Collaborating with industry: choices for Australian medicine and universities

Hamilton Moses III, Abbey Perumpanani and Jon Nicholson

ABSTRACT

- Collaboration between industry and academia is becoming increasingly prevalent and successful in Australia.
- To encourage and foster these relationships while preventing excesses, Australia needs to act now to create ethical, legal and legislative frameworks for collaboration.
- As the United States has progressed further than Australia in fostering and controlling collaboration between industry and academia, Australia has the opportunity to learn from the US experience.
- To speed the pace of development, Australia needs to consider making changes to legislation and increasing the level of government funding, either directly or by the creation of incentives for investment of venture capital and superannuation funds in biotechnology.

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SOME TIME AFTER codiscovering a law of proportions with German physician Wilhelm Weinberg in 1908, G H Hardy remarked that one of the joys of pure mathematics was knowing the results would never be applied to any human activity. Probably much to Hardy's chagrin, however, the Hardy–Weinberg law eventually became central to the study of many genetic problems. While this outcome was seemingly unforeseen, the leap between academic theory and practical application has become both more deliberate and commonplace, largely due to the growing expectation that academic institutions should become engines of economic development.

Over the past two decades, governments have strongly encouraged the commercialisation of discoveries by academics. Both parties have recognised compelling incentives to participate in industry–academia relationships, apart from the contribution that these arrangements can make to society. For example, medical institutions and investigators receive not just much-needed cash but also non-financial benefits (such as increased institutional professional recognition), which, in the long run, may prove even more important than funding. Companies that make the drugs and devices, on the other hand, gain access to research talent and an affiliation with a prestigious institutional name.

In trying to regulate industry–academia collaborations, governments have had to strike a balance between two extremes: allowing free and unfettered interaction, which can create conflicts of interest and compromise academic independence, or imposing heavy-handed regulation, which can stifle the translation of academic discoveries into commercial products. The challenge for regulatory authorities has been to design legislation that maximises potential gains from collaboration while deterring any damaging behaviour.

The United States has progressed much further than Australia in both fostering and controlling collaboration between industry and academia. In doing so, it has encountered a number of troublesome issues, such as conflicts between academic and industry priorities, and potentially dangerous compromises of academic independence. Australia therefore has an opportunity to use the US experience as an example of what to do (to foster greater interaction) and of what not to do (to avoid conflicts and compromises).

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The growth of collaboration in the United States

In 1999, academic institutions in the United States received about US$8 billion in biomedical funding from private foundations and US$17 billion from the federal government.[1] By comparison, corporate contributions to university laboratory-based investigations (excluding clinical trials) amounted to about US$3 billion, or about 7% of industry's total expenditure on biomedical research.[1] The contribution from industry increases every year, along with companies' influence on the course and conduct of academic research. Industry contributions, however, have not always been so prominent.

Between the 1940s and the early 1980s, most academic research in the US was federally funded, and the government retained ownership of the patents derived from the majority of academic innovations. Industry could have access to these patents, but not exclusive rights. Not surprisingly, efforts to attract private industry to transform these discoveries into economic value and growth were by and large unsuccessful, because what belongs to everyone belongs to no one. To complicate matters, there was no government-wide policy regarding access to inventions derived from federally funded research. The net result was a meagre flow of government-assisted inventions to the private sector. By the end of the 1970s, the government had about 30 000 patents, but only a small percentage of these led to new or improved products.[2]

A remedy emerged in 1980, when strong bipartisan congressional support led to the introduction of the Bayh–Dole Act. This legislation had two main provisions. First, it encouraged universities to seek their own patents on discoveries that were supported by public funding. Second, it prompted more industry funding for university research by delineating a clear protocol for sharing intellectual property, explicitly including intellectual property arising from publicly funded research. In interpreting the Bayh–Dole Act, universities also created incentives for individual investigators by sharing the rights with them. The Act was successful and very popular. Before the reform, universities were obtaining about 100 patents a year. By the close of the 1980s, this had risen to over 500. During the same period, industry's contribution to academic biomedical research, as a percentage of total industry-funded biomedical research, rose from 4% to 7%.[3]

These changes have had a staggering effect on productivity and a major economic impact. According to the Association of University Technology Managers, corporate licensing of university inventions in 1999 accounted for US$40 billion in economic activity in the United States, which, in turn, supports 270 000 private sector jobs.[1] In the fiscal year 1999, the top 10 universities alone received US$250 million in product royalties, with total royalties paid to universities of US$862 million.[1]

Conflicts and compromise

Conflicts arising from industry–academia collaboration fall into six categories.

Conflict of commitment. Financial conflicts usually involve the ownership of intellectual property. Academic conflicts arise from the use of university-paid time and facilities in for-profit activities. This could leave students in an uncertain position if their projects are assigned less because they are scientifically interesting or beneficial to their training, and more because the results are crucial to the company that their faculty mentor consults for or owns.[4] Similar interests might inhibit publication by postgraduate students and postdoctoral fellows, with a later adverse effect on their careers.

Conflict of interest. This arises when an investigator (or institution) plays multiple roles and has more than one master. The situation of the physician who also oversees trials on behalf of a company, and who may receive consulting fees from or have equity in the company, is one example that has received much attention, but the number of such relationships is unknown.[5]

In the United States, conflict of interest has been brought to the fore recently by the tragic events that occurred in gene transfer experiments that have been linked to the deaths of research participants.[5,6] In those cases, a clinical investigator and the investigator's institution held stock options in companies that sponsored the research. However, even when no equity interest is present, ethical questions arise. There is now considerable evidence that researchers with consulting relationships to drug companies are more likely to report results that are favourable to the products of those companies than researchers without such ties.[6] For these reasons, the most encompassing restrictions have been proposed to guard against the clinician playing these multiple roles.

Breach of trust. Loss of confidence in the independence of universities is also a fear, which can easily evolve from actual conflicts of interest. Another concern is the appearance of impropriety as the result of an institution itself having an economic interest in a commercial entity. Safeguards against this are now under active discussion, and are focusing on ground rules that separate roles and assure independent scrutiny of both preclinical (basic) and clinical research.

Distraction from basic discovery. This is the least explored, but in the long term perhaps the most important, concern. Over time, there is the prospect of a subtle shift away from basic research on fundamental biology and disease mechanisms and towards commercially oriented, later-stage research. This has been argued to be the case in Canada, where the growing number of CEO-scientists has led the Canadian Institutes for Health Research to increasingly reject grant applications on the basis that there may be a conflict of interest. There is also the potential for the diminution of research aimed at the general public good, where no specific commercial prize may exist. While no evidence has been published to indicate whether this fear is justified, such a scenario is certainly plausible.

Compromised academic independence. Commercial arrangements can threaten the fabric of free enquiry, open discussion, sharing of materials, and prompt and unfettered publication — ideally, the principles upon which academic research and graduate education should be based. In practice, of course, the race for precedence in publication already leads some academics to act more secretively than perhaps they should. This effect has been most pronounced in the arena of basic methods used in biotechnology and tools used in the early-discovery stage of pharmaceutical research, where it is the medical schools and teaching hospitals that have remained the fount of much new practical knowledge. Commercial pressures arising from the adverse effects of disclosure are likely to exacerbate this tendency.

Different mandates. For-profit businesses are pledged to increase the value of their investors' stock. This is quite different from the mission of medical schools. Imposing industry values on research institutions could result in more research on drugs and devices and less on insights into causes and mechanisms of disease. If, for example, it skewed research towards finding trivial differences between drugs, because those differences can be exploited for marketing purposes, this would be an unwelcome outcome.

These issues have given rise to a vigorous debate on how best to monitor, oversee, or possibly regulate, the relationship between industry and academia without stemming the flow of academic innovation into commercial reality. The fear of over-regulation has meant that many of the recommendations have been "light-touch", relying primarily on

the integrity of the involved parties. One of the earliest measures introduced was disclosure: academics publishing material in clinical journals were encouraged to declare any financial interests they held in the subject of the research. This measure was bolstered in the early 1990s, when several academic societies advocated disclosure as the most workable remedy for the management of individual and institutional financial conflicts of interest. In 2001, a group of leading international medical journals reaffirmed disclosure as a desirable safeguard, and went further, requiring authors who report clinical trials to have access to the source data in order to allow independent analysis.[7]

However, disclosure and open access to raw data alone are unlikely to provide a solution to the wide and varied conflicts. A recent article[8] suggested a new model for biomedical research based on four general principles:

- Veracity of basic research and clinical trials should not be compromised;
- Supervision should occur by a disinterested party;
- Proprietary rights and control of intellectual property ought to be acknowledged at the outset and assurances made regarding the right to publish; and
- Financial and non-financial incentives should be designed to address the needs of institutions, senior investigators and junior faculty.

The authors suggest that these principles can be translated into specific remedies, such as establishing a research institute, enhancing external supervision, or creating a new entity separate from the university to hold equity and receive royalties. These measures have been tried in different settings in the United States and could form the template for solutions that minimise the risk of conflict.

An Australian perspective

The Australian scientific community has been extremely vibrant. While Australia has 0.3% of the world's population, it produces nearly 2.8% of the world's research articles (an estimate based on Australia's share of major scientific journals indexed by ISI[9]). In addition, 1.3% of Australian publications fall in the world's top 1% of most-cited research articles. However, Australia has not been able to make full use of its academic talent to generate commercial innovation.[10] While Australia faces the same challenges as the United States in fostering industry–academia relationships, there are a number of specific local differences that have compounded the difficulties, particularly in the areas of legislation, funding and markets.

Legislative obstacles. Australia has yet to enact any law comparable to the Bayh–Dole Act, which would create a detailed protocol for technology transfer from academic institutions to industry. Institutions are still free to craft their own policies, and indeed are encouraged to do so by the National Health and Medical Research Council (NHMRC), which provides some broad guidelines.

Funding mix. There are two sources of non-government funding — industry and charitable institutions. In Australia, the incentives for either of these sources to provide funding are weaker than in the United States — some would argue, very much weaker. As a result, industry investment in health and medical research has remained small. As a percentage of gross domestic product, the investment of Australian industry in this area is a seventh that of Sweden, a fifth that of the United Kingdom, and a quarter that of Denmark.

In the United States, a major source of investment in biotechnology research is venture capital partnerships, which are attractive to institutional investors. In Australia, unlike in the United States, such funds are not able to employ limited liability partnerships without taxation penalty. Consequently, they face a 25%–40% lower return (depending on other taxes) in Australia than in the United Kingdom or the United States.

In the United States, around US$7.5 billion is provided by charitable institutions and foundations to medical research. To keep pace with the United States on a per capita basis, Australia would need around A$1.6 billion each year. Yet this source of funding has been largely absent in Australia, chiefly due to the absence of tax incentives. The recent government announcement of broader capital gains tax concessions for non-resident venture-capital investors is a step in the right direction, but there is still a long way to go to match current US incentives.

Scale. Being a geographically isolated, sparsely populated country has meant that most Australian inventions have migrated to the United States in search of funding, larger markets and stronger legislative frameworks. In recent years, however, the Australian government has been placing a stronger emphasis on addressing some of these issues, and on defining and directing the interaction of academic departments with industry.

In March 1998 a review was instituted by the Federal Government to identify future developments in health and medical research in Australia, and, in particular, the initiatives necessary to ensure that Australia remains at the forefront of health and medical research. The review, the Wills Report,[11] recommended closer interaction between industry, academic research organisations and government and an increase in funding for academic research. In response, the Federal Government announced a doubling of the base funding for the NHMRC over the next six years to A$614 million. (A similar shift in policy has occurred in Canada, with the Canadian government doubling federal funding of the Canadian Institutes for Health Research over the past four years.)

The NHMRC is the main source of funding for medical research in Australia. By doubling its budget, the government will provide a significant fillip to the research community. Additionally, the NHMRC has been skewing its funding towards research efforts that are likely to provide tangible benefit to the community and the economy. At the same time, it is encouraging academics to collaborate with industry through the use of matching funds.

These measures have yielded some limited but impressive results in recent years. One such Australian success story is the Bionic Ear Institute, founded in the Department of Otolaryngology at the University of Melbourne in 1984.

After 15 years of research, the Institute now produces a commercial "bionic ear" with a speech-understanding performance exceeding 70%. This has benefited over 26 000 people in over 50 countries. The most well known Australian example of a commercially successful scientific invention is ResMed's device for delivering positive pressure to the upper airways to relieve patients suffering from sleep apnoea. The research for this project was initially funded by the NHMRC. ResMed has since commercialised this product, listing on both the New York and Australian stock exchanges and having a two-year total return of 239% to 2001. There are other examples of successful collaboration between industry and academia, such as Biotron's commercialisation of biomedical projects developed from research at the John Curtin School of Medical Research and Ozgene's production of genetically modified mice for use by biotechnology and pharmaceutical companies as well as academic institutions.

Nevertheless, it remains a major concern that Australia will not reap the full potential of its research opportunities, in the same manner that the potential benefits of the revolution in information technology were not reaped in Australia, chiefly as a consequence of Australia's delayed focus on IT research.

We conducted discussions with various people from government and non-government bodies to gauge views on industry–academia collaboration. Martyn Evans, the former Shadow Minister for Industry, said in our interview: "We missed the IT revolution — we should not miss the biotech revolution." He believes a combination of modest legislative and more pronounced fiscal reforms will be needed to transform Australia into a "knowledge nation". A similar view was echoed by the former Shadow Minister for Trade, Carmen Lawrence, who believes that "legislative protocols need to be clarified" (along the lines of the Bayh–Dole Act). Professor Alan Pettigrew, the Chief Executive Officer of the NHMRC, thinks that, unlike in the United States, "academics and managers in industry lack an awareness of each other", which needs to be remedied by "upskilling both groups". Professor Gideon Polya, an academic at La Trobe University, expressed the concern, widely prevalent in the academic community, that the growth of "managerialism" in academic research could prevent the free spirit of scientific enquiry. Professor Glen Begley, Head of the Cancer Biology Laboratory at the Institute for Child Health Research, expressed a similar concern about the wide disparity in remuneration between doing academic research and doing industry-funded research, which provides a strong incentive to opt for the latter.

Conclusion

In the United States, collaboration between industry and academia has been overwhelmingly successful in creating wealth and hastening the pace of scientific development. The two keys are creating the right incentives to foster these relationships and enacting regulatory measures to prevent excesses. Recognising some distinct regional differences, Australia is following the trends in the United States. However, there remain many ethical, legal and legislative issues that will need attention as companies increase their collaboration with universities. Early implementation of legislation similar to the Bayh–Dole Act will help to speed up the pace of development. However, given the differences in the evolution of the relationship between industry and academia in Australia, a few specific measures tailored to Australian needs will be required, such as

- introducing incentives for investment of venture capital and superannuation funds in biotechnology; and
- improving the tax environment for philanthropy.

Australian educational institutions are currently being marketed to other nations as centres of excellence for higher education, and it is important that nothing be allowed to sully the image of these institutions. While the government tries to encourage industry–academia collaboration, it is necessary to do so in a controlled fashion so that the problems encountered elsewhere do not arise in Australia.

While there have been notable successes in collaboration between medical academics and industry in Australia, there is the opportunity for much more to be done. To encourage greater collaboration, the Australian government needs to carefully consider funding issues and protocols for collaboration.

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Competing interests

The authors serve as management consultants to many pharmaceutical and biotechnology companies, as well as academic medical centres, in the United States, Australia, and elsewhere in the world. None of the authors has a direct financial interest in this article.

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