Biotechnology Collaboration between New Zealand and Queensland: Opportunities for Growth

A report prepared for Industry New Zealand
by The Magic Pudding Company Pty Ltd*

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1 Background

Meetings between Prime Minister Helen Clark, Premier Peter Beattie and Ministers Pete Hodgson and Paul Lucas in Brisbane in May 2002 initiated a dialogue on potential collaborations between New Zealand and Queensland in the area of biotechnology.

This dialogue continued at the BIO 2002 meeting in Toronto in June and at the PacRim Biotechnology meeting in Auckland in November, and culminated in April 2003 with the signing of a memorandum of understanding between Minister Hodgson and Premier Beattie, agreeing to explore the potential for developing a strategic alliance in the biotechnology sector between New Zealand and Queensland.

In separate but parallel developments, both New Zealand and Queensland have identified biotechnology as a key plank in the development of their knowledge economies, and New Zealand has appointed a Taskforce to report on an action framework for growing the biotechnology sector.

This report has been commissioned in the latter context to explore collaborative opportunities between New Zealand and Queensland in the field of biotechnology.

2 State of Australasian biotechnology

2.1 SWOT analysis

Strengths

- **Human resources:** Although the combined population of Australia and New Zealand is only one third of 1% of the world's population, we do around 3% of the world's best science, including fundamental research in the disciplines of chemistry, biology and computing that underpin modern biotechnology.

- **Natural resources:** Australia and New Zealand offer an extraordinary level of plant, animal and microbial biodiversity, with up to 80% of our marine and terrestrial species being found nowhere else on the planet.

- **R&D costs:** The average costs of running agrifood, biomedical, pharmaceutical, diagnostics and clinical trial centres, including costs of salaries, laboratory space, equipment, consumables and support services, are as little as 50% of corresponding levels in the United States.

- **Clean and green:** Both Australia and New Zealand remain free of all Class A animal diseases, as listed by the OIE (Office International des Epizooties).

- **Quality of life:** International surveys of political, environmental, economic, safety, health, education and other quality of life factors in over 200 cities around the world show that New Zealand and Australian cities lead the world in terms of quality of life.

- **Infrastructure:** New Zealand spends more on IT infrastructure and communications (10.6% of GDP) than any other country in the world. Australia comes in fourth at 8.7% of GDP.

- **Commitment:** The New Zealand and Australian Governments, and those of many Australian States, have committed to the development of knowledge-based industries, and particularly biotechnology, as the basis for building their national economies.

Weaknesses

- **Technology managers:** Both Australia and New Zealand lack a critical mass of individuals with experience at the interface between science and business. Our scientists are too frequently illiterate in the language of business, and our business people in the language of science.

- **Cash:** Regardless of their stage of development, Australian and New Zealand companies raise less cash at lower valuations than their North American and European counterparts. This applies equally to seed investments from business angels, early stage venture capital and IPO's.

- **Culture:** We have been born and bred in an un-entrepreneurial, even anti-entrepreneurial, environment. Our scientists have been encouraged to publish rather than patent; our industries have chosen to imitate rather than innovate. Our investors have sought dividends rather than capital growth, and our governments have focused on three-year terms rather than thinking 30 years ahead.

Opportunities

- **Health:** The spate of mergers and acquisitions in the international pharmaceutical industry has changed the competitive landscape in favour of smaller knowledge-based companies. Roughly 25% of pharmaceutical industry R&D is now out-sourced, and will go to whichever biotechnology companies or research institutes offer the best opportunity to fill the pharmaceutical industry's pipelines.

- **Agriculture:** While the health applications of biotechnology provide a means to exploit our established strengths in biomedical research, agricultural applications offer us the unique opportunity to combine our brains *and* our resources to drive the social and economic transformation of our two countries. We are only 24 million people, but we own an awful lot of sheep!

- **Environment:** As for agriculture, environmental biotechnology is an area where Australia and New Zealand can exploit not only an outstanding research base, but also take marketing advantage of a relatively pristine environment. In the long term, our ability to develop biotechnological solutions to environmental problems will become a major source of revenue for Australasia.

Threats

There is only one threat, and that is failure to grasp these opportunities.

2.2 Potential

What contribution could biotechnology make to the economies of Australia and New Zealand?

Australia's current core biotechnology revenues (excluding pharmaceuticals, medical devices, food processing etc) are just over AU$1 billion. New Zealand currently earns around NZ$250m in biotechnology export revenues. Likely growth in these numbers can be estimated from current industry statistics or by comparison to other international targets.

International biotechnology targets

A simple guide to what might be achieved is the target published in 2000 by the five biotechnology-related Japanese government ministries (health, environment, agriculture, industry, energy). They have joined forces to invest US$18bn over five years in a national biotechnology strategy that they expect to give Japan approximately 1000 biotechnology companies by the year 2010. More importantly, they expect Japan's resulting annual revenues from biotechnology to rise from one trillion yen in 2000 to 25 trillion yen by 2010. That is equivalent to NZ$373 billion, or a bit more than half the combined GDP of Australia and New Zealand.

It is also a somewhat optimistic target, given that the already well-established US biotechnology industry will grow to only around NZ$200 billion by 2010 if it continues at its present growth rate. Interestingly, despite doubling national revenues every five years, the number of US biotechnology companies has barely changed, rising from around 1200 to 1500 over the past 10 years.

What would these figures mean for the Antipodes? Calculated on a population basis, the Japanese figures translate to targets of around 150 companies with revenues of NZ$50 billion for Australia and 30 companies with revenues of $10 billion for New Zealand by 2010. The US figures would suggest a similar number of companies, but with revenues of approximately NZ$15 billion for Australia and $3 billion for New Zealand. Given the relative maturity of the US industry, the latter targets seem more appropriate for Australia and New Zealand. The corresponding employment targets, extrapolated from projected US figures, would be 30,000 core biotechnology industry jobs in Australia and 6,000 in New Zealand.

Interestingly, we already have at least these numbers of companies in both countries, but their revenues and employee numbers are only a fraction of the corresponding international targets. A key requirement thus appears to be growth in individual company size and revenues, although, given our relative emphasis on the agricultural and environmental industries, it seems likely that we may always have a larger number of somewhat smaller companies.

Industry statistics

An alternative approach to estimating potential biotechnology industry outcomes is to use statistical data from similar economies. In these terms, the following indicators may be useful:

- **Number of biotech companies per million of population:** This number ranges from 2 in Japan to 25 in Israel, Finland and Sweden. The US has 5, while New Zealand, Canada and Australia are in the range 11 to 14. If we set an aggressive target of 25, Australia and New Zealand should have 500 and 100 core biotechnology companies respectively, ie about double the present number.

- **Biotech employees per 1000 of total population:** This number ranges from 0.2 in the Netherlands to 0.8 in Finland and Scotland. Australia and NZ are both around 0.3, while the US is 0.67, having grown from 0.3 in the last ten years. If we set an aggressive target of 1.5, which is where the US is projected to be in 2010, then total employment in the Australian and New Zealand biotech industries would be 30,000 and 6,000, respectively.

- **Biotech employees per company:** The company and employee numbers above translate to a target of 60 employees per company. This represents a substantial increase over current figures of 20 and 30 in Australia and New Zealand respectively, but still falls far short of the USA, which currently averages 130 employees per core biotech company. The latter figure and critical mass considerations suggest that a smaller number of larger companies may be the most effective growth path in the longer term.

- **Revenues per biotech employee:** These range from around US$100,000 per employee (Australia) to over $300,000 per employee (the Netherlands). The US and UK are both around $150,000 per employee, with the US figure having grown from $100,000 over the past ten years. An aggressive target of $250,000 per employee would result in revenues of US$7.5 billion (NZ$13.5b) and US$1.5 billion (NZ$2.7b) for Australia and New Zealand respectively.

- **Revenues per core biotech company:** The company numbers and revenues above translate to revenues of US$15 million per core biotech company. This compares to current figures ranging from US$2m per company (Australia) to US$20m per company (USA).

Ultimately, the most useful measure of success will be revenues generated by the biotechnology industry per head of population. At present, Australia generates approximately US$30 per person: New Zealand's biotechnology export revenues suggest a similar return. This does not compare favourably with our competitors: Belgium US$160, Finland US$130, United States US$100, the Netherlands US$70 and the United Kingdom US$50 per head.

The target numbers (of companies, employees, revenues per company and revenues per head) above, would result in biotechnology revenues of US$375 per head of population for both Australia and New Zealand. This is consistent with a direct extrapolation of the US data, but significantly less aggressive than Japan's target of $1600/head!

Targets for 2010

Based on either of these analyses, it would seem that Australia and/or New Zealand could reasonably hope to achieve up to ten times current biotechnology industry revenues by 2010. Queensland, with around 16% of Australia's population, but a substantial kick-start in biotechnology investment, might reasonably seek to attract 20% of the Australian total.

The following are proposed as appropriate targets:

	Australia	New Zealand	Queensland
Companies	500	100	100
Employees	30,000	6,000	6,000
Revenues (NZ$ m)	13,500	2,700	2,700

2.3 Which patch?

Achievement of these targets will require unprecedented levels of co-operation between researchers, investors, industries and governments throughout Australia and New Zealand. It will also require us to focus our efforts in those areas likely to secure the maximum returns on our investments. For reasons outlined below, these are most likely to be in the fields of human health and agricultural biotechnology.

Human health

There is no doubt that the single largest market for the products of biotechnology will continue to be human health. In 2002, world pharmaceutical sales reached US$400 billion, of which 51% was in North America, with an annual growth rate of 8%. Increasing demand in the developing world and the emergence of virulent new diseases will ensure this growth is sustained.

It is also evident that the future development of the pharmaceutical industry is now being driven by biotechnology. For example:

Novel targets*:* Although the human genome encodes upwards of 50,000 proteins, all of which are potential targets for new drugs, the pharmaceutical industry has traditionally targeted just 500 of these proteins for which the structures and functions were known. Sequencing of the human genome has expanded this range of potential pharmaceutical targets one hundred-fold.

Bioinformatics: An increasingly critical area of biotechnology is now the analysis and interpretation of the multitude of gene and protein sequences that are being identified. Strong skills in bioinformatics will allow rapid identification and validation of targets in the human genome and those of disease-causing organisms.

Structure-based drug design: Knowledge of target sequence and structure will facilitate rapid and increasingly automated drug discovery. This will be supported by significant increases in chemical diversity being created by companies combining molecular design and combinatorial chemistry.

Pharmacogenomics: The ability to identify SNP's (single nucleotide polymorphisms) in the genomes of individual patients will make it possible to not only identify the specific genes responsible for their disease, but also to tailor drugs to an individual's particular needs. This will result in drugs with increased efficacy and reduced side effects.

New varieties of drug molecules: Increased understanding of the roles of oligosaccharides and nucleic acids in governing biochemical processes within and between cells is leading to the recognition that traditional small molecule pharmaceuticals may not be of the appropriate size or shape to recognise and interact with many binding sites. As a result, there is a growing focus on the use of proteins, sugars and nucleotides as drug therapeutics.

The number of these opportunities, and the speed with which they are emerging, is exacerbating the trend for major pharmaceutical companies to focus more on sales and marketing, while either in-licensing new products or outsourcing research and early stage development to biotechnology companies and research organizations. Both Queensland and New Zealand are extremely well placed to take advantage of this trend, particularly given the strength of our track records for excellent research and relatively cheap R&D costs.

Agricultural biotechnology

World food production has doubled since 1960, and productivity from agricultural land and water usage has tripled. The population of the planet, on the other hand, has doubled since the 1950s, and is expected to double again by 2030. If sufficient food production is to be maintained, agriculture must become still more productive, as well as less damaging to the environment. In addition, globalisation of the food sector is resulting in growing pressure to use innovation to remain competitive.

It is evident that agricultural biotechnology (defined broadly to include any application of biotechnology to the development of plant and animal products, improvements in plant and animal productivity and, for present purposes, equivalent aspects of aquaculture) will play the major role in meeting these requirements. It will not only increase food production, but also reduce the dependence of agriculture on agrochemicals and the negative environmental impacts associated with traditional production methods.

In fact, the first generation of agricultural biotechnology, which focused primarily on the development of insect resistance, disease resistance and herbicide tolerance, is already history. Based on relatively simple, single-gene technologies, it was rapidly monopolised by companies such as Monsanto, Novartis and Dupont, who were able to corner the field by patenting or licensing the fundamental enabling technologies of plant gene transformation, gene expression and modification.

The second, and much more extensive, generation of agricultural biotechnology products will result from carefully tailored improvements in plant and animal traits based on modifications to much more complex, multigenic, pathways. For example:

Marker assisted breeding: By sequencing and mapping the genes, or groups of genes, responsible for any given trait we can vastly accelerate the breeding of plants and animals with improved characteristics, such as higher yielding trees, leaner meat, higher quality grains.

Biopharmaceutical products: Similarly, transfer or substitution of genes from one species to another offers the opportunity to create species capable of producing desired biopharmaceutical products in greater amounts or at substantially lower cost, eg pharmaceuticals manufactured by bacteria or plants, human protein products from the milk of animals. Less controversially, New Zealand's and Queensland's level A OIE disease-free status provides a strong foundation for the development of bioactives derived from agricultural animals and the marine environment.

New materials: Understanding the biochemical and genetic mechanisms of metabolic pathways will lead to products with novel food, pharmaceutical and industrial uses, for example, knowledge of lipid biosynthesis leading not only to higher yields from oil seeds, but also to new oils with potential applications ranging from nylon synthesis to industrial lubricants.

Environmentally adapted plants and animals: Understanding the molecular basis of the interactions of plants and animals with their environments will allow the transfer of genes providing environmental protection between species, thus producing crop plants resistant to drought, heat or salt, and plants or animals resistant to bacterial, viral or parasitic disease.

Safer, more nutritious foods: Development of DNA probes and on-line biosensors will vastly improve the efficiency and effectiveness of food contamination detection, and the ability to genetically modify food species will allow the production and marketing of foodstuffs tailor-made for patients with specific diets, allergies, or even simple food fads.

In short, the second generation of agricultural biotechnology will provide the products to underpin the global economies of the 21st century.

Given the importance of agriculture to both Australian and New Zealand economies, it seems clear that we should seek to play a key role in these developments in agricultural biotechnology. This has special relevance in the context of closer biotechnological relationships between New Zealand and Queensland, where agricultural biotechnology offers a unique opportunity to capitalise on the combination of our natural and human resources with our existing primary industries.

So, how do we secure seats at the second-generation agricultural biotechnology table? Certainly, no one company or institution in New Zealand or Queensland has all the competitive drivers required to do the job.

Between us, on the other hand, we certainly do. Our natural and bountiful biodiversity gives us access to a tremendous storehouse of valuable plant and animal traits, seeds and germ plasm. Our research base in agriculture and related sciences, although scattered over Crown Research Institutes, CSIRO, co-operative research centres, universities and various departments of primary industry, has underpinned the development of many novel herbicides and fungicides. The pool of expertise built up in our largely medical research-oriented institutions and their spin-out companies has given us world-class facilities in gene sequencing and functional genomics, combinatorial chemistry, high throughput screening and bioinformatics.

Where next?

How should we proceed? Clearly, our best bet will be to maintain and further develop our research base in both human health and agricultural biotechnology, and to link it to end-users through the formation of alliances and spin-off companies. Specifically, based on the international comparisons and statistics outlined above, New Zealand and Queensland should each be aiming to spin out around 10 biotechnology companies per annum from our universities and government research organisations in each of the next five years

Recommendation: New Zealand and Queensland should be jointly targeting the formation of 20 spin-off companies per annum in the fields of human health and agricultural biotechnology.

3 Opportunities for NZ/Qld biotechnology collaborations

To achieve this target New Zealand and Queensland will need to co-operate and collaborate at many levels. These include pooling mutually beneficial knowledge, joint investments in infrastructure, alliances between research organizations, and, most importantly, commercial collaborations between our evolving biotechnology industries.

The following is a helicopter view of some of the classes of collaboration that might be pursued.

3.1 Knowledge-based alliances

Generating knowledge, including proprietary know-how and patented IP, is expensive, and mechanisms that allow it to be shared without loss of competitive advantage will obviously create value for both Queensland and New Zealand. This is especially likely to apply in areas where the joint development of IP/knowledge can be separately applied to industries that rely on our temperate and tropical environments, respectively. Two examples are:

Bovine genomics/proteomics

The complementary nature of our domestic cattle industries (New Zealand dairy, Queensland beef) makes bovine genomics and proteomics an attractive target for joint development. Functional genomics, in particular, will enable the identification of groups of genes encoding for desirable characteristics in beef or dairy cattle as well as some that are common to both. So there is thus a real opportunity for knowledge of the bovine genome to be developed jointly by both partners, but made freely available to either party for individual applications.

A key input to this process will be the sequence of the bovine genome, which is likely to be completed by a consortium involving AgResearch, Baylor College of Medicine, the US Department of Agriculture and others by 2005, but most useful outcomes will require much more detailed understanding of both gene function and bovine proteomics.

These will come partly from genetic studies (eg those being conducted by the Livestock Improvement Corporation (LIC) in collaboration with Via Lactia), partly from gene silencing, marker analysis and related strategies (eg those being undertaken by Brisbane biotech companies Benitec Pty Ltd and Genetic Solutions Pty Ltd), and partly from proteomic studies (eg those proposed by Fonterra in collaboration with the University of Auckland and, prospectively, with IMB and CSIRO). An integrated approach to the generation of this knowledge base, akin to that already established by New Zealand's sheep industry through the Ovita consortium (and its subsidiary Covita) would bring great synergies to all concerned.

Biodiversity

Some 25% of all pharmaceutical products are directly or indirectly derived from chemicals isolated from plants, animals and micro-organisms. Of particular interest are species and environments that have not yet been well explored. These include most micr-organisms, many marine environments, and extreme ecosystems such as that of the Antarctic.

New Zealand and Queensland together have the capacity to span all these species and environments, but the real issue is the difficulty in matching these outstanding sources of chemical diversity with an adequate collection of biological screens to fully exploit them. Traditionally this is done through one-on-one arrangements with pharmaceutical companies or biotechnology companies with a range of proprietary screens. The Queensland Pharmaceutical Research Institute, for example, has attracted more than AU$50 million in funding from AstraZeneca over the past decade to screen extracts derived from Queensland's tropical rainforests.

There are numerous other players currently building major collections of extracts based on New Zealand's and Queensland's biodiversity. The Australian Institute of Marine Science (AIMS) and the National Institute of Water and Atmospheric Research (NIWA) both have very substantial collections of organisms from tropical and temperate marine environments, respectively. Other sources include the Cawthron Institute (marine bioactives), Xenome Ltd (marine toxins), IMB (marine micro-organisms), GNS (extremophiles), BioDiscovery New Zealand Ltd and Crop and Food (terrestrial plants).

Together, these groups offer an incredible range of chemical biodiversity. The development of mechanisms to share this resource and apply it to a much larger range of biological assays would give our biotechnology industries a clear competitive advantage in the discovery and development of biodiversity-based pharmaceuticals.

3.2 Infrastructural alliances

Investment in biotechnology infrastructure has been recognised as a key requirement in Australia and New Zealand. The Queensland Government, in particular, has made a number of major investments in bricks and mortar, and the Australian Government has invested in very large equipment items through the MNRF scheme.

Less emphasis has been placed on providing resources in areas where substantial new services are required to support the development of the biotechnology industry. This is partly because of the critical mass required to justify investment in these resources. They are thus obvious candidates for joint investments between Australia and New Zealand. Two widely cited examples are:

Bioinformatics

Bioinformatics is currently being developed in a piecemeal manner in both Australia and New Zealand. The biggest single initiative is the Institute for Molecular Bioscience (IMB) plan to recruit up to 70 bioinformaticians with the capacity to service major plant, animal and human biotechnology projects. The co-location of CSIRO's key animal biotechnology staff, and some of their plant biotechnologists, with IMB will further enhance this initiative.

In Auckland, the University and AgResearch have combined forces to establish a Bioinformatics Institute with emphasis on population genomics and structural biology.

As at IMB, there are close links to university strengths in mathematics, statistics and computational biology.

Ultimately, what is needed in both countries is a facility that provides high quality bioinformatics tools (mainly software) and training (at postgraduate level) for the biotechnology community at large. Such a facility would most obviously base its core operations in Brisbane and Auckland, but additional nodes could operate throughout New Zealand and Queensland.

Discussions on this concept with key players in Brisbane and Auckland suggests that the most beneficial mode of operation would involve individual nodes contributing specialist 'tools and training' to a shared resource that could then be applied by individual members for their own purposes. There would also be significant support for extending the concept to include shared supercomputing facilities.

Preclinical and clinical trial facilities

Although increasing numbers of preclinical candidates are being designed or discovered in Australia and New Zealand, there is no local capacity to undertake comprehensive preclinical or clinical trials.

There are, however, many potential contributors to this capacity scattered throughout Australasia, and many of the key players are located in New Zealand and Queensland. These include:

- A specialist Phase I facility established at Royal Brisbane Hospital by QPharm (a joint venture between the University of Queensland and the Queensland Institute of Medical Research),
- The Clinical Trials Centre being established by Auckland University in partnership with the Auckland District Health Board,
- Drug delivery expertise at the University of Otago,
- Pharmaceutical manufacturing at the Industrial Research Laboratories (IRL),
- Several small companies with specialist preclinical or clinical offerings.

Integrating these facilities, and complementing them with limited additional resources where appropriate, would significantly enhance the region's competitiveness in adding value to pharmaceutical, nutraceutical and other bioactive leads generated by research organisations and biotechnology companies.

3.3 Research alliances

While high quality research has always been one of Australasia's greatest strengths, we have been much less successful in its development and commercialisation. Fortunately, times are changing, and much of this change is being driven by the emergence of a new spirit of entrepreneurism amongst our research institutions. Alliances between such institutions have the potential to not only build critical research mass but also nurture their skills in its subsequent commercialisation.

IMB/CMB connection

The Institute for Molecular Bioscience (IMB) is the flagship of the Beattie government's investment in biotechnology, and the Centre for Molecular Biodiscovery (CMB) is one of five new national Centres of Research Excellence funded by the New Zealand government.

Both organisations bring together substantial resources at the interface of chemistry, biology and computing. In the case of IMB this is a physical juxtaposition, with some 250 IMB scientists moving into shared facilities with colleagues from CSIRO and the Queensland Department of Primary Industry during April 2003. CMB is more a virtual centre at this stage, being built around the mutual interests of five independent but complementary research groups at the University of Auckland.

Together, these two organisations offer serious critical mass in post-genomic drug design and development. There are, of course, substantial overlaps in their activities, but also important synergies and complementarities. Both organisations, for example, have a strong commitment to the mathematical modelling of cells and cellular processes, but they come to this exciting area from opposite directions, with IMB specialising in modelling at the molecular level whilst CMB has a history of modelling at the organ level.

IMB and CMB also share two very important commitments with respect to the future development of biotechnology in New Zealand and Queensland. The first is their commitment to facilitate the transfer of their human health expertise to plant and animal applications through their close interactions with organisations such as CSIRO and AgResearch. The second is to continue to develop and commercialise the applications of their research in collaboration with industry, including their own spin-out companies.

It is noteworthy that these two organisations are also clear leaders in the commercialisation of university research through spin-out companies. This includes the development of a level of entrepreneurism not previously seen in Australasian universities, and opens up opportunities for joint teaching and research programs in biotechnology commercialisation.

NIWA/AIMS connection

The Southern Hemisphere's two pre-eminent marine science organisations NIWA and AIMS also have many overlaps, synergies and complementarities. These include very substantial opportunities in marine biotechnology as well as in fisheries and oceanography.

Both NIWA and AIMS have substantial programmes collecting marine macro-organisms and micro-organisms. NIWA's program is focussed on the discovery and development of anti-inflammatory drugs in collaboration with the Malaghan Institute, while AIMS has placed particular emphasis on the search for novel anti-cancer and anti-infective agents. AIMS has also developed valuable leads with potential as sunscreens, antioxidants and herbicides, some of which are the subjects of joint ventures with national and international companies.

At the aquaculture level there are strong common interests in managing disease in intensive aquaculture farms, including the identification of new antibacterials from soil microbes, and in better understanding and application of the life cycle of shellfish and crustaceans, including the rock lobster.

Closer collaboration between NIWA and AIMS would not only bring together complementary collections of marine biodiversity (temperate and tropical, respectively) but also derive additional synergies in terms of skills, experience and facilities (eg NIWA deep water capacity).

3.4 Commercial alliances

There is little point in attempting an exhaustive analysis of all the individual opportunities for commercial collaborations between New Zealand and Queensland companies and research organizations. On the other hand, it is important to demonstrate that such opportunities exist. To that end, the following paragraphs provide outlines of opportunities in two aspects of human health and agricultural biotechnology: the design and development of new drugs, and the application of genomics to improved agricultural productivity.

The design and development of new drugs

An excellent example of the opportunities in drug development is provided by the work of Professor Bill Denny at the University of Auckland. Over the past 20 years, seven drugs designed in Denny's laboratory have proceeded to clinical trial. Of these, one is marketed and four are still being investigated. Drug design is also a strong point in Queensland, with Mark von Itzstein and Mark Smythe, two key players in the design of the anti-influenza drug Relenza, having founded new drug design companies in the past two years. Several of the spin-out companies of the IMB, which incorporates the former Centre for Drug Design and Development, also have compounds in or approaching clinical trial.

A common feature of several of the IMB spin-outs is their focus on the design of small molecules that mimic peptides and proteins. This process can be undertaken on a quite specific basis, designing a small molecule to mimic a particular peptide, but also lends itself to the generation of large libraries of molecules whose members may have the capacity to mimic the biological activity of any peptide, including those whose sequence or structure may be unknown. These libraries could clearly be partnered with a range of possible targets generated from companies with either human health or agricultural applications.

A specific example is that of oligosaccharides, many of which are now being identified as the molecules responsible for various intracellular and intercellular recognition phenomena. Brisbane-based Alchemia Pty Ltd has developed generic technology to enable the efficient chemical synthesis of oligosaccharides such as low molecular weight heparin. Many such oligosaccharides have shown clear clinical potential, but the cost of manufacturing has meant that only those that may be readily isolated from natural sources have achieved clinical application. Alchemia has solved this problem by creating a series of standard oligosaccharide building blocks, many of which are currently being manufactured by IRL. With the construction of IRL's new GlycoSyn facility there is a real opportunity to expand the present collaboration and develop new ones.

Another major area of interest for the development of new pharmaceutical products is the isolation of bioactive products from animal sources. This is an area where New Zealand has traditionally been much more active than Australia, with well-established companies such as New Zealand Pharmaceuticals involved in the extraction of pharmaceutical ingredients from animals. More recently, as in the case of AgResearch's work on bioactives from deer velvet, attention has shifted to biochemically and ecochemically driven searches for novel bioactives from a variety of marine and terrestrial plant and animal species.

Using genomics to improve agricultural productivity

It is important to recognise that genomics may be utilised to improve agricultural productivity without ever resorting to the use of genetically modified crops. Thus, for example, HortResearch has demonstrated the existence of common genes encoding desirable functions (taste, texture, etc) in a variety of temperate fruits. The genetic markers identified in this research may also have application in tropical fruits. A joint venture is planned in which HortResearch contributes skills and IP in marker-assisted breeding derived from temperate fruits, and QDPI contributes knowledge and experience of tropical fruit genetics.

However, while the emphasis in both Australian and New Zealand genetic improvement programs is clearly on marker-assisted breeding rather than genetically modified organisms, there is also a great deal of valuable transgenic research being undertaken.

An intriguing example of this potential is offered by IMB spin-out Cyclagen Pty Ltd, which has identified cyclic peptides produced by certain plant species that provide natural immunity to attack by insect pests. The company is currently working on the incorporation of the genes required to produce these peptides in commercial crop species. Related work at HortResearch has demonstrated that the incorporation of the gene producing streptavidin in plants has similar insecticidal effects. The complementary strengths of these two groups in chemistry, structural and molecular biology, insect physiology and ecology provides a rare opportunity to make substantial advances over existing genetically engineered insect resistance technologies.

4 Impediments

To capitalize on these opportunities we need to do three things. First, we must identify biotechnology, and particularly agricultural biotechnology, as a strategic priority and focus more of our research resources in this area. Second, we must create and implement mechanisms to train or attract a cadre of technology managers capable of developing and commercialising our R&D. Third, we must establish a financial environment which enables us to attract serious venture capital into Australasian biotechnology.

5 Solutions

5.1 Increased focus on agricultural biotechnology

A major part of the government-owned science resources of New Zealand and Queensland is already focused on agriculture, though only a relatively small component of this effort is devoted to agricultural biotechnology. Among universities and their spin-out companies there is much more emphasis on biotechnology, but this is predominantly directed towards human health rather than primary industry applications.

Co-location of universities and government research organizations, as in the case of the Biomolecular Science Precinct (comprising IMB, CSIRO Livestock Industries and the Queensland Department of Primary Industry's Agricultural Biotechnology Centre) at the University of Queensland, or the conglomeration of government and private research organisations surrounding Massey University at Palmerston North, will obviously go a long way towards addressing these issues. Further momentum could be gained by directing government-controlled resources towards agricultural biotechnology activity conducted at these and other public-private research interfaces, particularly where these involved subsequent commercial development.

An important secondary aspect of developing focus in the New Zealand/ Queensland collaboration is the opportunity to exploit the resulting critical mass internationally. In this context, Premier Beattie's proposed joint marketing strategy for Australasian biotechnology will be particularly valuable, as will moves to integrate our biotechnology industries through closer ties between Ausbiotech and BioteNZ.

Recommendation: That the Queensland and New Zealand governments make agricultural biotechnology a key component of their strategic alliance in biotechnology.

5.2 Attract, train and retain competent technology managers

The lack of experienced managers of biotechnology enterprises is often cited as a major impediment to the development of the Australian and New Zealand biotechnology industries.

In fact, there is no shortage of Australians and New Zealanders with this experience. The problem is that there are very few of them who are resident in Australia or New Zealand.

We need to find ways to encourage our expatriates to come back to help build our biotechnology businesses. Industry New Zealand's World Class New Zealanders program is a good step in this direction.

Of equal importance is the need to cross the cultural barrier between research and business, and the physical barrier between New Zealand and Australia. We need to find ways to enable our researchers to take time out from careers in universities and research organisations to work and gain experience in industry. And we need to find ways to enable New Zealanders and Australians to spend sufficient time in each other's laboratories and businesses to build real collaborative partnerships. This is an area where both governments could make a major contribution at relatively low cost.

Recommendation: That the Queensland and New Zealand Governments jointly establish a biotechnology exchange programme to facilitate exchanges of personnel between businesses and research organisations on both sides of the Tasman.

In a similar vein, we need to find ways in which the leaders of our biotechnology industry can draw on each other's skills and experiences for their mutual development. The role of CEO in a small biotechnology (or other knowledge-based) company is different from any other, and beginners in the game will clearly benefit from mentoring from their peers.

One way to achieve this is to bring the CEO community together for regular idea and experience-swapping meetings, and this is already happening on a small scale in both New Zealand and Queensland. An obvious extension would be to hold joint meetings of CEOs from New Zealand and Queensland. This would have the additional advantages of developing mutual knowledge of biotechnology activities on both sides of the Tasman and facilitating the generation of new and exciting collaborations.

The Biotech Meeting for Chief Executive Officers of biotechnology companies sponsored by Burrill & Company is a good example of the effectiveness of this strategy. It is held annually at Laguna Niguel in Southern California, and attracts over 175 top biotech executives who gather to share management ideas, set an agenda for the industry, and network with each other.

Recommendation: That the Queensland and New Zealand Governments jointly establish a CEO summit, to be held alternately in Queensland and New Zealand, which CEOs of biotechnology companies throughout Queensland and New Zealand would be invited to attend.

5.3 Establish a Trans-Tasman venture capital fund in biotechnology

Many in the investment community argue that the core issue in financing Australasia's biotechnology industry is not lack of capital but lack of investor readiness. In fact, both statements are true, and their effects are cyclic.

Lack of pre-seed funding aimed at establishing proof-of-concept, protecting intellectual property and facilitating business planning has meant that emerging biotechnology companies in Australia and New Zealand have traditionally been poorly prepared to attract venture capitalists or other professional investors. This issue is now being addressed in Australia through the Biotechnology Innovation Fund, which has awarded 138 grants of up to $250,000 over the past two years. A substantial proportion of these have gone to spin-out and start-up companies.

As a result, there are now more investor-ready companies seeking first round venture capital or equivalent funding, but ability to raise these funds in Australasia is generally limited to between 10% and 20% of capital raised for equivalent opportunities in the USA or Europe. This situation has been partly addressed by Australia's IIF scheme and New Zealand's VIF, although there is as yet no VIF specialising in any aspect of biotechnology.

In Queensland, the Queensland Investment Corporation, at the behest of the Beattie government, has established the $100 million Queensland BioCapital Fund, whose stated mandate is investment in human health applications, preferably at the stage of late preclinical and early clinical trials. The CEO of QBF has also indicated a willingness to invest in New Zealand, thus opening doors to joint ventures in the human health arena.

So, what of agricultural biotechnology? In fact, the only significant source of venture capital investment in agricultural biotechnology in Australasia are Gresham Rabo's Food and Agribusiness Investment Funds (FAIF1 and FAIF2), which have roughly $130 million available for expansion stage investments. This is supplemented by good connections to a small number of US funds with similar investment profiles, but so far these have not resulted in any substantial level of investment.

This level of capital availability is insufficient to address the targets outlined in 2.3 above. The establishment of 100 appropriately capitalised biotechnology spin-outs over five to seven years will need venture capital investments of around $500 to $1000 million. That is roughly equivalent to the combined budgets of all of Australia's IIF's and New Zealand's VIF's. On the other hand, it is less than one cent per "Quiwi" per day.

Experience with the VIF scheme suggests that this level of funding could be raised with 2:1 leveraging of government funds from private investors. Furthermore, there is developing interest among some government research organisations in making joint investments with private venture capital funds, thus bringing additional capital to the table and giving both parties access to better deal flow. Commitment from the Queensland and New Zealand governments of a fraction of the total requirement may therefore be sufficient to drive the establishment of a viable fund.

Recommendation: that the Queensland and New Zealand Governments establish a joint venture capital fund in biotechnology aimed at generating, with appropriate private sector leveraging, a total of $500 to $1000 million over five to seven years.

6 Conclusion

There is a real opportunity for New Zealand and Queensland to work together to build a formidable Australasian biotechnology industry by 2010. We already have strong and often complementary research strengths, competitive R&D costs, outstanding natural resources and magnificent environments. Between us, we have all the ingredients required to make major contributions to both human health and agricultural biotechnology.

To achieve this, we need to identify biotechnology, and particularly agricultural biotechnology, as a key driver for future growth. We need to build our skills in bioentrepreneurism, and further strengthen them by developing mutually supportive links between the managers of New Zealand and Queensland biotechnology companies. And we need to secure substantial public and private investment in a combined New Zealand/Queensland biotechnology fund, thus ensuring that we achieve the full potential of our emerging biotechnology industries.