Industry's Challenge to Academia: Changing the Bench to Bedside Paradigm

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The need for interdisciplinary collaboration is arising as a result of accelerating advances in basic science, including massive research and development funding by both government and industry, which has spurred the so-called "nanotechnology revolution" and developments at the intersection of the life and physical sciences, increasing emphasis by federal research funding agencies on interdisciplinary and inter-institutional research and by market influences. A number of barriers presently limit the interaction between academics and industry, including the typically very time-consuming and slow pace of technology transfer, which is compounded in the case of interdisciplinary and inter-institutional licensing, as well as the natural, and understandable, antipathies that exist between academia and industry as a result of their differing missions and approaches to scientific discovery. Moreover, if mechanisms are not in place at the outset of an inter-university collaboration, then the transition of inventions to clinical applications can be fraught with additional complexities and barriers. Policies suggested by the National Nanotechnology Initiative offer a number of ideas for overcoming barriers to multidisciplinary and inter-institutional research and illustrate some of the ways in which academia can structure partnerships with industry that will not only provide needed funding for multidisciplinary and inter-institutional biomedical research in an era of diminishing federal resources, but may permit academia, on the one hand, and industry, on the other, to benefit from the strengths provided by the other without compromising either academia's or industry's basic missions. Exp Biol Med 231:1257–1261, 2006

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In his message announcing the program for the 2006 Annual Meeting of the Association of Anatomy, Cell Biology and Neurobiology Chairpersons, Dr. Steven Goodman argues that scientific advances, including the completion of the human genome project, have brought about a "new era" in biomedical research and training in which large interdisciplinary teams will be required to answer the fundamental questions that will need to be answered in order to achieve the "next generation" of breakthrough advances in the field. He offers in support of his argument that a "new era" is upon us the fact that "inter-institutional and interdisciplinary consortia are springing up around the country." From my perspective as a lawyer who advises venture capitalists in connection with their investments in biotech-, bionanotech-, and other technology-based companies, as an advisor to the management of such companies, and as an active participant in the life sciences industry generally for more than a decade, Dr. Goodman is correct, both in his prediction about the increasing importance of interdisciplinary and inter-institutional approaches to life science research and development and his observations about the emergence of this new trend. Before turning to address the *consequences* of this trend, however, I would suggest that pausing a moment to reflect further on the *causes* of the movement towards interdisciplinary research will help us not only in seeking answers but in asking the right questions about how academia and industry need to change in response to the need for, and the movement towards, large interdisciplinary and inter-institutional research.

What is fueling the movement towards large interdisciplinary and inter-institutional research?

As a non-scientist, I dare not presume to understand, let alone articulate, all of the myriad ways in which yesterday's advances, including the understanding gained of the human genome, the collection of large amounts of proteomic data, and the development of even more powerful bioinformatics tools, to name a few developmental causes identified by Dr. Goodman, have created a condition in which increasingly interdisciplinary teams will be *required* to answer the fundamental questions in biomedical research. I leave it to you and the members of your departments, as basic science researchers, to do this. Nevertheless, my recent experience, albeit anecdotal, suggests that this is the case.

For example, I recently assisted Dr. Ellen Vitetta, one of the country's leading immunologists, a member of the

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National Academy of Science and Director of the Cancer Immunobiology Center at the University of Texas Southwestern Medical Center (UTSW), and Dr. Rocky Draper, a professor of molecular and cell biology at the University of Texas at Dallas and a leader in UTD's Bionanosciences Group, both of whom are members of the Institute of Biomedical Sciences and Technology, to team up with a bionanotechnology company to apply for a grant. This project had its genesis when the company assembled a broad interdisciplinary and inter-institutional collaboration with experts in biology, nanotechnology, chemistry, and physics from various research institutions across the United States. The project has potential applications in cancer and other therapies. Breakthrough projects such as this will not be possible without the collaboration of a broad, multidisciplinary, and indeed inter-institutional, team.

In addition to the need for interdisciplinary collaboration that is arising as a result of accelerating advances in basic science (1), a number of other forces are combining to fuel the movement towards large interdisciplinary and inter-institutional research, including massive research and development funding by both government and industry, which has spurred the so-called "nanotechnology revolution" and developments at the intersection of the life and physical sciences. In fact, governments, together with corporations and venture capitalists, spent approximately $8.6 billion worldwide in 2004 on nanotechnology research and development, a substantial portion of which was focused in the life sciences field. One analyst forecast that the United States' National Nanotechnology Initiative (NNI) will outstrip the human genome project as the most expensive U.S.-funded science initiative since the race to space (2). Moreover, federal research funding agencies increasingly emphasize interdisciplinary and inter-institutional research (3).

However, the trend towards greater interactions between different scientific disciplines is motivated, not alone by academic curiosity or even necessity, or by federal funding priorities, but by market influences, as evidenced by companies like Nanoco (4). For example, Lux Research of New York, which created a new index that is quoted on the American Stock Exchange (LUXNI) and is designed to track how financial markets value emerging nanotechnology applications, noted that 7 of the 17 companies listed in its initial index are classified as belonging to the healthcare and life sciences sector (5). Increasingly, academia and industry are partnering to undertake large-scale interdisciplinary research. The impetus for these collaborations is a quicker path from bench to bedside, which is fueled by rising expectations for better healthcare, spearheaded in part by patient advocacy groups and privately funded foundations that focus increasingly on the clinical applications of basic research (6), as well as public and government frustration at the enormous cost of drug and device development (7). Such frustration is leading federal funding agencies to examine ways to increase the odds that government funded research will yield new applications for preventing and treating injury and disease and their causes.

A further impetus behind the rise in interdisciplinary research, as well as one cause behind academia's increasing collaboration with industry, may be found in the fact that a substantial amount of interdisciplinary research, including in the bionanotechnology field, involves basic research, which universities are better suited to perform than industry. This is particularly the case in light of dwindling industry R&D budgets and a decreasing supply in the United States of qualified scientists and engineers. Naturally, universities' disproportionate involvement in basic research gives them an advantage in securing intellectual property (IP) rights, as well as an incentive to partner with industry to develop such rights (8).

What barriers presently exist for collaborations with industry?

In my involvement in the life sciences industry over the past decade, management of life sciences companies have often expressed frustration at the slow pace associated with university technology transfer. Anecdotally, in a very unscientific poll of certain partners in our Firm's global life sciences practice, the following response to the question, "How will the interaction between academics and industry need to change in response to the movement towards large interdisciplinary research," typifies such frustration: "My experience is that licensing out IP from academic institutions is very time-consuming and slow; interdisciplinary and inter-institutional licensing takes even longer, so one change that is needed is to speed up the process."

The traditional technology transfer process involves the award of funding, typically to a single researcher or laboratory, usually from a government research funding agency, and the disclosure by the inventor of an invention to the university technology licensing or transfer office (TLO). The office then conducts patentability and market reviews to determine whether or not to file a patent on the invention. Thereafter, the TLO seeks to either identify entities interested in licensing the university's patent rights, usually on an exclusive basis, or, less frequently, to form a company around the invention (usually with some level of involvement by the inventor), which involves not only licensing issues but identifying qualified management, including a scientific advisory board; generating a business plan; issuing equity to the key players, including possibly the university and the inventor; and seeking funding. All of this can take months (typically from nine months to a year or more), during which the marketplace, including potentially competitive products and companies, continues to rapidly evolve and scarce start-up funding is stretched and sometimes depleted.

Aside from the "mechanics" of the tech transfer process itself, however, perhaps even greater barriers are inherent in the natural, and understandable, antipathies that exist between academia and industry. Academia, for its part, tends to be suspicious, if not hostile, of the "results" or "market-oriented" approach of industry, which is viewed by many scientists as antithetical to the traditional hypothesis-driven methodology of science and its search for "truth" for truth's sake (9). Industry, which is driven and shaped by the accelerating rate of technological innovation, on the other hand, generally tends to be impatient with the more deliberate pace and the perceived bureaucratic hurdles associated with implementing academic discoveries.

How are these barriers exacerbated in the case of large interdisciplinary and inter-institutional research?

Obviously, the challenges that are inherent in the "traditional" model are greatly compounded when multiple investigators from different disciplines and possibly different institutions get involved. Generally as a matter of university policy, and often as an express term under a scientist's employment agreement, the work product that derives from such scientist's intellectual pursuits (with some limited exceptions) belongs to his or her university employer. Thus, in the first instance, all of the individuals involved in the inventive process must determine their relative contributions to the invention so as to determine each university's relative ownership of the underlying intellectual property rights.

An inventor is a natural person who has contributed, either individually or jointly with other individuals, to the subject matter of at least one of the patent claims (10). Thus, if determining inventorship among researchers at the same institution can sometimes be challenging, the difficulty compounds when research takes place at multiple institutions.

Under U.S. patent law, "inventors may apply for a patent jointly even though (a) they did not physically work together or at the same time, (b) each did not involve the same type or amount of contribution, or (c) each did not make a contribution to the subject matter of the patent" (11). Moreover, if a mechanism is not in place at the outset of the collaboration for joint ownership of any invention that comes out of the collaboration, as often is the case with inter-institutional collaborations, then such institutions in applying for patent protection must identify the inventor and invention date for each and every claim (12).

Moreover, it is imperative that university collaborations not only cooperate in order to secure their individual intellectual property right in the invention (13) but agree upon procedures relative to commercializing such rights. As a general matter, private companies, particularly those in their early stages that are underfunded and have limited resources, prefer to deal with one licensing entity, which is empowered to act on behalf of all patent holders, rather than incur the costs involved with negotiating with multiple universities. This is particularly critical in consequence of the basic tenet in U.S. patent law that, "in the absence of an agreement to the contrary, each of the joint owners of a patent may make, use, offer to sell, or sell the potential invention within the United States, or import the patented invention into the United States without the consent of and without accounting to the other owners" (14). Thus, if one university in an inter-institutional collaboration attempted to exclusively license an invention without the knowledge or consent of the second university, the second university could effectively undercut the first university's license by entering into a conflicting exclusive or nonexclusive license.

What can be done to change the way industry and academia interact to break down these barriers?

The NIH Roadmap announced a series of new awards intended to overcome some of the barriers described above and to "make it easier for scientists to conduct interdisciplinary research . . . including funding for: training of scientists in interdisciplinary strategies; creation of specialized centers to help scientists forge new and more advanced disciplines from existing ones [known as Exploratory Centers for Interdisciplinary Research]; supplements to existing awards which encourage interdisciplinary depth for an ongoing project; and planning of forward-looking conferences to catalyze collaboration among the life and physical sciences, important areas of research that historically have had limited interaction" (15).

Developments in the field of nanotechnology, including nanobiotechnology, offer similar ideas for overcoming barriers to multidisciplinary and inter-institutional research. For example, the NNI Strategic Plan specifically addresses many of the barriers to multidisciplinary research under Goal 2 of the Plan, namely to "facilitate transfer of new technologies into products for economic growth, jobs, and other public benefit," including the following:

Establishing "industry liaison groups with various commercial sectors to promote exchange of information on NNI research programs and industry needs that relate to nanotechnology";

Supporting "meetings at which researchers from academia, governments and industry exchange information on results and possible applications";

Fostering "interaction among industry, academic, and government researchers through the establishment or support of user facilities that are available to researchers from [public and private] sectors";

Requiring that "all NSF-funded Nanoscale Science and Engineering Centers . . . include industry partners";

Encouraging "exchange of researchers between universities and industry to allow university personnel to spend time in industry labs and vice versa";

Considering "new mechanisms to encourage technology transfer via licensing of intellectual property generated by NNI-funded research. Such mechanisms include forming of consortia among universities and other research institutions for purposes of pooling intellectual property and/or creating simplified or uniform technology transfer procedures"; and

Allowing "industry to communicate its needs at an early stage [in order to] enhance the likelihood that new ideas will ultimately be developed and commercialized" (16).

Nanoscale Science & Engineering Centers (NSECs), which have been funded by the National Science Foundation in connection with the U.S. NNI, provide a model to which multidisciplinary and inter-institutional biomedical centers and institutes may look for answers in initially assessing differing approaches to overcoming the barriers associated with such collaborations. Each NSEC includes several universities, private companies, and government laboratories that focus on an element of nanotechnology in which the members have demonstrated expertise (17). For example, the NSEC for Integrated Nanopatterning and Detection Technologies established at Northwestern University includes the University of Illinois at Champaign–Urbana, University of Chicago, Argonne National Laboratory, Lawrence Livermore National Laboratory, NASA, DuPont, Exxon-Mobil, Rohm and Haas, Motorola, IBM, and Unilever (18). In addition to including private sector partners in a multidisciplinary and inter-institutional research collaboration (whether focused on nanotechnology or biomedical research), other features highlighted in the NNI Strategic Plan, many of which have been implemented by NSECs, suggest approaches biomedical researchers and the federal agencies that fund them may wish to consider in response to the movement towards, and the creation of greater numbers of, interdisciplinary and inter-institutional biomedical research centers ("BMR Centers"), including the following:

Awarding a (perhaps modest) portion of federal research funding to the BMR Center director rather than to individual investigators, as is the case with NSCEs, which would enable each BMR Center considerable latitude in determining how it will be organized and allocate its resources;

Dedicating a significant percentage of federal biomedical research funding to multidisciplinary research programs (e.g., up to 20% of NNI's entire budget is dedicated to such research programs);

Include (possibly as a condition to receipt of federal funding) a requirement that each BMR Center have multi-investigative research teams comprised of investigators from the different members of the Center;

Adopting, per NNI's suggestion, simplified or uniform technology transfer procedures, including possibly the pooling of intellectual property, which will facilitate the transfer and licensing of intellectual property, including a mechanism for determining the patentability and licensability of IP generated by the Center;

Facilitating the transition of IP developed at a BMR Center to the private sector by including industry partners (possibly, as occurs with NSF funding of NSCEs, as a prerequisite to receiving federal funding) and creating internal programs designed to allow industry to communicate its needs at an early stage, thereby enhancing the likelihood that new ideas will ultimately be developed and commercialized;

Encouraging industry partners in the BMR Center to make unrestricted gifts at various levels depending on their desired level of involvement, as the Northwestern University NSEC has done, and later, when and if the potential relevance of the research to a company's specific objectives becomes clear, allowing such company to enter into a funded sponsored research arrangement in which the company supports the project with a specific company-centric focus;

Permitting IP developed under a sponsored research arrangement to be owned and protected by the private company sponsoring such research, provided it reimburses the universities for any associated costs; and

Adopting programs designed to enable the spin-out of companies through the creation of internal platforms for assessing market factors, drafting business plans, and attracting VC investors (19).

While the NNI's suggestions outlined above may be less appropriate in some respects for biomedical research centers (20), they illustrate some of the ways in which academia can structure partnerships with industry that will not only provide needed funding for multidisciplinary and inter-institutional biomedical research in an era of diminishing federal resources, but may permit academia on the one hand and industry on the other to benefit from each other's strengths without compromising either academia's or industry's basic missions.

1. The NIH Roadmap for Medical Research notes: ". . . as science has advanced over the past decade and the molecular secrets of life have become more accessible, two fundamental themes are apparent: the study of human biology and behavior is a wonderfully dynamic process, and the traditional divisions within health research may in some instances impede the pace of scientific discovery." Available at http://nihroadmap.nih.gov/interdisciplinary.
2. Lux Capital Group, LLC, *The Nanotech Report, 2004*, xi, 2004, as quoted in *Nanotechnology and the New Paradigm in University Tech Transfer*, Baluch A, available at http://www.foley.com/files/tbl_s31Publications/FileUpload137/3109/Baluch.pdf.
3. NIH Roadmap, *supra*, note 1.
4. Other examples of nanotechnology companies that, according to their websites, are developing products in the life sciences industry include: Insert Therapeutics, Inc. (focuses on designing and developing patented cyclodextrin-containing polymer delivery systems that combine with small-molecule drugs and nucleic acids to significantly improve drug solubility, stability, circulation, and targeting for enhanced safety and efficacy); Calando, Inc. (develops nanostructures for delivery and therapeutic use of RNA interference); Nanotechnica, Inc. (pursuing in the near term the development of several early-stage nanotechnologies such as scanning probes and integrated microfluidic systems for separation and detection of molecules); Potentia Pharmaceuticals, Inc. (an early stage biotechnology company focused on developing novel

therapeutics, primarily in the area of macular degeneration); Surface Logix Inc. (leverages its expertise in biophysical chemistry to create new small molecule drugs that are optimized to meet the challenges of human physiology, including multiple internal programs focused primarily on cardiovascular disease, oncology, and metabolic disorders); Nanosys (has a technology platform incorporating high performance inorganic nanostructures, with over 400 patent and patent applications, currently being applied to address opportunities in the energy, defense, electronics, computing, and life science industries); Nanosphere (commercializing certain nanoparticle probes, bio-barcode technology, and automated instruments that enable ultrasensitive detection of multiple proteins and nucleic acids simultaneously, direct genomic detection without amplification or enzymes, and 5–6 orders of magnitude more sensitive detection than ELISA-based methods for proteins); Ohmx Corporation (a protein biosensor company focused on the development of portable electrical detection devices for use in diagnostics, drug development, and industrial applications such as biodefense, food, water, animal, and environmental testing); Acumen Pharmaceutics, Inc. (a preclinical drug company focused on developing therapeutics and diagnostics for Alzheimer's disease and other memory-related disorders). See also Baluch A, *supra* note 2.

5. Lux Research, March 17, 2005, "Lux Nanotech Index™ Launches on American Stock Exchange" (press release), http://www.luxresearchinc.com/press/RELEASE_Index.pdf.
6. For example, Accelerate Brain Cancer Cure, Inc. (ABC^2), a nonprofit organization founded in 2001 by Daniel H. Case III, a leading investment banker who had been diagnosed with and subsequently died from brain cancer. "ABC^2 funds outstanding and novel translational science.... Central to our approach is a fast-track award process geared to provoke new ideas from scientists working in diverse areas of research. We give funding preference to applications focused on programs that will benefit patients with advanced brain cancer in the near term, although we also support projects with other relevant research guidelines." See http://www.abc2.org.
7. According to a widely cited Tufts University study from 2001, the average cost to develop a new drug is $802 million to $1 billion. Frantz A. "Biotech Battle," *Lowell Sun* (July 16, 2004). However, this estimate is not universally accepted. "The study included a 'highly selected' sample of the most expensive new drugs. The average cost of drugs in this sample came to $403 million." See, e.g., Angell M. "The Truth about the Drug Companies," *Chicago Sun-Times* (August 22, 2004). References available through LexisNexis news database.
8. Baluch A, *supra* note 2, at 3–7.
9. Krimsky S. *Science in the Private Interest: Has the Lure of Profits Corrupted Biomedical Research?* Lanham: Rowman Littlefield Publisher, 2003; Krimsky S. "Reforming Research Ethics in an Age of Multivested Science," in *Buying in or Selling Out*, ed. Stein D. New Brunswick, NJ: Rutgers University Press, 2004; Horton R. "The Dawn of McScience," *New York Review of Books*, March 11, 2004; Raube W. "The Emerging Partnerships Among the National Institutes of Health, Academic Health Centers and Industry," *Preparing for Science in the 21st Century*, eds. Harrison D, Osterweis M, and Rubin E. Association of Academic Health Centers, 1991; Krimsky S. "The Profit of Scientific Discovery and its Normative Implications," *Chicago-Kent Law Review*, 75:15–39, 1999; Editorial, "He Who Pays the Piper Calls the Tune," *J R Coll Physicians Edinb*, 33:229–234, 2003.
10. 37 CFR 1.45(c) (2005).
11. 35 U.S.C. § 116 (2005).
12. 37 CFR 1.56 (2005). *See* Baluch A, *supra* note 2, at 22.
13. The Manual of Patent Examining Procedures provides that "[a]ll parties having any portion of the ownership in [a] patent property must act **together** as a composite entity in patent matters before the [Patent and Trademark] Office." *The Manual of Patent Examining Procedures*, 8th ed., rev. 3:300–2 and 300–3, August 2005, quoted in Baluch A, *supra* note 2, at 23.
14. 35 U.S.C. § 262 (2005). See *id.*
15. NIH Roadmap, *supra*, note 1. For more information about the Exploratory Centers for Interdisciplinary Research. See http://nihroadmap.nih.gov/interdisciplinary/exploratorycenters.
16. *The National Nanotechnology Initiative Strategic Plan* http:www.nano.gov/NNI_Strategic_Plan_2004.pdf at 6 and 7.
17. Andrew S. Baluch describes the new paradigm in university technology transfer that the NSECs embody as an "evolutionary model" of tech transfer, as opposed to the more radical or "revolutionary" model typified by Albany Nanotech, the largest and best-funded nanotechnology research center in the United States, which is located in a new College of Nanoscale Science & Engineering at the State University of New York (SUNY) at Albany. Due in part to the fact that Albany Nanotech receives the majority of its funding from private companies and the State of New York rather than the federal government (including $493 million from IBM, Tokyo Electron Ltd., and International SeMaTech, matched by $310 million from New York), Albany Nanotech has a unique technology transfer process that is a byproduct of its public/private origins and its purpose "to provide a virtual 'one-stop-shop' for its business partners," which includes the following: "pre-competitive" collaboration among partners with common R&D interests at the early research or proof-of-concept research stage; a manufacturing capability, including a 200-mm wafer processing, characterization, and prototype fabrication facility and a network of over 100 corporate partners that comprise "the complete spectrum or 'food chain' of companies supporting the development of advanced devices, components, and systems"; and the provision of industry-compliant clean rooms and fabrication facilities for product testing. See Baluch A, *supra* note 2, at 13–21.
18. *Id.* at 14.
19. *See* Baluch A, *supra* note 2, at 13–18.
20. See discussion of ethical and other issues raised by the overdependence of academia on industry support and the public policies that contribute to such dependence, discussed in the references at note 9, *supra.*