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Proteome Systems Ltd: A Macquarie life-sciences spinoff

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The 20th November 2001, is a date to remember in the annals of the Australian biotechnology industry. This was the day when the Australian proteomics startup company, Proteome Systems Ltd (PSL), shocked the world biotech community with its announcement of a *global* strategic alliance with IBM Life Sciences. This announcement, and the depth of collaboration between PSL and IBM in the field of bioinformatics, indicated that this Australian company had "arrived" as a major player in the emerging biotech industry. It was not yet three years old, and had not even had its IPO. This was therefore a moment of great satisfaction for Dr Keith Williams, the founder and CEO of PSL, and world expert in proteomics. As he said:

"We chose IBM as our technology partner because we believe IBM is the only IT company that has a real understanding of the challenges presented by proteomics. The information generated in proteomics is massive and complex, and requires a highly integrated IT solution to make sense of this data and convert it into knowledge."

Likewise IBM expressed great satisfaction with the alliance. Dr Caroline Kovac, general manager of IBM's Life Sciences Division, said:

"This alliance combines IBM's leadership in software and servers with Proteome Systems' leadership in proteome analysis and bioinformatics, resulting in a rock-solid technology foundation that will meet global customers' needs now and in the future." The global customers she is referring to are the world's leading pharmaceutical and biotech companies, all scrambling to get aboard the proteomics train.

The IBM partnership is particularly gratifying for PSL and Keith Williams, because it is the final piece in a most important global technology platform – one of the world's first comprehensive instrumentation technology platforms for the new field of proteomic laboratory investigations. Partner firms such as Shimadzu-Biotech and Thermo-Finnigan have already been fitted into place, providing core mass spectrometry and instrumentation components of the platform; others such as Sigma-Aldrich and Millipore are providing essential chemical analysis and reagents components. But the big resource area that had been missing was bioinformatics. The identification and analysis of proteins for biotech and medical usage requires powerful and intelligent data-crunching abilities. Other proteomics and biotech firms have gone for alliances with IT firms such as Compaq and Oracle. But PSL was the first proteomics company selling technology to win the collaborative support of IBM – and it did so not by asking IBM for investment, which is a common basis for collaboration, but by offering IBM a business proposition. PSL offered IBM the opportunity to sell more IBM computers and middleware, as part of its comprehensive proteomics platform, ProteomIQ™. Thus are global partnerships born.

The year 2002 will now test whether PSL and IBM Life Sciences can turn this alliance into a revenue-generating business, as the core of a proteomics technology platform.

1. Introduction

Proteome Systems Limited (PSL) is a privately held Australian drug discovery and biotechnology company launched in January 1999. Located in the high-tech biohub of Sydney, with a subsidiary in Boston, Massachusetts, PSL is recognized as a world innovator in the development of proteomic technologies. In its just three years of existence, PSL has established itself as a player in the emerging "post-genomic" phase of biotechnology, where companies are scrambling to move beyond genetic manipulation to engage direct with the core building blocks of life, namely proteins and their biochemical linkages. PSL's four main areas of activity are drug discovery (human disease), discoveries in agricultural biotechnology, the commercialization of proteomics technology (scientific instruments and consumables) and bioinformatics (protein databases and tools). To support these activities, PSL has developed its own technology platform, in conjunction with leading partner firms supplying critical areas of technology, and is both using this platform for its own discovery efforts, and is at the same time commercializing the platform as a medium-term business strategy.

Proteomics, the science of proteins, is the global study of the expression, interaction and modification of proteins in the body. Since proteins are the intermediaries between genetic instructions and all forms of cell activity, both healthy and anomalous, the study of protein expression, protein interactions and protein synthesis promises to be the pathway to a detailed understanding of health and disease, in humans, and the furtherance of understanding in animal husbandry and agriculture. Advances in proteomics promise to provide insights into disease and to accelerate and systematise the discovery of new drugs. Proteomics offers medical research groups and drug companies the possibility of faster, safer, more effective drug design and a way to better diagnose disease.

The very word "Proteome" had been coined by one of the founders of PSL, Dr Marc Wilkins, when he was a PhD student of Dr Williams in the School of Biological Sciences at Macquarie University. The term describes the study and application of PROTEins expressed by a genOME. In other words, it is concerned with the *total range of protein expression* in living systems, utilizing the new techniques of high-throughput, automated protein analysis.

The science of protein expression has now become the biotechnology industry's next big wave following on from the mapping of the human genome by a team of scientists from around the world.[1] Despite the new genomics technologies, it takes 10 or 15 years to get a drug out of the laboratories for evaluation in animal and human trials and ultimately to market. Moreover, understanding the gene function alone does not provide answers to the critical questions of how the human body gets sick, how it recovers from illness, and how it grows and changes. That is where proteomics comes in.

Proteomics promises to shorten the lead-time to a few years by facilitating the process by which researchers identify safer and more effective medicines earlier in the

[1] For at least the past decade, the main biotechnology action has been in genomics: the study of human genetic make-up. The human genome project has essentially completed the task of sequencing the entire set of human genes. For the first time, the world now has a complete list of human genes, including the millions of chemical bases that eventually determine the make-up and function of the human body.

drug-development process.[2] The human genome project and the vast array of data generated from it is driving protein discovery. The basis of proteomics is using new technology to study proteins in a large-scale, automated way (similar to genomics) allowing researchers to identify and characterize thousands of proteins simultaneously. The defining aspects of proteomics, and the links with genomics, from the perspective of PSL, are explained in greater detail in Appendix 1.

The first stage of the proteomics revolution is being driven by the development of new, industrial-scale instrumentation, to take-over from the skilled labour-intensive and time-consuming processes of protein characterization, using gel electrophoresis and peptide "fingerprinting" via mass spectrometry. This is the market where PSL is situating itself initially. According to the respected market analysts, Frost & Sullivan, the market for proteomics instruments was worth US$1 billion in 2000 and should grow to US$5.8 billion by 2005.[3] PSL, one of Australia's most promising life-science companies, is well positioned to tap into this enormous potential market. The company is looking to make its mark with its core technology, which includes new ways of identifying proteins, compiling databases and developing analytical tools. PSL is producing a global technology platform for proteomics, involving inputs of hardware and software from a number of the world's leading corporations, such as Shimadzu Corporation of Japan, Sigma-Aldrich, Millipore Corporation, Thermo-Finnigan, Alpha Innotech, Kratos, and – the *coup de grace* – IBM Life Sciences (announced publicly, as mentioned above, on 20 November 2001). PSL builds and sells the platform, dubbed ProteomIQ™, with full support from the partners who supply and sell their own products as part of the joint effort. The advanced technology platform covers all the steps involved in protein analysis, identification and purification, with each commercial partner contributing a piece of relevant instrumentation, components, consumables or informatics. It is not just a remarkable accomplishment for such a young Australian company to coordinate such an endeavor, but it is also an interesting development in terms of the business-technology interface – one of very few global technology platforms that is jointly controlled by several companies, but perhaps pointing the way towards future developments.[4]

PSL is looking already beyond this platform towards its own evolution as a discovery company, and is working on several joint research ventures with leading laboratories in areas such as infectious disease, cancer, ageing, and pain in which the ultimate prize is drugs or early diagnostic markers. Thus PSL already has a sense of its own future development prospects, or what one might describe as a business model that has several phases to it.

PSL's business strategy involves the commercialization of proteome technology through (a) receipt of research and development payments, and a combination of milestone payments and royalties based on achievement of commercial outcomes from collaborating with companies in the AgBiotechnology

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[2] Licking, E., Carey, J., & Barrett, A. (10/04/00), Business Week Online, (http://www.businessweek.com/common_frames/bws.htm?http://www.businessweek.com/2000/00_15/b3676117.htm)

[3] This is a highly conservative estimate, taking into account solely sales of instruments and consumables. The addition of bioinformatics would expand the estimate of the market potential by an order of magnitude, while the market potential of drug discovery through proteomics is vast. But there are as yet no quantified estimates of these market sizes.

[4] Such platforms exist in the global semiconductor industry, such as the global partnership involved in introducing 300mm wafers from the former standard 200mm wafers. They are likely to become more common in the biotech sector.

and Pharmaceutical industries; (b) the development of intellectual property leading to the sale of proteome informatics solutions (with IBM); (c) the sale of scientific instruments and consumables, including the ProteomIQ™ platform; and (d) the application of proteomics technology to the research, discovery and development of AgBiotechnology products, drugs, molecular markers and diagnostics.

This case is concerned to bring out the way that an entrepreneurial endeavor like PSL has to put together a "package" of resources, routines and interfirm relations in order to get started as a business entity. These are the elements, the basic "molecules" of enterprise, and every company has to find a way to put them in place in order to get started. The particular distinctiveness of the resources assembled by a company (such as its technology, intellectual property and skilled staff), the routines that it builds or hires to activate these resources, and the relations it builds with other firms for the exchange and transfer of resources, stamp the firm with a strategic identity – as maintained by the now-dominant "resource-based view" of firm strategy.[5]

PSL is also of interest to MGSM as it is an unofficial spinoff from Macquarie University. The expertise of the founders of PSL was built up at Macquarie University, in the School of Biological Sciences, and in particular at the Australian Proteome Analysis Facility (APAF), a remarkable public sector innovation that was the world's first proteomics facility funded by a national government – and one of the successes of the then-government's Major National Research Facilities program. Part of the purpose of the case is to study this process through which knowledge is transferred from a knowledge institution like the University to a thriving private sector company. The case study, conducted through interviews with key PSL employees and staff from the University, and supported by documentary analysis, examines PSL's evolution over the three years since its incorporation, and the role of its resources, routines, and relations in generating the potential competitive advantages it is opening up for itself.[6]

2. Entrepreneurial origins of PSL at Macquarie University

Dr Keith Williams is an Australian scientist who has always combined entrepreneurial flair with the highest standards of scholarship. He spent four years as a Research group leader at the Max Planck Institute of Biochemistry in Germany in the early 1980s, before returning to Australia to take up the Chair in Biological Sciences at Macquarie University. Over the next 15 years he built up a group of faculty and students as collaborators, helping to turn Macquarie University into a powerhouse of biotechnology – which it continues to be, after his departure. In the 1980s he worked primarily on *Dictyostelium*, an amoeba – although he interacted with groups working

[5] The theoretical background to the reliance on resources, routines and relations between firms, as constituting the core of entrepreneurial initiatives, is given in Mathews (2001).

[6] Through the course of the study assistance has been obtained from many interviewees. At PSL itself we would like to acknowledge in particular the assistance of Dr Keith Williams, Dr Nicole Packer and Mr John Martin. At Macquarie Research Ltd (MRL) we would like to acknowledge the input of Richard Walker, Executive Director of MRL, and Warren Bailey, Manager, Technology Commercialisation; and at the Australian Proteome Analysis Facility (APAF) whence PSL sprung, we would like to acknowledge the insights of Professor Gary Cobon, Director of APAF, and Dr Brad Walsh, Facility Manager.

on a variety of other organisms. In choosing *Dictyostelium* as a model organism, he was in very good company; it is an excellent "model" for studying basic cellular and metabolic issues. [7]

Williams found himself drawn to issues that spanned basic research and scholarship and commercial inventiveness. He became a principal in the biotechnology firm, Australian Technological Innovation Corporation (ATIC), and in this capacity was drawn close to actual commercialization projects. For example, ATIC was involved in commercialising fungal parasites that showed promise as a biological control of parasitic nematodes (worms). Dr Williams found himself evaluating a breakthrough made in The Philippines involving a kind of fungus that naturally killed the worms. Williams saw big potential in this, on a scale far greater than had been conceived in The Philippines, and in the late 1980s he proceeded to investigate the possibilities, growing 100-200kg of fungus each week in a makeshift "fungus farm" located in an old building on the university campus, leased by ATIC. In what was to presage many of his later breakthroughs, he attracted Dow Chemical's interest to take over this program and make it a commercial success – only to see the deal vetoed by other ATIC principals, on the grounds that Dow was "too large" a partner and it was too early to form such an alliance. Other deals involving major firms as Novo also failed to be confirmed. As Williams saw it, he the technologist was being excluded from the deals by the "business experts' and the true potential of the arrangements was being lost. Little wonder that he developed a taste for seeing through deals in a form where he had a major influence on their structuring – as he does now within PSL.

The Australian Proteome Analysis Facility

At Macquarie University, Williams formed a strong group involved in protein analysis. At the time, many researchers were being drawn to the more fashionable field of genomics, but he and his group took the long view, that proteins would eventually be seen as the fundamental functional agents in the cell. In 1992 he established the **Macquarie University Centre for Analytical Biochemistry** (MUCAB) as a way to focus on these kinds of activities. (MUCAB still operates as one of Macquarie's biotechnological centres.) He was building a team of faculty and students, and increasingly focusing on the possibilities for improving instrumentation as a way of "industrializing" protein analyses, after the fashion of the industrialization of genomics wrought by Craig Venter and The Institute for Genomic Research (TIGR). Williams' big breakthrough in this regard came at the end of 1995, when he won funding from the Australian government's Major National Research Facility program for a research centre called the **Australian Proteome Analysis Facility** (APAF). With funding of A$7 million to set up an advanced facility, followed by a A$5.6 million R&D grant for the development of new instrumentation for high-throughput protein studies, his centre became one of the largest in Australia and a

[7] According to the Dictyostelium web resource:

Dictyostelium discoideum is a powerful system for basic biomedical research in cell and developmental biology. The organism has unique advantages for studying fundamental cellular processes with powerful molecular genetic tools. These processes include cytokinesis, motility, phagocytosis, chemotaxis, signal transduction, and aspects of development such as cell sorting, pattern formation, and cell-type determination. Many of these cellular behaviors and biochemical mechanisms are either absent or less accessible in other model organisms. For this reason, the NIH has chosen *D. discoideum* along with several other model organisms for functional analysis of sequenced genes.

See dictybase.org/tutorial/about_dictyostelium.htm

magnet for the new interest in proteins that was being heightened by the breakthroughs in genomics. The award was not without its critics, since Macquarie University was not considered a leading research university – but Williams proceeded to prove the validity of the award by turning APAF into a powerhouse of protein discovery and instrumentation development. It was his PhD student at APAF, Marc Wilkins, who invented the term "proteomics" (by analogy with genomics) as a way of describing the high-throughput study of the entire protein expression of an organism – a term that has stuck, and is now the term of preference to describe protein science. Dr Williams named his company, PSL, with this term. As Dr Williams described the issue:

> "We saw what was happening in genomics and we realized that we needed to industrialize protein science. In 1995 Paul Keating's government had a competition for major national facilities and we won a major facility. So through '96 we built that facility at Macquarie University. It was the world's first proteome facility funded by a national government, followed closely on our heels by the Danish Government and now there's lots of big facilities in the US that have sort of used our model" [8].

As an aside, it is worth noting that the decision by the then-government to launch the **Major National Research Facility** program was far-sighted, and has led to Australian prominence in many fields funded by the program, such as advanced telescopes and, more recently, photonics. (See Appendix 2 for background on the MNRF program.) The creation of PSL, and its performance over its first three years, must be seen as one of the most significant fruits of the MNRF program.[9]

Williams recruited a former student, Andrew Gooley, to head the APAF group. While APAF faculty were focused on basic research projects in cellular protein activity, they were at the same time also devoting more and more of their attention to issues of instrumentation, given the inadequacy of tradition benchtop approaches to protein analysis for large throughput analysis. To pursue these aspects, Williams and his group built very close relations with a series of instrumentation and reagents suppliers, working with them to improve the capacity and accuracy and automated character of protein laboratory equipment. One in particular was the instrumentation firm BioRad, which had headquarters in the USA but an active local subsidiary at North Ryde in Sydney, adjacent to the university; another was the Mass Spectrometer supplier, MicroMass, as well as the local Sydney company, Gradipore. The intellectual property that was generated in the BioRad collaboration was licensed by the university to BioRad, which proceeded to build one of the earliest versions of kits and instrumentation for proteome work, released as ProteomeWorks.™ This remains the platform used by APAF today in its own discovery work and its contract research undertaken for clients.

Williams and Gooley were already thinking beyond this, to a truly revolutionary way of speeding up and automating the process of protein analysis, using the idea of a "chemical printer". As opposed to traditional gel electrophoresis methods and benchtop operations, the idea was to stabilize separated proteins on membranes, and then "squirt" reagents onto the gel from a "chemical printer" adapted from the bubble jet printer used in offices. In 1995 this was an idea too far ahead of its time, as Gooley and Williams tried it out on several very large potential corporate

[8] Future of Biotechnology in Australia, 2/1/01, ABC Radio current affair special

[9] The APAF continues to operate at an advanced level even after the departure of Williams and his group, and in 2001 it was one of 15 facilities awarded a second round of MNRF funding, this time of A$16.5 million over 5 years.

partners. The idea was patented by the university, and eventually the patent reverted to the inventors (now at PSL) facilitating the commercial development of the idea. In 2001, it was announced that the chemical printer was being advanced to commercialization by PSL and its Japanese partner, Shimadzu Biotech – as discussed below.

The aborted bid for a Cooperative Research Centre

A turning point for Williams came with his attempt to create a major international centre out of APAF, in the form of a Cooperative Research Centre (CRC) for Proteome Technology. The CRC program itself was an Australian science and technology policy initiative launched in the 1980s to raise the level of collaboration between academia and industry in key areas of technological and economic importance. Williams and his group put together a proposal for funding under this program, worth a total of A$57 million, and involving not just APAF and Macquarie University, but also the ANU and the University of Geneva, as well as leading instrumentation companies Bio-Rad Laboratories, Beckman Instruments, MicroMass, Gradipore (a local Sydney company) and GBC Scientific Equipment. The proposal passed through a lengthy selection process but in the end was not successful. This was a setback, for Williams and his group, and arguably for proteomics in Australia.

After licking their wounds, Williams and his group realized that they would have to take a strong initiative in order to keep the group together, given the scale and frequency of the international job offers that were being made to them individually. They realized that they commanded great value as a team with high-level proteomics skills, fashioned through the research efforts at APAF. So if a world-class entity could not be created in the university sector, then Williams decided that the time had come to create such an entity in the private sector. The greatest asset of such a company would be precisely the set of skills accumulated by Williams and his team. Thus the moves towards creating PSL were set in motion.

Separation from Macquarie University

In 1997, the group around Keith Williams began to seriously consider the option of moving out of the University environment. At this point, Sydney lawyers John Martin and Stephen Menzies became involved, advising on legal and other issues that were critical for emerging enterprises. They were partners in the law firm Allen Allen & Hemsley and brought powerful "City" expertise and contacts for the group's commercialisation efforts. (John Martin later left the law firm and became Deputy CEO of the fledgling PSL, and at the same time co-founded the biotechnology incubator, Xcelerator Ltd, with Keith Williams and other shareholders.) The group also made contact at this time with another powerful figure from the world of finance, Mr Bruce Hogan; he had been Chairman of BT and on the board of Coles-Myer. The involvement of these figures, John Martin and Bruce Hogan and to a lesser extent, Stephen Menzies, no doubt concentrated minds on the commercial possibilities available to the group. The group's setback in not gaining the anticipated CRC funding favored the option of leaving the University, incorporating as a company, and moving to build a business based on the group's accumulated expertise and contacts.

Dr. Packer, one of Williams' key associates and a specialist in glycoproteins, described 1998, being the year leading up to the departure of the six co-founders from Macquarie University, as a "tortuous" year. The separation process was protracted. An opening offer of a form of commercialization was made by Professor Williams,

offering the University 5 percent equity in the venture, in return for transferring relevant intellectual property across to the new company. This offer was based on Williams' reading of the model of spinoffs developed at MIT. The university countered with an offer that it considered would protect its investment in APAF as well as meet guidelines laid down by the Commonwealth government as part of the funding of APAF. Negotiations proceeded until a non-binding "Heads of Agreement" was signed, in August 1998.

These heads of agreement represented the first "official" specification of guidelines for a spin-off company from Macquarie University, and as such are of interest. Broadly, they entailed the following points: 1) equity participation by the University, through Macquarie Research Ltd (MRL), of 20 percent; preservation of ownership of intellectual property by MRL, to be licensed exclusively to the new company; representation by the University on the new company's Board of Directors; and further subsidiary matters such as extension of the existing IR&D grant provisions to be shared by the new company with APAF, and provisions for an ongoing relationship between APAF and the new company, including continuing supervision of PhD students and such matters. The university was basing its position on studies of university spinoffs conducted by the University of British Columbia. [10]

Negotiations were continuing within the framework of these Heads of Agreement, through the latter months of 1998. By this time, Dr Craig Venter and his Celera company had startled the world of molecular biology with the announcement, in May 1998, that he would finish the sequencing of the human genome by the year 2000, entirely as a private sector effort. To accomplish this, Celera would work in partnership with the instrumentation firm Perkin-Elmer. As Dr Williams saw it, this put renewed urgency in their efforts to likewise create a private sector proteomics operation. He and his group felt frustration at the protracted nature of the negotiations, as the university called in its own legal advisers.

While the negotiations between Dr. Williams and MRL were in progress, the proteomics research group was also successful in landing a major contract from the multinational DowAgro Sciences, worth several million dollars, to pursue research in fundamental plant proteomics -- with an accompanying proviso that the research had to be done within a corporate environment. This was the lifeline that would allow the group to operate commercially for a year or more, independent of the university. This contract made the group's decision much easier – on Christmas Eve 1998, all six key founders announced their departure from their positions at Macquarie University, without reaching agreement with the university as to transfer of Intellectual Property. This was a difficult decision, not least because valuable superannuation entitlements had to be sacrificed.

The parting of the ways was frustrating for both parties. From the perspective of Williams and the group, there were undue delays in finalizing an agreement in a fast-moving area of biotechnological commercialization. For its part, Macquarie University ended up with no part in the commercial proteomics operation of its former researchers. Instead it retained the IP and associated royalties rights on a series of successful proteomics products that were then commercialized, under license to MRL, by BioRad. This remains a source of income for the University, but obviously one that is inferior to the potential equity holding that was under

[10] See Report on UBC spin-off company formation and growth, Livingstone (1998). The report discusses UBC's experience in spinning-off 71 new corporate ventures.

negotiation.[11] The University was also unhappy that the unresolved negotiations left APAF somewhat up in the air, and required strenuous efforts to renew Commonwealth government support for its operations. But for Dr Williams and his group, the year 1999 dawned with the possibility of creating their own proteomics company, free of university ties, but without any intellectual capital other than the brains of the six co-founders. This was their initial and original resource – and a powerful one it has turned out to be.

3. The founding of PSL

The six academic co-founders of PSL – Drs. Keith Williams, Andrew Gooley, Nicolle Packer, Marc Wilkins, Ben Herbert, and Jenny Harry – were all former Macquarie University research scientists. The Chief Executive Officer, Dr. Keith Williams, was the hub that connected all the other five. Each of the six had different strengths and skills that complemented the whole. What they lacked were complementary commercial, legal and financial skills. This is what Venture Capital firms frequently provide to startups – but at a price. In the case of PSL, these gaps were filled initially by the recruitment of skilled advisers and some very able people for the new Board. Dr. Williams injected a strong commercial base through the addition of Bruce Hogan and John Martin to the Board. Bruce Hogan, who became Chairman of the Board, came from the financial sector; John Martin was a senior partner with the law firm Allen Allen and Hemsley. He was eventually recruited as deputy CEO, giving up his senior partnership with the law firm and moving to a full-time position with PSL in early 2001. Background profiles on each of the key PSL personnel is provided in Appendix 4.

These recruitments at the top set the fledgling company on a good footing. It started with excellent advisers in the form of PwC as auditors (involving Andrew Sneddon); Allen Allen & Hemsley as lawyers; and F.B. Rice as patent attorneys. These were top-money advisers, but they opened doors for the fledgling company. At the same time, many new technical staff had to be recruited to service the growing business of PSL.

Dow Agrosciences project

The first stage of the company's growth strategy involved leveraging its existing proteomics knowledge base. This was done effectively at first through a partnership with Dow AgroSciences (DAS). In February 2000, Dow AgroSciences LLC and PSL announced a multi-year joint research agreement in proteomics (being an extension of a previous joint research agreement). The agreement increased the commitment by Dow AgroSciences in state-of-the-art proteomic technology, and broadened the scope of alliance between the two companies. [12]

[11] This is all that can be said at this point, since many of the details of these negotiations remain subject to commercial confidentiality provisions.

[12] Dow AgroSciences (DAS), based in Indianapolis, Indiana, is a global leader in providing pest management and biotechnology products that improve the quality and quantity of the earth's food supply and contribute to the safety, health and quality of life of the world's growing population. The company employs more than 3,000 people in over 50 countries and has worldwide sales of more than $2 billion. Dow AgroSciences is a wholly-owned subsidiary of The Dow Chemical Company. See

DAS and PSL collaborated on several projects in the area of proteomics. PSL achieved all milestones for Year 1. Milestones included the molecular characterization of an entirely new class of plant proteins being developed by Dow AgroSciences, the establishment of technologies to map diversity of protein families, and the development of tools to elucidate novel biosynthetic pathways in plants. PSL applied its emerging bioinformatics expertise in the construction of several new proteomic databases for the research and discovery program. The program was terminated early because the public hostility to Genetically Modified foods meant that the R&D activities of DAS, and indeed of most agro-biotech companies, came under severe pressure, leading to significant cutbacks.

The DAS program was extremely important for the fledgling PSL. First, it showed that the startup company could deliver services of value to a multinational, on-time and on-budget (in fact, improving on the timelines set). Second, it maintained the company in positive cashflow for its first year, relieving pressure on the financial front (and allowing PSL to avoid the pressures involved in Venture Capital funding). Third, it gave PSL an important reference group who were impressed with the expertise of the founders. Finally, it gave PSL insight into the needs of proteomics discovery companies, sharpening awareness of the need for adequate fast throughput instrumentation. Through the first year, this came to occupy more and more of the attention of the founding group, and accelerated the formulation of a viable business model for the startup company.

Facilities and growth of employment

At the founding of the company, its only assets were its initial knowledge resources, discovery and R&D routines brought across from Macquarie University, some intellectual property that the university had reverted to the inventors, and a set of relations with existing chemicals and equipment suppliers such as BioRad Laboratories and MicroMass. These relationships died, as the firms kept their links to the APAF facility within the University. The first few months of existence of PSL were spent in intensifying and broadening this initial base of resources , developing new partnerships and extending the network of relations through which further resources could be tapped. At the same time, the company was generating its first lines of revenue, and staff had to be employed to service these contracts – making for a period of very rapid growth and all the problems of adjustment associated with this.

At the most practical level, PSL needed initially some purpose-built laboratory as well as office space. Some equipment was purchased, and PSL also rented access to mass spectrometry facilities at APAF within the university. It was fortunate in finding suitable accommodation (both laboratories and office space) not far from the campus, in space vacated by Peptech, at the inception of the company. These premises have expanded, with new floors becoming available, and being converted to mass manufacture of the initial laboratory kit products. The space available to PSL has grown from 600 to 2000 to now 5000 square meters, all located in North Ryde – the "Silicon Valley" of Australia's biotech industry, and within 1km of Macquarie University.

Financing

Enriquez and Goldberg (2000) for a discussion of the life-science revolution that included the entry by Dow into this field.

When PSL was formed, 100% ownership was to remain with the founding six members plus Mr. Hogan, Mr. Martin and Mr. Menzies. It was not necessary to obtain short-term or medium-term capital at the outset, since the partnership with Dow AgroSciences provided funds to run the business initially, and get it started. However growth capital was needed for the advancement of proteome technology after year one.

PSL's financial resources in its first two years have primarily come from partnership funding and 'milestone' payments from technology partners – rather than from bank loans or venture capital injections. It is very rare for a fledgling company to be cash-flow positive in its first year of operations, and reflects the favourable circumstances of starting with a major contract, as PSL did with Dow – which of course was attributable directly to the group's prior reputation and facilities at Macquarie University. Government grants were also a source of revenue. For example, the Minister for Industry, Science and Resources, Senator Nick Minchin, announced on 26 September 2000 that PSL had been offered a $3.3 million Commonwealth Government grant under its R&D Start Program, to support a $12 million initiative by the company to develop instruments for proteomics research.[13]

Within the company's second year, PSL raised capital of A$16.3 million in September 2000, in a private capital placement process. Since this provided investors with 10% of the company's equity, it placed a value on the company of US$100 million (or around A$166 million at the time) – within less than two years of its founding. A year later, in September 2001, it completed a second private capital raising of A$5.3 million – this time valuing the company at US$175 million (or A$347 million). Early investors were of course impressed by this scale of growth.

The company has not yet had an IPO – preferring to wait until the turbulence in NASDAQ and world stock markets passes. Investors to date include Queensland Investment Corporation, a key shareholder in the company; BioTech Capital (the listed biotech development fund created by Challenger International Limited), as well as venture capital funds and high net worth individuals. (Refer to Appendix 5 for further details of BioTech Capital.) The funds were raised to assist the company to accelerate the delivery of its integrated proteomics technologies into the market.

4. Business strategy of PSL

PSL's business was premised on the significant opportunity arising from the commercialization of proteomics technology and the application of this technology (with the assistance of bioinformatics) to the discovery of biomarkers and drug targets. The company's business strategy evolved through several stages as the possibilities in this commercialization process became apparent.

Initially, the problem was to fund the company's early efforts and to generate cashflow. Utilizing their accumulated intellectual capital, i.e. their unrivalled knowledge of proteomics and reputation built during the years of operation at APAF and Macquarie University, the group was able to attract a high-level partnership with

[13] The grant was used to support development of three instruments (that allows quality screening in proteome-based research for drug discovery and agricultural biotechnology projects), viz. Xcise (involves removing samples from an array, treating them and then delivering them to a mass spectrometer), the Chemical Printer (involves use of Proteome Systems technology for microdispensing fluids on a protein array, followed by analysis in a mass spectrometer), and the PiezoLC (involves a miniaturised chromatography system for preparing protein samples for mass spectrometry).

Dow AgroSciences (DAS). This turned out to be very successful as a source of revenues, enabling the company to become established. (This is not always the outcome of spinoff ventures, as numerous entrepreneurs discover to their cost.)

As the research with Dow and others was completed, it became increasingly apparent that there were opportunities to develop and market high-throughput proteomics instruments. Dr Williams saw that it would be pointless for PSL to attempt to do this on its own, but that if collaborations could be established with leading suppliers of existing instruments, then PSL could play the role of orchestrator of new proteomics-focused "platforms." The first efforts in this direction were made with the Japanese firm Shimadzu, which has turned out to be a potent partner for PSL. (The activities with Shimadzu are described in the next section.) Collaborations with others followed, including the US chemicals and reagents group Sigma-Aldrich, leading to the announcement of **The Proteomics Alliance** in October 2000. This was the signal that PSL had "arrived" as a major proteomics player – although initially there were no products to back up the announced alliance. This set a pattern that PSL has consistently followed: first announce the vision, and then the products follow.

As PSL's involvement in these product and instrumentation development efforts intensified, so the confidence of the group in its abilities to design, produce and manufacture its own instruments, and supply kits for their operation, intensified. The PSL founders also saw that their first products, designed while at APAF and commercialized by BioRad, were becoming successful in the marketplace. Thus by 2001 the founding group were involved in intense activities to produce and launch their own proteomics technology platform. Some instrumentation and consumables would be manufactured by PSL; other parts would be supplied and marketed by partner firms, with PSL retaining the rights to market the entire platform as a coherent entity. Thus its focus turned increasingly to manufacturing, a direction in which the founders never envisaged themselves moving in at the time of their days at APAF.

Meanwhile PSL was also developing its own discovery programs, in anticipation of this taking over eventually as its major area of activity. Competing proteomics firms such as Oxford GlycoSciences (OGS) already operate in this fashion, in partnership with leading pharmaceuticals firms. In 2001 PSL took its first steps in the direction of medically-oriented discovery programs (searching for protein "markers" of medical conditions), again in collaboration with leading R&D groups in US medical research centers. These are described below.

In this way, PSL's business strategy has evolved, from initial dependence on an Ag-biotech discovery partnership for cash flow, to developing instrumentation, to orchestrating a global proteomics technology platform and developing its own unique instrumentation systems and consumables products (the chemical printer and protein "chips") as well as bioinformatics initiatives, to the taking of initial steps in medically-oriented protein discovery programs. In this evolution, over less than three years, it compresses what other companies go through in the course of decades.

US subsidiary

To complement its Australian operations, and acknowledging the value of an overseas presence and network, PSL acquired most of the Boston proteomics group of Genomic Solutions on 16 October 2000, opening up a US proteomics factory in Woburn, Massachusetts, by the end of 2000. The 21,000 square feet, state-of-the-art US operations allows PSL to carry out high throughput proteomics discovery programs and has accelerated the development of its proprietary high throughput proteomics technology platform. The Boston facility includes a demonstration and

training facility to showcase the company's leading edge proteomics capabilities. The facility is configured for GMP/GLP certification, which ensures adherence to the highest standards of manufacture and discovery program execution. The Boston group has become the site for the manufacturing of small consumables and kits, while Sydney focuses on the instrumentation.

5. Activities of PSL

According to Dr. Williams, PSL identified an immediate and large commercial opportunity for selling an integrated platform to both pharmaceutical companies and the research community. Since there has been a decade of little investment in protein science (caused by a lack of innovation in the enabling technology) and proteomics is now seen as a key enabling technology for discovery, a very large commercial opportunity exists for the company that builds an effective integrated platform. To achieve its ambitious plans quickly, PSL has chosen a partnering model for technology development. The company has put in place collaborations with numerous companies, including a major instrument company, Shimadzu (who own the high quality mass spectrometry company Kratos), Sigma-Aldrich, the world's leading supplier of fine chemicals, Thermo-Finnigan, the world's leading supplier of liquid chromatography mass spectrometry equipment, Alpha-Innotech, a leading image detection instrument supplier, and Millipore Corporation, a world leader in membrane development. PSL expects the technology platform to be the first in the market, and to sell initially for around US$2 million each.

In the short-term, PSL has done the groundwork to commence the roll out of the integrated platform for the first half of 2002. In the longer term, the company plans to be a discovery company that develops new diagnostics and drug targets, leveraging off the outstanding team who uses the integrated platform in-house for discovery. The in-house platform has many features not available in the commercial platform. With discovery programs in infectious disease, cancer, pain and aging, PSL expects to be amongst the first proteomics companies to provide valuable outcomes. PSL's products are aligned with the company's particular skills in the areas of solubilization and array technologies, new identification and characterisation technologies based on microprinting techniques, and informatics.

Technology partnerships

PSL's collaborative efforts in the areas of instrumentation and consumables are driven not just by its near-term revenue requirements, but by the leverage opportunities they generate to take PSL to "the top of the proteomics tree" (Keith Williams). In return for most of these collaborative endeavours, PSL receives research and development payments, and a combination of milestone payments and royalties based on commercial outcomes achieved. Although it has achieved quite an extensive number of alliances in this area, PSL is quite adamant that it is not just an instrumentation company.

PSL's most significant alliances in technology are with Shimadzu Corporation, including Kratos, a wholly-owned subsidiary mass spectrometry company; Thermo-Finnigan; Millipore Corporation; and Sigma-Aldrich (a chemicals supplier company). Its other technology alliances include Alpha Innotech and Protagen.

Shimadzu Corporation

The strategic alliance between Shimadzu and PSL was formalised in December 2000. The Japanese company has over a 100-year history as a leading manufacturer of scientific instruments, with particular skills in the manufacture and marketing of analytical instruments, medical instruments and mass spectrometry through ownership of Kratos Analytical. Recently Shimadzu announced the release of its high throughput DNA sequencer to establish its presence in the field of genomics. It is using its alliance with PSL to leverage entry into proteomics.

While the proposed chemical printer was the subject of initial talks with Shimadzu, the collaboration with Shimadzu-Kratos achieved its first practical outcome with the development of a patented product for protein identification, the **Xcise**. This is an instrument designed to speed up the excision and manipulation of protein spots from gels in the process of 2-dimensional gel electrophoresis (2DGE) – the set of procedures that remains the basic technology in protein identification and analysis. The partners split the development costs evenly, while Shimadzu-Kratos would take charge of marketing the finished product. PSL worked with the Sydney company, Pneumatic Products, to assemble the prototype, and later with Niche Innovation, a Melbourne-based robotics and motion control company that provided much-needed design and manufacturing expertise. The Xcise project provided PSL with its first real experience of manufacturing an instrument itself, and laid the platform for subsequent experiences with the ProteomIQ platform and chemical printer.

PSL and Kratos Analytical (part of newly formed Shimadzu Biotech) announced an expansion of their Proteomics Alliance in March 2001. This involves partnering on software development for further automating Kratos' new AXIMA mass spectrometry proteomics applications.

This program is focused on addressing many of the current bottlenecks in high throughput automation for MALDI mass spectrometer applications in proteomics. The core of the program will be the integration of PSL's advanced sample preparation technologies, such as the Xcise and the proposed chemical printer (jointly developed by Proteome Systems and Shimadzu) with the AXIMA family of MALDI-TOF mass spectrometers.

Chemical printer

The idea for the chemical printer originated with Andrew Gooley, one of the PSL founders and now Chief Scientific Officer for the company. While the idea had been pursued prior to PSL's formation, and there was a high level of interest shown by potential partners, no-one was prepared to fund what was seen as a high-risk project. The exception was Shimadzu, which expressed great interest in the concept early in PSL's existence. The stumbling block early on was the fact that PSL had to leave Macquarie University without the vital patents to the chemical printer concept. In spite of this, progress was achieved in bringing the concept closer to realization in research in 2000. In November 2000 PSL acquired the right to use the "matrix jet" technology for squirting minute quantities of chemical reagents from the U.S. firm MicroFab Technologies, of Plano, TX. By this time the key patents had reverted to PSL (under a university policy of allowing patent to "revert to the inventor" when they are not commercialized) and it announced the achievement of a major milestone with Shimadzu in December 2000, involving the development of membrane-based printing protocols for peptide-mass fingerprinting applications.

By October 2001 the two companies were able to announce the successful conclusion of the R&D stage of the chemical printer project, with a move into immediate commercialization in 2002. The chemical printer in its final form is a revolutionary technology for protein identification and characterization. Whereas traditional benchtop processes involved bringing the protein to the instruments (and destroying a sample in the process) the chemical printer brings the instrument to the protein, and uses only a tiny portion of a sample; it is based on microprinting reagents on a spot of the protein sample, using PSL's breakthrough gel chip technologies. It is planned to include the chemical printer as an update to the ProteomIQ platform, due for release in 2002.

Sigma-Aldrich

In May 2001, Sigma-Aldrich Corporation (NASDAQ: SIAL), a $1.1 billion life science and high technology company, announced an agreement with PSL, under which Sigma-Aldrich would manufacture and/or exclusively distribute certain products developed in collaboration with PSL. Sigma-Aldrich produces biochemical and organic chemical products and kits used in scientific and genomic research, biotechnology, pharmaceutical development, the diagnosis of disease and chemical manufacturing. The company has customers in life science companies, university and government institutions, hospitals, and in industry. Sigma-Aldrich operates in 33 countries and has over 6,000 employees.

The recently introduced **ProteoPrep™** line of sample preparation kits is the first in a number of product groups that will be launched as a result of this agreement. This set of products consists of three kits and two stand-alone reagents that are optimised for use in proteomic research, but also work extremely well for standard research applications. These kits include new and innovative detergent formulations that improve solubility and allow for higher protein loads, study of membrane proteins and greater visibility of low abundance proteins in 2D gels. Sigma-Aldrich and PSL plan to expand this collaborative relationship to include the development of other proprietary technologies and systems used in proteomic research.[14]

Millipore Corporation

PSL and Millipore Corporation (NYSE:MIL) announced the signing of an agreement to develop and market novel kits in the rapidly emerging field of proteomics on March 2001. Millipore is a multinational, high technology company that applies its purification technology to critical research and manufacturing applications in the microelectronics and biosciences industries.

The new kits will leverage the proteomics expertise of PSL with the device and sample preparation expertise of Millipore. The initial kits, the first in a series, are based upon Millipore's innovative Multiscreen and Zip Tip product platforms and are targeted for protein digestion prior to detection by MALDI-TOF mass spectrometry. PSL has exclusive assembly rights for the kits, and Millipore is the exclusive distributor. The first kits are manufactured by PSL in Boston and were released by Millipore at the end of 2001.

[14] Dave Julien, President of the Biotechnology Division of Sigma-Aldrich said, "We believe our agreement with Proteome Systems is truly synergistic. Sigma-Aldrich's R&D, manufacturing, and distribution capabilities, coupled with Proteome System's expertise and comprehensive approach, will allow rapid availability of innovative products for an exciting new market."

Thermo Finnigan

On 21 August 2001, Thermo Finnigan, a Thermo Electron business (NYSE: TMO), and PSL entered into a strategic partnership that combines the strengths of both companies to deliver total solutions to proteomics researchers. Thermo Finnigan is a leading supplier of total laboratory solutions for the analytical and life sciences industries. Product offerings include mass spectrometers, liquid chromatography equipment, gas chromatography equipment and multi-instrument combinations of these products, as well as a complete range of advanced software solutions.

Under the agreement, PSL will augment its integrated proteomics technology system by incorporating the following Thermo Finnigan products: the Surveyor(TM) liquid chromatography system; the LCQ Deca XP ion-trap mass spectrometer, the workhorse analytical instrument of proteomics; TurboSEQUEST(R), Thermo Finnigan's proprietary protein identification software; and chromatography columns and packings from Thermo Hypersil-Keystone. Thermo Finnigan gains access to PSL's sample preparation technology for the electrospray mass spectrometer, which includes technology for introducing protein samples from gels into mass spectrometers.[15] The entire platform, known commercially as **ProteomIQ™**, is expected to be available early in 2002. Its details are spelt out in Appendix 6.

Manufacturing of proteomics platforms by PSL

PSL struck up a relationship with the Melbourne-based product development group Niche Innovation, to enter into manufacturing of proteomics instruments.[16] The relationship has blossomed, and resulted in a formal takeover of Niche by PSL effective from 1 July 2001, with the Niche staff moving from Melbourne to Sydney. Niche Innovation had been working with PSL on the proteomic range of instruments, of which the Xcise, an integrated robot for sample preparation, is the most sophisticated product.

Niche Innovation's extensive experience in developing high-throughput sample preparation instruments, in commercialising technology, and in establishing manufacturing operations complemented PSL's core development capabilities. Consequently, Niche Innovation's integration with PSL enables PSL to improve its time to market and quality, as well as benefiting from the team synergies as a result of the co-location of the instrument and consumables development team with its scientists.

Bioinformatics

A large number of computer-driven tools have been developed at PSL that facilitate the identification of proteins from gene sequences, among others. PSL has built informatics systems (taking two forms: tools for hands-off data analysis of mass spectrometric data and various customised applications, and the construction and

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[15] "We see this partnership as a critical step in Thermo Finnigan's evolution from a manufacturer of proteomics hardware and software into a provider of complete solutions for proteomics researchers," said Dr. Ian Jardine, president of Thermo Finnigan. "It is exciting to be able to bring such innovation to our customers."

[16] Niche Innovation was established and founded by Bill Hunter in 1994. Niche became one of Australia's leading contract development organizations with its past clients including organizations such as Astra Zeneca, Cochlear CRC, Cryovac, CSL Bioplasma, Fosters Brewing, Herron Pharmaceuticals, and Sola Optical.

manipulation of databases) to enable its large-scale proteomics partnerships. To do this, PSL has aligned itself with informatics companies skilled in the areas of data analysis and database management.

GeneBio

On 5 September 2000, PSL and GeneBio (Geneva Bioinformatics) announced the signing of an exclusive agreement for the worldwide distribution of PSL's GlycoSuite database. The GlycoSuiteDB is the world's first relational database of protein glycosylation (a diverse group of protein modifications important in protein function and diseases such as cancer). PSL has curated a large part of the scientific literature on protein glycosylation, previously scattered throughout the literature in numerous publications, to make it available in an easily searchable form. The GlycoSuiteDB is a natural extension of GeneBio's SWISS-PROT protein database, and in combination should enhance researchers abilities to solve problems in the field of proteomics.[17]

IBM Life Sciences

On 20 November 2001, PSL and IBM Life Sciences announced their global strategic partnership in bioinformatics. Through this agreement, IBM provides powerful IT systems that will henceforth form the backbone of the ProteomIQ platform as well as PSL's own in-house discovery systems. The PSL-developed IT infrastructure is known as BioinformatIQ™ and forms an essential component of the entire platform. Depending on the scale of the ProteomIQ offering, the new PSL IT infrastructure will include IBM's p660 servers and the new p690 eServer™ (code named "Regatta"), which is based on IBM's next-generation POWER4 microprocessor. The latter features self-healing technologies that can help provide uninterrupted operation even during major power failures and outages, thus further "industrializing" the processes of protein identification and analysis. This is the hardware. The system also includes IBM's advanced software systems, such as its DB2™ universal database, disk storage systems and IBM's DiscoveryLink™ data integration technology. All this means that PSL and the ProteomIQ platform will have unprecedented bioinformatics power, as well as access to IBM's worldwide support services, technical support and training. It is anticipated that BioinformatIQ™ will become available as part of ProteomIQ in the first quarter of 2002.

Discovery program

PSL's longer-term strategic imperative is to make significant inroads, underpinned by its leading-edge proteomics technology and informatics systems, in discoveries in AgBiotechnology and human disease. Its initial collaborations with the Buck Institute, Eukarion and The University of Missouri-Columbia represent the first

[17] Geneva Bioinformatics (GeneBio) S.A. is a bioinformatics company based in Geneva, Switzerland. Founded in November 1997, GeneBio's mission is to provide high quality proteomics databases, software tools, services and customized solutions through in-house development and strategic alliances with key research institutions and companies. GeneBio is the exclusive commercial representative for the Swiss Institute of Bioinformatics (SIB), and provides key proteomic tools and protein databases like SIB's SWISS-PROT, PROSITE and SWISS-2DPAGE, the protein analysis software package Melanie-3, and the world famous ExPASy proteomics web server that provides access to a suite of proteomics tools and databases. These high-value proteomics databases and services, along with innovative, state of the art products and services developed in-house, form the foundation of GeneBio's product line.

stage (i.e. collaborative research) in PSL's ambitious plans to ultimately discover and develop diagnostics and cures for human diseases.

Buck Institute

On 17 August 2001, PSL and the Buck Institute for Age Research announced a collaborative program on the proteomics of aging. A pilot program will focus on mitochondrial oxidative stress and the role of mitochondrial dysfunction in degenerative neurological disease. The proteomic analysis of brain mitochondria will allow us to identify the proteins, or their modifications, that are associated with oxidative stress and aging. Beginning to understand the key molecules will give insight into aging and help guide studies on age-related disease.[18]

The Buck Institute is a non-profit organization that conducts biomedical research into the basic mechanisms of the aging process and of age-related diseases like cancer, stroke and Alzheimer's disease. Its mission is to extend the healthy, productive years of life through basic research. The Buck Institute has brought together a multi-disciplinary group of researchers, and state-of–the-art technologies and resources, to focus on the complex challenge of discovering why we develop diseases as we age and developing therapeutics to prevent these debilitating conditions. The Buck Institute for Age Research, located 20 miles north of San Francisco, California, is the only institute of its kind in the United States, and one of just three such institutes world-wide.

Eukarion

PSL announced a three-way discovery collaboration with the Buck Institute and Eukarion Inc, in December 2001, to further investigate the proteomics of ageing. The program is to focus on mitochondrial stress and dysfunction in ageing and degenerative neurological disease. Eukarion will provide synthetic pharmacological compounds that augment natural anti-oxidant pathways for studies on longevity in mice.[19]

University of Missouri

PSL established a proteomics collaboration with The University of Missouri-Columbia in the area of cancer research on 21 June 2001, which involves the identification of critical pathways in anti-cancer drug resistance and potential protein targets for therapeutic intervention using proteomics.[20] According to Dr Packer of PSL, this alliance has two goals. First, it is a strategic "smart" cancer project aimed at building IP in this area. Second, it is strategic promotion of PSL technology, geared to promoting later sales of its products as the academic world becomes aware of the

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[18] "Proteomic profiling using mouse models for aging and neurological disease will enable us to track the molecular changes that occur at the functional level in cells", said Dr Simon Melov, one of the founding faculty at the Buck Institute and key collaborator on this program, which also includes Drs. Julie Andersen and David Nicholls.

[19] Eukarion, Inc., a privately held biopharmaceutical company located in Bedford, MA, is developing small molecule drugs for the treatment of degenerative and age-related disorders. The company's principal focus is on its patented synthetic catalytic scavenger technology for the treatment of conditions associated with oxidative stress. In addition to its synthetic catalytic scavenger technology, Eukarion is also developing proprietary technology to adapt monoclonal antibodies for intracellular use.

[20] The University of Missouri-Columbia is the state of Missouri's flagship, land-grant campus and is a top research institution in the United States. In the past year, it had more than $100 million in research expenditures and is home to several nationally and internationally known scientists.

power of the proteomics platform via this demonstration effect. Thus this collaboration will raise the profile of PSL within the proteomics academic community. Professor Stephen Alexander from the Division of Biological Sciences at UM will lead the university team. His team has wide expertise in using a model organism to study how anti-cancer drugs work in cells. PSL will integrate this project into a larger in-house cancer program. The agreement entails PSL providing expert advice to the university on use of proteomics to drive research.

6. PSL's competitive position

As befitting a totally new area like proteomics, there are a few highly specialized firms – like PSL – as well as genomics and biotech firms that are developing proteomics businesses, all competing vigorously with each other. The instrument makers and bioinformatics firms are also becoming involved – like IBM Life Sciences with its alliance with PSL. At this early stage of the field, there is intense variation in terms of strategies, business models, and technology, which can be expected to lead to consolidation as market selection processes mark out some choices as superior to others.

Six years ago, only one fledgling proteomics firm was in operation; today there are dozens (van Brunt 2001; Garber 1999). Leading proteomics firms include the Applied Biosystems division of Applera (which includes Celera, the world's first specialist in genomics, now expanding into proteomics); Amersham BioSciences, which was formed from a merger between Amersham Life Sciences (UK) and Pharmacia Biotech (Sweden), a specialist in protein separation, and the new alliance between BioRad Laboratories(US) and Micromass (UK), termed the "Global Proteomics Alliance."[21] The current market leaders are Amersham Pharmacia and the BioRad-MicroMass alliance; they pose a strong competitive incumbency position that is to be challenged by PSL's new platform ProteomIQ™.

There are other small startups entering this field alongside PSL. LumiCyte is one such proteomics startup, based in Fremont, CA, and likewise working through a strategic alliance with Shimadzu Biotech for the supply of AXIMA mass spectrometers to drive its SELDI approach to biochips. Alliances between mass spectrometer firms such as Applied Biosystems, Bruker AXS, Bruker Daltonics (with GeneProt) and Bruker Biospin (with IPI) are also driving the proteomics platform technology race, where PSL has chosen to compete. Its partner Shimadzu Biotech is also allied with LumiCyte Inc (in the field of protein biochips) while IBM Life Sciences and MDS Proteomics are also involved with Structural Bioinformatics Inc, of San Diego, CA. Firms like Genomic Solutions are finding the going tough in the new competitive conditions, and are shedding staff that can be picked up by new players such as PSL; indeed this was the origin of the formation of the new Boston team by PSL.

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[21] Bio-Rad Laboratories, Inc. (www.bio-rad.com) is a multinational manufacturer and distributor of life science research products and clinical diagnostics. It is based in Hercules, California, and serves more than 70,000 research and industry customers worldwide through a network of more than 30 wholly owned subsidiary offices. For further details on the Global Proteomics Alliance, and the ProteomeWorks platform, see www.proteomeworks.bio-rad.com.

The proteomics laboratory services and discovery field itself is an emerging industry in which there are as yet few players. The key players in the global market for sophisticated cataloguing of proteins are Oxford GlycoSciences in Oxford, England; Large Scale Biology in Rockville, Maryland; MDS Proteomics (Toronto) and Geneva Proteins (GeneProt), all of whom have developed sophisticated, reliable methods of miniaturising the sheets of jello-like polymer that are used to separate individual proteins from the many thousands contained in a serum or urine sample. They have even found ways to sequence the 20 different building blocks rapidly but accurately.[22] Other participants include MDS in Toronto, and the various pharmaceutical companies that are developing in-house proteomics expertise. Pharmaceutical companies really want to understand the protein changes that occur when a normal cell becomes diseased. This is a highly competitive field into which PSL is venturing.

Other new biotech companies like Curagen, Myriad Genetics, and Hybrigenics, have opted for a simpler approach to protein analysis. They are fishing out specific groups of new proteins related to, for example, insulin levels, and then determining the proteins' functions. In a study with a pharmaceutical company, Myriad scientists took 10 proteins known to be involved in a particular disease and used them to uncover 200 additional proteins – and one of them looked like a promising drug target. In just a few months of work, Myriad scientists were able to provide the pharmaceutical company not only with critical biological information but also with valuable clues about a potential blockbuster medicine. Many proteomics companies are developing what they call "protein chips" – pioneered by Ciphergen and also pursued by startup companies like Zyomyx, CombiMatrix Corp, and Packard Biochip Technologies (bought by Perkin Elmer, an instrument maker that is getting strategic about proteomics). The basic idea is that any biological sample can be applied to the "chip" which will give an automated readout of the proteins present in the sample. PSL is about to actively compete in this sector with its chemical printer.

These technical and commercial upheavals are all consistent with the way in which the capitalist evolutionary process works its way through a new field, involving creative construction of the new and creative destruction of the old. Proteomics is simply the newest front in this well-known process. The major proteomics firms today are listed in Appendix 7.

Promoting local biotech and proteomics cluster

PSL has taken an enlightened attitude towards the promotion of a biotechnology cluster in its immediate vicinity, seeing this as good not only for Australia but also for PSL itself. A thriving cluster will encourage the formation of specialized firms, and the creation of complementarities between firms, thus expanding the capabilities of the cluster as a whole, and making it more attractive as a source of business relationships with the wider world.

PSL has taken specific steps in this direction, starting with the establishment of a technology-based firm incubator, called Xcelerator Ltd. This is a business in its own right, with the remit to "incubate" new spinoff and startup companies. Established in February 2000, it is housed initially in the same premises as PSL, but as an independent entity. It provides complete support to start-up companies working in the biotechnology sector and an environment and infrastructure which is highly

[22] Licking, E., Carey, J., & Barrett, A. (10/04/00), Business Week Online.

conducive to allowing start-up businesses to get on with the task of developing their new venture and growing rapidly. As it grows it could well seek its own premises. To date, the firm that has most benefited from Xcelerator is BioTechnology Frontiers – another unofficial spinoff from Macquarie University, jointly founded by Dr. Graham Vesey and Mr. Mark Gauci, was incorporated on 1 March 1999. BTF has a range of products designed specifically to facilitate rapid, accurate testing for Cryptosporidium and Giardia in environmental samples.[23]

More generally, PSL has favored the formation of a biotech cluster in Sydney's North Ryde biohub and northern Sydney more generally. In 2001 this concept was formalized as the BioMed North cluster, involving over 60 research institutions, biotech firms, and investors, as well as major universities including Macquarie University. Under state government funding, the BioMed North cluster was able to appoint a CEO in November 2001, with a remit to develop a cluster identity and drive business interaction between the member firms and institutions.

7. Resources, routines and relations

We wish now to take stock of the PSL story in its brief three years existence, focusing on the resources, routines and relations that have fed and driven the development of the business. PSL has been remarkably successful in constructing an ambitious business model within such a short time of its founding. This is partly attributable to the accelerated pace of change in the proteomics industry, but must be attributed mainly to the strategic vision that informs PSL and its founders. The business model is based on identifying a variety of sources of revenues, and allocating them according to short-term, medium-term and long-term objectives and possibilities.

The short-term sources of revenue include milestone payments derived from partner firms. This is a way for PSL to leverage its knowledge capital in its initial stages – capital that was built on expertise developed, and relations formed, while the founding group were at Macquarie University. The second stream of revenues for the medium-term include laboratory instrumentation and products directed towards biotech laboratories as customers. The first of these, sample preparation kits for proteomics research, were released in the second half of 2001, and are expected to generate significant revenue streams from 2002 onwards. This revenue stream is expected to take a quantum leap with the release of the comprehensive proteomics integrated platform, developed by PSL in collaboration with leading instruments suppliers, and as it moves through more advanced versions, involving PSL's proprietary "chemical printing" technology. The third source of revenues is expected to come from diagnostics and drug and pharmaceutical products, obtained through the

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[23] BTF was formed to capitalise on the unique combination Vesey and Gauci had developed whilst working together in the research laboratories of Macquarie University, Sydney. There, Vesey (microbiologist) and Gauci (optoelectronics engineer) collaborated on the development of laser flow cytometric assays for the detection and characterisation of microorganisms in environmental samples. BTF uses this combination of expertise in leading edge biotechnology and optical and electronic technology, to create a unique library of problem-solving skills. BTF has a range of products designed specifically to facilitate rapid, accurate testing for *Cryptosporidium* and *Giardia* in environmental samples.

processes of discovery launched by PSL on its own and in collaboration with partners. This is for the longer-term – but it is significant that PSL is already actively engaged in several collaborations oriented towards the development of such biomedical products.

The approach that has made such a business model feasible, is that of early alliance building. PSL has adopted the realistic stance that it possesses advanced and highly distinctive knowledge of proteomics – but lacks all the resources needed to apply this knowledge in the marketplace. It has no intention of attempting to build its own extensive sales and marketing teams, nor to become a major manufacturer in its own right. PSL has therefore embarked on a series of collaborative alliances, detailed above, designed to "bridge" the resource gaps that separate its strategic goals from its actual possibilities. PSL has targeted leading international firms to cover each of the "resource segments" involved in building technology platforms for proteomics, each of which has strong sales and marketing presence in its own right. These include: Shimadzu (Jpn) and Kratos Analytical (UK) as well as Thermo-Finnigan (US) for mass spectrometric instrumentation; MicroFab Technologies (USA) for microdispensing and precision printing; Sigma-Aldrich (USA) for chemical reagents; Millipore (USA) for life science laboratory instrumentation; and the local small firm, Pneumatic Products, for manufacturing capabilities (now taken into the adjacent small-firm incubator, Xcelerator, as a new startup, BioRobotic Systems). As noted in the Prelude, the only resource missing from this line-up has been, until recently, a bioinformatics partnership – now consolidated through the linkup with IBM Life Sciences.

The capabilities that PSL possessed initially were confined almost exclusively to bioscience R&D. The founding of the company meant that new capabilities, in business plan drafting, in Board formation, in finance, in management of contracts and relations with other firms, all had to be acquired and learnt quickly. The development of product lines, in the form initially of laboratory kits, meant that new capabilities had to be developed in pilot production and manufacture, and then in customer service. All of this meant explosive growth for PSL, particularly in the crucial area of middle-level management. At the time of writing, the company is moving into the transition from being a small, relatively intimate operation with tight bonding between the senior managers, towards a more diversified commercial operation dependent on specialization and division of labor, and needing organizational structure to ensure that operations are effectively coordinated and resources utilized efficiently. Approximately half of the over 70 staff recruited by mid-2001 have PhDs. Thus PSL is essentially a knowledge-intensive company.
The rapid growth of the company through alliance formation has also brought in its wake quite specific kinds of management demands. PSL is a tiny startup company compared with the well-established giant firms it is partnering, such as Shimadzu, Sigma-Aldrich, Millipore, Thermo-Finnigan or IBM. The partnership could end up being very lopsided, with the giant making increasing demands on the small partner, seeing it (quite accurately) as a convenient source of knowledge on all aspects of the new industrial sector of proteomics. Thus the partnerships have to be managed with as much care as the internal operations such as product development or manufacturing or sales and marketing – if not with more care, since errors made with partners can have very damaging effects.

A measure of the strength of the partnerships that PSL forged with established firms, is the degree to which these firms are prepared to commit resources and routines to the partnership. Resources come in the form of people, technology, or

customers. These are the very reason why PSL would seek to enter into the partnership in the first place. Routines would mean the investment by the partners in joint business processes – such as the kinds of processes that are needed to operate the joint proteomics technology platform being assembled. For example, Sigma have formed a team that is responsible in-house for coordinating all aspects of the relationship with PSL. With Shimadzu there is a growing relationship, with Shimadzu regularly sending engineers to the Sydney laboratories, and co-locating its Boston facility with PSL's new facilities there. At the time of writing, as the proteomics platform ProteomIQ™ is coming close to launch, the various partners are intensively coordinating their internal business processes, such as for billing customers and keeping track of periodic payments, and maintaining customer service records. It is these activities that test the joint investment by partner firms of resources and routines in their coordinated initiatives.

One of the critical resources for a knowledge-intensive company is its Intellectual Property (IP) portfolio. Within just two years, PSL has already acquired a portfolio of approximately 25 patents applications, after leaving Macquarie University with just two – covering chemical printing and sugar chemistry. More important in PSL's eyes is the IP coverage of the partner firms, which strengthens the IP protection of the ProteomIQ platform. The IP portfolio is of strategic significance not just in terms of the protection it potentially provides (provided the company is prepared to enforce this protection in the courts) but in terms of representing a "stake" in the competitive game with other biotech players. Patents granted and pending are listed in Appendix 8.

8. Next steps for PSL

Proteome Systems Ltd is a remarkable story of a company cleverly leveraging its initial critical resources – largely the knowledge possessed by the six founders – into a leading position in what promises to be one of the most significant new industries of the 21st century. In less than three years it has built a formidable array of capabilities from its initial R&D specialization to encompass new product development, manufacturing, sales and customer support, as well as partnership management, intellectual property protection, and all the public activities that go with contributing to the development of a new discipline and new industry. PSL leading staff are in constant demand as speakers at scientific and business conferences. This exemplifies the character of a knowledge-intensive company: by giving of their expertise to public events, they acquire and enhance their reputation, and create opportunities for further knowledge leverage.

The test for the company lies in the future – as it passes through the familiar milestones of accomplishing its IPO (being postponed until the US Stock Market settles down) and building its revenues and customer base. But the signs point to PSL taking these in its stride. It is building a strong base in terms of its resources, routines and relations with other firms.

Finally, PSL is already attempting to mend fences with Macquarie University, the academic home of its founders, and is building links with many other universities. Dr Williams is an adjunct professor at both Macquarie University and the University of Sydney. PSL has sponsored a Lectureship in proteomics in the Molecular Biotechnology program at the University of Sydney, and has sponsored scholarships for students at MU, University of Sydney and the University of NSW. Going further afield, PSL has sponsored commercially-focused programs at the University of

Verona in Italy, and at the University of Missouri at Columbia in the USA. Thus PSL is cementing its access to knowledge capital in the burgeoning field of proteomics, in a synergistic manner that benefits the universities as well as its own future prospects.

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Appendices

1. The concepts of proteome and proteomics

Central to the understanding of the new fields of Genomics and Proteomics is an understanding of the link between genes, proteins and disease. Proteins comprise approximately half of the dry matter of living organisms. They are complex molecules required for the structure, function and regulation of the body's cells, tissues and organs. Changes in the composition or abundance of proteins can lead to disease. This can occur either directly or indirectly through interactions with other molecules. Many of the best selling drugs either act by targeting proteins or are proteins themselves. In addition, many molecular markers of disease, which are also the basis of diagnostics, are proteins.

Until recently, the analysis of proteins in tissues was a laborious exercise, in marked contrast with the sequence analysis of genes, which for several years has been a rapid automated process. For many years this meant that proteins were studied indirectly through their gene sequences. Now Proteomics enables proteins to be analysed in a high throughput, automated way similar to how genes have been studied. This advance will have major implications for pharmaceutical research and development. A protein consists of a chain of amino acids, which folds into a characteristic shape and may be modified chemically before it becomes physiologically active. Each individual protein is encoded by a separate gene. The gene specifies the order in which the individual amino acids that make up the chain are arranged. The genetic code is carried in the form of DNA. It is estimated that there may be up to some 35,000 genes in the human genome. The protein readout from each gene can be differently formed or modified, so there may be as many as 1,000,000 differently modified proteins in humans. The complete genetic code, or genome, required by a living organism for the manufacture of all the protein molecules necessary for survival and growth, is found in the cell's nucleus.

Source: PSL webpage

The development of company strategy in the new field of proteomics is intimately connected to the scientific view of the field taken. In the case of PSL, this is quite distinctive. According to Dr Keith Williams:

"Just as we took a lonely position (vis a vis genomics) in 1994, in 2001 our view on proteomics is different to our competitors. More than 20 years of studying protein science gives us a perspective that few others have. Our focus is on authentic proteins as expressed in the cells under study. We believe that at this early stage of proteomics the next step is to understand what the cell does as it translates the message of the genome, and to understand what changes when things go wrong (eg disease). We have worked hard to develop enabling technologies to help us in this quest. We do not reject new approaches such as protein chips, but we do seek to introduce such technologies with a view to studying native proteins. Indeed our protein chip instrument, which is currently under development, accesses authentic rather than genetically engineered proteins.

We do have views about protein-protein interactions and protein structure, but these views are in the context of studying authentic proteins. We see great technology being used in many of the studies of our competitors, but often we think this

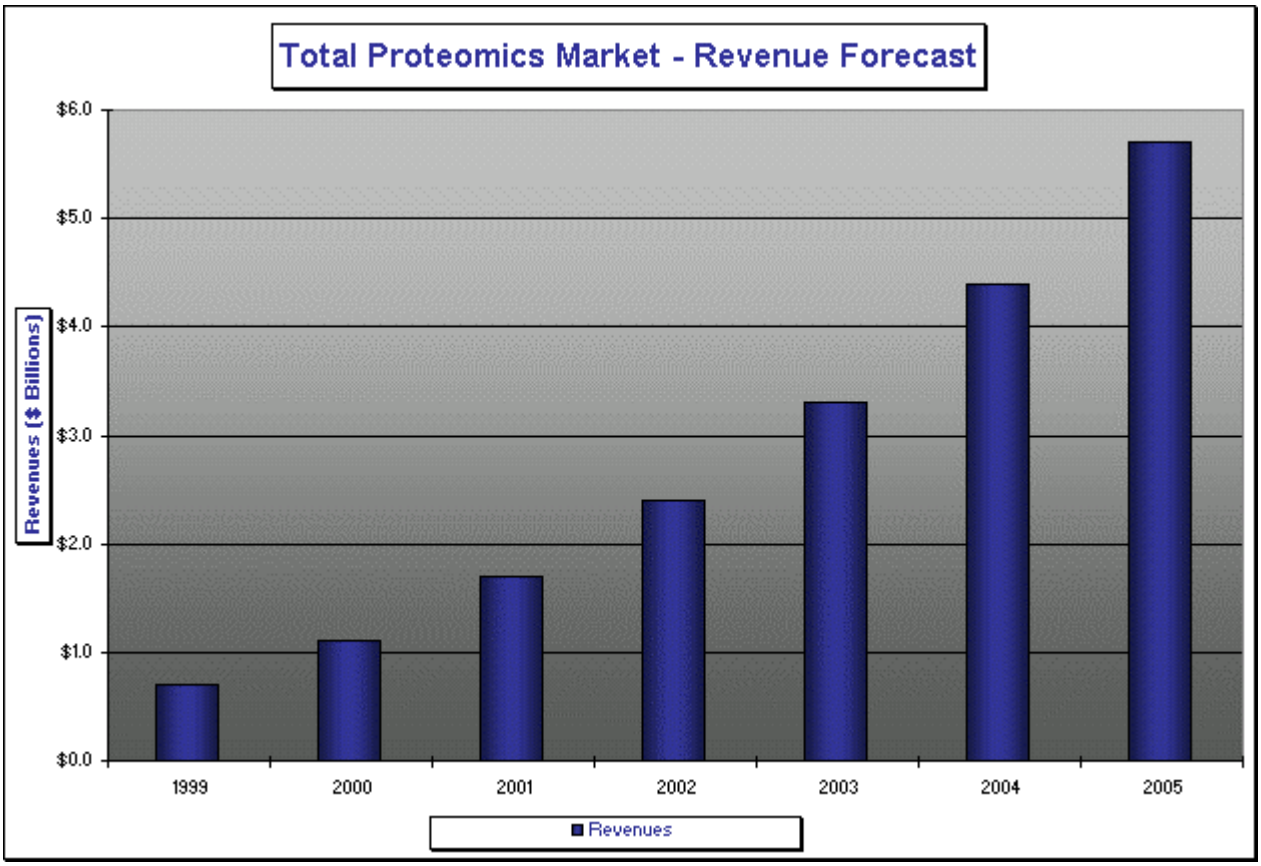
technology fails the utility test. In our view technology must not only be fast, it must be enabling.

So what do we do? We focus on real tissues and developing means of solubilizing them so that we can display all of the proteins. We emphasise purifying the proteins, as only with pure proteins can one study the modifications which we believe are the critical aspects of proteins that enable function and provide the diversity needed to make complex organisms. We then develop identification and characterisation tools (largely but not exclusively mass spectrometry based) that enable us to get a true picture of the proteome. With this as a basic approach, we believe we are well placed to be one of a small group of companies who will drive the proteomics revolution."

Source: Message from the CEO, PSL webpage

2. Market projections for proteomics

In August 2000, the widely respected firm of technology and market consultants, Frost & Sullivan (founded in New York in 1961) published a major market research report on the emerging proteomics industry and market development. It placed a value overall on the proteomics sector in 2000 of US$1 billion, anticipating growth over five years to nearly US$6 billion in 2005.



Source: Frost & Sullivan

Frost & Sullivan broke the market down into the following segments:

- Laboratory instruments and supplies – instruments, wet technologies, reagents, consumables, and tightly-integrated computer hardware and software;
- Laboratory services – instrumented and wet analytical services, contract services;
- Informatics – databases, stand-alone analysis software, and contract work.

Of these, by far the largest at this stage is the market for laboratory instruments and supplies; this is where PSL has positioned itself in its early years – with a view to moving into the other segments as well, and going further afield into drug discovery and protein interaction analysis. Frost & Sullivan see bioinformatics moving increasingly to centre-stage as the field matures – and again, PSL sees itself moving with this trend.

3. The APAF and Australian Major National Research Facilities program

The Major National Research Facilities (MNRF) program has since the mid-1990s supported the establishment in Australia of major facilities that would be unlikely to be provided by the private sector, but which are nevertheless of fundamental importance in driving new science-based and knowledge-intensive industries. One of

the most important of the MNRF projects has been the establishment of the Australian Proteome Analysis Facility (APAF) at Macquarie University, under the guidance and direction of Professor Keith Williams.

A further 15 support decisions were announced in August 2001, backed by funding of A$155 million over five years. This included continuing support for APAF at Macquarie University (ensuring its survival as a leading international research centre and public resource for promoting the proteomics industry in Australia) together with renewed funding for the Australian Genomics Research Facility (with nodes in Brisbane and Melbourne) and the new Australian Phenomics Facility, announced in 2001, to be based at the ANU in Canberra.

To the extent that the success of the MNRF program can be judged a success in terms of spin-off companies generated in the private sector, APAF must be counted as by far the most successful facility to date, since it gave rise directly to Proteome Systems Ltd.

Source: MNRF program, Department of Industry, Tourism and Resources

4. PSL's founders and leading managers

Keith L. Williams, PhD (CEO)

Keith Williams, Chief Executive Officer and Executive Director of PSL, was the founder and Director of The Australian Proteome Analysis Facility (APAF), the world's first national proteome facility, from July 1996 until July 1998. In September 1998 he structured PSL's multi-year project with Dow AgroSciences and developed strategic alliances with various instrument companies, the results of which include several products in the ProteomeWorks product range released by Bio-Rad.
Prior to 1999, Dr. Williams was a Professor in Biological Sciences at Macquarie University in Sydney and Founder and Director of the Macquarie University Centre for Analytical Biotechnology (MUCAB). He has trained 30 PhD students and built a team of 25 scientists who established a patent portfolio and designed and commercialised various instruments and kits. Dr. Williams has at least 5 granted patents, at least 15 patents at Patent Convention Treat (PCT) phase and over 250 publications in the field of cell, molecular and developmental biology.

John D. Martin, BA, LLB (Hons)(Deputy CEO)

John Martin is a former Executive Partner of the corporate group of the Sydney based law firm Allen Allen and Hemsley. John's areas of specialisation include mergers and acquisitions, fundraising and advising high growth companies in emerging technologies, particularly biotechnology. He has worked with Dr. Williams on structuring PSL since its inception. He continues to consult with the Life Sciences practice of Allens. John is a co-founder of the biotechnology incubator, Xcelerator Ltd., and provides advice to the incubator companies on business development.

Andrew A. Gooley, PhD (Chief Scientific Officer)

Andrew Gooley, Director and Chief Scientific Officer, was Director of Protein Technology in the APAF from 1996 until December 1998. Dr.Gooley has 15 years experience in instrument and application development in proteomics with major corporations including, Bio-Rad, Novo Nordisk and GenenTech. Recently he has focussed on the integration of automation into proteomics with the development of several motion control systems to automate many of the steps in proteomics. In collaboration with MicroFab Technologies (USA) he has pioneered the use of

piezoelectric micro-dispensing in proteomics and is project leader for the design and prototype development of two new instruments in collaboration with the Shimadzu Corporation.

Nicolle H. Packer, PhD (Head of Glycoproteomics)

Nicolle Packer, Executive Vice President and Head of PSL's Glycoproteomics program, has 20 years experience in glycobiology and biochemistry. Dr Packer was part of the team which established the Australian Proteome Analysis Facility, a Major National Research Facility at Macquarie University, Sydney in 1996 until she left the university to co-found PSL in 1999.

Her research interests have included the analysis of lipopolysaccharides and the site-specific glycosylation of mucins as well as the micro-characterisation of glycoproteins separated by 2-D electrophoresis and she has been invited as a guest speaker to several international conferences in these areas. Her work has required the development of new methodologies for the analysis of oligosaccharides and she holds several key patents in glycobiology. More recently she has co-ordinated the development of a curated and annotated relational database on published glycan structures on proteins.

Dr Packer has collaborated with major corporations such as Beckman and Bio-Rad on methods development and is on the Editorial Board of the Proteomics journal, serving as Guest Editor for a special issue on post translational modifications in proteomics. She has authored 48 publications in refereed journals, 10 book chapters, is an editor of a book and journal issue, and holds 6 patents.

Marc R. Wilkins, PhD (Head of Bioinformatics)

Marc Wilkins, Vice President and Head of Bioinformatics co-developed the concept of the proteome and coined the term. Prior to joining PSL in 1999, he was a senior post-doctoral fellow in the Australian Proteome Analysis Facility, and held a post-doctoral fellowship from 1995-1997 at the University of Geneva, Switzerland working with Prof. Denis Hochstrasser and Dr. Amos Bairoch. Marc has 8+ years experience in cell and developmental biology more than 6 years experience in developing bioinformatic databases and tools; he co-developed many of the protein analysis tools available on the ExPASy Web server, including FindMod, PeptIdent and TagIdent. In 1997, Marc co-edited the first book on proteomics, Proteome Research: New Frontiers in Functional Genomics (Springer Verlag), and has published more than 50 research and review articles. In PSL, Dr. Wilkins has been responsible for the planning and execution of a major research project in collaboration with Dow AgroSciences, and has established and co-ordinates PSL's integrated bioinformatics platform for protein identification, characterisation and the organisation of discovery project information.

Ben R. Herbert, PhD (Head of Array Technology)

Ben Herbert, Vice President and Head of Array Technology, was a Ph.D. student in the laboratory of Dr. Williams from 1995 to 1997. From December 1997 until December 1998 Dr. Herbert was a post-doctoral fellow in the Australian Proteome Analysis Facility. Dr. Herbert has gained international recognition as one of key innovators in the use of 2-D PAGE for protein separation and has over 20 publications and several key patents in the area of separation science methods development. He has 15 years experience in protein sample preparation and electrophoresis and 5 years experience in product development, including playing a

key role in the development of the Bio-Rad ProteomeWorks package. In collaboration with Prof. Pier Giorgio Righetti (Verona University, Italy) he is pioneering new technology and instrumentation for sample prefractionation.

Jenny Harry, PhD (Head of Discovery Programs)

Jenny Harry structures Proteome Systems' discovery programs and oversees the implementation of Proteome Systems' proteomics discovery platform. Jenny has directed collaborative projects with industry partners and co-ordinated proteomic research projects in-house. Until recently, the major program has been with Dow AgroSciences, which consisted of three research projects in different areas of AgBiotechnology. Jenny is now developing discovery initiatives and alliances in the area of human health. These programs involve partnering with leading medical and research institutions and corporate organisations in Australia, the USA and China. Prior to Proteome Systems, Jenny directed discovery programs in the Australian Proteome Analysis Facility (APAF) from July 1997 until December 1998, during which time she implemented APAF's first commercial project investigating differential protein expression in colon cancer in collaboration with the Chiron Corporation USA. Prior to 1997, Dr. Harry was a post-doctoral research fellow at the University of Melbourne working on differential gene expression in mammals. She has 10 years experience in developmental biology and molecular genetics.

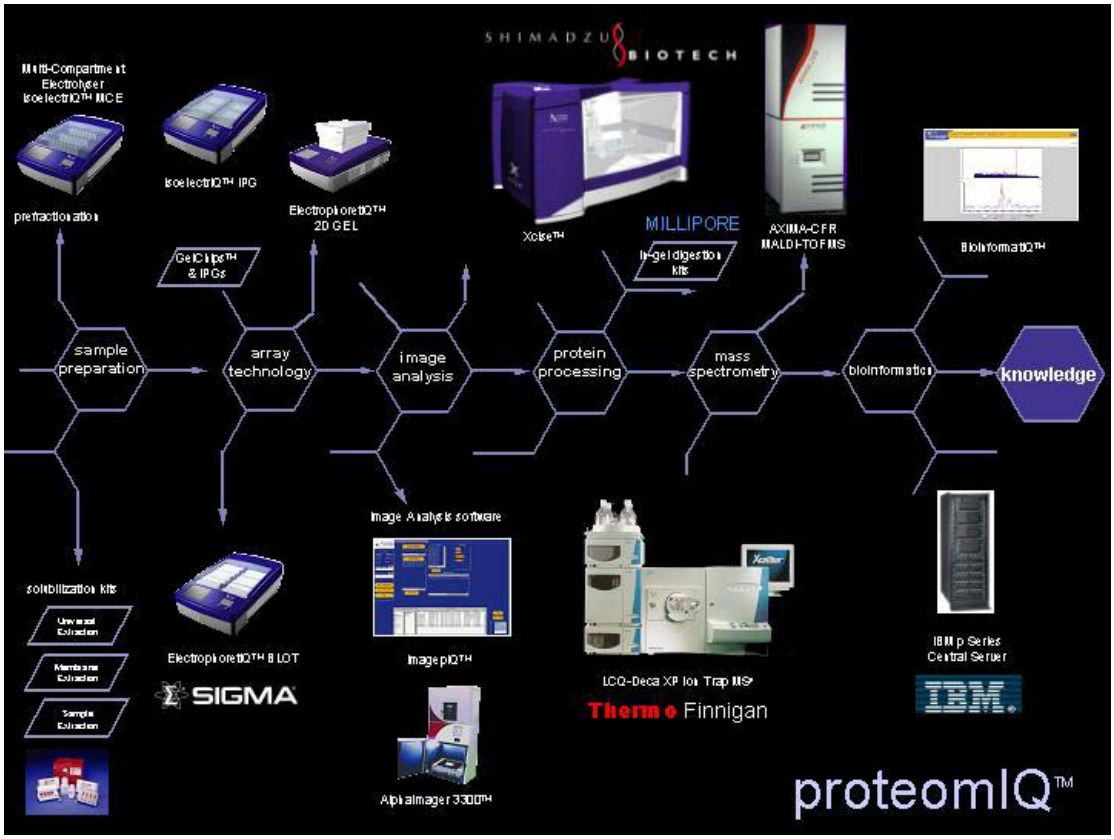
5. BioTech Capital Ltd

BioTech Capital Ltd is the largest individual shareholder in PSL apart from those directors and managers directly involved in the company. It is a Venture Capital Fund formed by Challenger International Limited, which went public in August 2000 with a capital raising of A$40 million. Its first investment, of A$3 million, was in PSL. BioTech is a cornerstone investor in Proteome Systems Ltd.

The main areas on which BioTech will be focussing are genomics, proteomics, medical devices, bioinformatics and enabling technologies. The fund's team of advisors and board members include Fund Chairman, Bill Ireland, and Fund Manager Harry Karelis; other Board members include Irene Lee, former Managing Director of Sealcorp Holdings Ltd and Michael Boyd, Director of Sonic Healthcare, Silex Systems and Chairman of Foundation Healthcare - all of which are listed on the Australian Stock Exchange.

Since its investment in PSL, BioTech Capital has also invested in four further Australian biotech companies: Pacific Knowledge Systems; Alchemia; X-Ray Technologies; and Xenome.

6. Proteomics platform: ProteomIQ



7. Competing proteomics companies

Company	Location	Business approach	Major collaborators
Amersham BioScience	Amersham, UK	Functional proteomics	
Applied Biosystems Inc (ABI)	Foster City, CA	Proteomics platform	Perkin Elmer; subsidiary of Applera; sister company of Celera
AxCell Biosciences Corp.	Princeton, NJ; Newtown, PA	Protein pathway database	Subsidiary of Cytogen Corp.
Caprion Pharmaceuticals Inc	Montreal, Quebec	Subcellular proteomics	Sun Microsystems
Cellzome GmbH	Heidelberg, Germany	Functional proteomics	European Molecular Biology Lab.
Ciphergen Biosystems Inc.	Palo Alto, CA	Protein chips	Pfizer; Invitrogen
CombiMatrix Corp.	Seattle, WA	Protein chips	
Compugen Ltd	Jamesburg, NJ	Computational proteomics	Mitsui Knowledge (Jp)
Curagen Corp	New Haven, CT	Drug target discovery	Warner-Lambert
GeneFormatics Inc	San Diego, CA	Structural proteomics	Bruker MS companies (BioSpin, AXS, Daltonics)
Geneva Proteomics (GeneProt) Inc.	Geneva, Switz and New Jersey	Large-scale proteomics	
Genomic Solutions Inc	Ann Arbor, MI	Automated 2-D gel/MA platform	Perkin Elmer
Hybrigenics SA	Paris, Fr	Protein-protein interaction	Pasteur Inst; Small Molecules Therapeutics Inc.
Integrative Proteomics Inc (IPI)	Toronto, Ontario	Integrated proteomics platform	Aurora Bioscience; Bruker MS companies (Biospin, AXS, Daltonics)
Large Scale Proteomics Corp	Rockville, MD and Vacaville, CA	Integrated proteomics platform; Biological assay	Subsidiary of Large Scale Biology Corp.
LumiCyte Inc	Fremont, CA	SELDI process for protein biochips	Shimadzu Biotech
MDS Proteomics	Toronto, Ontario	Functional	IPI

Inc		proteomics	
MelTec GmbH	Magdeburg, Germany	Topological proteomics; whole cell fingerprinting	Evotec OAI
Myriad Genetics Inc	Salt Lake City, UT	Proteomics platform	Bayer, Eli Lilly, Hitachi et al
Oxford GlycoSciences plc	Oxford, UK	Biological assay; protein databases	Incyte Pharmaceuticals; Pfizer Inc
Packard Biochip Technologies LLC	Meriden, CT and Billerica, MA	Proteomics platform	Subsidiary of Packard BioScience
PerSeptive Biosystems Inc	Framingham, MA	Protein analysis; Proteomics Solution 1™	Subsidiary of PE Biosystems
Phylos Inc	Lexington, MA	Functional proteomics; Trinectin™ proteome chip	Aventis; NCI; Cubist Pharmaceuticals
ProteoLogics Inc	Orangeburg, NY and Rehovot, Israel	Sub-cellular proteomics	
Signature BioScience Inc	Hayward, CA	Functional proteomics; phenodynamic profiling	MDS Sciex
Structural Bioinformatics Inc	San Diego, CA	Computational proteomics	IBM Life Sciences
Structural GenomiX Inc (SGX)	San Diego, CA	3-D protein structure	Celera
Syrrx Inc	San Diego, CA	Structural proteomics	Cubist; Novartis; Molsoft
Zyomyx Inc	Hayward, CA	Protein biochips	

9. PSL IP portfolio

	Country	***Title***
Granted		
722578	Australia	Analysis of molecules
68447	Singapore	Analysis of molecules
US06077951	USA	Glycosylhydrazines*
US05831077	USA	" *
703243	Australia	" *

Pending (national phase)

543310/98	Japan	Analysis of molecules
09/403196	USA	"
2289688	Canada	"
98914705.3	Europe	"

Pending (patent convention treaty)

PCT/AU00/01065	Electrophoresis apparatus
PCT/AU00/00194	Method and apparatus for manipulating arrays
PCT/AU01/00366	Macromolecule detection
PCT/AU00/01391	Electrolyser
PCT/AU00/00688	Apparatus and methods for high-resolution separation

* Licensed to Proteome Systems by inventors