Speaking of Pharmacology

Editorial

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Today's learners and the use of Web 2.0 in teaching

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Significant developments in the World Wide Web, producing a "Web 2.0," allow users to extract and create content and to communicate with peers and groups in new and interesting ways. This new digital culture, fundamental to today's health science learners, challenges modern pharmacology teachers to suit the learning style of the Net Generation by using tools such as podcasting, wikis, blogs, videos, and social networking sites. Adoption of these new approachs will be essential to engage today's learners of pharmacology.

Much has been written about how today's students are, in terms of their approach to learning, different from previous generations (see pull quotes). Many observers have stressed that the important work we as educators face must be carried out in an atmosphere of great change. First, our students, having grown up with digital technology, are different. Second, the World Wide Web—the single greatest factor that has shaped the new learning environment—has itself undergone a radical transformation since its inception. The purpose of this brief article is to describe this new generation of students and to discuss the new Web technologies that can help us do our job and achieve our objectives more effectively so that no pharmacology teacher is left behind.

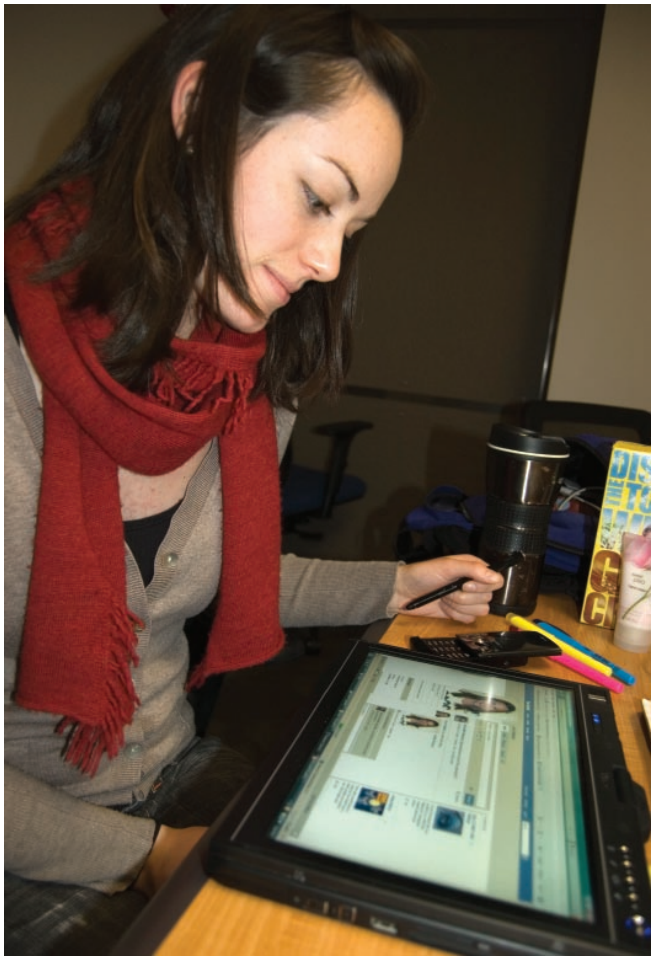
"Students today are different, but a lot of educational material is not" (1).

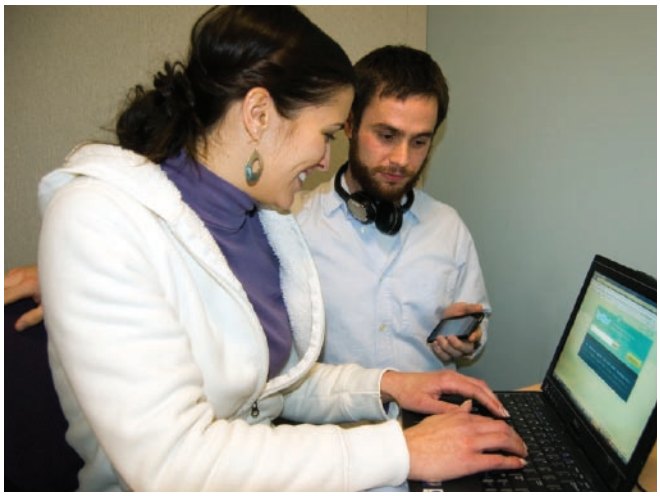
Digital Natives

In their book *Millennials Rising: the Next Great Generation*, Howe and Strauss use the term "millennials" to label the generation born approximately between 1977 and 1997. According to these authors, millennials can be typified by seven traits: they are special, sheltered, confident, team-oriented, conventional, pressured, and achieving *(4)*. Although academics may argue whether this description accurately describes this generation *(5)*, one factor that is indisputable is that millennials have been shaped by the digital technologies with which they grew up. This defining influence has also inspired such terms as "Digital Natives" *(2)* and "Net Generation" *(6)*.

With respect to the use of technology itself by digital natives, or Net-geners, eight parameters appear to be at play, including: freedom of choice, customization, collaboration, scrutiny, integrity, fun, speed, and innovation *(6)*. [To this list, Prensky adds multitasking *(2)*.]

Our own students portray many of the characteristics given above. They use Google pages to collaborate in groups; during lectures, they sometimes log on to social networking sites with their notebook computers; and they are in constant contact with their friends and family through their cell phones. Some of our faculty colleagues have been critical of these tendencies, but the derision of students for their use of technology is increasingly giving way to acceptance, and educators have begun to examine how the technologies that students use may be better exploited for teaching purposes. Additionally, we as educators need to consider the technologies that our students will face in their careers.





Web 2.0

In the mid 1990s, the World Wide Web emerged as a venue in which information was prepackaged and widely accessible to learners. Thus, the Web of that era simply presented another way to access information – the presentation was new but the content similar to that available in the pre-Web era. The language of this version of the Web (Web 1.0) was acquired by many professional baby-boomers, who could be regarded as "digital immigrants," having arrived as adults into the new Internet culture; in contrast, the "millennial" students of today are "digital natives," having used this language all their lives *(2)*.

As the Web evolved, users and programmers began to explore new ways of creating and sharing information. The resulting technology has been described as Web 2.0, a second iteration of the Web *(7)*. Web 2.0 is vastly different from the version learned by digital immigrants, and its usefulness is much farther-reaching. Web 2.0 represents a platform for creating content, collecting and interacting with many sources, and collaborating with others. Tools such as blogs, wikis, social networks, tagging systems, mashups, and content-sharing sites are examples of a new user-centric infrastructure that emphasizes participation (e.g., creating, re-mixing) over presentation, that encourages focused conversation and short briefs rather than traditional publication, and that facilitates innovative explorations, experimentations, and purposeful tinkerings that often form the basis of a situated understanding that emerges from action rather than passivity *(8)*. Learners in this environment become empowered to acquire and organize knowledge that is immediately meaningful and useful to them, which has significant implications for medical education.

Web 2.0 is still a relatively new entity, for digital natives as well as for digital immigrants. Undoubtedly, digital natives have learned to use Web 2.0 tools more readily than digital immigrants. But can these tools foster effective learning? This is the question faced by educators—that is, digital immigrants—as we attempt to convey vast content knowledge to our technology-driven students.

Web 2.0 In Medical Science Education

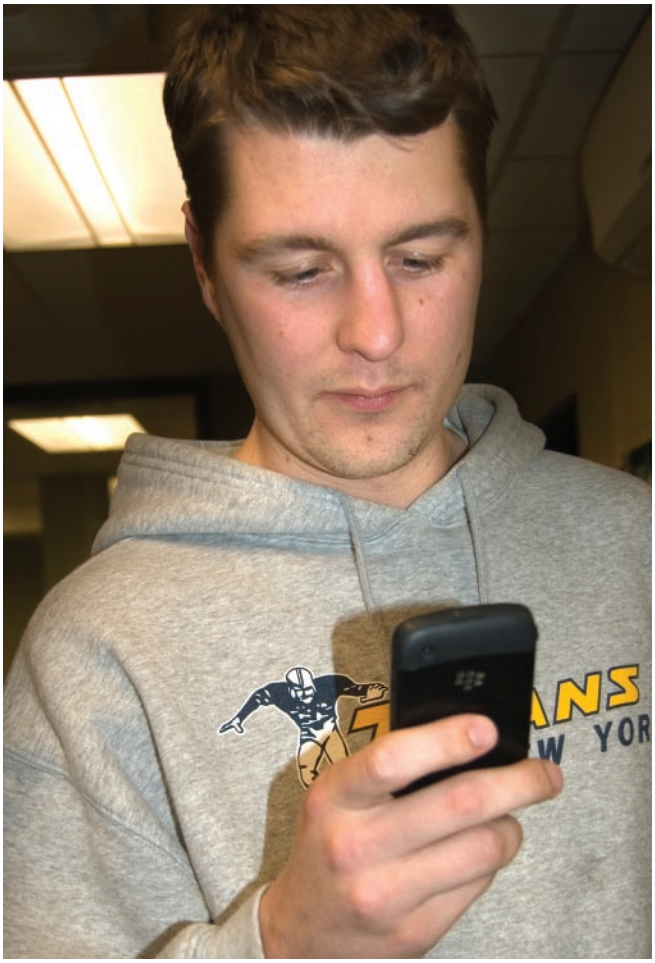
Web 2.0 technologies such as podcasts have been detailed elsewhere (see Glossary). Many health science programs routinely record faculty lectures and syndicate them for student use. Blogs and wikis, along with the more traditional message board, have likewise found acceptance in health science education *(9)*. Blogs are typically driven by the viewpoint of a single author, such as a teacher attempting to supplement material from the classroom or laboratory. Wikis are collaborative documents, well-suited for student assignments that pose a question or require student groups to develop a treatise on a single topic. The message board, with its threaded discussions, is best for stimulating interaction between teacher and student on various topics. Most institutions have these learning tools embedded in their learning management systems. A list of interesting science blogs and wikis is shown in Table 1.

The use of social networking sites, also known as social media (Table 2), has exploded over the past several years. These sites, such as Facebook, with 400 million users, subserve online communities of members based on a common interest or background. Social networking sites allow users to develop applications (usually games and quizzes) for the community. Educational and professional institutions (including ASPET) have capitalized on the popularity of such sites by presenting promotional pages intended to attract applicants or members; however, there has been little movement toward the use of these sites by health sciences institutions for instructional purposes. Health science journals, such as the *New England Journal of Medicine*, have begun to put pages on Facebook, with links back to case content, but these efforts appear to be largely promotional rather than educational. We believe that most students simply do not want their Facebook circle of friends to be accessed by their educators and men-

Table 1. Biomedical Science Education Blogs and Wikis

Name	URL
Pharmamotion	pharmamotion.com.ar
Clinical Correlations	clinicalcorrelations.org
Neuroscientifically Challenged	neuroscientificallychallenged.blogspot.com
Dr. Shock	shockmd.com
WikiTox	wikitox.org
Wikia: Open Science Wiki	science.wikia.com
Pharmtalk: The ASPET President's Blog	aspet.org/blog

"Today's students are no longer the people our educational system was designed to teach" (2).



tors. Other social networks (e.g., the Student Doctor Network, studentdoctor.net) have arisen to provide a niche for those interested in the social aspects of health science education.

A more recent Web 2.0 medium generating educational interest is Twitter *(10)*. Twitter is a microblogging/social networking site (twitter.com) that allows an individual or organization to keep their "followers" updated, via 140-character alerts ("tweets"), as to events of common interest. Tweets can contain links to other Web sites or merely inform followers of the poster's whereabouts or activities. Tweets can be sent via RSS and read via a computer or wireless device such as a smart phone. The Twitter user, in addition to receiving automatic status updates, also develops a series of followers. The unique aspects of the medium (i.e., small message size and rapid communication to a large number of followers) allow rapid propagation of messages. In this way, students can follow a course or individual instructor and receive tweets regarding course changes, general information, and journal

Table 2. Some Social Networking Sites

Site/URL	Comment
Facebook facebook.com	With 400 million users, the largest social networking site. Users post their status, personal information, photos, etc., and develop a network of friends.
MySpace myspace.com	Formerly the most popular social networking site, it remains strong in the area of music and entertainment.
Friendster friendster.com	The most popular social networking site in Asia.
Bebo bebo.com	Similar to other social networking sites, Bebo is an acronym for "blog early, blog often."
Twitter twitter.com	Microblogging/social networking site; tweets are limited 140 characters.
LinkedIn linkedin.com	A professional social networking platform, primarily for making employment and work collaboration connections.
Ning ning.com	Free Web platform that allows users to create their own social networks. Users can be members of multiple distinct networks for social, work and education purposes.
Flickr flickr.com	Online community for posting and discussing photographs. Online bloggers often use Flickr as a host for their images.
YouTube youtube.com	Web site in which users can post videos. Users can comment on videos, tag, and search. The social impact of this site has been tremendous, creating a democratization of video entertainment.
Mashable mashable.com	Online guide to social media sites. Excellent resource for social media culture, containing how-to guides and commentary.

links. For good or ill, students can also communicate with each other during class. Users can also produce lists that allow collaboration and consolidation of Twitter resources (e.g., the Laikas list of biomedical journals on Twitter: twitter.com/laikas/biomedical-journals). Twebinars (twitter.com/twebinars) are Web conferences (or mashups) during which Twitter conversations about the subject of the webinar occur in real time. A drawback of Twitter is that the aforementioned information sharing occurs in a public platform. Edmondo is a private social networking platform designed for students and teachers (edmondo.com) that has a microblogging function similar to Twitter, but only for a prescribed group. Learning management systems like Blackboard (blackboard.com) are now developing similar features. Since this social networking phenomenon is still evolving (18 million users in 2009, 75 million in 2010), it is difficult to predict its ultimate role in health sciences education.

YouTube (youtube.com) allows users to upload video files, which are rendered into low-resolution flash files. Videos posted on YouTube can be easily "embedded" in other sites, such as blogs or social networking platforms. Interesting

Glossary of Web 2.0 Terms

App: Application software designed to perform a specific task; often refers to application software for a mobile device.
Blog: Contraction of the phrase "we**b log**" to connote a Web site containing serial commentaries that can include links, graphics and video. Blogs usually have a single author and provide sequential commentary on a single theme or a variety of topics similar to a diary. *Examples:*

- Pharmamotion blogcatalog.com/blog/pharmacology-animations-resources-and-unbiased-news
- Clinical Correlations clinicalcorrelations.org

Cloud computing: Use of resources, services, and software through the Internet (the "cloud"). In this model, the physical infrastructure needed for computing services is relegated to a third party and the user pays the provider for services used. The purported advantage is that each user does not have to maintain an internal array of software and hardware, with attendant costs for maintenance, licensing, servers, etc. The user pays a fee similar to a utility bill.
Mashup: Web site or service that incorporates content from multiple external sources (e.g., Web sites, news feeds, blogs, journals, Web application software, search engines, etc) to create a new service *(12). Example:* ubio.org
Podcast: Digital audio or video files made available in a serial fashion for download via Web syndication. *Example:* nature.com/bjp/podcast/index.html
RSS ("Rich Site Summary"): Delivery of regularly changing Web content (i.e., a Web feed) in XML format to a user or Web site. RSS is sometimes defined as "Really Simple Syndication." RSS files are needed to subscribe to news feed, podcasts, etc. *More info:* whatisrss.com
Social networking: Grouping of individuals into specific groups, based on previous relationships, common interests, etc. Social networking is usually facilitated through the development of an online community that allows participants to share information, chat, organize, play games, etc. *Examples:*

- Facebook facebook.com
- LinkedIn linkedin.com
- Twitter twitter.com
- BioMedExperts biomedexperts.com

Tag: Word chosen and assigned by a user to an object on a Web site for the purpose of categorizing or cataloging it. A **tag cloud** (or word cloud) is a graphic of a group of tags indicated according to relative importance or usage frequency.
Web syndication: Process by which Web material can be made automatically available to other Web sites, usually via subscription.
Wiki (from Hawaiian word for "fast"): Website that allows collaborative creation and editing of text and graphical material via a Web browser. Typically designed for a specific purpose and is editable by anyone in the community established for that wiki. *Example:* Open Science Wiki science.wikia.com

videos can be rapidly propagated ("going viral"). YouTube has recently begun to be used for educational purposes. For example, over 1200 videos are currently on YouTube with the tag "pharmacology," and over 80 with the tag "norepinephrine." Some of these videos are commercially produced, some are recordings of medical school lectures, and many are of students or self-professed experts speaking on a variety of pharmacological topics. The drawback is that there is no quality review. However, faculty can select or create videos to share with students via embedding into course materials or showing them in the classroom. (For an example of a commercially produced video on the mechanism of action of botulinum toxin, see youtube.com/watch?v=R-A8YI7Ik4g). To ensure quality and ensure privacy, some educational institutions are creating their own video interfaces. For example, Creighton University has developed BluView, which allows students to create and upload their own videos in a social network created by individual course directors. In this venue, students can be assigned to create videos or can upload third-party videos as part of class assignments. All the features of a social network site are also present, such as tagging, searching, commenting, and embedding.

The newest Web 2.0 technology that could potentially have an impact on pharmacology education is Google Wave (wave.google.com). This platform is a real-time collaboration tool that allows users to share opinions, use and develop applications, edit content of other users, play back content, automatically translate text, and share files. As of this writing, this tool is available only in a limited preview. However, it has the capacity to unite all of the previously discussed technologies on a single platform and create new ways to educate students in an interactive environment.

"[S]tudents have been left to negotiate a cultural paradigm shift, comparable to the print and industrial revolutions, with inadequate support from the institutions created to help them" (3).

The Eductor's Role: A Mission Of Change

By exploring the use of Web 2.0, do educators merely pander to this generation of digital natives? We don't think so, because the reality is that students already apply this technology in and out of the classroom. Although faculty members may bemoan the fact that some students are not attending class, these students tell us that they are able to accomplish

more on their own. Are we forcing them into a mold that we are comfortable with but it is not optimal for them? We know that there are certain pieces of information that students need to know and comprehend, but our roles as caretakers of this information have been transformed by and transferred to the Internet *(6)*. Over the next few years, there will be an increased use of cloud computing, mobile devices, and the personal Web *(1)*. Will we as teachers be ready? In addition to being content experts, we need to explore these technologies and determine how best to use them to help students learn. In order to facilitate the latter, we need to collaborate with our students in the effective use of technology.

There are four steps to help us accomplish the change from the old system, in which the teacher delivered the same lecture to all students, to a focus on individual learners (6). First, we have to leave the lectern and establish a dialogue with our students; we have to adopt a more interactive approach. Second, we need to encourage students to enter a process of discovery and critical thinking instead of just memorizing drug information. There is a vast array of educational tools and resources available to our students, but this vastness raises issues of relevancy and accuracy for our students. Thus, while encouraging them to discover for themselves, we need to coach them. Third, we need to expand the learning environment by encouraging our students to collaborate among themselves and with others outside the school. Finally, we need to explore how we can tailor the style of education to our students' individual learning styles, as has been discussed elsewhere *(11)*.

It is not going to be easy. Leaving the lectern moves many of us out of our comfort zone, but we do not need to deal with this discomfort alone[1]. More importantly, we need to begin to collaborate with our learners and learn from them.

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1 A workshop on Web 2.0 technologies, sponsored by the ASPET Division for Pharmacology Education, is programmed at EB2010.

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Private Development Companies: Transforming Academic Research into New Treatment Options for Cancer

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In 1971, President Nixon signed the National Cancer Act into law. Intended to eradicate cancer as a major cause of death, the Act functioned, in part, to make funds available for the identification of new molecular targets. Nearly forty years later, with expenditures of over $200 billion, the age-adjusted death rate for cancer in the US remains unchanged *(1, 2)*. In contrast, over this same period of time, with expenditures approaching only half of those invested in cancer research, deaths from coronary disease declined from over 375 to under 150 per 100,00 individuals *(3, 4)*. Early on, this disparity could have been attributed to our lack of an understanding of tumor cell biology. In the last fifteen years, however, our knowledge of both tumor cell biology and the human genome has grown exponentially, yet cancer deaths continue to surpass cardiovascular deaths (Figure 1). It is clear that we are not spending our money in a way that best leverages what we have funded and what we have learned. We urgently need new models for cancer drug development.

Private development companies could provide the means for meeting this need. Such companies would shepherd first-in-class molecules emerging from competitively funded academic oncology research centers into rigorous regulatory-directed development programs. These companies could "de-risk" experimental therapeutic innovations which, having no clearly defined pathway toward commercialization, often languish in the academic institutions where they are conceived. By providing translational pathways, private development companies would expedite the availability of these innovations to the marketplace by making them viable candidates for licensing to the pharmaceutical sector, which uniquely possesses the funding resources and expertise for clinical development and global marketing.

The current paucity of translational routes for antitumor drugs is a problem that can be linked to three key events that occurred in 1980. To understand the critical role that private development companies could play in solving this problem, it is worthwhile to understand its history, which involves a Supreme Court decision and two pieces of legislation. First, in *Diamond v. Chakrabarty*, the Supreme Court decided that genetically engineered microorganisms could be viewed as new compositions of matter. The litigants in this case were Al Chakrabarty, a General Electric microbiologist who developed a strain of *Pseudomonas* capable of using crude oil as a substrate, and Sydney Diamond, the US Commissioner of Patents, who in principle opposed patenting life. Chief Justice Burger, writing the majority opinion in a 5-4 decision, held that "any product of human ingenuity" was patentable. This landmark ruling enabled the nascent biotechnology industry to flourish. Although Genentech was founded four years earlier, in 1976, it would clearly rely on this decision. Also in 1980, Congress passed the Bayh-Dole Act (i.e., the University and Small Business Patent Procedure Act), which gave universities and research institutions the right to hold patents. The Act obligated patent-holding institutions to competitively license their intellectual property for maximum returns while giving preference to small businesses. These conditions essentially required the creation of technology transfer offices. Finally, Congress passed the Stevenson-Wydler Technology Innovation Act of 1980, which in turn required federal research institutions, along with universities, to attempt to competitively license their intellectual property.

As a consequence of the 1980 legislation, universities were placed upon a tripartite axis with pharmaceutical corporations and the newly emerging biotechnology industry (which they helped spawn and which grew in propinquity to them) as part of a plan to deliver the products of federally funded research back to the taxpayer and to improve the health of the American public (Figure 2). In this way, universities, for the first time, were actively encouraged to market their intellectual property. The legislation, however, failed to recognize the not-for-profit ethos in which academe is so deeply rooted. In fact, many universities had long-standing policies explicitly forbidding the marketing of biomedical research. As early as 1934, the President and Fellows of Harvard University had decided, "no patents primarily concerned with therapeutics or public health may be taken out by any member of the university." Although these inveterate policies were rescinded in the 1970s, they continue to color the thinking at many universities. This, coupled with legal concerns associated with institutional tax-exempt status, still make it difficult for important drugs to reach the market.

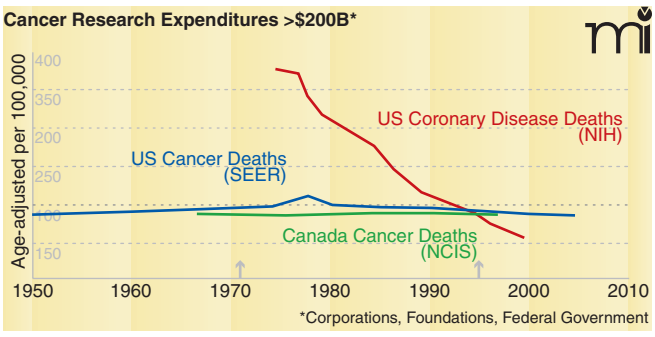

Figure 1. Age-adjusted death rates for cancer and coronary disease.

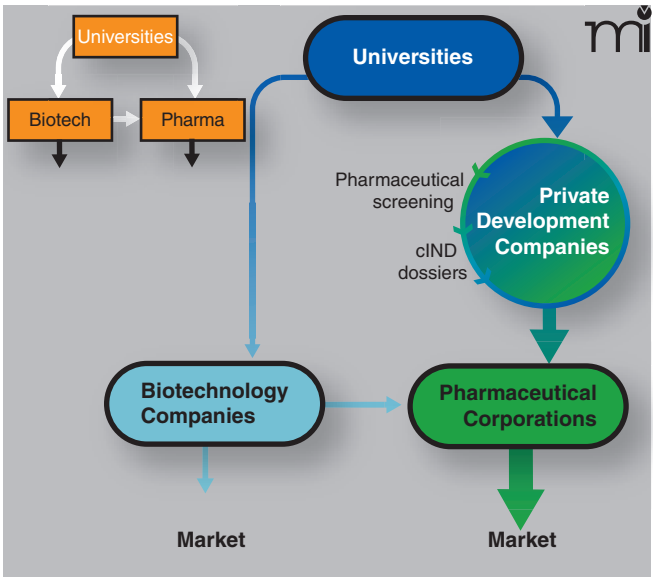

Figure 2. The University/Pharmaceutical/Biotechnology axis remodeled. *Upper inset.* The familiar tripartite axis, representing a pathway for intellectual property to be developed into marketable therapeutics, resulted in 1980 from *Diamond v Charkrabarty*, the Bayh-Dole Act, and the Stevenson-Wydler Act (see text for details). White arrows represent the flow of intellectual property; black arrows represent a pathway to market. *Main flowchart.* In oncology, where the commercialization of effective drugs has been sluggish, private development companies are needed to transform academic research into new treatment options that reach the market. Private development companies would utilize experienced pharmaceutical review boards to select molecules emerging from competitively funded federal research programs and subject them to rigorous regulatory-directed development programs resulting in commercial Investigational New Drug (cIND) dossiers. These dossiers could be licensed to pharmaceutical clients, facilitating a route to market.

Nevertheless, research investments into the university/pharmaceutical/biotechnology axis have not been insignificant. In 2008, $29.8 billion of NIH funds, nearly $5 billion explicitly earmarked for cancer, flowed into universities and research institutions *(4)*. Venture capital investments specifically targeted to biotechnology were slightly greater than $6 billion, more than double the amount invested across all sectors in 1990, and more than ten times the amount invested in 1980 *(5, 6)*. Corporate research and development expenses at pharmaceutical corporations exceeded $50 billion, ten percent of which was spent extramurally *(7)*.

Given the large sums of money that have been poured into drug development along the university-pharmaceutical-biotechnological axis, one must wonder what the return on this investment has been. If we focus on cancer, we find that six antitumor drugs accounted for one-third of the $66 billion in revenues posted by the twenty-five top-selling biotechnology drugs of 2008. Genentech developed the top three revenue producers worldwide: Rituxan, approved for non-Hodgkin's lymphoma, grossed $5.1 billion; Avastin, approved for colorectal and non-small cell lung cancer, grossed $4.5 billion; and Herceptin, approved for first-line treatment of metastatic breast cancer, grossed $2.6 billion. Novartis's Gleevac, for chronic myelogenous leukemia, grossed $3.7 billion worldwide, and Taxotere, a Sanofi-Aventis drug approved for second-line treatment of metastatic breast cancer, yielded $2.6 billion. Finally, Erbitux, approved for colorectal cancer, grossed $1.5 billion for ImClone. All in all, twenty-three cancer drugs had worldwide revenues of greater than $1 billion in 2008, and total worldwide revenues for antitumor drugs exceeded $40 billion *(8)*.

Although the drugs we are developing for cancer produce significant revenue, their efficacies leave much to be desired. With the exception of Rituxan, which produced a five-year survival in lymphoma patients of over 50%, and Gleevac, which resulted in a one-year survival of 97%—both invented by company scientists *(9,10)* —the benefits these drugs provided, according to FDA-approved labeling at launch, have been less than stellar. Avastin extended survival by 4.7 months, whereas patients treated with Herceptin lived with no overall increase in tumor burden for an additional 2.7 months. Patients treated with Taxotere lived 2.7 months longer, whereas Erbitux gave patients the benefit of living only 6 weeks longer with no overall increase in tumor burden *(11)*. In general, the rate of cancer drug approval in the US from 1987 to 2008 (about 3.5 drugs per annum) suggests that most cancer drugs that enter development do not work very well or do not work at all *(12)*. And this must change.

This leads us to ask what our prospects might be for new effective antitumor agents. Data collected from some 160 universities and research institutions over ten years by the Association of University Technology Managers clearly suggests that, at present, we cannot rely on discoveries made in universities *(13)*. Alarmingly, only one half of one percent of university patents licensed to industry produced income (both in fees and royalties) of greater than $1 million. With research expenditures reported at $200 billion and 25,000 patents licensed over the survey period, it now costs about $1.6 billion to produce a $1 million license. For large institutions (i.e., those spending over $250 million per annum on research), the median return on investment in 2007 was a paltry 1.5%, although the maximum return was 265.6% [the latter reflecting $791 million collected by New York University, largely associated with Remicade royalties *(14)*]. Despite the fact that the survey was not limited to biotherapeutics, to say we are inefficient in mining discoveries made in publicly funded research institutions, or that there is room for improvement, nevertheless, understates the dilemma.

The problem remains that universities and research institutions are not-for-profit organizations. As such, they do not war-

rant their patents, represent that these patents are not subject to competing blocking patents, nor guarantee the technical validity of their science. These institutions therefore license their intellectual property at a deep discount, to pharmaceutical clients who purchase these licenses defensively and, wary of the development risk, often do not exploit them. Thus, if inventions do not languish in universities, they languish in pharmaceutical corporations.

If we cannot rely on discoveries made in universities to populate a cancer discovery pipeline, what about privately funded premarket biotechnology companies? These companies have typically spun off from academic centers, taking with them, through technology transfer agreements, both key inventors and intellectual property. With regard to cancer therapeutics, such companies tend to position themselves for acquisition following proof-of-concept phase 2 trials. But it is difficult to see how this model can remain profitable. The issue is clinical development risk. Clinical development risk increases dramatically if clinical development is underfunded, as it almost always is at these small companies, reliant as they are on limited private equity funds. They typically can afford only one phase 2 trial per disease indication to create value.

The difficulty in cancer, in contrast to cardiovascular diseases, is that there are no biomarkers to allow companies to rationally pick dosing schedules, let alone determine activity after phase 1 data *(15)*. This is likely why we have made such strides in treating coronary disease but not cancer. The clinical trials are so much easier. So for small companies focused on cancer, to expect real value accretion after limited phase 2 data is beyond wishful thinking. And this is where the biotechnology model fails in oncology.

Premarket biotechnology companies that undertake to develop new treatments for cancer, however, continue to be funded by a sequacious investment strategy that forces them to live or die on positive outcomes in one tumor type. Because it typically takes $100 million and eight to ten years to get to a point where success can be evaluated; because there is high clinical development risk; and because valuations must be extremely high in order to achieve a significant return on investment at acquisition: many investors are now starting to adopt an ABC policy (Anything But Cancer). This limits development opportunities for new drugs.

Private development companies offer the opportunity to address this dilemma by reorganizing the university/ pharmaceutical/ biotechnology axis (Figure 2). These companies would have access to a constellation of concepts already crystallized through federal funds, and could foster the development of many of the thousands of university patents issued annually [almost 4000 in 2007 *(16)*]. Alongside professional review boards and experienced oncology development teams, these private companies would work to find first-in-class molecules against novel targets, evaluate their patentability and existence of blocking patents, assess their preclinical efficacy, and determine their scalability and stability. Selected molecules would undergo intense regulatory-directed development studies which, if accomplished correctly, would allow the development company to compile commercial Investigational New Drug (cIND) dossiers. These dossiers could be competitively marketed to pharmaceutical clients (Figure 2).

In concept, a cIND dossier would be a ready-to-file document, comprising the major components of an IND following the common technical document format recognized by licensees and regulatory agencies worldwide. The cIND would homologate the pharmaceutical and regulatory development risks that often kill drug candidates between discovery and the onset of clinical trials. Moreover, a cIND could be warranted by the development company and thus of be of greater value than a university license.

Although they would compete with biotechnology companies for pharmaceutical clients, private development companies would structure themselves to license cIND dossiers rather than position themselves for acquisition. These companies would diversify risk by choosing from a number of first-in-class drug candidates, against novel targets, that are currently being produced in competitively funded federal research programs. With low internal costs—a private development company could outsource most of its work—each compound would require only a few million dollars in external costs over three years to reach a cIND endpoint that would generate license fees, and over time, milestone payments and royalties. Moreover, private development companies could become self-sustaining in a short time, depending on the value of the cINDs they produce.

One way to assess how a cIND might be valued in oncology is to assess how industry values early-stage data involving novel targets. Over the last year, deals made between biotechnology firms and pharmaceutical corporations involving inhibitors of novel targets with only incomplete phase 1 data garnered, according to company announcements, from $0.5 billion to just over $1.0 billion, excluding royalties. Examples of such deals include: i) an agreement between Bristol–Myers Squibb and PDL BioPharma to develop a monoclonal antibody inhibitor of CS-1, a novel cell surface glycoprotein (upfront payment: $30 million; total deal value:$1.2 billion); ii) an agreement between Merck Serono and Lpath to develop a monoclonal antibody inhibitor of Sphingosine-1-

phosphate (upfront payment: $23 million; total deal value: $0.5 billion); iii) an agreement between Sanofi- Aventis and Merrimack to develop a monoclonal antibody inhibitor of ErbB, a novel epidermal growth factor receptor (upfront payment: $60 million; total deal value: $0.5 billion); iv) an agreement between Onyx and S*Bio to develop a small molecule inhibitor of JAK2, a Janus kinase (upfront payment: $25 million; total deal value $0.6 billion); and v) an agreement between Sanofi -Aventis and Exelixis to develop a small-molecule inhibitor of PI3K, a phosphatidyl inositol 3 kinase (upfront payment:$140 million; total deal value $1.2 billion). Clearly, there is a perceived need and an appetite for early-stage data involving inhibitors of novel tumor targets. And without doubt, the gross margins of these deals would have been far greater had they involved private development companies operating with far less infrastructure compared to biotechnology companies.

To become a reality and to address the dearth of new treatment options for cancer, the need for private development companies must be understood by those who craft policy in the federal granting system, universities, and the private equity community. For too long it has been underappreciated that universities cannot efficiently license their patents to industry and that pre-market biotechnology companies cannot undertake the high commercial risk of developing new cancer therapies. Thus, the university/pharmaceutical/biotechnology tripartite axis dating from the 1980s, although formed with good intent, must be remodeled. Private development companies could re-invent a more productive architecture. By operating outside of universities, but in consort with them, they could add significant value to existing federally funded intellectual property and define a clear path to market for early-stage concepts. These companies would require relatively little cash, but their impact on cancer and other inadequately treated diseases could be large. doi:10.1124/mi.10.2.2

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