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PATENTS, PASTEUR, AND PRODUCTIVITY

A Model for Promoting Scientific and Economic Growth at the National Institutes of Health

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Executive Summary

The primary goal of scientific research supported by the National Institutes of Health (NIH) is to advance knowledge that will ultimately improve human health. However, some of the research funded by the institutes and centers of the NIH also creates economically valuable technologies and inventions, often reflected in patents.

This study evaluates patents obtained as the result of NIH-sponsored research grants and contract spending, comparing the number and quality generated by the NIH's various institutes. Inventions and associated scientific publications are important inputs for the American biotech and pharmaceutical sectors, where new knowledge and technologies, embodied in patentable new ideas, are uniquely linked to the creation of new commercial ventures and growth in these important sectors of the U.S. economy.

Our research showed a wide variation in the invention output of NIH-funded research, as reflected in patents generated per dollar of federal funding invested. Congress has occasionally shifted resources in response to compelling or urgent scientific priorities, such as Alzheimer's disease, Ebola outbreaks, or personalized-medicine initiatives. But the NIH's strongest areas of patent production have experienced some of the slowest growth since 2000.

We believe that this creates an untapped opportunity for policymakers to leverage NIH's highly valuable patent portfolio, and we recommend that policymakers act to reverse this paradigm through a sustainable, growth-oriented approach to the NIH. Specifically, while scientific opportunities should remain paramount, the evidence suggests that significant gains in economic output could be realized through targeted investment in programs that have demonstrated historically strong records of technological innovation and invention. Doing so will not only result in new tools and technologies that help move science and discoveries forward; it will also help meet the urgent calls for programs that can spur productivity and growth at the national level.

Because the prime motivation for federally funded biomedical research is to reduce the burden of disease and to improve human health, calls to take into account other aspects of return on investment—such as patent productivity and downstream commercial activity—may be regarded as off-mission. Yet a closer look at NIH's patent portfolio suggests that these goals and attributes are often shared. We find that some of the highest-impact science, as indicated by 33 of the most recent NIH-funded Nobel Prize winners, has been highly productive in the area of patentable inventions. We also explore the idea that research programs marked by high patent productivity often combine strategies of basic and applied research to address a well-defined, use-inspired need.

It is clear that broad reductions to the NIH budget will also reduce patent output—and thus, reduce the innovation capacity of the biotech sector. Alternatively, our findings suggest that sustainable and targeted allocations to the NIH can provide a substantial boost to the U.S. economy while enhancing the ability to generate advances that reduce the burden of disease and improve health, the goal at the heart of the NIH mission.

PATENTS, PASTEUR, AND PRODUCTIVITY

A Model for Promoting Scientific and Economic Growth at the National Institutes of Health

Introduction

Behind the stubborn slowdown in U.S. GDP growth lies the story of innovation and productivity. U.S. firms, particularly in innovation-facing sectors, have encountered challenges in attempting to steadily boost productivity—creating strong headwinds for economic growth. Citing this trend in her most recent Semiannual Monetary Report to the Congress, Federal Reserve chair Janet Yellen expressed an urgent mandate to policymakers: in lieu of tax cuts or stimulus programs, seek out sustainable policies that are best capable of stimulating long-term productivity.[1]

To this end, many other countries are attempting to harness the causal connection between innovation, technology, and productivity. Specifically, many nations are strategically directing resources within their public R&D programs to areas that are more likely to produce the patents, technologies, and innovations that fuel economic growth.

In the U.S., there has traditionally been less emphasis on steering science in such a fashion. While the overall NIH budget has increased over time, funding allocations to the agency's 27 institutes and centers (ICs) have remained largely unchanged over the last 25 years.[2] Perhaps signaling a new approach on the horizon, the NIH has been developing evidence-based metrics to help evaluate the differences in *scientific* impact and quality across some of its programs.[3] But while the agency tracks data on outcomes directly related to firm creation and *economic* impact (e.g., patents), the historical propensity of programs to contribute to productive capacity in the commercial life-sciences sector has not been featured as a prominent criterion for identifying and scaling programs.

From an economic perspective, this may present an untapped and powerful approach to NIH, given the calls to spur productivity. Because innovative new tools, technologies, and processes are key drivers of long-term productivity—in terms of accelerating exciting new areas of scientific discovery and for new firm creation beyond the period of public-sector support—prioritizing the agency's strong producers of these outputs within a multiyear approach to NIH support could help meet an urgent national need.

Patent-Based Outcome Metrics, the NIH, and the Life Sciences

While most NIH-funded research is focused on basic life science, diagnosing and treating disease, and advancing health, many programs do so in a way that also creates new, economically valuable technologies. These inventions are often formally recognized by the granting of patents.

Patents are natural products of genuine innovation and represent a verifiable signal from the U.S. Patent and Trademark Office (USPTO) that the advances meet established legal criteria for innovation, significance, and usefulness.

There is considerable evidence that invention and patent production are important contributors to economic growth. As summed up by a Brookings Institution study: "Inventions, embodied in patents, are a major driver of long-term regional economic performance, especially if the patents are of higher quality. In recent decades, patenting is associated with higher productivity growth, lower unemployment rates, and the creation of more publicly-traded companies."[4]

This strong link between patents and economic growth makes assessing patent output from federal R&D programs a potentially attractive and relevant productivity measure. However, while measuring total patent output per program may be important, it does not tell the whole story. Patents can vary greatly in their ultimate impact. A method frequently used to assess patent quality or impact is to count "forward citations": the number of later patents that cite that earlier patent as relevant to a new invention.

From a science- and technology-policy perspective, forward citation statistics may illuminate federal R&D programs that contribute to economic activity well beyond the end of the grant or contract—a primary goal for innovation policy. Therefore, given the rich and objective bibliographical data contained in USPTO records, patent frequency and citation rates seem to be attractive metrics to help identify areas of federal R&D investment likely to contribute to downstream economic activity long past the initial taxpayer investment.

Applicability to the Biotech and Life-Science Sector

Patents are often a critical prerequisite for life-science companies focusing on moving discoveries from the laboratory to the benefit of patients.[5] R&D costs leading to major discoveries and important technologies are extremely high, while the costs of imitation and reverse engineering are low. The patent system addresses this situation by providing a period of protection for companies that invest in innovation against such imitation. The essential nature of patents in translating inventions into useful products was summed up by MIT economist Pierre Azoulay: "It's hard to think of an innovation [in biomedicine] that doesn't have a patent."[6]

From a policy perspective, it is important to remember that the "primary" product of NIH research—new

NIH Institutes and Centers

- (NCI) National Cancer Institute
- (NEI) National Eye Institute
- (NHLBI) National Heart, Lung, and Blood Institute
- (NHGRI) National Human Genome Research Institute
- (NIA) National Institute on Aging
- (NIAAA) National Institute on Alcohol Abuse and Alcoholism
- (NIAID) National Institute of Allergy and Infectious Diseases
- (NIAMS) National Institute of Arthritis and Musculoskeletal and Skin Diseases
- (NIBIB) National Institute of Biomedical Imaging and Bioengineering
- (NICHD) Eunice Kennedy Shriver National Institute of Child Health and Human Development
- (NIDCD) National Institute on Deafness and Other Communication Disorders
- (NIDCR) National Institute of Dental and Craniofacial Research
- (NIDDK) National Institute of Diabetes and Digestive and Kidney Diseases
- (NIDA) National Institute on Drug Abuse
- (NIEHS) National Institute of Environmental Health Sciences
- (NIGMS) National Institute of General Medical Sciences
- (NIMH) National Institute of Mental Health
- (NIMHD) National Institute on Minority Health and Health Disparities
- (NINDS) National Institute of Neurological Disorders and Stroke
- (NINR) National Institute of Nursing Research
- (NLM) National Library of Medicine
- (CIT) Center for Information Technology
- (CC) Clinical Center
- (CSR) Center for Scientific Review
- (FIC) Fogarty International Center
- (NCATS) National Center for Advancing Translational Sciences
- (NCCIH) National Center for Complementary and Integrative Health

Source: National Institutes of Health, "NIH Institutes, Centers, and Offices," Feb. 8, 2017 knowledge through scientific publications—can also lead to commercial innovation. A recent study found that scientific publications stemming from NIH-sponsored research are often cited by patents for inventions developed by the commercial biomedical sector.[7] In a knowledge-based economy, this remains a critical factor for ensuring broad support for NIH as a whole.

Given the synergy of research investment, inventions, and economic growth in the biotech and pharmaceutical sectors, it would seem appropriate to take into account invention production as a measure of productivity when considering science and technology investments at the federal level. As a key output that furthers the core mission of NIH to improve human health, federally funded patents are not some "less pure" derivative of public science. There is good historical evidence that, in biomedical research, high-quality science and invention productivity are often linked.

When assessing a potential new discovery for patentability, university technology transfer officers recognize that "[h]igh impact basic science serves as an entry ticket to the patenting arena for universities."[8] The growing recognition that patents can be a marker for high-quality science has led to recommendations that innovation-based measures be embedded into faculty performance reviews at U.S. academic institutions. For instance, a number of university presidents and senior officers have urged that "universities should expand their criteria to treat patents, licensing, and commercialization activity by faculty as an important consideration for merit, tenure, and career advancement, along with publishing, teaching, and service."[9]

Inventions and Patents Resulting from NIH-Funded Research

To uncover highly productive programs at NIH (in terms of patent output), we gathered publicly available summary project and patent data from primary sources, including the NIH RePORTER (Research Portfolio Online Reporting Tools for Expenditures and Results) database, the USPTO, and AcclaimIP, a subscription-based global patent database.

To match IC patents with actual grant dollars, we implemented a three-year lag in deflated budget dollars (2000–2009). This lag is consistent with previously published work to account for patent filing and approval.[10]

To assess differences in quality of patentable new inventions, we also looked at the average number of forward citations, per patents issued to ICs, from 2006 to 2008. This practice of looking at a relatively narrow "vintage," or window, of patents within a larger portfolio helps control for the fact that patent citations gather over time.[11] For example, a portfolio with a large number of older patents (e.g., from 2003 and 2004) will likely have more citations, given the long period to accumulate them. Likewise, programs that are increasing in their overall innovation output will have more recent patents, which will not have had adequate time to build up citations and will appear to perform poorly from a citation perspective. Although there are limitations with this methodology, it is a widely accepted practice for measuring the economic value, or technological and economic significance, of a portfolio of patents.

After a bulk download of NIH RePORTER grant and patent data, we removed duplicate reported patents from our data set and sorted by core IC. For the patent period 2003–12, this resulted in a total universe of 8,476 unique and direct patents across the 21 primary grant-making NIH ICs. The mean number of patents per IC was 403.6, with a median of 177.0. The National Cancer Institute (NCI) reported the highest number of patents (1,853) over the 10-year period.

NIH institutes vary greatly in their annual budget authority. In the budget window analyzed (2000–2009), NCI research helped spur its 1,853 unique patents on a budget of just over $37.4 billion. This was more than 2.5 times higher than the average IC budget—of slightly more than $10 billion—for this period. To control for differences in budget authority, we calculated patent volume per $100 million in grant and contract funding (**Figure 1**). For comparison purposes, we compiled similar data for several other individually appropriated federal R&D programs, including the Defense Advanced Research Projects Agency (DARPA), National Science Foundation (NSF), the National Aeronautics and Space Administration (NASA), and the Department of Energy (DOE).

To identify patents associated with these programs, we used the AcclaimIP database to retrieve patents that state a connection to a federal research program in their "government interest" statements in USPTO bibliographical data. This resulted in a universe of 20,135 unique patents that are a direct result of federal R&D.

The aggregate results (**Figure 2**) for the budget period, 2000–2012 (and patent output during 2003–15), indicate that NIH-sponsored research led to 5.5 patents per $100 million in grant and contract spending, or approximately $18.1 million per patent.

FIGURE 1.

Patent Productivity, 2003–12

Agency/IC	Patents/$100M (real dollars)	Citations (2006–08)	Combined direct and indirect patents/$100M (real dollars)
NIBIB	17.76	23.7	420.88
NHGRI	3.83	52.6	201.31
NIGMS	8.38	14.6	122.35
NIAMS	4.94	20.8	102.77
NCI	5.53	13.3	73.57
NIDCD	3.81	18.3	69.70
NIDCR	5.64	10.9	61.46
NIDDK	4.16	14.1	58.64
NINDS	3.97	14.6	57.98
NEI	3.81	13.3	50.69
NHLBI	4.18	11.7	48.88
NIAID	4.14	10.8	44.76
NIEHS	2.00	12.9	25.80
NIA	2.63	9.8	25.76
NICHD	1.79	8.8	15.72
NIMH	1.19	13.1	15.62
NIDA	2.25	6.1	13.70
NCCIH	0.93	3.3	3.07
NIMHD	0.59	2.0	1.19
NIAAA	0.49	1.2	0.59
NINR	0.18	0	-
NIH Average	5.50	13.9	76.45
DARPA (Defense Advanced Research Projects Agency)	9.30	26.8	249.24
NSF (National Science Foundation)	8.05	22.3	179.52
NASA (National Aeronautics and Space Administration)	1.24	33.5	41.54
DOE (Department of Energy)	14.45	20.4	294.78

Source: Authors' analysis

This cost per patent is lower than the reported average R&D cost per patent for private-sector pharmaceuticals and medicines, as reported by the National Science Foundation, which found a worldwide average of $20.5 million in R&D expense per patent in 2008.[13] But it is more than the $9.2 million per patent reported for the U.S. biopharmaceutical sector.[14] It is also higher than the $3.2 million per patent in the medical-instrument and technology sector.[15] Direct comparisons with the private sector must also take into account the unique public role of NIH in supporting an array of activities that would not be expected to yield patents but are nevertheless critical to the long-term pipeline of American science—such as training young scientists.

In terms of overall patent quality, we also found that the weighted mean for "Citations per Patent" (x-axis in Figure 2) was 13.9. This degree of quality (as measured by citations) is higher than found in other studies and indicates a significant degree of downstream R&D interest in NIH's patent discoveries.[16] We also compiled results using the proprietary scoring algorithm provided in the AcclaimIP database, the "P-score," to compare the NIH patent portfolio against the entire universe of USPTO patents. According to AcclaimIP, "patents that rank high on the P-score scale tend to be better patents, with a higher likelihood of being infringed, being used in a company's products, or having current or future monetization potential."

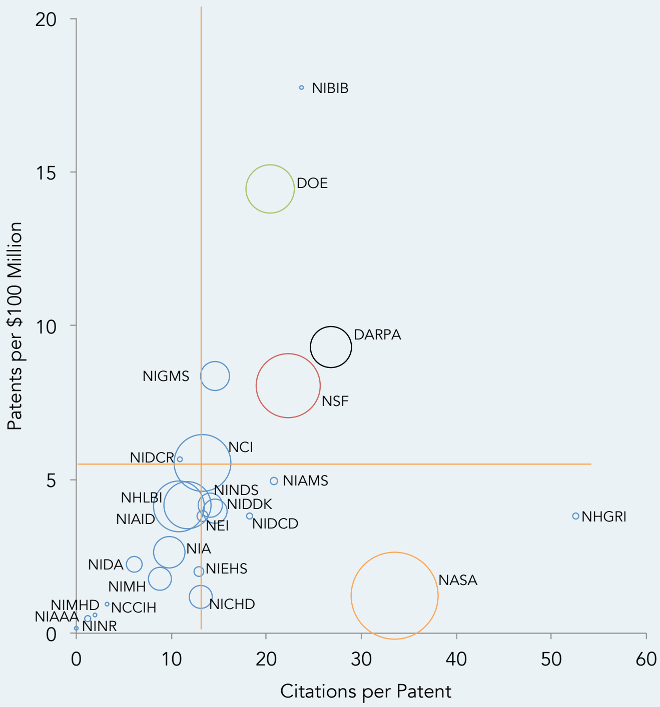
Altogether, the aggregate NIH portfolio scored 70.4 on a normalized scale of 0–100, meaning that NIH patents engender 20.4% more economic value than the general population of USPTO patents.[17] In terms of the highest-quality programs at NIH, NHGRI's P-score of 86.9 and NIBIB's P-score of 79.5 rated very high: their entire patent portfolio during 2006–08 represented some of the most fundamental pieces of new knowledge produced anywhere during that period. This finding supports the conclusion that the overall invention portfolio stemming from NIH-funded research is a significant, and economically valuable public good, particularly in an innovation-based economy.

To assess the downstream economic impact, we use a common variable for the average cost of a downstream patent—which, as noted above, has been estimated to be $9.2 million in the U.S. pharmaceutical sector. This calculation indicates that every $100 million invested in NIH-funded research is associated with an impressive $598 million in additional downstream R&D in the U.S. biotechnology and pharmaceutical sectors (5.5 patents per $100 million x [13.9 forward citations x $9.2 million per downstream patent] x 0.85).[18]

Our analysis shows that a number of programs at NIH have particularly strong return on investment, as reflected in invention volume and quality metrics. The NIBIB and the NHGRI stand out. Both programs performed at least three standard deviations above their metric of note. NIBIB-funded research produced 17.8 patents per $100 million, while the NHGRI patent portfolio was distinguished by an astonishing 52.6

FIGURE 2.

Patent Output per Program*



*Circle size corresponds to total current annual budget authority.[12]
Source: Authors' analysis

forward citations per patent.[19] Based on the methodology described above, each $100 million invested in NHGRI-funded research yields an estimated downstream R&D investment of nearly $1.6 billion. A similar calculation for NIBIB-funded research indicates that each $100 million in investment results in an enormous $3.3 billion in downstream R&D investment, making it by far the most productive appropriated federal R&D program that we analyzed. Despite this outsize productivity, these two programs[20] are among the smallest at NIH, as measured by annual budget authority—accounting for just 2.7% of the annual NIH budget.

The National Institute of General Medical Sciences (NIGMS)—recognized as the home for fundamental basic science at NIH—also stands out for its high invention output. At 8.4 patents per $100 million in grant and contract funding, it is nearly one standard deviation above the NIH mean. Combined with its above-average rate of 14.6 forward citations per patent, NIGMS is associated with $956.8 million in subsequent R&D activity, nearly twice the aggregated NIH average.[21] At the other end of the spectrum, 15 of the 21 NIH primary grant-making ICs fall below the mean for total patent productivity, accounting for over 81% of the total NIH budget.[22] In some ways, the NIH's overall patent productivity appears to mirror current trends at the global level, where total R&D productivity is being concentrated in the hands of a few highly productive firms.[23]

Pasteur's Quadrant

The past 70 years have marked a golden age in American science. A cornerstone for this progress was laid at the conclusion of World War II, when President Franklin Roosevelt asked science advisor Vannevar Bush to outline a plan for the future of American science.[24]

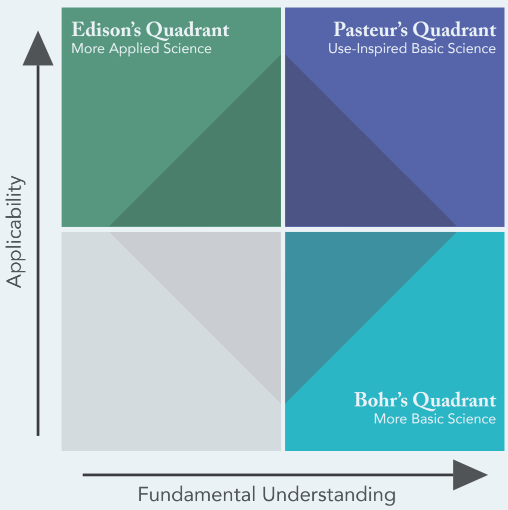
A key concept at the heart of Bush's influential 1945 report to the president, *Science, the Endless Frontier,* was the idea that research could be characterized along a spectrum of basic to applied science. Basic research seeks to explore and understand nature for the primary purpose of advancing knowledge. At the other end of the spectrum is applied science, which uses the knowledge generated by basic research to create practical applications. Bush emphasized a linear model of scientific progress, starting with the freedom and creativity of basic science, followed by the methods of applied science, followed by, in some cases, the introduction of new technologies and products.

While this perspective has dominated U.S. federal science policy since World War II, other views have been proposed. In *Pasteur's Quadrant: Basic Science and Technological Innovation,*[25] political scientist Donald Stokes of Princeton University challenged the linear model of scientific progress, pointing to many historical examples when applied science and the introduction of new technologies preceded—and, crucially, enabled—new basic-science discoveries. Indeed, from advanced medical-imaging techniques to labs-on-a-chip, the technological advancements of the past 20 years have had a profound influence on the direction of NIH science itself, challenging the idea that technological development cannot and should not influence the direction of purely basic science—a powerful paradigm shift recognized by the late Steve Jobs: "[T]he biggest innovations of the 21st century will be at the intersection of biology and technology."[26]

Overall, Stokes argued for a "use-inspired" approach to research that, from the very beginning, integrates the power of interdisciplinary basic and applied science. He proposed a model for classifying scientific research according to a two-by-two grid (**Figure 3**). On one axis, he ranked research on the extent to which it is focused on advancing human knowledge. On the other axis, he characterized the extent to which the research was directed at solving

FIGURE 3.

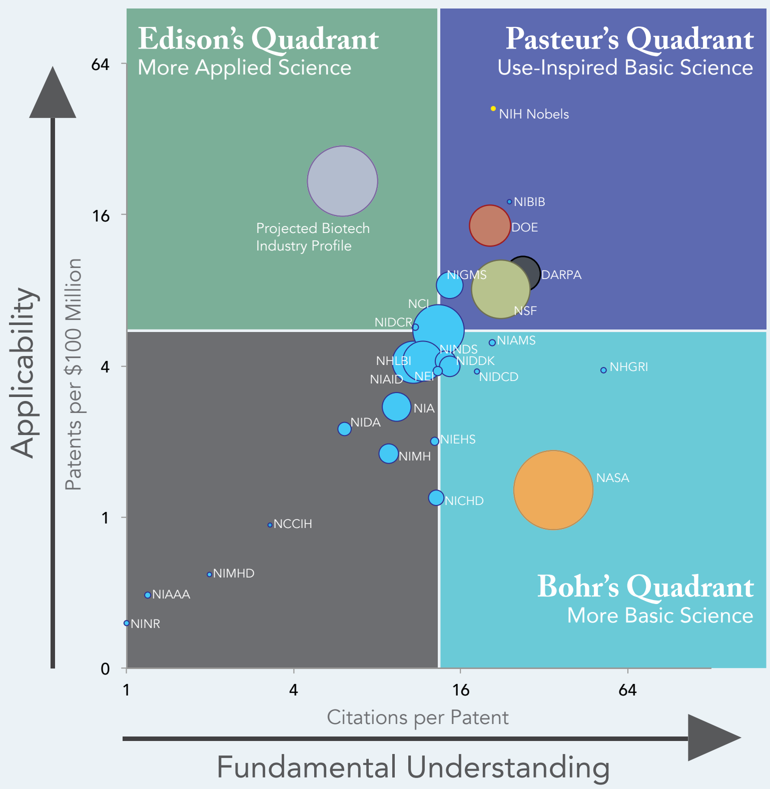
Pasteur's Quadrant



Source: Adapted from Donald Stokes, *Pasteur's Quadrant* (Washington, DC: Brookings Institution, 1997)

FIGURE 4.

NIH Patents and Pasteur's Quadrant[30]



Source: Authors' calculations, based on Figure 3

a practical problem. Stokes designated the quadrant of the figure corresponding to traditional basic research as "Bohr's Quadrant" because "there were no immediate considerations of use in mind as Niels Bohr groped toward an adequate model of the structure of the atom; although note that when he found it, his ideas remade the world."[27] Stokes designated the opposite quadrant, corresponding to applied science, as "Edison's Quadrant" because Thomas Edison "never allowed himself five minutes to consider the underlying significance of what they were discovering in their headlong rush toward [commercialization]."[28]

Stokes then called attention to the top right quadrant, where researchers motivated by specific problems harness the strategies of basic and applied research in pursuit of discovery and new knowledge. Stokes called this "Pasteur's Quadrant" because Louis Pasteur's research always had a clear use in mind (vaccines for public health); yet his fundamental contributions to the understanding of microbiology represented the birth of an entirely new scientific discipline. Indeed, the hallmark of Pasteur's Quadrant is its pursuit of topics where mission-oriented goals are not seen as repressing the imagination and creativity that are required for discovery.

The concept and reality of use-inspired research has been viewed as significant for science and technology policy at the federal level. For example, a 2013 article by Dugan and Gabriel in *Harvard Business Review* examined the innovation record of DARPA, an agency in the U.S. Department of Defense responsible for advanced R&D. The authors argued that "a central reason DARPA has been so successful over time is its unwavering commitment to work in Pasteur's Quadrant," resulting in what is arguably "the longest-standing, most consistent track record of radical invention in history."[29]

To evaluate this paradigm from a data-driven perspective, **Figure 4** represents a "thought experiment" in applying Stokes's model to the NIH patent metric data. According to U.S. patent law, a key prerequisite for patent validity is *usefulness*. Hence, the vertical axis (patent volume) might be considered as corresponding to the *applicability* axis of Stokes's diagram. Patents that are highly significant—the kinds of discoveries that can serve as the foundation for transformative new fields—tend to be highly cited. Therefore, the horizontal axis in Figure 4 may share similarities with the *fundamental understanding* axis of Stokes's figure.

This figure shows a strong and positive relationship between patent frequency and patent quality for most portfolios, suggesting that there is no strong trade-off between quality and quantity in these programs when increasing the frequency of their inventions. Programs that do depart from this pattern trend toward Bohr's Quadrant, as might be expected, given that federally supported R&D should support the type of risky basic science that the private sector likely would not be able to support.

Alternatively, we find no federal R&D programs operating solely in Edison's Quadrant. Instead, this tends to be the domain of industry-sponsored R&D.

As an exercise to further explore and validate the significance of the relationships illustrated in this figure, we compiled patent metric data for NIH-supported Nobel Prize winners in chemistry or medicine/physiology from 1990 to 2010. This portfolio comprised 33 teams responsible for some of the best science that NIH has ever produced (and a testament to the role of NIH in transforming medicine).[31]

In addition to groundbreaking research, more than three-quarters of these teams yielded patented inventions. The overall volume of patents in this portfolio was extraordinarily high: 46.2 patents per $100 million of NIH investment. The invention quality metric was also high: an average of 21 forward citations. These results place the Nobel portfolio squarely within Pasteur's Quadrant, illustrating that some of the most transformative discoveries in biomedicine are also characterized by a high return on investment, with respect to inventions. Clearly, such research—and high correlation with patent activity—in this quadrant is aligned with, and does not compromise, the core mission of the NIH.

Overall, these findings align with a recent analysis that found virtually no difference in the rate of patenting between "basic" and "applied" research at NIH.[32] In fact, using patent-based outcomes measures to empirically evaluate Stokes's paradigm appears to affirm that the basic compact between science and government is operating as designed. Invention from federal science funding bends slightly toward the creation of new-to-the-world knowledge (basic science), while industry-sponsored research decidedly favors more applicable solutions. Interestingly, these metrics also reveal areas of science that achieve both missions simultaneously, producing the sort of game-changing innovation and radical new technologies that can have a truly transformative impact on medicine and human health.

Increasing Patent Output Would Increase GDP Significantly

Several studies have assessed factors that contribute to GDP growth in advanced economies, such as the number of universities, education levels, and rate of scientific publications. These studies have shown that the rate of patent creation is strongly associated with the growth rate of the national economy. A 1% increase in a nation's domestic patent stock has generally been associated with a 0.22% growth in productivity and, on average, a 0.18% increase in a nation's rate of growth in GDP.[33]

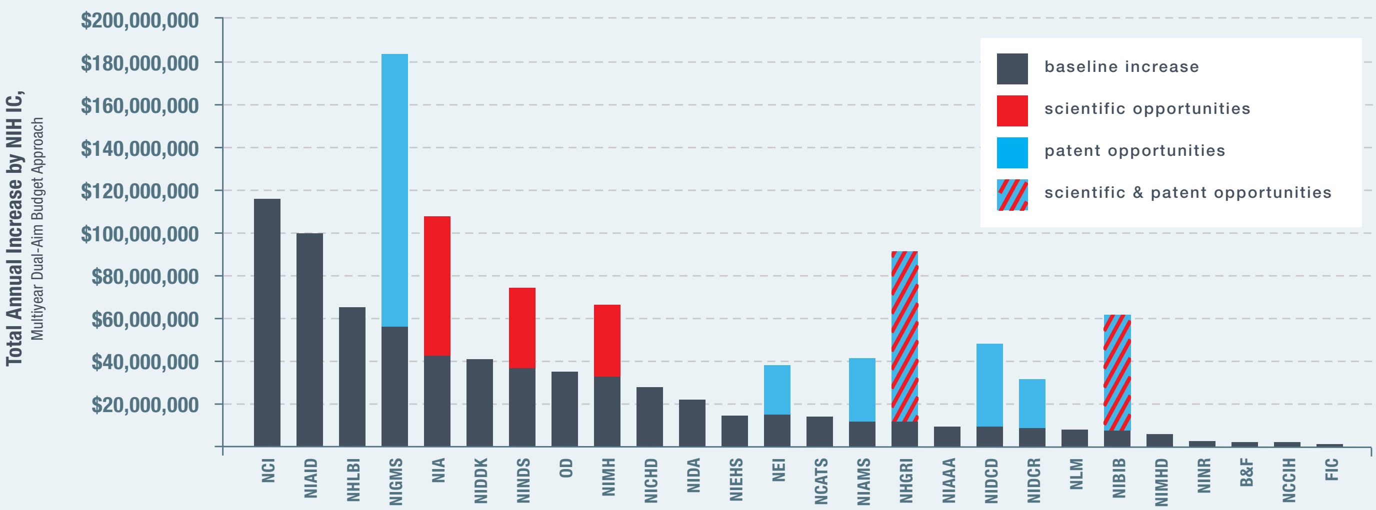
Based on USPTO data, the growth rate in U.S. domestic patents since 2000 has been 3.8% per year, with the total number of U.S. utility[34] patent grants reaching 140,000 in 2016. This suggests that to increase the U.S. domestic patent rate by 1% per year, on average—and to attain the resultant 0.18% increase in annual GDP—one strategy would be to embrace policies that could help foster approximately 1,400 more domestic utility patents annually over the current pace.

Our research suggests that policymakers could stimulate this level of additional patent creation by modest, but steady, investment in the NIH. At the current pace, we estimate that NIH R&D is already associated with approximately 3,500 direct and downstream (indirect) patents per year. To grow total U.S. domestic patent production by 1% (+1,400 patents per year) and capture an additional 0.18% of GDP growth, NIH would have to increase its patent output by 40%.

This may seem like a high bar. Yet this result may not only be attainable; it may be affordable, too—by embracing growth-oriented models that pair traditional, compelling, scientific priorities with modest, targeted investments made within portfolios with the highest historical performance in invention productivity. In one possible model (**Figure 5**), programs with strong patent productivity (such as NIBIB, NHGRI, NIGMS, NIAMS, and NIDCD) would see a 7%–15% budget increase per year, depending on total innovation capacity and budget size (i.e., smaller programs would be scaled closer to 15%, while NIGMS would be scaled closer to 7%, given its relatively larger existing budget authority). In this model, other NIH programs are incremented at 2% from the baseline, for five years, to maintain their current level of patent production.

FIGURE 5.

NIH Budget Model with Targeted Increases for Scientific and Economic Opportunities



Source: Authors' calculations. OD is the Office of the Director, and B&F is Buildings and Facilities.

This budget model would cost roughly $6 billion over a five-year period (a modest 3.4% per year overall increase to the NIH baseline budget). However, the model predicts that it would add approximately 2,060 (+58.8%) new direct and indirect patents per year over the subsequent 10-year period—a greater than 1% increase to the U.S. domestic utility patent base. According to published literature cited in endnote 33, in advanced economies, such a level of increased domestic patent production would be correlated with 0.24% growth in annual GDP. Keeping in mind the cumulative impact of increasing GDP, a 0.24% increase in economic growth is further associated with 230,000 more high-quality jobs and over $800 billion in deficit reduction over a 10-year period.[35] Importantly, since this level of economic activity would be built in to the NIH base moving forward, this would be a sustainable path to higher productivity and economic growth, not simply a one-time stimulative bump.

As such, Figure 5 is an example of a dual-purpose budget, outlining year one of a five-year approach. In this model, all ICs received a baseline 2% inflationary increase (black bars) to maintain their current rate of scientific and patent production. Examples of potential scientific opportunities (red bars) are scaled further, while patent opportunities are also scaled (blue bars) above the baseline increase. Thus, as the lead on combating Alzheimer's disease, the NIA (National Institute on Aging) would be allocated a budget authority of $2.1 billion—or $64 million above the 2% baseline increase. The NHGRI (National Human Genome Research Institute) would receive $608 million, $79 million above the 2% baseline, to fuel more patentable innovation in the genomics arena. Another strong patent producer, the National Institute for General Medical Sciences (NIGMS), would receive a budget of $2.8 billion—a $64 million (4.5%) increase over the baseline adjustment.

Some ICs are candidates for both scientific and economic adjustments (blue bars with red stripes): NHGRI (Precision Medicine Initiative) and NIBIB (BRAIN Initiative). Note that despite the potential impact on economic growth, the majority of the economic adjustments are relatively modest, as the baseline inflationary adjustments to many ICs are still larger than the targeted adjustments for economic opportunities.

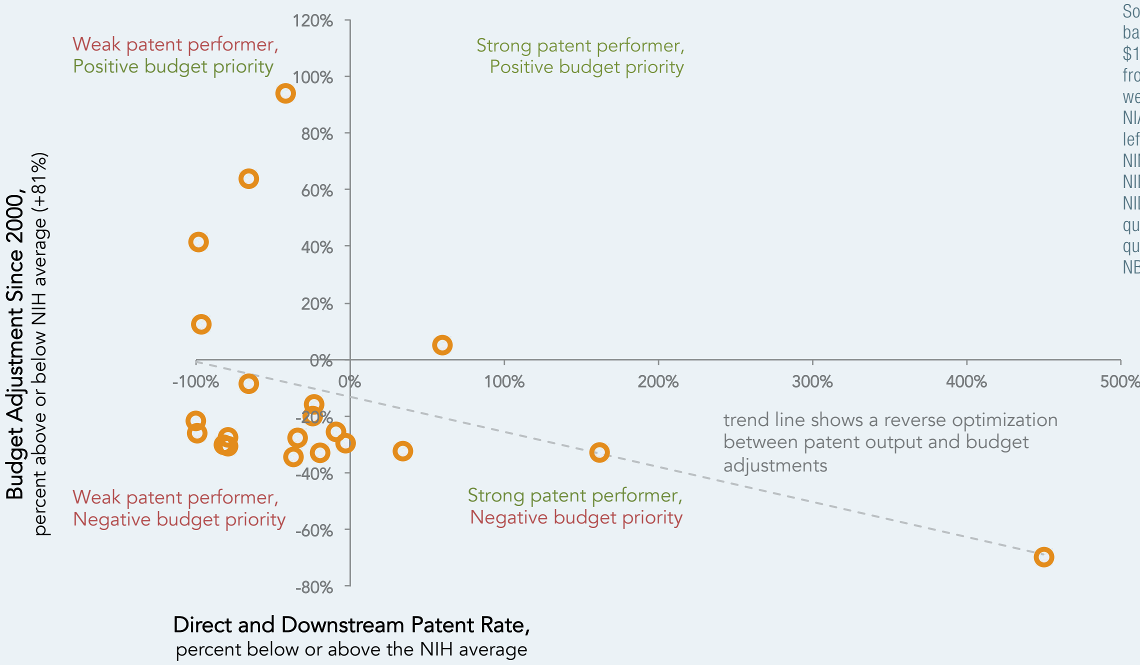
Recommendations

Policy recommendations regarding patent-based output metrics should be viewed appropriately within their context and goals. First and foremost, NIH does not primarily exist to spur commercial innovation. Indeed, the vast majority of products from NIH research—new scientific knowledge, theories, diagnoses, methods, and techniques—will not result in patentable innovations.

The main "products" from NIH-supported science are ultimately better human health and longer life spans, a public benefit that has had an immeasurable

FIGURE 6.

2000–2016 Budget Increases vs. Patent Rate, Normalized



Source: Authors' calculations, based on Figure 2 (patents per $100 million) and budget data from the NIH Office of Budget website. Top left quadrant: NIAID, NIA, NIMHD, and NCCIH; lower left quadrant: NIEHS, NIDDK, NINDS, NINR, NIDCD, NIAAA, NIMH, NEI, NCI, NIDA, NICHD, NIDCR, and NHLBI; top right quadrant: NIGMS; lower right quadrant: NIAMS, NHGRI, and NBIB.

return on investment. Therefore, patent-based output metrics should not be viewed as the primary measure of research performance. Nevertheless, it is hard to justify, in light of calls for increased economic growth, not paying greater attention to these important metrics at one of the federal government's premier science institutions.

There are a number of important tech transfer strategies that others have identified to facilitate the translation of technologies to the marketplace (tax policy, the NSF I-Corps™ Program, etc.). These are highly meritorious programs and proposals. However, at the start of the pipeline—at the point of resource allocation at the grant-making stage—we must appreciate that private-sector R&D and commercial development result from NIH-funded research, and it can be strategically beneficial for government officials to understand which programmatic areas of research have the highest propensity to generate economically significant inventions.

Compelling scientific opportunities should remain paramount in setting NIH allocations. Still, we suggest that policymakers seek to add a secondary budget strategy that prioritizes resources to programs that demonstrate a high level of R&D productivity, as measured by patent-based outcome metrics.

To illustrate why a more systematic assessment of patent output is critical from a national science- and technology-policy perspective, consider the changes in patent productivity vis-à-vis the budget for NIH-funded programs since 2000, in the absence of consideration for such metrics (**Figure 6**).

In general, we find that the relative investment in some of the portfolios with the strongest invention metrics decreased linearly during 2000–2016. For example, in the lower right is NIBIB (National Institute of Biomedical Imaging and Bioengineering), which has generated inventions at a rate approximately 450% greater than the NIH average. Yet in budget adjustments over the years, NIBIB received about 70% less than the average across the NIH ICs (+81% overall since 2000). A similar trend is seen for many of NIH's strongest patent producers. This result implies that modest changes to the NIH budget over time may have resulted in a lower than natural rate of patent productivity—an area that may yet be exploited for future growth.

Fortunately, for budget purposes, most of NIH's most prolific patent producers—NIBIB, NHGRI, and NIGMS, as well as others, such as NIAMS, NIDCD, and NIDCR—are among the NIH's smallest by budget authority. This means that very modest adjustments in allocation can have a substantial impact in patent productivity, particularly in a budget process where sustainable investments in the NIH are paired with marginal, but targeted, increases in the agency's most inventive programs.

Conclusion

NIH-sponsored research produces lifesaving discoveries, making it one of America's most valuable federal investments. In addition to furthering its core mission, NIH-funded research produces inventions and patents that are crucial prerequisites for making these lifesaving advances available to patients and that provide a strong benefit to the U.S. economy. Many important metrics can be used to assess the return on investment for NIH-funded research. Traditional criteria, such as peer-reviewed scientific publications and outcome measures (e.g., disease-specific morbidity and mortality statistics), will always provide primary guidance in this regard.

Given the translational and economic significance of inventions, it is appropriate to consider patent metrics when allocating budget resources. The evidence reviewed here suggests that there is a substantial opportunity to significantly boost invention production and downstream benefit to the American economy from NIH-funded research—through modest, targeted investments in areas with the highest productivity.

Moreover, the evidence that the high-quality science achieved by NIH-supported Nobel Prize winners is also characterized by high patent productivity suggests that informing budget allocations to consider this perspective will not compromise the scientific mission of the NIH. Instead, it will enhance NIH's scientific mission by encouraging the Pasteur's Quadrant paradigm—a useful reminder that patents are not "less pure," commercially driven, derivatives of science but a representation of true scientific breakthroughs that can lead to entirely new health-care industries. If the U.S. hopes to compete with the rest of the developed world for a robust biotechnology sector—and the jobs, firms, exports, and growth that come with it—it should embrace R&D productivity models and make the output of high-quality patents a higher priority from federal science programs.

Appendix

Similar to the authors' previous analysis of NIH patents,[36] the summary data and descriptive statistics in this report were gathered from a number of primary sources, including the NIH RePORTER (Research Portfolio Online Reporting Tools for Expenditures and Results) database, the U.S. Patent and Trademark Office (USPTO), and AcclaimIP, a subscription-based global patent database. For curating a list of NIH patents, we relied on those that were self-reported by principal investigators to the NIH RePORTER site. NIH budget data came from the NIH RePORTER for grant and contract funding, while full appropriations historical data came from the NIH Office of Budget website.

For patents associated with other federal R&D programs, we searched the USPTO bibliographic data, via the AcclaimIP tool, for "government interest" statements that link patents back to their relevant federal agency. Department of Energy budget data included only programs under the Office of Science (not the Advanced Research Projects Agency—Energy program), while the NASA budget included only projects from the science, aero, exploration, and education programs. All budget data were deflated according to the Biomedical Research and Development Price Index.

In dealing with IC reorganizations during the period examined, we relied on the NIH's method for assigning funds to the core IC. We excluded one of the newest ICs, the National Center for Advancing Translational Science, as well as the Office of the Director, because of incomplete reported data and significant funding overlap between ICs. In the case of NIBIB, which was created in 2002, we included only a truncated time frame of summary project data from 2003–09 and patent data from 2006–12 per the three-year lag for all ICs.

A relatively modest number of patents contained funding from more than one IC. In total, there were a small number of "type 8/9 transfers" from one IC to another, particularly following the creation of NIBIB. In dealing with these instances, we deferred to the NIH's attribution to the project's core IC. As noted by the Battelle Technology Partnership Practice, there are several exceptions: NIBIB's raw patent count would be about 50% higher, in terms of frequency; and NIGMS would be about 1% higher.[37] We did not include this adjustment in the data presented.

One limitation with the data set in this report is that not all grantees are compliant with reporting patents issued as a result of an NIH grant, particularly if that grantee is no longer supported by the agency. Again, Battelle found that augmenting the NIH RePORTER database by searching USPTO "government interest" statements raised total patent counts nearly uniformly for each NIH Institute Center by 30%–40%, although slightly more for the NEI (National Eye Institute) and the NIAAA (National Institute on Alcohol Abuse and Alcoholism). However, in the three years since the Battelle data were gathered, we found that total patents reported in the NIH RePORTER database were significantly higher (by 29%). Given these corrections within the NIH RePORTER database, we did not think that it was necessary to adjust project summary data based on the Battelle methodology. However, future studies would benefit from an assessment of the NIH RePORTER results vis-à-vis USPTO "government interest" statements that identify NIH funding.

Project summary data are not available for other federal R&D agencies, such as DARPA, DOE, and NASA. Therefore, funding totals for these programs included administrative costs that were able to be backed out of the NIH totals. With the advent of Federal RePORTER (a government-wide iteration of the NIH RePORTER), we hope that such summary project data will be available for all federal R&D agencies in the future.

The NIH website has information regarding agency-supported Nobel laureates for 1990–2010.[38] We also used the NIH RePORTER database to evaluate patent frequency data, aggregating patents and awards when a team of investigators was awarded a Nobel Prize. For forward-citation data, we used the USPTO website, which does not include citations to patent applications in its time frame. This likely resulted in a slightly lower quality for the aggregate Nobel profile vis-à-vis the individual ICs. A vintage of patents to calculate forward citations was not possible because of sample-size concerns.

Endnotes

1 Janet L. Yellen, “Semiannual Monetary Policy Report to the Congress,” Feb. 14, 2017.

2 From 1993 to 2015, according to the authors’ analysis of NIH budget data, the average adjustment per each NIH institute and center as its percentage of the agency’s total budget has been just 0.06%, with a median of 0.23%. The primary outlier was the National Institute of Allergy and Infectious Diseases (NIAID), which grew from 9.5% of the budget in 1993 to 14.4% in 2015. Also, the Office of the Director grew from 1.8% in 1993 to 4.7% in 2015. Otherwise, the majority of ICs maintained roughly the same proportion of the budget then as they do now. Budget data for institutes or centers that were created from existing programmatic activity during this period (e.g., NHGRI, NIBIB, and NCATS) were calculated based on their first full year of grant-making activity.

3 National Institutes of Health, Office of Portfolio Analysis, iCite.

4 Jonathan Rothwell et al., “Patenting Prosperity: Invention and Economic Performance in the United State and Its Metropolitan Areas,” Brookings Institution, Feb. 2013. See also Paul Romer, “The Origins of Endogenous Growth,” *Journal of Economic Perspectives* 8, no. 1 (Winter 1994): 3–22; idem, “Endogenous Technological Change,” *Journal of Political Economy* 98, no. 5 (1990): S71–S102; Robert E. Lucas, “On the Mechanics of Economic Development,” *Journal of Monetary Economics* 22, no. 1 (Feb. 1988): 3–42; Robert Barro and Xavier Sala-i-Martin, *Economic Growth* (Cambridge, MA: MIT Press, 2003); Elhanan Helpman, *The Mystery of Economic Growth* (Cambridge, MA: Belknap/Harvard, 2005); and Charles I. Jones, “Sources of U.S. Economic Growth in a World of Ideas,” *American Economic Review* 92, no. 1 (Mar. 2002): 220–39.

5 Organisation for Economic Co-operation and Development, *Genetic Inventions, IPRs and Licensing Practices* (Paris: OECD, 2002).

6 Quoted in Peter Dizikes, “Study: NIH Funding Generates Large Numbers of Private-Sector Patents,” MIT News, Mar. 30, 2017.

7 Danielle Li, Pierre Azoulay, and Bhaven N. Sampat, “The Applied Value of Public Investments in Biomedical Research,” *Science* 356, no. 6333 (Apr. 7, 2017): 78–81.

8 Jason Owen-Smith and Walter W. Powell, “The Expanding Role of University Patenting in the Life Sciences: Assessing the Importance of Experience and Connectivity,” *Research Policy* 32, no. 9 (Oct. 2003): 1695–1711.

9 Paul R. Sanberg et al., “Changing the Academic Culture: Valuing Patents and Commercialization Toward Tenure and Career Advancement,” *Proceedings of the National Academy of Sciences* 111, no. 18 (Apr. 28, 2014): 6542–47.

10 David Hirshleifer, Po-Hsuan Hsu, and Dongmei Li, “Innovative Efficiency and Stock Returns,” *Journal of Financial Economics* 107, no. 3 (Mar. 2013): 632–54.

11 Because forward citations accumulate over time and a large portfolio of patents can have unequal distributions of grant-year patents, analyses of raw forward citations can suffer from inconsistent reporting periods. To correct for this issue, it is common to select only a relatively narrow range of patents. In this analysis, we tried to balance selecting a narrow range of patents while including enough years to ensure adequate sample sizes for most ICs.

12 The expected annual budget for each federal agency in FY17 is: NIH, $34.3 billion; DARPA, $2.9 billion; NSF, $7.4 billion; NASA, $13.6 billion (R&D activity only); and DOE, $5.3 billion (nonnuclear security R&D). See Matt Hourihan and David Parkes, “Congress Rejects White House Approach, Pursues Targeted Science and Technology Boosts,” American Association for the Advancement of Science, May 1, 2017.

13 Brandon Schackelford, “One in Five Businesses with R&D Applied for a U.S. Patent in 2008,” National Science Foundation, National Center for Science and Engineering Statistics, Info Brief NSF 13-307, Feb. 2013.

14 Battelle Technology Partnership Practice, “The U.S. Biopharmaceutical Industry: Perspectives on Future Growth and the Factors That Will Drive It,” 2014.

15 See Schackelford, “One in Five Businesses.”

16 The primary cause for a higher rate of forward citations in this study is that the AcclaimIP database tool includes citations to pre-grant patent applications. Most studies look at citations only to the final approved patent. But in the time from when the patent application is made public and is finally approved (which can take 24–36 months), other subsequent patents can cite the pre-grant application. Since these pre-grant citations are important indicators of additional downstream R&D conducted during the pendency time, we have included these as well.

17 See “Quantitative Patent Scoring” at AcclaimIP. We hope to evaluate this metric more thoroughly in the future, given its consideration of factors beyond citations. However, for our purposes here, the correlation between forward citations and P-score was fairly robust (0.55, $p<0.001$, range 0.0–86.9), perhaps reflecting the recognition of citations as an indication of economic significance.

18 Based on our analysis, approximately 15% of forward citations come from the same or other academic research sites. If we assume that these subsequent patents were generated using additional federal or state grant dollars, a conservative approach would be to back these out from estimates of additional downstream R&D in the private sector—despite the possibility that some of those patents may have been supported through a Master Research Agreement or licensing arrangement with private-sector dollars.

19 NHGRI’s patent rate (patents per $100 million) is likely to be depressed because of the fact that some of the main products of discovery, genes, were deemed non-patentable by both the science community and U.S. courts.

20 In looking at the missions of these programs, note that engineering fields are twice as likely to patent as life-science fields—even when controlling for the same number of publications. See Paula E. Stephan et al., “Who’s Patenting in the University? Evidence from the Survey of Doctorate Recipients,” *Economics of Innovation and New Technology* 16, no. 2 (Mar. 2007): 71–99. In general, most NIH grantees are life-science researchers—which can help explain the higher propensity to patent from the more engineering-based programs at NSF, DARPA, and DOE. But even considering the fact that NIBIB’s and NHGRI’s programs are often engineering in nature, their overall R&D productivity is still more than five times and three times greater, respectively, than the mean at the NIH. Therefore, controlling for mission-specific factors still leaves significant R&D productivity that cannot be explained simply because of field of study. Nor is it clear from a policy perspective that we should apply these controls: the goal is precisely to identify areas of R&D with a higher propensity for patentable discoveries, not to attempt to mitigate the significance of higher levels of patent performance.

21 Making this figure even more impressive: NIGMS has a unique charge to support a large number of training awards across the research enterprise. Considering that training awards would not be expected to generate new innovations, NIGMS’s productivity metrics would most likely be moderately higher if measured by simply its research grants and contracts.

22 Again, it is worth remembering that well-cited patents are not the NIH’s main scientific output, and patent laggards are still producing many non-patentable innovations and health advances.

[23] Organisation for Economic Co-operation and Development, *The Future of Productivity* (Paris: OECD, 2015).

[24] Vannevar Bush, *Science, the Endless Frontier: A Report to the President* (Washington, DC: Government Printing Office, 1945).

[25] Donald E. Stokes, *Pasteur's Quadrant: Basic Science and Technological Innovation* (Washington, DC: Brookings Institution Press, 1997).

[26] Quoted in Walter Isaacson, *Steve Jobs* (New York: Simon & Schuster, 2011), 539.

[27] Donald E. Stokes, "Completing the Bush Model: Pasteur's Quadrant," conference paper, 1994.

[28] Ibid.

[29] Regina E. Dugan and Kaigham J. Gabriel, " 'Special Forces Innovation': How DARPA Attacks Problems," *Harvard Business Review* 10 (Oct. 2013): 74–82.

[30] Note that the location of each bubble in this figure is determined by the average value of metrics within that portfolio. Individual research programs within each portfolio would be more widely distributed across the figure. For estimating the Biotech Industry Profile, we referred to the Brookings Patent Report (Rothwell, "Patenting Prosperity"), which found a forward citation rate for private companies without government funding to be just 6.9. For patents per $100 million in R&D, the NSF report (Schackelford, "One in Five Businesses") notes that industry tends to produce one patent for every $3.2 million–$10 million in R&D funding. As such, we have placed their overall profile at about 20 patents per $100m in R&D funding. Given the large amount of R&D conducted by private-sector biotech and pharmaceutical firms, their circle size is not fully representative of their total R&D intensity, which would be significantly larger.

[31] See data and methodology appendix for more details on the data sources and methodology regarding the analysis of these teams.

[32] See Li et al., "The Applied Value of Public Investments."

[33] See Derek H. C. Chen and Carl J. Dahlman, "Knowledge and Development: A Cross-Section Approach," Policy Research Working Paper 3366, World Bank, Aug. 2004; Michael E. Porter and Scott Stern, "Measuring the 'Ideas' Production Function: Evidence from International Patent Output," NBER Working Paper no. 7894, Sep. 2000; and Dushko Josheski and Cane Koteski, "The Causal Relationship Between Patent Growth and Growth of GDP with Quarterly Data in the G7 Countries: Cointegration, ARDL and Error Correction Models," SSRN, Sep. 3, 2011.

[34] In contrast to, e.g., "design patents" or "plant patents," a "utility patent" is "issued for the invention of a new and useful process, machine, manufacture, or composition of matter, or a new and useful improvement thereof." See USPTO, "Types of Patents."

[35] Congressional Budget Office, "The Budget and Economic Outlook: Fiscal Years 2012–2022," Jan. 2012.

[36] Richard L. Ehman and Michael J. Kalutkiewicz, "Patents as Proxies: NIH Hubs of Innovation," *Nature Biotechnology* 32, no. 6 (June 2014): 536–37.

[37] Battelle Technology Partnership Practice, "The U.S. Biopharmaceutical Industry:Perspectives on Future Growth and the Factors That Will Drive It."

[38] National Institutes of Health, The NIH Almanac, "Nobel Laureates."

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Abstract

All scientific research supported by the National Institutes of Health aims to advance knowledge that will ultimately improve human health. However, some of the agency's many institutes and centers do so in a way that tends to create economically valuable new technologies. This research is most often embodied through high-quality new intellectual property and patents.

This paper looks at the patents granted as the result of NIH-sponsored research grants and contract spending, comparing the number and quality generated by the agency's various institutes. We find a wide variation in what can be called patent productivity at NIH, in terms of patents generated as compared with federal funds invested. Furthermore, while Congress has occasionally shifted resources in response to compelling or exciting scientific priorities, NIH's strongest areas of patent production have experienced some of the slowest growth since 2000.

This creates an untapped opportunity for policymakers to leverage NIH's highly valuable patent portfolio: policymakers should reinvest in the programs at NIH that have evidence of strong rates of technological innovation. Doing so will not only result in new tools and technologies that help move science and discoveries forward; it will also help meet the urgent calls to seek out programs that can help spur productivity and growth at the national level.

The vast majority of research—new scientific knowledge, theories, diagnoses, methods, and techniques—will not result in patentable innovations. Yet the highest-impact science at NIH, as pursued by 33 of the most recent NIH-funded Nobel Prize winners, overwhelmingly led to the development of new patents. Especially in the life sciences, the line between basic and applied research is not as stark as policymakers and the general public believe. Research undertaken to explore or solve a well-defined, use-inspired need or problem can also push the frontiers of fundamental knowledge.

This paper suggests that modest, sustainable, and targeted allocations to the several programs of the National Institutes of Health can provide a larger boost to the U.S. economy while furthering its core mission.

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