Biomedical research in Australia may have chalked up some successes, but it has also let some money-spinning ideas slip through its fingers. Having learned its lesson, this nascent industry is now beginning to flex its muscles. David Blake reports.

DREW BERRY/WEHI

Gaining medical momentum

Four letters sum up the how and why of Australian biomedical research as it stands today: GCSF. This abbreviation, which stands for granulocyte colony stimulating factor, will always be known as the one that got away.

Discovered in 1986 by Don Metcalf at Melbourne's Walter and Eliza Hall Institute (WEHI), GCSF is a hormone-like protein that stimulates certain bone marrow cells to make specialized white blood cells. It was patented and commercialized by the California-based biotechnology giant Amgen, and is now routinely used to help patients recover from cancer therapy. Sold under the brand names Neupogen and Neulasta, GCSF has yielded a massive US$5.7 billion in sales in the past three years alone.

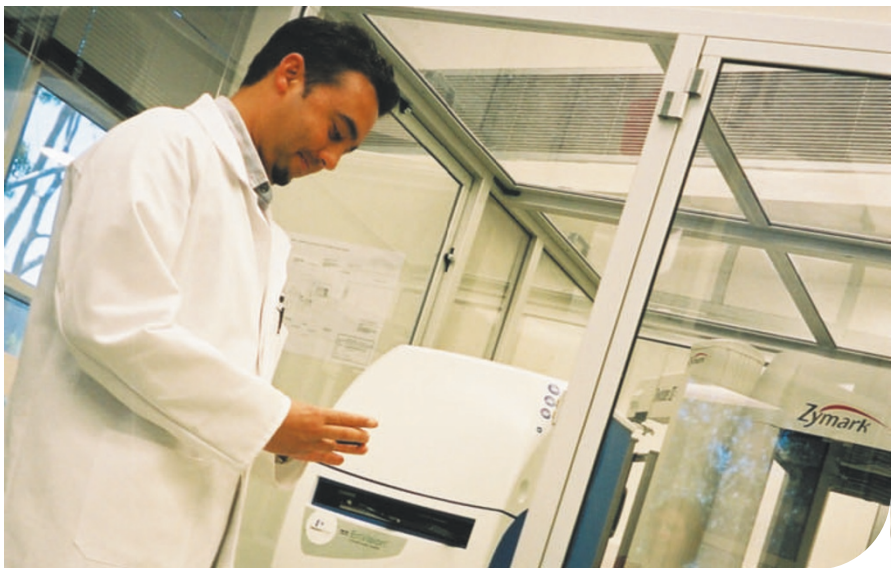
But rather than representing Australia's inability to exploit its discoveries properly, GCSF is a turning point. Some would argue that it had to be taken up by another party and become a huge money-spinner to initiate a sea change in Australian medical research. In the mid-1980s "the world was naive and the sorts of agents we were producing and cloning had no known commercial value", Metcalf recalls. "Pharmaceutical companies were uninterested in growth factors."

Metcalf and the WEHI learned from GCSF. Shortly afterwards a related cytokine, GMCSF, was successfully patented and the royalties flowed. GCSF also created the backdrop for Amrad, now a stalwart of the Australian biotech industry. In many ways, Amrad's story represents the sector's story.

Amrad was established by the Victorian state government in 1986 as a vehicle to develop and commercialize technology from four Melbourne-based research institutes, the WEHI (immunology), the Macfarlane Burnet Institute (virology), the Murdoch Childrens Research Institute and the Howard Florey Institute (brain research).

A survivor

The company went on to expand its partnerships, add extra business activities, list on the Australian Stock Exchange, experience a string of clinical trial failures, divest businesses and go through a 'rough patch'. Surprisingly, it is still in business. But now it is a leaner, cashed-up company with an



ADVANCED LABS

DREW BERRY

Pete Smith has overseen a change of direction at biotech firm Amrad.

express focus on cytokine biology and drug development, with a market value of about A$100 million (US$70 million) and A$60 million in the bank. Its projects are still dominated by research emanating from the WEHI.

Leading Amrad is Pete Smith, who is typical of the new breed of Australian biotech managers. Formerly a biotech and healthcare analyst for several merchant banks in the United Kingdom, he was also a co-founder of Onvyax, a British immunotherapy firm.

Smith is not the only new recruit for Australian biotech. Numerous companies are headed by returning expats, drawn back to Australia for various reasons, including attractive government incentives, the desire to raise their children in the relaxed antipodean lifestyle, and the challenge of working in a youthful and vibrant industry.

Although the medical-research sector has learned the lessons of GCSF, all is still not perfect. Ian Frazer from University of Queensland — developer of two vaccines against human papilloma virus — believes that universities still struggle with technology transfer. "There is still a problem with the business models, particularly when things are spun out of universities," he says. "Universities haven't learned to let go yet, but that will be resolved as market forces take over and determine how things are allowed to develop."

For John Stocker, of consulting group Foursight Associates, a major challenge confronting the medical biotech sector in Australia is the paucity of licensing executives who have strong experience in protecting the intellectual property of discoveries and in commercialization. "We need to understand how to extract real value when forging deals. We will probably have to do so by recruitment," says Stocker.

Another pressing challenge for Australian researchers is to move their work a lot further down the track before contemplating starting a company or even getting the pharmaceutical industry interested, says Peter Colman, head of the WEHI's Structural Biology Division. Last November, the WEHI opened an A$27-million biotechnology centre. Its director, Suzanne Cory, expects the new centre to allow researchers to take their basic-science discoveries further along the research and development pipeline. The centre includes a high-throughput chemical screening facility unique in Australia.

Lack of confidence

Michael Aldridge of Peplin Biotech, a Brisbane-based cancer-drug-development company, notes that players in the local therapeutics industry are not confident that they can create and build a business in Australia. "There's an expectation or trend to license to Merck, GlaxoSmithKline and Pfizer. There is no recognition that you can license to more focused players, who will provide you with a more collaborative role in the development process," he says. "There's also the opportunity to do these things independently and take them to the market yourself. But significantly more resources will have to become available for companies to achieve that."

However, the recent decision by a Singapore biotech company CyGenics to move to Melbourne may signify a promising new trend. CyGenics grows stem and blood cells to treat AIDS, leukaemia and blood disorders. The company recently announced plans to trial in Melbourne a technology to grow a person's own stem cells in synthetic bone marrow outside the body.

And Living Cell Technologies — a New Zealand company — recently transferred to Adelaide ahead of a planned listing on the Australian Stock Exchange to fund its development of a cell therapy tool for tissue repair.

These recent events are promising signs that the Australian capital market is starting to deliver the right formula for medical biotechnology. ■

David Blake is co-editor of *Bioshares*, a specialist biotech stock report.

BLAIN CRELLIN/VIRAX

David Boyle and his colleagues turned their work on poultry vaccines into a vector for HIV vaccines (see page A23).

Immunological strengths lead to new vaccines

Ian Frazer represents the cutting edge of vaccine development in Australia. Not only has his research team at the University of Queensland in Brisbane developed a vaccine to stop the spread of human papilloma virus (HPV) — the virus responsible for almost all cases of cervical cancer — but it has also tackled the much harder problem of creating a vaccine to treat the infection.

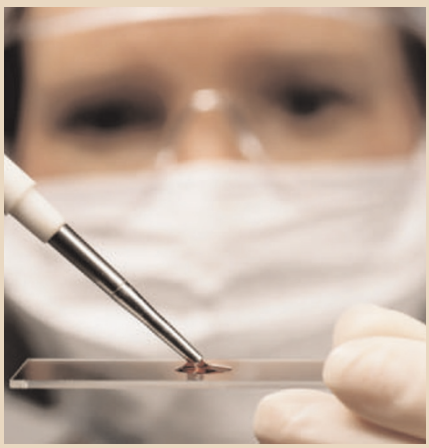
"Our vaccines are a great example of how to fight disease on several fronts at once," says Frazer. The preventive vaccine is currently in phase III clinical trials being conducted and funded by GlaxoSmithKline, Merck Sharp Dohme and CSL, and involving 20,000 women. The treatment vaccine is in phase I trials.

"The two vaccines used together have the potential to save millions more lives, decades sooner than using one alone," says Frazer, a Scot who emigrated to Australia because of its rich heritage in immunology.

He says most vaccine development in Australia can be traced back to Nobel laureate MacFarlane Burnett, who turned research at the Walter and Eliza Hall Institute in Melbourne from virology to immunology in the 1950s.

In the 1940s, Burnett was concerned with the threat of an influenza pandemic, and embarked on a virological investigation that led eventually to the world's first anti-influenza treatment. He then turned to vaccines and immunology. His theory of clonal selection and how we acquire immunological tolerance led to a Nobel prize in 1960. Perhaps more importantly, he mentored a cohort of scientists who went on to become leading immunologists, including Gordon Ada, Ian Gust, Gustav Nossal and Ian McKay.

A young Frank Fenner was recruited by Burnett to work on mousepox. Later he became the foundation professor of the John Curtin School of Medical Research (JCSMR) in Canberra, and then headed the Global Commission for the Certification of Smallpox Eradication. Fenner in turn recruited veterinarian Peter Doherty who with Rolf Zinkernagel won a Nobel prize for the discovery of the role of cell-mediated immunity in recognizing and destroying virus-infected cells.



The scientific legacy of these pioneers led directly to the invention of Co-X-Gene, a fowlpox vaccine vector, by teams headed by David Boyle of the Commonwealth Scientific and Industrial Research Organisation (CSIRO) and Ian Ramshaw of the JCSMR in the 1980s. This vector is now being used for two prototype HIV vaccines — it carries genes from HIV and a human cytokine to cells in the human body with the aim of triggering a directed immune response.

Boyle had been working on poultry vaccines when he realized that his fowlpox vaccine vector had human applications. Today an Australian public–private partnership is completing phase I trials of a preventive vaccine for HIV with funding from the US National Institutes of Health. And Virax, a Melbourne-based biotech company, is developing a treatment vaccine that is commencing phase II trials. Both trials are being managed by the National Centre for HIV Epidemiology and Clinical Research (NCHECR) in Sydney.

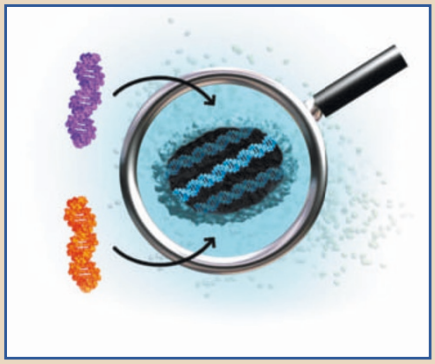
Clinical trials afoot

Today, the Cooperative Research Centre (CRC) for Vaccine Technology has reunited many of Burnett's protégé organizations across the country. Under the CRC's auspices a wide range of vaccines are currently being developed to fight streptococcal infections — a major issue for indigenous communities; Epstein–Barr virus — the cause of glandular fever and nasopharyngeal carcinoma, a particular scourge in China — and cytomegalovirus, a significant cause of birth defects.

"Australia's strengths are in our immunological foundations, and the motivation of our researchers to make a difference in the fight against disease," says Anne Kelso, director of the Vaccine CRC.

"Malaria research has been an Australian strength for decades. An effective vaccine is urgently needed, as drug-resistant malaria has begun to terrorize Australia's neighbours," says Beryl Morris, chief executive of Vaccine Solutions, a Brisbane-based vaccine commercialization company. Vaccine Solutions is working with the Vaccine CRC on two of three Australian malaria-vaccine initiatives funded by the Bill and Melinda Gates Foundation.

"No Australian partner has the resources to run a A$500-million (US$344-million) phase III trial. So international partnering is still essential. But we have good facilities for early phase trials," says Kelso.



DREW BERRY

Directed response: the Co-X-Gene is being used to ferry genes from the AIDS virus and from human cytokines into other human cells in an effort to encourage the immune system to fight back.

"Many small Australian biotechs still take their trials overseas when they could be adding value by doing the trials at home," says Tony Webber, director of Clinical Network Services, a Brisbane-based clinical-research management company. In fact, most of his work comes from companies in the United States drawn to Australia by a combination of high quality, low prices, a capacity to service tropical, sub-tropical and temperate disease issues, and a regulatory framework respected by the US Food and Drug Administration.

"Australia has developed a special expertise in HIV clinical trials," says Sean Emery, head of therapeutic and vaccine research at the NCHECR. The Australian government responded to the AIDS crisis with a national strategy that created three research centres devoted to virology, clinical research and social research. That 1990 decision has led to an infrastructure supporting both research and clinical trials. The NCHECR is now coordinating ten major HIV trials across four continents.

Webber says that there has been strong growth in contract clinical trials in recent years. "This is good for Australia's infrastructure, but we need to be sure we can consistently deliver patients for the trials from our relatively small population."

Emery is more cautious. "The growth in Australia's clinical-trial infrastructure is exciting but it's important that we maintain the academic integrity of the system," he says.

"Australia's regulatory authorities have the balance between risk and benefit about right," notes Frazer, although he says there needs to be better public-sector funding for large-scale clinical trials. "We can't rely on commercial trials alone, in determining the most effective ways to use the products of biotechnology in the community," he says.

Niall Byrne