The emerging role of academia in commercializing innovation

Shreefal Mehta

The university has been slowly changing from ivory tower to economic engine. Publicly funded research organizations are becoming increasingly adept at protecting intellectual property (IP), spinning out new companies, licensing technology to the private sector and even developing their own venture arms to finance commercial development of their discoveries. The migration of universities into more translational research will likely enhance their ability to capitalize on IP assets and ultimately could reduce the internal cost of producing new medicines

Corporate academia

The Bayh-Dole act of 1980 created an incentive for US universities to translate academic research discoveries into innovative commercial products by granting them ownership of patents arising from federally funded research. In subsequent decades, US universities have licensed many thousands of patents to the private sector, indirectly resulting in the commercialization of hundreds of lifesaving treatments[1].

Elsewhere, other countries have struggled to match the capacity of US universities to capitalize on their discoveries. In Germany, for example, although university professors were allowed to own patents, the external environment was not conducive to commercialization of these patents (data from 1980 to 1996); as a result many innovations stagnated until new incentives were introduced a few years ago[2]. Similarly, until recently, French inventors had little incentive to commercialize and were not allowed to hold equity or board positions in companies with which they had cooperation arrangements. Recent changes in the French system have removed these disincentives, enabling technology transfer to be funded more aggressively[3]. But it is the United States that is the benchmark, with lucrative licensing revenues, an entrepreneurial market and the relative abundance of venture capital galvanizing institutions to commercialize their discoveries.

Growth in the US biotech industry has been facilitated by the increasingly aggressive licensing of publicly funded research. Academic institutions have traditionally provided the basic biological discoveries that form the basis for the majority of biotech enterprises. However, research universities are now positioning themselves to move from basic research into more translational research and the more aggressive acquisition of downstream IP. Universities increasingly take equity in companies as part of a diversified technology transfer license structure[4]. Licensing revenues to universities and industry-academic collaborations are also growing[5,6].

Moreover, the ties between industry and universities have strengthened, as reflected in the 60% growth in university-industry R&D centers in the 1980s[7] and the more than eightfold increase in US university technology transfer offices between 1980 and 1995 (ref. 8).

Table 1 Selected university venture arms for supporting spinouts/startups ordered chronologically by foundation date

Fund	Founded	URL
Purdue University's Trask Venture Fund	1974	http://www.otc.purdue.edu/
Boston University's Community Technology Fund	1975	http://www.bu.edu/ctf/
Oklahoma State University's Seed Fund	1977	http://www.osuf.org/index.html
University of Chicago's ARCH Venture Partners	1987	http://www.archventure.com/directors.html
Michigan's Wolverine Venture Fund	1997	http://www.zli.bus.umich.edu/wvf/
UK Medical Research Council's Medical Ventures Fund	1998	http://www.mrc.ac.uk/
Stanford University's Office of Technology Licensing's Seed Funds	1999	http://otl.stanford.edu/inventors/resources/gap.html
Australia's Uniseed Venture Fund	2000	http://www.uniseed.com/
Cornell University's BR Venture Fund	2002	http://brv.cornell.edu/
University of Kentucky's Research and Development Voucher Fund	2002	http://gov.state.ky.us/legislativeinits/2002/econinit2.htm
Imperial College's (UK) UCLA and BML Ventures Imperial Fund	2003	http://www.imperialinnovations.co.uk/
Tel Aviv University's RAMOT Fund	2003	http://www.tau.ac.il/ramot/

Shreefal Mehta is at the Lally School of Management and Technology, Rensselaer Polytechnic Institute, 110 Eighth St., Troy, New York 12180, USA. e-mail: mehtas@rpi.edu

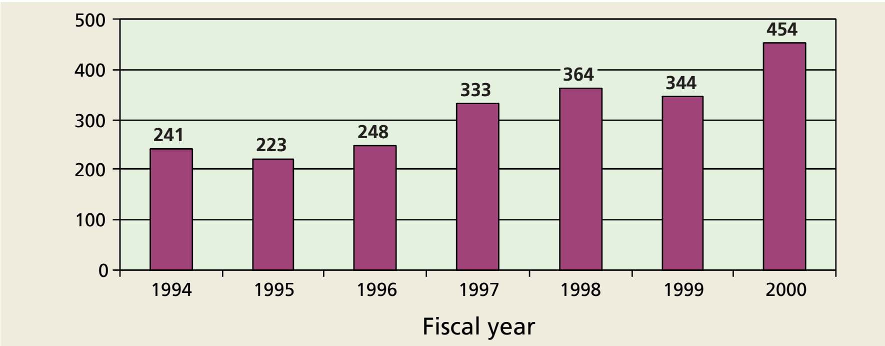

Figure 1 Number of startups initiated by university technology transfer processes.

Commercial awareness on every campus is increasing and business opportunities are no longer anathema to academic departments. This change in attitude is particularly striking in departments of life sciences research and reflects the increasingly high profile of the biotech sector in the academic world, the trend of the National Institutes of Health (NIH; Bethesda, MD, USA) to fund more applied/technology-driven research (and the founding of the NIH's Biomedical Engineering Division[9]),and the widening involvement in startup companies of faculty colleagues who simultaneously run academic research groups[8] (see **Fig. 1**). It also reflects the need for universities to diversify their revenues in the light of slowing growth in state support, individual giving and reduced endowments[10], particularly in recent years.

In addition to providing licensing revenues that can be ploughed back into intramural research, US universities are developing recognition of their role as regional economic engines. The core of every bioscience industry cluster consists of leading research universities (notable exceptions where clusters have not arisen around a universities include: the University of Texas Southwestern Medical Center, Austin, TX, USA; Johns Hopkins University, Baltimore, MD, USA and the Oregon Health Sciences Center, OR, USA). If technology transfer efforts can be enhanced and local commercialization activities supported with the institutional infrastructure, universities can generate wealth for themselves and jobs for the local economy.

More universities are hiring executives and entrepreneurs from the commercial world to lead their institutes[11]— examples include San Diego State University's new dean of the Business School (Gail K. Naughton, formerly a founder of Advanced Tissue Sciences, who also held the posts of president and director), the new director of Arizona State University Center for Applied Nanobioscience (George Poste, a senior executive from SmithKline Beecham) and the recently appointed presidents of the University of Kentucky (Lee T. Todd, Jr., formerly senior vice president at Lotus Corporation), among others.

Many institutions are encouraging life science researchers to commercialize their discoveries by making available university-backed venture funding (see **Table 1**) and facilitating interaction with other department with complementary expertise for startups; for example, partnering with business students to help with business plans, engineering students to help with product design and testing, and law students to iron out IP and other legal issues. A recent article in *Inc. Magazine*[12] provides some specific examples.

A recent report[13] summarizes its findings on best practices in university technology transfer in the United States, redefining the goals of research universities as follows: "an institution…[not only] can be national or world class in its research, scholarship, and educational programs, but also can be effective at a variety of partnering activities that enhance regional economies and contribute to the growth of technology industry. In short, universities can be smart, do well financially, and do well in a public mission sense, all at the same time."

Academia and drug development

Despite their pivotal role in seeding new biotech ventures, universities have had less of a role in the subsequent process of converting those discoveries into marketable medicines. In fact, the cost of developing new drug products from basic research has traditionally been borne almost exclusively by the private sector. Demasi *et al.*[14] estimate that taking a drug to market costs an average of $403 million in out-of-pocket costs ($802 million in capitalized costs). A comparison of the investments made by industry and the NIH in R&D shows that in 2001, the pharma industry invested roughly $30 billion[15], whereas the entire NIH budget was $20.3 billion. The bulk of the costs for product development, namely the costs for clinical trials, are borne by industry, with ~$10 billion invested in 2001. In comparison, only $2.1 billion from NIH funds went toward clinical research in 2001 (ref. 16).

Another study by the NIH[17] found that of the 47 drugs that achieved sales above $500 million in 2000, only four could be shown to have use or ownership rights traced back to government-funded research. Of the 284 new drugs approved in the United States from 1990 to 1999, 93.3% originated from industrial sources, with government sources accounting for 3.2% of the approvals and other nonprofits accounting for the other 3.5%[18].

Thus, the highly risky and expensive drug-development process has been driven primarily by companies. Although basic research supported by public monies may be exploited by the private sector in their research, drugs would not make it to the public without substantial additional investment and risk-taking by industry.

Goal-oriented academia?

As universities' appetites for commercializing research grow and high-throughput platforms are increasingly adopted in public research programs, should universities apply their technologies and programs to more goal-oriented biological and pharmaceutical research? It appears that it may already be happening.

Although some centers for translational discovery and development of new drugs were established more than 20 years ago, many more have been recently formed with the specific goal of translational research. Centers dating from the 1980s include the University of Florida's Center for Drug Discovery (http://www.cop.ufl.edu/centers/cdd, founded in 1985), Purdue University's Cancer Research Center (http://www.cancer.purdue.edu/, founded in 1976), the University of Texas at Austin's Drug Dynamics Institute (http://www.utexas.edu/pharmacy/research/interdis/ddi.html, founded in 1974), the University of Michigan's Cancer Center (http://www.cancer.med.umich.edu/, founded in 1986); they are primarily focused on neurology or oncology diseases.

Some examples of recently started centers for translational drug discovery, design and development are provided in **Table 2**. These centers focus on translational research or on discovering new chemical compounds using industrial techniques and tools, such as high-throughput screening and computational chemistry. Although most of the centers were founded with a mission to target specialized diseases that might be too small a market for pharma companies, these centers' capabilities are clearly industrial and commercial in nature[18].

As a significant part of the expense of preclinical studies is the outlay and running costs of high-throughput screening and discovery of appropriate chemical compounds, the trend toward more goal-oriented research centers at universities is in keeping with industry efforts to curtail R&D expenditure. Today, large pharma is moving toward a business model that meets the university initiatives. Big pharma is increasingly focusing on clinical development and regulatory/marketing expertise and early-stage drug development is increasingly being contracted out[19]with estimates of drug discovery outsourcing to increase from a $2 billion market today to $6 billion in 2007 (ref. 20). In general, the global pharmaceutical R&D outsourcing market continues to grow at about 8–10% annually[21].

The trend for large pharma is to move toward the commercialization functions of regulatory, marketing, distribution and reimbursement. An example of a pharma company that increasingly views R&D functions as noncore is GlaxoSmithKline (GSK; Brentford, UK). In 2001, it restructured business and R&D units and launched a hub-and-spoke model, where the R&D units are independently organized around a core hub containing clinical phase 3 management capabilities, marketing, manufacturing and corporate functions. "In the middle stages of R&D … GSK has created six Centers of Excellence for Drug Discovery, or CEDDs. Each CEDD is dedicated to specific therapeutic categories; each is responsible for taking lead compounds forward to the point where the therapeutic rationale for those compounds is demonstrated sufficiently to justify the start of large-scale clinical trials"[22]. Since this reorganization, GSK has added at least two external alliances with Exelixis (S. San Francisco, CA, USA) and Ranbaxy (New Delhi, India) with the same deliverables as its CEDDs, effectively creating external CEDDs. Tadataka Yamada, head of R&D at GSK, has also indicated the possibility of spinning out its CEDDs at a later stage if appropriate[23].

Implications

Giving a greater emphasis to goal-oriented research in publicly funded organizations has several implications. In the case of inventions related to marketed drugs, most patents are either method patents or composition-of-matter patents. The former defends the right to treat a disease by a specific pathway or protein target and the latter defends a particular composition of a compound that can effectively address the target to treat the disease. Until now, most research universities obtained method patents because basic research is directed at uncovering novel disease mechanisms; much less publicly funded research has been oriented toward synthesizing the pharmaceutical products for addressing the targets in disease pathways.

Because method patents often make broad claims, attempts by universities to enforce such patents sometimes have been controversial. In particular, it has been argued that these basic mechanism-of-use patents can potentially block novel products from reaching the public in a cost-effective or timely manner. Two examples include a patent granted to the Massachusetts Institute of Technology (Cambridge, MA, USA), the Whitehead Institute for Biomedical Research (Cambridge, MA, USA), and Harvard University (Cambridge, MA, USA) on the NF-κB signaling pathway[24], and a University of Rochester (NY, USA) patent on the method of activity of an entire class of popular drugs known as cyclooxygenase 2 (Cox-2) inhibitors[25]. The former patent has created controversy because it was licensed exclusively to Ariad Pharmaceuticals (Cambridge, MA, USA), which has proceeded to sue for infringement Eli Lilly, which was already marketing two drugs that target NF-κB: raloxifene (Evista) for osteoporosis and drotrecogin alfa (Xigris) for septic shock. In the latter case, however, the University of Rochester patent was found by a court to be too generic to support an infringement claim against makers of the class of drugs known as Cox-2 inhibitors. The patent was deemed invalid, too broad and nonspecific by the presiding judge, as the university scientists did not take what he called the "last, critical step" of actually isolating a drug compound themselves[26].

By focusing more resources on goal-oriented research, universities have the opportunity to make a further claim on the final product, which is not available in the basic discovery and patent around a critical new pathway or target. In the case of drug screening, work remains clearly research-oriented (involving structure-function analysis of proteins and chemical compounds) and relatively less routine than other later steps in drug development (*e.g.*, toxicology). The attractiveness of owning IP (composition-of-matter patents) in the area of novel drug compound structures is thus a very compelling reason for the creation of applied research centers at universities. It is also likely that pharmaceutical companies or intermediate venture organizations will increase partnerships with universities to fund work at these applied drug discovery centers to get first rights to such patents.

The increasingly proactive role of universities in drug development could also have an impact on the need for large R&D spending in industry. As outlined above, the cost of developing drug products has traditionally been borne almost exclusively by the private sector. With greater investment in expensive screening and high-throughput technologies by publicly funded organizations, it is possible that

Table 2 Centers for translational drug discovery, design and development ordered chronologically by foundation date

Center	Founded	URL
University of Pittsburgh's Drug Development Program	1995	http://www.upmc.edu/ClinPharm/Discovery.htm
University of Texas Southwestern Medical Center's Center for Biomedical Inventions	1997	http://cbi.swmed.edu/
Georgia State University's CollabTech	1999	http://biology.gsu.edu/industry/incubator.html
The State University of New York, Buffalo's Center for Drug Discovery and Experimental Therapeutics	2000	http://cddet.buffalo.edu/
Harvard University's Laboratory for Drug Discovery	2001	http://www.hcnr.med.harvard.edu/d_drug/
PharmaSTART Stanford University, SRI International, University of California, San Diego/San Francisco and the Institute for Quantitative Biomedical Research (QB3)	2003	http://www.pharmastart.org/

the drug industry may be able to collaborate and outlicense more preclinical research to universities, with associated savings for industry R&D.

Perhaps the most contentious issue, however, is whether academic institutions can balance the shift of focus to goal-oriented research and wealth creation with their altruistic mission of education and the pursuit of knowledge for knowledge's sake. Several studies have suggested that the increasing complexity of licensing negotiations and the mounting cost of licensing associated with patenting is an impediment to scientific progress[27–30].

But a change in patenting strategy at universities from more traditional methods patents with broad claims to composition-of-matter patents could in fact lessen the impact of patents on basic academic research, with methods patents being licensed out nonexclusively, and composition-of-matter patent licenses being granted exclusively. And with industry increasingly reluctant to take on the risk of commercializing fundamental research because of tightening spending budgets and more venture capital going to later stage companies, the increasing emphasis on translational drug discovery and development research at universities will ensure that basic discoveries have a better chance of translation into life-saving treatments.

1. http://www.autm.net/
2. Casper, S. & Kettler, H. *Industry Innovation* **8**, 5–30 (April 2001).
3. Triendl, R. *Res. Technol. Management* **42**, 5–7 (Mar/Apr 1999).
4. Feldman, M. *et al. Management Sci.* **48**, 105–121 (2002).
5. Press, E. & Washburn, J. *Atl. Mon.* **285**, 39–54 (March 2000).
6. Munro, N. *Natl. J.* 580–585 (22 February, 2003).
7. Cohen, W.M., Florida, R., Randazzese, L. & Walsh, J. in *Challenges to Research Universities* (ed. R. Noll) 171199 (Brookings Institution Press, Washington, DC, 1998).
8. Pressman, L. (ed.). AUTM Licensing Survey: FY 2001 Survey Summary (AUTM, Northbrook, Il, USA, 2003) (http://www.autm.net/surveys/01/01summarypublicversion.pdf).
9. http://www.nibib.nih.gov/
10. Pulley, J. *Chronicle Higher Edu.* **49**, A23 (January 24, 2003).
11. Basinger, J. *Chronicle Higher Edu.* **49**, A32 (December 13, 2002).
12. Barker, E. *Inc. Magazine*, p. 66 (November, 2002).
13. Tornatzky, L.G., Waugaman, P.G. & Gray, D.O. *Innovation University: New University Roles In A Knowledge Economy* (Southern Technology Council and Southern Growth Policies Board, Research Triangle Park, NC, 2002).
14. DiMasi, J.A., Hansen, R.W. & Grabowski, H.G. *J. Health Economics* **22**, 151–185 (2003).
15. The Pharmaceutical Research and Manufacturers of America. New Drug Approvals in 2001 (PhRMA, Washington, DC, USA) p. 17 (January 2002) (http://www.phrma.org/newmedicines/resources/2002-01-25.46.pdf).
16. Guyer, R.L. People doing science (NIH, Bethseda, MD, USA) (http://www4.od.nih.gov/officeofbudget/FY04pub/MechanismTotal.PDF)
17. Department of Health and Human Services. NIH Response to the Conference Report Request for a Plan to Ensure Taxpayers' Interests are Protected (NIH, Bethseda, MD, USA) (July 2001) (http://www.nih.gov/news/070101wyden.htm).
18. Pollack, A. UCSD getting more involved in drug trials. *SignOnSanDiego.com*, 31 July 2003 (http://www.signonsandiego.com/news/business/biotech/20030731-9999_1b31biotech.html).
19. Gwynne, P. *Drug Disc. Dev.*, p. 81 (October 1, 2002).
20. Kalorama Information. *Outsourcing in Drug Discovery* (Kalorama Information, New York, NY, USA, 2003).
21. Waltham, M.M. (ed.). *Parexel's Pharmaceutical R&D Statistical Sourcebook.* p. 25 (Parexel International Corporation, Waltham, MA, USA, 2001).
22. GlaxoSmithKline. GlaxoSmithKline unveils strategy for growth (GSK, Brentford, UK) (February 22, 2001) (http://www.gsk.com/press_archive/press_02222001.htm).
23. Dyer, G. *Financial Times*, p. 19, London edn, (January 25, 2002).
24. Baltimore, D. *et al.* US Patent 6,410,516 (issued June 25, 2002).
25. Young, D.A. *et al.* US Patent 6,048,850 (issued April 11, 2000).
26. Shulman, S. *MIT Technol. Rev.* **106**, 75 (2003).
27. Russo, E. *The Scientist*, **14**, 8 (2000).
28. Rai, A.K. & Eisenberg, R.S. *Law Contemp. Problems* **66**, 289 (2003).
29. Rai, A.K. & Eisenberg, R.S. *Am. Sci.* **91**, 52 (2003).
30. Agres, T. *The Scientist* **17**, 58–59 (2003).