Supplementary Materials for

The applied value of public investments in biomedical research

Danielle Li,* Pierre Azoulay, Bhaven N. Sampat

*Corresponding author. Email: dli@hbs.edu

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This PDF file includes:

Appendices A to G
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Data and Code: Available on Bhaven Sampat's Dataverse:
https://dataverse.harvard.edu/dataverse.xhtml?alias=boffindata

The uploaded data include everything necessary to replicate the main paper figures, as well as the discrete time hazard models in Appendix G. The results in Table G1 make use of restricted access data from the Association of American Medical Colleges (AAMC), used to assign gender, age, and degree. Table G2 re-estimates our models without these variables, to allow for replication with publicly available data. To access restricted AAMC data, please contact datarequest@aamc.org

Appendix A: A Primer on NIH Funding

The National Institutes of Health (NIH) is the primary organization within the United States government with responsibilities for health-related research, with an annual budget of approximately $30 billion. NIH's mission is "to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability" (*29*).

NIH includes 21 different Institutes (and several centers, though these are not included in our analyses). The Institutes have distinct though sometimes overlapping research foci. For example, the National Institute for Mental Health focuses on mental health related research. It shares interests with the National Institute of Aging on issues related to dementia. All Institutes receive their funding directly from Congress, and manage their own budgets.

More than 80% of the total budget supports extramural research through competitive grants that are awarded to universities, medical schools, and other research institutions, primarily in the United States. The largest and most established of these grant mechanisms is the R01, a project-based renewable research grant which constitutes half of all NIH grant spending and is the primary funding source for most academic biomedical labs in the United States. There are currently 27,000 outstanding awards, with 4,000 new projects approved each year. The average size of each award is 1.7 million dollars spread over 3 to 5 years, and the application success rate is approximately 20 percent (*30*).

Institutes included in the analysis. While there are 21 different Institutes, we exclude grants from the National Library of Medicine (NLM), the National Institute of Nursing Research (NINR), and the National Institute on Minority Health and Health Disparities (NIMHD), which together represent less than 3% of NIH's total budget. We drop the NLM because it seldom supports extramural researchers. We drop NINR and NIMHD because we found no instances of the grants funded by these Institutes generating publications referenced in private-sector patents. Doing so effectively focuses our analysis on component institutes that are "at risk" of being linked to patents.

Grant Characteristics. Our analytic sample consists of 365,380 NIH grants awarded between 1980 and 2007. Approximately 8% of these grants are directly linked to academic patents and 30% are indirectly linked to commercial patents. Table A1 describes the breakdown by grant type for our full set of grants, and each of these subsets of patent-linked grants.

Table A1: Grant Characteristics

		Grants Linked to Patents	
	Full Sample	**Directly Linked**	**Indirectly Linked**
Sample Coverage			
# Grants	365,380	30,829	112,408
Grant Characteristics			
% R01 equivalent grants	44.99	34.73	42.74
% RFA	23.89	17.90	15.13
% Disease-related keywords	50.23	49.64	51.50
By "highest" organism-related keyword			
Human	48.63	44.52	44.42
Primate	0.47	0.28	0.59
Other Mammal	3.05	2.35	2.72
Rodent	8.46	8.18	8.70
Vertebrate	1.06	0.73	0.73
Invertebrate	1.38	0.98	0.94
Eukaryote, multicellular	0.82	0.83	0.75
Eukaryote, unicellular	0.77	0.61	0.86
Prokaryote	1.91	1.93	2.19
Virus	1.26	1.67	1.76
Undefined	32.19	37.91	36.34

Note: Sample is the set of all NIH-funded grants from 1980-2007, excluding NINR, NLM, and NIMHD grants. The sample is restricted to new and competitive renewal grants so that there is one observation per successful grant application cycle. A grant is defined as directly linked if it is acknowledged by a patent. A grant is defined as indirectly linked if there exists a patent that cites a publication that acknowledges funding from that grant. A grant is matched with a publication if it acknowledges the project number of the grant and is published within 5 years of the grant's funding year. A patent is citation-linked to a grant if it cites a publication that is linked to a grant. R01 equivalents include the R23, R29, and R37.

Appendix B: "Life Science" Patents

To assess the indirect impact of NIH funding, we need to define a universe of life science patents. While we do not want to impose strong restrictions on where NIH funding could have an effect (e.g., by looking in specific disease areas) focusing on a specific subset of the universe of issued patents is necessary because linking NIH publications to patents requires probabilistic matching (see Appendix E), and the rate of false positives is much lower if we restrict the set of potential matches.

To do so, we started with the 5,269,968 patents issued by the USPTO between 1980 and 2012. Then, using the NBER patent categorization described in Hall et al. (*31*), we focused on patents in the classes belonging to NBER Categories 1 (Chemicals) and 3 (Drugs and Medical). This left 1,310,700 patents. Of these patents, 565,593 cite at least one non-patent reference. Using the algorithm described in Azoulay et al. (*32*) and Sampat and Lichtenberg (*9*) we determined that 312,903 patents cite an article indexed in PubMed. We refer to this set—patents in NBER Classes 1 and 3 that cite to at least one PubMed indexed article—as "life science patents." Classes 1 and 3 cover a range of subcategories, listed in Table B1.

Private sector vs. public sector patents. We are primarily interested in the effect of NIH funding on the rate of production of private-sector patents, excluding those assigned to public research entities such as universities, research institutes, academic medical centers, or government agencies (e.g., the intramural campus of NIH). This focus is justified by our desire to focus on disembodied knowledge flows. Since the Bayh-Dole act, life science academics have considerably increased their rate of patenting (*33, 34*). Previous scholarship has documented the growing importance of patent-paper pairs (*35*) where a given piece of academic knowledge gives rise to both an article and a patent listing the authors of the article as inventors and their employer (often a public institution) as assignee. Including these patents in our analyses would make the interpretation of our results (which emphasizes indirect spillovers of knowledge) difficult. To separate private-sector from public-sector patents, we adapted Bronwyn Hall's patent assignee name matching algorithm to isolate private-sector assignees (*36*). Using this method, we restrict the sample to 232,276 patents, or 74% of the life science patents. This creates no obvious biases if we limit our inferences to the effects of NIH research on private sector innovation.

Patents on FDA approved drugs. Though a substantial share of the life science patents are "pharmaceuticals" not all are therapeutic molecules or proteins. Even among those that are, there is substantial heterogeneity in value, since only a small share of drugs enter trials, and of these a small share receive marketing approval.

To examine heterogeneity of the effects of NIH funding, and to assess the effects on drug development, we isolated patents associated with drugs. We began with all patents from current and archival versions of the FDA's Orange Book (officially named Approved Drug Product with Therapeutic Equivalence Evaluations). Since the 1984 Hatch-Waxman Act, branded firms are required to list on the Orange Book patent issued before drug approval with at least one claim covering a drug's active ingredient, formulation, or methods of use for approved indications. Though there is strong incentive to list patents issued after drug approval as well (*37*), strictly speaking this is not required. We can link patents to products for pharmaceuticals because of unique regulations requiring listing of patents for each product in this industry (Hemphill and Sampat 2012). Unfortunately similar information is not available for other life-science patents associated with successful products, e.g. medical device approvals.

Table B1: Relevant Patent Classes

Cat. Code	Category Name	Sub-Cat. Code	Sub-Category Name	Patent Classes
1	Chemical	11	Agriculture, Food, Textiles	8, 19, 71, 127, 442, 504
		12	Coating	106,118, 401, 427
		13	Gas	48, 55, 95, 96
		14	Organic Compounds	534, 536, 540, 544, 546, 548, 549, 552, 554, 556, 558, 560, 562, 564, 568, 570
		15	Resins	520, 521, 522, 523, 524, 525, 526, 527, 528, 530
		19	Miscellaneous	23, 34, 44, 102, 117, 149, 156, 159, 162, 196, 201, 202, 203, 204, 205, 208, 210, 216, 222, 252, 260, 261, 349, 366, 416, 422, 423, 430, 436, 494, 501, 502, 510, 512, 516, 518, 585, 588
3	Drugs & Medical	31	Drugs	424, 514
		32	Surgery & Medical Instruments	128, 600, 601, 602, 604, 606, 607
		33	Biotechnology	435, 800
		39	Miscellaneous	351, 433, 623

Appendix C: Linking NIH Grants to Patents Directly [Bayh-Dole Linkage]

Recipients of NIH grants and contracts are allowed to seek patent protection on project results. This practice emerged in the 1970s under Institutional Patent Arrangements between individual grantees (and contractors) and the Department of Health, Education, and Welfare, and intensified after the implementation of the Bayh-Dole Act in 1981.

One Bayh-Dole requirement is for recipients of federal research funds to report to the funding agency any patent application they file. This information is stored in the Interagency Edison (iEdison) database. Another requirement is to acknowledge on patent documents the existence of federal funding and the fact that the government retains certain rights, in so-called "government interest" statements.

Recently iEdison data has been made available through NIH RePORTER. Since there is likely under-reporting of patents by grantees to the NIH (*23*) our data provide a lower-bound for the share of grants resulting in "Bayh-Dole" patents.

Appendix D: Linking NIH Grants to Publications that Acknowledge NIH Support

The NIH asks grantees to acknowledge the agency's support in any publications resulting from a grant, and to do so in a very specific format (*38*). Since the early 1980s, PubMed has recorded these acknowledgements in a separate field, and we use these data to link every grant in the NIH Compound Grant Applicant File (CGAF) with the publications that result. The process used to systematically map publication-to-grant linkages is relatively straightforward, but may be prone to measurement error. We discuss two potential issues below.

Dynamic linking inconsistency. In the vast majority of the cases, a grant acknowledgement provides a grant mechanism, a funding institute, and a grant serial number (as in R01GM987654), but typically no reference to a particular grant cycle. This limitation is potentially serious, since some of our analyses aim to measure the time elapsed between the receipt of funding and the citation to a publication listed in a patent. This duration is the sum of a publication pendency (the amount of time between grant funding and a publication) and a citation pendency (the amount of time necessary for a patent to cite the publication). Indeterminate grant cycles may add error to the measurement of publication pendency lag.

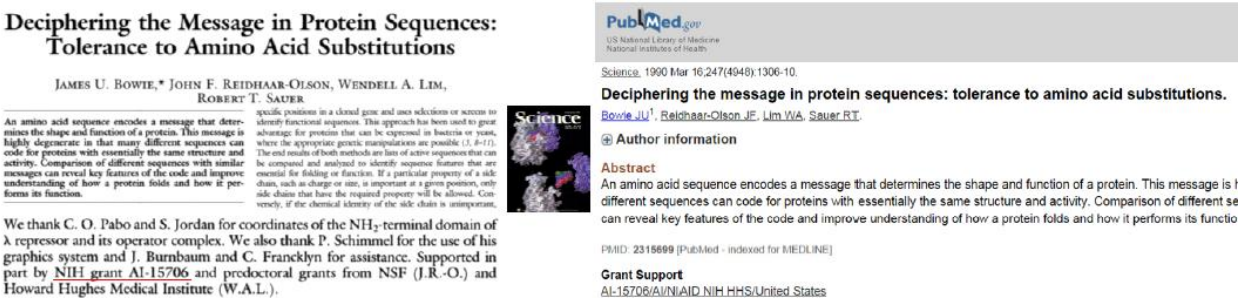
How did we address this? Our final dataset uses information from 987,799 unique publications that acknowledge a grant funded by NIH. 100% of these acknowledgements occur in a window of ten years before the year in which the article appeared in print. 93% of these publications are linked to the same grant within seven years, 83% within five years, and 47% within two years. To find the relevant grant cycle for each publication acknowledging a grant, we adopted the following procedure: (i) look up the year of publication t_{pub} for the acknowledging publication; (ii) create a five year "catchment window" $[t_{pub}\text{-}5; t_{pub}]$; (iii) identify the most recent fiscal year t_{grant} in that window during which the grant was funded either as a new grant or as a competitive renewal; and (iv) link the publication to the funding institute identified in the grant acknowledgement, the study section that evaluated this grant according to NIH records, in the year t_{grant}. While we cannot directly observe whether a publication was funded by a different grant cycle, we have verified that our benchmark results are robust to alternative choices for the length of the catchment window: $[t_{pub}\text{-}2; t_{pub}]$, $[t_{pub}\text{-}7; t_{pub}]$, $[t_{pub}\text{-}10; t_{pub}]$.

Overclaiming of publications. NIH grant renewal is dependent on the research and publications stemming from that stream of funding. To our knowledge, NIH does not audit the acknowledgement trail systematically—this is left to the discretion of scientific review officers (the federal employees who manage the flow of information between reviewers in a particular study section and the NIH funding apparatus). Therefore, grantees may have an incentive to "over-attribute" publications—e.g., to credit some publications to the support of a grant, even if they were in fact enabled by other streams of funding. This raises the concern that we identify more linkages between individual grants and patents than are warranted, through the spurious channel of false attributions.

We believe that our results are unlikely to be driven by this behavior. The vast majority of public biomedical research funding in the US comes from NIH, meaning that most scientists do not have meaningful amounts of funding from other sources to support their research (*39*). Note that while scientists often use grant funding to subsidize research projects that are not directly related to the topic of their grant, in our view these projects should still be counted as a product of grant funding.

Example. We illustrate the procedure with the case of particular publication, *Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions,* by Bowie et al., which appeared in the journal Science on March 16th, 1990 (see the left side of Figure D1). The publication credits grant support from NIH, specifically grant AI-15706. Despite the fact that this acknowledgement appears at the very end of the paper as the ultimate reference in the bibliography (reference #46 on page 1310), PubMed captures this data accurately (see the right side of Figure D1). Note that the acknowledgement omits the grant mechanism, as well as the leading zero in the grant serial number. These issues, which are typical in the PubMed grant acknowledgement data, turn out to be unimportant. In particular, the National Institute of Allergy and Infectious Diseases (NIAID, code-named AI) has only one grant with serial number 015706: A project R01 grant first awarded to Robert T. Sauer, an investigator in the biology department at MIT, in 1979, and competitively renewed in 1982, 1987, 1992, 1997, and 2002. The grant was evaluated by the BBCA (Molecular and Cellular Biophysics) study section; its title is *Sequence Determinants of Protein Structure & Stability*, with a budget of $1,211,685 for the cycle that began in 1987, three years before the date of the publication above (whose last author is also Robert Sauer).

Figure D1: Example of Grant Acknowledgement



Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions

JAMES U. BOWIE,* JOHN F. REIDHAAR-OLSON, WENDELL A. LIM, ROBERT T. SAUER

An amino acid sequence encodes a message that determines the shape and function of a protein. This message is highly degenerate in that many different sequences can code for proteins with essentially the same structure and activity. Comparison of different sequences with similar messages can reveal key features of the code and improve understanding of how a protein folds and how it performs its function.

We thank C. O. Pabo and S. Jordan for coordinates of the NH_2-terminal domain of λ repressor and its operator complex. We also thank P. Schimmel for the use of his graphics system and J. Burnbaum and C. Francklyn for assistance. Supported in part by NIH grant AI-15706 and predoctoral grants from NSF (J.R.-O.) and Howard Hughes Medical Institute (W.A.L.).

PubMed.gov
US National Library of Medicine
National Institutes of Health

Science. 1990 Mar 16;247(4948):1306-10.

Deciphering the message in protein sequences: tolerance to amino acid substitutions.

Bowie JU[1], Reidhaar-Olson JF, Lim WA, Sauer RT.

Author information

Abstract

An amino acid sequence encodes a message that determines the shape and function of a protein. This message is h
different sequences can code for proteins with essentially the same structure and activity. Comparison of different se
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PMID: 2315699 [PubMed - indexed for MEDLINE]

Grant Support

AI-15706/AI/NIAID NIH HHS/United States

Appendix E: Linking PubMed References to USPTO Patents

We use patent-publication citation information to identify patents that build on NIH-funded research. Patent applicants are required to disclose any previous patents or articles that are relevant to the patentabilty of their inventions. Failure to do so can result in strong penalties for the applicant and attorney, and invalidation of the patent (*40*). There is a long history of using patent-patent citation data as measures of intellectual influence or knowledge flows between public and private sector research (*41, 42*). Recent work (*25, 43*), however, shows that patent examiners rather than applicants insert many patent-patent citations, casting doubt on their utility as measures of knowledge flows or spillovers (*44*).

We instead use information on patent citations to published scientific articles. (These "front page" citations are also included in the References Cited section of issued patents.) This is appealing both because publications rather than patents are the main output of scientific researchers (*45*), but also because the vast majority of patent-paper citations, over 90 percent, come from applicants rather than examiners, and are thus more plausibly indicators of real knowledge flows than patent-patent citations (*5*). Roach and Cohen (*6*) provide empirical evidence on this point.

Determining whether patents cite publications is more difficult than tracing patent citations: while the cited patents are unique seven-digit numbers, cited publications are free-form text (*46*). Moreover, the USPTO does not require that applicants submit references to literature in a standard format. For example, Harold Varmus's 1988 Science article "Retroviruses" is cited in 29 distinct patents, but in numerous different formats, including Varmus. "Retroviruses" Science 240:1427-1435 (1988) (in patent 6794141) and Varmus et al., 1988, Science 240:1427-1439 (in patent 6805882). As this example illustrates, there can be errors in author lists and page numbers. Even more problematic, in some cases certain fields (e.g. author name) are included, in others they are not. Journal names may be abbreviated in some patents, but not in others.

To address these difficulties, we developed a matching algorithm that compared each of several PubMed fields—first author, page numbers, volume, and the beginning of the title, publication year, or journal name—to all references in all biomedical and chemical patents issued by the USPTO since 1976. Biomedical patents are identified by technology class, using the patent class-field concordance developed by the National Bureau of Economic Research (*31*). We considered a dyad to be a match if four of the fields from PubMed were listed in a USPTO reference.

Overall, the algorithm returned 1,058,893 distinct PMIDs cited in distinct 322,385 patents. Azoulay, Graff- Zivin, and Sampat (*32*) report that the algorithm performs well against hand matching, returning correct PMID information 86 percent of the time, with few false positives. In a more recent validation exercise we found similar results when comparing to hand collected references for a sample of patents associated with neurology drugs. For the 314 references, the algorithm returned the correct PMID (including none, in cases when hand matching suggests the reference does not match a PMID) 90 percent of the time. For less than 3 percent of the references the algorithm produced a false positive: it incorrectly found a PMID where hand matching did not find one. For 8 percent of the references the algorithm produced a false negative: hand matching identified a PMID, but the algorithm did not. In our setting, the presence of false negatives means that we will underestimate the share of grants cited in NIH patents.

Example. We illustrate the procedure with the case of particular patent, #6,687,006, issued on March 15, 2005 and assigned to the biopharmaceutical firm Human Genome Sciences, Inc. In the section of the patent entitled "Other Publications", we can find a citation to "Bowie, J.U., et al., Deciphering the Message in Protein Sequences…," precisely the publication we took as an example in Appendix D.

Figure E1: Example of Patent-to-Publication Citation

(12) **United States Patent**
Li et al.

(10) **Patent No.: US 6,867,006 B2**
(45) **Date of Patent: Mar. 15, 2005**

(54) **ANTIBODIES TO HUMAN CHEMOTACTIC PROTEIN**

(75) Inventors: **Haodong Li**, Gaithersburg, MD (US); **Steven M. Ruben**, Olney, MD (US); **Granger Sutton, III**, Columbia, MD (US)

(73) Assignee: **Human Genome Sciences, Inc.**, Rockville, MD (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 230 days.

(21) Appl. No.: **10/141,965**

(22) Filed: **May 10, 2002**

WO	WO 96/38559	12/1996
WO	WO 96/40762	12/1996
WO	WO 97/15594	5/1997
WO	WO-98/44118	10/1998

OTHER PUBLICATIONS

Beall, C.J., et al., "Conversion of Monocyte Chemoattractant Protein–1 into a Neutrophil Attractant by Substitution of Two Amino Acids," *J. Biol. Chem. 267*:3455–3459, American Society for Biochemistry and Molecular Biology, Inc. (1992).

Berkhout, T.A., et al., "Cloning, in Vitro Expression, and Functional Characterization of a Novel Human CC Chemokine of the Monocyte Chemotactic Protein (MCP) Family (MCP–4) That Binds and Signals through the CC Chemokine Receptor 2B," *J. Biol. Chem. 272*:16404–16413, American Society for Biochemistry and Molecular Biology, Inc. (Jun. 1997).

Bowie, J.U., et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," *Science 247*:1306–1310, American Association for the Advancement of Science (1990).

Appendix F: "Measuring Basicness"
Linking NIH Grants and their Abstracts to MeSH Keywords

An important and longstanding challenge in understanding the allocation of research funding across types of research has been the ability to classify grants according to the "basicness" of the research they support.

We attempt to capture different dimensions of basicness. For several of the measures we use information from the title and full-text abstract for each grant (*47*). Specifically, we map words in the title and abstract to terms from the MeSH thesaurus, using a natural language processing tool, the Medical Text Indexer (MTI), a natural language processing tool which enables researchers to map full text paragraphs onto the MeSH controlled thesaurus (*48*). We batch process each grant title and abstract with the MTI tool, resulting in 18,557,642 unique grant-MeSH term combinations for 1,423,873 distinct grant applications. On average, MTI maps a grant to 13 MeSH terms. (The median is also 13; the range is from one to 101).

The MeSH keywords are used to construct three of the measures. The first is whether a grant is targeted at a particular disease. 4,586 unique MeSH terms (16.70% of the terms in the MeSH thesaurus) correspond to diseases (*49*). 52.54% of the grants in the data are supporting research that is targeted at a disease. Figure F1 provides a graph for the evolution of the relative importance of disease vs. non-disease targeted research over time.

Another measure based on the MeSH hierarchy is based the model organism that NIH-funded PIs rely upon for their research. Although there is a long list of potential model organisms, there is a shorter list of organisms that have been used extensively over the years as common models, making them standards in research. Examples include the fruit fly *drosophila melanogaster*, the tapeworm *caenorhabditis elegans*, the zebrafish *danio reiro*, the yeast *saccharomyces cerevisiae*, or the plant *arabidopsis thaliana*, in addition to mammals such as mice, rats, and non-human primates. Helpfully, model organisms can be identified unambiguously through MeSH terms as well. 2,508 unique MeSH terms (9.13% of the terms in the MeSH thesaurus) correspond to model organisms (*50*). Model organisms differ in their costs, the number of offspring they generate, reproduction time, and biological complexity. We divide model organisms in the following ten categories, from least to most complex: (i) viruses; (ii) prokaryotes; (iii) unicellular eukaryotes; (iv) multicellular eukaryotes; (v) invertebrates; (vi) rodents; (vii) other mammals; (viii) primates; and finally (ix) humans. Figure F2 provides a frequency distribution of these organisms in the grant data, focusing only on the set of grants that are not disease-targeted (*51*). Humans are most commonly studied, followed by rodents.

The analyses also distinguish between patient-oriented research and other research. We use the same approach for constructing this measure. In a third measure, grants studying the "human" organism are classified as patient-oriented.

To measure the fourth dimension of basicness, we take a different approach. This measure is not based on grant keywords, but rather whether the grant is the result of a Request for Applications (RFA). RFAs are used by the NIH to solicit specific research, and are viewed as more targeted grants than "investigator-initiated" research projects (*19, 52*). We obtained data on which grants were the result of RFAs from NIH RePORTER.

It is difficult to validate our measures against an objective yardstick of basicness since, to our knowledge, none exists. One intuitive check is to examine whether grants funded by the National Institute of General Medical Sciences (NIGMS)—which considers itself the Institute most responsible for funding basic research (*53*)—are indeed more basic according to our measures of disease and patient orientation. We find that NIGMS grants are less likely to be disease-oriented (19 percent vs. 54 percent for all other institutes) and less likely to be patient-oriented (23 percent vs. 52 percent), providing some evidence of face validity. Further, though our basicness designations capture different dimensions, they are also internally consistent: for example, among non-disease oriented grants, 34 percent focus on humans, compared to 63 percent among disease-oriented grants.

Figure F1: Disease-Targeted vs. Non-Disease Targeted Grants, 1972-2007

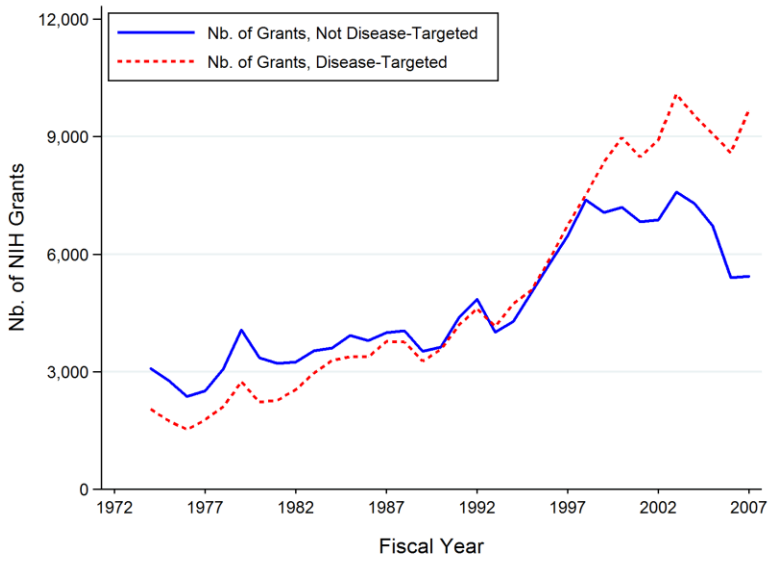

Figure F2: Classification by Model Organisms. N=365,380 grants, not disease-targeted

Type	Example	Frequency	
Viruses	bacteriophage λ	8,290	1.79%
Prokaryotes	*escherichia coli*	21,994	4.74%
Unicellular eukaryotes	*saccharomyces cerevisiae*	8,937	1.92%
Multicellular eukaryotes	*cryptococcus neoformans*	9,163	1.97%
Invertebrates	*caenorhabditis elegans*	15,057	3.24%
Vertebrates	*xenopus laevis*	13,785	2.97%
Rodents	rats, sprague-dawley	69,472	14.96%
Other mammals	rabbits	31,377	6.76%
Non-human Primates	*macaca mulatta*	4,515	0.97%
Humans		281,795	60.68%

Appendix G: Discrete-time Hazard Models

The analysis presented in the main body of the manuscript consists of plots of the proportion of grants that are linked (directly or indirectly) to patents, by grant age. The advantage of this graphical approach is that it is transparent and non-parametric. There are two main disadvantages. First, these curves conflate analysis time and calendar time, by pooling grants *t* years after issue, regardless of the calendar year in which they were awarded. Second, the graphical approach does not lend itself easily to multiple levels of stratification.

Accordingly, as a complement to the graphical exposition, we also provide multivariate analyses below. In order to accommodate the discrete nature of patenting events, we employ discrete-time hazard rate models (*54, 55*). The use of discrete-time models (as opposed to continuous-time models such as the Cox (*56*) is motivated by the fact that survival times in our data are grouped into discrete intervals (years). For a grant *i* during experience interval *t*, let the discrete-time hazard rate be $p_{it} = \text{Prob}[T_i = t \mid T_i \geq t, X_i]$, where T_i is the time at which grant *i* experiences an event and X_i a vector of covariates.

Discrete-time survival models can be estimated via maximum likelihood. Estimation makes use of the property that the sample likelihood can be rewritten in a form identical to the likelihood for a binary dependent variable and applied to a specially organized dataset (*57*). Specifically, we use a logistic regression function to link the hazard rate with time and the explanatory covariates:

$$Ln\left[\frac{p_{it}}{1-p_{it}}\right] = \alpha_t + \beta' X_{it}$$

where p_{it} is a set of experience interval indicator variables. This is otherwise known as the discrete-time proportional hazards model, with a piecewise constant baseline hazard (*58*).

Covariates. Covariates include characteristics of the grant and its principal investigator (PI). Grant-specific covariates include: (i) an indicator for new grant application (to distinguish them from competing continuations); (ii) the budget of the grant (deflated by the Producer Price Index for Biomedical R&D) over it entire cycle; (iii) and the grant type (fellowship and training grants, R01 and R01-equivalent project grants, research center grants, and other research grants). PI-level covariates were obtained by merging the NIH Compound Applicant Grant File (CGAF) with the Faculty Roster from the Association of American Medical Colleges (AAMC). Included in the specifications are: (i) an indicator variable for PI gender (assigned probabilistically based on first names); (ii) PI highest degree (MD, PhD, or MD/PhD—we dropped from the samples a handful of grants where the PI's highest degree was a Master's degree); and (iii) the PI's career age and its square.

In addition to these control covariates, our specifications also include several variables of more substantive interest: whether the grant is disease-oriented; whether it is patient-oriented; and whether the application is a response to a Request for Application (RFA). All specifications also include a full set of funding institute indicator variables, funding year indicator variables, and organism indicator variables.

Sample and Results. The resulting sample includes 226,781 grants funded between the years 1980 and 2005. This is smaller than the sample in the main body of the manuscript because the PI covariates are not available for the universe of grants, but only for the subsample of grant applicants who appeared in the AAMC Faculty Roster between 1980 and 2005. We separately model four distinct events. The first model, reported in Column 1, focuses on whether the grant is associated with a patent through a direct (Bayh-Dole) link or through an indirect (citation) link. The second column reports results form a model that limits the patents to those with indirect (citation) links. The third column restricts the sample further, to only private sector assignees. Finally the fourth focused only on patents associated with FDA-approved drugs.

Table G1 displays the results as exponentiated coefficients. (Coefficient estimates equal to 1.00 mean a variable has no effect.) The results are consistent across columns. Grants from female PIs are much less likely to be associated with a patent, a finding consistent with prior research (*59*). The propensity for a grant to be linked to a patent decreases monotonically with PI age, and PIs with only a PhD degree are less likely to see their grants associated with patents, relative to MD-degree and MD/PhD- degree holders.

Of the grant level covariates, we find that the budget of a grant clearly matters. In the first column, the average marginal effect for the grant budget covariate implies that a 1% increase in budget boosts the odds of being associated with a patent by about 1% (recall that we already hold constant grant type). New grant applications are also much less likely to yield a patent than are follow-on grant cycles.

There is no clear pattern across the measures in the effects of "basicness." Disease-oriented grants are associated with a 15 to 20% greater patent propensity, but this is not the case for patient-oriented grants, even controlling for other organism types. Grants that were funded through requests for applications are less likely to be associated with a patent, though this effect is not statistically significant.

Table G2 replicates the specifications displayed in Table G1, with one modification: we omit the PI gender, age, and degree variables which cannot be shared publicly because of our license with AAMC. The results are qualitatively similar.

Table G3 provides evidence that we can separately identify the effects of the different measures of "basicness," by introducing them one-by-one into the model (the risk modeled is that of a link, direct or indirect, to any life science patent). Column 6 of Table G3 and the first column of Table G1 are identical.

Table G1: Discrete-time Hazard Specifications

	All Patents	Excluding "Bayh-Dole" Patents	Excluding Patents with Non-corporate Assignees	Patents Associated with an FDA-approved Drug
Disease-oriented	1.148***	1.140***	1.164***	1.185**
	(0.014)	(0.015)	(0.015)	(0.062)
Patient-Oriented	0.993	0.975	0.994	1.099
	(0.015)	(0.015)	(0.016)	(0.068)
Disease-oriented & Patient-oriented	0.998	1.010	0.988	0.911
	(0.017)	(0.019)	(0.019)	(0.069)
Request for Applications (RFA)	0.839***	0.842***	0.844***	0.953
	(0.014)	(0.015)	(0.015)	(0.064)
New Grant Application	0.652***	0.656***	0.639***	0.644***
	(0.006)	(0.007)	(0.006)	(0.026)
Center Grants (P, M)	0.910***	0.863***	0.922**	0.998
	(0.024)	(0.026)	(0.025)	(0.091)
R01 & R01-equivalent Grants	0.838***	0.882***	0.834***	0.697***
	(0.014)	(0.016)	(0.015)	(0.051)
Other Research Grants (R, K, U)	0.539***	0.553***	0.533***	0.637***
	(0.010)	(0.011)	(0.011)	(0.056)
Log(Grant Budget)	1.601***	1.544***	1.631***	1.867***
	(0.008)	(0.009)	(0.009)	(0.041)
MD	0.946***	0.932***	0.944***	1.327***
	(0.015)	(0.016)	(0.016)	(0.087)
PhD	0.788***	0.786***	0.773***	0.826**
	(0.011)	(0.012)	(0.012)	(0.052)
Female PI	0.739***	0.753***	0.725***	0.650***
	(0.008)	(0.009)	(0.009)	(0.039)
PI Career Age	0.982***	0.984***	0.983***	0.961***
	(0.001)	(0.001)	(0.001)	(0.006)
PI Career Age, squared	1.000***	1.000***	1.000***	1.001***
	(0.000)	(0.000)	(0.000)	(0.000)
Nb. of Grant Applications	224,131	209,705	212,305	223,268
Nb. of Obs.	3,380,837	3,311,943	3,348,762	4,416,464
Adjusted R2	0.089	0.083	0.093	0.085

Note: Estimates from logistic specifications. All models incorporate a full suite of application year effects, funding institute effects, grant type effects, and organism type effects. Displayed estimates correspond to exponentiated coefficients. For example, the estimates in the first column imply that disease-oriented grants are 14.8% more likely than non-disease, non-patient-oriented grants to be associated with a patent.

Robust standard errors in parentheses, clustered at the level of the grant. $^{\dagger}p < 0.10$, $^{*}p < 0.05$, $^{**}p < 0.01$

Table G2: Discrete-time Hazard Specifications, with publicly available data

	All Patents	Excluding "Bayh-Dole" Patents	Excluding Patents with Non-corporate Assignees	Patents Associated with an FDA-approved Drug
Disease-oriented	1.165***	1.156***	1.183***	1.232***
	(0.014)	(0.015)	(0.015)	(0.064)
Patient-Oriented	0.994	0.975	0.995	1.128
	(0.014)	(0.015)	(0.016)	(0.070)
Disease-oriented & Patient-oriented	1.005	1.017	0.996	0.923
	(0.018)	(0.019)	(0.019)	(0.070)
Request for Applications (RFA)	0.837***	0.840***	0.844***	0.952
	(0.013)	(0.015)	(0.014)	(0.064)
New Grant Application	0.689***	0.691***	0.675***	0.683***
	(0.006)	(0.007)	(0.006)	(0.027)
Center Grants (P, M)	0.889***	0.841***	0.904***	0.993
	(0.023)	(0.024)	(0.024)	(0.088)
R01 & R01-equivalent Grants	0.798***	0.840***	0.793***	0.622***
	(0.013)	(0.015)	(0.013)	(0.044)
Other Research Grants (R, K, U)	0.526***	0.539***	0.522***	0.630***
	(0.010)	(0.011)	(0.010)	(0.055)
Log(Grant Budget)	1.586***	1.533***	1.618***	1.857***
	(0.008)	(0.008)	(0.008)	(0.039)
Nb. of Grant Applications	224,131	209,705	212,305	223,268
Nb. of Obs.	3,380,837	3,311,943	3,348,762	4,416,464
Adjusted R2	0.086	0.081	0.090	0.081

Note: Estimates from logistic specifications. All models incorporate a full suite of application year effects, funding institute effects, grant type effects, and organism type effects. Displayed estimates correspond to exponentiated coefficients. For example, the estimates in the first column imply that disease-oriented grants are 14.8% more likely than non-disease, non-patient-oriented grants to be associated with a patent.

Robust standard errors in parentheses, clustered at the level of the grant. $^{\dagger}p < 0.10$, $^{*}p < 0.05$, $^{**}p < 0.01$

Table G3: Discrete-time Hazard Specifications, All Patents

	(1)	(2)	(3)	(4)	(5)	(6)
Disease-oriented		1.143***		1.185***		1.148***
		(0.010)		(0.014)		(0.014)
Patient-Oriented			0.957***	0.948***		0.993
			(0.009)	(0.013)		(0.015)
Disease-oriented & Patient-oriented				0.958*		0.998
				(0.017)		(0.017)
Request for Applications (RFA)					0.838***	0.839***
					(0.014)	(0.014)
New Grant Application	0.640***	0.635***	0.642***	0.639***	0.654***	0.652***
	(0.006)	(0.006)	(0.006)	(0.006)	(0.006)	(0.006)
Center Grants (P, M)	0.939*	0.932**	0.942*	0.936*	0.935*	0.910***
	(0.025)	(0.024)	(0.025)	(0.025)	(0.025)	(0.024)
R01 & R01-equivalent Grants	0.895***	0.866***	0.905***	0.878***	0.887***	0.838***
	(0.014)	(0.014)	(0.014)	(0.014)	(0.014)	(0.014)
Other Research Grants (R, K, U)	0.548***	0.530***	0.556***	0.541***	0.561***	0.539***
	(0.010)	(0.010)	(0.010)	(0.010)	(0.010)	(0.010)
Log(Grant Budget)	1.581***	1.577***	1.584***	1.582***	1.599***	1.601***
	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)
MD	0.947***	0.936***	0.950**	0.941***	0.950***	0.946***
	(0.015)	(0.015)	(0.015)	(0.015)	(0.015)	(0.015)
PhD	0.778***	0.788***	0.776***	0.785***	0.777***	0.788***
	(0.011)	(0.011)	(0.011)	(0.011)	(0.011)	(0.011)
Female PI	0.742***	0.738***	0.744***	0.742***	0.743***	0.739***
	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)	(0.008)
PI Career Age	0.982***	0.982***	0.982***	0.982***	0.982***	0.982***
	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)	(0.001)
PI Career Age, squared	1.000***	1.000***	1.000***	1.000***	1.000***	1.000***
	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)	(0.000)
Nb. of Grant Applications	224,131	224,131	224,131	224,131	224,131	224,131
Nb. of Obs.	3,380,837	3,380,837	3,380,837	3,380,837	3,380,837	3,380,837
Adjusted R2	0.087	0.088	0.087	0.088	0.088	0.089

Note: Estimates from logistic specifications. All models incorporate a full suite of application year effects, funding institute effects, grant type effects, and organism type effects. Displayed estimates correspond to exponentiated coefficients. For example, the estimates in column 6 imply that disease-oriented grants are 14.8% more likely than non-disease, non-patient-oriented grants to be associated with a patent.

Robust standard errors in parentheses, clustered at the level of the grant. $^{\dagger}p < 0.10$, $^{*}p < 0.05$, $^{**}p < 0.01$.

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49. For instance, MeSH term C02.782.815.616.400.040 correspond to "Acquired Immunodeficiency Syndrome." All disease terms are in one branch of the MeSH tree—all of them begin with the letter C.
50. For instance, MeSH term B01.050.150.900.090.180.610.500 correspond to xenopus laevis, a common type of aquatic frog often used in developmental biology. All model organisms are in one branch of the MeSH tree—all of them begin with the letter B (including humans).
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