand. That's an important insight because a lot of us academics see ourselves as doing basic stuff and it's companies that do applied."

However, he thinks there can potentially be a clash of cultures between researchers and the men and women in business suits, and that's where people like Findlay are valuable "buffers" and "translators".

"Hamish brings a whole different range of skills and a way of thinking … One of the things he's very good at is recognising the boundaries: his role is to think through the commercial side of it and who we can approach as a partner. And my job is to think through the science.

"He's also very good at explaining to me what I need to tell corporate investors, what they need to hear. Interacting with the business people is not just a one-way street – I'm also learning. I have to explain what I want and how to get it. It's just part of my training. It's actually quite fun."

Photo: Alan Dove

Commercialisation manager Hamish Findlay (left) and Associate Professor Ian McLennan: one thinks through the commercial aspects and the other thinks through the science.