Robbie Wilson, Hayden Paul and Ilana Gerber with Dr Wayne Patrick (second from left) discuss the results of their DNA ligase experiments.

Engineering enzymes

Dr Wayne Patrick is the first university-based academic to be awarded Young Biotechnologist of the Year. He talks to Jennifer Little.

When Dr Wayne Patrick was named Young Biotechnologist of the Year in March, he was mightily pleased for a number of reasons.

Sure, the recognition and accolade for the work carried out in his lab at the Institute of Natural Sciences on the Albany campus, to engineer new and improved versions of the DNA "pasting" enzyme, ligase, were welcome on a personal level. His "obsession" with improving its function could have far-reaching implications for next-generation DNA sequencing technologies and the speedier development, for example, of molecular tools that break down harmful chemicals used in farming and horticulture.

But he was especially chuffed to learn he is the first university-based academic to win the award, reflecting growing recognition by the biotechnology community that fundamental scientific research is important in advancing new technologies.

Added to this was the pride the biochemistry senior lecturer felt in the cadre of talented undergraduate students, or "Team Ligase" as he fondly calls them, who played their part in winning the award. The white-coated squad of young scientists consisted of Robbie Wilson, Ankita Patel, Hayden Paul and Ilana Gerber.

Supervised by Patrick, the team fused DNA-binding proteins to the ligase enzyme, then tested the modified molecules for an improved ability to join DNA strands together.

"The team have now made and tested 13 prototypes, several of which out perform their unmodified counterparts," he says. The results of their research are being scrutinised by two American biomedical, or "life science", companies, with the prospect of a patent and full-scale commercial development of this core technology that underpins all of molecular biology.

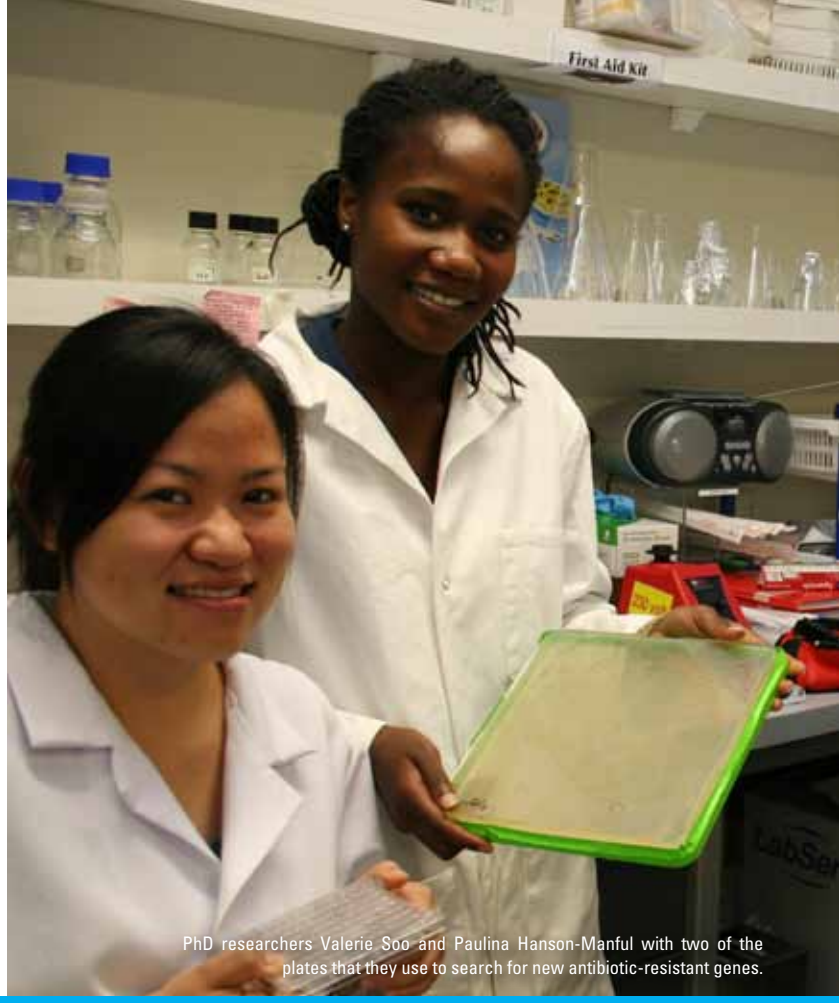
Wilson, 22, graduated with a first class Honours degree in April before taking up a doctoral scholarship at the Australian National University in Canberra. The others have all graduated with Massey Bachelor of Science degrees, with Patel and Paul now doing postgraduate studies at the University of Auckland, while Gerber is teacher training at the Auckland University of Technology.

In its current commercially available form, DNA ligase is expensive and unreliable, Patrick says. "It was discovered in the 1960s and its DNA-joining activity is indispensible for modern recombinant DNA technology, but no-one's ever tried to make it better."

"Without ligase's ability to paste together genes in a test tube, diabetics would still be using insulin from pigs and our human growth hormone would still be extracted from cadavers. In addition, whole new therapeutic approaches – like monoclonal antibodies (Herceptin, Humira, etc) – would never have been developed."

Patrick, who was awarded first-class honours in biochemistry at the University of Otago before completing a PhD in biochemistry at the University of Cambridge, hopes that his award signals a

Robbie Wilson in the final stages of purifying an improved DNA ligase.



PhD researchers Valerie Soo and Paulina Hanson-Manful with two of the plates that they use to search for new antibiotic-resistant genes.

change of attitude in New Zealand regarding the relationship between fundamental and applied research.

"The research in my lab group addresses fundamental questions about the evolution of enzyme structure and function, and we use that fundamental understanding to help us engineer biomolecules with new or improved functions," he says. "The award is an acknowledgement that biotechnological innovation can come from fundamental research, and I am excited that we here in New Zealand recognise that fact."

The award, from NZBIO and supported by the Ministry of Research, Science and Technology, is presented to a scientist under the age of 40 whose work demonstrates the potential for future leadership in biotechnology. The judging committee said Patrick, aged 32, stood out as a candidate for the award because of his world-class research and development in the field of DNA ligase enzymes.

"More than anything, the NZBIO Young Biotechnologist of Year award is about potential for the future. I hope that my own best work is still to come; but thanks to my students, I am certain that the future of New Zealand biotechnology is bright," he said at the awards dinner. Part of his prize includes participation in a New Zealand delegation to the 2010 Bio International Convention, in Chicago, Illinois, this month.

Patrick, who joined Massey in October 2007 after four years of post-doctoral research at Emory University in Atlanta, one of the world's leading research universities, says he strongly believes in fostering a spirit of cooperative inquiry and collegiality in his students. Cheerful comradeship underpins serious scientific work by the current crop of international PhD researchers Valerie Soo, Malaysia, Mack Saraswat, India, Paulina Hanson-Manful, Ghana via Belgium and Matteo Ferla, Italy and Britain at the Patrick Lab, or P-Lab as they jokingly refer to it.

Their studies revolve around different aspects of the molecular processes that underlie adaptive evolution, such as the "multi-tasking" abilities of proteins seen in the bacterium, Escherichia coli, and investigating the evolution of antibiotic resistance.

"Contrary to the traditional 'one enzyme, one substrate' view of enzyme specificity, our results suggest that many proteins (and perhaps all) possess secondary activities that become physiologically relevant, given an appropriate evolutionary pressure," says Patrick.

Making a positive contribution to society by transferring the results of fundamental research – some of it funded by two Marsden research grants totalling $1.3 million in the past two years – in the form of improved biomolecules is his driving force, he says.

"In the Patrick Lab, we borrow tools from functional genomics, directed evolution, microbiology and enzymology to address a fundamental question in molecular evolution: "Where do new enzymes and metabolic pathways come from?" Grappling with this question gives us insights into problems affecting the health of humans, and the health of the New Zealand environment." ■