LABORATORY PROFILE

Proteomics unleashed

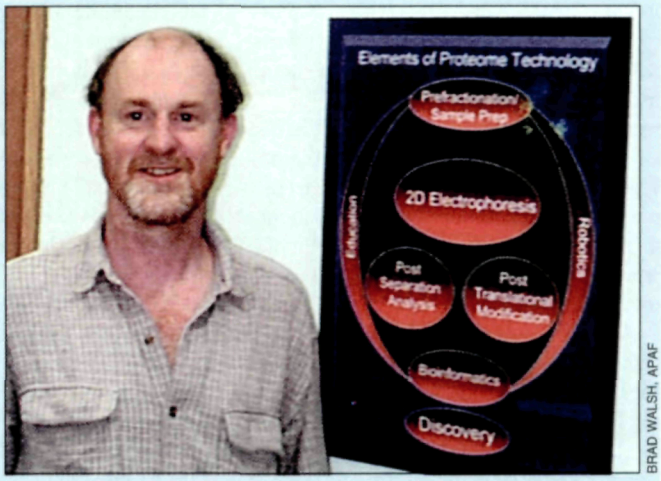
It's not yet a household word, but if Keith Williams, director of the Australian Proteome Analysis Facility (APAF) at Macquarie University in Sydney, has anything to do with it, "proteome"—the protein complement of an organism—will soon roll off the tongue as easily as "genome". And proteomics will complement genetics in our understanding of biological processes.

APAF is the first research establishment in the world devoted to proteomics. It was set up with a $7 million grant in late 1995, as one of the former Labour government's last minute, pre-election forays into promoting innovation, which established seven National Major Facilities.

The ever-increasing number of APAF staff had been working in temporary laboratories until earlier this year, when they moved into their permanent home on the Macquarie University campus. The almost pristine laboratories have the largest collection of protein sequencers in the southern hemisphere. They overlook verdant hills destined to house a new technology park, where Williams's fertile imagination already sees profitable APAF spinoffs.

For those unfamiliar with the term, the name "proteome" was coined by APAF researcher Marc Wilkins in 1994, when he was a Ph.D. student under Williams. "It simply refers to the protein complement of the genome," explains APAF Operations Manager, Brad Walsh. "The problem with genomics is that if you stop at the genome, you still don't know much about the levels of protein expression." After all, he points out, it is well-known that proteins can remain in the cell far longer than their mRNA. Thus, whereas genomics is predictive, proteomics deals with the actual end product.

Proteomics got its start in the Macquarie University Centre for Analytical Biotechnology (MUCAB), which was established by Williams in 1991. "MUCAB is a dream," rhapsodizes Williams today. "It is a vehicle for researchers in both the Schools of Biological Sciences and Chemistry to dream up things and to use MUCAB to achieve outcomes."



BRAD WALSH, APAF

Keith Williams is excited about the future of the proteome.

In an era of shrinking federal research funds, MUCAB has been able to attract substantial industry funding for both analytical research and instrument development. Proteomics was conceived and nurtured in its cramped laboratories, which have spawned some of the best Australian protein scientists of this decade. Williams is planning to step down as MUCAB director to devote his energy to APAF.

The APAF facility was built to handle large-volume protein sequencing. Walsh says the goal is to analyze 1000 proteins a week and process 1000 2-D electrophoretic gels by the year 1999.

There are three laboratories—one for separation and two for sequencing and analysis. Here, two MALDI-TOF mass spectrometers, top of the line sequencers (including the only C-terminal sequencer in Australia), and a brand new robot await mass production.

The technology used is a combination of standard 2-D electrophoresis, Edman sequencing, and novel analytical techniques, such as peptide mass fingerprinting. The sophisticated bioinformatics used are developed in collaboration with Denis Hochstrasser's group at the University Hospital in Geneva (Switzerland). Hochstrasser is also an APAF director.

The separation lab has room for a maximum of 16 personnel. The high volume will be achievable by using commercially available mini-gels, Walsh says.

In the analytical laboratory, new equipment is still being delivered, but work is already in progress to increase productivity. APAF has the capability to design and develop its own instrumentation as the need arises. This is being done through an R&D grant, called Australian Proteome Industrial Research and Development (APIRD).

"The goal behind APIRD is to develop new instrumentation for proteomics," Williams told *Analytical Chemistry*. He says the federal funding, which runs out in 2000, is for building and equipment only, which means that APAF must raise its operating funds from research grants and fee-for-service activities. It can also collaborate with its commercial partners—Beckman Instruments, Hewlett Packard, Gradipore, Bio-Rad, GBC, and the Australian robotics company ARRM—to develop new instrumentation.

As a National Facility, APAF is in a good position to achieve its goals. To date, major projects include an analysis of human tears, mapping the *E. coli* proteome, and mapping the proteomes of wool and whey.

Williams says the proteome provides a new insight into biology. "There is a finiteness to biology that people haven't really conceived of before. I think people previously thought that everything is so horrendously complicated that you'll never get to the end of it. What we are saying is that there is an end. An organism has only so many genes, and while there are a lot of proteins that get modified, there is still a finite number of modified proteins."

Elizabeth Ban