ADVANCING TRANSLATIONAL RESEARCH FOR BIOMEDICAL INNOVATION

MEASURING INDUSTRY-ACADEMIC CONNECTIONS

Biotechnology Industry Organization

Prepared for the Biotechnology Industry Organization
by the Battelle Technology Partnership Practice

June 2015

Battelle
The Business of Innovation

Biotechnology Industry Organization

Innovations Transforming Our World

BIO—Biotechnology Industry Organization—is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers and related organizations across the United States and in more than 30 other nations. BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products. BIO also produces the BIO International Convention, the world's largest gathering of the biotechnology industry, along with industry-leading investor and partnering meetings held around the world. BIOtechNOW is BIO's blog chronicling "innovations transforming our world" and the BIO Newsletter is the organization's bi-weekly email newsletter.

Battelle

The Business *of* Innovation

Solving What Matters Most

Battelle is the world's largest nonprofit independent research and development organization, providing innovative solutions to the world's most pressing needs through its four global businesses: Laboratory Management, National Security, Energy, Environment and Material Sciences, and Health and Life Sciences. It advances scientific discovery and application by conducting approximately $5 billion in global R&D annually through contract research, laboratory management and technology commercialization.

Battelle's Technology Partnership Practice (TPP) assists local, state, and regional organizations, universities, nonprofit technology organizations, and others in designing, implementing, and assessing technology-based economic development programs. For more information on TPP, please contact Mitch Horowitz, Vice President and Managing Director, at horowitzm@battelle.org.

EXECUTIVE SUMMARY

More than a decade ago, the NIH Roadmap and the FDA Critical Path Report brought significant public attention and new programmatic efforts to advance translational research as the bridge between the promise of bioscience discoveries and the advancement of new biomedical innovations to improve the lives of patients. Of particular importance for accelerating translational research and overcoming the challenging environment for bioscience innovation is advancing collaborations between industry and academia as a means to both improving R&D productivity and reducing the costs of translating discoveries into new medical products.

The call for greater industry-academia partnerships reflects the unique nature of bioscience innovation when compared to other industrial sectors. For instance, not only is there a greater commitment by the bioscience industry to conduct internal R&D, there is also existing close ties between industry, clinical care, and academic communities due to the necessary interface of "bench and bedside" required for biomedical innovation to move forward.

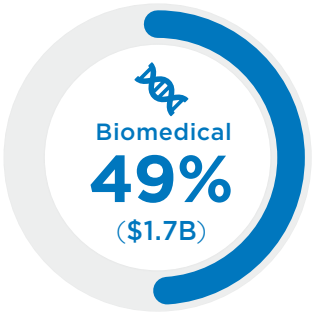
It is particularly fitting for BIO, the world's largest biotechnology-focused trade association representing both industry and academic institutions, to take the lead in assessing the volume of activity and trends in industry-university collaborations that are critical for accelerating translational research.

This first-ever measurement of the extent of current industry-academic collaborations considers both the rich environment of engagement and the contribution between industry and academic partners across the four stages that all translational research must pass through in bringing new treatments to patients—basic and applied, technology development, clinical trials, and new product launch.

Bio Biotechnology Industry Organization
Battelle The Business of Innovation

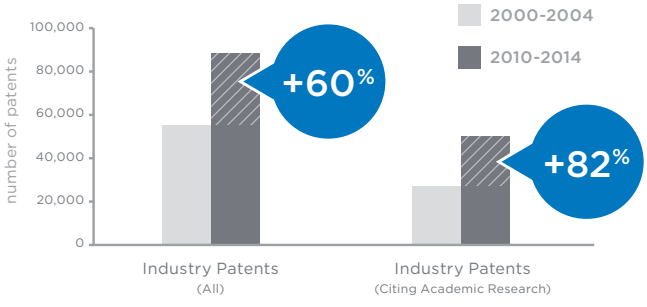
KEY DATA FINDINGS

In basic and applied research, industry engagement of academic partners in biomedical research stands out. Industry direct funding for university biomedical-related research stands at 49% of all industry-funded university research in 2013, reaching $1.73 billion or just over 5% of total university biomedical-related research. Joint industry-academic (including university, hospital or research institute) publications in biomedical-related fields grew by almost 23% over the past decade.



Industry-Funded University Research
2013

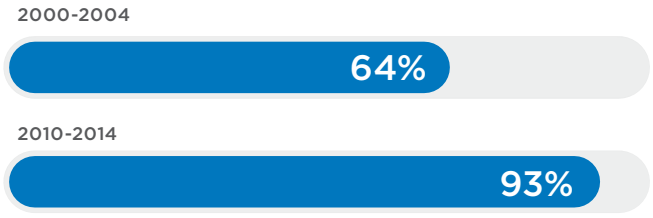
In technology development, industry is relying more and more on academic research in support of their industry patents. Industry patents citing academic research articles increased over the past decade from 27,549 from 2000–2004 to 49,997 from 2010–2014, representing a growth of 81.5% (significantly exceeded the overall rate of growth in industry biomedical patenting of 59.7%).



Academic Linkages to US Granted Biomedical Patents

In clinical trials, academic institutions are far more than just sites for conducting industry-sponsored trials. One in eight industry sponsored clinical trial has an academic institution as a co-sponsor or collaborator. While this is substantial, it may be one area where increased industry-academic collaborations are fostered.

In newly launched products, there has been a sharp rise in the share of patents associated with new therapies citing academic research—further proof of the growing connections between academic research and new drug therapies reaching patients. Over the 2010–2014 period, 93% of novel chemical entity drugs and novel biologics associated with patent-protected intellectual property cited academic research. This is up significantly from the 2000–2004 period, when 64% of novel chemical entity drugs and 79% of novel biologics cited academic research.



Percent of Patents Associated with New Therapies Citing Academic Research

Emerging Models: What To Do

Beyond just the numbers, there is a "real world" context of exciting developments taking place in industry-academic collaboration activities to advance translational research.

In basic and applied research, industry-university research collaborations are evolving. Two significant developments are taking hold in advancing collaborations at the research stage that hold promise in reaching a new level of scale beyond which individual

Bio Biotechnology Industry Organization

Battelle The Business of Innovation

company sponsoring and jointly conducting research with an academic institution can achieve, including:

- **Rise of multi-institutional and multi-company collaborations**
- **Rise of open innovation models that provide academic researchers broader access to research tools and even funding from industry in a more streamlined and open process**

In technology development, industry-academic collaborations are increasingly focused on advancing systematic, replicable approaches for creating value through leveraging scientific, clinical, and business know-how versus a more ad hoc project-by-project approach. Two areas where these more systematic, replicable approaches are taking hold include:

- **Advancing partnerships of clinicians with engineers and scientists**
- **Fostering new venture development approaches**

In clinical trials, industry-academic collaborations may be an area that offers opportunities for increased activities, especially in light of the complexity of clinical trials. Among the examples of emerging best practices, models include:

- **Regional clinical trials consortia**
- **CRO-CTSI partnerships**
- **Centralized patient repository**

In launching new products, industry-academic collaborations are benefiting from more applied research capacities that academic institutions are advancing, particularly in two areas:

- **Experimental therapeutics centers**
- **Advanced biomanufacturing centers**

Opportunities for BIO to Help Accelerate Industry-Academic Translational Research Collaborations

BIO, in bridging the worlds of biotechnology industry and academic research, can play a critical role in convening and disseminating emerging models. In convening, BIO can scale-up the localized efforts on collaborations to have a larger footprint as well as possibly impacting how federal and state initiatives to advance bioscience development proceed. Among opportunity areas for convening would be:

- Working with patient advocacy groups to initiate larger scale multi-institutional and multi-company translational research collaborations.
- Advancing larger scale, multi-institutional patient registries.
- Promoting more engagement between contract research organizations and NIH-funded clinical and translational research institutes.

In dissemination of emerging models and resources available, there is much to be done, including:

- Better cataloging the many available translational research activities taking place involving open innovation, applied academic research resource centers, and ongoing partnerships of industry, clinicians, engineers and scientists.

Tracking the success and impact these industry-university translational research efforts are having and focusing increased discussion on best practices and how to achieve increased scale.

TABLE OF CONTENTS

Bio Biotechnology Industry Organization

Battelle *The Business of Innovation*

“INNOVATION OR STAGNATION”

The imperative for translational research and the critical role for industry-university collaborations.

Battelle
The Business of Innovation

INTRODUCTION

"Innovation or Stagnation" was the riveting title of the 2004 Food and Drug Administration (FDA) report on the Challenges and Opportunity on the Critical Path to New Medical Products (commonly referred to as the Critical Path Report). The report brought to public attention the growing concern that "at a time when basic biomedical knowledge is increasing exponentially, the gap between bench discovery and bedside application appears to be expanding[1]."

At roughly the same time, the National Institutes of Health (NIH) Roadmap was getting underway and bringing a new focus on accelerating translation from bench to bedside and creating an academic home for translational research, which is now embedded in the recently formed NIH National Center for Advancing Translational Sciences.

Despite the efforts of FDA and NIH, the challenge of addressing the translational research gap between promising bioscience discoveries and the advancement of new biomedical innovations has seemingly deepened. In particular, the funding environment for bioscience research and development is greatly constrained due to the loss of industry revenues caused by expiring patents and the challenging federal funding environment for the NIH. Industry is also under pressure to raise the effectiveness of R&D expenditures as it tackles ever more complex diseases using advanced multi-disciplinary research approaches.

At the same time, venture capital needed to foster new bioscience firm formation and growth faces strong competition from alternative opportunities that offer the prospect of more near term returns, particularly in web-based applications, Big Data and social media, and as a result bioscience venture capital has shifted from early-stage bioscience companies developing new products to those in later stages of development that are ready to enter clinical trials.

The result of this difficult environment for bioscience innovation is leading to increased emphasis on an alternative model for biomedical commercial R&D—one that is rooted in research and development partnerships between industry and academia as a means to both improving R&D productivity and reducing the costs of translating discoveries into new medical products.

Elias Zerhouni, former Director of the NIH, in explaining the NIH Roadmap in Science in 2003 noted: "The private sector will play an essential role in this new paradigm.[2]" The FDA in the Critical Path Report (2004) noted that "there is currently an urgent need for additional public-private collaborative work on applying technologies such as genomics, proteomics, bioinformatics systems and new imaging technologies to the science of medical product development.[3]"

These calls for industry-academic partnerships reflect the unique nature of biosciences innovation. Not only is there a major commitment by industry to R&D, but there is also especially close ties between industry, clinical care and academic communities due to the necessary interface of "bench and bedside" required for biomedical innovation to move forward.

Measuring Up: A First-Ever Measurement System of Industry-Academic Partnerships Across the Stages of Translational Research

Now, a decade after the NIH Roadmap and the FDA Critical Path Report brought significant public attention and new programmatic efforts to advance translational research, it is important to take stock of the progress that has been made in advancing industry-academic collaboration.

1 FDA, Innovation or Stagnation: Crisis and Opportunity on the Critical Path to New Medical Products, March 2004, page 3.
2 Elias Zerhouni, The NIH Roadmap, Science, Vol. 302, October 3, 2003, page 64.
3 FDA, Innovation or Stagnation: Challenges and Opportunity on the Critical Path to New Medical Products, March 2004, page 15.

BROAD STAGES OF TRANSLATIONAL RESEARCH FOR MEASURING INDUSTRY-ACADEMIC LINKAGES

The nature of translational research and the many steps involved in advancing bioscience innovation makes it difficult to establish a single metric to capture industry-academic collaborations. Translational research is a complex continuum across which industry-academic collaborations occur with much bi-directional interaction between basic, applied and clinical sciences. Still there are common types or stages of activities across which translational research must pass that can help in focusing attention on the level and trends in collaboration taking place between industry and academic partners. For this first ever measurement of industry-academic collaborations, the focus is on measuring collaborations at four broad stages that all translational research must pass through:

- Basic and applied research collaborations to address scientific questions, typically with an uncertain outcome
- Technology development collaborations to take scientific innovations forward through proof-of-concept tests and more applied research development
- Clinical trials collaboration to test new investigational drugs and devices to ensure their safety and efficacy
- New product launches in which final regulatory approval is secured after the lengthy, complex, costly and uncertain process that defines translational research

As the above illustration depicts, measuring industry-academic connections across these stages of translational research serves to demonstrate the complex and multi-faceted nature of industry-academic engagement and contributions that are taking place to advance translational research.

More Than Just Data

Beyond just the numbers, there is a "real world" context of exciting developments taking place in industry-academic collaboration activities to advance translational research. Of primary interest are those emerging efforts that go beyond traditional one company to one academic institutional partnerships to involving multiple companies and/or multiple academic institutions to gain more scale and impact. To offer a sense of the range of efforts and their different approaches, we set out an illustrative listing in Appendix A and draw upon a number of these examples in our discussion.

BASIC & APPLIED RESEARCH: MEASURING INDUSTRY-UNIVERSITY CONNECTIONS

Translational research requires close industry-academic connections at the research stage so that industry-led biomedical product innovations keep up with the astonishing speed of advances in biotechnology—advances that are reshaping how we discover and develop new treatments and diagnostics for diseases and medical conditions.

Biotechnology is shaping two new medical revolutions that will require close connections between academia and industry to bring benefits to patients. One is the rise of genomic-based medicine that is moving medicine from being an inexact art of detection and treatment to a science of prediction, prevention and strategic intervention or what is popularly referred to as "personalized or precision" medicine. The other is regenerative medicine in which biotechnology is being applied to restore bodily functions, replace failing body components and organs, and addressing many currently incurable diseases with cell-based therapies.

Specific Measures of Industry-University Connections in Research

Industry-Funded University Research

Biomedical industry stands out in its investment in research-driven innovations. Roughly one in five dollars spent on R&D by U.S. businesses is accounted for by the biomedical industry—the highest level of all industries in the U.S. What better way to measure the connection of industry research with that of academia then by considering how industry directly funds academic research.

Data from the National Science Foundation's research expenditure surveys of universities, since 2010, tracks direct industry support to university research in medical sciences, biological sciences, and bioengineering.

Among the areas of analysis are:

- Trends in industry funded research for university biomedical-related research
- The geographic footprint of industry funded research for university biomedical-related research

Joint Industry-Academic Publications

The collaboration of industry and academia in publishing joint scientific articles in peer-reviewed journals reflects both the quality of collaborations leading to scientific findings as well as the depth (though often informal) of links comprising flows of personnel, tacit knowledge and technology.[4]

Data from Thomson Reuter's Web of Science tracks the level of joint publications in bioscience fields by industry and academic authors.

Among the areas of analysis are:

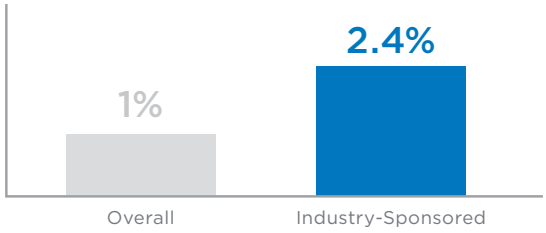
- Trends in joint industry-academic publications
- Leading fields of joint industry-academic publications

4 See Keith Pavitt, "Do Patents Reflect the Useful Research Output of Universities," Research Evaluation, August 1998, page 110.

Analysis

Trends in Industry-Funded University Research

- In 2013 industry funded research for university biomedical-related research totaled $1.73 billion or just over 5% of total university biomedical-related research
- Biomedical-related research funding by industry comprised over 49% of all industry-funded university research in 2013.
- From 2012 to 2013, industry funding for university biomedical-related research grew by $40 million, a gain of 2.4% from 2012 to 2013 levels, out-pacing overall university-related biomedical sciences growth of 1% (see Table 1).



Percentage Growth University Biomedical R&D 2012-2013

Table 1: Trends in Biomedical-Related University Research Funded by Industry

Industry-Sponsored R&D, 2013		Percentage Growth, 2012–2013	
Expenditure	Share	Industry Funded University Research	Total University Research
$1,726,761	**5.04%**	**2.4%**	**1.0%**

Geographic Footprint of Industry-Funded University Research (By State)

From 2010 to 2013, the average state share of industry funding of university biomedical-related research reached 5%, with a high of 13.9% in North Carolina. The next highest state was Louisiana at 7.7%. Table 2 lists data for the top ten states receiving industry funding for biomedical-related university research.

Among the fastest growing states in industry funding of university biomedical-related research, it is useful to consider those with large existing university biomedical research bases and those with smaller university biomedical research base that are making strong gains.

As indicated in the data provided in Table 3, Utah stands out among the states with a large existing university biomedical research base, with nearly 4x growth of its industry funding of university biomedical research from 2010 to 2013. Other states making strong gains in industry funding of university biomedical research included Wisconsin, Georgia, New York, and Connecticut.

Table 2: Top 10 States in Share of Industry Funding for Biomedical-Related University Research

State	Value
North Carolina	13.9%
Louisiana	7.7%
Colorado	7.0%
Missouri	6.6%
Ohio	6.5%
Hawaii	6.3%
Indiana	5.4%
California	5.3%
Texas	5.2%
Nebraska	5.1%

Table 3: Top States in Growth of Industry Funding for University Biomedical-Related Research, 2010–2013

Research Funding Above $1 Billion		Research Funding Under $1 Billion	
State	Growth	State	Growth
Utah	388.8%	Alaska	574.0%
Wisconsin	64.8%	Maine	105.7%
Georgia	52.9%	Montana	89.4%
New York	44.9%	Kansas	61.5%
Connecticut	43.0%	Mississippi	59.4%

Among smaller states, Alaska, Maine, Montana, Kansas, and Mississippi all made strong gains in industry funding of university biomedical research from 2010 to 2013.

Level of Joint Industry-University Publications Over Time

Joint industry-academic (including university, hospital or research institute) publications in biomedical-related fields grew by almost 23% over the past decade – this slightly outpaced the overall growth of biomedical-related publications which grew 21.6% and well outpaced overall industry biomedical-related publications growth of 14.7%. (See data provided in Table 4.)

Leading Fields of Joint Industry-Academic Publications

The biomedical-related field with the most joint industry-academic publications in 2010–2014 was pharmacology and toxicology. Other fields with significant joint publications in 2010–2014 include public health, oncology, and neurosciences.

The biomedical-related fields with at least 250 publications with the greatest increase in joint industry-academic publications over the past decade include neurology (119% growth), surgery (113% growth), health care sciences and services (111% growth), public health (104% growth), and rheumatology (101% growth). (See data provided in Table 5.)

Table 4: Trends in Biomedical-Related Publications

	Total Count	Industry	Joint Industry-Academic
2000–2004	551,636	35,390	27,229
2010–2014	671,030	40,604	33,457
Percentage Change	21.6%	14.7%	22.9%

*Joint industry-academic publications includes at least one collaborator across universities, hospitals/medical centers, and research institutes, though often it includes multiple collaborators.

The close connection in industry-university research remains one of the hallmarks of biosciences development. In the face of a challenging environment for translational research, industry-academic research collaborations are evolving to reach a new level of scale beyond that which individual company sponsoring and jointly conducting research with an academic institution can achieve.

Top 10 Fields in Number of Joint Industry-Academic Publications

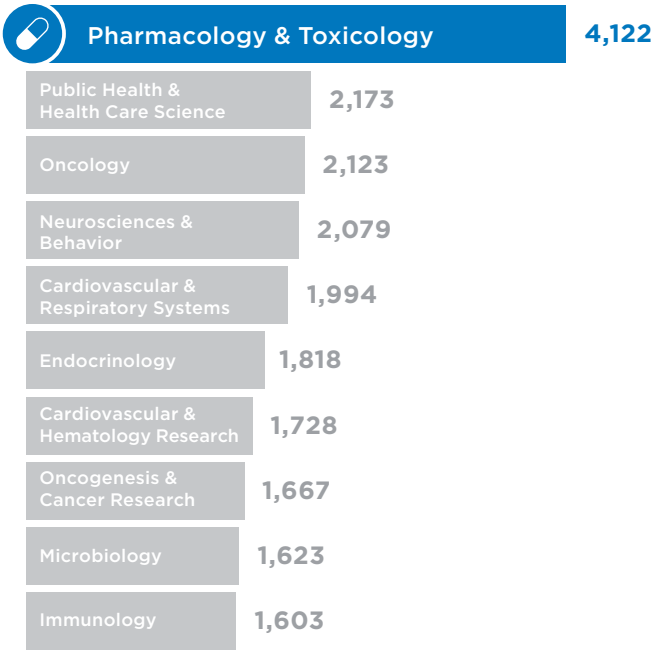


Table 5: Leading Biomedical-Related Fields Represented in Industry-Academic Publications

Top 10 Growth Fields Over the Decade	
Field	**Growth**
Neurology	118.90%
Surgery	112.70%
Health Care Sciences & Services	111.10%
Public Health & Health Care Science	103.80%
Rheumatology	100.80%
Metabolism & Nutrition	94.60%
Environmental Medicine & Public Health	85.20%
Hematology	71.00%
Gastroenterology & Hepatology	68.70%
Ophthalmology	65.20%

EMERGING MODELS: WHAT TO DO?

The close connection in industry-university research remains one of the hallmarks of biosciences development. In the face of a challenging environment for translational research, industry-academic research collaborations are evolving to reach a new level of scale beyond that which individual company sponsoring and jointly conducting research with an academic institution can achieve.

One is the rise of multi-institutional and multi-company collaborations. This broader engagement of industry and academia has its roots in approaches put forward by the National Science Foundation through its Industry/University Cooperative Research Centers and its Engineering Research Centers. Among such ongoing efforts in biosciences is the ERC on Biomimetic Microelectronic Systems (BMES), a research center dedicated to the development of implantable microelectronic devices for the treatment of presently incurable ophthalmic and neurological diseases involving University of Southern California, Caltech and UC Santa Clara and nearly 20 industry partners, and the I/UCRC Center for Pharmaceutical Development involving Georgia Tech and University of Kentucky advancing novel biocatalysts for synthesis of small molecule drugs with 6 company partners.

New efforts in such multi-institutional/multi-company research collaborations includes: the Tuberculosis Drug Accelerator Consortium with the goal of developing five new preclinical drug candidates; the Asian Cohort Consortium bringing US and Asia partners together to identify markers of early disease based on genetics, environmental exposure and etiology of disease; and the Strategic Pharma-Academic Research Consortium for Translational Medicine bringing the University of Indiana, Washington University, Ohio State and Northwestern together with Eli Lilly and Takeda Pharmaceuticals to advance research on autoimmune diseases.

The other is the rise of open innovation models. These open innovation models are typically sponsored by an individual company to significantly reduce the barriers to industry-university collaborations by cutting through much of the red-tape and negotiations of more formal scientific relationships. Academics can typically directly apply to the companies with their ideas through a confidential, but open process so that the best ideas regardless of institution can be considered. Through these open innovation models the companies offer a range of assistance from grants, access to research tools such as molecular profiling and screening tools and access to company scientists. Among the companies with formal open innovation programs are AstraZeneca, Eli Lilly & Co., GlaxoSmithKline, and Merck.

TECHNOLOGY DEVELOPMENT: MEASURING INDUSTRY-UNIVERSITY CONNECTIONS

The technology development stage in translational research involves the advancement of innovations that can lead to new therapeutics, diagnostics, devices or other biomedical products. These bioscience innovations or inventions often have close connections to academic research, either directly relating to discoveries from research efforts or to insights from research that can lead to new discoveries and technology breakthroughs. In drug discovery, for instance, basic research into disease processes can help in identifying possible targets for novel therapeutic development, which then requires considerable effort in drug discovery before a novel therapeutic is advanced.

Typically bioscience inventions advanced through technology development are protected as intellectual property through patents, which provides the predictable legal protection necessary to ensure private investment for technology development.

The bioscience inventions that generate patents must still be developed into viable technology solutions with much additional applied research and development as well as pre-clinical testing before it can qualify for the next stage of development involving clinical testing.

Specific Measures of Industry-University Connections

Industry patent citation of academic research: One broad measure of the extent to which academic research is connected to industry-led technology development is whether industry bioscience patents cite specific journal articles as major sources of knowledge upon which their invention builds. This use of patent citations of scientific journals to assess the extent to which knowledge from academic research contributes to bioscience invention is well established in science research policy. Pioneering work using scientific journal citations from patents was used by Narin and Noma to show the strong dependence of the early patents in biotechnology on knowledge published in scientific papers.[5]

The data for tracking patent citations of academic publications comes directly from patent records reported by the U.S. Patent and Trademarks Office. For this analysis, the Thomson Reuters Innovation database system was used to analyze the patent records reported by U.S. PTO.

The analysis of industry patent citations of academic scientific journals can provide significant insights into how academic research informs bioscience innovations, including:

- How the extent of industry patent citation of scientific journals is changing.
- What is the geographic footprint of industry patents citing scientific research?
- What are the leading technology areas of industry patents citing scientific research?

Analysis

Trends in Industry IP Citing Academic Publications

With the continued advances in biosciences research, industry is relying more and more on academic research in support of their industry patents. As shown in the data breakdown provided in Table 6, industry patents citing academic research articles increased over the past decade from 27,549 from 2000–2004 to 49,997 from 2010–2014; this represents a growth of 81.5% (significantly exceeding the overall rate of growth in industry biomedical patenting of 59.7%).

Table 6: Academic Linkages to U.S. Biomedical Patents

Parameter	Patent Count	
	Total with Industry Assignees	Patents Citing Academic Research
2000–2004	55,513	27,549
2010–2014	88,631	49,997
Percentage Change	59.7%	81.5%

Geographic Footprint of Industry Patents Linked to Academic Research (By State)

Among states with at least 250 industry biomedical patents from 2010–2014, Maryland leads the nation in share of industry patents citing academic research with nearly 75% of its industry patents over the period 2010–2014 citing academic research. Among other states with at least 7 out of 10 industry patents citing academic research were Washington, Colorado, and Massachusetts. (See Table 7.)

Oregon was the state with the highest growth (216% growth) over the past decade in generating industry-assigned biomedical patents citing academic research for states with over 200 patents invented during the 2010–2014 period, followed closely by Tennessee (206% growth). The average share of patents citing academic research journals from 2010–2014 was approximately 56% of all industry-assigned biomedical patents invented in a given state.

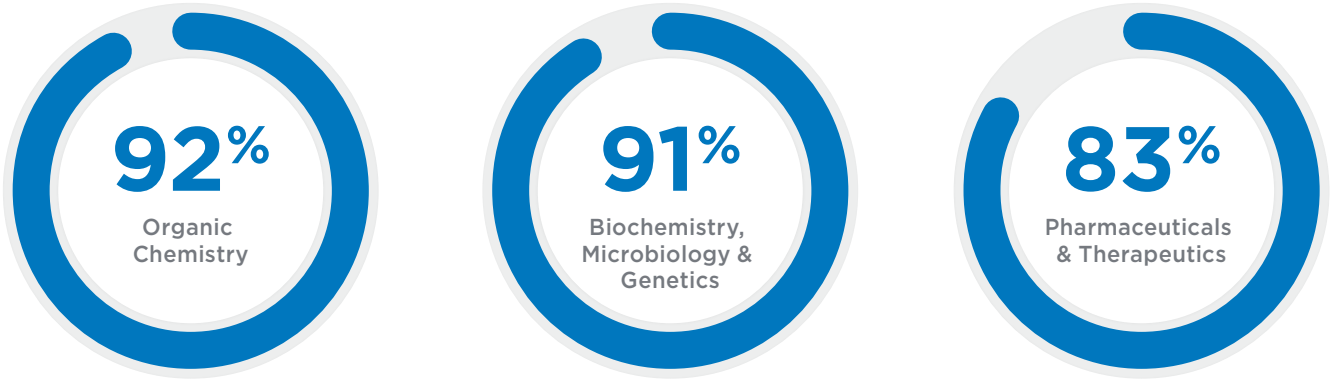
Table 7: Top Ten States with at Least 250 Industry Biomedical Patents Citing Academic Research, 2010–2014

State	Percent Share	State	Percent Growth
Maryland	74.50%	Oregon	216.30%
Washington	71.50%	Tennessee	206.30%
Colorado	71.10%	Minnesota	159.10%
Massachusetts	69.90%	Delaware	124.10%
North Carolina	67.70%	Florida	122.20%
California	67.40%	Illinois	106.40%
Connecticut	63.80%	Ohio	97.20%
Texas	62.40%	California	78.80%
New York	60.90%	Arizona	78.70%
Pennsylvania	60.80%	Colorado	78.50%

Leading Class Areas of Patents Linked to Academic Research

Patents with applications in organic chemistry and biochemistry, microbiology, and genetics as well as patents for pharmaceuticals and therapeutics each had very high proportions of overall industry patents with citations to academic journals (with 92.4%, 91.3% and 82.6% of patents referencing academic research respectively).

As shown in Table 8, these proportions were significantly higher than any other major biomedical patent category in industry (other than organic chemistry primary class patents with secondary biomedical classes). Detailed class areas in pharmaceuticals containing organic active ingredients as well as measuring and testing processes involving enzymes had 88% and 92% of their industry publications citing academic research journals respectively, among the highest of all detailed patent classes with over 500 patents invented from 2010–2014.



Percent of Industry-Assigned Biomedical Patents with Citations to Academic Journals by Primary Class Area

2010-2014

- The two application areas with the highest number of industry patents citing academic research were medical device applications and pharmaceuticals and therapeutics—each with over 10,000 patents from 2010–2014.
- The fastest growing area of industry patents citing university research—albeit from a low base—was in bioinformatics and health information technology with over fivefold growth. Also growing fast in industry patents citing university research was medical devices and procedures with a 1.5x growth.

Table 8: Primary Patent Class Areas for Industry-Assigned Biomedical Patents with Academic Linkages

Primary Patent Class Area*	2000–2004	2010–2014	% Change	% of All Industry Patents 2010–2014
Lab Equipment	324	349	7.7%	35.4%
Medical Devices & Procedures	7,351	18,911	157.3%	40.7%
Organic Macromolecular Compounds	230	359	56.1%	62.8%
Pharmaceuticals & Therapeutics	5,916	10,395	75.7%	82.6%
Bioinformatics & Health IT	43	277	544.2%	86.6%
Biochemistry, Microbiology, Genetics	5,246	6,669	27.1%	91.3%
Organic Chemistry	4,842	6,433	32.9%	92.4%

*Patents can be labeled using multiple classes—this table lists the primary classification all patents that are labeled as having relevance to at least one biomedical class area, even if that area is a secondary one. For example, a patent's primary classification might be in a non-biomedical area but it may also have a secondary biomedical class label if part of its intended IP protection is relevant to a specific biomedical application. Patents with primary classes outside biomedical applications but with at least one biomedical secondary class are listed under the non-biomedical related patenting area category.

EMERGING MODELS: WHAT TO DO?

Industry-academic collaborations in technology development are increasingly focused on advancing systematic, replicable approaches for creating value through leveraging scientific, clinical and business know-how versus a more ad hoc project-by-project approach. Two areas where these more systematic, replicable approaches are taking hold include:

Advancing partnerships of clinicians with engineers and scientists. Through the use of facilitative processes around focused commercial milestones, a number of initiatives are allowing clinicians to define opportunities for innovation (often in strategically targeted areas) and then leveraging engineering and scientific experts to offer solutions with active industry engagement. Perhaps the "grand-daddy" of this approach is the Center for the Integration of Medicine and Innovative Technology (CIMIT) that brings together 12 academic institutions including teaching hospitals and engineering schools in the Boston areas, with an active industry liaison program involving 40+ members. Another example is the Coulter Foundation, which through its Centers for Translational Research has defined their own processes for increasing clinical innovations through bringing clinicians and engineers together and have replicated with 15 different university partners.

Fostering new venture development approaches. New venture development is a key means for industry-academic collaboration to move through the technology development and later stages of translational research. An interesting spin is having larger companies provide a full range of support to helping to launch and support the growth of new ventures well beyond simply corporate venture financing. Johnson & Johnson's Innovation Centers, for example, offers an integrated model of new venture development including incubation facilities, entrepreneur mentoring and venture financing. Another example is the Accelerator Corporation started in Seattle and now expanding to NYC with investments from Eli Lilly, Johnson & Johnson and Pfizer, among others, that partners with academic institutions in a structured process to bring together a full range of venture start-up services led by a core team of serial entrepreneurs to identify and evaluate the commercial potential of promising bioscience discoveries and technologies and then serve as the initial management teams to form and advance new start-up companies within dedicated bioscience incubation space.

These emerging best practices suggests new targeted public funding approaches for supporting biosciences technology development through more systematic, replicable value-added approaches. Already the State of Michigan is advancing the Coulter Center for Translational Research approach to its universities.

CLINICAL TRIALS STAGE: MEASURING INDUSTRY-UNIVERSITY CONNECTIONS

A unique challenge for bioscience innovation is the need for multiple phases of clinical testing in humans to demonstrate the safety and efficacy under strict FDA regulatory oversight of investigational therapeutics as well as novel types of devices. A recent analysis of the economic impact of industry funded clinical trials found that in 2013 industry sponsored 6,199 clinical trials of medicines in the U.S. involving more than 1 million participants.[5] A separate study finds that about 70% of the potential medicines in development representing novel approaches to addressing disease in areas such as neurology, cancer, diabetes and immunology.[6]

The Tufts Center for the Study of Drug Development reports that industry clinical trials are becoming both more science-driven and complex, requiring significantly more eligibility criteria, procedures and overall work burden.[7] For these more scientifically challenging and complex clinical trials, academic medical centers and academic hospitals offer industry the deep insights of physician-researchers to help in leading industry funded clinical trials, sites that offer more scientific capabilities across its staff and equipment, and a rich environment for recruiting patients.

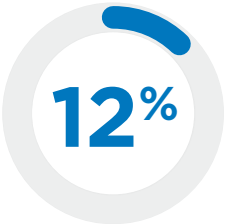
Specific Measures of Industry-University Connections

Industry funded clinical trials with academic collaborators or sponsors. Academic institutions, including universities, medical schools, hospitals and non-profit research institutions, can serve as collaborators and sponsors of clinical trials together with industry that go well beyond simply being a site for hosting a clinical trial. Sponsors are organizations that fund and oversee the clinical study and are responsible for analyzing the study data, while collaborators are other organizations involved in design, implementation, data analysis or reporting functions (as well as providing partial funding).

Data on clinical trials is available from ClinicalTrials.gov, a registry of clinical trials maintained by the U.S. National Institutes of Health, as required under Food and Drug Administration Modernization Act of 1997. It contains data on both publicly and privately supported clinical studies with human participants and its coverage has increased markedly over time as more policies and laws requiring registration have been enacted and as more sponsors and investigators voluntarily register their studies.[8]

Analysis

12.3% or roughly one in eight industry sponsored clinical trials has an academic institution as a co-sponsor or collaborator. While this suggests that academic institutions are far more than just sites for conducting industry-sponsored trials, it also suggests that this might be one area where increased industry-academic collaborations are fostered.

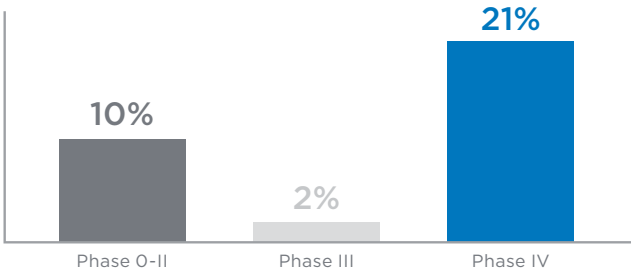


of Industry-Funded Trials had a
University Sponsor/Collaborator

5 Battelle Technology Partnership Practice, Biopharmaceutical Industry-Sponsored Clinical Trials: Impact on State Economies, March 2015.
6 The Analysis Group, "Innovation in the Biopharmaceutical Pipeline: A Multi-Dimensional View," 2012.
7 See Tufts Center for the Study of Drug Development, Briefing: Cost of Developing a New Drug, November 18, 2014.
8 https://clinicaltrials.gov/ct2/resources/trends.

By Phase

University engagement was lowest for large-scale Phase III clinical trials, but reached more than 10% for early phase trials and, interestingly, over 20% for Phase IV clinical trials involved with monitoring safety and long-term side effects. (See data breakdown in Table 9.)



Share of Industry Funded Trials with University Sponsor/Collaborator
2012-2013

By Type of Intervention

- The largest number of industry funded trials with university sponsor or collaborator is found in drug interventions.
- As a share of industry funded trials by type of intervention, university sponsors and collaborators stand out in the areas of behavioral, radiation, procedural and genetic interventions. (See data breakdown in Table 10.)

Table 9: Overview of Industry-Funded Clinical Trials by Phase

Phase	With University Sponsor or Collaborator	Without University Sponsor or Collaborator	Total, All Industry Trials	Share of Industry Funded Trials with University Sponsor/ Collaborator
Phase 0–II	831	7,103	7,934	10.47%
Phase III	60	2,591	2,651	2.26%
Phase IV	239	910	1,149	20.80%
Grand Total (w/Phase Info)	**1,130**	**10,604**	**11,734**	**9.63%**
Grand Total (all trials)	**1,887**	**13,459**	**15,346**	**12.30%**

Table 10: Overview of Industry Sponsored/Collaborative Clinical Trials by Intervention Type

	All Industry (N=15,346)		With University Sponsor or Collaborator (N=1,887)		Share of All Industry Funded Trials
Intervention Type*	Count	Percent	Count	Percent	Percent
Drug	10,382	68%	1,077	57%	10.37%
Device	2,004	13%	255	14%	12.72%
Biological	1,310	9%	92	5%	7.02%
Behavioral	195	1%	73	4%	37.44%
Genetic	40	0%	11	12%	18.51%
Procedure	454	3%	125	7%	27.53%
Radiation	114	1%	43	2%	37.72%
Other	1,183	8%	219	12%	18.51%

*Trials can be classified into more than one Intervention Type.

OUTLINE OF DISTINCT PHASES OF DRUG DEVELOPMENT

Phase 0 Clinical Trials

Fairly new designation identifying exploratory studies involving very limited human exposure to a drug, with no therapeutic or diagnostic goals (for example, screening studies, micro-dosing studies). These studies are designed to understand the cellular level effects of a potential new drug (also known as an experimental drug) by working with extremely low level dosing unlikely to cause any therapeutic or adverse results.

Phase I Clinical Trials

Typically conducted with a small number of health volunteers, typically less than 100, to determine the safety, tolerability, pharmacokinetics, and pharmacodynamics of the potential drug (i.e., researchers assess how the potential drug behaves in the body and the relationship between the compound's molecular structure and its effects on volunteers).

Phase II Clinical Trials

Begin if the drug successfully passes Phase I testing. This phase generally involves between 100 and 500 human volunteers to assess the efficacy and dose response of the drug in development, including identification of common, short-term potential side effects.

Phase III Clinical Trials

Initiated if the potential new medicine is found to be both safe and efficacious through Phase I and II testing. Phase III trials may enroll 1,000 to 5,000 patients or more across numerous clinical trials sites across states and around the world. These randomized, controlled trials generate large amounts of data to support submission to the FDA for approval.

Phase IV Post-Approval Research & Monitoring

Following approval, companies are often required to conduct extensive post-approval research to monitor safety and long-term side effects in patients using the medicine. Under certain circumstances, the FDA may also require companies to conduct risk evaluation and mitigation strategies (REMS) to ensure that the benefits continue to outweigh the risks of a particular medicine.

EMERGING MODELS: WHAT TO DO?

Industry-academic collaborations in clinical trials may be an area in translational research that offers opportunities for increased activities, especially in light of the complexity of clinical trials. Among the examples of emerging best practices, many are building collaborations that involve contract research organizations as a potential partner for academics.

Regional clinical trials consortia – The Biomedical Research Alliance of New York has advanced an alliance among academic-based clinical sites that offers many high value turnkey services to expedite clinical trials start-up and ongoing operations. It has forged a collaboration as a primate site with Quintiles, one of the nation's leading contract research organizations.

CRO-CTSI Partnerships – A number of NIH-awarded Clinical and Translational Science Institutes are starting to develop partnerships with contract research organizations. UCSF in its CTSI has established a preclinical CRO vendor program to offer a wide array of drug development services needed for preclinical development and testing of new investigational drugs. The Indiana CTSI has partnered with Covance, a leading contract research organization, on a Phase I clinical research unit partnership involving shared use of sites in Indianapolis and Evansville.

Centralized patient repository – The University of California Biomedical Research Acceleration, Integration and Development (BRAID) effort brings the five medical campuses of the UC system together. An initial effort was to create a cross-campus searchable database of patient level study data to help inform ongoing and future clinical research efforts.

NEW PRODUCTS LAUNCHED: MEASURING INDUSTRY-UNIVERSITY CONNECTIONS

The ties between academic basic research discoveries and industry product development within the biosciences sector are substantially closer than those found in most other technology fields. The biosciences industry has a deeply rooted and integral relationship with academic research and development. Paula Stephan in her 2012 book, How Economics Shapes Science, published by Harvard University Press, summarizes the literature demonstrating these extensive connections:[9]

- "Nowhere is the contribution of public research more clear-cut than in the areas of pharmaceuticals. Three-quarters of the most important therapeutic drugs introduced between 1965 and 1992 had their origins in public sector research conducted in universities, NIH and non-profit research institutions—almost all of the drugs coming out of biotechnology companies originated at universities—virtually all important vaccines introduced in the past 25 years have come from research conducted in the public sector."

This strong track record of academic research contributing to new medicines that have been brought forward is perhaps the most important measure of the value of academic research.

Specific Measures of Industry-University Connections

Connection between new medicines approved and academic research. A broad gauge of the connection between new medicines advanced by industry for approval and academic research is the citations of academic research for the patents related to the new medicines approved. While this is a similar measure to that used in technology development, the set of industry patents that result in approved medicines is a much more select universe. The Tufts Center for the Study of Drug Development estimated that in 2013 less than 12% of investigational drugs reaching clinical trials were eventually approved as new medicines.[10]

The complicated part is identifying what patents are associated with new medicines approved. For "small molecule" chemical entity drugs identifying the patents is not a challenge in large part because these small molecule chemical entities have well-defined chemical structures and are produced through chemical synthesis that combines specific chemical ingredients in an ordered process. Given that the novelty of these new drugs is dependent upon their patents, the FDA cites the patents in its publication Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the Orange Book).

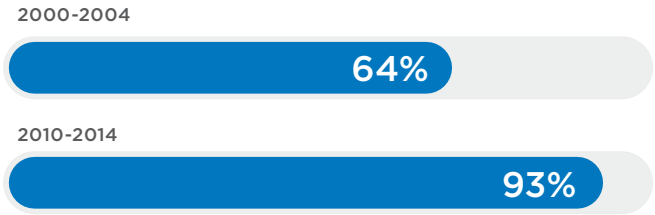
When it comes to biologics, however, the situation is more complicated. FDA does set out the new approved biologics in its publication, Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations (now known as the Purple Book). However, for biologics, which are very large, complex molecules produced using biotechnology techniques on human, animal or microorganism cells, it is very difficult to

9 Paula E. Stephan, How Economics Shapes Science, Harvard University Press, 2012, page 207.
10 Tufts Center for the Study of Drug Development, "Briefing: Cost of Developing a New Drug," November 18, 2014.

know the precise chemical structure and the "product" is actually the process of scaling up the cells produced using biotechnology techniques, some of which are combinations of proprietary formulation and synthesis technologies. Plus, given the different nature of biologics from chemical entity drugs, Congress has developed a different framework for providing new biologics a period of product exclusivity that differs from referencing patents and depends upon therapeutic equivalence. Therefore, FDA has decided not to explicitly track patents for biologics and so no public database exists that directly ties patents to approved biologics.

However, using targeted patent searches reflecting the biologic names and companies involved, a set of patents associated with the biologic product approved from 2000–2004 and from 2010–2014 were developed that cover at least a partial portion of the core intellectual property surrounding the formulation, manufacture, or therapeutic usage of new biologics products from the Purple Book. This listing of patents serves as a complement to the patents explicitly identified in the Orange Book, and while not a complete listing of all patents represents the majority of IP held by biologic product owners that is actively used to protect those products on the current market.

Analysis



Percent of Patents Associated with New Therapies Citing Academic Research

Trends in Patent Citations to Academic Research for New Chemical Entity Drugs

Among novel new chemical entity drugs approved, there has been a sharp rise in the share of patents associated with new therapies citing academic research—further proof of the growing connections between academic research and new drug therapies reaching patients. From 2000–2004 64% of the 229 new chemical entity drug therapies associated with patent-protected intellectual property cited academic research; by the 2010–2014 period it rose to 93% and in 2014 reached to almost 100% in 2014. (See data breakdown provided in Table 11.)

Trends in Patent Citations to Academic Research for New Biologics Products

Among patents associated with new biologics products approved, there was also a significant rise in the share citing academic research indicating that connections to academic research are also critical for bringing biologics products to market. From 2000–2004, 79% of the 53 new biologic products that had patent-protected intellectual property related to their manufacture or formulation cited academic research; by the 2010–2014 period it rose to 93% even with increasing numbers of biologics applications and approvals for market use. (See data breakdown provided in Table 12.)

Table 11: Patent Linkages to Academic Research

Metric	A Period of Interest	
	2000–2004	2010–2014
Total new drug product patents	229	222
Total patents referencing SCI academic journals in citations	147	207
Percent referencing SCI journals	64%	93%

Table 12: Patent Linkages to Academic Research for FDA Purple Book Biologics

Metric	A Period of Interest	
	2000–2004	2010–2014
Total new biologics product patents	53	104
Total patents referencing SCI academic journals in citations	42	97
Percent referencing SCI journals	79%	93%

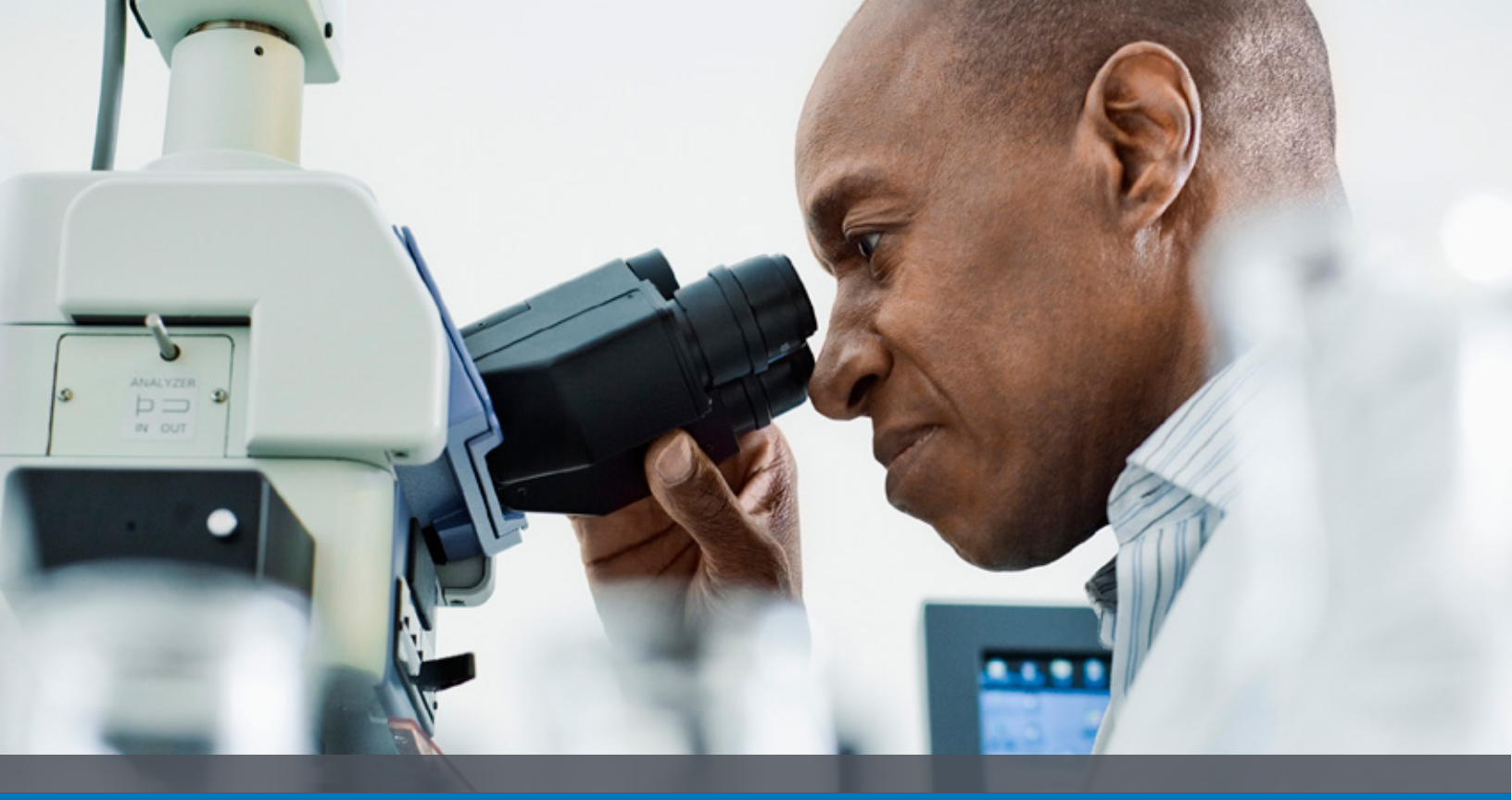
EMERGING MODELS: WHAT TO DO?

Industry-academic collaborations for launching new products are benefiting from more applied research capacities that academic institutions are advancing, often with the support of NIH to establish new resource centers for advanced technology platforms such as high throughput screening, bioinformatics, and molecular imaging. These applied academic capacities are particularly critical for collaborating with emerging bioscience companies, but also hold the promise of "de-risking" early discoveries for collaborations with larger, more established bioscience companies.

Two key areas where academic institutions are bringing advanced applied research capabilities include:

Experimental Therapeutics Centers: These centers bridge the drug development gap that is typically found in many academic medical centers. Often these centers will bring together the medicinal chemistry and pharmacology expertise to identify compounds with a specific target, enhance the compound's selectivity and test its safety. Examples include Harvard's Laboratory for Drug Discovery in Neurodegeneration and Vanderbilt's Center for Neuroscience Drug Discovery.

Advanced Biomanufacturing Centers for Complex Biologics: One of the most complicated and difficult aspects of advancing new biologics is having the know-how to do the bio-scale-up of novel applications of vaccines, cell therapies, and antibodies. As PriceWaterhouseCoopers notes in its report Pharma 2020, "Biologics are particularly hard to manufacture and transport, because they are more fragile than small molecules and more susceptible to impurities in the manufacturing process." The Association of Academic Biologics Manufacturers now numbers nearly 50 institutions. One excellent example is the City of Hope Center for Biomedicine and Genetics that offers a Good Manufacturing Practices biologics production facility with regulatory expertise to support phase I and II clinical trials at City of Hope. It also offers a Production Partnership Program to collaborate with biotechnology companies and academic institutions.



CONCLUSION

Since 2004 when the FDA released its report on the Challenges and Opportunity on the Critical Path to New Medical Products, the decade has experienced innovation in translational research driven by industry-university collaborations, as evidenced by the fact that:

- In basic and applied, industry engagement of academic partners in biomedical research stands out. Industry direct funding for university biomedical-related research stands at 49% of all industry-funded university research in 2013, reaching $1.73 billion or just over 5% of total university biomedical-related research. Joint industry-academic (including university, hospital or research institute) publications in biomedical-related fields grew by almost 23% over the past decade.
- In technology development, industry is relying more and more on academic research in support of their industry patents. Industry patents citing academic research articles increased over the past decade from 27,549 from 2000–2004 to 49,997 from 2010–2014, representing a growth of 81.5% (significantly exceeded the overall rate of growth in industry biomedical patenting of 59.7%).
- In clinical trials, academic institutions are far more than just sites for conducting industry-sponsored trials. One in eight industry sponsored clinical trial has an academic institution as a co-sponsor or collaborator. While this is substantial, it may be one area where increased industry-academic collaborations are fostered.
- In newly launched products, there was been a sharp rise in the share of patents associated with new therapies citing academic research—further proof of the growing connections between academic research and new drug therapies reaching patients. Over the 2010–2014 period,

93% of novel chemical entity drugs and novel biologics associated with patent-protected intellectual property cited academic research. This is up significantly from the 2000–2004 period, when 64% of novel chemical entity drugs and 79% of novel biologics cited academic research in the 2000–2004 period.

However, despite this progress, the challenge of addressing the translational research gap between promising bioscience discoveries and the advancement of new biomedical innovations continues. Key challenges include:

- Pressures on industry to raise the effectiveness of R&D expenditures in light of an observed decline in R&D productivity (likely attributable to more complex diseases being addressed and increasingly more sophisticated scientific approaches being utilized).
- A constrained funding environment in the U.S. for bioscience research and development to fuel innovations. Constraints are fueled by both for the loss of industry revenues caused by expiring patents and the challenging federal funding environment for the NIH.
- Strong competition for the venture capital needed to foster new bioscience firm formation and growth. Competition principally stems from alternative opportunities in social media and other information technology fields that offer high returns in the near-term and often face less risk, as well as a shift in bioscience venture capital from early-stage bioscience companies to those that are ready to enter clinical trials.

As a result of this difficult environment for bioscience innovation, it is even more critical today that innovations in alternative models for industry-academic collaboration activities be found to catalyze and advance translational research. Emerging areas that need to be further supported include:

- In basic and applied, advancing collaborations at the research stage that hold promise in reaching a new level of scale beyond that which individual company sponsoring and jointly conducting research with an academic institution can achieve, such as:
  - Rise of multi-institutional and multi-company collaborations.
  - Rise of open innovation models that provide academic researchers broader access to research tools and even funding from industry in a more streamlined and open process.
- In technology development, advancing systematic, replicable approaches for creating value through leveraging scientific, clinical and business know-how versus a more ad hoc project-by-project approach. Emerging areas that need to be further supported include:
  - Advancing partnerships of clinicians with engineers and scientists
  - Fostering new venture development approaches.
- In clinical trials, advancing collaborations that offer opportunities for increased activities, especially in light of the complexity of clinical trials. Emerging areas that need to be further supported include:
  - Regional clinical trials consortia
  - CRO-CTSI Partnerships
  - Centralized patient repository.
- In product development, industry-academic collaborations for launching new products are benefiting from more applied research capacities that academic institutions are advancing, particularly in two areas:
  - Experimental therapeutics centers
  - Advanced biomanufacturing centers.

CONCLUSION

By continuing to develop innovative models for collaboration that reflect the unique nature of translational bioscience innovation, industry-academic relationships can continue to be accelerated to address the critical challenges facing the bioscience industry.

BIO in bridging the worlds of biotechnology industry and academic research can play a critical role in convening and disseminating emerging models.

In convening, BIO can scale-up the localized efforts on collaborations to have a larger footprint as well as possibly impacting how federal and state initiatives to advance biosciences development proceed. Among opportunity areas for convening would be:

- Working with patient advocacy groups to initiate larger scale multi-institutional and multi-company translational research collaborations.
- Advancing larger scale, multi-institutional patient registries.
- Promoting more engagement between contract research organizations and NIH-funded clinical and translational research institutes.

In dissemination of emerging models and resources available, there is much to be done:

- Better catalog the many available translational research activities taking place involving open innovation, applied academic research resource centers, and ongoing partnerships of industry, clinicians, engineers and scientists.
- Track the success and impact these industry-university translational research are having and focus on increased discussion of best practices and how to achieve increased scale.

APPENDIX A

Examples of Wide Range of Industry-Academic Partnerships with Multiple Partners

This Appendix illustrates many of the existing developments taking place in industry-academic collaboration activities to advance translational research. While not exhaustive, it is a beginning step to offer a sense of the range of efforts and their different approaches to emerging translational research partnership efforts that go beyond traditional one company to one academic institutional partnerships to involving multiple companies and/or multiple academic institutions to gain more scale and impact.

Potential Case Study	Translational Research Stage	Who Is Involved	Key Features of Approach
Asian Cohort Consortium	Basic research	US: Fred Hutchinson Cancer Research Center South Korea: Seoul National University of Medicine Investigators from China, India, Japan, Malaysia, Singapore and Taiwan, among others Not clear from web site the role of industry	• Multi-national effort to identify markers of early disease based on the relationship of genetics, environmental exposures and etiology of disease. • Track a large cohort of at least 1 million healthy people to various disease endpoints. • Make use of molecular testing as well as information on variety of factors shaping disease including environmental exposures. • First study on BMI and mortality in Asian populations.
AstraZeneca Open Innovation	Multi-stage		• AZ seeks to create drug discovery and development partnerships with academics through "co-create" projects and co-author publications. • AZ offers researchers with an innovative target idea access to new molecular profiling, clinical compound bank and pharmacology toolbox. • Among open partnerships mentioned on web site: Oncology ISS; NIH/NCATS; MRC (UK); NRPB (Taiwan); Oncology Toolbox; CRT/CRUK (UK); DNDi; European Lead Factory; Karolinska Institute (SWE); Lead Discovery Center (GER); MRCT (UK); and NEOMED (Canada).
Bayer's Grants4Targets	Technology development to validate targets in variety of diseases	Bayer Healthcare 59 grants funded out of 380 applications after 4th round of calls	• Focus on proof-of-concept. • Crowdsourcing approach. • IP remains with the participating institutions (not Bayer).
Biomedical Research Alliance of New York (BRANY)	Clinical development advancing an alliance of clinical research sites affiliated with academic medical centers and academic hospitals	Started in 1998 as an initiative with NY Academy of Medicine with NYU School of Medicine, Montefiore Medical Center, Mount Sinai School of Medicine, North Shore-LI Jewish Health System. Includes over 200 affiliates. Prime site for Quintiles	• Offers turnkey solutions for expedited site identification and study start up. • Collaborative IRB. • Advanced clinical trials tools.
Center for the Integration of Medicine and Innovative Technology (CIMIT)	Technology development consortium to address unmet clinical medicine needs for innovation	12 member institutions involving teaching hospitals and engineering schools in the Boston area Active industry liaison program—of both small and large companies who join as members of CIMIT—40+ members including: AstraZeneca; Boston Scientific; Covidien; Johnson & Johnson; Pfizer; Smith & Nephew	• Bring clinicians and engineering expertise together. • Focus on strategic opportunities areas (point of care, neurohealth, etc.). • Use of facilitative processes, including site minders. • Phased grant funding. • Pro-active industry engagement. • Since its founding, CIMT reports: 550+ projects; 500+ publications; 30+ patents issued; 10+ licenses; 15 companies formed.

APPENDIX A

Potential Case Study	Translational Research Stage	Who Is Involved	Key Features of Approach
GlaxoSmithKline Discovery Fast Track Challenge	Multi-stage	2014 award winners: • Sandford-Burnham Institute • JHU • Penn • UT Southwestern Medical Center • University of Iowa • University of Toronto	• Open process in which academics can propose drug discovery projects for funding. • Match together leading academics with GSK drug discovery expertise to form joint teams with open sharing of information. • GSK provides funding as pre-defined, pre-clinical and clinical milestones are reached with royalty payments for launching of a new medicine.
Harvard Laboratory for Drug Discovery in Neurodegeneration	Basic research effort to close gap from scientific discovery to drug discovery	Harvard Several sponsored research agreements with biotechnology/ pharmaceutical companies	• Leading university-based drug discovery institute. • Industry experienced staff. • Reports 40 drug discovery collaborations. • One new company launched. • One license executed of a drug discovery candidate and several options in place.
Indiana Biosciences Research Institute	Basic research effort where industry led consortium is directly investing in for a new biomedical research institute	Eli Lilly and Company Roche Diagnostics Dow AgroSciences Cook Medical Biomet IU and IU Health	• Public-private partnership. • Direct industry involvement in defining research focus. • Raised over $50 million, but just getting started.
Johnson & Johnson's Innovation Centers	Technology development involving full ecosystem efforts to help validate, develop and launch new companies and products	Four innovation centers: Boston, California, London and Shanghai. Plus network of incubators with primary one in San Diego	• Integrated model for advancing innovation: • Incubation facilities. • Entrepreneur Innovator Program (IP owned by entrepreneur). • Venture capital investment arm.
Lilly Clinical Open Innovation	Clinical development to make it easier for patients and those close to patients to find clinical trials that are right for them	Eli Lilly and Company Information technology companies for advancing APIs	• Integration of social media tools to engage patients: • Sponsored a Patient Engagement App Challenge. • Pilot project to improve interaction with patients on study websites.
Lilly Open Innovation Drug Discovery	Research		• Seeks to advance novel targets by allowing academic researchers to submit on a confidential basis their proprietary compounds for screening by Lilly using its proprietary, disease-relevant phenotypic and target-based assays as an in-kind contribution. • Uses a web-site to facilitate process of submission and sharing results. • Uses a single universal Material Transfer Agreement. • Lilly selects proposed targets for screening by using an automatic algorithm. • Once a compound generates promising results, academic investigators have the option to reveal the structure to Lilly and pursue licensing and co-development.
Merck's California Institute for Biomedical Research	Offers drug screening and animal models for new spin-off companies Technology development to validate targets in variety of diseases	Merck Partnerships with academic researchers across the world	• New dedicated institute in San Diego. • Merck reported to have committed $90 million.

APPENDIX A

Potential Case Study	Translational Research Stage	Who Is Involved	Key Features of Approach
Merck Initiatives for New Targets	Basic research effort to close gap from scientific discovery to drug discovery	Merck Multiple academic institutions	• Committed funding from Merck. • Access to Merck drug discovery tools. • Generating many of Merck's new drug leads.
NSF Industry/ University Cooperative Research Centers and Engineering Research Centers	Research	Current I/UCRCs and ERCs involved in biotechnology: Center for Pharmaceutical Development – Georgia Tech, University of Kentucky with 6 company members Center for Innovative Instrumentation Technology (nanotech sensor platforms) – University of Illinois at Urbana-Champaign with 13 partners including Abbott, Baxter, Elanco Animal Health, Dow Agrosciences, Monsanto ERC on Biomimetic Microelectronic Systems (BMES), a research center dedicated to the development of implantable microelectronic devices for the treatment of presently incurable ophthalmic and neurological diseases involving University of Southern California, Caltech and UC Santa Clara and nearly 20 industry partners	• Targeted to specific research areas. • Leverages NSF funding 10-15 times with industry support.
Pfizer's Center for Therapeutic Innovation	Basic research effort to close gap from scientific discovery to drug discovery	Pfizer More than 23 academic institutions across four regional sites	• Pfizer and academic teams work side-by-side to shortcut traditional linear process of target discovery. • Four locations across US: Boston, NY, San Diego and San Francisco. • Makes use of master agreements. • Provides access to Pfizer drug discovery tools.
Stanford Program in Biodesign	Technology development to advance innovations of new health technologies through interdisciplinary research and education	Stanford, drawing on faculty across university. Industry sponsors include Abbott, BD Medical, Boston Scientific, Edwards Life Sciences, Johnson & Johnson, St. Jude Medical, among others	• Multi-disciplinary with strong engagement of students. • Unique curriculum. • Industry mentors. • Growing globally with international programs. • 2014 annual report notes: 350,000 patients treated with technologies advanced; 37 companies formed; and $325m in capital raised.
Strategic Pharma-Academic Research Consortium for Translational Medicine, or SPARC	Research	Broad consortium of Midwestern universities, including Indiana CTSI (IU, Purdue and Notre Dame), Washington University, Ohio State University and Northwestern University. Eli Lilly and Co. and Takeda Pharmaceuticals International Inc	• Advancing research on autoimmune diseases. • Leverages and broadens the Indiana Clinical and Translational Sciences Institute.
Tuberculosis Drug Accelerator Consortium	Research to identify new lead compounds	Abbot, AstraZeneca, Bayer, Eli Lilly, GlaxoSmithKline, Merck and Sanofi Infectious Disease Research Institute, NIAID, Texas A&M and Weill Cornell Medical College Gates Foundation	• Pursuing goal of creating a TB drug regimen that cures patients in one month. Aims to develop 5 new preclinical drug candidates. Begun in 2012.

APPENDIX A

Potential Case Study	Translational Research Stage	Who Is Involved	Key Features of Approach
UC BRAID (Biomedical Research Acceleration, Integration, and Development)	Multi-stage	Five medical campuses of UC system: UC Davis, UC Irvine, UCLA, UC San Diego and UCSF. With funding support from UC Office of the President Limited information on industry partners in web site	• A resource for identifying clinical and translational needs and enabling partnerships across 5 medical campuses associated with UC System. • Among accomplishments noted: • Facilitating the linking of clinical trial networks across UC campuses. • Cross-campus searchable database of patient level study data from all UC medical centers that today provides researchers access to 13.6 million patient records.
University of Washington Research Affiliates Program on Transporters	Technology Development	UW School of Pharmacy AstraZeneca, Genentech and Merck	• Predict the fate of new drugs early in development and better predict the potential for drug-drug interactions and the influence of genetics.
Vanderbilt Center for Neuroscience Drug Discovery (VCNDD)	Basic research effort to close gap from scientific discovery to drug discovery	Vanderbilt Mention industry support from AstraZeneca, Bristol-Myers Squipp and Janssen Pharmaceuticals Many patient disease foundation supporters as well	• Leading university-based drug discovery institute. • Industry experienced staff. • Reports many publications and patents generated.
Wallace H. Coulter Centers for Translational Research	Technology development involving increasing clinical innovations by bringing clinicians and engineers together	15 university partners (9 in first round and 6 added): BU; CSWR; Drexel; Duke; Georgia Tech; Stanford; U of MI; UVA; U of WA; U of WI; Columbia; JHU; U of Louisville; Pitt; USC Many industry collaborators through advisory committees of each center	• Advanced a defined and replicable process for clinical innovation. • Now launching self-sustaining innovation centers. • Many successes via university partners.

APPENDIX B

Detailed Source Notes on Data Used

Basic & Applied Research

National Science Foundation's Higher Education R&D (HERD) Survey has collected data annually since 2010 on R&D expenditures at 891 institutions across the US reporting at least $150,000 in expenditures the previous fiscal year. This data identifies funding by broad research areas in addition to source of funds.

Thomson Reuter's Web of Science contains detailed information on academic journal articles published from 1998 to present including abstracts, relevant research fields and academic disciplines, and organizations involved in authoring articles. A set of research fields relevant to human biosciences was used to create extracts of all US research articles from 2000-2005 and from 2010-2015. Industry publications were then identified through text searching algorithms with fields identifying organizations involved in authoring articles, with further text searching algorithms identifying industry publications which also contained university authors.

Technology Development

The Thomson Reuters Innovation platform was used to extract data from US Patent and Trademark Office (USPTO) records from 2000-2005 and from 2010-2015 in areas related to human bioscience. Human bioscience patents were identified through Common Patent Classification (CPC) patent classes primarily related to bioscience fields with human (as opposed to animal or agricultural) applications, which categorize the intellectual property outlined in a patent record according to the anticipated market use. Patent records list the primary and all secondary assignees, or owners, of a patent. Text searching algorithms were used to identify all human bioscience patent records with industry assignees. Patents were then linked to academic journals through examination of non-patent document citation lists attached to each patent record that identify all relevant prior references that contribute to the establishment of new intellectual property.

Academic journal titles were identified in these lists through a text matching algorithm which probabilistically evaluated similarities to academic journals in the Science Citation Index, a listing of around 6,500 significant journals considered to be leading sources of science and technology research. Journal articles in the SCI which were cited by patents were further evaluated to confirm direct author connection to academic institutions.

Clinical Trials

Data on clinical trials is available from clinicaltrials.gov, a registry of clinical trials maintained by the U.S. National Institutes of Health, as required under Food and Drug Administration Modernization Act of 1997. As part of this database, ClinicalTrials.gov requires information on all sponsors and collaborators involved in each clinical trial.

New Product Launch

The US Food and Drug Administration's (FDA) Approved Drug Products with Therapeutic Equivalence Evaluations, known more commonly as the Orange Book, was used to identify patents explicitly linked to new drug products granted approval. The FDA publishes the relevant patents for new products covered by their approvals process with the exception of some products not covered by Title I of the FDA Modernization Act of 1997, typically due to legacy reasons. US patent numbers for all drug products in the Orange Book from 2000-2005 and 2010-2015 were used to extract patent records from Thomson Innovation for the relevant drug products, which in turn were analyzed using the same methods as those described under Technology Development.

The FDA's Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations, more commonly known as the Purple Book, give information on

approval dates, trade names, and owners for biologics products. Explicit linking of patents to biologics is not performed by FDA, primarily due to the fact that biologics are typically covered by groups patents related to the manufacture and synthesis of these products in addition to their formulation. Targeted patent searches in Thomson Innovation were used to identify the patent "sets" relevant to each Purple Book product using the owner company listed in the database in addition to research from other sources of information on biologics patents such as annual company financial disclosures of relevant intellectual property for flagship products. The patents associated with each biologic product approved by the FDA from 2000-2005 and from 2010-2015 were then analyzed using the same methods as those described under Technology Development.