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An Outcome Evaluation of the National Institutes of Health (NIH) Director's Pioneer Award (NDPA) Program, FY 2004–2006

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About this Publication

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Executive Summary

The National Institutes of Health (NIH) Director's Pioneer Award (NDPA) was initiated in fiscal year (FY) 2004 to support individual scientists of exceptional creativity who propose pioneering approaches to major contemporary challenges in biomedical research. The program is approaching its tenth year, which is likely to be the last year it will be fully supported through the NIH Common Fund. To help steer the future directions of the program, the NIH therefore requested that the IDA Science and Technology Policy Institute (STPI) evaluate the NDPA program.

Goals and Parameters of the Evaluation

This evaluation addressed two primary study questions that followed from the program goals stated in the NDPA solicitations: To what extent does the research supported by the NDPA (or the "Pioneer") program produce unusually high impact, and to what extent are the research approaches used by the NDPA grantees (or the "Pioneers") highly innovative? The evaluation also addressed two secondary questions: To what extent is the Pioneers' research interdisciplinary, and to what extent are the Pioneers collaborative?

The evaluation focused on scientific publications between the date of award and the end of 2011. To ensure the entire 5-year NDPA grant period would be covered, the STPI study team included only the first three cohorts of the Pioneers (35 in total), limiting the analysis to awardees in the period FY 2004–2006.

Because some of the study questions are expressed as statements of relative value (e.g., unusually high impact), and because NIH intends to use the evaluation to help decide the future of the program in light of its full portfolio, the study questions were addressed comparatively against the five comparison groups described in the following section.

Comparison Groups

The first comparison group was a matched set of 35 new grants from the NIH Research Project Grant Program (R01) awarded from FY 2004 through FY 2006. The R01 set was constructed statistically using matching methods to ensure that the R01 grantees "looked" enough like the Pioneers that any differences in outcomes could potentially be attributed to the NDPA rather than to characteristics of the investigators.

The second comparison group was the set of 35 recipients of the matched R01 grants. The first group allowed comparison with the NDPA grants (grant-level analysis), and the second group, with the Pioneers (researcher level analysis).

The third group comprised the 39 Howard Hughes Medical Institute (HHMI) investigators who received awards in FY 2005. This group allowed comparison of Pioneer outcomes with those of researchers from a similar research program that purports to fund similarly high-risk high-reward research.

The team chose the 30 NDPA finalists from FY 2004–2006 as a fourth comparison group because finalists have demonstrated the most similarity to the Pioneers with respect to being exceptionally creative researchers having proposed high-risk ideas deemed worthy of consideration to be interviewed in the final round.

The fifth group comprised 30 sets or portfolios of randomly selected new grants issued from FY 2004 through FY 2006. Each set was selected to ensure that their direct costs added up to the same total direct costs as the NDPA portfolio. The portfolio level analysis allowed us to assess how much "impact" the same amount of direct funding would buy in the mainstream grant universe.

Method

The STPI study team performed analyses at both the grant level and the researcher level; grant-attributed publications represent the body of work produced as a result of a particular award, while researcher-attributed publications reflect the effect of multiple grants and funding sources on a researcher's published work. The team analyzed over 20,000 publications and associated meta-data using Thomson Reuters' Web of Science database and the NIH's electronic Scientific Portfolio Assistant (eSPA), Scientific Publication Information Retrieval and Evaluation System (SPIRES), and SPIRES+ databases. The final set included 15,165 grant-attributed publications (518 Pioneer, 295 matched R01, and 14,352 from the random R01 portfolio) and 8,859 researcher-level publications (3,287 Pioneer, 3,274 matched R01, and 2,298 from the NDPA finalists).

The study team employed both bibliometric analyses and expert reviews to measure the scientific impact of researchers and their NDPA research and the innovativeness of their research approaches. Bibliometric analyses included computations of the numbers of citations of awardees, grants, and publications; SCImago Journal Rankings, a measure of journal impact; and h-indices, a measure of scientific productivity and impact based on numbers of publications and citations.

To complement the bibliometric analyses and their associated limitations, PI publications were also reviewed by experts to assess their impact and innovativeness. A total of 94 experts were recruited, and they reviewed 108 sets of "top five" papers from the NDPA award, the matched R01 grants, and the HHMI investigators. A total of 1,923

reviews led to assessments in the form of quantitative ratings and qualitative comments on the impact and innovativeness of the research approaches at a "body of work" and individual paper levels.

Findings and Observations

On indicators of impact, the team found that the Pioneers—at both the grant level and the researcher level—scored as well as or higher than the matched R01 grants and PIs. The reasons for the differences are likely complex. By design, the two groups were well-matched on pre-award PI characteristics and research areas. However, the Pioneers received more funding than the matched R01 PIs, through a grant mechanism intended to provide more flexibility and to fund riskier ideas. The differences between the matched R01 grants and NDPAs are likely not attributable to PI differences or differences in research area, but may be due to differences in funding or programmatic differences.

The random portfolio included 2-3 times as many grants as the Pioneer portfolio, and also produced more publications. However, on bibliometric measures of impact (number of citations, journal impact factors, and h-indices), the Pioneer portfolio scored as well as or higher than the 30 similarly sized random R01 portfolios. Since funding levels for the two portfolios were about the same, the differences between these groups are likely not attributable to funding, but may be due to differences in PI characteristics, research area, or program characteristics.

The Pioneers scored as well as or lower than HHMI investigators scored on all indicators of impact. While both programs provide flexibility and aim to fund riskier ideas, NDPA provides less funding than HHMI. The differences in outcomes are likely due to funding levels, differences in PIs, or differences in areas of science, or other programmatic characteristics.

Last, the Pioneers scored as well as or higher than the NDPA finalists on all measures except interdisciplinarity. The Pioneers and NDPA finalists were well-matched on pre-award characteristics, so these differences are possibly attributable to differences in subsequent funding or research area. The following tables summarize the differences across all groups visually.

Productivity of NDPA Compared with Other Groups

	Matched R01 (Grant Level)	Random R01 Portfolios	HHMI Investigators	Matched R01 (Researcher Level)	NDPA Finalists
Number of publications					
Number of publications per grant funding amount				N/A	N/A

Note: Green indicates that the NDPA group rated *higher* than the comparison group, yellow indicates that the NDPA rated about the *same as* the comparison group, and red indicates that the NDPA rated *lower*. N/A indicates that it was not feasible to perform the requisite analysis.

Bibliometric Impact of NDPA Compared with Other Groups

	Matched R01 (Grant Level)	Random R01 Portfolios	HHMI Investigators	Matched R01 (Researcher Level)	NDPA Finalists
Number of citations per awardee					
Number of citations per grant funding amount				N/A	N/A
Number of citations per publication					
H-index		N/A			
Journal ranking					

Expert Assessed Impact of NDPA Compared with Other Groups

	Matched R01 (Grant Level)	HHMI Investigators
Packets		
Papers		

Expert Assessed Innovativeness of NDPA Research Approaches

	Matched R01 (Grant Level)	HHMI Investigators
Packets		
Papers		

Bibliometric Interdisciplinarity and Collaborations of NDPAs

	Matched R01 (Grant Level)	HHMI Investigators	Matched R01 (Researcher Level)	NDPA Finalists
Integration score				
Number of co-authors				
Number of co-author affiliations				

Note: Green indicates that the NDPA group rated *higher* than the comparison group, yellow indicates that the NDPA rated about the *same as* the comparison group, and red indicates that the NDPA rated *lower*. N/A indicates that it was not feasible to perform the requisite analysis.

Contents

1. Introduction

A. Overview of the Program

The National Institutes of Health (NIH) Director's Pioneer Award (NDPA) was initiated in fiscal year (FY) 2004 "to support individual scientists of exceptional creativity who propose pioneering approaches to major contemporary challenges in biomedical research" (NIH 2004). It grew out of concerns that the traditional NIH peer review process had become overly conservative and the belief that the NIH required specific means to fund high-risk research (Brenner 1998, Mervis 2004).

The program provides individual researchers (called "Pioneers") with $500,000 in direct costs for each of the 5 years, for a total direct cost of $2.5 million. Compared to the average NIH Research Project Grant Program (R01) grant, the NDPA provides a greater amount of funding per year over a longer duration, and does not require a project budget specifying how the funds will be allocated.

The NDPA is currently administered through the NIH Office of the Director and is annually awarded to a small number of researchers across a range of scientific disciplines. Since 2004, the NDPA has been awarded to over a hundred Pioneers.

B. Purpose of the Outcome Evaluation

FY 2013 will be the NDPA's tenth year and its last supported fully through the NIH Common Fund, which supports trans-NIH programs with participation of two or more NIH Institutes and Centers (ICs). After this year, the program will remain within the Office of the Director, but only the first year of the awards will be funded by the Common Fund; future years of the program are expected to be funded or co-funded by the individual ICs.[1]

To facilitate future IC participation, NIH Director Francis Collins requested that the IDA Science and Technology Policy Institute (STPI) compare NDPA to other grant programs in order to evaluate its effectiveness in producing high-impact research. Prior process and outcome evaluations of the NDPA program provide details on the program's inception, evolution, selection, outputs, and outcomes.[2]

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[1] Email correspondence with an NIH program officer.

[2] The reports summarizing these analyses are available on the NIH Common Fund website, http://commonfund.nih.gov/pdf/Pioneer_Award_Outcome%20Evaluation_FY2004-2005.pdf and http://commonfund.nih.gov/pdf/PioneerAwardProcessEvaluation_2004-2008.pdf, accessed June 11, 2012.

C. Study Questions

The NDPA solicitation provides the framework for the goals of this evaluation. The 2012 solicitation, which has not changed significantly since the program's inception, begins with the following statement:[3]

> Pioneer Awards are designed to support individual scientists of exceptional creativity who propose pioneering—and possibly transforming—approaches to major challenges in biomedical and behavioral research. The term "pioneering" is used to describe *highly innovative approaches* that have the potential to produce an *unusually high impact* on a broad area of biomedical or behavioral research…. (Italics added.)

This program goal established the evaluation's primary study questions, which are:

- To what extent does NDPA-funded research produce *unusually high impact*?
- To what extent are the *research approaches* used by the Pioneers highly innovative?

The evaluation also addresses two secondary questions that emerged from NIH leadership's interest in high-risk, high-reward research and are of special interest to the science and technology policy community. They also have strong policy implications. The secondary questions are:

- To what extent is the Pioneers' research interdisciplinary?
- To what extent are the Pioneers collaborative?

D. Scope of the Evaluation

1. Conceptualizing the Approach

Science progresses through a combination of incremental and breakthrough research—both are essential for progress. In the current traditional research portfolio (e.g., R01), some percentage of the funded research outcomes are breakthrough—primarily through serendipity. If there is to be a focused effort on producing breakthrough research through a set-aside program (such as the NDPA), to justify the new program, either the percentage of breakthrough research must be greater for the set-aside program than the traditional program, or the amount of "breakthrough-ness" achieved per breakthrough must be greater.

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[3] Department of Health and Human Services, Funding Opportunity Announcement RFA-RM-11-004, August 5, 2011, http://grants.nih.gov/grants/guide/rfa-files/RFA-RM-11-004.html, accessed December 12, 2011.

The Pioneer program does several things to distinguish itself from traditional research programs. For example, it attracts highly meritorious researchers, whether recognized as such in the community or not; encourages them to propose high-risk ideas; gives them a larger sum of money and a longer time horizon; and gives them the flexibility to do what they need to do to pursue their high-risk ideas. The combination of exceptionally bright people pursuing high-risk ideas, in theory, increases either the probability of producing pioneering research outcomes—as distinct from incremental advances, or the degree of "pioneeringness" of the research outcomes.

Building on this rationale, the study team developed a conceptual approach to the evaluation. The evaluation examined how NPDA outcomes differentiate themselves from traditional research outcomes. There are two ways this differentiation could manifest itself. In one manifestation, the distribution of pioneeringness, however it is measured, shifts rightward, meaning that as a result of NDPA support, the overall pioneeringness of an entire group of researchers improves. This is represented in Figure 1 by the notional normal curve shifted below wholesale (dotted blue line). Alternatively, NDPA support could enable a larger number of instances of extreme pioneeringness. This could occur were NDPA support to increase the variance of the distribution by changing the shape of the distribution so that there was a longer tail in Figure 1 (dotted red line). In either case, NDPA could increase pioneeringness, although in the latter case, increased pioneeringness as measured by a longer tail comes at the cost of an increased percentage of supported awards that are unsuccessful.

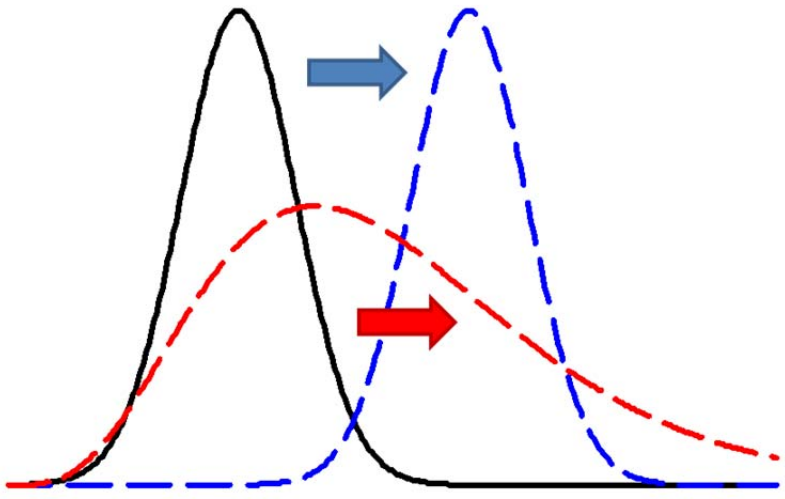


Figure 1. Notional Manifestation of Two Types of Differences (Shifts) in Performance

2. Operationalizing Terms of Interest

After conceptualizing the evaluation, the study team considered ways to operationalize the key metrics of interest. The first primary study question focused on the concept of unusually high impact. The term "impact" is not defined in the solicitations, and in general is a concept that is difficult to quantify or standardize. Unusually high impact is even more problematic to quantify. The solicitation attempted to clarify its expectations, and requested that, in their research strategy sections, applicants explicitly address the question: "What are the pioneering, and possibly high-risk, approaches that, if successful, might lead to groundbreaking or paradigm-shifting results?" However, terms such as "paradigm shifting" and "groundbreaking" are no easier to define and operationalize than "impact."

Godin and Dore (2004) propose a broad definition of scientific impact: the contributions to research through publications, including diffusion and appropriation of new knowledge, theories, methodologies, models, and facts; the formation and development of specialties and disciplines; the diversification of the type of research conducted (basic, applied, strategic), and the development of interdisciplinary, intersectoral, and international research. As a first step, in this evaluation, the team took a narrow definition of scientific impact and examined impact only as expressed in scientific publications of researchers.

The second study question explores the concept of the innovativeness of research approaches. Again, while the term has many interpretations, it is difficult to standardize. Given these difficulties, the team approached the evaluation from two directions.

First, the team decided to follow a multi-method approach to include both objective and subjective assessments. The objective approach involved identifying bibliometric indicators of interest (Chapter 3 describes them in detail), and the subjective approach involved asking experts to provide a rating and discussion of impact and innovation with regard to the research in question. While the experts were provided high-level guidance on how to think about impact and innovation of research approaches, ultimately it was a subjective judgment on their part.

Second, the team determined that any assessment of NDPAs or the Pioneers would be meaningful only in comparison. (Whether NDPAs yield "more" impact begs the question "compared to what.") This required a choice of comparison groups that were meaningful and had policy relevance. To fully isolate the effect of the Pioneer program would require randomizing principal investigators (PIs) to grant mechanisms; failing this, the team chose comparison groups that overlap with NDPA in substantive ways.

3. Other Parameters to Bound the Evaluation

While the Pioneer program is ongoing, and eight cohorts of awards have been made since inception, this evaluation covers the 35 NDPAs from the first three cohorts (FYs 2004–2006). This was to ensure that the award period was complete and that (almost) all outputs of the awards had had a chance to be reviewed in the community.

As discussed previously, while there are many ways research creates impact, this evaluation focuses on impact as evident in scientific publications. Excluding materials like textbooks, websites, databases, and other outputs of research certainly limits the scope of the evaluation; however, it makes the data and findings more comparable.

Since researchers typically received multiple grants, to ensure appropriate comparison, analyses were performed at both the grant level and the researcher level. Grant-level analyses allow for the comparison of just the output of grants; researcher-level analyses permit inclusion of the publications of multiple grants and funding sources.

E. Overview of the Report

Chapter 2 describes the methods used to select and construct the comparison groups and summarizes data collection approaches. Chapter 3 describes the analytic methods used both for the bibliometric analyses and for the expert review. Chapter 4 presents findings on impact and innovation at the grant level. Chapter 5 presents these findings at the researcher level. Chapter 6 explains qualitative findings from the expert assessment, and Chapter 7 provides findings related to interdisciplinarity and collaboration. Chapter 8 summarizes all the findings. Appendix A provides lists of figures and tables in the main report, and Appendix B through Appendix I provide supporting details.

2. Data

A. Description of Comparison Groups

The study team used five different groups of awards/awardees for comparison with the NDPA and Pioneers. These groups, which are described in the following subsections, are: a matched set of 35 FY 2004–2006 NIH Research Project Grant Program (R01) grants, the 35 PIs on the same R01 grants, 30 FY 2004–2006 random R01 portfolios that received comparable amounts of funding to the NDPA portfolio, 39 FY 2005 Howard Hughes Medical Institute (HHMI) investigators, and 30 FY 2004–2006 NDPA finalists. Appendix B describes these groups and additional comparison groups considered before settling on these five groups. Appendix C provides profiles of the researchers that form the groups used for comparison purposes.

1. Matched Set of R01 Grants and PIs

The R01 is the original and historically oldest grant mechanism used by the NIH to support biomedical research and health-related research and development.[4] R01 applications may be initiated by the investigator or in response to a program announcement or request for applications.

Successful R01 applications are funded through one or more of the NIH's 27 Institutes and Centers, which have research agendas that often focus on specific diseases or body systems.[5] Grants are generally awarded for up to 5 years. In FY 2011, R01 PIs received an average of $440,000 for one year.[6]

From FYs 2004 to 2006, the NIH funded 12,007 new (Type 1) R01 applications. This is the population of R01 grants from which the team derived the matched set of R01 grants. Since R01 grants are the most traditional research grant at the NIH, they provide a comparison group that helps clarify the effect of the mechanism on research impact and innovation. The scope of the R01 set was limited to Type 1 applications because NDPA projects support new research ideas.[7] The team considered R01 PIs from FY 2004

[4] For more information on the R01 mechanism, visit: http://grants.nih.gov/grants/funding/r01.htm.

[5] For more information on the NIH's Institutes and Centers, visit: http://www.nih.gov/icd/.

[6] For more information on awards, visit NIH RePORT Funding Facts at http://report.nih.gov/fundingfacts/index.cfm.

[7] For more information on NIH application types, visit: http://grants.nih.gov/grants/glossary.htm#A27.

through 2006 to keep the bibliometric measures, which are time sensitive, as comparable as possible.

a. Construction of the Matched R01 Set

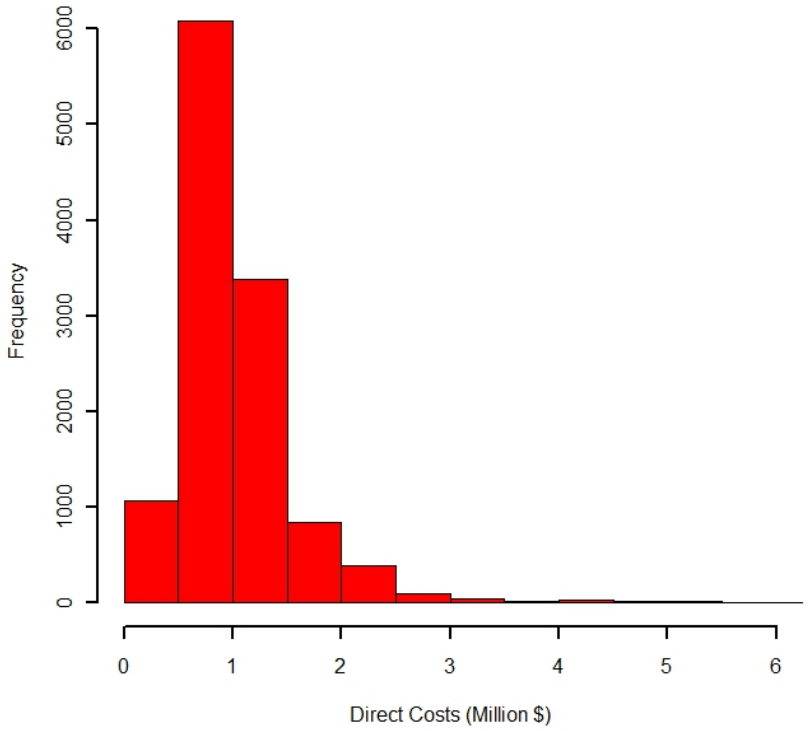
The matched R01 comparison groups were not selected randomly. This particular part of the evaluation used a quasi-experimental design. Quasi-experimental designs are typically developed when the evaluator must collect data after the program has been initiated or even completed. Because of these characteristics, evaluators compare the outcomes of the people who participated in the program with individuals that did not, and use statistical methods or research design methodologies to estimate the causal impact of the program. These methods are required because the causal impact can be difficult to disambiguate without them for several reasons, most notably non-random assignment to the program or treatment.

Non-random assignment happens because characteristics that predict which individuals self-select or are selected into a program or treatment are correlated with the outcome variable. An example would be nutritional classes for overweight people. If the participants self-select into a class (people who are motivated are more likely to sign up for these classes and therefore lose more weight), the measured treatment effect (for example, pounds lost), may be biased if the outcome is compared to people who did not participate, since the changes may be due to the motivation and not the actual treatment.

For this evaluation, the study team constructed a control group that removes many of these differences between the control and comparison groups. The construction of a control group can be done many different ways (Guo and Fraser 2010); this evaluation uses matching methods. Matching has been defined broadly as a method that aims to create a comparison group with equal or "balanced" distribution of specific covariates between the treated and the comparison group (Stuart 2010). Specifically, this evaluation used the rank-scale Mahalanobis distance approach, which uses a robust distance metric to account for nominal, ordinal, and continuous covariates (Rosenbaum 2005). This method was useful because the construction of the comparison group also included additional constraints, discussed below.

To construct a matched set of R01 grants, the team started with the 12,007 Type 1 R01 grants awarded in FYs 2004–2006. One observed covariate is the total direct cost of the grant. For NDPA, this is $2.5 million (M) over 5 years. For the population of Type 1 R01 grants awarded in FYs 2004–2006, the distribution of direct costs is given in Figure 2. Grants of $2.5M are uncommon; only 2% of the R01 grants considered received $2.5M or more. (As a note, 84% of these were awarded for 4 or 5 years, with one awarded for 6 years and the remainder for 1 to 3 years.)

As a first step, the team considered comparably sized R01 grants by restricting the set to the 183 R01 grants with total direct costs between $2.25M and $2.75M. Each of these was identified as either basic or clinical; approximately 85% of the R01 grants with these direct costs were clinical. NDPA, on the other hand, funds more basic research (Lal et al. 2010). The team decided that a comparison of the outcomes of basic and clinical research would introduce an uncontrolled source of variation into the results and would be an inappropriate comparison group.



Note: Seventeen awards with total direct costs above $6M are not displayed here.

Figure 2. Distribution of Direct Costs for Type 1 R01 Grants, FY 2004–2006 (*n* = 12,007)

The team next focused on identifying R01 grants that were topically similar to the NDPAs. In collaboration with Edmund Talley of the NIH, the study team used the NIH Topic Mapping Tool (Talley et al. 2011) to identify 821 R01 grants that were topically similar to the research being conducted by the Pioneers. This methodology uses Latent Dirichlet Allocation to categorize unstructured text. Some R01 grants were topically similar to more than one NDPA; overall there were 730 unique R01 grants identified. This evaluation uses the term “research strata” to refer to the groups of R01s that are similar to the NDPAs.

Exactly one R01 was chosen from each research stratum under the constraint that the 35 R01s chosen must (1) contain the same distribution as for the NDPAs (9 awarded in FY 2004, 13, in FY 2005, and 13, in FY 2006) and (2) be as close as possible to the NDPAs on a set of other characteristics. Choosing one R01 from each research stratum requires *fine balance*. "Closeness" is measured using the rank-scale Mahalanobis distance described by Rosenbaum (2005). The variables used are year since degree, institutional prestige, prior NIH funding, terminal degree(s) received, receipt of early career awards, and receipt of R01 award within 5 years of most recent research or clinical doctorate. These variables are described in more detail in the next section.

A comparison of the funding received by the matched R01 awards and an NDPA award is shown in Figure 3. The specific R01 grants selected for the comparison group are listed in Table 1.

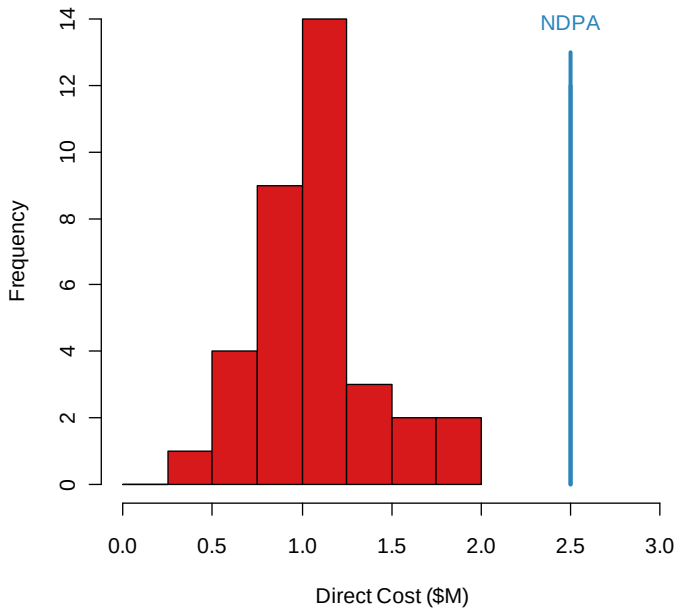


Figure 3. Matched R01 Funding Compared to NDPA Funding

Table 1. R01 Grants Selected for Comparison Group

IC	R01	Grant
NCI	R01CA107338	Mechanisms of HPV DNA Segregation
NCI	R01CA120480	Molecular Contrast Agents Based on Gold Nanocages for OCT Imaging of Cancer
NCI	R01CA112075	Using Viral Nanoparticles to Target Cancer
NCRR	R01RR019652	A Microscale Sorting Cytometer for Cell-Based Screens
NEI	R01EY014454	Functional Circuitry of Visual Adaptation
NEI	R01EY015788	Mechanisms of Visual Map Development
NHLBI	R01HL080627	Hematopoietic Development From ES Cells
NHLBI	R01HL077095	Immune Response to Pneumocystis in Simian Model of AIDS
NIA	R01AG024398	A Unique Murine Model for Human Aging
NIA	R01AG023321	Regulation of Apoptosis in C. elegans
NIA	R01AG028490	Molecular Structures and Kinetics of Amyloid Intermediates by Solid-State NMR
NIAID	R01AI069341	Measuring Entomological Risk for Dengue
NIAID	R01AI067712	Surface Protein Dynamics in Live Bacterial Pathogens
NIAID	R01AI067704	Mechanisms of Genomic RNA Packaging in Influenza Virus
NIAID	R01AI054515	Structure and Function of Antimicrobial Peptides
NIAMS	R01AR052672	Cloning and Genetics of Human Pemphigus Autoantibodies
NIAMS	R01AR052713	The Regulation of Keratinocyte Stem Cells
NIBIB	R01EB003537	Interferometric Nano-sensing for Biochemical Analysis
NIDA	R01DA018799	Mapping Neural Circuits Using Pseudorabies Virus Vectors
NIDCD	R01DC007124	Dynamics of Vocal Tract Shaping
NIDCR	R01DE015847	New Pathogens for Childhood Caries
NIDDK	R01DK072234	Damage and Regeneration in the Hematopoietic System
NIEHS	R01ES015165	Identification and Characterization of Epigenetically Labile Genes
NIGMS	R01GM073089	Interconversion of Specificity within Enzyme Families
NIGMS	R01GM073655	Molecular Mechanisms of Cellular Mechanics
NIGMS	R01GM069551	Eukaryotic Phosphofructokinase: Structure/Function
NIGMS	R01GM074756	Foldamers: Novel Ligands for Diverse Protein Surfaces
NIGMS	R01GM074746	Tetrahymena Basal Body Duplication
NIGMS	R01GM077331	Microfluidic Temperature Steps to Understand Robustness of Embryonic Development
NIGMS	R01GM068462	Repeat-Proteins: Stability, Folding Kinetics, and Evolution
NIMH	R01MH074847	Neuroanatomy of Anticipation in Anxiety Disorders
NIMH	R01MH073435	Role of Hypocretin in Metabolic Effects of Sleep Loss
NIMH	R01MH077769	Use-Dependent Intrinsic Plasticity in the Cerebellum
NINDS	R01NS045702	A Common Glial-Neuronal Progenitor in Postnatal Brain
NINDS	R01NS048435	Role of IL-12/IL-23 in Intravenous Tolerance

Note: See the abbreviation list at the end of this report for the full names of the ICs abbreviated here.

a. Variables Used

A quasi-experimental design requires the construction of a comparison group that looks like the group of interest in ways that predict treatment and affect outcome. This section describes the covariates used to develop a sample of R01s. For both populations, the team collected data from Query/View/Response (QVR), the NIH's internal interface for accessing information on funded and unfunded grant applications (NIH 2007). Additional data were collected from collaborations with an NIH topic modeling group, the National Science Foundation (NSF) website and award search database,[8] press releases, and program websites.

1) Subject Area Distribution

Edmund Talley's topic modeling group at the NIH generated a graph-based layout algorithm of two-dimensional visualized output for all funded NIH grants whereby documents are clustered based on their topic- and word-based similarity over a visual map (Talley et al. 2011). Figure 4 is a visualization of NDPAs in the overall NIH grant landscape. The team reasoned that subject area would have an effect on the bibliometric research outcomes because Cameron (2005) suggests that different research fields have different publishing patterns and citing conventions.

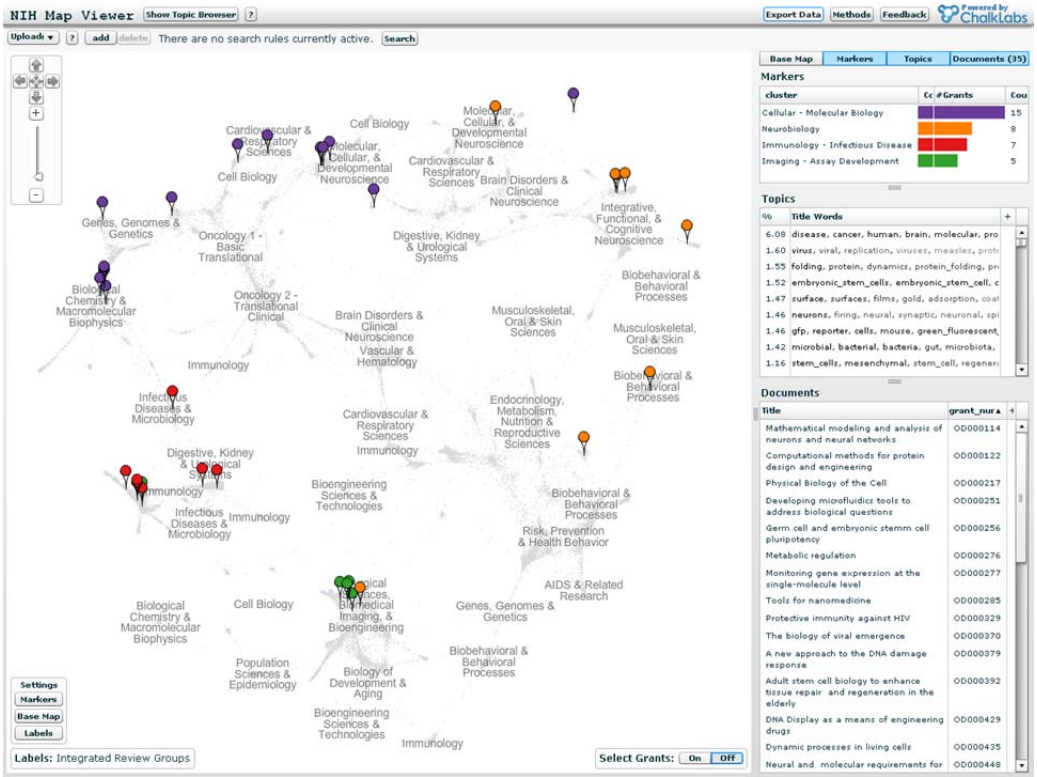


Figure 4. Map of NDPA Research Areas within the NIH Landscape

[8] NSF's award search database can be accessed at http://www.nsf.gov/awardsearch/.

2) Principal Investigator (PI) Characteristics

Using QVR, the study team gathered information about the personal characteristics of the PIs in the NDPA and R01 populations. Data were obtained on institution at the time of award, year of doctoral degree conferral, and doctoral degree type(s). Using the SCImago Institutions Ranking (SIR), the team gathered information on the rank of each PI's institution at time of award.[9] The team also determined whether individuals in the NDPA and R01 populations received early career awards in the years prior to and including their year of grant receipt.

Using public sources such as NSF's award search page[10] and NSF and NIH program-related press releases,[11] the team collected information on the following prestigious early career award programs that target their support towards early tenure-track faculty members and award scientists across different fields of research:

- NSF Faculty Early Career Development (CAREER)
- NSF Presidential Young Investigator (PYI)
- NSF Young Investigator (NYI)
- NSF Presidential Faculty Fellowship (PFF)
- NIH Presidential Early Career Awards for Scientists and Engineers (PECASE)[12]

Previous NIH funding data are available from QVR, the NIH's web-based tool on grant applications and awards. In a compiled database of all NIH funding prior to 2007, automated steps and human judgment were used to clean PI names, and CVs were compared to grant information to verify grant attribution. The prior NIH funding variable is a sum of the direct and indirect costs awarded through the R01 mechanism prior to and including FY 2004. Funding amounts were reported in current dollars each year, and there was no attempt to normalize the data for real dollar amounts. In addition to total R01 funding, another covariate available through QVR is the year of first R01 receipt. This variable denotes the year in which the PI of interest was awarded the first R01 as the lead PI.

Raw degree data for PIs were also obtained through QVR. The degrees obtained were categorized into "research" and "clinical" doctorates. As a starting point for identifying which doctoral degrees may be considered research doctorates, the NSF's

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[9] For more information on SIR, visit: http://www.scimagoir.com/.

[10] NSF's award search page can be accessed here: http://www.nsf.gov/awardsearch/.

[11] Further information on the National Science Foundation early career awards chosen for these analyses can be found in National Science Foundation (2001), available at http://www.nsf.gov/pubs/2001/nsf01118/nsf01118.pdf.

[12] Further information on the NIH PECASE program is available at: http://grants.nih.gov/grants/policy/pecase.htm.

Survey of Earned Doctorates was consulted.[13] Additional judgment was used to categorize clinical degrees and doctorates not explicitly mentioned in the Survey of Earned Doctorates. Table 2 identifies which degrees were considered research and which were considered clinical. Number of years since degree was calculated from the most recent research or clinical doctorate.

Table 2. Research and Clinical Degrees

Research Degrees	Clinical Degrees
doctor of philosophy	doctor of dental surgery
doctor of public health	doctor of dental medicine
doctor of education	other doctorate of medical dentistry,
doctor of social work	doctor of nursing science
doctor of science	doctor of nursing practice
	doctor of osteopathy
	doctor of podiatric medicine
	doctor of veterinary medicine
	other doctor of veterinary medicine
	bachelor of medicine
	bachelor of medicine and bachelor of surgery
	doctor of medicine
	doctor of optometry
	doctor of pharmacy
	doctor of psychology

Note: Only degrees found among the Pioneer and R01 PI populations are listed in the table.

One of the NDPA review criteria in FYs 2004–2006 was "evidence of prior willingness to take risks or inclination towards creative and innovative research." Receipt of an early career award is an observable variable that has been linked to creativity and innovation (Azoulay et al. 2011).

After data on early career awardees were obtained, individuals were matched by their full names. Year of early career award receipt was also noted. Once the early career awardees were matched to the correct PIs in the compiled dataset, the team derived the binary variable "Receipt of Early Career Award." This variable indicates whether the researcher received at least one early career award in a year prior to or including the year of grant receipt.

The team chose to use the SIR to assess the prestige of the institution at which the PI was employed at the time of grant award (SCImago Research Group 2011a). The

[13] Data from NSF's Survey of Earned Doctorates is summarized in NSF (2010), http://www.nsf.gov/statistics/nsf11306/. Research degrees are identified in appendix table A-2: Research degrees included in the Survey of Earned Doctorates: 2005-09.

SCImago Research Group uses four indicators based on scientific output and citations to evaluate institutional research performance. The data for these rankings comes from Scopus. The indicators are output (number of scientific papers, pro-rated for co-authorship), percentage of international collaborations, normalized impact[14] ("the ratio between the average scientific impact of an institution and the world average impact of publications in the same time frame, document type, and subject area"), and the ratio of publications in first quartile journals.

The team reasoned that these PI-level characteristics would have an effect both on the likelihood of being selected for an NDPA and on the research outcomes of the award. Year of degree conferral is a proxy for research experience, SIR is a proxy for the research infrastructure supporting the PI, and early career award receipt is a proxy for the researcher's potential for conducting high-impact research.

The team used the American rankings for institutions; institutions outside the United States were assigned the ranking of the American institution closest to but below it in the World Rankings.

3) Research Grant Characteristics

Using QVR, the study team gathered information on the R01 the fiscal year of the award, grant's award length, and the sum of the direct costs of funded Type 1, Type 3, and Type 5 awards attributed to that grant number.

Since bibliometric measures of impact are time-sensitive, the fiscal year of the award became an important consideration in creating the matched R01 set. Two of the unique features of the NDPA mechanism are the 5-year award length and the $2.5M direct costs, so the team reasoned that matching R01s on award length and direct costs would help with understanding the effects of the NDPA and R01 mechanisms as opposed to the effect of disparities in research funding support.

2. R01 Portfolios

Another comparison group of R01 grants was constructed to enable a comparison by direct cost. Using the same 12,007 base set of R01-funded grant applications used in developing the matched R01 group, the team selected 30 random samples of Type 1 R01 grants based on total direct cost. No matching was done for PI characteristics or for area of science. The direct costs of the random samples were stratified by year such that the total direct cost for grants in a given start year from FY 2004 through FY 2006) mirrored

[14] Normalized impact is computed using a methodology established by the Karolinska Intitutet in Sweden, where it is named "item oriented field normalized citation score average."

that of NDPA.[15] While it was not possible to get an exact match on direct costs, matches were made as close as possible. Figure 5 shows the distribution of total direct costs for the 30 R01 portfolios compared with that for NDPA.

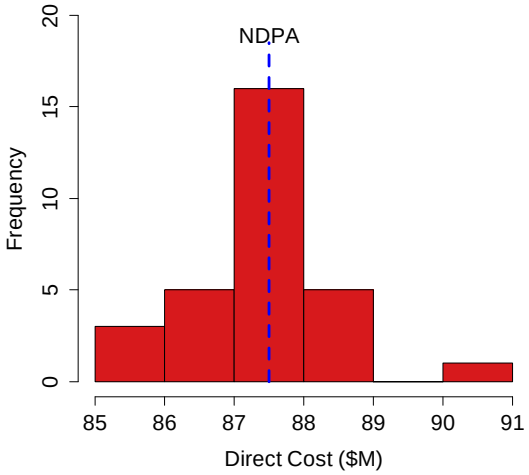

Figure 5. Distribution of Total Direct Cost for the 30 R01 Portfolios

A difference in funding levels between R01s and NDPAs (on a per grant basis) resulted in a larger number of grants per R01 portfolio when compared to the NDPA portfolio. Figure 6 compares the distribution of R01 grants per portfolio with that of NDPA.

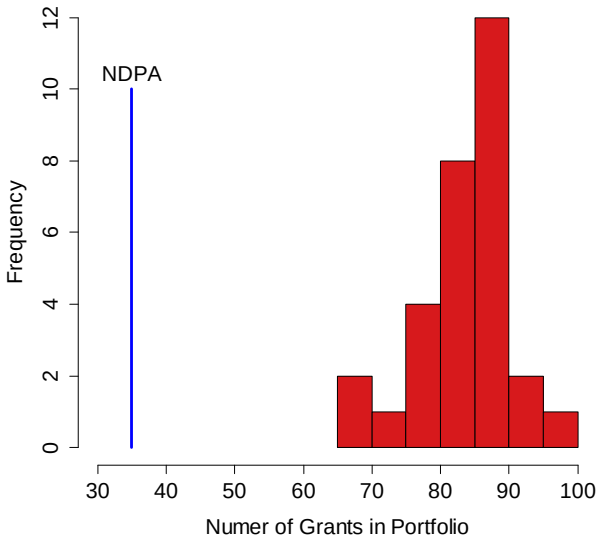

Figure 6. Distribution of Number of R01 Grants per Portfolio Compared with NDPAs

[15] NDPA issued 9 grants in FY 2004 (direct cost ~$22.5M), 13 grants in FY 2005 (direct cost ~$32.5M), and 13 grants in FY 2006 (direct cost ~$32.5M).

3. HHMI Investigators

HHMI investigators were included as a comparison group because, like the Pioneers, they are also high-performing researchers funded at significantly higher levels than the traditional R01 awards. The Howard Hughes Medical Institute is one of the largest nonprofit biomedical research institutes in the world. There are approximately 330 current HHMI investigators. This prestigious group of researchers includes 13 Nobel laureates and 147 members of the National Academy of Sciences The HHMI website describes the program purpose as follows:[16]

> By appointing scientists as Hughes investigators, rather than awarding them grants for specific research projects, the investigators are provided with long-term flexible funding that gives them the freedom to explore and, if necessary, to change direction in their research. Moreover, they have support to follow their ideas through to fruition—even if that process takes a very long time.

In support of this purpose, HHMI has had a variety of selection processes over the years. In 1995, the first formal competition took place when HHMI solicited the presidents and deans of the top 200 NIH-funded universities for researcher nominations.[17] The comparison group of 39 FY 2005 HHMI investigators was selected using this process. The May 2004 solicitation asked for "candidates from the full range of biological and biomedical inquiry who demonstrate exceptional promise early in their careers as independent researchers"[18] It also required that the investigators be 4 to 10 years from their first faculty appointment.

Starting in 2009, HHMI changed the selection process from a nomination-based process to an open competition. The frequency of the competitions varies and is at the discretion of the HHMI staff.

Additional characteristics of HHMI investigator support underscore the "person focus" as opposed to a traditional "project focus" of the award. When HHMI investigators are selected, they and some of their staff become employers of HHMI while the university where they work becomes the host institution. Total direct costs are approximately $650,000 per year.[19] Funding amounts differ between investigators for a variety of reasons, one being that investigators can apply for equipment funds, which are awarded as needed. They are also required to spend at least 75% of their time conducting biomedical research. Chapter 5 provides additional information about HHMI funding.

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[16] About HHMI Investigators: http://www.hhmi.org/research/investigators/.

[17] HHMI Institute News, "HHMI Taps 43 of the Nation's Most Promising Scientists," http://www.hhmi.org/news/032105.html, March 21, 2005.

[18] HHMI Research News, "Howard Hughes Medical Institute Seeks Up to 50 New Scientists," May 13, 2004, http://www.hhmi.org/news/pdf/051304.pdf.

[19] Figure comes from discussions with HHMI staff and program leadership.

Finally, in the belief that truly transformative research is accomplished over a long period of time, reappointment at the end of the 5-year award period is possible. A review panel evaluates the past achievements of the investigator; reappointment rate is approximately 80%, and investigators usually stay with HHMI for an average of 15 years.[20]

4. NDPA Finalists

In each year of the NDPA, the NDPA Oversight Committee co-chairs selected between 22 and 25 of the most promising applicants to present their ideas and interview with a panel of external experts at the NIH campus. These application finalists were selected using a combination of criteria, which included average overall application scores, "top four" scoring designations, other potential funding sources (e.g., interviews were not given to candidates who received HHMI fellowships while in consideration for the NDPA), and factors related to demographic and scientific diversity.[21]

Each finalist gave a 15-minute presentation and answered questions from the external review panel. Panelists then placed the finalists into three tiers. Interviewees in the top tier were recommended by the panel for funding, those in the middle tier were suggested for funding if money was available, and those in the bottom tier were not recommended for funding.

There is little documentation of the final phase of the NDPA selection process, though it is known that the NIH Director and the Advisory Committee to the Director, with input from NDPA program leadership, made final decisions on the award winners in all years. The likelihood of receiving an award was not based solely on the tiered decisions made by the interview panelists; program leadership also considered more subjective factors (i.e., existing funding, other potential funding sources, likelihood that the research could be funded with R01s, etc.) in the final phase of the selection process.[22]

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[20] Conversation with Philip Perlman, VP of Research, HHMI, December 19, 2011.

[21] Finalists cannot be predicted solely from average overall scores and top four designations. In each year, individuals who had higher scores and more top four designations than some of the interviewees (and awardees) were not asked to interview. Conversely, some individuals asked to interview had lower scores and only one top four designation. Talks with NDPA program leadership revealed that other funding sources, demographic diversity, and scientific diversity were additional factors in the finalist selection process.

[22] For further information on the NDPA selection process, see Lal et al. (2010), https://commonfund.nih.gov/pdf/PioneerAwardProcessEvaluation_2004-2008.pdf.

The NDPA finalist comparison group of 30 NDPA applicants who did not receive NDPA funding in FYs 2004–2006[23] had several limitations. First, whether the finalists' NDPA-proposed ideas were subsequently pursued and funded was unknown. Further, information was incomplete regarding the amount of research funding finalist received subsequent to their application to the NDPA. Nevertheless, the team made the assumption that finalists continue to be productive biomedical researchers after their unsuccessful NDPA application. Due to the quality of the researchers and their potential for pioneering research, NDPA finalists were useful in comparisons to Pioneers at the researcher level.

B. Comparison Groups at Time of Award

To assess the appropriateness of the comparison groups selected, the study team examined several other variables that might influence post-award outcomes at baseline, that is, at time of award. As Figures 7 through 12 indicate, the Pioneers look similar to the matched R01 PIs, HHMI investigators, and NDPA finalists on most of these accounts. Although the covariates shown in Figures 7 through 12 were not used to select any of the comparison groups, overall, the groups appear to be quite comparable at time of award.

Figure 7 shows box plots for years since degree for the comparison groups. Results of a Kolmogorov-Smirnov test (K-S) indicates the HHMI group is statistically younger than the NDPA Pioneer group (K-S, $p = 0.0007$), which is not surprising since the HHMI investigators are chosen to be 4 to 10 years from first faculty appointment. The PIs from the grants selected in the random R01 portfolios ($n = 2297$) are also statistically different from the NDPA Pioneers (K-S, $p = 0.004$).

Figure 8 shows box plots for the SIRs for researchers' home institutions at time of award. The rankings for the NDPA Pioneers were similar to those for the matched R01 PIs (K-S, $p = 0.97$), HHMI investigators (K-S, $p = 0.91$), and NDPA finalists (K-S, $p = 0.99$). The rankings for the institutions of the random R01 portfolios are statistically different from those of the NDPA Pioneers (K-S, $p < 0.0001$).

Figure 9 shows box plots for the number of publications per researcher at time of award. NDPA Pioneers had similar citation distributions as the matched R01 PIs (K-S, $p = 0.63$), HHMI investigators (K-S, $p = 0.44$), and NDPA finalists (K-S, $p = 0.62$). Figure 10 shows box plots for the number of citations per researcher at time of award. NDPA Pioneers had similar citation distributions as the matched R01 PIs (K-S, $p = 0.63$), HHMI investigators (K-S, $p = 0.44$), and NDPA finalists (K-S, $p = 0.62$). Figure 11

[23] Two of the 32 NDPA finalists from the FY 2004–2006 application processes were removed to compose the comparison group of 30 finalists. One 2004 finalist was excluded because she received an NDPA in 2005 and is evaluated as an NDPA awardee. A second investigator (Steve Benner) was a finalist in both 2004 and 2006. The study team considered him only once as a 2004 finalist because the information on his application was more complete for that year.

shows box plots of the researcher h-index at time of award. The NDPA Pioneers had similar h-index values as the matched R01 PIs (K-S, $p = 0.80$), HHMIs (K-S, $p = 0.62$), and NDPA finalists (K-S, $p = 0.19$).

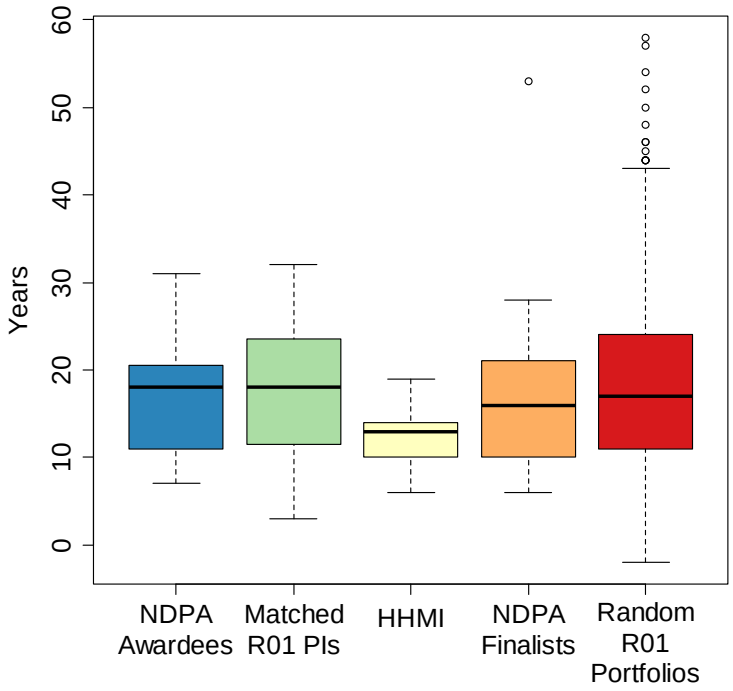


Figure 7. Years since Degree at Time of Award

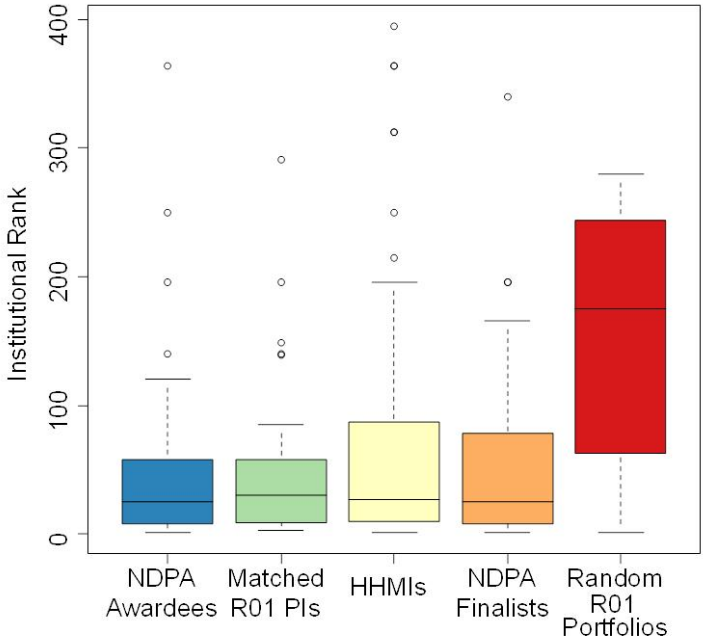


Figure 8. SCImago Institutions Rankings at Time of Award

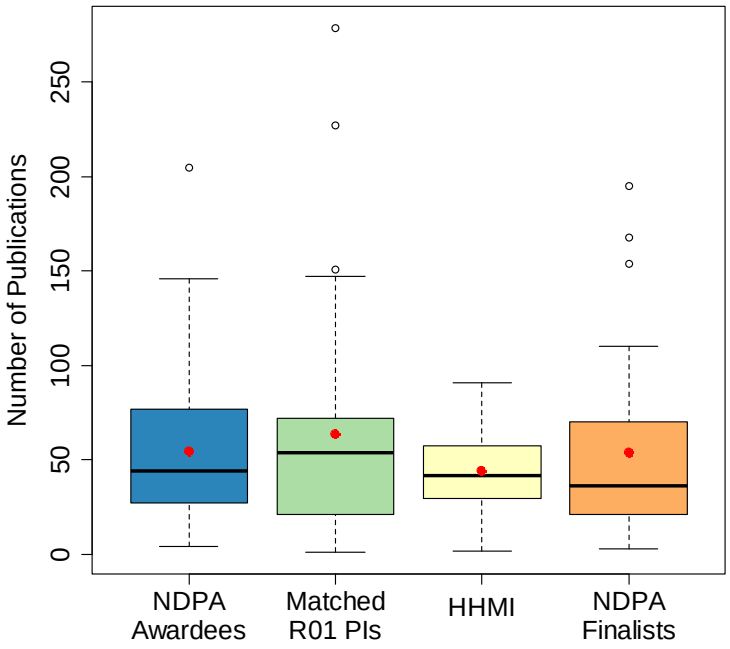
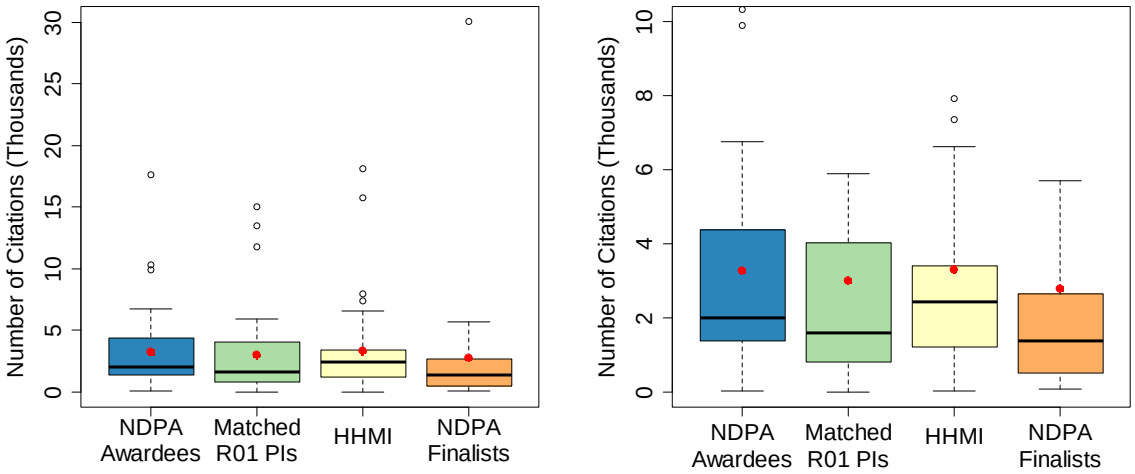


Figure 9. Number of Publications at Time of Award



Complete **Magnified**

Figure 10. Number of Citations at Time of Award (Complete and Magnified)

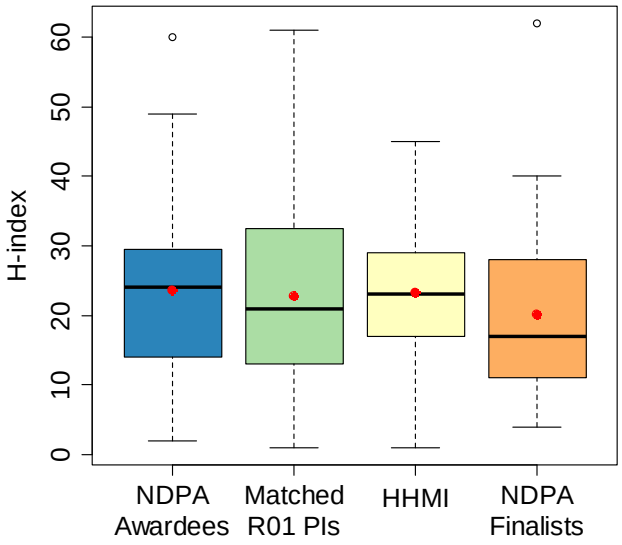


Figure 11. H-index at Time of Award

Figure 12 shows box plots of the integration score at time of award. Integration score is a measure of interdisciplinarity and is discussed in detail in Chapter 3. NDPA Pioneers are similar to the matched R01 PIs (K-S, $p = 0.64$) and the NDPA finalists (K-S, $p = 0.23$), but are more interdisciplinary than HHMI investigators (K-S, $p = 0.03$).

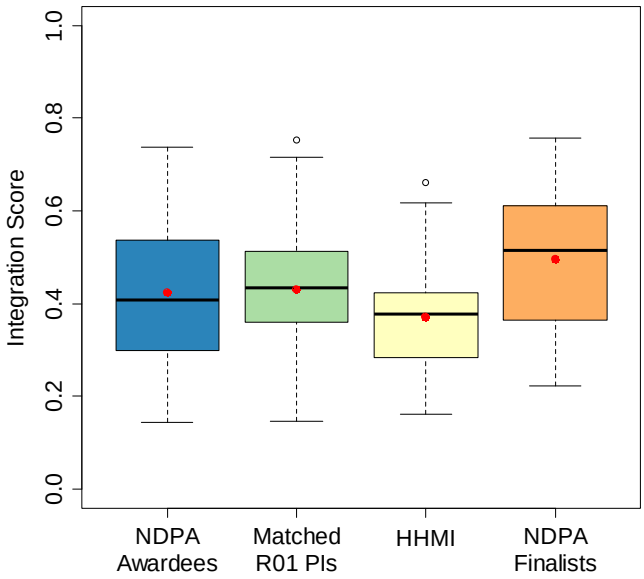


Figure 12. Integration Score at Time of Award

Figure 13 shows box plots of the number of unique co-authors working with each researcher prior to time of award. NDPA Pioneers are similar to the matched R01 PIs, HHMI investigators, and NDPA finalists (K-S, $p = 0.63, 0.82, 0.21$).

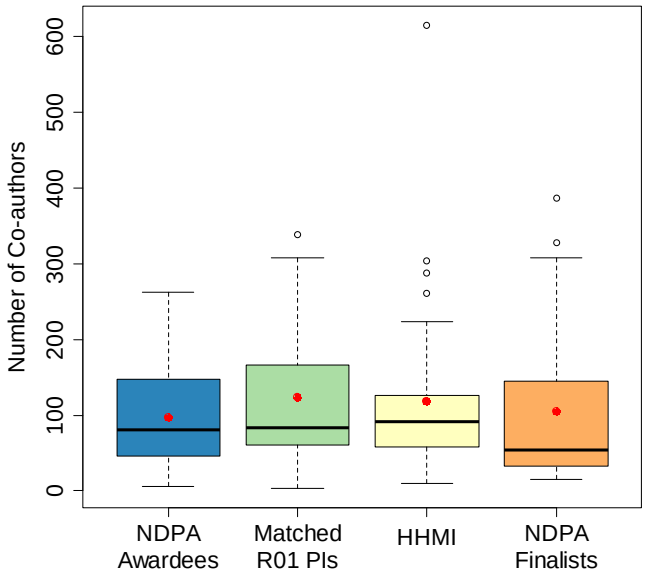


Figure 13. Number of Unique Co-authors at Time of Award

Figure 14 shows box plots of the number of unique institutions associated with co-authors working with each researcher prior to time of award. NDPA Pioneers are similar to the matched R01 PIs, HHMI investigators, and NDPA finalists (K-S, p = 0.78, 0.11, 0.72).

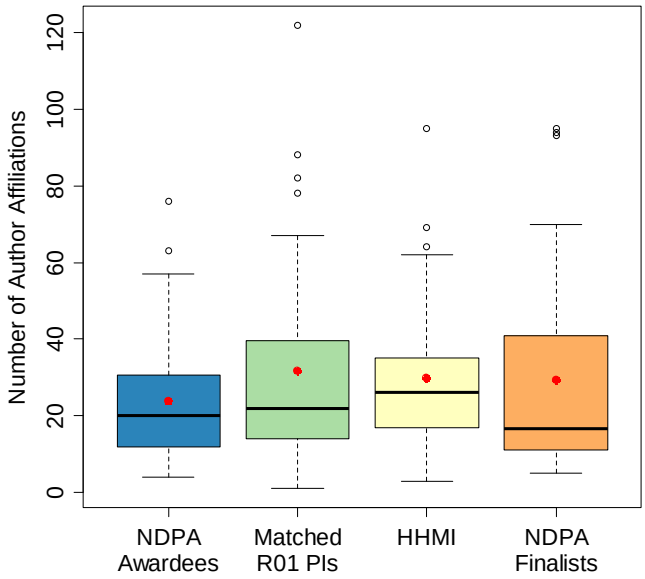


Figure 14. Number of Unique Co-author Affiliations at Time of Award

Table 3 summarizes all comparison groups, the study questions they specifically address, and their advantages and limitations. Table 4 summarizes the differences across the groups.

Table 3. Summary of the Five Comparison Groups

Comparison Group	*Description*	Study *Question*	*Advantages*	*Limitation*
Matched R01 grants N = 35	*R01 grants matched on PI characteristics within similar research areas*	*To what extent do the Pioneer award outcomes have more (or less) impact compared with traditional NIH grants given to similarly qualified researchers?*	*Controls for PI-related characteristics that may impact outcome*	*Does not control for award size*
Matched R01 grantees N = 35	*Grantees of the matched R01 grants*	*To what extent do the Pioneer outcomes have more (or less) impact compared with similarly qualified researchers from traditional grant programs?*	*Controls for PI-related characteristics that may impact outcome*	*Does not control for award size*
Random R01 Portfolios N_av = 85	*R01s with a portfolio direct cost comparable to that of the NDPA portfolio*	*To what extent* do *Pioneer award outcomes* have *more (or less) impact compared with portfolios of randomly selected R01* grants *the same size as the NDPA portfolio?*	*Controls for the portfolio award sizes that may impact outcome*	*Portfolios contai*n different numbers of grants; d*oes not control for PI characteristics*
HHMI N = 39	*2005 Howard Hughes Medical Institute Investigators*	*To what extent* do *Pioneer award outcomes* have *more (or less) impact compared with a similarly high-prestige research program?*	*High-prestige program that funds high-risk high-reward research in a way that is similar to NDPA in many aspects; reputation for innovative investigators*	*Does not explicitly control for PI characteristics or award size*
NDPA Finalists N = 30	*Individuals who were invited to interview, but were not awarded an NDPA from 2004–2006*	*To what extent are Pioneer award outcomes more (or less) impactful as compared with researchers who were almost as qualified as the Pioneers but did not get the Pioneer award?*	*Examines the outcomes of PIs who are "almost as exceptionally creative," and capable of producing high impact outcomes*	*Variable post-application funding amounts*

Table 4. Summary of the Differences across the Comparison Groups

Comparison Group	*Funding Level*	*Subject Area*	*PI Characteristics*	*High-Risk Research/ Flexibility*
Matched R01 grant	*Lower*	*Matched*	*Similar*	*No*
Matched R01 grantee	*Unknown*	*Matched*	*Similar*	*No*
"Random" R01 Portfolios	*Equal*	*Not matched*	*Different*	*No*
HHMI	*Higher*	*Not matched*	*Different*	*Yes*
NDPA Finalists	*Unknown*	*Not matched*	*Similar*	*N/A*

C. Collection of Data

Bibliometric data were collected in order to analyze the publication-based research outcomes of the matched R01 set, the FY 2005 HHMI investigators, the FY 2004–2006 NDPA finalists, and the FY 2004–2006 R01 portfolio set in comparison to the NDPAs and Pioneers. The primary sources of bibliometric data were the Thomson Reuters Web of Science (WOS) database and the internal NIH electronic Scientific Portfolio Assistant (eSPA) database.[24] Additional information was gathered from the SCImago Journal Rank (SJR), a measure of journal impact (SCImago Research Group 2001b). Appendix H provides the protocols for downloading and cleaning of the bibliometric data. Expert data were collected from topic-specific experts through a review of the five publications with the most impact ("top five") by each NDPA, matched R01 grants, and HHMI investigator.

1. Publication Data (Matched R01 PIs, HHMI Investigators, and NDPA Finalists)

Bibliometric data were collected at three levels: researcher, grant, and top five publications. Researcher-level publications are defined as research articles where the PI of interest appears as an author.[25] Researcher-level data were collected from 1980 through the end of 2011 for the Pioneers, matched R01 PIs, HHMI investigators, and NDPA finalists in the comparison groups.[26] Grant-level publications are research articles that can be attributed to the grant number of interest through funding acknowledgments

[24] For more information on WOS, visit the Thomson Reuters product page at: http://thomsonreuters.com/products_services/science/science_products/a-z/web_of_science/. For more information on eSPA, visit: http://thomsonreuters.com/content/press_room/science/468364.

[25] Research articles are publications produced from original research output. They exclude reviews, letters, notes, proceedings papers, etc.

[26] The WOS publication database extends only as far back as 1980.

in WOS, PubMed, or eSPA. Grant-level data were collected for NDPAs, matched R01 grants, and R01 portfolios. Top-five publications are the set of publications used in the expert review analysis. Top five data were collected for NDPAs, matched R01 grants, and HHMI investigators. The process for identifying the top five publications is described in greater detail in Section 2.C.4 where the expert review is discussed. Review papers were excluded from grant and researcher level analyses.

Top five publications were included in the grant-level set if they were research articles and published prior to 2012. Grant-level publications were included in the researcher-level set if the PI was an author on the publication. The following information was collected for each publication record: publication title, authors, publication year, journal, citations accumulated each year from 1980 to 2011, document type, WOS category, and SCImago Journal Ranking.[27]

VantagePoint software was used to clean the WOS publication data[28] for use in analyses of the matched R01 grants and PIs, HHMI investigators, and NDPA finalists. The software was used to identify and remove publication records that were incorrectly attributed to the PIs and grants of interest, disambiguate author names and institutional affiliations, and match cited journals to WOS categories in an effort to understand interdisciplinarity.

The resulting data set contains 12,232 total publications of which 510 are top five, 813 are grant level, and 12,172 are researcher level.

2. Publication Data (R01 Portfolios)

Publication and citation data for each portfolio of grants (random R01 portfolios, NDPA, and the matched R01 groups) were collected via eSPA. Grant-attributed publications in eSPA were found via the SPIRES+ algorithm[29] and constrained to research publication using the "Research" flag in eSPA data export. Publication data coverage in eSPA is truncated at the end of 2010. The following information was collected for each publication record: publication title, authors, journal, attributed NIH

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[27] WOS categories compose a framework for understanding the topical coverage of a journal that is indexed by WOS. Several subject categories may be assigned to one journal. For a list of the 249 WOS categories, visit: http://images.webofknowledge.com/WOKRS56B5/help/WOS/hp_subject_category_terms_tasca.html

[28] For more information about VantagePoint, a text mining software for cleaning and analyzing search results from patent and literature databases, visit: http://www.thevantagepoint.com/products/vantagepoint.html.

[29] A combination of the NIH's Scientific Publication Information Retrieval and Evaluation System (SPIRES) and a Thompson Reuters-developed algorithm for matching MEDLINE articles to NIH projects. The algorithm is detailed here: https://espa.niaid.nih.gov/eSPA/Help/Documents/eSPAWG_PublicationMatching_20091210a.pptx.

grant numbers, and total citations.[30] Data for the R01 portfolio analyses did not undergo further cleaning after download. Publication data collection via eSPA yielded 266 grant attributed research publications for both the NDPA portfolio and the matched R01portfolio, of which 206 and 213, respectively, had citation count values in eSPA. Each of the 30 random R01 portfolios have more grant attributed research publications than the NDPA and matched R01 portfolios. Combined, the random R01 portfolios had a total of 14,352 unique research publications, of which 11,262 had citation count values in eSPA.

3. Publication Data (Text Mining)

Publication titles and abstracts were extracted from grant-attributed publications in the NDPA, matched R01 grants, random R01 portfolios, and HHMI investigator groups. The data sets were limited to those publications that have PubMed IDs and were in the SPIRES database between 2007 and the first March 2012. Publication data from the random R01 portfolios were further constrained by eSPA to publication dates of 2007 to 2010.

4. Expert Review Data

The expert review was conducted using the top five publications with the most impact. For the HHMI group, these publications were selected by each of the 39 HHMI investigators as part of their 2011 review. For NDPAs, the study team requested that the Pioneers select these publications, and 26 of them provided selections. For the matched R01 grants, the team asked the program officers to make the selections, and 12 of them provided publications. The grant mechanism of the publications was blinded before the expert review, although the authors and journal titles were not.

For NDPAs and matched R01 grants for which the PIs and program officers provided fewer than five publications, the team developed an algorithm to select publications from their remaining bodies of work. The algorithm chose two titles with the highest journal impact factors, two titles that were most highly cited, and one title with the highest citation rate, which was calculated by dividing total number of citations and number of years since publication. This algorithm was compared to other algorithms with different combinations of bibliometric impact by using the PI- and program-officer-chosen publications as a training set, but minimal differences were observed.

The team also compared the algorithms' retrieval to the PI- and program officer-selected data and then sub-selected from among algorithms that produced the closest results. The team-developed algorithm was preferred on a theoretical basis; the team

[30] According to eSPA help desk, eSPA was last updated in April 2011. It is unclear if the citation count are truncated at Dec 2010, or if they are from April 2011.

reasoned that journal impact factor was more appropriate than total number of citations as a bibliometric proxy for impact in short timeframes after publication. Where grants had fewer than five grant-attributed publications, the team used as many as were available in the expert review. Overall, there were 518 papers, of which 23 were review papers and 4 were review book chapters. Of these 27 reviews, 11 were authored by Pioneers and 16 by the matched R01 PIs.

The study team designed the expert review protocol to collect expert ratings for both the impact and the innovation of a researcher's publications. In addition, three questions related to the expert reviewer's personal and educational background were included. In total, the following data were collected:

- The impact of a researcher's individual papers on a five-point scale from extremely to not at all
- The impact of a researcher's set of papers, taken as a whole, on a five-point scale from extremely to not at all
- The innovativeness of the approaches of a researcher's individual papers on a five-point scale from extremely to not at all,
- The innovativeness of a researcher's set of papers, taken as a whole, on a five-point scale from extremely to not at all,
- The alignment between the research in each set of papers and the expert reviewer's own research area
- Year of birth
- Gender
- Educational degrees awarded

Refer to Appendix D for information on the characteristics of the reviewers, Appendix E for the protocol design, and Appendix F for data summaries of the expert reviewer's ratings of impact and innovation.

3. Methods

The team used bibliometric techniques and expert review to measure the scientific impact and innovativeness of the approaches used by researchers, research groups, and grants.

A. Bibliometric Methods

The application of bibliometrics in a comparative evaluation can provide a partial indication of impact (Cozzens 1996; Moed 2005; Martin and Irvine 1983).[31] In addition to communicating research findings, publications provide information on the author and co-authors, affiliations, journal, publication year, citations, cited references, and the journal's scientific area.

As Table 5 indicates, the study team conducted bibliometric analyses[32] on the comparison groups at the grant-level for NDPAs, matched R01 grants, and random R01 portfolios, and at the researcher-level for all comparison groups except the random R01 portfolios.

Table 5. Bibliometric Analyses for Groups and Metrics Calculated

Group (award years)	Grant-Level	Researcher-Level
NDPA Pioneers (FYs 2004–2006)	X	X
Matched R01 PIs (FYs 2004–2006)	X	X
HHMI Investigators (FY 2005)		X
NDPA Finalists (FYs 2004–2006)		X
Random R01 Portfolios (FYs 2004–2006)	X	

[31] Martin and Irvine (1983, 66) noted the use of publications and citations as partial indicators of the "level of scientific progress made by the individual or group." For example, researchers are motivated to publish "not only to present valuable results, but also for social, political, and career reasons" and other factors.

[32] Bibliometric analysis refers to the study of publication data including the authors, journals, and cited references, from scholarly literature to produce quantitative or statistical analysis. For further on bibliometric analysis, see van Raan (2003).

1. Background

A substantial body of literature demonstrates the use and limitations of bibliometrics for scientific evaluations. Bibliometrics are most often used to evaluate research performance on basic research (Melkers 1993). The technique allows for a variety of metrics that focus on different portions of publication data and associated meta-data. For example, bibliometrics can be used to assess the scientific production of a country, an institution, a program, or an individual researcher. In 2010, the National Science Board used a country-specific metric to benchmark the U.S. national science capacity against other countries of interest (NSB 2010; Moed et al. 1995). The technique has also been used to measure the research performance of universities and research groups and associated institutions (Moed et al. 1985). Furthermore, the NIH and the NSF have long used publications counts and citations as evaluative indicators of a program's scientific activity (Narin 1976; Cozzens 1996).

2. Approach

The team adapted Godin and Doré's (2004) definition of scientific impact to operationalize the bibliometric analysis. They assert that scientific impact can be measured in the following ways:

- Contributions to research through publications, including diffusion and appropriation of new knowledge, theories, methodologies, models, and facts
- Formation and development of specialties and disciplines
- Diversification of the type of research conducted (basic, applied, and strategic)
- Development of interdisciplinary, intersectoral, and international research

Many of these dimensions can be quantified through both simple and sophisticated analysis of information provided through publications and citations (National Academy of Sciences 1999, 2011; Cozzens 1996; van Raan 2003). After reviewing the scientometric and bibliometric analysis literature, the team identified 11 traditional and emerging metrics within five broad categories—(1) productivity, (2) citation impact, (3) journal impact, (4) interdisciplinarity and diversity, and (5) collaborations and networks.

Table 6 lists the metrics the team used, explains the rationale for using them, and indicates the data requirements for each.

Table 6. Metrics used in Bibliometric Analysis by Category

Category	Metric	Rationale	Data Requirements
Productivity	1. Number of publications	Indication of the production and diffusion of knowledge, theories, methodologies, models, and facts	Publication counts
	2. Number of publications per grant funding amount	Indication of the productivity per funding dollars provided to the award	Publication counts Total direct funding
Citation Impact	3. Number of citations per awardee	Indication of actual appropriation of diffused knowledge in the scientific community	Publication citations
	4. Number of citations per grant funding amount	Indication of the appropriation of knowledge per funding dollars provided to the award	Publication citations Total direct funding
	5. Number of citations per publication	Indication of the actual appropriation of diffused knowledge per individual publication	Publication citations Publication counts
	6. H-index	Indication of unusually high appropriation of knowledge relative to other scholarly work in a similar field	Publication counts Publication citations
Journal Impact	7. SCImago Journal Rank (SJR)	Indication of the publication's potential for diffusion; possibly accounting for the publication's visibility in the scientific community and citation counts	Journal titles Journal ranking*
	8. Proportion of publications by journal percentiles	Indication of the aggregate publications' potential for diffusion; possibly accounting for the publication's visibility in the scientific community and citation counts	Journal titles Journal ranking*
Interdisciplinarity and Diversity	9. Integration score	Indication of the integration of diverse knowledge or the diversification of the type of research being performed	Journal subject areas^
	10. Number of co-authors	Indication of the growth in number of co-authors in publications	Co-authors
Collaborations and Networks	11. Number of co-author affiliations	Indication of the growth in number of affiliations associated with co-authors in publications	Institutional affiliations of co-authors

* SCImago Research Group (2011b), retrieved February 5, 2012 from http://www.scimagojr.com/journalrank.php.

^ Subject areas are assigned by Thomson Reuters as Subject Categories. See Thomson Reuters, Journal Search, http://ip-science.thomsonreuters.com/cgi-bin/jrnlst/jlsubcatg.cgi?PC=D.

3. Analyses Conducted

Three of the five comparison groups—NDPA Pioneers, matched R01 PIs, and random R01 portfolios—were used in the grant-level analyses. All bibliometric indicators were calculated for the NDPA Pioneer grants and the matched R01 grants, while only three metrics (1, 3, and 5) relating to impact were calculated for the random R01 portfolios due to time constraints and data availability.

Four of the five comparison groups—NDPA Pioneers, matched R01 PIs, HHMI investigators, and NDPA finalists—were used in the researcher-level analyses. Nine of the 11 bibliometrics measures (1, 3, 5, 6, 7, 8, 9, 10, and 11) were analyzed. Metrics 2 and 4 (number of publications per grant funding amount and number of citations per grant funding amount) were calculated for the Pioneers and HHMI investigators, but not for the other two groups.

For researcher-level analysis, a distinction was made between the bodies of work published prior to the grant or grant application (i.e., 1980 to year of grant) and the bodies of work published post-award/application (i.e., year of grant to 2011). See Chapter 2 for details on the differences among these data. This distinction enabled the team to create a baseline for the comparison groups across many of the metrics. The random R01 portfolios were not included in the research-level analysis due to time constraints.

The study team performed various statistical tests (where applicable) to ascertain the significance of differences between the NDPA Pioneers and the comparison groups across the metrics. Statistical tests performed included the Kolmogorov-Smirnov test to determine if the group distributions differ significantly, and the chi-square test to observe significant differences for categorical data.

a. Productivity Metrics

The team calculated two productivity metrics:

- Number of publications
- Number of publications per grant funding amount

Van Raan (2003) notes that "communication, i.e. the exchange of research results, is the driving force in science" and considers publications as direct research outputs that are critical to understanding the diffusion of knowledge. The number of publications over a researcher's career indicates the level of activity or productivity of a researcher in a particular field. However, there are limitations when comparing publication counts across fields since some fields have a stronger tradition of publishing than others (Cozzens 1996). For the purposes of this study, comparisons of publication counts are less

problematic because the NIH and comparison group researchers are all conducting research within the biomedical and health-related domains. Additionally, publication counts depend on the length of the researcher's career and their respective institutional support. This analysis shows that the four comparison groups for which data were available had similar publication counts prior to the award date (see Chapter 2).

b. Appropriation of Knowledge

Four metrics represent the appropriation of knowledge:

- Number of citations
- Number of citations per grant funding amount
- Number of citations per publication
- H-index

Garfield (1955) finds that citations to a publication indicate an association between two publications that can be used to measure the publication's scientific impact. Moreover, some studies have concluded there is a positive relationship between citation counts and the outcomes of peer review (Oppenheim 1995 and 1997). While there are widely acknowledged issues with the use of citations for understanding scientific impact, citation counts have been accepted in the literature due to the relative ease of data collection and its representation of the direct research impact on the scientific community (Bornmann and Hans-Dieter 2008).[33] The total number of citations received may be influenced by the funding the researcher received as well as the number of publications that they produced. Thus, the team also compared distributions of the number of citations normalized by the award funding amount and citations per publication in order to provide other perspectives of the research quality.

One limitation to analyzing citations is that they are accumulated over time, thus recent publications will have had less time to accumulate citations. To understand the citation distributions over time across the groups, the team calculated the time to citation for grant-level NDPA and matched R01 publications. Other metrics, such as the h-index, are derived from citations and attempt to improve upon the limitations of simple citation counts for researcher-attributed analyses.

The h-index draws upon the idea that knowledge diffusion is dependent upon and integrates both publication and citation counts into one metric (Hirsch 2005). Variations on the h-index attempt to render impact more comparable across researchers by

[33] The unifying factor in these limitations is the lack of discrimination for the nature of the citation. An article receives one citation count regardless of whether the citation was based on a positive, negative, scientific, or non-scientific rationale. In addition, the citation could also have been the author's self-citation.

accounting for differences in the length of a researcher's career (Burrell 2007) and differences in citation patterns from diverse scientific fields (Iglesias and Pecharroman 2007). The h-index was further validated as a metric for research quality and impact when van Raan (2005) concluded that the h-index is positively correlated with the peer judgments for articles published by 147 chemistry research groups in the Netherlands.

In the bibliometrics literature, the h-index has been calculated at various degrees of aggregation: from a single researcher, to a laboratory, to a research field, to a set of journals, to a country (Hirsch 2005, Alonso et al. 2009, Jascó 2011). The study team calculated the h-index for the subset of grant-attributed publications as well as broad sets of publications (1980–2011) from a researcher's career.

c. Journal Impact

The team used two metrics using journal impact scores:

- SCImago Journal Rank (SJR)
- Proportion of publications by journal percentiles

The team used the SJR indicator to measure the prestige of the journals in which the researchers from the comparison groups publish. The concept of a journal's impact is derived from citation analysis. It provides a proxy measure of the journal's effectiveness to communicate research results (Garfield 1979). The number of citations a journal receives per articles published provides an indication of the journal's impact on the scientific community (Garfield 1972). Moreover, there is a greater capacity for knowledge diffusion in journals with higher citations and impact.

Bibliometric researchers and companies have developed several journal impact indicators, including the Journal Impact Factor (JIF) developed by Thomson Reuters[34] and the SJR developed by the SCImago Research Group[35] (Garfield 2005; Moed 2010). The JIF is calculated by dividing the number of citations in the current year to all items published in a journal the previous 2 years with the number of publications in the journal during the previous 2 years. The SJR not only considers the citation counts but also the quality of the citation measured by the prestige of the journal from which the citation is coming. The importance of the journal is thereby measured by the importance of the citations they receive. SCImago researchers González-Pereira, Guerrero-Bote, and Moya-Anegón (n.d.) assert there is a strong correlation between the JIF and SJR as tested for journals in the biochemistry, genetics and molecular biology, and psychology fields. The

[34] About the JIF: http://thomsonreuters.com/products_services/science/free/essays/impact_factor.

[35] About SJR: http://www.scimagojr.com/aboutus.php.

team chose the 2011 SJR to measure journal impact due to the public availability of the metric (SCImago Research Group 2011b).

Two important considerations when comparing journal impact measures include (1) the time horizon used in the calculations and (2) the inclusion of reviews, editorials, and letters. Both the JIF and the SJR measure a journal's relative importance in a particular field in a specific time period and should be compared with impact factors for other journals calculated based on that same time period. Additionally, journals include reviews, editorials, and letters that often receive many more citations than other research or experimental publications (Seglen 1997). These publication types can easily distort the journal impact metric.

d. Interdisciplinarity and Diversity

The study team used two interdisciplinarity measures to capture the diversity of the researcher's body of work:

- Integration score
- Subject area analysis

While interdisciplinarity has many meanings in scholarship, the team defined "interdisciplinarity" as the integration of traditional disciplines of knowledge into newly synthesized fields or niche areas of research within an existing field.[36] Scientists have developed emerging metrics, such as the integration score, to measure the level in which researchers have integrated knowledge from various disciplines into their published work. The integration score measures the knowledge within a body of research based on the journal's subject area from a publication's cited references; therefore, it is a backward-looking metric (Porter et al. 2007; van Raan 2002). The team used a set of 221 journal subject areas assigned by Thomson Reuters to WOS indexed journals. While there are other measures of diversity, Rafols and Meyer (2010) noted that the integration score is the only measure that integrates the three aspects of diversity—variety, balance, and disparity—into one index. Variety represents the number of disciplines cited by the publication, balance signifies the distribution of citations among the disciplines, and disparity shows the similarity of dissimilarity of the subject areas to one another (Porter and Rafols 2009).

The proportions of subject areas from the cited reference's journals were used to qualitatively represent the diversity of researchers' publications. The 221 subject area assignments from Thomson Reuters were organized into 18 macro-subject area clusters based on the factor analysis performed in Leydesdorff and Rafols (2009). The team used

[36] For further clarification, refer to the discussion of "content integration" and the distinction between "interdisciplinary" and "integrative" in the social science in Klein (1990, 26–27).

the macro-subject areas in two analyses: (1) the frequency of cited references in each subject area normalized such that each cited reference and all publications had the same weight, and (2) the frequency of cited references in each subject area normalized such that each researcher had the same weight, regardless of number of publications. Both analyses represent a different perspective on the diversity of the research being funded by the program. The latter analysis enabled the team to observe whether a highly productive researcher exerts disproportionate influence on the differences in the distributions across or within any one of the 18 macro-subject areas.

The use of subject areas based on Thomson Reuters in this study presented a couple of difficulties: (1) the low accuracy of the subject area categories assigned to journals and (2) the aggregation of subject areas into macro-subject areas. Thomson Reuters assigns from one to six subject areas to WOS indexed journals based on a combination of factors, including the cited references in the journal publications. Rafols, Porter, and Leydesdorff (2010) measured the error associated with this assignment to be around 50%, meaning nearly half the indexed journals have at least one subject category assigned that is mismatched (Rafols and Leydesdorff 2009). However, most of the mismatched journals appear to fall in subject areas within the close vicinity of the macro-subject area categories (Rafols, Porter, and Leydesdorff 2010). In addition, the multidisciplinary sciences subject area is problematic since it includes too diverse an array of publications to categorize within any other subject area. This subject area is assigned to journals such as *Nature* and *Science*. In aggregating the 221 subject areas into 18 macro-subject areas, the multidisciplinary sciences subject area is grouped into the biomedical science macro-discipline. A judicious look should be taken when comparing the biomedical science macro-discipline across the groups.

e. Collaborations and Networks

The study team used two metrics to gain insight into the individual researcher collaboration networks among the groups:

- Number of co-authors
- Number of co-author institutional affiliations

De Solla Price (1970) explained that not only do publications provide information, but they also can reveal relationships among the people publishing the scholarly work. Given a researcher's body of work, the number of co-authors and institutional affiliations associated with that work reveals the magnitude of the researchers' co-author and institutional collaboration networks after application for or receipt of the award.

B. Expert Review

1. Expert Panel Experimental Design and Analysis

The expert panel assessment was conducted on a total of 510 papers in 108 sets of "top five" papers ("packets") from the NDPAs, the matched R01 grants, and the HHMI investigators. The packets were divided into groups of between three and eight papers of similar research areas. An expert read at most four packets within a particular group, and each packet was read by three or four experts. Within the groups, the experts were assigned to papers using an alias-optimal design to make it as easy as possible to estimate separate expert and paper effects. Overall, 336 packet evaluations and 1,587 paper evaluations were included in the analysis. All 94 recruited experts completed the evaluation. One matched R01 PI was inadvertently used as an expert, but his ratings were excluded from the analysis to avoid any conflict of interest.

The analysis of the data was based on the multi-rater ordinal data methodology developed in Johnson and Albert (1999). The study team assumed that each paper and packet has an underlying impact (innovativeness) that can be measured. When an expert assesses the impact of a packet, the team assumed that this "measurement" is made with some variability. This measurement was not observed directly; instead, a discretized version was observed, much like the grade on an examination being discretized to a letter grade. Each expert discretized the impact (innovativeness) scale differently, and the "grade" cutoffs were estimated from the data. The underlying impact (innovativeness) was also estimated, as were the measurement variations for each expert. Since each packet was read by multiple experts, large estimated measurement variations indicated that the expert assessed packets differently from other experts. Similar assumptions were made for paper "measurements," with the additional assumption that paper impact (innovativeness) would be distributed around packet impact with some variation.

In addition, several covariates were incorporated into the analysis to determine whether they are predictive of the expert-assessed impact (innovativeness). At the packet level, the team considered grant mechanism, number of citations at time of award for the PI, number of publications at time of award for the PI, h-index at time of award for the PI, SIR at time of award, years since degree, receipt of early career award, and, for the matched R01 packets, total direct costs. At the paper level, the team considered journal impact factor and total citations to date. Details of the analyses are discussed in Appendix I.

2. Analysis of Qualitative Data from the Expert Panel

The study team initiated a qualitative analysis of the open-ended responses collected from the experts to provide insight on how impact and innovation were assessed. The expert review protocol is reproduced in Appendix E. The goals of this exercise were to

determine whether the experts used the given typologies when evaluating the research and whether the experts considered impact and innovation to be related to one another, given that the two factors were found to be highly correlated through the quantitative analysis.

a. Data

Data for the qualitative analysis came from open-ended responses from experts following the impact and innovation questions, which were asked in separate sections via the protocol. Each section of the protocol begins with a sentence on how each factor relates to the overall goals of the NDPA program. For example, the impact section begins with the following: "NDPA was created to promote highly innovative and potentially transformative approaches that have the potential to produce extremely high impact on a broad area of biomedical or behavior research." Reviewers were provided with a list of factors to consider when assessing impact and innovation within the context of this evaluation. These factors were based on the Heinze et al. (2007) and Colwell (2003) typologies of research outcomes and research risks.

For impact, "extremely high impact" refers to research that accomplishes one or more of the following:

- Radically changes present understand of an important existing scientific or engineering concept
- Leads to the creation of a new paradigm or field of science or engineering
- Challenges present understanding in the field(s)
- Provides pathways to new frontiers
- Challenges conventional wisdom
- Leads to unexpected insights that enable new techniques or methodologies
- Redefines the boundaries of science or engineering

For innovation, "extremely innovative" refers to approaches that can be characterized in one or more of the following ways:

- The ideas underlying the research are at odds with prevailing wisdom
- The research requires the use of equipment or techniques that have not been proven or are considered extraordinarily difficult
- The research involves a unique combination of disciplines

After assessing each paper and the packet as a whole, reviewers were asked to write responses to the following question in both sections: "What about these papers, individual or as a whole, made you choose your answers above?" Responses were

voluntary and had no character limits. Out of the 340 reviews that were collected, 334 and 309 provided answers for the impact and innovation questions, respectively.

b. Method

Responses were coded inductively using content analysis assisted by NVivo, a software tool used for analyzing qualitative data. Content analysis is a systematic approach widely used to extract common themes from unstructured data (Lasswell and Leites 1968).

An initial coding framework, or codebook, was developed from the rubrics listed previously and from examining samples of responses. In contrast to quantitative data analysis, qualitative data analysis is an evolving process dependent on themes emerging from the text. Categories were added and refined after all responses were coded using the initial coding framework. The final codebook is available in Appendix G, which also provides representative examples of responses coded under each theme.

C. Potential Limitations

The evaluation has limitations along three dimensions: measurement validity (which relates to accuracy of measurement), measurement reliability (which relates to repeatability of measurement), and internal validity (which relates to establishing causality).

With respect to measurement validity, the biggest concern is how well the abstract concepts of impact and innovativeness of research approaches were turned into empirically observable indicators. A key assumption was that publications capture the intended effects. It is possible that transformative research is more likely to be rejected by peer-reviewed journals or that, given the database limitations, not all of the publications attributed to the grant or researcher were captured. As a specific illustration, the team assumed that interdisciplinarity of publications is a close-enough proxy for the interdisciplinarity of research. It is likely that researchers are bringing interdisciplinarity into their research (for example, through formal or informal interactions with colleagues from other disciplines) without it reflecting in the subject area distribution of their publications. Publications, as the “currency” of science, however, were the most appropriate research outcome to assess impact and innovativeness in the evaluation.

Going beyond the limitation of using publications as a proxy for research, there are other limitations related to measurement validity. For example, the team assumed that citations to research publications, researchers’ h-index, and journal reputations were good proxies of impact. The assumption is supported in the literature, but it is an assumption nevertheless that should be made explicit. Similarly, the team assumed that the number of co-authors was a good proxy for collaborations, and the integration score was a good

proxy for interdisciplinarity. For the latter case especially, this may not be the case. The calculation of these scores is based on the diversity of subject categories assigned to journals by Thomson Reuter's Institute for Scientific Information (ISI) and the degree to which a subject category (SC) relates to a particular journal. This is somewhat problematic. First, the validity of the I-Score is dependent on the accuracy of the publication dataset used to describe a PI's publication history. The I-Score analysis used the publications from the WOS database, which indexes a limited selection of conference papers and proceedings, with coverage varying by research area. This point is particularly important in calculating the proposal I-Score from cited references, since many of the PI records contained conference proceedings that were not included in the WOS database and, thus, not matched to a SC. Second, the I-Score calculation is based on the diversity of SCs matched to the journals of a publication dataset; however, the accuracy of the matched SC(s) to classify a journal may vary (Boyack, Klavans, and Borner 2005). Boyack, Klavans, and Borner also note that for approximately 50% of the SCs, there is a high level of accuracy regarding the matched journal and SC. For the other 50%, there is less accuracy in the attribution.

With respect to measurement reliability, one potential limitation of the evaluation is that the impact and innovativeness assessments are based on experts' ratings of researcher publications. This is a subjective approach. Presumably a different set of evaluators might have given the research different ratings.

Many of the issues related to measurement validity and reliability were addressed by using a multi-method approach that combined bibliometrics with expert reviews and text mining.

The three most important limitations that pose threats to internal validity of the evaluation relate to the appropriateness of the matched R01 set, the selection of the publications for analysis, and the timing of the evaluation.

With respect to the matched set, every attempt was made to ensure that the researchers in the comparison group were as similar as possible to the NDPA group. They were matched on areas of research, demographics, and other attributes of importance. An analysis showed the two groups to be highly comparable, including on bibliometric measures that were not used to select the comparison group. Nevertheless, there is still a chance that the matched set of R01s is not an apt comparison group, in which case any differences or lack of differences in outcome cannot be attributed to the receipt of the NDPA award.

Publications selected—for both the bibliometric analysis and the expert assessment—can pose a threat to internal validity (i.e., ability to assign causality) as well. While extreme effort was expended on accurate data disambiguation, download, and cleanup, an assumption was made that Thomson Reuter's WOS database and the NIH's

eSPA, SPIRE, and SPIRE+ databases accurately capture research publications. This may not have been the case.

Similarly, for the expert review, top five publications with the most impact were selected. While most of the Pioneers and HHMI investigators selected these publications themselves, for some of the Pioneers and the matched set of R01 PIs, these publications were selected either by the NIH program officers or the STPI study team (using a carefully designed and validated algorithm to ensure comparability). There is a possibility, however, that the publications selected were not those with the most impact.

With respect to timing, the challenge is that transformative research is often not evident for years (even decades) after being conducted. This evaluation was done for research only 5 years after award of funds. There is a good chance, therefore, that at least for some of the research, the evidence base—whether the number of citations or expert judgment as to impact—is absent. Conversely, research considered to have high impact now, may, in fact, be disproved in a few years. And what is being measured could be noise rather than signal.

The study team addressed these potential limitations by operationalizing concepts in multiple ways and using multiple methods of analyses.

4. Impact and Innovation: Grant-Level Findings

This chapter presents evaluation findings with respect to the impact of research and the innovativeness of research approaches. It compares the NDPAs first to the matched R01 set of grants and then to the random R01 portfolios. For the matched R01 grants, the first eight bibliometric indicators are discussed here; the final four are discussed in Chapter 7. In addition, this chapter provides the results from analyses of expert assessments of the impact and innovativeness of the top five publications. For the random R01 portfolios, the findings from the analyses of three bibliometric indicators are discussed.

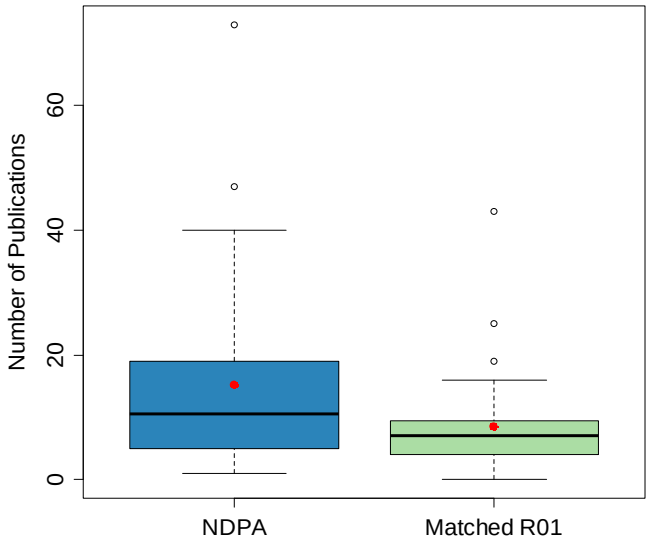
A. Matched R01 Grants

The study team compared impact and innovation of the matched R01 grants to impact and innovation of the NDPAs through bibliometrics and expert review. The results are presented graphically as box plots that show the relative distributions. Kolmogorov-Smirnov (K-S) tests were performed to determine whether the group distributions differ significantly.

1. Bibliometric Findings

a. Number of Publications

NDPAs produced more grant-attributed publications than the matched R01 grants (*K-S*, $p = 0.04$) (Figure 15).

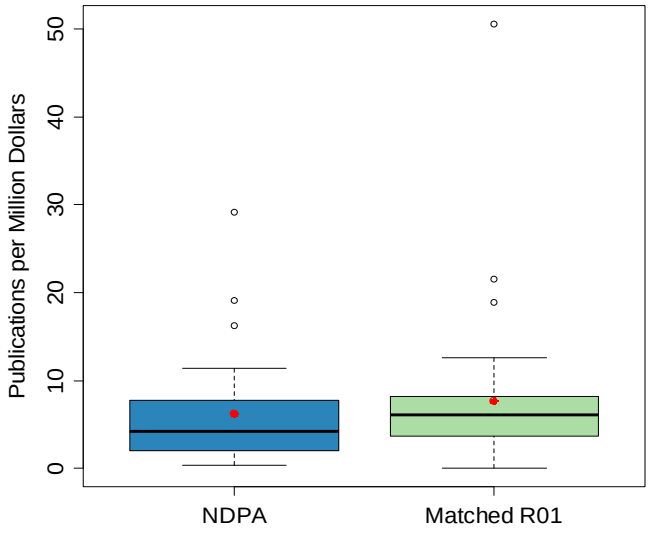


Note: One observation equals one grant.

Figure 15. Grant-Level Publications

b. Number of Publications per Grant Funding Amount

When accounting for grant size (as measured by direct cost), there was no difference in the number of publications output by the two grant mechanisms (K-S, $p = 0.31$) (Figure 16).

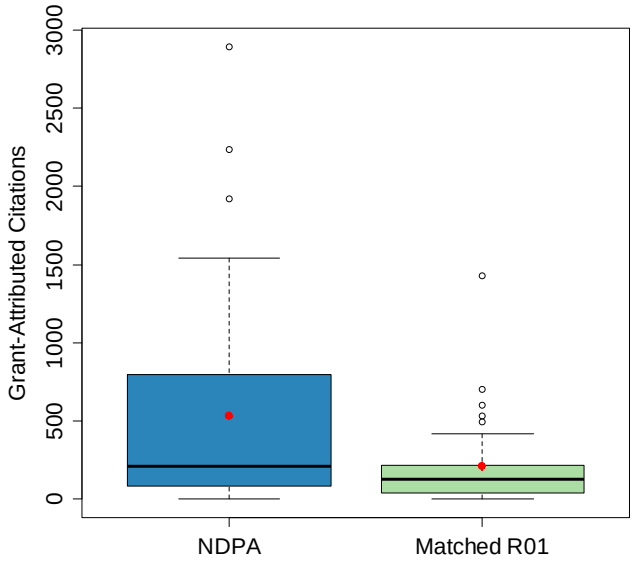


Note: One observation equals one grant.

Figure 16. Grant-Level Publications per Million Dollars in Direct Costs

c. Number of Citations

There was no statistical difference between the Pioneers and the matched R01 PIs in citations to grant-attributed publications (K-S, $p = 0.06$) (Figure 17).

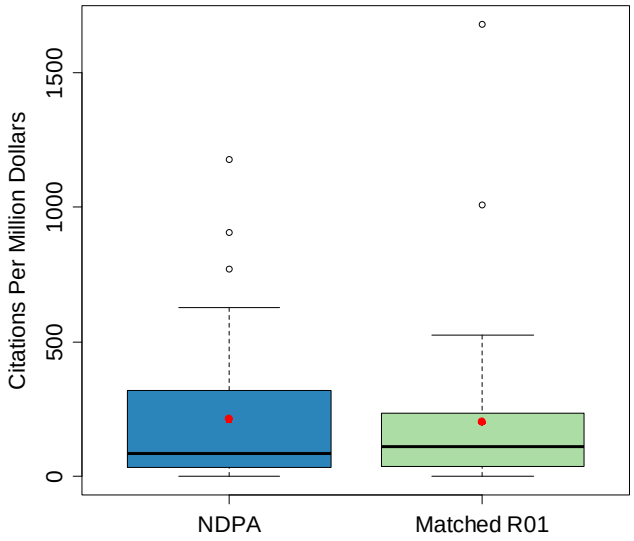


Note: One observation equals one grant.

Figure 17. Grant-Level Citations

d. Number of Citations per Grant Funding Amount

When accounting for grant size, there continued to be no difference in the citations to grant-attributed publications (K-S, $p = 0.89$) (Figure 18).

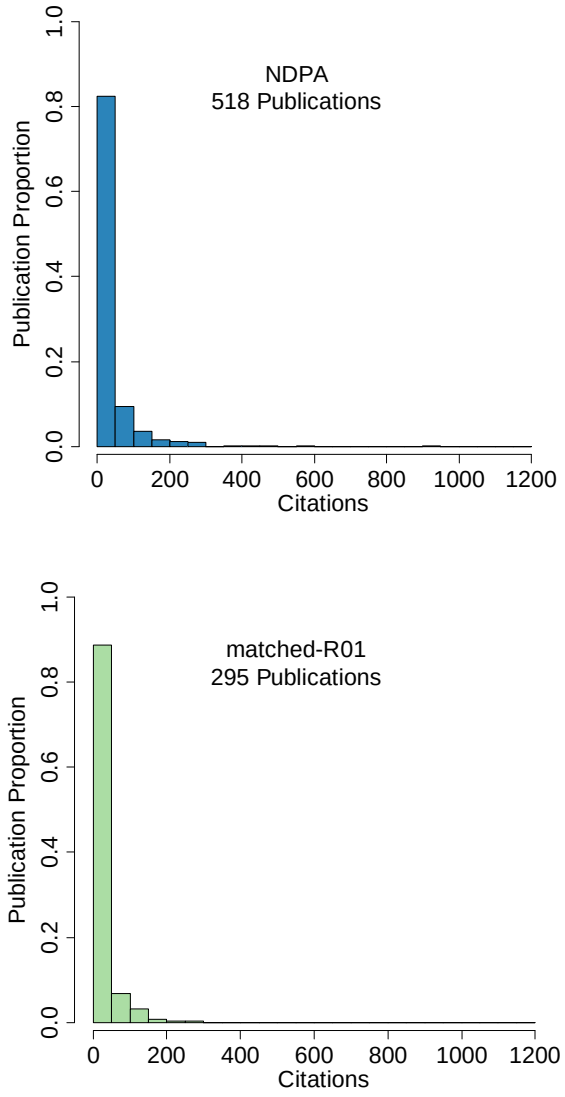


Note: One observation equals one grant.

Figure 18. Grant-Level Citations per Million Dollars in Direct Costs

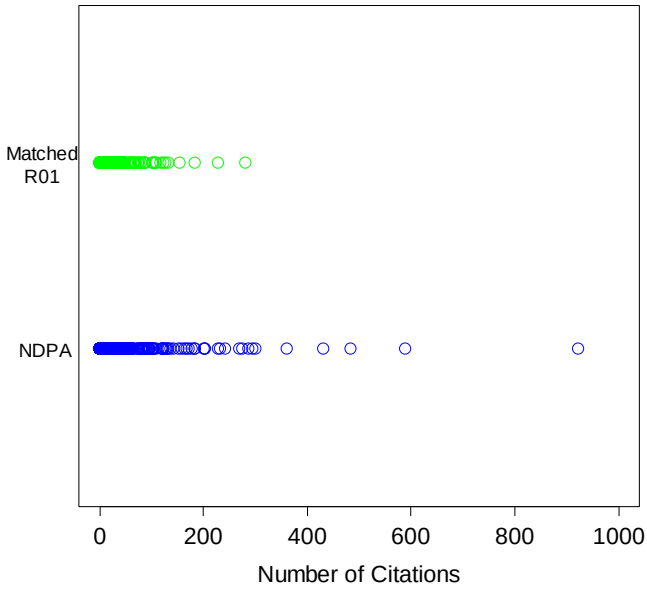
e. Number of Citations per Publication

At the publication level, NDPAs and matched R01 grants had statistically similar citation distributions (K-S, $p = 0.34$) (Figure 19 and Figure 20). Nevertheless, it is notable that the NDPA distribution of citations has a longer positive tail. Several NDPA publications had 400 or more citations, while the matched R01 publications had no more than 281 citations. This might suggest that the most successful NDPAs had a greater impact than the most successful matched R01 grants.



Note: One observation equals one publication.

Figure 19. Grant-Level Citations per Publication—Histogram



Note: One observation equals one publication.

Figure 20. Grant-Level Citations per Publication

f. Additional Analysis on Publications and Citations

Calculations show that NDPAs produced publications more slowly than the matched R01 grants (chi-sq, $p < 0.0001$) (Figure 21), but their publications, once released, were cited more rapidly (chi-sq, $p < 0.0001$) (Figure 22). These plots are a snapshot of publications and citations through the end of 2011. Figure 22, in particular, will continue to change as publications accrue citations.

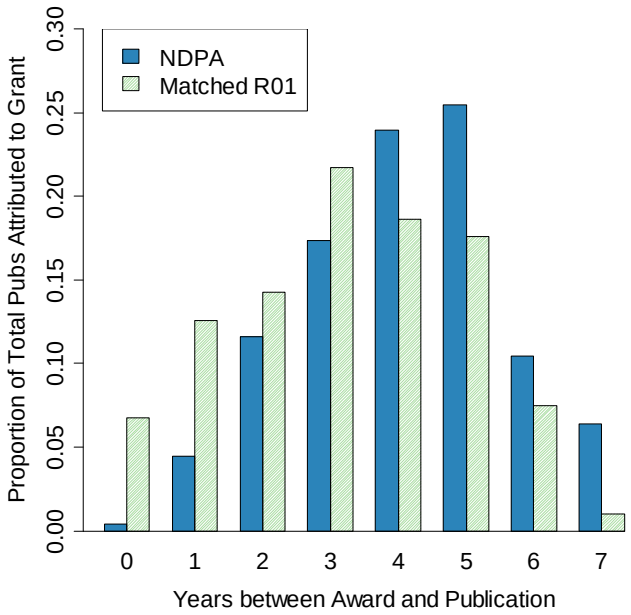


Figure 21. Lag time between Publication and Award Year

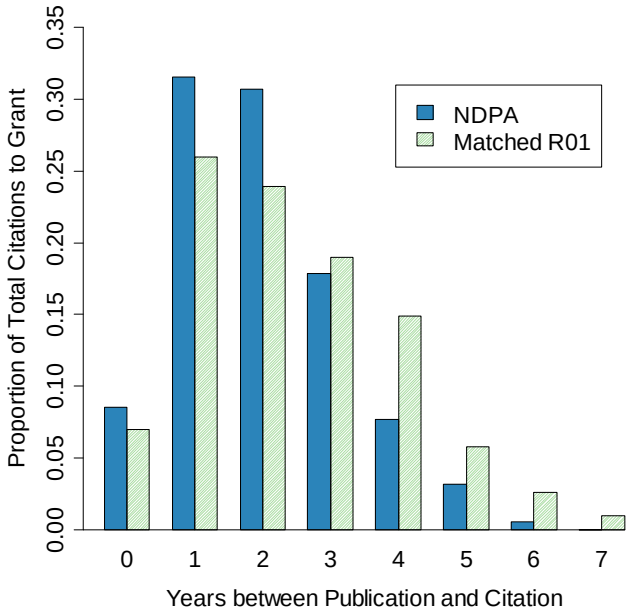
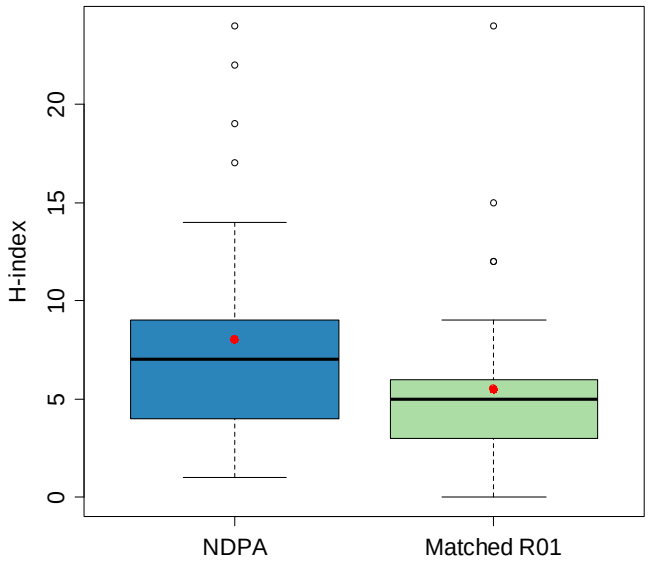


Figure 22. Lag Time between Citation and Publication Year

g. H-index

NDPAs have larger h-index values than matched R01 grants (K-S, $p = 0.003$) (Figure 23).

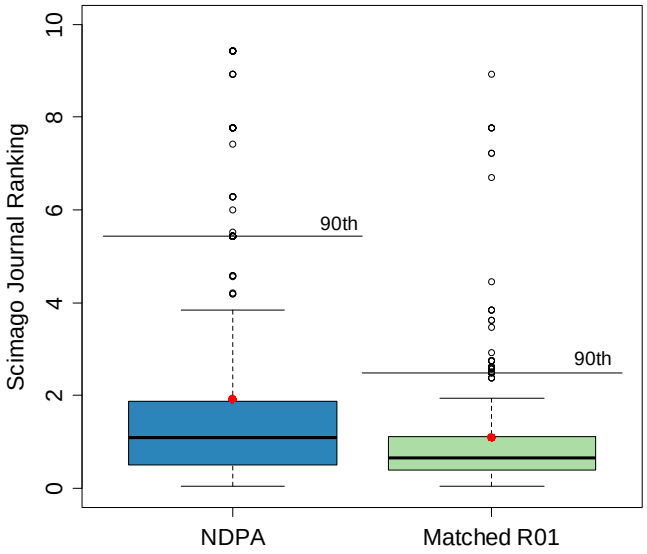


Note: One observation equals one grant.

Figure 23. Grant-Level H-Index

h. SCImago Journal Rank

NDPA publications appeared in journals with higher journal impact factors than those of matched R01 publications, and there was a notable difference between the 90th quantiles in the distributions of the two groups (K-S, $p < 0.0001$) (Figure 24).



Note: One observation equals one publication.

Figure 24. Grant-Level Journal Impact Factors

i. Proportion of Publications by Journal Percentiles

Approximately 25% of NDPA-attributed publications appeared in the top 0.5% of all SCImago-indexed journals, approximately 50% of NDPA publications appeared in the top 1% of all SCImago-indexed journals, and just over 30% of the matched R01 publications appear in the top 1% (chi-sq, $p < 0.0001$) (Figure 25).

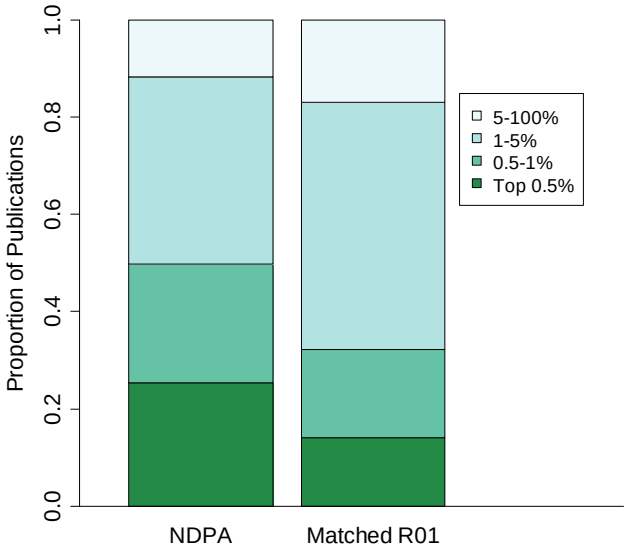
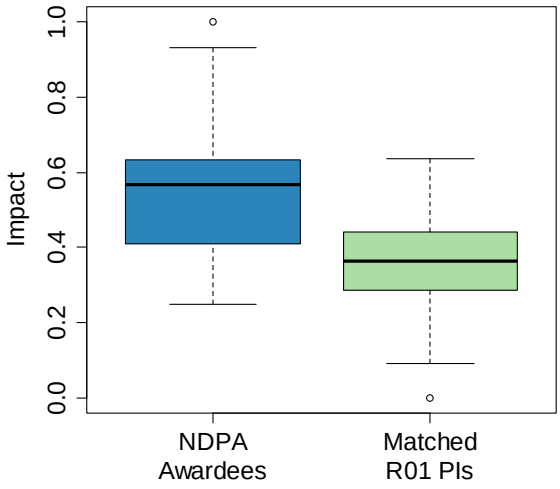


Figure 25. Grant-Level Proportion of Publications by Journal Percentiles

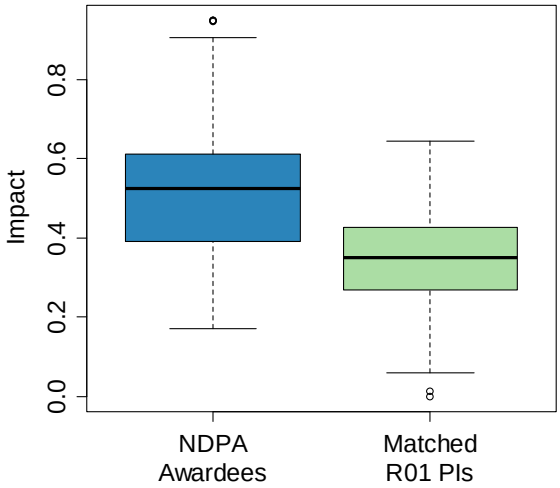
2. Expert Review Findings

The expert review assessed impact and innovation of both packets and papers. Figure 26 is a box plot of the estimated impact for NDPA and matched R01 packets. The Pioneers had a significantly higher impact (t-test, $p < 0.0001$, K-S $p = 0.0002$). Similar results are seen for papers (t-test, $p < 0.0001$, K-S, $p < 0.0001$) in Figure 27.



Note: One observation equals one grant.

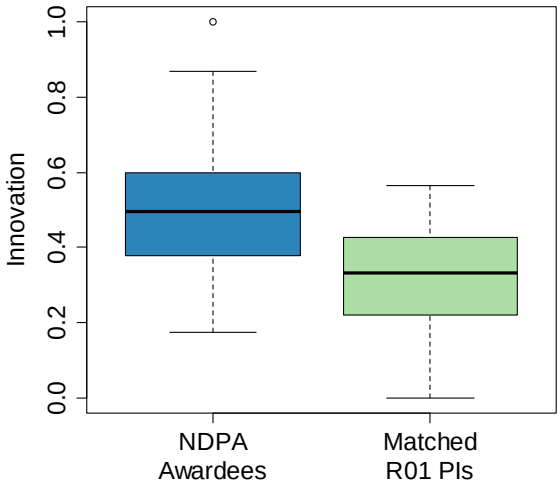
Figure 26. Expert-Assessed Packet Impact



Note: One observation equals one paper.

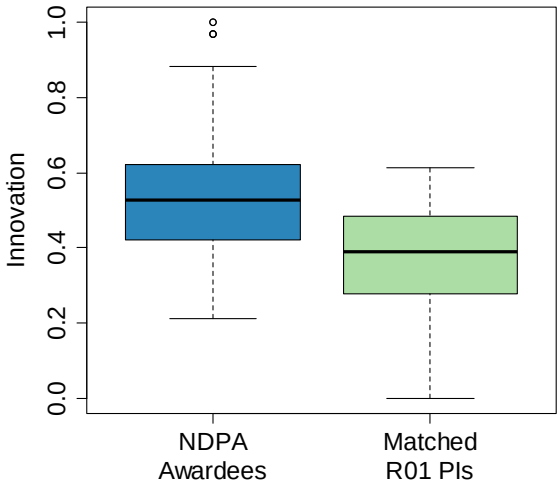
Figure 27. Expert-Assessed Paper Impact

Figure 28 and Figure 29 summarize the results for packet and paper innovation. Again, the experts assessed NDPA packets (t-test, $p < 0.0001$, K-S, $p = 0.0005$) and papers (t-test, $p < 0.0001$, K-S, $p < 0.0001$) to be significantly more innovative than the matched R01s.



Note: One observation equals one grant.

Figure 28. Expert-Assessed Packet Innovation



Note: One observation equals one paper.

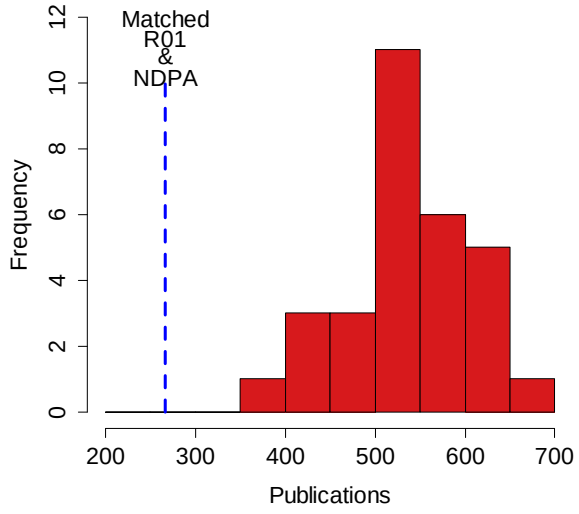
Figure 29. Expert-Assessed Paper Innovation

B. Random R01 Portfolios

The impact of the random R01 portfolios was compared to that of the NDPA and matched R01 portfolios in a limited bibliometric analysis. Figure 5 and Figure 6 (presented previously in Chapter 3) are plots of the total direct costs of each randomly selected portfolio and the number of grants in each portfolio (the range is from 66 to 96 with a median of 86).

1. Number of Publications

Each random R01 portfolio consists of a greater number of grants than the NDPA portfolio (Figure 6) with similar direct costs (Figure 5). Figure 30 shows the number of publications in the 30 random R01 portfolios, compared to that of the NDPA portfolio and the matched R01 portfolio.

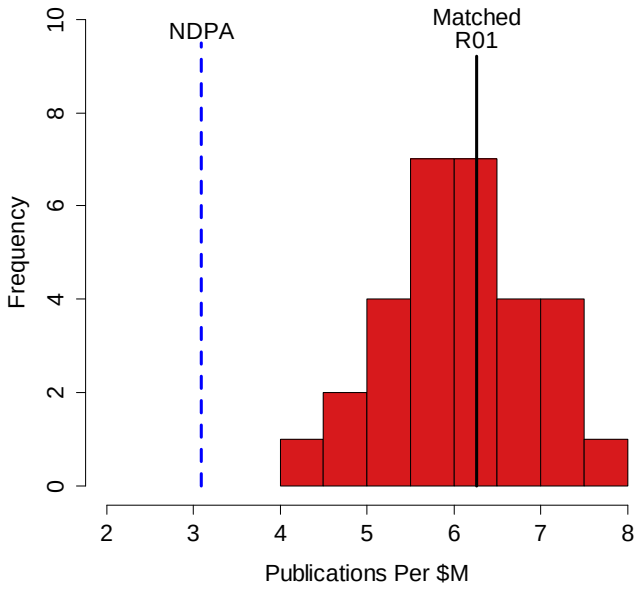


Note: One observation equals one portfolio.

Figure 30. Random R01 Portfolio Grants and Publications

2. Number of Publications by Portfolio Funding Amount

Figure 31 shows the number of publications for NDPA and the matched R01 portfolios when divided by the total direct costs of the portfolio. While the NDPA portfolio has fewer publications per dollar, the matched R01 portfolio is quite comparable to the random portfolios.

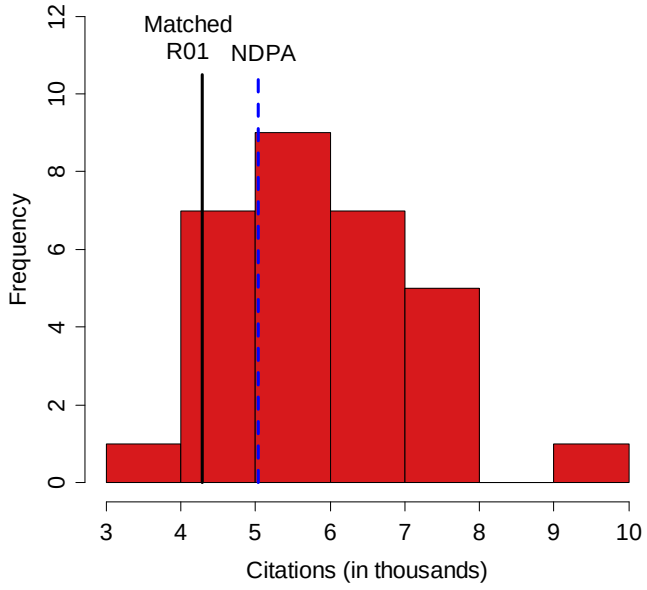


Note: One observation equals one portfolio.

Figure 31. Number of Publications Divided by Total Direct Costs of Portfolio

3. Number of Citations

Despite having fewer publications, the NDPA portfolio of grants received a similar number of citations as the matched R01 portfolio (Figure 32).

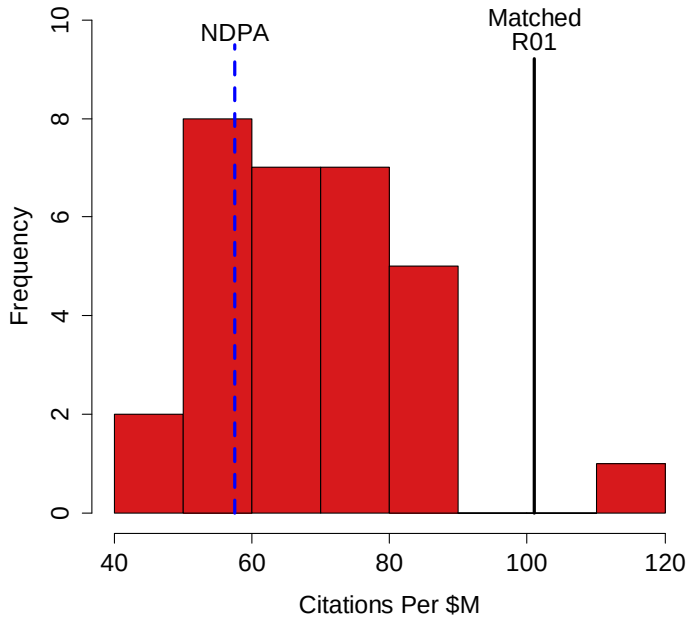


Note: One observation equals one portfolio.

Figure 32. R01 Portfolio Citations

4. Number of Citations per Portfolio Funding Amount

Figure 33 shows that when normalized by total direct costs of the portfolio, the NDPA and matched R01 portfolios still have similar numbers of citations as the random R01 portfolios.



Note: One observation equals one portfolio.

Figure 33. Number of Citations Divided by Total Direct Costs of Portfolio

5. Citations per Publication

The density estimations of the distributions of citations per unique publication displays a shift in the right side of the distributions for the NDPA and matched R01 portfolios when compared to the combined random R01 portfolio distribution (Figure 34).

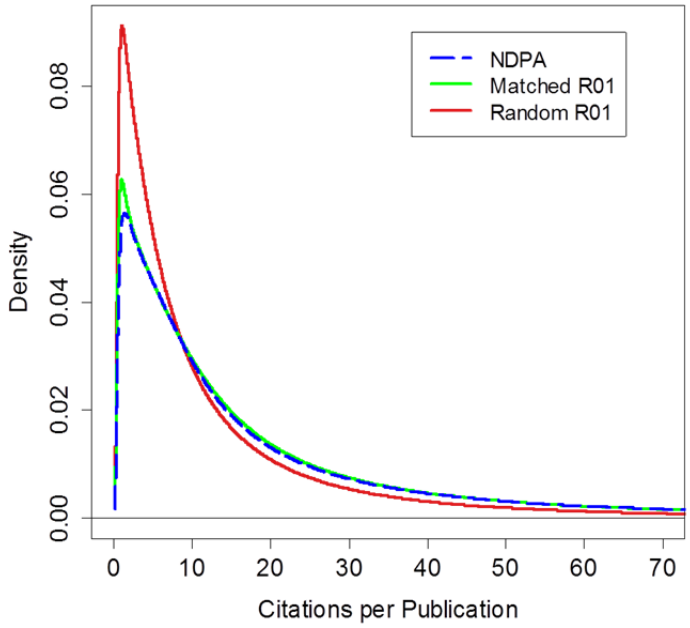
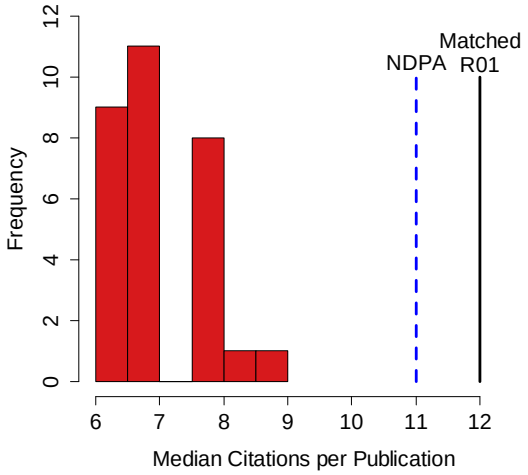
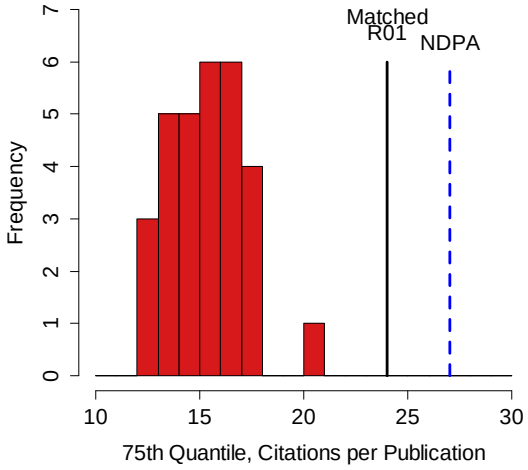
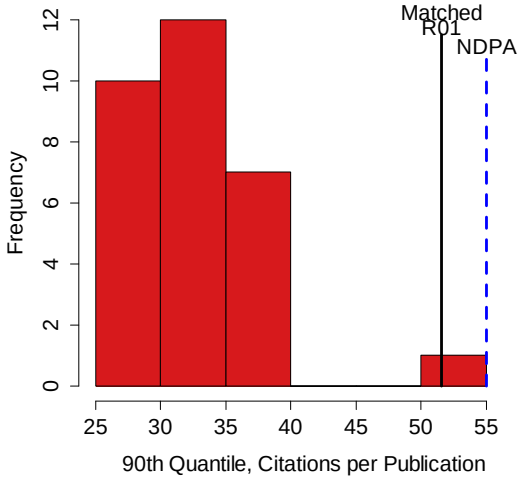


Figure 34. Density Estimations of the Distributions of Citations per Unique Publication for the NDPA, Matched R01, and Random R01 Portfolios

When considering the distribution of citations over publications, the NDPA portfolio had a higher median, 75th quantile, and 90th quantile than the R01 portfolios (Figure 35). The matched R01 portfolio, similarly, had a higher median, 75th quantile, and 90th quantile than the random R01 portfolios; the NDPA portfolio performed better than the matched R01s at the higher quantiles. Table 7 shows the spread in values (minimum/maximum) at each of the reported quantiles for the random R01 portfolio, the NDPA, and the matched R01 portfolios.







Note: One observation equals one portfolio.

Figure 35. Distribution of R01 Portfolio Citations per Publication (Median, 70th, and 90th Quantile)

Table 7. Spread in Values (Minimum/Maximum) at Each Reported Quantile of Comparison among Groups

	Median			75th Quantile			90th Quantile		
	Min		Max	Min		Max	Min		Max
NDPA	--	11	--	--	27	--	--	55	--
Matched R01	--	12	--	--	24	--	--	52	--
Random R01	6	7	9	13	15	21	26	32	51

6. SCImago Journal Ranking

NDPA eSPA publications have higher journal impact factors than those of matched R01 and random R01 portfolio eSPA publications (K-S, $p = 0.02$, <0 .0001 respectively) (Figure 36). In addition, the 90th percentile of NDPA publications has a higher impact factor than the 90th percentiles of the matched R01 and random R01 portfolios.

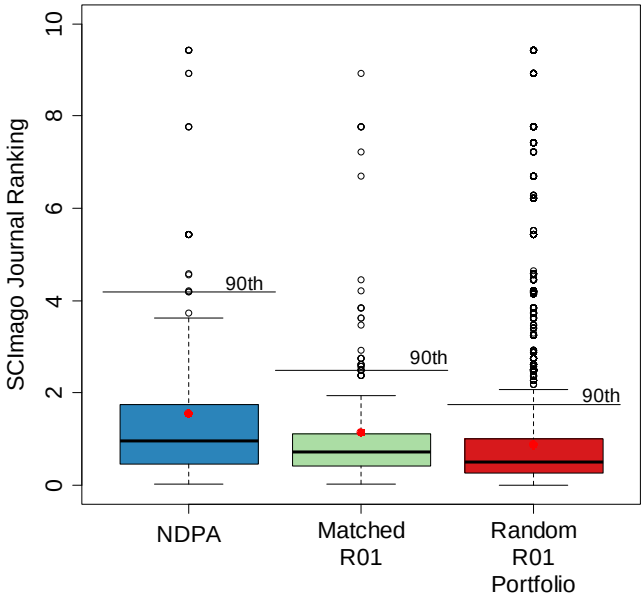


Figure 36. Journal Impact Factors for NDPA, Matched R01, and Random R01 Portfolios

7. Proportion of Publications by Journal Percentiles

Approximately 21% of NDPA eSPA publications appeared in the top 0.5% of all SCImago-indexed journals, and approximately 44% of NDPA publications appeared in the top 1% of all SCImago-indexed journals (Figure 37). The distribution for the random R01 portfolios differs from that of NDPA (chi-sq, $p < .0001$); only 7% and 21% of random R01 portfolio publications appeared in the top 0.5% and top 1% of journals,

respectively. NDPA and matched R01 publications had similar distributions, with 15% of matched R01 publications in the top 0.5% and 35% in the top 1% (chi-sq, $p = 0.14$). (Note that the comparison of NDPA and matched R01s differs from that presented previously in Figure 25 because of the different data set that was used for portfolio comparisons.)

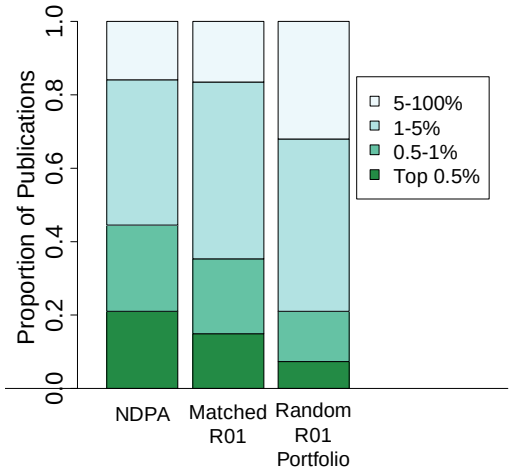


Figure 37. Proportion of Publications by Journal Percentiles for NDPA, Matched R01, and Random R01 Portfolios

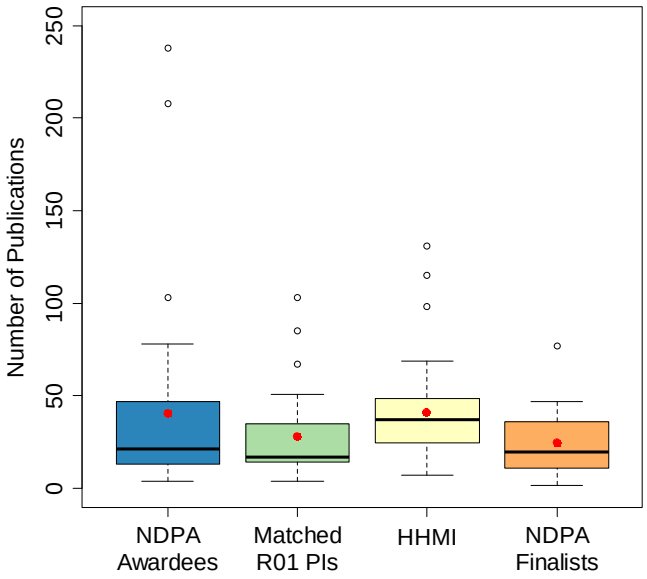
5. Impact and Innovation: Researcher-Level Findings

The impact of the matched R01, HHMI, and NDPA finalist researchers was compared to that of Pioneers through six bibliometrics. Additionally, the impact and innovation of HHMI researchers was compared to that of the NDPA and matched R01 grants through expert review.

A. Bibliometric Findings

1. Number of Publications

In the years after award and application, Pioneers were similarly productive to the matched R01 PIs and NDPA finalists, and published fewer research articles than HHMI investigators (K-S, p = 0.58, 0.37, 0.02 respectively) (Figure 38).

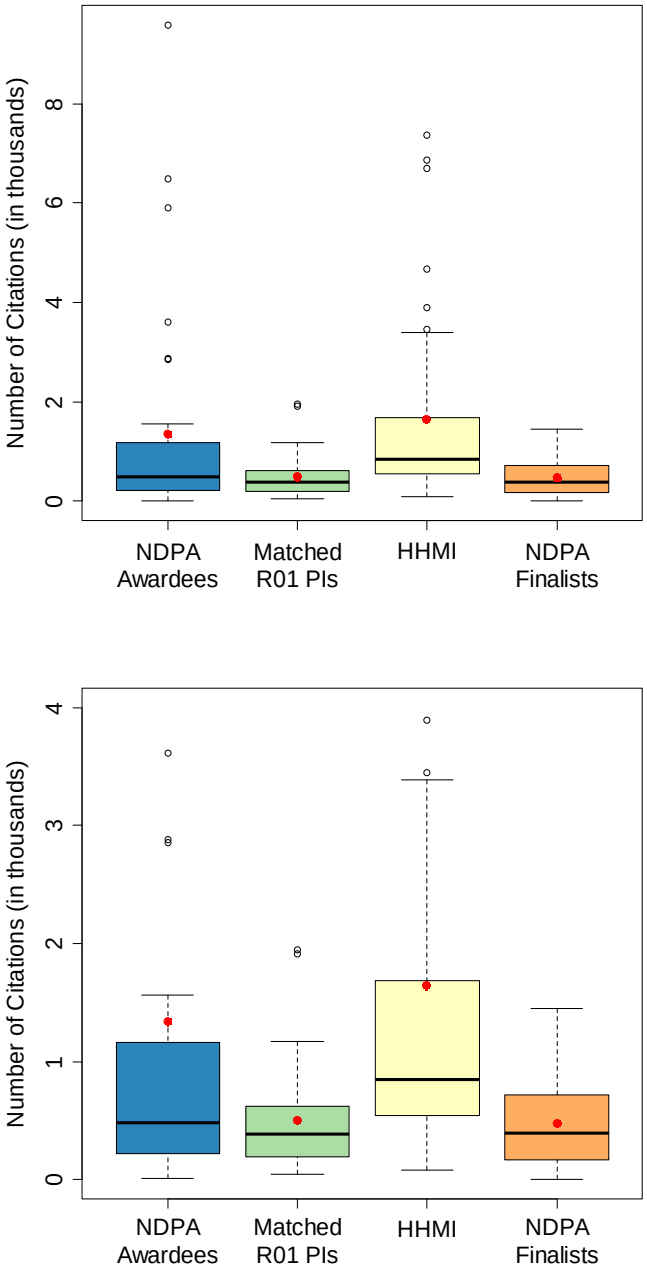


Note: One observation equals one PI.

Figure 38. Researcher-Level Post-Award Publications

2. Number of Citations

Citations to publications from the post-award period observed the same trend among the groups; NDPA awardee publications received similar numbers of citations as the matched R01 PI and NDPA finalist publications, and received fewer citations than HHMI publications (K-S, p = 0.33, 0.16, 0.01 respectively) (Figure 39).

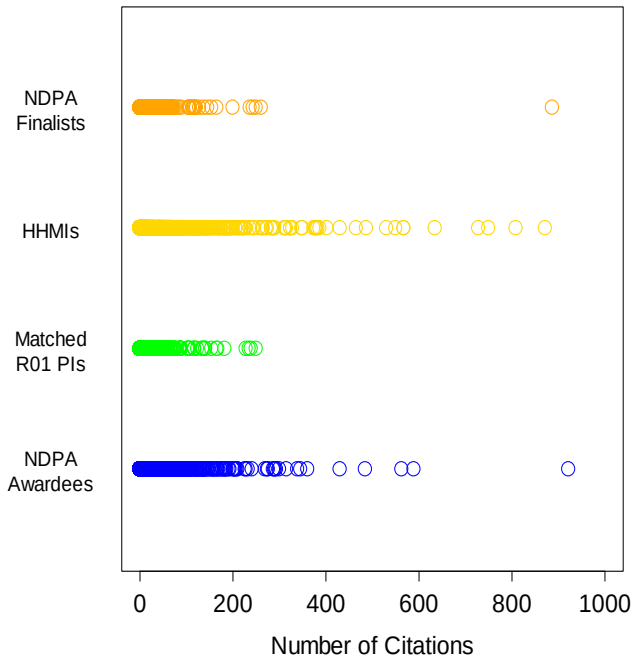


Note: One observation equals one PI.

Figure 39. Researcher-Level Post-Award Citations

3. Number of Citations per Publication

At the publication level, Pioneers had greater citation counts than matched R01 PIs and NDPA finalists, and similar citation counts as HHMI investigators in the post-award period (K-S, $p < 0.001$, <0.001, $= 0.12$ respectively) (Figure 40). The most notable similarity between the NDPA and HHMI distributions in comparison to those of the other groups is the distinctive tail of publications with large numbers of citations.

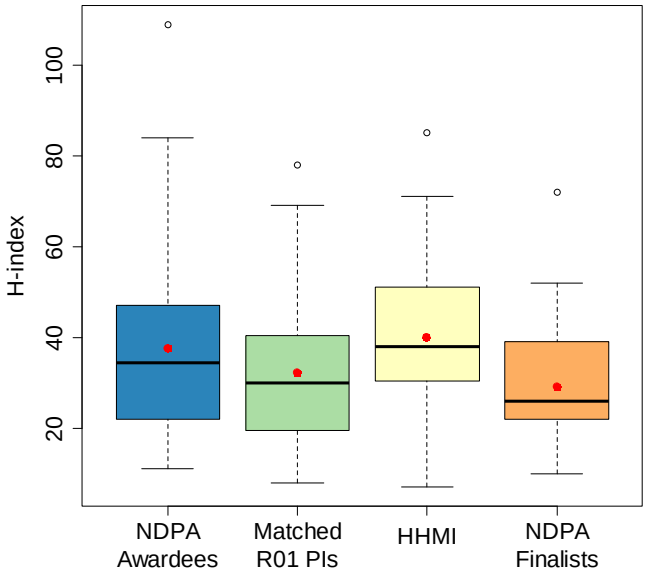


Note: One observation equals one publication.

Figure 40. Researcher-Level Post-Award Citations per Publication

4. H-index

Full career h-index, another proxy for a researcher's impact, showed no significant differences between Pioneers and matched R01 PIs, HHMI investigators, or NDPA finalists (K-S, $p = 0.42$, 0.72, 0.08 respectively) (Figure 41). H-index is cumulative over a researcher's career, so it is a less direct proxy of post-award research impact. Also, recall that there were no significant differences between the h-index values of the groups at time of award.

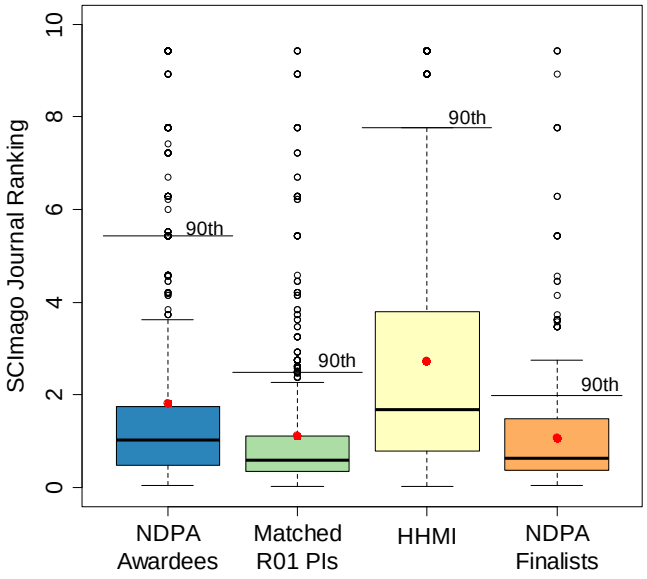


Note: One observation equals one PI.

Figure 41. Researcher-Level H-Index to 2011

5. SCImago Journal Ranking

Journal impact factor was another bibliometric proxy for research impact. NDPA researchers published in journals with higher impact factors than matched R01 PIs and NDPA finalists, and published in journals with lower impact factors than HHMI investigators in the post-award period (K-S, $p < 0.001$ for all comparisons) (Figure 42). The 90th quantiles for HHMI publications and NDPA publications are distinctly different than the 90th quantiles for the other two groups.



Note: One observation equals one publication.

Figure 42. Researcher-Level Post-Award Journal Impact Factors

6. Proportion of Publications by Journal Percentiles

Both the HHMI investigators and the NDPA Pioneers published more frequently than the matched R01 PIs and the NDPA finalists in the top 0.5% of SCImago-indexed journals in the post-award period. The HHMI investigators published in the highest ranking journals. A total of 41% of HHMI investigator publications were published in the top 0.5% of all SCImago-indexed journals. Pioneer publications in the top 0.5% accounted for 25% of the group's total publications, while the matched R01 PIs and NDPA finalists produced 12% and 11% in the top 0.5% of SCImago-indexed journals, respectively (Figure 43).

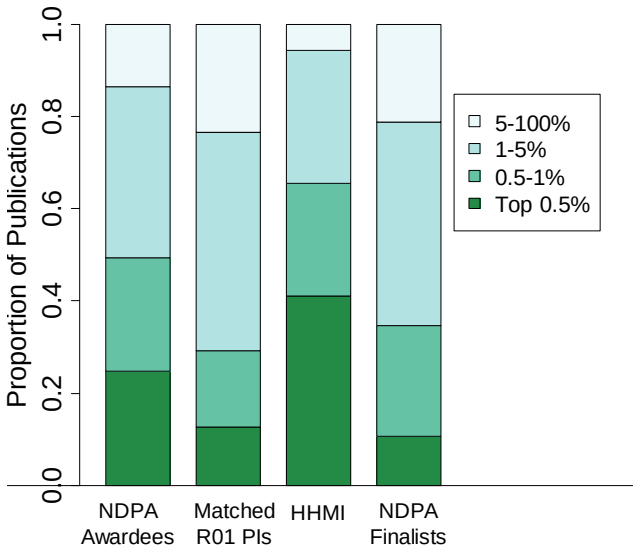


Figure 43. Researcher-Level Post-Award Proportion of Publications by Journal Percentiles

7. Additional Bibliometric Analyses: Outcomes per Selected Direct Costs

An additional set of analyses were performed on the Pioneer and HHMI investigator groups. These analyses compared the number of publications and citations per selected direct cost awards received by each PI. Due to the challenges of data collection and data availability for funding amounts, there are several limitations to this analysis. For each of the Pioneers and HHMI investigators, the study team collected information on all non-NDPA, NIH direct cost awards from the year of NDPA/HHMI receipt through the end of 2011, and used estimates for the following values based on information on the groups: NDPA direct cost amounts for the duration of the NDPA funding period, average annual half-salary[37] support for Pioneer awards, overall annual means for HHMI investigator operating and equipment budgets starting the year of NDPA/HHMI receipt through the end of 2011, and average annual salary support for HHMI investigator awards.[38]

Non-NDPA NIH award amounts were included only if the Pioneer or HHMI investigator was the contact PI on the NIH application. The team was unable to collect data for grants on which the PI of interest was a co-PI or otherwise affiliated with the grant.

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[37] Fifty percent of the average annual salary support provided for NDPA awards.

[38] Non-NDPA NIH funding was collected from the NIH QVR system. Pioneer award funding and 50% salary amounts were estimated based on discussions with NDPA program staff. HHMI investigator average funding and salary amounts were estimated based on discussions with HHMI program staff.

NDPA direct cost amounts were uniformly set at $500,000 per year for the 5-year designated funding period, although NIH's QVR system reports that some investigators received less than $500,000 in some years. The annual half-salary amount for Pioneer awards was estimated to be at $100,000. In consequence, each Pioneer was assigned $600,000 per year of NDPA funding.

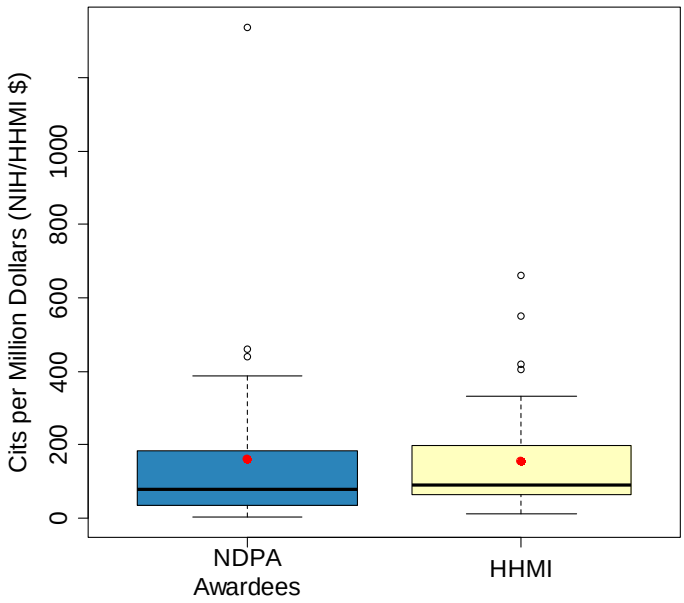
HHMI investigator direct cost awards were unknown for individual PIs. The team was provided with the overall annual mean for the 5-year period from 2005 through 2010 for forty of the 2005 HHMI investigators. The average annual operating budget for forty 2005 HHMI investigators from 2005 to 2010 was $580,543. The average annual equipment budget for that same group was $179,169.[39] After adding the annual salary amount for HHMI investigators, approximately $200,000, each individual who received an HHMI investigator award (includes some Pioneers) was rounded to $960,000 per year of HHMI funding. It should be noted that all individuals in the study who received HHMI investigator awards were renewed for HHMI funding in 2010 and the $960,000 per year figure was extended to account for HHMI funding these individuals would have received during their renewal period in 2010 and 2011.

Due to data availability, NIH and HHMI investigator funding were the only sources included in this analysis, but it is known that these researchers have many other sources of funding (e.g., NSF awards, HHMI Early Career Scientist Awards, private foundation support). In addition, the team could not account for PI funding support from research collaborations or lab members.

a. Number of Publications per Selected Direct Costs

In the years after award, Pioneers and HHMI investigators were similarly productive when accounting for NIH and HHMI investigator funding (K-S, $p = 0.47$) (Figure 44).

[39] HHMI program staff note that there are substantial variations in actual funding among the HHMI investigator awards.

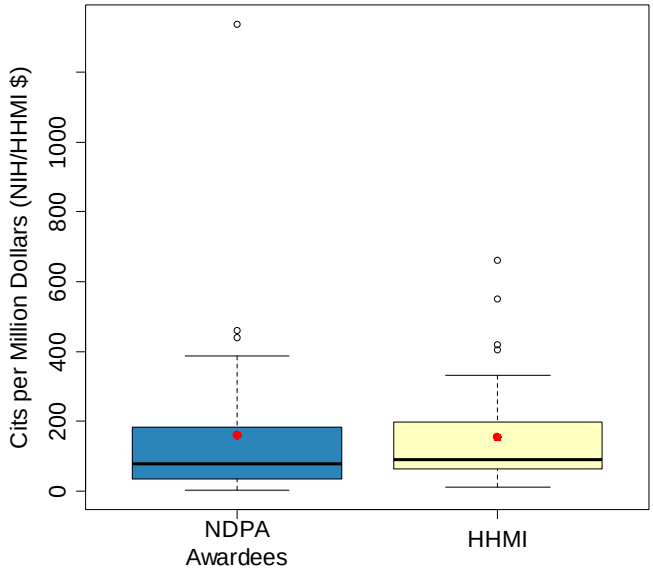


Note: One observation equals one PI.

Figure 44. Pioneer and HHMI Investigator Publications per Selected Direct Costs

b. Number of Citations per Selected Direct Costs

Pioneers and HHMI investigators received similar numbers of citations to publications in the post-award period when accounting for NIH and HHMI investigator funding (K-S, $p = 0.32$) (Figure 45).



Note: One observation equals one PI.

Figure 45. Pioneer and HHMI Investigator Citations per Selected Direct Costs

8. Additional Analyses: Text Mining

In addition to bibliometrics and expert review, the study team conducted a text-mining analysis of publications that were attributed to grants across the comparison groups. The goal of this analysis was to determine how dense and similar the topical areas of the grant-attributed publications are. This emerging method of analysis might be able to predict areas of innovation. Areas of low density, for example, might indicate transformative research topics.

Two analyses were conducted on the Pioneers, the HHMI recipients, the matched R01 comparison group, and the random R01 portfolio group:

- A comparison of the differences (i.e., the divergence) between publications in each comparison group and the NIH-SPIRES background (2007–March 2012)
- A comparison of topics among the grant-attributed publications

For the first analysis, the pairwise Kullback-Leibler (KL) divergence between title and abstract corpa were provided by Edmund Talley's group. The divergences were calculated between each grant-attributed publication and the set of funded grant applications and publications in SPIRES (2007–March 2012). The 500 smallest pairwise KL divergences for each grant-attributed publication were aggregated by comparison group and filtered to include only pairwise publication comparisons (e.g., the 500 publications in SPIRES with the smallest divergence from each of the NDPA-attributed publications are grouped). The 10th quantile from each of these "top 500" groups were calculated and compared in order to see how each group differed from the SPIRES background.

The analysis showed no statistical difference between the 10th quantiles of the KL pairwise divergence of the comparison group publications and SPIRES (Figure 46). This demonstrates, on the whole, that grant-attributed publications[40] have comparable numbers of similar papers (on a contextual basis) in SPIRES. Thus, any observed difference in citations among the comparison groups is due to something other than a difference in publication and citation habits or a paucity of research in an area.

[40] For HHMI investigators, only "top five" papers were used.

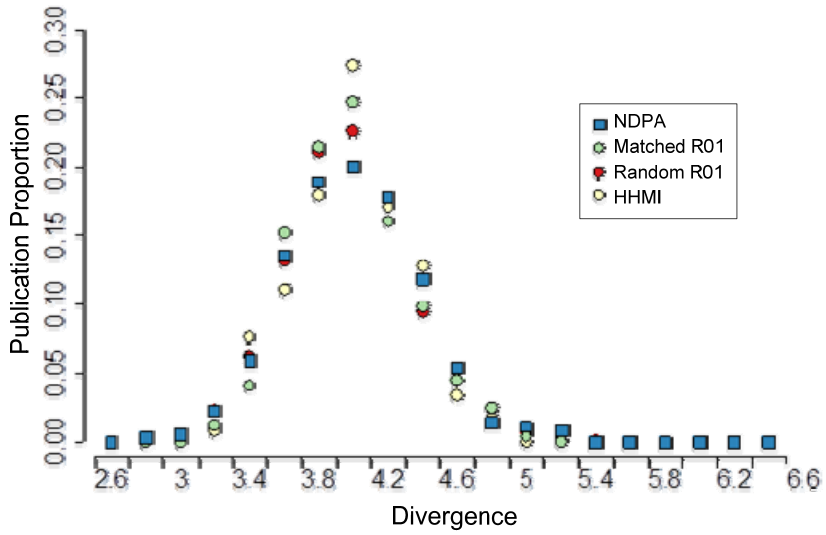
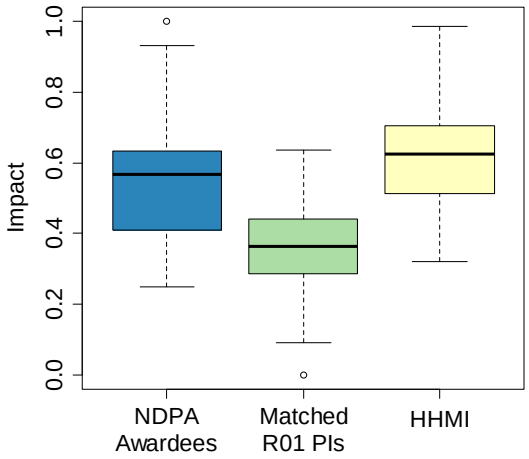


Figure 46. Difference from SPIRES Publications

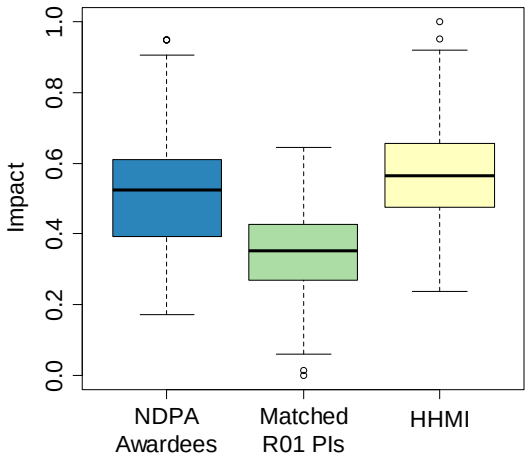
B. Expert Review Findings

Figure 47 and Figure 48 display box plots of the expert-assessed impact of packets and papers. NDPA and HHMI packets have significantly more impact than the matched R01s (t-test, $p < 0.0001$, K-S, $p = 0.0002$), with no significant difference between NDPA and HHMI (t-test, $p = 0.08$, K-S, $p = 0.17$). However, for papers, HHMI grants have significantly more impact than the NDPAs (t-test, $p = 0.0008$, K-S, $p = 0.004$), which again have significantly more impact than matched R01s (t-test, $p < 0.0001$, K-S, $p < 0.0001$).



Note: One observation equals one grant.

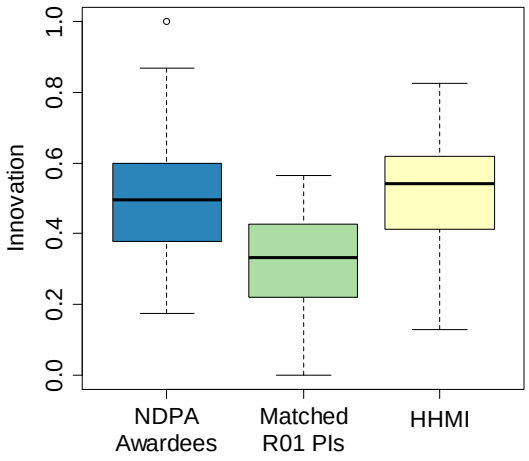
Figure 47. Expert-Assessed Packet Impact



Note: One observation equals one paper.

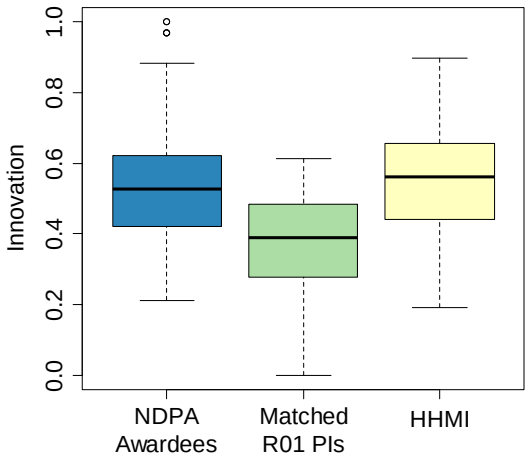
Figure 48. Expert-Assessed Paper Impact

Figure 49 and Figure 50 display box plots of the expert-assessed innovation of packets and papers. NDPA and HHMI packets are significantly more innovative than the matched R01s (t-test, $p < 0.0001$, K-S, $p = 0.0005$), with no significant difference between NDPA and HHMI (t-test, $p = 0.71$, K-S, $p = 0.88$). NDPA and HHMI papers are significantly more innovative than the matched R01s (t-test, $p < 0.0001$, K-S, $p < 0.0001$), with no significant difference between NDPA and HHMI (t-test, $p = 0.53$, K-S, $p = 0.14$).



Note: One observation equals one grant.

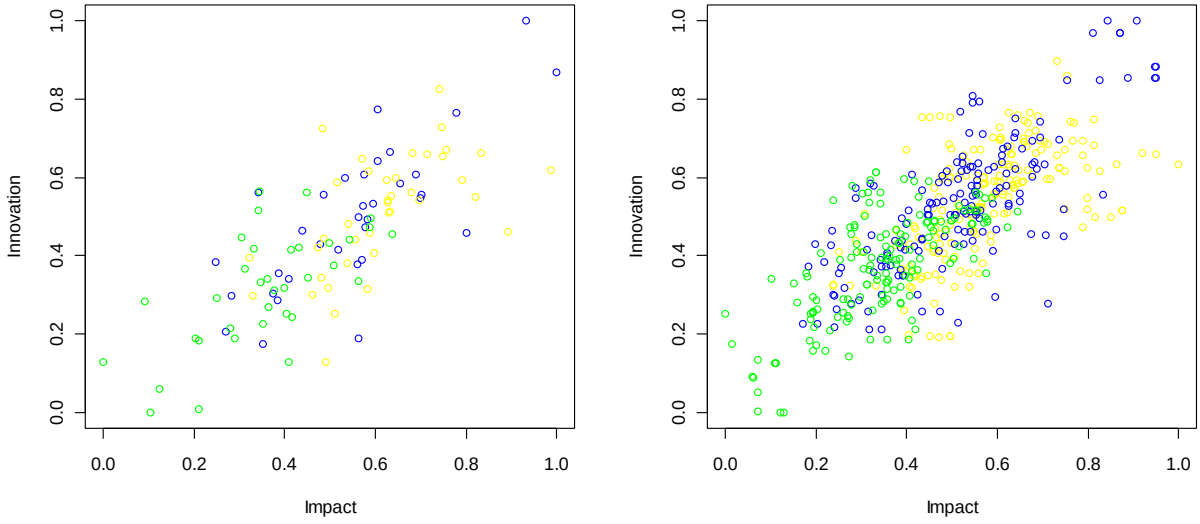
Figure 49. Expert-Assessed Packet Innovation



Note: One observation equals one paper.

Figure 50. Expert-Assessed Paper Innovation

Figure 51 shows a strong correlation between expert-assessed impact and innovation ($\rho = 0.76$ for packets and $\rho = 0.75$ for papers).



Papers **Packets**

Figure 51. Correlation of Impact to Innovation for Papers and Packets

Figure 52 and Figure 53 plot the estimated ranks packet impact and innovativeness. Note that the matched R01s are not among the top packets in the expert rankings. Figure 54 and Figure 55 plot the estimated ranks of paper impact and innovation.

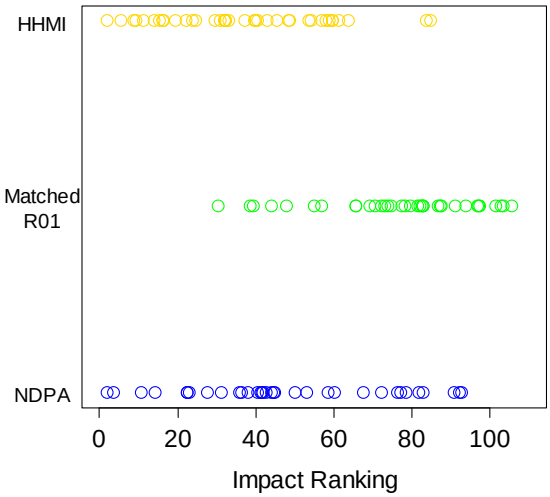


Figure 52. Expert-Assessed Packet Impact Rankings

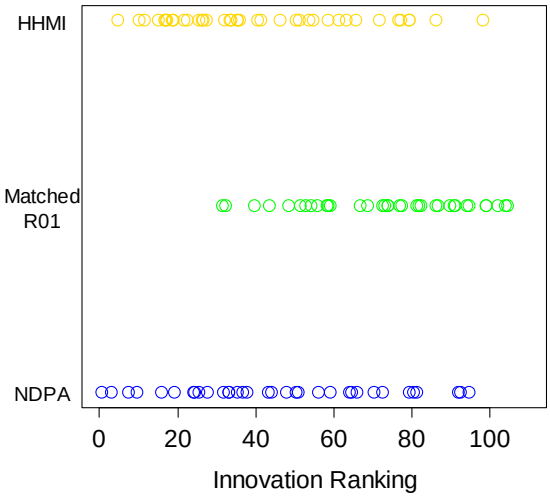


Figure 53. Expert-Assessed Packet Innovation Rankings

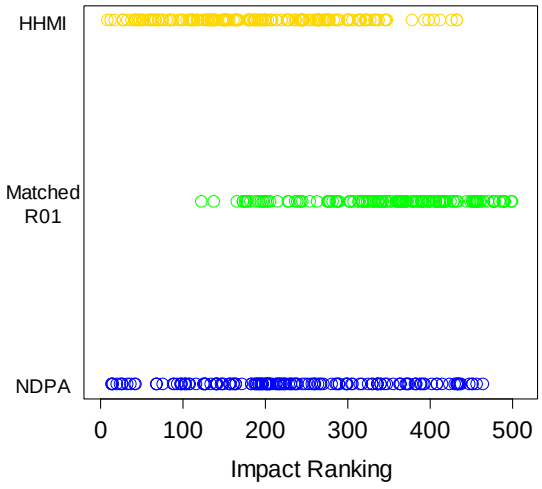


Figure 54. Expert-Assessed Paper Impact Rankings

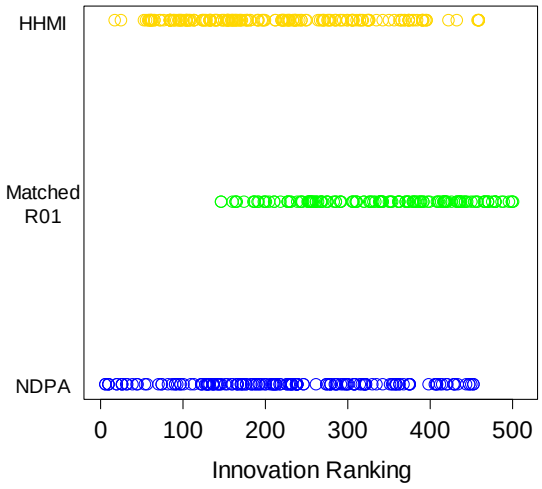


Figure 55. Expert-Assessed Paper Innovation Rankings

Additional discussion of the qualitative comments from the expert review can be found in Chapter 6.

C. Regression Analyses

A regression model linking expert ratings, bibliometric indicators of performance, and information about individual awards was developed to identify which variables were predictive of the underlying packet or paper impact as assessed by the experts. The study team had no expectation that the regression model would be a good surrogate for the expert ratings: it is unlikely that knowing the grant mechanism, the characteristics of the PI, and the journal that published the paper will fully characterize its level of impact or

innovation. Details of the model are discussed in Appendix I, and Table I-1 and Table I-2 summarize the coefficients of the fitted regression models.

The covariates considered were: granting mechanism (NDPA, R01, HHMI), number of pre-award citations for the PI, SCImago Institutions Ranking (SIR) for the PI at time of award, number of pre-award publications for the PI, PI h-index at time of award, years since degree, receipt of early career award, and, for the R01 awards, total direct costs.

For impact of the packet, the covariates that affected the rating (those that are significantly different from zero) are whether a PI received an HHMI or matched R01 award and the PI's pre-award lifetime number of citations. The impact of individual papers was affected positively by the impact factor of the journal in which the paper was published and the total number of citations to the paper. There was a negative impact when the paper was a review paper. Direct costs were included for matched R01 awards, and it is interesting to note that the size of the grant was not a statistically significant predictor of the impact rating of its five papers with the most impact.

With respect to ratings of the innovativeness of approaches, whether a PI got an NDPA or HHMI award was a factor in the rating, as was the PI's citations at award. Innovativeness of the approaches of the individual papers was (as with impact) affected positively by the impact factor of the journal in which it was published, and (again as with impact) there was a negative impact when the paper was a review paper. Again, it is interesting to point out that the size of the matched R01 grant was not a statistically significant predictor of the innovativeness rating of its five papers with the most impact.

6. Impact and Innovation: Qualitative Findings from Expert Assessment

As part of the expert assessment, reviewers were asked to provide comments about how they made their assessments of impact and innovation. Out of the 340 reviews the experts completed, 307 contained an open-ended discussion of the specific factors that influenced his or her assessment of impact, and 288 contained discussion of the specific factors influencing the assessment of innovativeness. This chapter discusses the findings from the analysis of those responses, which provide context for the quantitative analysis of the expert ratings.

A. Assessing Impact

Experts were asked to rate the level of impact in the research on a five-point scale from extreme to no impact. They also responded to the following open-ended question:

> *What about these papers, individually or as a whole, made you choose your answers above?*

The following prompt was given within the survey:

> *NDPA was created to promote highly innovative and potentially transformative approaches that have the potential to produce extremely high impact on a broad area of biomedical or behavioral research. In this context, "extremely high impact" refers to research that accomplishes one or more of the following:*
>
> - *radically changes present understanding of an important existing scientific or engineering concept*
> - *leads to the creation of a new paradigm or field of science or engineering,*
> - *challenges present understanding in the field(s) involved,*
> - *provides pathways to new frontiers,*
> - *challenges conventional wisdom,*
> - *leads to unexpected insights that enable new techniques or methodologies, or*
> - *redefines the boundaries of science or engineering.*

Of the 340 responses, 307 contained a discussion of specific factors influencing the assessment of impact. Five themes, summarized in Table 8. Counts for Major Themes

Used by Experts to Discuss Impact of Packets, were commonly discussed. (Appendix G includes a detailed list of the themes identified and coded.) Table 8 contains the number of responses that mentioned a particular theme broken out by the expert's quantitative ranking of the packet.

Table 8. Counts for Major Themes Used by Experts to Discuss Impact of Packets

Theme	Extreme or Very High Impact (*n* = 168)	Moderate Impact (*n* = 107)	Slight or No Impact (*n* = 35)
Foundational research	60	45	16
Elucidation of pathways or mechanisms	42	18	1
Translational or clinical potential	37	9	3
Changing present understanding	36	24	10
Pathways to new frontiers	28	11	0

"Foundational research" and "changing present understanding" were the general themes that experts used to express either positive or negative assessments of impact. They have large relative counts across all packet ratings.

"Elucidation of pathways or mechanisms" encompassed three primary ideas:

- Research that provided entirely new or important mechanistic insight
- Research that solved long-standing questions in a particular pathway or process and provided future opportunities for moving forward
- Research that definitely identified the role of a specific element in the pathway, which was previously unexplored or not well-understood

In research deemed to have extreme or very high impact, the foundational research theme appeared more often in the discussion of HHMI (28%) and NDPA (26%) packets than in assessments of the matched R01 packets (14%). Examples of experts' comments that fell under this category include:

> *"…Paper #5 was extremely impactful because it revealed a new connection between histone post-translational modifications and DNA replication, which is a largely unexplored but important aspect of eukaryotic biology."* (HHMI)

> *"The major papers in this group address a crucial issue in the development of the nervous system: how are specific connections formed between source and target structures during development. Two of the papers address this issue in the vertebrate retina, where beautiful lamination and sublamination provides an elegant example of specificity of connections. One paper that I regard as extremely impactful shows how*

inputs segregate on to pyramidal neurons of layer 5 in the cerebral cortex—a major issue in development of the cerebral cortex. Another impactful paper shows the role of other semaphorins in formation of connections in the fruitfly drosophila. Together, they build an insightful picture of the role of a class of molecule, semaphorins, in the development of specific projection systems in the brain." (HHMI)

"Studies presented in these papers identified novel signaling components and signaling events in pathways mediating apoptosis, necroptosis and autophage. Two of these studies also identified inhibitors of these signaling pathways, which are potential lead compounds for anti-cancer drug. These findings made significant contributions to the understanding of the mechanisms of cell death and autophage, and advanced the field." (NDPA)

"Human TFG is a tumor suppressor or an oncogene in several human cancers but its mechanisms of action remain unclear. This paper demonstrates that the C. elegans homolog TFG-1 acts as both a novel apoptotic suppressor and an activator of cell growth." (R01)

"Translation or clinical potential" encompassed four primary ideas:

- Research that identifies interventional or therapeutic targets
- Research that closes the gap between basic science and clinical delivery
- Utilization of animal models to demonstrate clinical potential
- Development of previously nonexistent culture systems

In research deemed to have extreme or very high impact, this theme appeared more often in the discussion of matched R01 (31%) and NDPA (26%) packets than in assessments of the HHMI packets (14%). Examples of experts' comments that fell under this category include:

"The investigators have mapped several regulatory pathways that connect the binding of auto inducers at sites on the surface to functional changes within the cell. For public health a highly important result is the elucidation of the pathway that leads to expression of virulence factors when many Vibrio cholerae are present. They have also studied how the ability of the auto inducers to trigger quorum sensing relates to their chemical structure by synthesizing auto inducers with modified structures. This work has revealed ways in which the effect of the auto inducers could be blocked, suggesting routes to therapies. This work and studies like this are of the utmost significance for the mission of the NIH in the medium and longer term." (HHMI)

"The studies in aggregate are highly significant and made important advances in our understanding of the signaling pathways that operate in HSC [hematopoietic stem cells] and leukemia. These findings, although [they] do not radically change our current understanding of the field, have

led to significant scientific insights and the identification of pathways that could be manipulated for leukemia treatment." (R01)

"Development of a culture system for HPV is of very high impact, allowing therapeutic testing in culture, viral genetics, virus-host interactions, replication and in vitro models of oncogenesis. Very nice." (R01)

"This is an extremely impressive body of work. The high level of impact derives not only from the application of cutting edge techniques, several of which are novel and used for the first time, but also from the relevance to human disease. This work has high significance at the levels of basic and translational research and to clinical science. Adding to the impressiveness of this series of papers from the [Daley] lab is that they were all published over only a 3 year period. These papers truly advance understanding of stem cells and how they can be used in innovative ways in medicine." (NDPA)

"It has long been a goal to expand hematopoietic stem cells in culture, but the field has been marked by controversy and reports that were not reproducible. In most cases, the precious property of self-renewal has been quickly lost when the cells have been placed in culture. Many investigators have tried co-cultures with a variety of stromal cell types in hopes that one might provide a supportive stem cell niche. If particular endothelial cells work as described in the first of this group of papers, there will be tremendous impact and implications for clinical treatments. This is provided of course that the work is reproducible." (HHMI)

"These papers present a picture of the spread and genetics of the virus. They directly impact treatment." (NDPA)

"Collectively these papers helped identify key regulatory pathways involved in HSC function and or leukemic stem/progenitor cell progression. The primary impact of these papers is the identification of additional pathways that can be manipulated for therapy. Some of the work provided hard proof of pathway involvement that had been theorized before the work based on gene expression patterns in hematopoiesis/leukemogenesis. Each paper identified unrelated pathways and are therefore key advances in their own right. It is unusual for a single laboratory to make so many independent significant advances." (HHMI)

"Pathways to new frontiers" was a theme presented to experts as a potential indicator of high impact research and was used when the experts' discussions specifically cited opportunities for future exploration. Specific ideas include:

- The specific methods chosen and research findings clearly define the path for moving forward

- New methods, techniques, or resources (clone libraries, genetic maps, etc.) were developed, especially for areas where there was a critical need
- The research pursued issues that were far ahead of mainstream, in an entirely new frontier
- The research findings have applications not just for a particular research topic, but with broad applicability
- Other researchers have followed suit, and are pursuing this line of investigation

In research deemed to have extreme or very high impact, the pathways to new frontiers theme was discussed in 19% of the NDPA responses, 17% of the matched R01 responses, and 14% of the HHMI responses. Examples of experts' comments that fell under this category include:

> *"This work forms a foundation for the use of viruses as genetically encoded nanoparticles. A nice array of applications is explored - fluorescent imaging, MR imaging, tumor targeting. Quite a few investigators in the field have subsequently jumped on this band wagon, and the exploitation of viruses as nanoparticles is really emerging as a significant thrust."* (R01)

> *"The inventive development and application of large-scale microfluidics and of high-throughput sequencing by the group of Stephen Quake have made these techniques among the most powerful discovery tools of molecular and cellular biology where the throughput is critically needed. The clever design and operation of his signature microfluidics have opened many research opportunities for his group and potentially others as well."* (NDPA)

> *"As a group, these papers are extremely impactful. The "Mapping and sequencing" paper provides pathways to new frontiers by providing the first high-resolution sequence map of human structural variation. The "A burst of segmental duplication" paper addresses a long standing question, "how humans evolved from the great apes." It leads to the creation of a new paradigm that a burst of genome duplication activity (rather than cytogenic rearrangements, single-base-pair changes, or retro-transposon activity) occurred during the period when humans diverged from the great apes. The "diversity of human copy number" paper provides pathways to new frontiers, by making ~ 1000 genes accessible to genetic studies of disease association (e.g., intellectual disability, autism, schizophrenia and epilepsy). The "duplication architecture" paper and the "punctuated cores of human genome evolution" paper, although slightly less impactful in their own right, set the stage for the subsequent extremely impactful papers."* (HHMI)

B. Assessing Innovation

As part of the research assessment, experts were also asked to rate the level of innovation, specifically for the research approaches, on a five-point scale from extreme to no innovation. They also responded to the following open-ended question:

> *Regardless of its impact, how innovative are the approaches described in this set of papers, taken as a whole?*

The following prompt was given in the survey:

> *NDPA was created to promote highly innovative and potentially transformative approaches that have the potential to produce unusually high impacts on a broad area of biomedical or behavioral research. In this context, an approach may be considered extremely innovative if it accomplishes one or more of the following:*
>
> - *the ideas underlying the research are at odds with prevailing wisdom,*
> - *the research requires the use of equipment or techniques that have not been proven or are considered extraordinarily difficult, or*
> - *the research involves a unique combination of disciplines.*

288 of the 340 responses contained a discussion of specific factors influencing the assessment of innovativeness. Four themes, summarized in Table 9, were commonly discussed. Table 9 contains the number of responses that mentioned a particular theme broken out by the expert's quantitative ranking of the packet.

Table 9. Counts for Major Themes Used by Experts to Discuss Innovation of Packets

Theme	Extreme or Very High Impact (*n* = 130)	Moderate Impact (*n* = 115)	Slight or No Impact (*n* = 43)
Research requires the use of equipment or techniques that have not been proven or considered difficult	61	33	2
Creative utilization or improvement of existing techniques	41	23	6
Standard methods	19	60	28
Changing present understanding	24	27	6

"Changing present understanding" was a general theme that experts used to express either positive or negative assessments of innovation.

Use of "standard methods" was commonly cited when a paper or packet was not judged to be highly innovative. Examples of expert comments include:

"The use of Zebrafish genetics combined with electrophysiological and molecular approaches is not novel. They are well done in these papers, but do not demonstrate a novel or uniquely strong approach. The results have not significantly challenged prevailing wisdom." (HHMI)

"While innovation is often in the eyes of the beholder, these are typical studies that are using standard methods (statistics for the epidemiological studies, clustering methods to trace evolutionary relatedness)." (NDPA)

"While these studies were carefully undertaken, there is little in them in the way of innovation. There are very much examining well-studied areas using very conventional approaches." (R01)

The "use of equipment or techniques that have not been proven or considered difficult" encompassed three primary ideas:

- Successfully completing technically sophisticated experiments, for which other investigators had previously been unsuccessful
- Research that completed laborious techniques, which was considered to be a "service" to other researchers in the field
- Research that was difficult due to inaccessibility of research materials

In "extremely" or "very" innovative work, difficult technique was mentioned in 55% of HHMI responses, 45% of matched R01s, and 38% of NDPA. Examples of the experts' comments that fell in this category include:

"Most of these achievements are not incremental advances achieved by applying safe, proven methods. Instead, they take rather radically new, unproven approaches." (HHMI)

"Creativity was high and innovative, developing a robust culture system for HPV. Important for numerous researchers across the field." (R01)

"This work is extremely novel and exciting. The techniques are very difficult, and prior to this group accomplishing their goals, most would have not considered most of the work in these papers to have been feasible. The work is highly interdisciplinary." (NDPA)

"These manuscripts all make use of cutting-edge technologies that are very difficult. They all include a broad range of approaches to generate data that supports their conclusions." (HHMI)

The "creative use of existing techniques" encompassed two primary ideas:

- Clever integration of complementary approaches
- Techniques applied in an innovative way to address the specific study question

In "extremely" or "very" innovative work, creative technique was mentioned in 29% of HHMI responses, 33% of matched R01s, and 35% of NDPA. Examples of the experts' comments that fell in this category include:

> *"It may not use any new techniques per se, but the demonstrated application is very powerful and constitutes a new method of fundamental biological research…."* (NDPA)

> *"I feel that the most innovative aspects of this research was the collaborative study on beta-catenin function. With that said, this study really does not represent a technical breakthrough, rather, the innovation aspect stems from clever integration of live cell imaging with biochemical and ultrastructural approaches to discover a completely new function for beta-catenin."* (R01)

> *"As noted in the previous section, each of these papers pinpoints a central biological question and employs excellent methodology to solve the question. The most obviously innovative contributions are the new telomere protection assay and the creation of the ts mutations in TRF2, but the use of live-cell monitoring of telomere movement in the 53BP1 paper was also stunning. Other techniques, such as FUCCI and the Shld1-regulated Pot1 were developed by others, but skillfully exploited."* (NDPA)

> *"These are clever applications of molecular genetics tools and approaches, including mutant fruitflies and mice, to address the role of several members of a class of molecule—the semaphorins—in brain development."* (HHMI)

> *"The techniques used here—flow cytometry, RNAi, gene profiling, for example—are not in themselves innovative. They have been applied to the study of mammalian stem cells and other developmental systems. What is unique and innovative about these studies is the collective application of these techniques to a model system, planaria, to which these techniques have not been systematically applied."* (HHMI)

C. Summary of Qualitative Findings

When assessing impact, the experts used foundational research and changing present understanding as themes to distinguish work as having more or less impact. Changing present understanding was also the general theme used to distinguish innovative research.

However, additional specific themes emerged as important in describing high-impact work. The first specific theme was elucidation of pathways or mechanisms. This was more commonly cited among HHMI investigators and Pioneers than among the matched R01 PIs. The second theme was translational or clinical potential, which was more commonly cited among the Pioneers and matched R01 PIs than for HHMI

investigators. The third theme was pathway to new frontiers, which was cited similarly among the groups.

For innovation, the specific themes that emerged related to the difficulty and creativity of technique. HHMI investigators were cited for using difficult technique the most often, followed by Pioneers, followed by matched R01 PIs. Creative technique was mentioned in approximately similar proportions across the comparison groups.

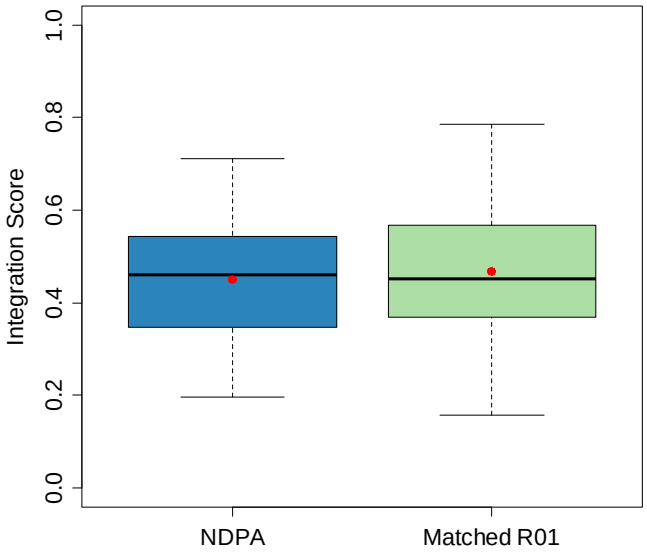
7. Interdisciplinarity and Collaborations Findings

The findings to the secondary study questions—around interdisciplinarity and co-authorship patterns—are presented for all comparison groups. This includes the assessment of four bibliometrics for the matched R01 set of grants and three for the HHMI investigators and NDPA finalists.

A. Interdisciplinarity

1. Integration Score

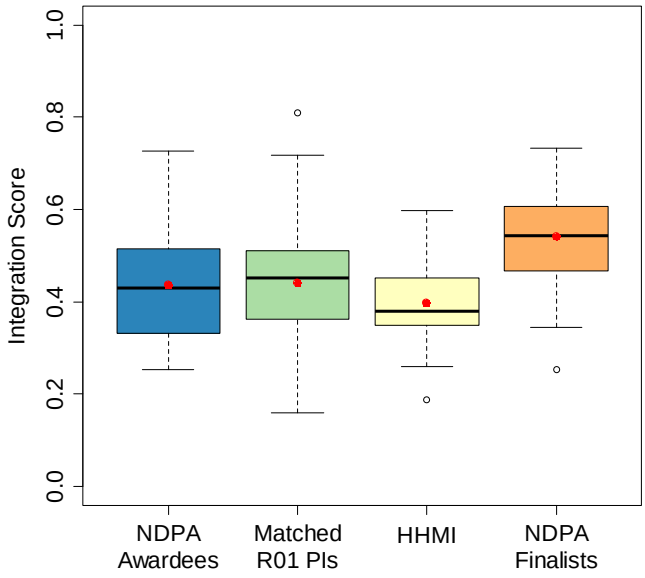
NDPAs and matched R01 grants have similar grant-level integration scores (K-S, $p = 0.82$) (Figure 56). The R01 grants and NDPAs were matched on the topical similarity of their applications, so the similarity in how these grant-attributed publications integrate knowledge suggests that the topics addressed by the grants may indeed be similar.



Note: One observation equals one PI.

Figure 56. Grant-Level Integration Score

In the period after the award, the researcher-level integration score (Figure 57) for Pioneers, matched R01 PIs, and HHMI investigators are similar (K-S, $p = 0.74$, 0.06). NDPA finalists, however, had higher integration scores than NDPA Pioneers during this time (K-S, $p = 0.01$).



Note: One observation equals one PI.

Figure 57. Researcher-Level Post-Award Integration Score

2. Additional Analyses: Proportion of Subject Area Categories

The study team conducted additional analyses to quantitatively represent the diversity of research publications by the NDPA and matched R01 grant groups, as reflected in the subject categories Thomas Reuters assigns to the publications the two groups cited in their published work. The 221 subject area assignments from Thomson Reuters were organized into 18 macro-subject area clusters for use in two analyses: (1) the proportion of referenced articles in each subject area were normalized such that each NDPA and R01 publication has the same weight (Figure 58), and (2) the proportion of citations in each subject area were normalized such that each researcher has the same weight, regardless of their number of publications (Figure 59). Neither figure suggests strong differences in the subject areas cited as a result of NDPAs and matched R01 grants.

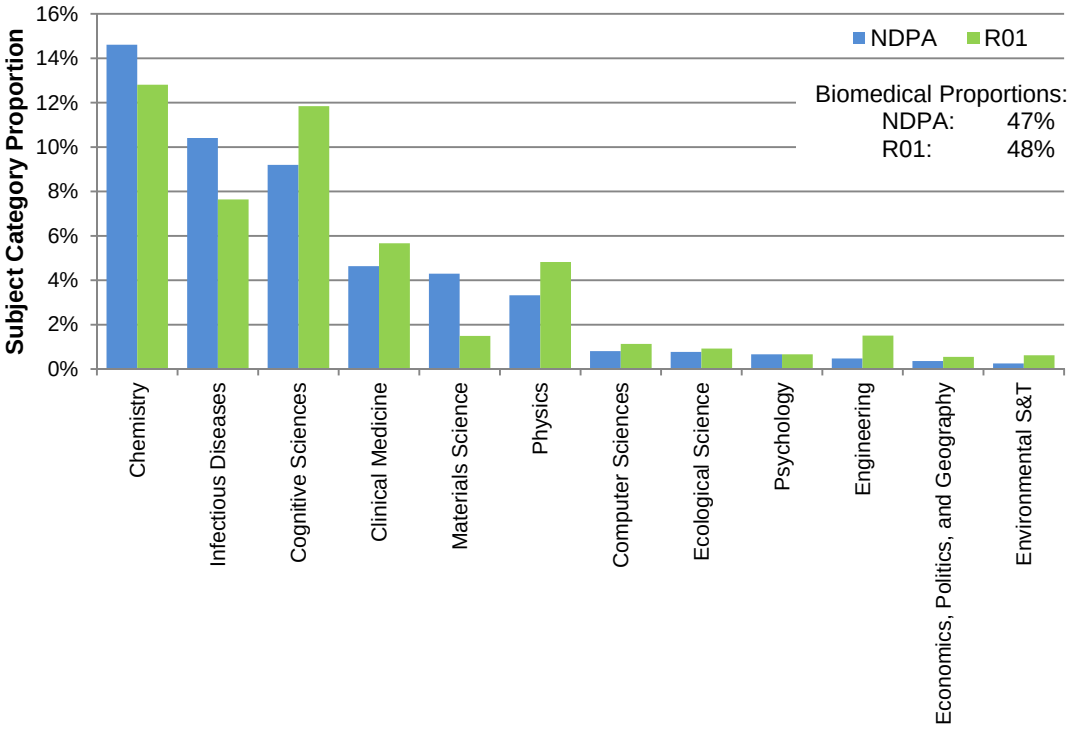


Figure 58. Subject Categories, Aggregated by Publication

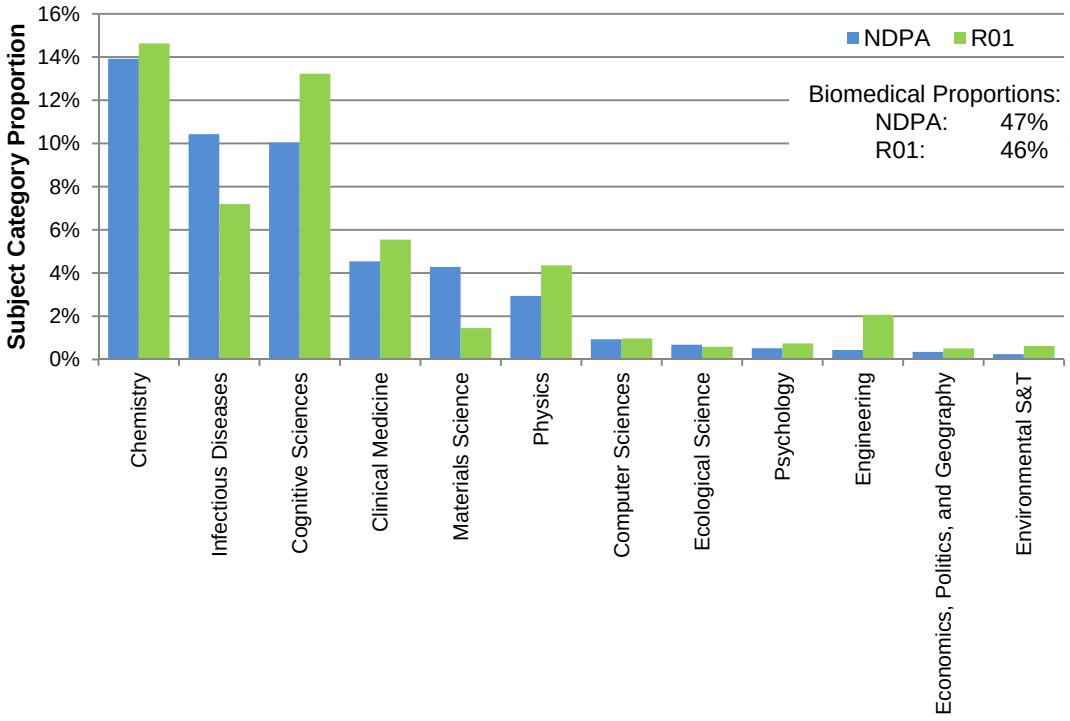
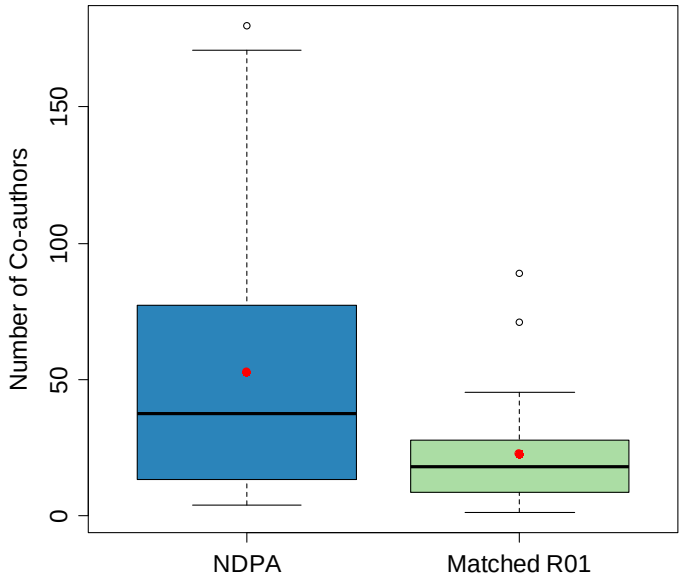


Figure 59. Subject Categories, Aggregated by PI

B. Collaborations

1. Number of Co-authors

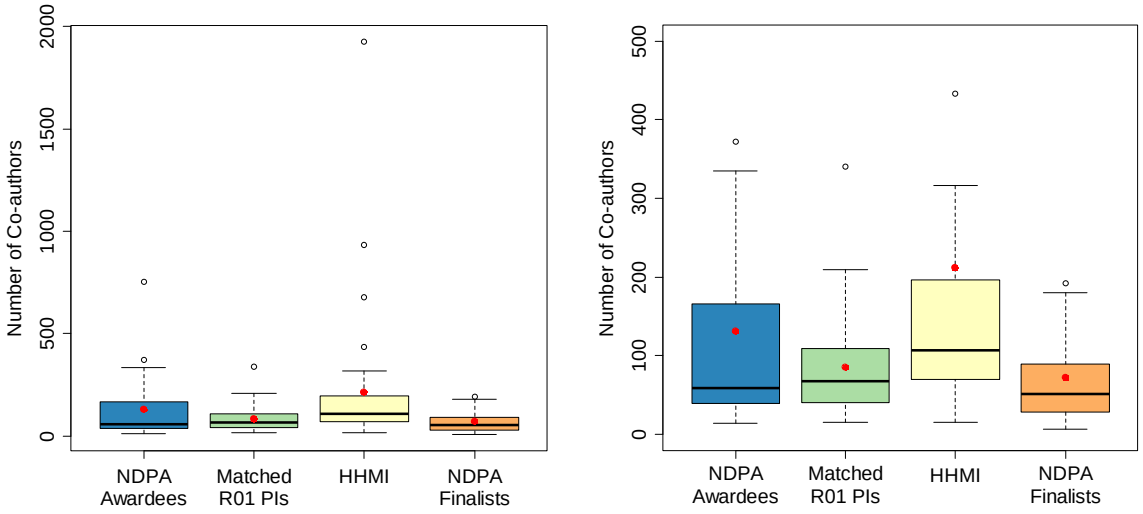
NDPA-attributed publications had greater numbers of authors than matched R01 grant-attributed publications (K-S, $p = 0.01$) (Figure 60).



Note: One observation equals one grant.

Figure 60. Grant-Level Unique Co-authors

NDPA Pioneers published with similar numbers of co-authors as matched R01 and NDPA finalist researchers in the post-award period (K-S, $p = 0.34$, 0.24) (Figure 61). HHMI investigators, however, published with a greater number of co-authors (K-S, $p = 0.007$). Since all of the groups published with a similar number of authors prior to the award period, it would appear that HHMI investigators formed a greater number of new collaborations than NDPA Pioneers after receiving the award.

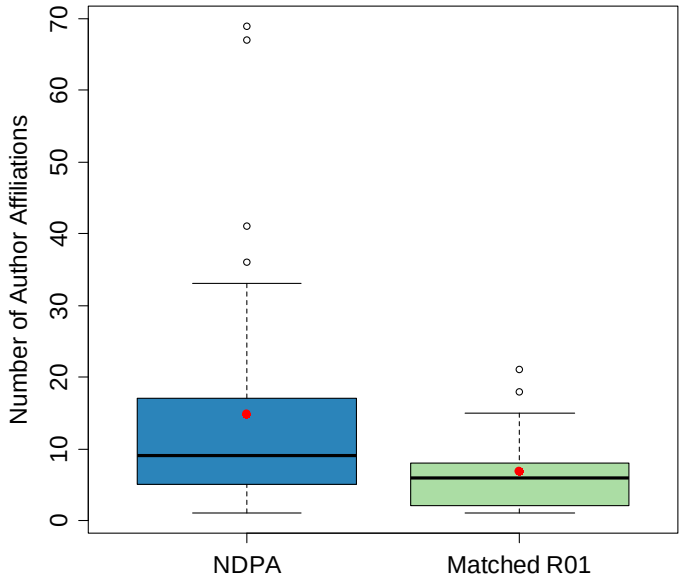


Note: One observation equals one PI.

Figure 61. Researcher-Level Post-Award Unique Co-authors (Complete and Magnified)

2. Number of Co-author Affiliations

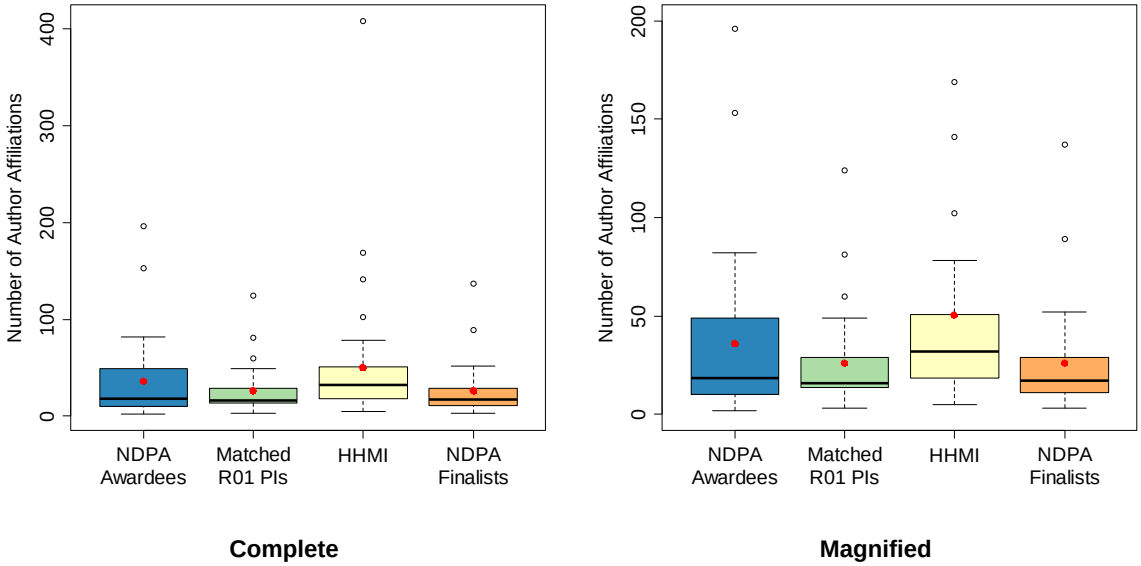
NDPA and matched R01 grant-attributed publications were published by researchers from similar numbers of institutional affiliations (K-S, $p = 0.07$) (Figure 62).



Note: One observation equals one grant.

Figure 62. Grant-Level Unique Author Affiliations

Unique author affiliations follow the same trend as co-authors; NDPA awardee publications have similar numbers of institutional affiliations as matched R01 and NDPA finalist researcher publications and fewer institutional affiliations than HHMI investigator publications in the post-award period (K-S, p = 0.19, 0.58, 0.04 respectively) (Figure 63).



Note: One observation equals one PI.

Figure 63. Researcher-Level Post-Award Unique Author Affiliations (Complete and Magnified)

8. Summary of Findings

This chapter summarizes the findings detailed in Chapters 4–7.

A. Grant-Level Analyses of Impact and Innovativeness

Grant-level analyses were performed on three sets of grants—Pioneer grants from the first three cohorts (2004-2006), matched R01 grants in the same time period, and grant in 30 randomly selected portfolios of R01 grants (again from the same time period).

Bibliometric analyses indicate that the Pioneer grants resulted in a larger number of published papers (518) than the matched R01 grants (295). NDPA grants were larger than the matched R01 grants, and when considered per dollar, NDPA and matched R01 grants produced similar numbers of publications.

The 30 random R01 portfolios, each valued at $87.5 million, published more papers (median of 530) than the NDPA portfolio (266). When considered per dollar, the NDPA portfolio still had a slightly smaller number of publications than the random R01 portfolios.

Impact was assessed using three bibliometric (citations, journal impact and h-index) and two expert review-based ("packet" and paper level subjective assessment) indicators. Turning first to the number of citations per grant, NDPA awards received a similar number of citations as the matched R01 set of grants. The NDPA and matched R01 portfolios had a comparable number of citations (5,031 and 4,293, respectively) to the random R01 portfolios (median of 5,757), even though the random portfolios contained a greater number of publications.

On a per-publication basis, NDPA and the matched R01 grants have similar distributions. For example, 50% of NDPA and 56% of matched R01 grant-attributed publications received greater than or equal to 13 citations. It is important to note that there were several NDPA-attributed publications with over 400 citations and no matched R01-attributed publications with over 281 citations (none of the papers in the bibliometric analyses were review papers), indicating perhaps that a small number of Pioneers have been very successful.

Both NDPAs and matched R01 grants, however, received more citations per publications than were attributed to the random portfolios. For example, 10% of NDPA and 7% of matched R01 publications, as opposed to only 3% of unique random R01 portfolio publications, had accumulated greater than 55 citations. While the Pioneers

tended to publish later in the grant period than the matched R01 PIs, their papers, once published, were cited more quickly.

Looking at the statistics on journal prestige, the team found that the Pioneers' NDPA-attributed publications appeared in journals with higher impact factors than matched R01s. The Pioneers also had a larger fraction of their NDPA-funded publications in top journals than the other two groups—half of NDPA grant-attributed publications appeared in the top 1% of all science journals, compared to under one-third (32%) of the matched R01 publications appeared in the top 1%. Only 7% of the random R01 portfolio publications were in the top 0.5% of journals and 21% were in the top 1% of journals.

The h-index, an indicator that integrates both publication and citation counts into one metric, was greater for the NDPA-attributed publication portfolio than that of the matched R01s. For instance, 25% of NDPA grants and 15% of matched R01 grants had an h-index value greater than or equal to 9.

Expert assessment of impact (conducted on the five highest-impact publications of Pioneers and matched R01 publications) reflected the bibliometric analyses, finding NDPAs to have uniformly more impact than the matched R01 awards, at the level of both the packet and the individual papers.

Two methods were used to assess the innovativeness of research approaches in the grant-attributed publications. Expert assessment found NDPA "top five" publications to have research methods that were more innovative than the matched R01s, at both the "packet" level and the paper level. Qualitative analysis of expert comments, summarized below, illustrates some systematic differences between the two groups. Text mining analysis did not find the NDPA research areas to be more "distant" from the NIH SPIRES background than the matched R01s.

B. Researcher-Level Analyses of Impact and Innovativeness

Researcher-level analyses were performed on four sets of researchers—Pioneers and NDPA finalists from the first three cohorts, matched R01 grantees in the same time period, and HHMI investigators from 2005. The researcher level analysis was valuable in two regards. By including publications funded by a larger set of grants, going beyond just the Pioneer award, it provided a fuller picture of the accomplishments of Pioneers and the matched set of PIs. More importantly, it allowed for comparisons with HHMI investigators and NDPA finalists, which are groups that do not have specific grants outputs for comparison.

Comparisons with the researchers in the matched R01 set and finalist groups show the Pioneers to be similar to both groups with respect to the number of publications. Pioneers, however, had higher citations counts at both the PI level and the publication

levels (for instance, 10% of Pioneer, 3% of matched R01 PI, and 3% of finalist post-award publications had greater than or equal to 86 citations by the end of 2011). Pioneers also had higher journal impact factors, and a higher fraction of publications in journals with the most impact. In fact, twice as many (as a proportion of the total) Pioneer publications were in the top 0.5 % of all SCImago-indexed journals than was found for the other two groups. Pioneers were similar to both groups with respect to h-indices For instance, 50% of Pioneers, 43% of matched R01 PIs, and 27% of finalists had an h-index value greater than or equal to 34.5 at the end of 2011).

Comparisons with the HHMI investigators are more nuanced. HHMI investigators outperform Pioneers with respect to the number of publications. The HHMI investigators from 2005 produced a median of 37 papers, as compared with a median of 21.5 for the Pioneers.

When looking at the total numbers, HHMI investigators have a greater number of citations (25% of Pioneers and 38% of HHMI investigators had received greater than or equal to 1,157 citations to post-award publications by the end of 2011). However, when examined on a per *NIH and HHMI dollar* basis (see the detailed caveats in Chapter 5), the two groups produce a comparable number of citations. The two groups also have a similar number of citations *per publication* (50% of NDPA and 52% of HHMI post-award publications had greater than or equal to 15 citations by the end of 2011). One additional similarity between the NDPA and HHMI publications is the distinctively long tail of publications with large numbers of citations (10% of NDPA and 12% of HHMI post-award publications had greater than or equal to 86 citations by the end of 2011).

HHMI investigators publish in higher impact journals, and have twice the proportion of their publications in the top 0.5% of the journals as the Pioneers. Experts found the individual publications of the HHMI investigators to have more impact than those of the Pioneers, although there was no difference between the groups in the assessment of the body of work represented by the "top five" publications. There was no difference between the Pioneers and HHMI investigators with respect to career h-index (50% of Pioneers and 54% of HHMI investigators had h-index values greater than or equal to 34.5).

Expert assessments included assessment of HHMI Investigators as well (but not the NDPA finalists, because there was no single attributable "body of work" that could be assessed). With respect to innovativeness of research approaches, both in their numeric and qualitative assessment, experts found Pioneer publications to have research methods that were similarly innovative as the HHMI investigators, at both the packet level and the paper level.

C. Qualitative Findings from Expert Assessment

Out of the 340 reviews experts completed of the three sets of researchers (Pioneers, Matched R01 grantees and HHMI Investigators), 307 contained an open-ended discussion of the specific factors that influenced his or her assessment of impact, and 288 contained discussion of the specific factors influencing the assessment of innovativeness.

When assessing impact, the general themes used by the experts to distinguish work with more or less impact were how foundational the research was and how much it changed present understanding. The first specific scientific theme was elucidation of pathways or mechanisms. This was more commonly cited among HHMI investigators and Pioneers than among the matched R01s. The second theme was translational or clinical potential, which was more commonly cited among the NDPA and matched R01 PIs than for HHMI investigators. The third theme was pathways to new frontiers, which was cited similarly among the groups.

For innovativeness, the specific themes that emerged related to the difficulty and creativity of technique. HHMI investigators were cited for using difficult technique the most often, followed by NDPA, followed by matched R01. Creative technique was mentioned in approximately similar proportions across the comparison groups.

D. Regression Analysis

A regression model linking expert ratings, bibliometric indicators of performance, and information about individual awards, was developed to determine which variables were predictive of the underlying packet or paper impact as assessed by the experts. For impact *of the packet*, there were two covariates that affected the rating: whether a PI received an HHMI or matched R01 award, and the PI's pre-award number of citations.

Impact of the *individual papers* was affected positively by the impact factor of the journal in which it was published, and the total number of citations to the paper, and there was a negative impact when the paper was a review article. Direct costs were included in the analysis for matched R01 awards, and it is interesting to note that the size of the grant was not a statistically significant predictor of the impact rating of the packet.

With respect to ratings of the *innovativeness of approaches*, whether a PI got an NDPA or HHMI was a factor in the rating, as was the PI's citations at award. Innovativeness of the approaches of the individual papers was (as with impact) affected positively by the impact factor of the journal in which it was published, and (again as with impact) there was a negative impact when the paper was a review paper. Again, it is notable that the size of the matched R01 grant was not a statistically significant predictor of the innovativeness rating of the packet.

E. Analyses on Interdisciplinarity and Collaborations

Pioneers' grant-attributed and researcher-level publications were similarly interdisciplinary as all other groups other than the finalists (50% of Pioneers, 51% of matched R01 PIs, 33% of HHMI investigators, as compared to 83% of finalists, had post-award integration scores greater than 0.43). With respect to the subject areas integrated into the research, there appeared to be no strong differences in the areas cited by the Pioneer publications as compared with the matched R01s.

With respect to the number of co-authors on post-award publications, the Pioneers had a similar distribution to those of the matched R01 PIs (at the researcher level) and NDPA finalists, and fewer co-authors compared with HHMI investigators (50% of Pioneers, 57% of matched R01 PIs, and 43% of finalists, as compared to 85% of HHMI investigators, had greater than or equal to 60 unique co-authors). The Pioneers had a greater number of co-authors compared with the matched R01 PIs (grant level) (for instance, 50% of NDPA and 17% of matched R01 grant-attributed publications had greater than or equal to 38 unique co-authors).

With respect to institutional collaborations, the number of collaborating institutions for the Pioneers was similar to all groups except HHMI, which had a larger number of institutional collaborations (for instance, 50% of Pioneers, 43% of matched R01 PIs, and 47% of finalists, in contrast with 74% of HHMIs, had greater than or equal to 19 unique institutional collaborations).

F. Conclusion

As the sections above explain, a bibliometric and expert-review-based evaluation of the Pioneer program compared with four other programs of interest found several differences across the groups (note limitations of the analysis in Section 3C). The study team found, for example, that on a range of impact indicators, the Pioneers scored as well as or higher than the matched R01 PIs at both the grant level and the researcher level. On the same impact indicators, at a portfolio level too, the Pioneer portfolio scored as well as or higher than the random R01 portfolios. At the researcher level, the Pioneers scored similar to or higher than the NDPA finalists. Finally, the team found that the Pioneers had comparable performance on some impact indicators and lower on others as compared with HHMI investigators. This section briefly considers the potential reasons for some of the differences.

For the first finding—that the Pioneers scored as well as or higher than the matched R01 PIs—the study team noted that the Pioneers received more funding than the matched R01s (Figure 3) through a grant mechanism intended to provide more flexibility and to fund riskier ideas. The two groups were well matched on pre-award PI characteristics (Figure 7 through Figure 14). By construction, the NDPA and matched R01 grants

worked in similar areas of science. **The differences between the matched R01 grants and NDPA are likely not attributable to PI differences or differences in research area, but may be due to differences in funding or program characteristics (such as increased flexibility).**

The Pioneer portfolio also scored as well as or higher than the random R01 portfolios on the number of citations and journal impact factor. The portfolios were constructed to have similar direct cost amounts (Figure 5). The groups were otherwise randomly selected; they had different PI characteristics (Figure 7 and Figure 8), the grant mechanisms had different levels of funding and risk, and the areas of science were not controlled. **The differences between the random R01 portfolios and the NDPA portfolio are likely not attributable to funding, but may be due to differences in PI characteristics, research area, or program characteristics.**

The Pioneers did not outperform the HHMI investigators. While both programs provide flexibility and aim to fund riskier ideas, NDPA provided less funding than HHMI (how much less has been difficult to assess). In addition, there were differences in pre-award PI characteristics (Figure 7 through Figure 14), and the researchers may have been working in different areas of science. **The differences between HHMI and NDPA are likely not attributable to flexibility of research, or riskiness of ideas, but may be due to funding, differences in PIs, or differences in areas of science.**

The Pioneer also scored as well as or higher than the NDPA finalists. While the finalists were similar to the Pioneers with respect to PI characteristics (Figure 7 through Figure 14), the team did not know enough about the funding profile of the finalists to comment on these similarities and differences.

As a final observation, it is interesting to note that the matched R01 portfolio performed better than the random R01 portfolios across bibliometric measures of impact. Matched R01s had more citations per publication than the random portfolios (Figure 34 and Figure 35), and the publications appeared in journals with higher impact factors (Figure 36 and Figure 37). While these groups shared a funding mechanism, the matched R01 portfolio received less funding, there are potential differences in the areas of science, and there were differences in PI characteristics—the matched R01s are elite researchers (Figure 7 and Figure 8). **The differences between matched R01 grants and the random R01 portfolios are likely not attributable to grant mechanism or funding, but may be due to PI characteristics or differences in research area.**

Appendix A
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Appendix B
Potential Comparison Groups

The study team considered several samples and populations as potential comparison groups for this evaluation. Based on the availability of data and interest of the sponsor, the pool was limited to primarily National Institutes of Health (NIH) funding mechanisms and groups. Howard Hughes Medical Institute (HHMI) investigators were the only non-NIH mechanism considered, and they were included after much assistance from the HHMI. Table B-1 presents information on a select number of groups that were considered.

Table B-1. Potential Comparison Groups

Potential Comparison Group	Description	Advantages	Disadvantages	Study Question	In Study?
Matched R01 Grantees (PI Characteristics)	R01 grantees matched on PI characteristics within similar research areas	Controls for PI-related characteristics that may affect outcome	Cannot control for award size	How do NDPA awardee outcomes compare to those of PIs with equally pioneering potential?	X
Random R01 Portfolios	R01 grantees with a portfolio direct-cost comparable to that of the NDPA portfolio	Controls for the portfolio award sizes that may affect outcome	Portfolios contain different numbers of grants; does not control for PI characteristics	How do NDPA awardee outcomes compare to those of R01 portfolios that have received similar amounts of funding?	X

Potential Comparison Group	Description	Advantages	Disadvantages	Study Question	In Study?
HHMI	2005 Howard Hughes Medical Institute Investigators	High-prestige program that funds high-risk, high-reward research in a way that is similar to NDPA in many aspects; reputation for innovative investigators	Does not explicitly control for PI characteristics or award size	Does longer term, greater funding, and more flexibility result in more outcomes with greater impact than NDPA?	X
NDPA Finalists	Individuals who were invited to interview, but were not awarded an NDPA during FY 2004–2006	Examines the outcomes of PIs who are "almost as exceptionally creative," and capable of producing high-impact outcomes	Variable post-application funding amounts	How do NDPA awardee outcomes compare to PIs of equally pioneering potential?	X
Random R01 Grantees	Randomly chosen Type 1 R01 grantees	Allows for comparisons to average PIs	Cannot attribute differences to population differences or funding mechanism	How do the Pioneers' outcomes compare to those of the average R01 grantee?	
MERIT (Method to Extend Research in Time) Awardees	PIs with superior research competence and productivity selected by program staff for long-term grant support; Less than 5% of NIH-funded investigators.*	Indirectly selects for PI productivity, PI character-istics, and possibly innovative-ness	MERIT awardees have a long track record with NIH funding on their existing projects and NDPA projects are more likely to be new ideas without preliminary data	How do the Pioneers' outcomes compare to the most productive NIH researchers?	

Potential Comparison Group	Description	Advantages	Disadvantages	Study Question	In Study?
R01 Grantees designated as high-performing by IC leadership	Selected for superior competence and outstanding productivity	May control for productivity and PI potential	Does not control for additional PI characteristics or award size	How do the Pioneers' outcomes compare to the "most reputable" R01 grantees?	
Matched R01 Grants (Size of Award)	R01 grants with similar direct costs	Controls for the impact of the size of award on outcomes	Cannot control for PI characteristics or similar research areas due to characteristics of the R01 population	How do the Pioneers' outcomes compare to those from comparable sized R01 grants?	

* https://dcb.nci.nih.gov/Pages/MERITAwardees.aspx.

Appendix C
Researcher Profiles

This appendix provides basic information on each of the researchers across four groups—NDPA Pioneers, matched R01 PIs, HHMI investigators, and NDPA finalists. The study team collected the information from the NIH's internal database, QVR; the HHMI website and program leadership; and publicly available sources. Table C-1 contains the following fields: analysis group, researcher name, year of award or application receipt, grant number, institutional affiliation at time of award, year of doctoral degree attainment, doctoral degrees attained, and current lab website (as of June 2012).

Table C-1. Researcher Profiles

Group	Name	Award/ App FY	Grant Number	Institution at Award	Degree Year[a]	Degrees	Current Lab Website[b]
NDPA Pioneers	Laurence Abbott	2004	DP1OD000114	Brandeis University	1977	PhD	http://www.neurotheory.columbia.edu/larry.html
	George Daley	2004	DP1OD000256	Harvard University	1991	MD/PhD	https://daley.med.harvard.edu/
	Homme Hellinga	2004	DP1OD000122	Duke University	1986	PhD	http://www.biochem.duke.edu/modules/biochem_hellinga_lab/index.php?id=1
	Joseph McCune	2004	DP1OD000329	University of California San Francisco	1982	MD/PhD	http://cancer.ucsf.edu/people/mccune_joseph.php
	Steven McKnight	2004	DP1OD000276	University of Texas Southwestern Medical Center	1977	PhD	http://www4.utsouthwestern.edu/mcknightlab/
Awardee	Chad Mirkin	2004	DP1OD000285	Northwestern University	1989	PhD	http://chemgroups.northwestern.edu/mirkingroup/
Awardee	Rob Phillips	2004	DP1OD000217	California Institute of Technology	1989	PhD	http://www.rpgroup.caltech.edu/
Awardee	Stephen Quake	2004	DP1OD000251	California Institute of Technology	1994	PhD	http://thebigone.stanford.edu/
Awardee	Sunney Xie	2004	DP1OD000277	Harvard University	1990	PhD	http://bernstein.harvard.edu/
Awardee	Vicki Chandler	2005	DP1OD000575	University of Arizona	1983	PhD	http://bio5.arizona.edu/node/1196
Awardee	Hollis Cline	2005	DP1OD000458	Cold Spring Harbor Laboratory	1985	PhD	http://clinelab.cshl.edu/
Awardee	Leda Cosmides	2005	DP1OD000516	University of California Santa Barbara	1985	PhD	http://www.psych.ucsb.edu/research/cep/codirectors/codirectors.html
Awardee	Titia de Lange	2005	DP1OD000379	Rockefeller University	1985	PhD	http://delangelab.rockefeller.edu/
Awardee	Karl Deisseroth	2005	DP1OD000616	Stanford University	1998	MD/PhD	http://www.stanford.edu/group/dlab/index.html
Awardee	Pehr Harbury	2005	DP1OD000429	Stanford University	1994	PhD	http://cmgm.stanford.edu/biochem/harbury/
Awardee	Erich Jarvis	2005	DP1OD000448	Duke University	1995	PhD	http://jarvislab.net/
Awardee	Thomas Rando	2005	DP1OD000392	Stanford University	1987	MD/PhD	http://www.stanford.edu/~casco/
Awardee	Derek Smith	2005	DP1OD000490	University of Cambridge	1997	PhD	http://www.zoo.cam.ac.uk/zoostaff/smithd.html

Group	Name	Award/ App FY	Grant Number	Institution at Award	Degree Year[a]	Degrees	Current Lab Website[b]
Awardee	Giulio Tononi	2005	DP1OD000579	University of Wisconsin Madison	1988	MD/PhD	http://tononi.psychiatry.wisc.edu/index.html
Awardee	Clare Waterman-Storer	2005	DP1OD000435	Scripps Research Institute	1995	PhD	https://intramural.nhlbi.nih.gov/labs/LCTM/Pages/default.aspx
Awardee	Nathan Wolfe	2005	DP1OD000370	Johns Hopkins University	1998	ScD	http://gvfi.org/index.php
Awardee	Junying Yuan	2005	DP1OD000580	Harvard University	1989	PhD	https://yuan.med.harvard.edu/
Awardee	Kwabena Boahen	2006	DP1OD000965	Stanford University	1997	PhD	http://www.stanford.edu/group/brainsinsilicon/
Awardee	Arup Chakraborty	2006	DP1OD001022	Massachusetts Institute of Technology	1988	PhD	http://web.mit.edu/akcgroup/
Awardee	Lila Gierasch	2006	DP1OD000945	University of Massachusetts Amherst	1975	PhD	https://people.chem.umass.edu/gieraschlab/
Awardee	Rebecca Heald	2006	DP1OD000818	University of California Berkeley	1993	PhD	http://mcb.berkeley.edu/labs/heald/
Awardee	Karla Kirkegaard	2006	DP1OD000827	Stanford University	1983	PhD	http://www.stanford.edu/group/kirkegaard/
Awardee	Thomas Kodadek	2006	DP1OD000663	University of Texas Southwestern Medical Center	1985	PhD	http://www.scripps.edu/kodadek/
Awardee	Cheng Chi Lee	2006	DP1OD000895	University of Texas Health Science Center at Houston	1986	PhD	http://www.uth.tmc.edu/bmb/faculty/cheng-chi-lee.html
Awardee	Evgeny Nudler	2006	DP1OD000799	New York University	1995	PhD	http://nudlerlab.info/
Awardee	Gary Pielak	2006	DP1OD000783	University of North Carolina Chapel Hill	1983	PhD	http://www.chem.unc.edu/people/faculty/pielak/group/
Awardee	David Relman	2006	DP1OD000964	Stanford University	1982	MD	https://sites.google.com/site/davidrelmanlab/
Awardee	Rosalind Segal	2006	DP1OD000839	Harvard University	1986	MD/PhD	http://research4.dfci.harvard.edu/segallab/
Awardee	James Sherley	2006	DP1OD000805	Massachusetts Institute of Technology	1988	MD/PhD	http://www.bbri.org/index.php/our_scientists/articles/sherley.html
Awardee	Younan Xia	2006	DP1OD000798	University of Washington	1996	PhD	http://www.nanocages.com/
Matched R01	Louise T Chow	2004	R01CA107338	University of Alabama at Birmingham	1973	PhD	http://www.uab.edu/gbs/bsb/biochemistry-a-molecular-genetics/faculty/louise-t-chow-phd

Group	Name	Award/ App FY	Grant Number	Institution at Award	Degree Year[a]	Degrees	Current Lab Website[b]
Matched R01	Vittorio Gallo	2004	R01NS045702	Children's Research Institute	1979	PhD	http://www.childrensnational.org/research/faculty/bios/cnr/Gallo_v.aspx
Matched R01	Lea A Harrington	2004	R01AG024398	Ontario Cancer Institute	1993	PhD	http://medbio.utoronto.ca/faculty/harrington.html
Matched R01	Emmanuel J Mignot	2004	R01MH073435	Stanford University	1986	MD/PhD	http://med.stanford.edu/school/Psychiatry/narcolepsy/mignot.html
Matched R01	Ayyalusamy Ramamoorthy	2004	R01AI054515	University of Michigan at Ann Arbor	1990	PhD	http://rams.biop.lsa.umich.edu/
Matched R01	Abdolmohamad Rostami	2004	R01NS048435	Thomas Jefferson University	1981	MD/PhD	http://www.jefferson.edu/facint/details.cfm?key=axr146
Matched R01	Joel H Rothman	2004	R01AG023321	University of California Santa Barbara	1988	PhD	http://www.lifesci.ucsb.edu/mcdb/labs/rothman/labpage.htm
Matched R01	Teresa Ruiz	2004	R01GM069551	University of Vermont & St Agric College	1990	PhD	http://physiology.uvm.edu/ruiz/; http://vermontcancer.org/index.php?id=147
Matched R01	Joel Voldman	2004	R01RR019652	Massachusetts Institute of Technology	2001	PhD	http://www.rle.mit.edu/biomicro/
Matched R01	Douglas E Barrick	2005	R01GM068462	Johns Hopkins University	1993	PhD	http://biophysics.jhu.edu/faculty-pages/barrick.html
Matched R01	Darryl J Bornhop	2005	R01EB003537	Vanderbilt University	1987	PhD	http://www.vanderbilt.edu/AnS/Chemistry/groups/bornhop/
Matched R01	Michael Crair	2005	R01EY015788	Baylor College of Medicine	1991	PhD	http://crair.medicine.yale.edu/
Matched R01	Jonathan B Demb	2005	R01EY014454	University of Michigan at Ann Arbor	1997	PhD	http://www.umich.edu/~neurosci/faculty/jdemb.htm
Matched R01	Jeffrey M Friedman	2005	R01DA018799	Rockefeller University	1986	MD/PhD	http://www.rockefeller.edu/research/faculty/labheads/JeffreyFriedman/
Matched R01	George Georgiou	2005	R01GM073089	University of Texas Austin	1987	PhD	http://www.che.utexas.edu/georgiou/index.html
Matched R01	Gordon Keller	2005	R01HL080627	Mount Sinai School of Medicine of NYU	1979	PhD	http://medbio.utoronto.ca/faculty/keller.html

Group	Name	Award/ App FY	Grant Number	Institution at Award	Degree Year[a]	Degrees	Current Lab Website[b]
Matched R01	Marianne Manchester	2005	R01CA112075	Scripps Research Institute	1992	PhD	http://pharmacy.ucsd.edu/faculty/manchester.shtml
Matched R01	Shrikanth Narayanan	2005	R01DC007124	University of Southern California	1995	PhD	http://sail.usc.edu/shri.php
Matched R01	Jack B Nitschke	2005	R01MH074847	University of Wisconsin Madison	1998	PhD	http://www.waisman.wisc.edu/nitschkelab/jack.htm
Matched R01	Karen A Norris	2005	R01HL077095	University of Pittsburgh at Pittsburgh	1985	PhD	http://www.cvr.pitt.edu/Personnel/view.asp?uid=kan1
Matched R01	Alanna Schepartz	2005	R01GM074756	Yale University	1987	PhD	http://www.schepartzlab.yale.edu/
Matched R01	Anne C R Tanner	2005	R01DE015847	Forsyth Institute	1981	PhD	http://www.forsyth.org/research/scientists/profiles/annetanner.html
Matched R01	Yoshitaka Ishii	2006	R01AG028490	University of Illinois at Chicago	1997	PhD	http://www.chem.uic.edu/ishii/group/
Matched R01	Rustem F Ismagilov	2006	R01GM077331	University of Chicago	1998	PhD	http://ismagilovlab.caltech.edu/
Matched R01	Randy L Jirtle	2006	R01ES015165	Duke University	1976	PhD	http://www.geneimprint.com/lab/
Matched R01	Xingde Li	2006	R01CA120480	University of Washington	1998	PhD	http://bit.bme.jhu.edu/Home.php
Matched R01	David J Linden	2006	R01MH077769	Johns Hopkins University	1989	PhD	http://neuroscience.jhu.edu/DavidLinden.php
Matched R01	Rebecca Jane Morris	2006	R01AR052713	Columbia University	1981	PhD	http://www.hi.umn.edu/stem_cells_cancer.html
Matched R01	Tristram G Parslow	2006	R01AI067704	Emory University	1985	MD/PhD	http://pathology.emory.edu/AdminFacultyMember.cfm?Name_seq=919
Matched R01	Tannishtha Reya	2006	R01DK072234	Duke University	1996	PhD	http://www.reyalab.org/
Matched R01	Klaus Schulten	2006	R01GM073655	University of Illinois Urbana-Champaign	1974	PhD	http://www.ks.uiuc.edu/~kschulte/

Group	Name	Award/ App FY	Grant Number	Institution at Award	Degree Year[a]	Degrees	Current Lab Website[b]
Matched R01	Thomas Wallace Scott	2006	R01AI069341	University of California Davis	1981	PhD	http://entomology.ucdavis.edu/faculty/scott/index.cfm
Matched R01	John R Stanley	2006	R01AR052672	University of Pennsylvania	1974	MD	http://www.uphs.upenn.edu/dermatol/faculty/stanley.html
Matched R01	Julie A Theriot	2006	R01AI067712	Stanford University	1993	PhD	http://cmgm.stanford.edu/theriot/
Matched R01	Mark Winey	2006	R01GM074746	University of Colorado at Boulder	1988	PhD	http://mcdb.colorado.edu/labs/winey/index.html
HHMI	Susan Ackerman	2005	NA	The Jackson Laboratory	1987	PhD	http://research.jax.org/faculty/susan_ackerman.html
HHMI	James Bardwell	2005	NA	University of Michigan	1987	PhD	http://www.mcdb.lsa.umich.edu/labs/bardwell/
HHMI	David Bartel	2005	NA	Massachusetts Institute of Technology	1993	PhD	http://web.wi.mit.edu/bartel/pub/
HHMI	Bonnie Bassler	2005	NA	Princeton	1990	PhD	http://www.molbio1.princeton.edu/labs/bassler/
HHMI	Albert Bendelac	2005	NA	University of Chicago	1992	MD/PhD	http://biomed.uchicago.edu/common/faculty/bendelac.html
HHMI	Ronald Breaker	2005	NA	Yale University	1992	PhD	http://www.yale.edu/breaker/index.htm
HHMI	Andrew Camilli	2005	NA	Tufts University	1992	PhD	http://sackler.tufts.edu/Academics/Degree-Programs/PhD-Programs/Faculty-Research-Pages/Andrew-Camilli.aspx
HHMI	Edwin Chapman	2005	NA	University of Wisconsin	1992	PhD	http://www.physiology.wisc.edu/chapman/Chapman_Lab/Home.html
HHMI	Zhijian James Chen	2005	NA	University of Texas Southwestern Medical Center	1991	PhD	http://www.utsouthwestern.edu/fis/faculty/29110/zhijian-chen.html
HHMI	Joseph Derisi	2005	NA	University of California San Francisco	1999	PhD	http://derisilab.ucsf.edu/
HHMI	Sascha Du Lac	2005	NA	Salk Institute	1989	PhD	http://www.salk.edu/faculty/faculty_details.php?id=17
HHMI	Evan Eichler	2005	NA	University of Washington	1995	PhD	http://eichlerlab.gs.washington.edu/
HHMI	Christopher Garcia	2005	NA	Stanford University	1992	PhD	http://garcia-lab.stanford.edu/Welcome.html

Group	Name	Award/ App FY	Grant Number	Institution at Award	Degree Year[a]	Degrees	Current Lab Website[b]
HHMI	Taekjip Ha	2005	NA	University of Illinois	1996	PhD	http://bio.physics.illinois.edu/
HHMI	Gregory Hannon	2005	NA	Cold Spring Harbor Laboratory	1992	PhD	http://hannonlab.cshl.edu/
HHMI	Oliver Hobert	2005	NA	Columbia University	1995	PhD	http://cpmcnet.columbia.edu/dept/gsas/biochem/labs/hobert/
HHMI	Steven Jacobsen	2005	NA	University of California Los Angeles	1993	PhD	http://www.mcdb.ucla.edu/Research/Jacobsen/LabWebSite/P_Index.shtml
HHMI	Erik Jorgensen	2005	NA	University of Utah	1989	PhD	http://biologylabs.utah.edu/jorgensen/
HHMI	Dorothee Kern	2005	NA	Brandeis University	1994	PhD	http://www.bio.brandeis.edu/kernlab/
HHMI	Alex Kolodkin	2005	NA	Johns Hopkins University	1987	PhD	http://www.neuroscience.jhu.edu/AlexKolodkin.php
HHMI	David Liu	2005	NA	Harvard University	1999	PhD	http://evolve.harvard.edu/
HHMI	Scott Lowe	2005	NA	Cold Spring Harbor Laboratory	1994	PhD	http://www.mskcc.org/research/lab/scott-lowe
HHMI	Karolin Luger	2005	NA	Colorado State University	1989	PhD	http://lugerlab.org/
HHMI	Liqun Luo	2005	NA	Stanford University	1992	PhD	http://www.stanford.edu/group/luolab/
HHMI	Milan Mrksich	2005	NA	University of Chicago	1994	PhD	http://chemgroups.northwestern.edu/mrksich/
HHMI	Dianne Newman	2005	NA	California Institute Of Technology	1997	PhD	http://www.dknlab.caltech.edu/Newman_Lab/Newman_Lab.html
HHMI	Teresa Nicolson	2005	NA	Oregon Health Sci University	1995	PhD	http://zfin.org/cgi-bin/webdriver?MIval=aa-labview.apg&OID=ZDB-LAB-001113-2
HHMI	Joseph Noel	2005	NA	Salk Institute	1990	PhD	http://www.salk.edu/faculty/noel.html
HHMI	Shahin Rafii	2005	NA	Weill Cornell Medical College	1986	MD	http://www.med.cornell.edu/research/shahinrafii/index.html
HHMI	Frederick Rieke	2005	NA	University of Washington	1995	PhD	http://rieke-server.physiol.washington.edu/
HHMI	Michael Rosen	2005	NA	University of Texas Southwestern Medical Center	1993	PhD	http://www.utsouthwestern.edu/fis/faculty/53929/michael-rosen.html
HHMI	Alejandro Sanchez-Alvarado	2005	NA	University of Utah School of Medicine	1992	PhD	http://planaria.stowers.org/index.php

Group	Name	Award/ App FY	Grant Number	Institution at Award	Degree Year[a]	Degrees	Current Lab Website[b]
HHMI	Brenda Schulman	2005	NA	St. Jude Children's Hospital	1996	PhD	http://www.stjude.org/schulman
HHMI	Geraldine Seydoux	2005	NA	Johns Hopkins University	1991	PhD	http://www.bs.jhmi.edu/MBG/SeydouxLab/
HHMI	Kevan Shokat	2005	NA	University of California San Francisco	1991	PhD	http://shokatlab.ucsf.edu/
HHMI	Thomas Tuschl	2005	NA	Rockefeller University	1995	PhD	http://www.rockefeller.edu/labheads/tuschl/
HHMI	Rafael Yuste	2005	NA	Columbia University	1992	MD/PhD	http://www.columbia.edu/cu/biology/faculty/yuste/index.html
HHMI	Yi Zhang	2005	NA	University of North Carolina	1995	PhD	http://www.med.unc.edu/~zhangyi/lab.htm
HHMI	Xiaowei Zhuang	2005	NA	Harvard University	1996	PhD	http://zhuang.harvard.edu/
Finalist	Cynthia Beall	2004	NA	Case Western Reserve University	1976	PhD	http://www.case.edu/affil/tibet/currentStaff/beall.htm
Finalist	Steven Benner	2004	NA	University of Florida	1979	PhD	http://ffame.org/sbenner.php
Finalist	Carl Bergstrom	2004	NA	University of Washington	1998	PhD	http://octavia.zoology.washington.edu/Homepage.html
Finalist	David Heeger	2004	NA	New York University	1987	PhD	http://www.cns.nyu.edu/heegerlab/
Finalist	Stephen Johnston	2004	NA	University of Texas Southwestern Medical Center	1981	PhD	http://www.biodesign.asu.edu/people/stephen-johnston
Finalist	Leonid Mirny	2004	NA	Massachusetts Institute of Technology	1998	PhD	http://web.mit.edu/leonid/www/index.html
Finalist	Mark Roth	2004	NA	Fred Hutchinson Cancer Research Center	1984	PhD	http://labs.fhcrc.org/roth/
Finalist	David Scheinberg	2004	NA	Memorial Sloan-Kettering Cancer Center	1983	MD/PhD	http://www.mskcc.org/research/lab/david-scheinberg
Finalist	David Schneider	2004	NA	Stanford University	1992	PhD	http://www.stanford.edu/group/schneider_lab/Schneider_lab_2011/Home.html
Finalist	Oliver Smithies	2004	NA	University of North Carolina Chapel Hill	1951	PhD	http://www.unc.edu/~krfloyd/

Group	Name	Award/ App FY	Grant Number	Institution at Award	Degree Year[a]	Degrees	Current Lab Website[b]
Finalist	John Tooby	2004	NA	University of California Santa Barbara	1989	PhD	http://www.psych.ucsb.edu/research/cep/
Finalist	Eric Betzig	2005	NA	New Millennium Research, LLC	1988	PhD	http://www.janelia.org/lab/betzig-lab
Finalist	Chris Beyrer	2005	NA	Johns Hopkins University	1988	MD	http://www.jhsph.edu/faculty/directory/profile/690/Beyrer/Chris
Finalist	Donald Doyle	2005	NA	Georgia Institute of Technology	1996	PhD	http://ww2.chemistry.gatech.edu/~doyle/index.html
Finalist	Alessio Fasano	2005	NA	University of Maryland School of Medicine	1981	MD	http://medschool.umaryland.edu/facultyresearchprofile/viewprofile.aspx?id=1891
Finalist	Laura Kiessling	2005	NA	University of Wisconsin Madison	1989	PhD	http://www.biochem.wisc.edu/faculty/kiessling/lab/
Finalist	Laksh-minarayanan Mahadevan	2005	NA	Harvard University	1995	PhD	http://www.seas.harvard.edu/softmat/index.html
Finalist	Laurence Tecott	2005	NA	University of California San Francisco	1987	MD/PhD	http://psych.ucsf.edu/faculty.aspx?id=190
Finalist	Rhoda Alani	2006	NA	Johns Hopkins University	1991	MD	http://www.bumc.bu.edu/derm/rhoda-m-alani-md/
Finalist	Nancy Carrasco	2006	NA	Yeshiva University	1980	MD	http://bbs.yale.edu/people/nancy_carrasco-1.profile
Finalist	Joseph DeSimone	2006	NA	University of North Carolina Chapel Hill	1990	PhD	http://www.desimone-group.chem.unc.edu/
Finalist	Drew Endy	2006	NA	Massachusetts Institute of Technology	1998	PhD	http://openwetware.org/wiki/Endy:Lab
Finalist	Joerg Lahann	2006	NA	University of Michigan at Ann Arbor	1998	PhD	http://www.engin.umich.edu/research/lahann/index.htm
Finalist	Marcelo Magnasco	2006	NA	Rockefeller University	1991	PhD	http://sur.rockefeller.edu/Plone
Finalist	Hongkun Park	2006	NA	Harvard University	1996	PhD	http://people.fas.harvard.edu/~parklab/index.html
Finalist	Lynne Regan	2006	NA	Yale University	1987	PhD	http://www.yale.edu/reganlab/index.html
Finalist	Ram Samudrala	2006	NA	University of Washington	1997	PhD	http://compbio.washington.edu/

Group	Name	Award/ App FY	Grant Number	Institution at Award	Degree Year[a]	Degrees	Current Lab Website[b]
Finalist	Scott Small	2006	NA	Columbia University	1992	MD	http://www.neuroscience.columbia.edu/?page=28&bio=192
Finalist	Simon Spivack	2006	NA	New York State Department of Health	1985	MD	http://www.einstein.yu.edu/faculty/profile.asp?id=11003
Finalist	C Erec Stebbins	2006	NA	Rockefeller University	1999	PhD	http://www.rockefeller.edu/research/faculty/labheads/ErecStebbins/

[a] If the PI received multiple doctoral degrees, the most recent doctoral degree year was reported.

[b] Current as of June 2012.

Appendix D
Expert Reviewer Characteristics

The study team collected data to characterize the experts who participated in the expert review. These data were collected from researcher websites and self-reported by the expert reviewers in the expert review protocol. In addition, these data were supplemented by information gathered from the NIH's internal database, QVR. This appendix presents information on age, gender, degree type, institutional affiliation, and job title.

Age and Gender

The average age of the expert reviewer population is 52 years, and the minimum and maximum ages are 38 years and 72 years, respectively (Figure D-1). Of the 93 expert reviewers, 72 (77%) were male and 21 (23%) were female.

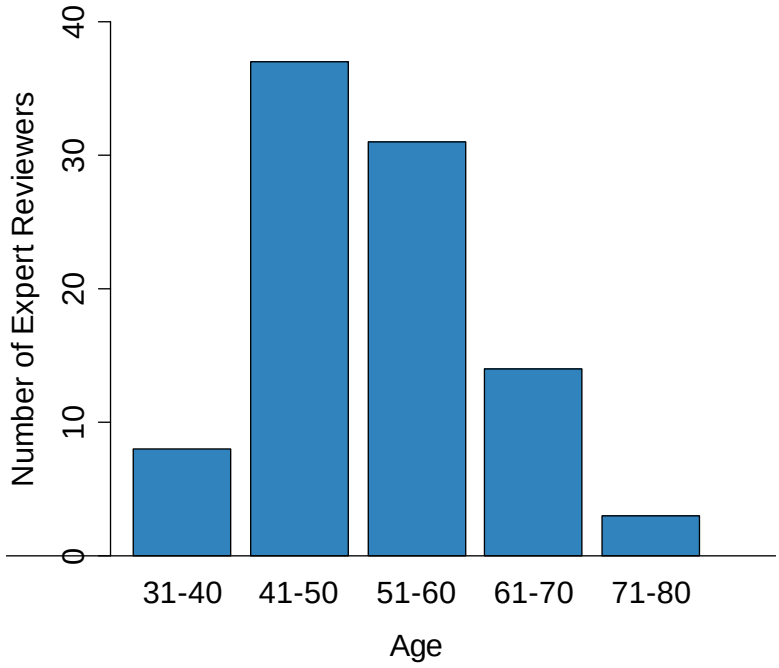


Figure D-1. Age Distribution of the Expert Reviewers

Degree Type

The study team requested that the expert reviewers report the highest degrees they have attained. All the expert reviewers had received at least one type of doctoral degree. Out of 93 expert reviewers, 92 (99%) had received a research doctorate (PhD or equivalent). In addition, six (6%) had received a medical doctorate (MD or equivalent), and four (4%) had received a doctor of veterinary medicine (DVM or equivalent).

Institutional Affiliations

Table D-1 lists the institutional affiliations of the 93 expert reviewers.

Table D-1. Institutional Affiliations of the Expert Reviewers

Institution	Count	Institution	Count
Harvard University	5	La Jolla Institute for Allergy and Immunology	1
Emory University	3	Markey Cancer Center	1
The Scripps Research Institute	3	New York University	1
University of Pittsburgh	3	North Carolina State University Raleigh	1
University of Washington	3	Oklahoma Medical Research Foundation	1
Washington University	3	Princeton University	1
Carnegie-Mellon University	2	Rensselaer Polytechnic Institute	1
Johns Hopkins University	2	Rice University	1
Massachusetts Institute of Technology	2	Rutgers The State University of New Jersey New Brunswick	1
Northwestern University	2	Sanford-Burnham Medical Research Institute	1
Stanford University	2	Seattle Biomedical Research Institute	1
State University New York Stony Brook	2	St. Jude Children's Research Hospital	1
University of California Berkeley	2	Texas A&M University	1
University of California Davis	2	University California San Francisco-Gladstone Institute	1
University of California Irvine	2	University of Arizona	1
University of California San Francisco	2	University of California Los Angeles	1
University of Iowa	2	University of California San Diego	1
University of Pennsylvania	2	University of Chicago	1
University of Wisconsin Madison	2	University of Florida	1
Yale University	2	University of Maryland College Park	1
Baylor College of Medicine	1	University of Massachusetts Medical School Worcester	1
Beth Israel Deaconess Medical Center	1	University of Michigan Ann Arbor	1

Institution	Count	Institution	Count
Brandeis University	1	University of Minnesota Twin Cities	1
Brigham Young University	1	University of North Carolina Chapel Hill	1
Brown University	1	University of Oregon	1
California Institute of Technology	1	University of Texas at Austin	1
City University of New York	1	University of Texas MD Anderson Cancer Center	1
Columbia University	1	University of Texas Southwestern Medical Center Dallas	1
Cornell University	1	Vanderbilt University	1
Duke University	1	Virginia Polytechnic Institute and State University	1
George Mason University	1	Weill Cornell Medical College	1
Georgia Institute of Technology	1	Wellesley College	1
Indiana University School of Medicine	1	Yeshiva University Albert Einstein College of Medicine	1

Note: One expert reviewer was counted twice because the individual held a joint appointment to Harvard and Beth Israel Deaconess Medical Center.

Job Title

Job title information was collected for the 93 expert reviewers (Table D-2). A majority of the recruited experts are tenure-track faculty members at universities. Five of the 93 (5%) expert reviewers were not affiliated with universities, but held leadership positions at medical or research institutes. Seven of the 93 expert reviewers (8%) are chairs in their departments (Table D-3).

Table D-2. Academic Rank or Position of the Expert Reviewers

Position or Title	Number of Reviewers
Distinguished Professor	11
Professor	46
Associate Professor	21
Assistant Professor	7
Adjunct Professor	1
Adjunct Associate Professor	1
Associate Research Professor	1
President and Chief Scientific Officer*	1
President*	1
Vice-President of Research*	1
Associate Member*	2

* These positions were affiliated with medical or research institutes.

Table D-3. Chair Positions for the Expert Reviewers

Chair Position	Number of Reviewers
Chair	3
Vice-Chair	3
Associate Chair	1

Appendix E
Expert Review Protocol

The expert review protocol reproduced herein included an introduction and non-disclosure agreement, instructions, three sections of questions for each set of papers (Impact of Research, Innovativeness of the Approaches, and Research Experience), and three personal information questions.

Introduction

Dear Dr. {LastName},

The IDA Science and Technology Policy Institute (STPI) is conducting an expert review for the National Institutes of Health (NIH). The information collected in this review will be used to assess the impact and innovativeness of research funded by NIH's Director's Pioneer Award (NDPA), NIH R01 award, and the Howard Hughes Medical Institute (HHMI) Investigators program.

Your Participation:

We selected you for participation in this review based on your expertise in biomedical research. We have determined that you have no known conflicts of interest with any of the authors you have been assigned to evaluate. If you believe you have a conflict of interest, please contact Amy Richards, who may be reached at arichard@ida.org or (202) 419-3731.

We expect the review to take about eight hours. Please use only the papers provided to you to answer the questions, and do not do outside research.

Due Date and Compensation:

Please finish the expert review by {DueDate}. STPI will process your compensation within four weeks of receiving your full set of responses.

Financial Information:

You will be paid an honorarium of $750 by check for your participation following the completion of all questions in the review.

Confidentiality:

Unless required by law, only IDA Science and Technology Policy Institute (STPI) staff will have access to your responses to this online questionnaire. STPI staff are required to maintain confidentiality regarding your identity. Results of this review may be used for research, publications, or presentations; however, if your individual results are discussed, your identity will be protected by using a code number rather than your name or other identifying information. Review responses will be collected and downloaded from secure, web-based software, and stored on our secure systems, and all responses will be password-protected.

Your Rights:

Your participation is completely voluntary, and you are free to withdraw from the review at any time. However, the honorarium would be paid only upon completion of all questions in the review.

Contact Information:

Direct any questions about this expert review to Amy Richards at STPI, arichard@ida.org or (202) 419-3731.

Non-Disclosure Agreement:

All information that I receive from the IDA Science and Technology Policy Institute (STPI) shall be deemed proprietary information. I understand that until either (a) the information is made public or (b) STPI grants me specific written approval, I will, both during the review and after the review, treat the information as confidential, not use the information for any purposes other than to answer the questions below, and not disclose the information to a third party.

○ ○ I agree. (You will be directed to the INSTRUCTIONS page)

[If selected "I agree," skip to Section 2. Instructions.]

○ ○ I do not agree. (You will EXIT the website, and no longer participate in the study)

[If selected "I do not agree," display the question.]

If you marked I do not agree in error, please select PREVIOUS to change your selection to I agree and proceed with the NIH review.

To exit the review and no longer participate, select below and SUBMIT.

○ ○ I would not like to participate in the NIH expert review.

[EXIT SURVEY]

Instructions

You have been provided with {Total Packets} sets of papers, each set representing a grant or funding mechanism. Please review each set of papers, and then answer questions related to:

- the impact of each paper, and the set of papers, taken as a whole
- the innovativeness of the approaches of each paper, and the set of papers, taken as a whole
- the alignment between the research in each set of papers and your own research area.

At the end of the review, you will be asked three questions about yourself.

To navigate the instrument please use the PREVIOUS and NEXT buttons and not press the browser's back and forward buttons. If you have cookies enabled on your computer, your responses will be saved allowing you to pause, if needed, or continue on the same computer.

The questionnaire has been tested on Internet Explorer, Chrome and Firefox browsers. If you are using a different browser or mobile device or find navigating difficult, please let us know, and we will email you a copy of the questionnaire and acrobat files of the papers.

Please press the NEXT button when you are ready to proceed to the first set of papers.

Expert Review Questions

Impact of Research

NDPA was created to promote highly innovative and potentially transformative approaches that have the potential to produce extremely high impact on a broad area of biomedical or behavioral research. In this context, "extremely high impact" refers to research that accomplishes one or more of the following:

- radically changes present understanding of an important existing scientific or engineering concept
- leads to the creation of a new paradigm or field of science or engineering,
- challenges present understanding in the field(s) involved,
- provides pathways to new frontiers,
- challenges conventional wisdom,
- leads to unexpected insights that enable new techniques or methodologies, or

- redefines the boundaries of science or engineering.

1. How would you categorize the impact of the research in each of the following papers?

Choose one answer for each paper. Click on the paper's title to download and, if needed, print the paper.

> **Note:** You will not be able to proceed to the next page of questions unless you have responded to this question.

	Extremely Impactful	Very Impactful	Moderately Impactful	Slightly Impactful	Not At All Impactful
[Title of Paper 1 hyperlinked to actual paper]	○	○	○	○	○
[Title of Paper 2 hyperlinked to actual paper]	○	○	○	○	○
[Title of Paper 3 hyperlinked to actual paper]	○	○	○	○	○
[Title of Paper 4 hyperlinked to actual paper]	○	○	○	○	○
[Title of Paper 5 hyperlinked to actual paper]	○	○	○	○	○

2. How impactful is the research described in this set of papers, taken as a whole?

> **Note:** You will not be able to proceed to the next page of questions unless you have responded to this question.

- ○ Extremely Impactful
- ○ Very Impactful
- ○ Moderately Impactful
- ○ Slightly Impactful
- ○ Not At All Impactful

3. What about these papers, individually or as a whole, made you choose your answers above?

There are no character limits in the space provided and you may expand the text box to better view your response.

[open-ended text entry]

Innovativeness of the Approaches

NDPA was created to promote highly innovative and potentially transformative approaches that have the potential to produce unusually high impacts on a broad area of biomedical or behavioral research. In this context, an approach may be considered extremely innovative if it accomplishes one or more of the following:

- the ideas underlying the research are at odds with prevailing wisdom,
- the research requires the use of equipment or techniques that have not been proven or are considered extraordinarily difficult, or
- the research involves a unique combination of disciplines.

4. Regardless of the impact, how would you categorize the innovativeness of the approaches taken in the research described in each of the following papers?

Choose one answer for each paper. Click on the paper's title to download and, if needed, print the paper.

Note: You will not be able to proceed to the next page of questions unless you have responded to this question.

	Extremely Innovative	Very Innovative	Moderately Innovative	Slightly Innovative	Not At All Innovative
[Title of Paper 1 hyperlinked to actual paper]	☐	☐	☐	☐	☐
[Title of Paper 2 hyperlinked to actual paper]	☐	☐	☐	☐	☐
[Title of Paper 3 hyperlinked to actual paper]	☐	☐	☐	☐	☐
[Title of Paper 4 hyperlinked to actual paper]	☐	☐	☐	☐	☐
[Title of Paper 5 hyperlinked to actual paper]	☐	☐	☐	☐	☐

5. Regardless of its impact, how innovative are the approaches described in this set of papers, taken as a whole?

Note: You will not be able to proceed to the next page of questions unless you have responded to this question.

☐ Extremely Innovative

☐ Very Innovative

☐ Moderately Innovative

- [ ] Slightly Innovative
- [ ] Not At All Innovative

6. What about these papers, individually or as a whole, made you choose your answers above?

There are no character limits in the space provided and you may expand the text box to better view your response.

[open-ended text entry]

Research Experience

7. How aligned is your own research expertise with that of the research presented in the papers as a whole?

Note: You will not be able to proceed to the next page of questions unless you have responded to this question.

- [ ] Extremely Aligned
- [ ] Somewhat Aligned
- [ ] Not Very Aligned
- [ ] Not At All Aligned

You have completed a review of the first set of ${e://Field/Total%20Packets} sets of papers.

At this time, if you need to review your answers, please select PREVIOUS. Once you proceed, you will not be able to return to this section.

To continue, select NEXT.

[Repeat questions in Section 3. Expert Review Questions and Section 4. Research Experience for each of {Total Packets}. There is a maximum of four Total Packets per expert.]

Personal Information

This information will be used only to contextualize your responses in the review.

[Questions 8–10 responses are optional.]

8. What is your year of birth? {YYYY}

9. What is your gender?

- ○ Male
- ○ Female

10. What are the highest degrees that you have obtained? Check all that apply.

- ☐ PhD or equivalent
- ☐ MD or equivalent
- ☐ DDS or equivalent
- ☐ DVM or equivalent
- ☐ Other (please specify): [open-ended text entry]

You have now completed all responses to the NIH expert review. Thank you for your time and input.

Select the SUBMIT button to record your responses.

If you wish to revise your responses to the questionnaire, please contact Amy Richards (arichard@ida.org, 202 419-3731) to resend you the link.

[EXIT SURVEY]

Appendix F
Expert Review Data

The expert reviews were completed by all 94 experts that agreed to participate in the expert review. The paper- and packet-level ratings for each group were distributed evenly between the impact and innovativeness questions (1,587 paper-level ratings and 336 packet-level ratings for each of the two sections).

Of the 3,174 paper-level ratings, the NDPA Pioneers, matched R01 PIs, and HHMI investigators received 1,024, 978, and 1,172 ratings, respectively.

Of the 672 packet-level ratings, the NDPA Pioneers, matched R01 PIs, and HHMI investigators received 216, 220, and 236 ratings, respectively.

Figure F-1 and Figure F-2 present the paper-level rating distributions, and Figure F-3 and Figure F-4 show the packet-level rating distributions for each of the three groups. The data are represented without the statistical corrections that STPI used to test for significant differences among the groups.

Figure F-5, Figure F-6, and Figure F-7 show the distributions of rating proportions for each of the researchers in the three groups for impact paper ratings, and Figure F-8, Figure F-9, and Figure F-10 show these distributions for innovation paper ratings. Figure F-11, Figure F-12, and Figure F-13 show rating proportions for each of the researchers in the three groups for impact packet ratings, and Figure F-14, Figure F-15, and Figure F-16 show these proportions for innovation packet ratings.

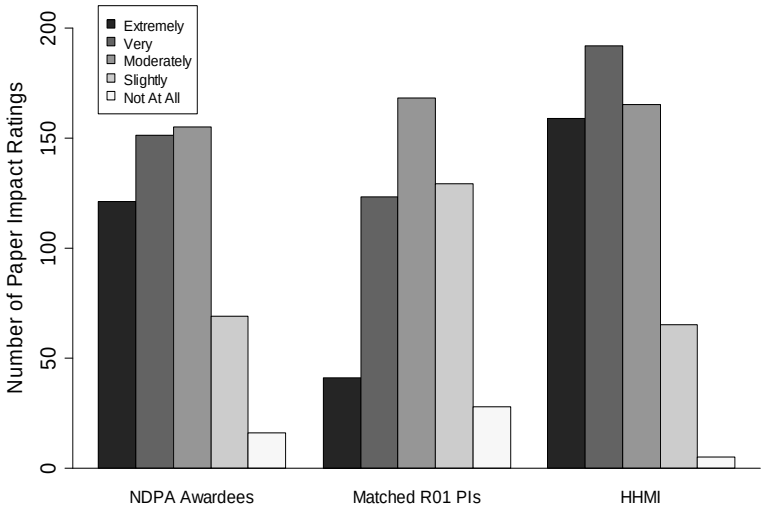


Figure F-1. Impact Distributions for Paper-Level Ratings

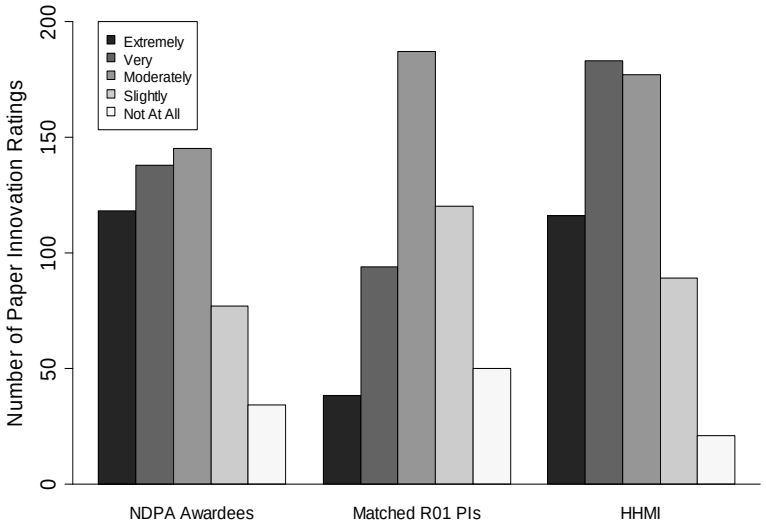


Figure F-2. Innovation Distributions for Paper-Level Ratings

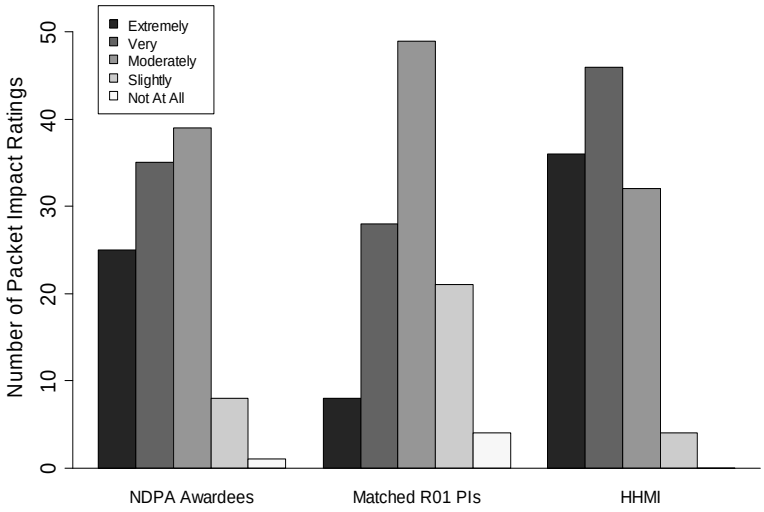


Figure F-3. Impact Distributions for Packet-Level Ratings

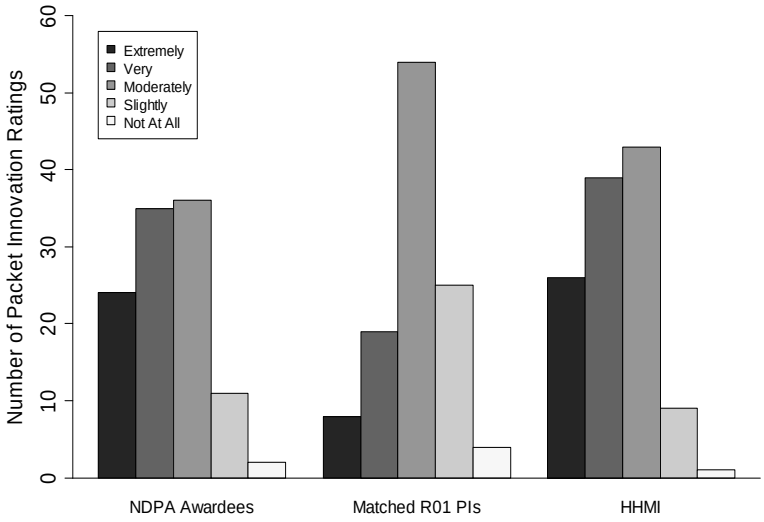


Figure F-4. Innovation Distributions for Packet-Level Ratings

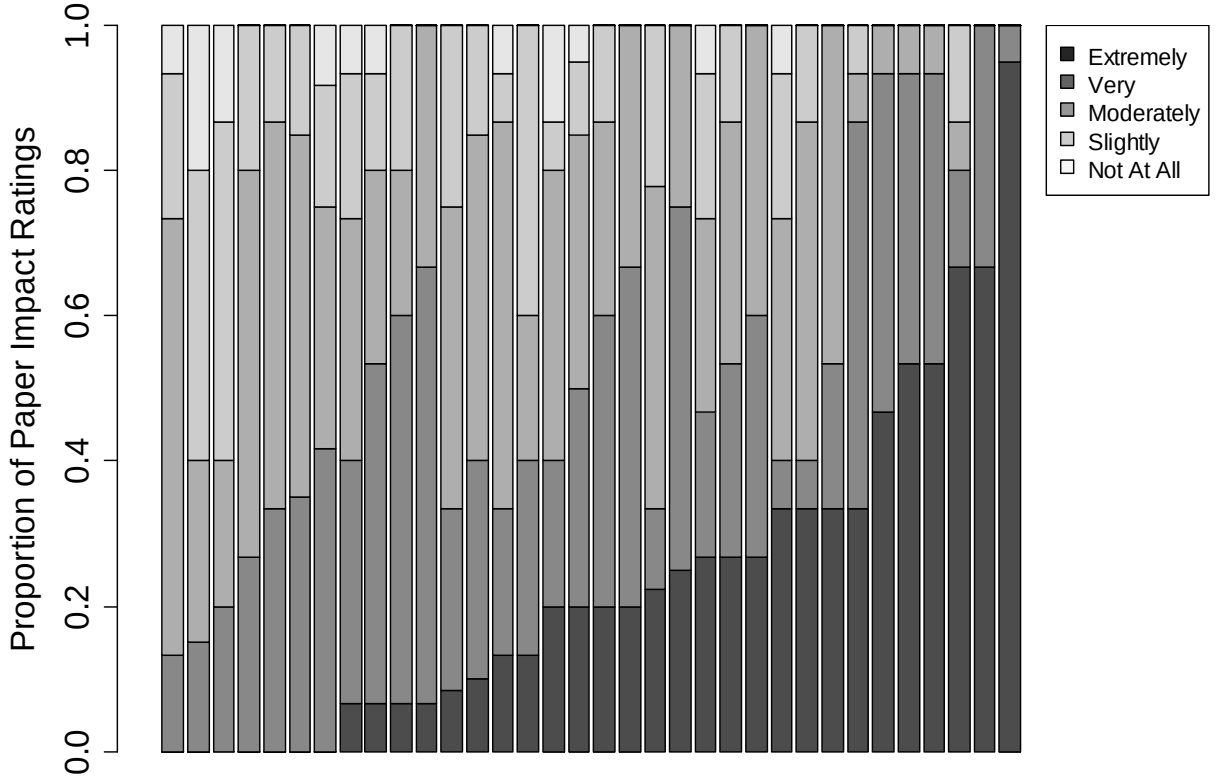


Figure F-5. Impact Distributions by Researcher for Paper-Level Rating Proportions for NDPA Pioneers

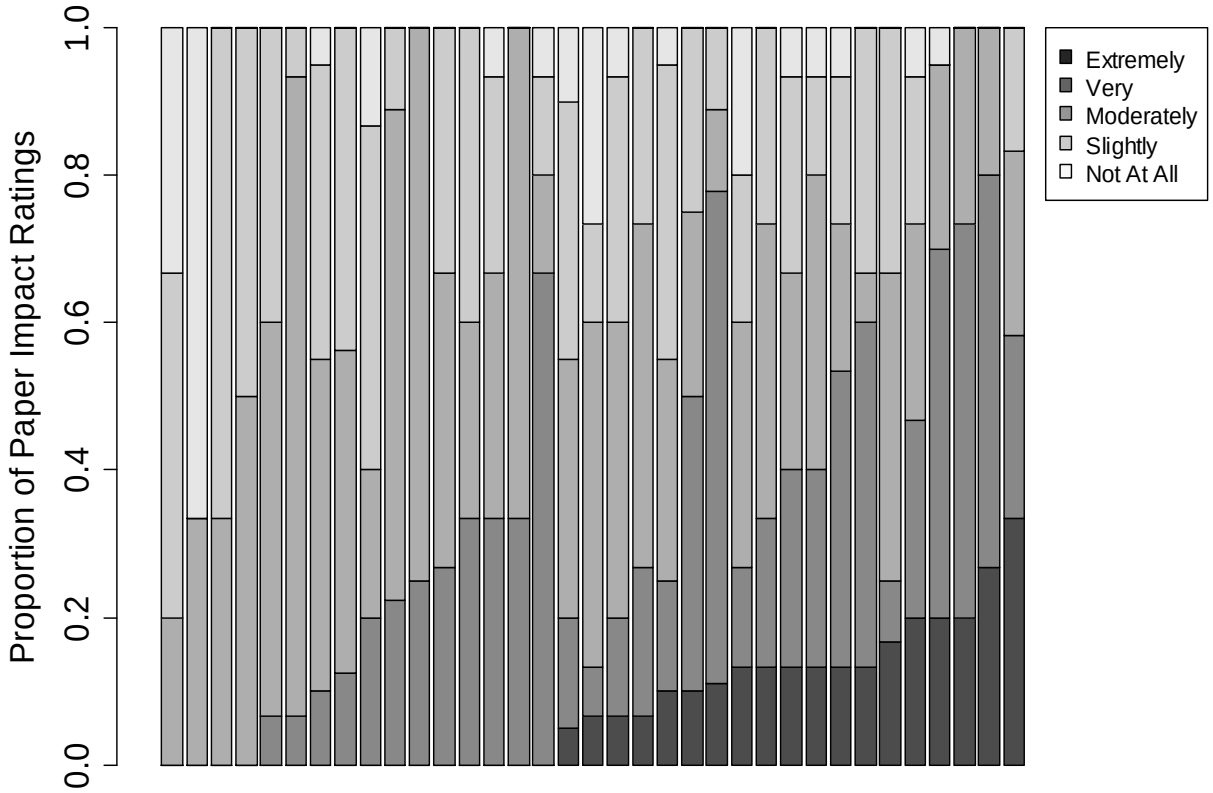


Figure F-6. Impact Distributions by Researcher for Paper-Level Rating Proportions for Matched R01 PIs

Figure F-7. Impact Distributions by Researcher for Paper-Level Rating Proportions for HHMI Investigators

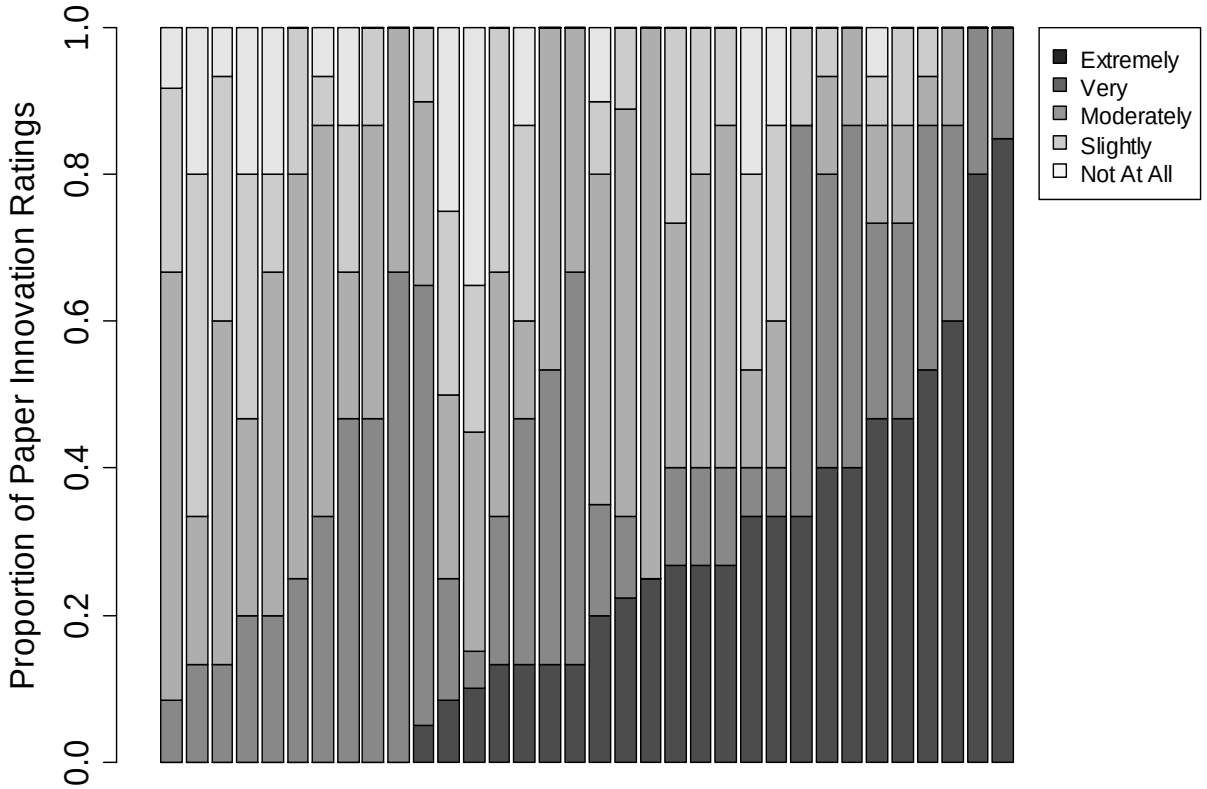


Figure F-8. Innovation Distributions by Researcher for Paper-Level Rating Proportions for NDPA Pioneers

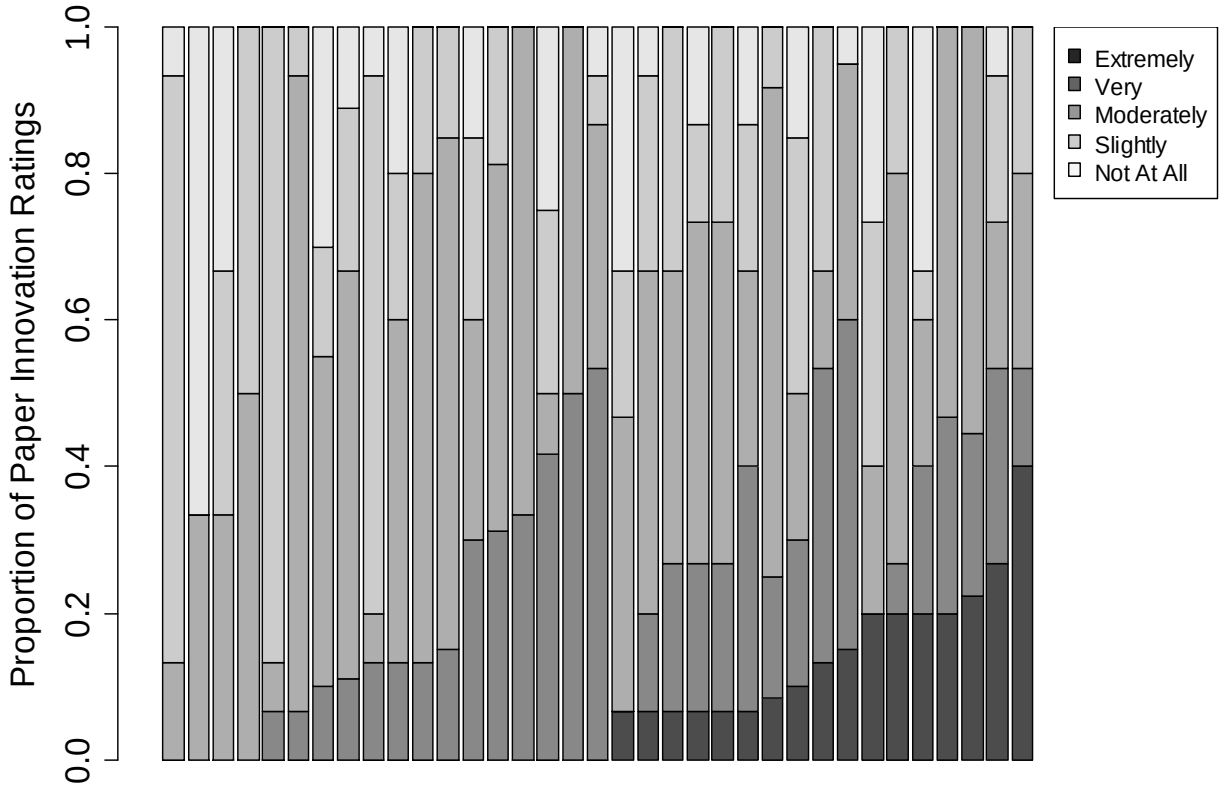


Figure F-9. Innovation Distributions by Researcher for Paper-Level Rating Proportions for Matched R01 PIs

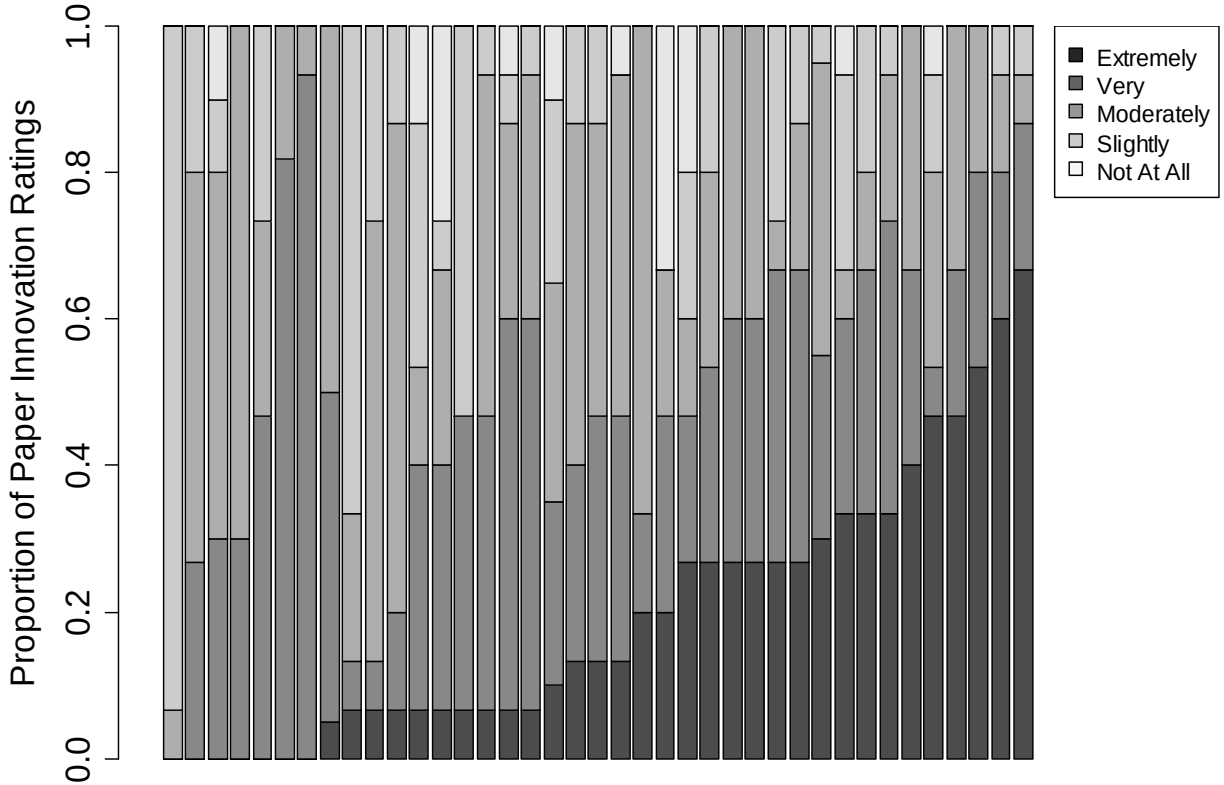


Figure F-10. Innovation Distributions by Researcher for Paper-Level Rating Proportions for HHMI Investigators

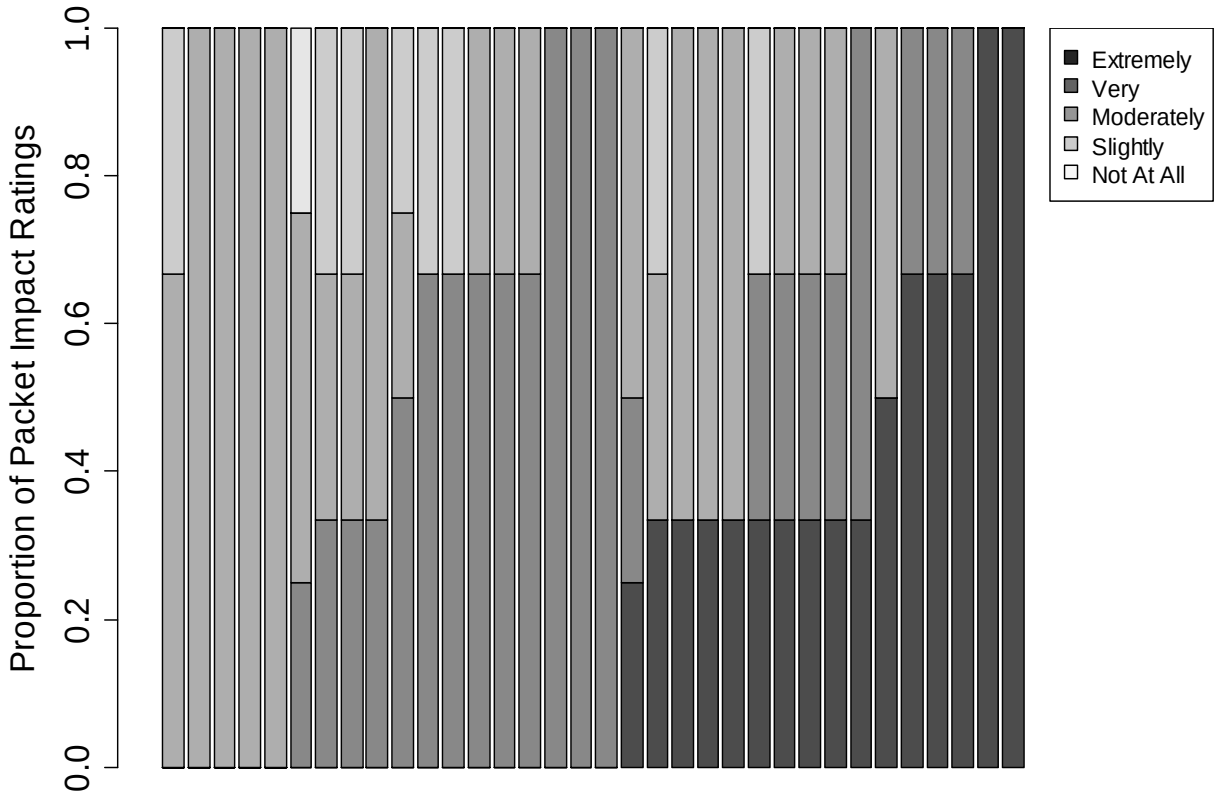


Figure F-11. Impact Distributions by Researcher for Packet-Level Rating Proportions by NDPA Pioneers

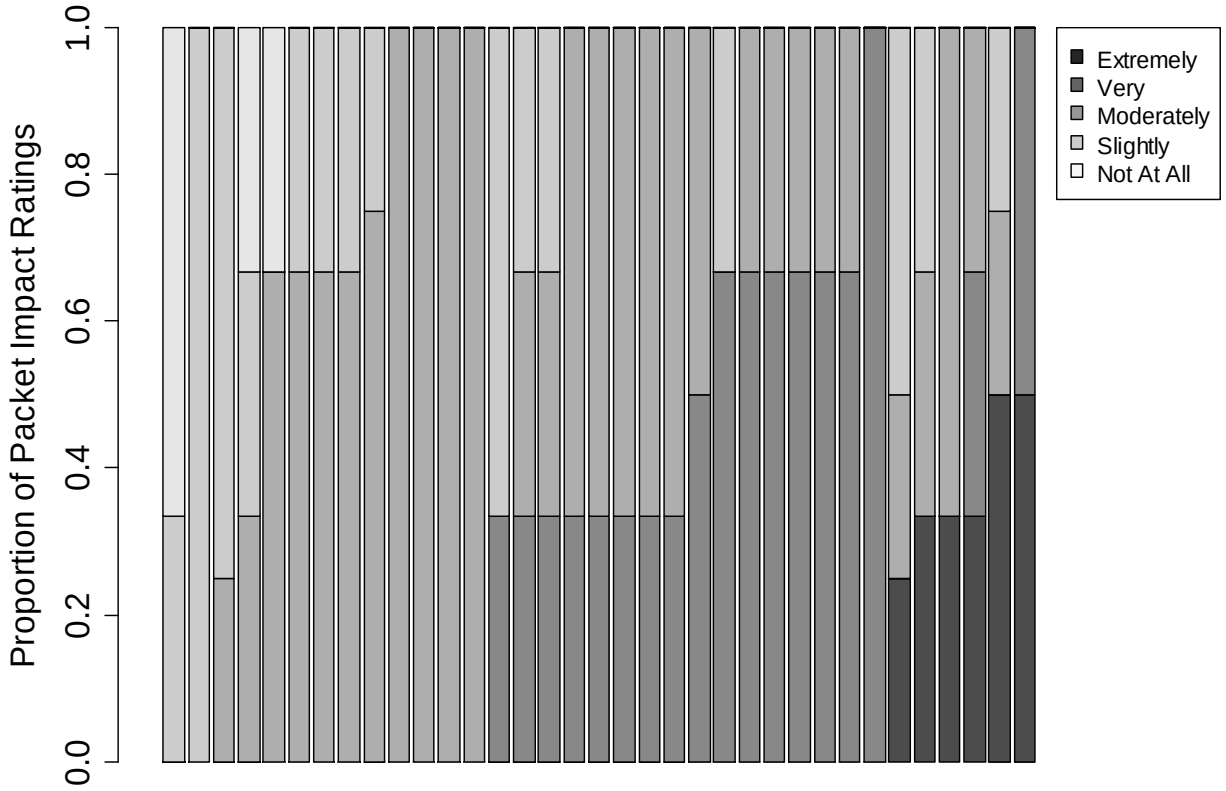


Figure F-12. Impact Distributions by Researcher for Packet-Level Rating Proportions by Matched R01 PIs

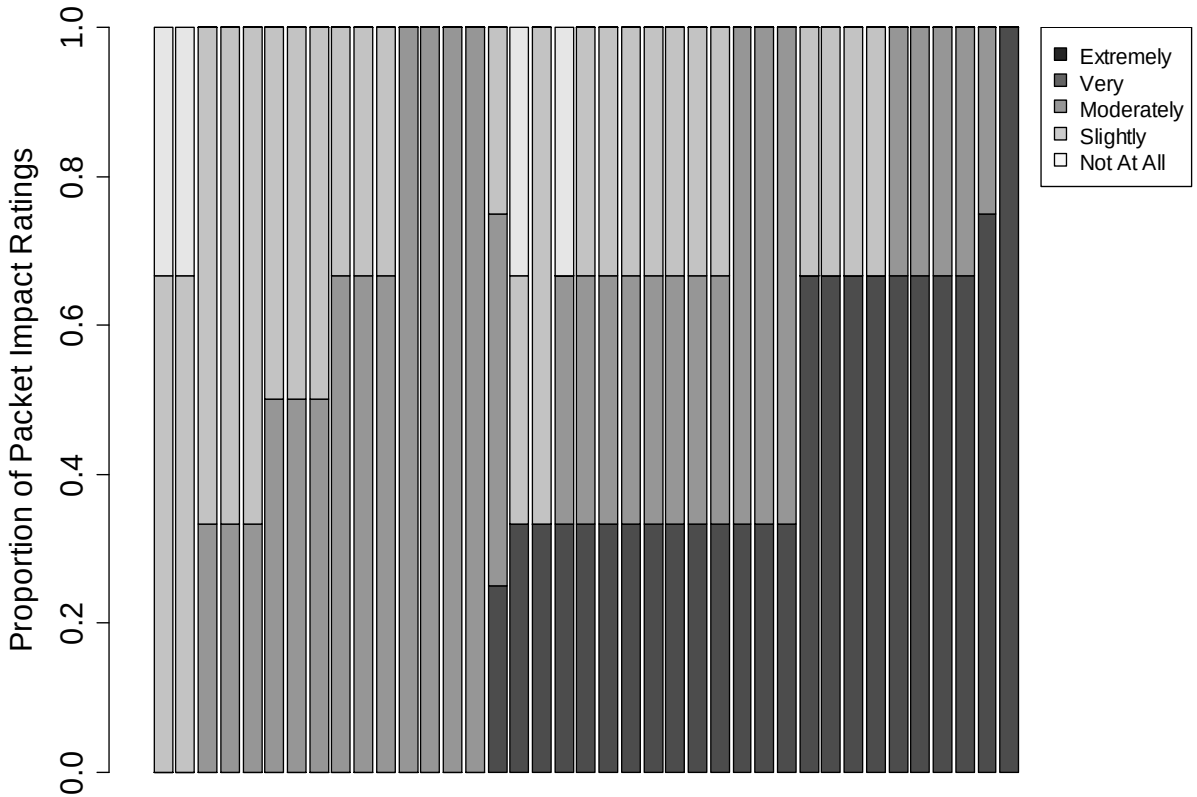


Figure F-13. Impact Distributions by Researcher for Packet-Level Rating Proportions by HHMI Investigators

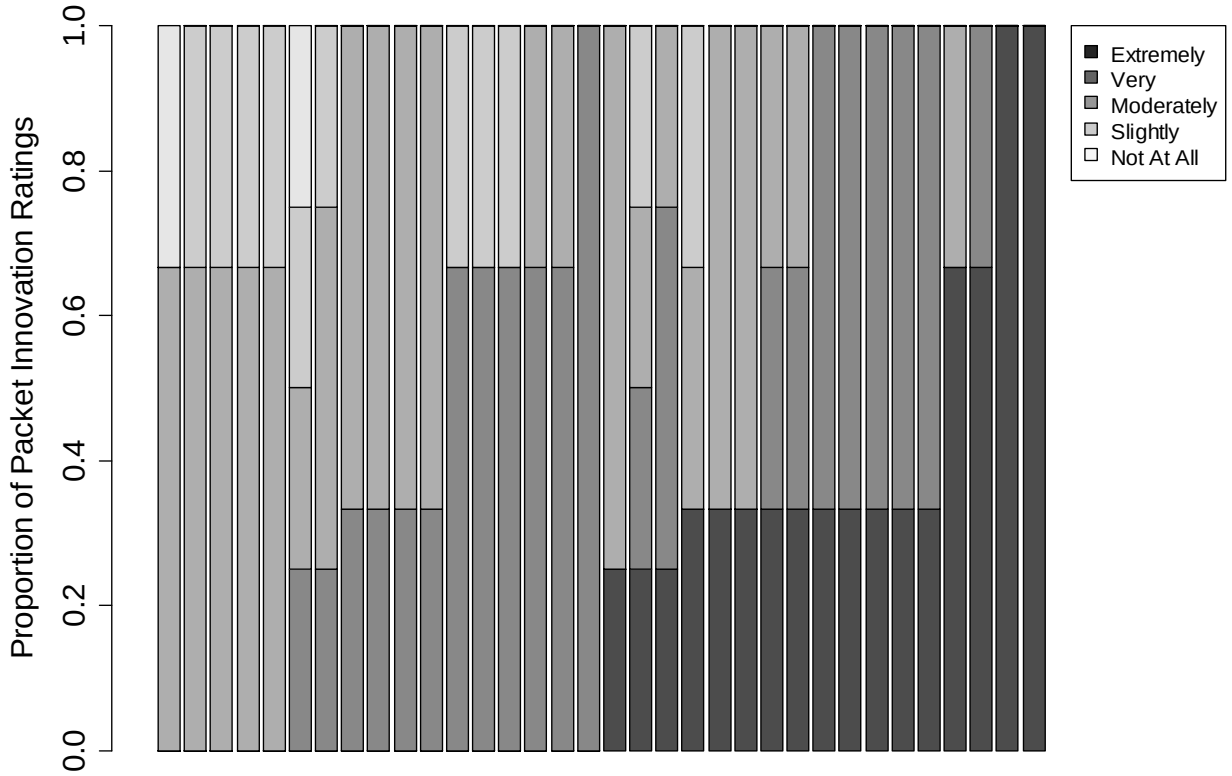


Figure F-14. Innovation Distributions by Researcher for Packet-Level Rating Proportions by NDPA Pioneers

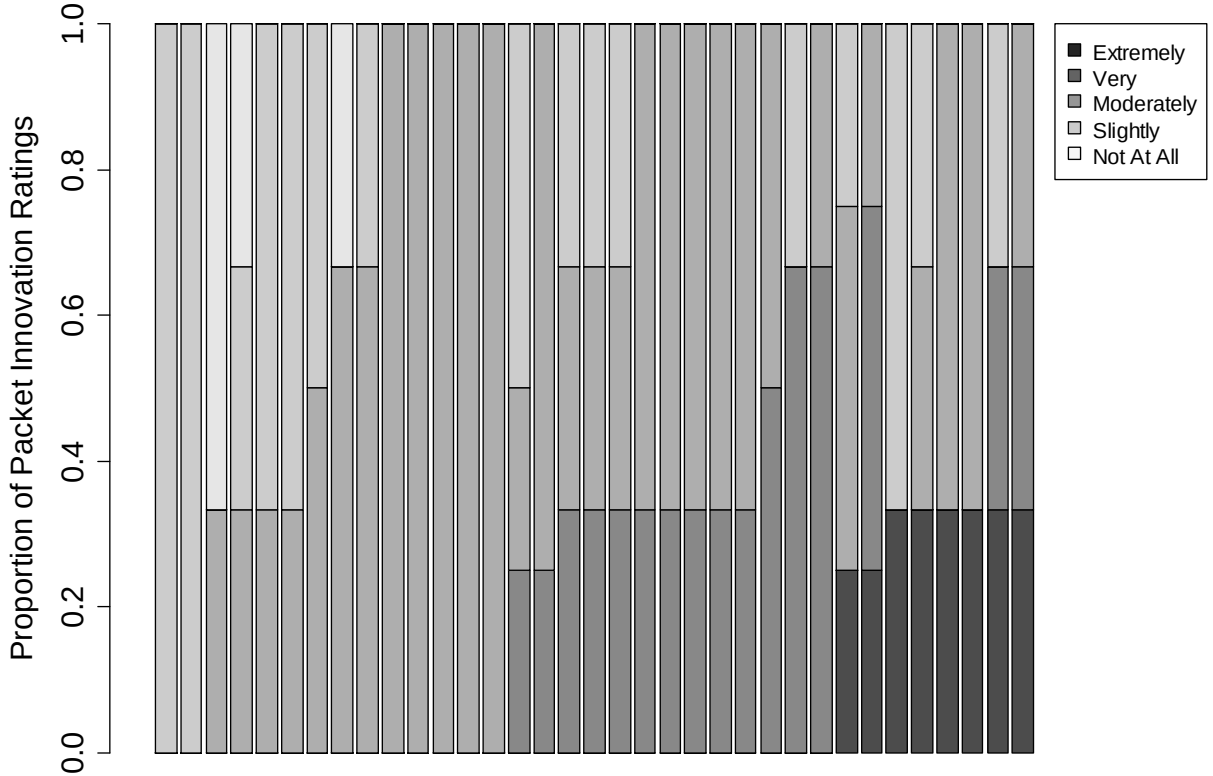


Figure F-15. Innovation Distributions by Researcher for Packet-Level Rating Proportions for Matched R01 PIs

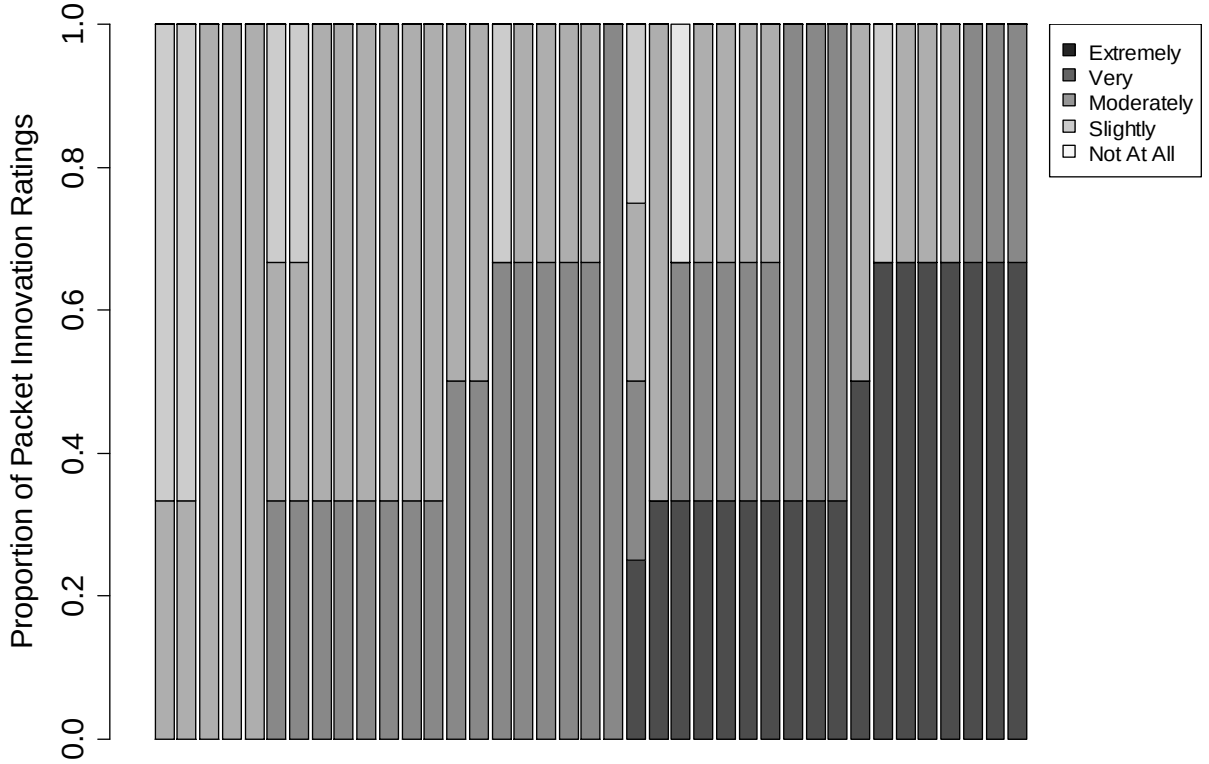


Figure F-16. Innovation Distributions by Researcher for Packet-Level Rating Proportions for HHMI Investigators

Appendix G
Qualitative Analysis Codebook

To better understand why experts characterized papers as having impact or being innovative, qualitative coding was performed on the expert reviewer open comments. Codes and subcodes were developed to find patterns across expert comments. For responses related to the impact of the research, statements were categorized under one of the following broad codes: evaluation strategy, impact, or impact decision (Table G-1). For responses related to the innovativeness of the research, statements were categorized under one of the following broad codes: evaluation strategy, innovation, or innovation decision (Table G-2). Subcodes under each of the broad codes further characterized the nature of the statement. Representative examples from experts are provided for each of the impact and innovation subcodes (Table G-3 and Table G-4).

Table G-1. Code Descriptions for Impact

Code/Subcode	Description
EVALUATION STRATEGY	Reviewers' approach to providing rationale for impact/innovation ratings.
Entire packet	Rationale centered on the packet as a whole.
Multiple papers	Rationale included discussion of innovation/impact of more than one paper as a group.
Single paper	Rationale included discussion of innovation/impact for a single paper.
Unclear	Unclear whether rationale was based on a single paper, multiple papers, or the entire packet.
IMPACT	Discussion of research impact.
Impactful	Research was considered impactful.
Moderate or incremental	Research was considered to have moderate impact or is considered incremental science.
No response	No explicit discussion of impact.
Not impactful	Research was considered not impactful.
IMPACT DECISION	Discussion of how impact assessments were made.
Scientific Discovery	Discussion of research impact focused on the scientific discovery.
Elucidation of pathways or mechanism of action	Elucidation of pathways or understanding mechanism of action were the primary reasons without further descriptions that would allow for further coding into the rubric categories.

Code/Subcode	Description
Foundational research	Decision was based on the scale of impact on a specific field or across fields, including whether other researchers have built on the research, with no other explanation lending to placement inside one of the rubric categories.
Reproduced/Reproducible	Decision was based in whole or in part on whether the findings have been reproduced or whether they are reproducible.
Translational or clinical potential	The research was/was not translational or had/did not have the potential to directly impact patient health or outcomes without further descriptions that would allow for further coding into rubric categories.
Scale-crossing	The research crossed/could not cross scales of organism complexity (cells, tissues, organs, organ systems, and organisms) without further descriptions that would allow for further coding into rubric categories.
Rubric	Discussion of impact of the scientific discovery was based on the rubric given for the impact questions.
Challenges present understanding	The research challenged or did not challenge present understanding.
Changes present understanding	The research changed or did not change present understanding.
Insights that enable new techniques	The research provided insights that enabled new techniques or technologies.
New paradigms	The research provided pathways to new paradigms.
Pathways to new frontiers	The research provided pathways to new frontiers.
Redefines the boundaries of science and engineering	The research redefined the boundaries of science and engineering.
Scientific Method	Discussion of impact focused on the scientific method or approach.
Standard or established methods	Reviewer mentions that standard or established methods were used.
Rubric	Discussion of impact of the scientific method was based on the rubric given for the Innovation questions.
Underlying research is at odds with prevailing wisdom	[Not used]
Research involves a combination of disciplines	The method or approach used was drawn from multiple disciplines.
Research requires the use of equipment or techniques that have not been proven or considered difficult	The method or approach used equipment or techniques that have not been proven or are considered difficult.
Scientific Team Composition	Composition of the team, including the reputation of the PI, was mentioned as part of the justification.
Other	Other factors influencing assessment of research.
Citations	Citations were discussed as part of the rationale.

Code/Subcode	Description
Claims outweigh data	Decision was based on the conclusions not being supported by the results or approach used.
Journal prestige	Journal prestige was discussed as part of the rationale.
Not published yet or recently published	Impact was too soon to tell because the manuscript was recently published or not yet published.
Review	The publication being a review paper, as opposed to an original scientific publication, was mentioned as part of the rationale.

Table G-2. Code Descriptions for Innovation

Code/Subcode	Description
EVALUATION STRATEGY	Reviewers' approach to providing rationale for impact/innovation ratings.
Entire packet	Rationale centered on the packet as a whole.
Multiple papers	Rationale included discussion of innovation/impact of more than one paper as a group.
Single paper	Rationale included discussion of innovation/impact for a single paper.
Unclear	Unclear whether rationale was based on a single paper, multiple papers, or the entire packet.
INNOVATION	Discussion of research innovation.
Innovative	Research was considered innovative.
Moderate or incremental	Research was considered to be moderately innovative.
No response	No explicit discussion of innovation.
Not innovation	Research was considered not innovative.
INNOVATION DECISION	Discussion of how innovation assessments were made
Methodology	Discussion of Innovation focused on the scientific method or approach.
Standard or established methods	Reviewer mentions that standard or established methods were used.
Rubric	Discussion of innovation of the scientific method was based on the rubric given for the innovation questions.
Underlying research is at odds with prevailing wisdom	The underlying research used was at odds with prevailing wisdom.
Research involves a combination of disciplines	The method or approach used was drawn from multiple disciplines.
Research requires the use of equipment or techniques that have not been proven or considered difficult	The method or approach used equipment or techniques that have not been proven or are considered difficult.
Creative utilization or improvement of existing techniques	Discussion of innovation was based on the creative use or improvement of existing techniques.
Other	Discussion of innovation included other aspects of the methodology which were not consistent with the rubric, or with the other methodology categories.
Discovery	Discussion of research innovation focused on the scientific discovery.
Elucidation of pathways or mechanism of action	Elucidation of pathways or understanding mechanism of action were the primary reasons without further descriptions that would allow for further coding into the rubric categories.

Code/Subcode	Description
Foundational research	Decision was based on the scale of impact on a specific field or across fields, including whether other researchers have built on the research, with no other explanation lending to placement inside one of the rubric categories.
Reproduced/Reproducible	Decision was based in whole or in part on whether the findings have been reproduced or whether they are reproducible.
Translational or clinical potential	The research was/was not translational or had/did not have the potential to directly impact patient health or outcomes without further descriptions that would allow for further coding into rubric categories.
Scale-crossing	The research crossed/could not cross scales of organism complexity (cells, tissues, organs, organ systems, and organisms) without further descriptions that would allow for further coding into rubric categories.
Rubric	Discussion of innovation of the discovery was based on the rubric given for the Impact questions.
Challenges present understanding	The research challenged or did not challenge present understanding.
Changes present understanding	The research changed or did not change present understanding.
Insights that enable new techniques	The research provided insights that enabled new techniques or technologies.
New paradigms	The research provided pathways to new paradigms.
Pathways to new frontiers	The research provided pathways to new frontiers.
Redefines the boundaries of science and engineering	The research redefined the boundaries of science and engineering.
Creative Hypotheses or Ideas	Decision was based on the creativity in the concepts or hypotheses underlying the research.
Team Composition	Composition of the team, including the reputation of the PI, was mentioned as part of the justification.
Synonymous with Impact	The reviewer referred to his or her discussion for the impact question for justification of his or her innovation rating, or specifically cited that innovation was perceived to be synonymous with impact.
Other	Other factors influencing assessment of research innovation.
Review	The publication being a review paper, as opposed to an original scientific publication, was mentioned as part of the rationale.

Table G-3. Code Examples for Impact

Code/Subcode	Description
EVALUATION STRATEGY	
Entire packet	"As a whole, the work is important because it provides mechanistic insights into the pathology of viral infections and suggests strategies for prevention."
Multiple papers	"I was less enthusiastic about the last two papers because, while solid, I just did not find the insights derived from the studies to be that profound."
Single paper	"The paper concerning malaria was a comparative genetic analysis of strains of Plasmodium that are species specific, and the conclusion was that the human-specific form had evolved from the chimpanzee-specific strain. Not very surprising."
Unclear	"Ok, but not outstanding." [Only response]
IMPACT	
Impactful	"The optogenetics technology is revolutionizing neuroscience. Some of the applications are more interesting than others, some papers are over-hyped, but it is a huge advance, perhaps the most important in the last two decades of neuroscience."
Moderate or incremental	"As with the previous set of papers these finding seem to modify incrementally our understand[ing] of these systems. I found none of them revolutionary."
No response	[Not applicable]
Not impactful	"Paper 3 is a very detailed analysis of the mechanism of terpene formation that I don't expect to have a big impact outside this limited field."
IMPACT DECISION	
Scientific Discovery	
Elucidation of pathways or mechanism of action	"In totality this work is highly impactful in understanding mechanisms regulating stem cell renewal and differentiation."
Foundational research	"The paper chosen as extremely impactful demonstrates an important function of myosin II in driving keratocyte cell motility through activation of actin disassembly. This paper will be highly cited and will serve as the basis for a substantial body of work in cell motility."
Reproduced/Reproducible	"There are aspects of these papers that are interesting, particularly the claimed finding of reprogramming pancreatic cells without transcription factors. However, this has not been reported by anybody else and raises questions about reproducibility. …I am really curious if that reprogramming protocol is reproducible. Overall, I would not say these reports have had a high impact. If that were the case, the claimed reprogramming protocol would have been in every local newspaper."

Code/Subcode	Description
Translational or clinical potential	"The gold-silver nanocage may be a novelty in nanofabrication, but it has no impact on drug delivery. There is no way such structures can be translated for drug delivery. .. The lack of a medical perspective significant dampens the impact of the work."
Scale-crossing	"The other two papers do not address questions that are as fundamental as the three articles cited above. While the quality of the work is high, I did not find these stories as compelling. The article by Cheng et al. (2009) seemed the least impactful because it focuses on very specific molecules and is not likely to have the major impact on the field or across species, that the other papers are likely to have."
Rubric	
Challenges present understanding	"I would not score this work as Extremely Impactful as it does not challenge wisdom, create a new paradigm or give unexpected insight. This work is excellent, timely, very impactful and rigorous and identifies upstream mechanisms of what is anticipated to be a critical new pathway for understanding neurodegenerative mechanisms."
Changes present understanding	"Each of these papers is really stellar, and changes the way we think about regulation of transcription and translation in cells."
Insights that enable new techniques	"The first paper demonstrates the use of plant viruses to image and differentiate arterial and venous capillaries. It introduces what appears to be a novel platform for imaging."
New paradigms	"The impact of this work is particularly high because essentially either nothing (or highly controversial information) was known on the effect of molecular crowding and nonspecific protein-protein interactions on protein stability, before these studies by Pielak. Impact and innovation are highly connected in these pioneering paradigm-shifting studies."
Pathways to new frontiers	"While each individual paper does not achieve a novel result (that had not already been achieved by other chemical backbones), when taken as a whole the body of work did explore a new chemical frontier and led to some unexpected insight, particularly into the physical basis for the stability of designed structures."
Redefines the boundaries of science and engineering	"However, I give it less impact than the whole body of work in the previous set, because it will not break down boundaries. It will develop new techniques, but the techniques will be accepted by the field."

Code/Subcode	Description
Scientific Method	
Standard or established methods	"The PLOS genetics paper using this same approach to uncover the underlying mutation in flincher and toppler strains in Lass1 is of significance with the impact on lipofuscin accumulation, but it does not reach the high impact of some of the others, most likely due to this same approach of using mouse mutants leading to ataxia and then finding underlying mutations."
Rubric	
Underlying research is at odds with prevailing wisdom	[Not used]
Research involves a combination of disciplines	"excellent mix of basic science molecular approaches, genome biology, physiology of bacteria as they associate with host, cause disease, etc. The breadth of knowledge and approaches is unusual for many labs [that] typically focus on one thing and do it over and over. This PI is cutting edge in many fields."
Research requires the use of equipment or techniques that have not been proven or considered difficult	"This is an extremely impressive body of work. The high level of impact derives not only from the application of cutting edge techniques, several of which are novel and used for the first time, but also from the relevance to human disease."
Scientific Team Composition	"Prof. [name removed] has applied molecular dynamics simulations more broadly than anyone else. He is prolific and his papers are characterized by a rigor and attention to detail."
Other	
Citations	"The five papers together have only been cited a total of 57 times, which isn't bad, but by no means highly impactful. "
Claims outweigh data	"Most of this work is highly speculative. The claims far outweigh the data."
Journal prestige	"For starters the authors address important aspects of stem cell development. Clearly the authors are at the cutting edge in their area. This is reflected by the type of journals they publish in and by the methods used to accomplish their goals. There is no doubt that this science has an impact in the organism system they work in."
Not published yet or recently published	"The Seiler et al. manuscript was just published in Nature Immunology, so its scientific impact has not yet been evaluated by the scientific community."
Review	"The review paper is well done, but cannot be held to have the impact of a primary science paper."

Table G-4. Code Examples for Innovation

Code/Subcode	Description
EVALUATION STRATEGY	
Entire packet	"My score for the set is modestly higher than for each taken alone — because together they do apply state-of-the-art (albeit not novel) methods in a new way to a new preparation. As stated above, this establishes a solid foundation for future and hopefully more innovative work."
Multiple papers	"Papers #1, #2, and #3 were moderately innovative both in the starting hypothesis and in the methods that were used. These studies were logical extensions of the knowledge in the field using mostly standard tools for molecular biology. All three of these papers involved collaborations with groups that had appropriate expertise for specialized methods. Paper #4 was highly innovative because it was the first demonstration of a new technology, including development of new data analysis tools. Paper #5 was very innovative because it combined cell sorting and Next Generation DNA sequencing to get at the question of which parts of the genome are dysregulated in a histone methyltransferase mutant."
Single paper	"The 'human movement...' paper develops a new model."
Unclear	"The questions poised are cutting edge and the approaches taken are relatively novel." [Only response]
INNOVATION	
Innovative	"These studies illustrate boldness in challenging conventional wisdom and a careful approach, using whatever means available to address issues of key importance. This includes the innovative creation and implementation of novel techniques and approaches, such as the use of better EM imaging techniques and genetic methods to create targeted knockouts in C.elegans."
Moderate or incremental	"Paper 1 combines structure analysis with information on the spatial and developmental expression of the enzymes and the functional effects of their knockout: moderate innovation. Paper 2 is a straightforward crystallographic analysis that I would consider slightly innovative. Paper 3 seemed like a pretty straightforward crystal structure analysis with some computational modeling that I rank slightly innovative. I rank paper 4 as moderately innovative for combining evolutionary mutation information with a chromatography based analysis of the enzymatic activity of the enzymes generated. I rank paper 5 as moderately innovative for combining the chemical metabolite analysis, crystal structure data and in vivo assays. I rank the group as a whole moderately innovative.
No response	[Not applicable]

Code/Subcode	Description
Not innovation	"Techniques here are pretty standard in the field...they are applied to a new circuit/system, but the approach is not dramatically innovative."
INNOVATION DECISION	
Methodology	
Standard or established methods	"These studies used well-established methods and a traditional approach. The hypotheses were largely derived from previous evidence. The authors performed a series of direct experimental tests of the mechanisms that might underlie specific behaviors. The behavioral connection could not be validated since all experiments were performed in vitro. The data are definitely novel and interesting for the cerebellar physiologists. The approach is conventional."
Rubric	
Underlying research is at odds with prevailing wisdom	"These studies illustrate boldness in challenging conventional wisdom and a careful approach, using whatever means available to address issues of key importance. This includes the innovative creation and implementation of novel techniques and approaches, such as the use of better EM imaging techniques and genetic methods to create targeted knockouts in C.elegans.."
Research involves a combination of disciplines	"These studies are all highly innovative as the investigators were able to combine theoretical and computational statistical physics, experimental immunology, and clinical data to address outstanding questions that are fundamental to the field. The approaches are unconventional and require both deep understanding of the biological questions and effective implementation of statistical and computational methods."
Research requires the use of equipment or techniques that have not been proven or considered difficult	"The approach is technically innovative, in the sense that authors did not only implement the real time MRI technology but also modified it for speech analysis. I cannot judge how much the authors contributed to the development of this new technology since I did not follow the history of how real time MRI developed and evolved, but nevertheless, those studies do present a significant technical advance."

Code/Subcode	Description
Creative utilization or improvement of existing techniques	"While many of the approaches are not necessarily innovative in and of themselves, the way they were used is highly novel. For instance, the clarity of fax sorting NG2+ SVZ versus cortical cells to evaluate EGFP expression and activity on migration was a very innovative approach at the time. The methods to evaluate direct interactions between NPCs and NSCs in the Notch/EGFR Nature 2010 paper is also a highly novel way to address the question posed. Finally in the chordin 2010 Nat Neurosci paper, the approach to use a demyelinating insult to address differences in migration and differentiation and site from which migration occurs was a novel use of system."
Other	"The approaches chosen are able to answer the questions the authors asked. All the approaches are creative and not limited to the organism in question."
Discovery	
Elucidation of pathways or mechanism of action	"Novel signaling components and protein modifications that mediate cell death and autophagy were identified in these papers. However, these studies did not rely on novel techniques, and the results are within the framework of existing pathways."
Foundational research	[Not used]
Reproduced/Reproducible	"#1 -Logic — very innovative — combines many approaches and bioinformatics; unique combination of methods is innovative. #2, 3,4 — Moderately innovative. Interesting concepts and results, but these are not out of the norm of typical research. #5, extremely innovative. This is a complex in vivo screen, but led to a hit from a subset of a compound library that could then be explored further. I would have bet against this screen working, but they found interesting and reproducible results with it."
Translational or clinical potential	"For the most part these papers use state-of-the-art mouse genetics to help define important roles for endothelial cells in stem cell niche formation. The most innovative paper dealt with the generation of multi potent stem cells from the germ line. It identified new markers that can potentially help create a whole new approach for fertility treatments. The other papers were innovative not for their technical approaches, which could be done in many labs, but for the unique insights and advances in defining the vascular niche."
Scale-crossing	"This paper is intellectually innovative, as its reach is so broad. While the findings are not at odds with prevailing wisdom, they push the envelope much further by charting brand new territory in terms of the functionality of the Shh pathway and the importance of the proteoglycans. A tremendous, lovely story."

Code/Subcode	Description
Rubric	"The PLOS genetics paper using this same approach to uncover the underlying mutation in flincher and toppler strains in Lass1 is of significance with the impact on lipofuscin accumulation, but it does not reach the high impact of some of the others, most likely due to this same approach of using mouse mutants leading to ataxia and then finding underlying mutations."
Challenges present understanding	"The work illustrates the power of combination of disciplines and the application of especially sophisticated techniques. The results challenge, or even overturn, some prevailing ideas about DNA structure, and offer new approaches that may actually be useful."
Changes present understanding	"There is only one paper in this group. The novelty of this work is 1) the discovery of cell death genes can also regulate cell size and 2) therefore the cell death process and cell size program can be coupled. These connections would not been predicated based on prior knowledge."
Insights that enable new techniques	"The most innovative contribution of these papers is the use of fluorinated side chains to better enable the visualization of proteins in intact cells. Although much of the spectacular resolution associated with traditional biomolecular NMR is lost in this approach, it does enable the detection of protein NMR signal in vivo, even for larger globular proteins, a feat that has largely defied methods based on traditional labeling schemes. Further innovation is provided by considering the specific character of proteins as the primary crowding agent within cells, and noting that they differ from traditional agents used to mimic cellular crowding in vitro."
New paradigms	"Paper 1 I consider very innovative in the sense that it conceived of a whole new field of regulation. Paper 2 — Extends the analysis to metabolites which was cutting edge technology at the time, so it gets slight innovation for that. Paper 3 — Extends the analysis to a functional endpoint. Beyond the first two papers, I would rate it high for impact but probably not for innovation. Paper 4 — Monitoring metabolites was pretty new technology so some innovation points should be awarded. Paper 5 — The findings are potentially of high impact but the approach is not particularly innovative. Overall it is a moderately innovative package, with the metabolism monitoring representing the most innovative of the technologies."

Code/Subcode	Description
Pathways to new frontiers	"In this work 'the whole is greater than the sum of its parts.' Heald's use of cytoplasmic extracts to reconstitute complex cellular functions was not new; however, it was essential for generating a data set robust enough to be used for mathematical modeling. It was the skill with which the studies leveraged these two complimentary approaches that was the most compelling innovative aspect for me. Especially interesting were the predictions of how "putative factors" that affect microtubule plus or minus end dynamics will affect spindle length. These predictions prompt quite a few interesting future experiments. It is trendy for investigators to attempt to combine basic cell biological research with mathematical modeling but the results are not typically as provocative as these are. "
Redefines the boundaries of science and engineering	"These papers exactly fall into the category of 'development of new frontiers' that 'redefine the boundaries of science and engineering.' This has been achieved through a combination of novel genetic engineering and transformative application of the technology to study awake behaving animals while selectively manipulating neuronal activity by light. Importantly, this novel technology is transferrable to other research groups, making it a true community resource with a huge impact."
Creative Hypotheses or Ideas	"The main innovations in these paper are conceptual. The experimental techniques applied are relatively standard, but the kinds of analysis and the posing of the questions allows the authors to re-frame long-standing questions about the visual system and to connect the biological features of retinal circuitry with computational problems faced by the visual system. Because these papers did not directly deal with treatment of a human disease, it is difficult to compare their long-term impact to that of papers that directly address the causes and effects of disease on human health. Nonetheless, I believe that these papers have [been] and will continue to be very important for our understanding of early sensory processing in a number of systems."
Team Composition	"This is a tough choice. These papers build off of many years of mouse ES cell biology to help suggest possible approaches for successful hES cultures. Human ES are much more technically challenging to work with and making these technical advances are very important to and necessary for the field. The challenges are often empiric and difficult to accomplish, but not massive departures from what has worked in other systems. Dr Keller is a leader in these efforts and helped develop much of the mouse ES biology that the human work is often patterned after."

Code/Subcode	Description
Synonymous with Impact	“Here again, innovation clearly parallels impact. The technique appears to be completely novel in the context of biomolecules — i.e. if you include the Science paper — but of necessity I am guessing. I assume that standardization is required for most of the systems studied — however for routine measurements, this technique appears to have great promise.”
Other	“About all sets of papers — Innovation (in approach) must be evaluated with careful validations. Please see my detailed comments on individual papers regarding the impact of the research. Only the 4th and 5th papers were done with reasonable validation. Individual paper — #1 Science Review. This is review paper and innovation cannot be evaluated. #2 Nature Neuroscience — This paper may be innovative, but I don’t think the approach was validated. #3 Science vol 324 — Same as #2 paper. #4 Science vol 332 — Several unique approaches, including the use of circadian arrhythmic mutant flies and an enriched environment (fly mall) are very innovative. #5 Nature — Standard methodology was used, but careful analysis revealed an innovative discovery which lead to an innovative idea for local sleep.”
Review	“The fact that it is a review article made it difficult to examine the innovativeness of the approaches.”

Appendix H
Protocols for Downloading and Cleaning Publication Data for Bibliometric Analysis

Background

The study team obtained and cleaned publication data at the researcher and grant levels. Researcher-level publications are defined as research articles where the PI of interest appears as an author. Researcher-level data were collected for NDPA Pioneers, matched R01 PIs, HHMI investigators, and NDPA finalists. Grant-level publications are defined as research articles that can be attributed to the grant number of interest through funding acknowledgments in Web of Science (WOS), PubMed, or NIH electronic Scientific Portfolio Assistant (eSPA). Grant-level data were collected for NDPAs, matched R01s, and R01 portfolios.

The protocols described in this appendix detail the data download and cleaning processes at the researcher level. At the researcher level, the WOS database was used to download publication data and disambiguate researchers. Commercially available software called VantagePoint (VP) was used to clean and prepare the publication data for statistical analysis using R.

At the grant level, publication data that corresponded to grant numbers as opposed to authors was downloaded and the data-cleaning methods were altered to render them appropriate for the grant-level data. The study team collected the grant-attributed titles using a combination of the eSPA database and WOS. For the matched R01 PIs, the team performed queries by grant number, and for NDPA Pioneers, the team queried the text "DP1," the NDPA activity code, and "Pioneer" to get a comprehensive list of titles. The complete publication data for these titles were then downloaded from WOS and cleaned in the manner described in the data-cleaning protocol.

In addition to cleaning the researcher-level and grant-level data with VP, the team continued to fix errors that were observed throughout the bibliometric analysis process to develop the cleanest dataset possible. The errors that were observed arose from a combination of errors from the WOS database, the eSPA database, and human judgment. All analyses presented in the report reflect the most accurate dataset.

The downloading protocol and data-cleaning protocol follow.

Start

To begin, you will need to access the Thomson Reuters WOS publication database.

1. Create a Researcher ID to keep track of and save queries.
2. Copy the most up-to-date fuzzy files, import filters, macros, and thesauri (VantagePoint file types) to the appropriate Program Files folder on your computer

You will also be provided with a folder of NIH application biographical sketches (biosketches) or curriculum vitae (CV) for the researchers in the comparison group that is assigned to you. Additional materials for data cleaning include: a spreadsheet of the PI's full name, award year, and STPI-assigned "STPICode" for each researcher; a spreadsheet that matches WOS indexed journals to WOS Subject Categories (WOS SC-Journals spreadsheet); and a summary spreadsheet at the PI data rate in which to record metrics of interest. Time estimates are provided as a rough guide for the amount of time that should be spent on each process.

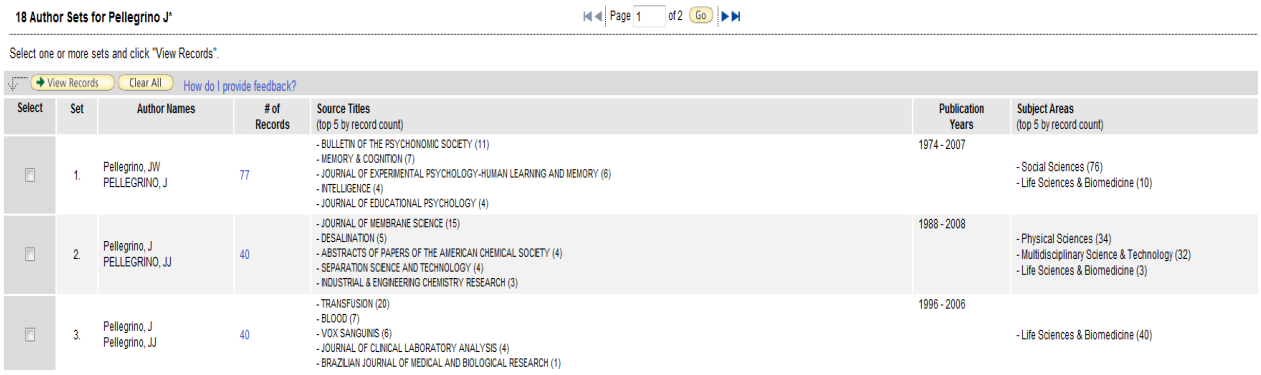
Data Downloading Protocol (Researcher Level)

Download the Publications [TOTAL TIME: 10-20 Minutes]

3. Perform an "Author Finder" search using last name and first initial.
    a. For example, Abbott L is the search query for Larry F. Abbott.
    b. For people with common last names, refer to the biographical sketch/CV and the format of the name from the publications listed; use judgment in whether a middle initial should also be included in this search query. Including the middle name will help you sort through the distinct author sets more efficiently and determine which author is the correct one.
4. Select the appropriate "Distinct Author Set" by referring to the provided biographical sketch/CV (Figure H-1). Judgment should be used here in selecting the correct author set. Some things that might help you identify the correct distinct author set are:
    a. Look at the middle initial in a person's name.
    b. Match field of study with related "source titles for the author" in WOS (although sometimes this is not accurate because people don't perform research in the field in which they got their degree).
    c. Look at the year in which they received their PhD to ensure that the "publication years" in WOS roughly make sense (we assume that people will start publishing around the time they get their PhDs or a little before).

d. Match the "last known institution" in WOS to the institution of employment listed on the biosketch/CV (the biosketches and CVs are from 2004-2006 so this may or may not be useful if the individual has moved institutions in the last few years).

e. You may choose one or more author sets, based on your judgment of whether the publication years and subject areas listed are compatible with the information provided on the author.



18 Author Sets for Pellegrino J*

Page 1 of 2 Go

Select one or more sets and click "View Records".

View Records | Clear All | How do I provide feedback?

Select	Set	Author Names	# of Records	Source Titles (top 5 by record count)	Publication Years	Subject Areas (top 5 by record count)
☐	1.	Pellegrino, JW PELLEGRINO, J	77	- BULLETIN OF THE PSYCHONOMIC SOCIETY (11) - MEMORY & COGNITION (7) - JOURNAL OF EXPERIMENTAL PSYCHOLOGY-HUMAN LEARNING AND MEMORY (6) - INTELLIGENCE (4) - JOURNAL OF EDUCATIONAL PSYCHOLOGY (4)	1974 - 2007	- Social Sciences (76) - Life Sciences & Biomedicine (10)
☐	2.	Pellegrino, J PELLEGRINO, JJ	40	- JOURNAL OF MEMBRANE SCIENCE (15) - DESALINATION (5) - ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY (4) - SEPARATION SCIENCE AND TECHNOLOGY (4) - INDUSTRIAL & ENGINEERING CHEMISTRY RESEARCH (3)	1988 - 2008	- Physical Sciences (34) - Multidisciplinary Science & Technology (32) - Life Sciences & Biomedicine (3)
☐	3.	Pellegrino, J Pellegrino, JJ	40	- TRANSFUSION (20) - BLOOD (7) - VOX SANGUINIS (6) - JOURNAL OF CLINICAL LABORATORY ANALYSIS (4) - BRAZILIAN JOURNAL OF MEDICAL AND BIOLOGICAL RESEARCH (1)	1996 - 2006	- Life Sciences & Biomedicine (40)

Figure H-1. Distinct Author Sets Resulting from the Author Finder Search in Web of Science

5. Click on "View Records."
6. Do a quick comparison of the publication titles listed in the biosketch/CV and the titles that have been returned in the search query in order to make sure that you have the correct person (keeping in mind that the CV/biosketch is from 2004-2006). If you do not find any of the publications listed in the biosketch/CV, there may be an error—go back and look at the distinct author sets again.
7. On the left, see the "Refine Results" box. Under the "Document Types" arrow, refine by the "article" document type.
8. Also under the "Refine Results" box, filter for publications up to and including 2011.
9. Return to the refined list of query hits. At the bottom of the page, find the box that says "Output Records" (Figure H-2).
10. Select the radio button with the option "Records __ to __". In the blank boxes, input "1" and "*the number of results from the search query*" in order to download data for all of the publications you've found.

Note: You may download a maximum of 500 records from WOS at any one time, so it may be necessary to download the records in parts.

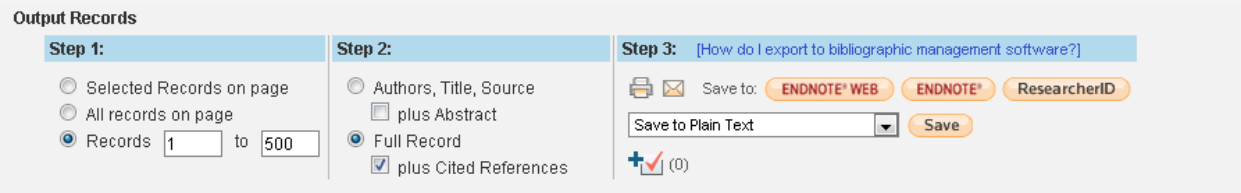


Figure H-2. Output Records in Web of Science

11. Select the radio button "Full Record" and check the box "plus Cited References".
12. Select the option "Save to Plain Text" in the drop down menu. Click the "Save" button.
13. Rename the downloaded file as the query you used in the "Author Finder" search (e.g., Abbott L.txt; e.g., Abbott L2.txt; etc.).
14. In the browser, return to the results page and click "Create Citation Report."
15. At the bottom of the resulting Citation Report page, select the radio button with the option "Records __ to __". In the blank boxes, input "1" and "*the number of results from the search query*" in order to download data for all of the publications you've found (Figure H-3).
16. Select the option "Save as Excel file," and click the "Save" button. Rename the resulting file with the STPICode. The citation report data will form the foundation for the publication data in spreadsheet form.

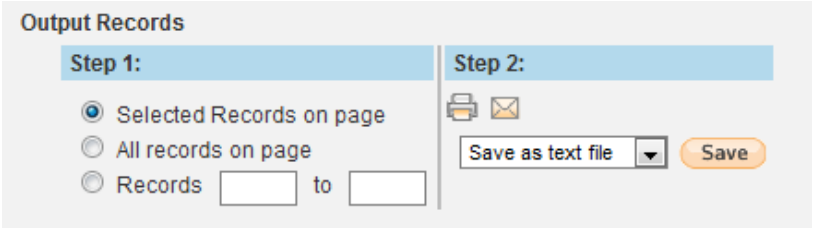


Figure H-3. Output Citation Report in Web of Science

Data Cleaning Protocol

Import Text Files into VantagePoint

Import each Text File individually into VP, saving the filename as the STPICode for each researcher (e.g., "Awardee1.vpt").

17. Select the files that need to be imported using the "Raw Data File (Use Import Filter)" (under File or when the window pops up when you first open VP).
18. The Import Filter that you will use is: "WOK-WOS (Field-Tagged text)," a filter custom-made for our purposes.

Note: if the file does not initially show up—select "Select New Filter Directory" button in the bottom of the window and you can navigate to wherever you've saved the Import Filter file on your computer.

19. Select all primary fields and add the secondary fields you want to import: select using Ctrl+
    a. Cited Journal
    b. Cited Authors
    c. Cited References
    d. Funding Award Numbers
    e. Funding Organization
20. Select Finish and let the file load.

FIELD 1: Authors [TOTAL TIME: 10-15 Minutes]

For **Authors—make sure that your final cleaned Authors field is labeled **"Authors FINAL"****

Note: you can rename the final cleaned field or create a copy of the field by right-clicking on the field name in the Summary window—copy rather than rename the field if you have undergone a major cleanup process (used the most recent thesaurus) to create the field.

21. Under Fields>List Cleanup—highlight the field "Authors" and use the General.fuz file in your Fuzzy folder (Figure H-4) (**do not** check "Verify Matches w/another Field"); you can specify the New Field to create and label this as the thesaurus or fuzzy function you are using (e.g., "Authors RunGeneral.fuz").
22. In Cleanup Confirm window—make sure any groupings make sense and given your time allotted for cleaning, try to focus on those authors that have more rather than less Number of Records.
    a. Selecting All Items and Right-clicking to Sort>All Items>By Name will make it easier to see similar names.
    b. You can drag any names to a similar name to group names—please follow the standardization instructions below.

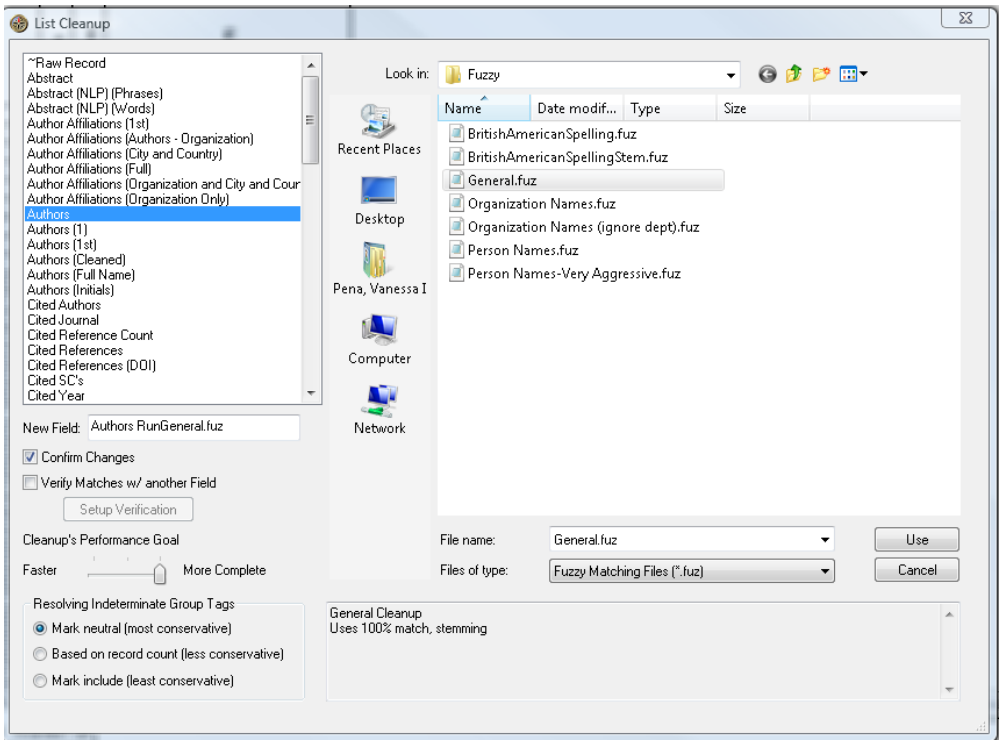


Figure H-4. List Cleanup Window in VantagePoint

Note: When grouping names you think are similar, and if initials are missing and the last name is sufficiently "uncommon" (e.g., Turrigiano, G; Turrigiano G G, and Turrigiano, GG), then always group the one without the middle initial and without spaces into the name with the middle initial (e.g., new group name: Turrigiano, GG).

Note: When grouping similar names and one part of the name is spelled out and one isn't (e.g., Swinehart, Christian D and Swinehart, CD); then always group the spelled out name into the initial name (e.g., new group name: Swinehart, CD).

Note: For less common names (e.g., Zhang, Z and Zhang ZY) do not try grouping these until you have checked their affiliations in "(Optional) Step 24." It is best to stay conservative with your groupings.

23. Once you are done grouping names, "Save as Thesaurus"—this will access your Thesaurus folder and save the File name as "NDPA-YourGroup-Authors" (e.g., NDPA- Pioneers -Authors.the).

Note: You can now use this file in the future when cleaning authors for other PIs.

24. (Optional) Making further changes — If there were similar names for which you would like to check their affiliations or look at all the publication record fields to determine if they are indeed the same individual, then you can view the new author list ("Authors RunGeneral.fuz") you have created and highlight the names you would like to investigate.

a. There is a default detail window to the left of VP that shows the Title of the publications for any highlighted cells in your list.

Note: a general check may be to compare the publication titles of the individuals and check for similar keywords or context of the publications for those with similar names.

b. You can add additional detail windows to the right of the interface by right-clicking and selecting “Create Detail Window”; you can choose a field to look at to compare affiliations, publication years, and subject categories of the names you’ve highlighted (Figure H-5).

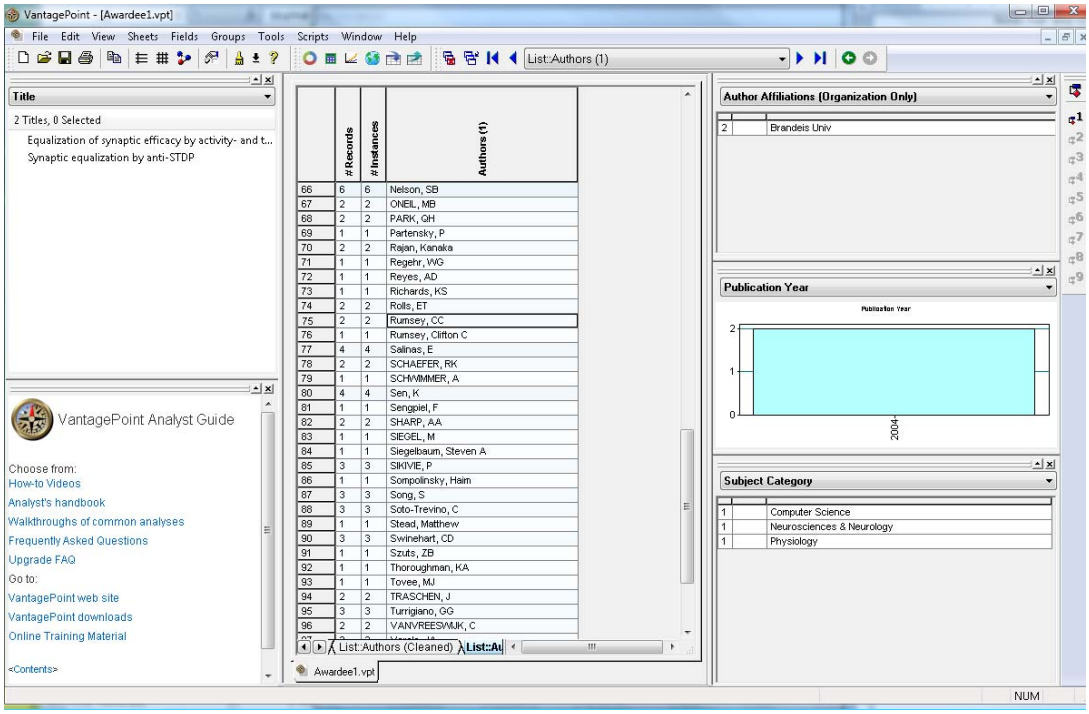


Figure H-5. Highlighted Similar Names and Detail Windows in VantagePoint

Note: a general check on the Affiliations (Organization Only), Publication Year, and Subject Category should provide more than enough information to tell whether the similar names are really the same individual.

c. If you would like to make additional changes to the list, you can edit and run the new Authors thesaurus (“NDPA- Pioneers -Authors.the”)

d. To edit the Authors thesaurus—select Tools>Thesaurus editor…; open the Authors thesaurus, select the newest Authors field (“Author RunGeneral.fuz”).

e. You will be adding a “Top Level Item” by right clicking on the second window that lists the contents of the thesaurus—you will then type in the

new label for the name (e.g., I have added Rumsey below by typing out the New Item name “Rumsey, CC” and highlighting the two Rumsey names in the Authors list (left) and dropping it into the “Rumsey, CC” top level item [Figure H-6]). Save.

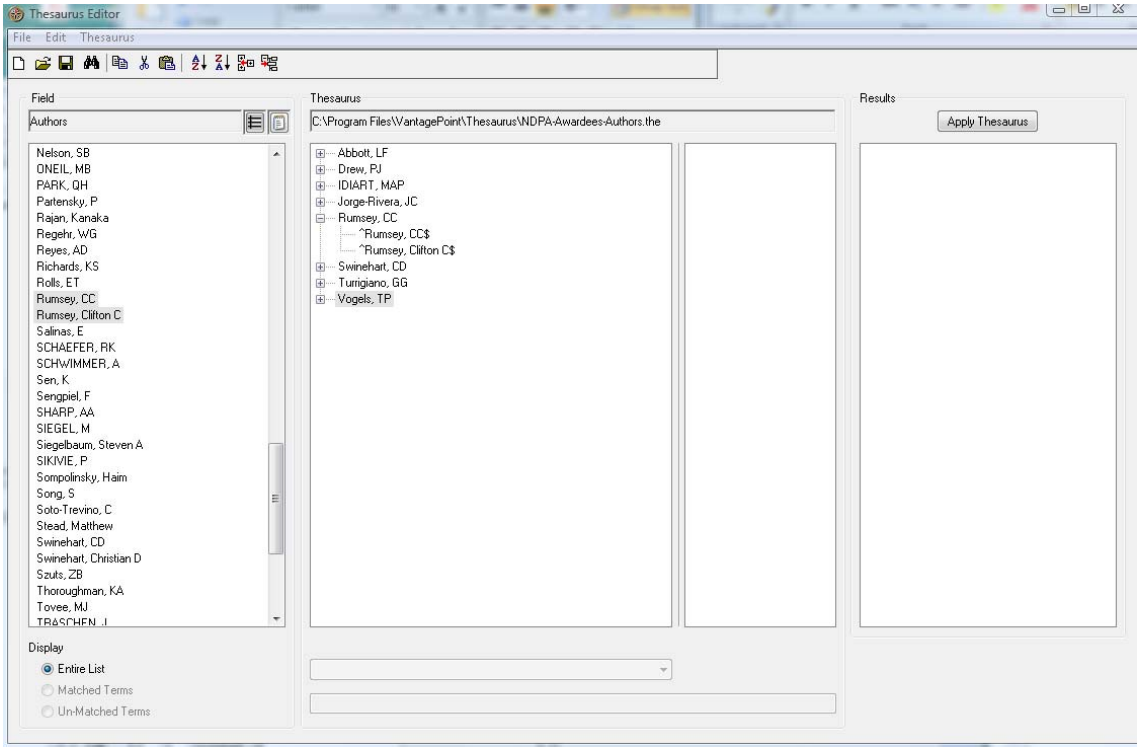


Figure H-6. Thesaurus Editor Editing an Authors List and Thesaurus in VantagePoint

Note: The thesaurus editor automatically inserts any notations necessary when you drag and drop and there’s no need to further edit the names inserted in the group.

Note: You can check whether the thesaurus now recognizes Rumsey, Clifton C by selecting “Apply Thesaurus” and displaying Matched Terms (whether now this name is in the matched term list) or Un-matched Terms (whether the name is no longer in this list).

f. Using the new edited thesaurus on your latest cleaned Authors list, you will specify a name for the new field.

25. If you are done with the Author cleanup process, then specify this field as “**Authors FINAL”**.

FIELD 2: Author Affiliations [TOTAL TIME: 10-15 Minutes]

For Author Affiliations (Organization Only)—make sure that your final cleaned Affiliations field is labeled “Author Affiliations (Organization Only) FINAL”

26. Review the list of Author Affiliations (to get a sense of similar affiliations).
27. Under Fields>List Cleanup…—highlight the field "Author Affiliations (Organization Only)" and use the "NDPA-Organization-Names.fuz" file in your Fuzzy folder (**do not** check "Verify Matches w/another Field"); you can specify the New Field to create and label this as the thesaurus or fuzzy function you are using (e.g., "Author Affiliations (Organization Only) RunNDPAOrg.fuz").
28. In Cleanup Confirm window—add or remove groupings if necessary as indicated in Field1: Authors—Step 2.
29. Once you are done grouping names, "Save as Thesaurus"—this will access your Thesaurus folder and save the File name as "NDPA-*YourGroup*-Affiliations" (e.g., NDPA- Pioneers -Affiliations.the).

Note: You can now use this file in the future when cleaning affiliations for other PIs.

Note: Similarly, you can edit the new Affiliations thesaurus if you find after reviewing that your new Affiliations list requires further cleaning—Field1: Authors-(Optional) Step 4.

30. If you are done with the Author Affiliation cleanup process, then specify this field as **"Author Affiliations (Organization Only) FINAL".**

Grouping by Publication Years [TOTAL TIME: 20-30 Minutes]

31. Refer to the provided data where the PI's award year is noted.
32. In the Summary window, double-click on the Publication Year field and right-click to sort by year.
    a. Highlight all the years previous to and including the year in which the PI received the award and right-click to "Add Selection to Group…". Label the New Group as "Before".
    b. Highlight all the years after the award year of the PI and right-click to "Add Selection to Group…", and label the New Group as "After".
33. Add Detailed Windows (right-click) to show the fields: (1) Authors FINAL and (2) Author Affiliations (Organizations Only) FINAL (Figure H-7).
34. Count the unique authors and affiliations.
    a. Highlight the "Before" column created in your Publication Year list and count the number of unique authors and affiliations are associated with that time period. Record these numbers.

b. Highlight the "After" column created in your Publication Year list and count the number of unique authors and affiliations are associated with that time period. Record these numbers.

Note: Save the excel file as their STPI_Code (e.g., "Awardee1VPData.xlsx") for our records.

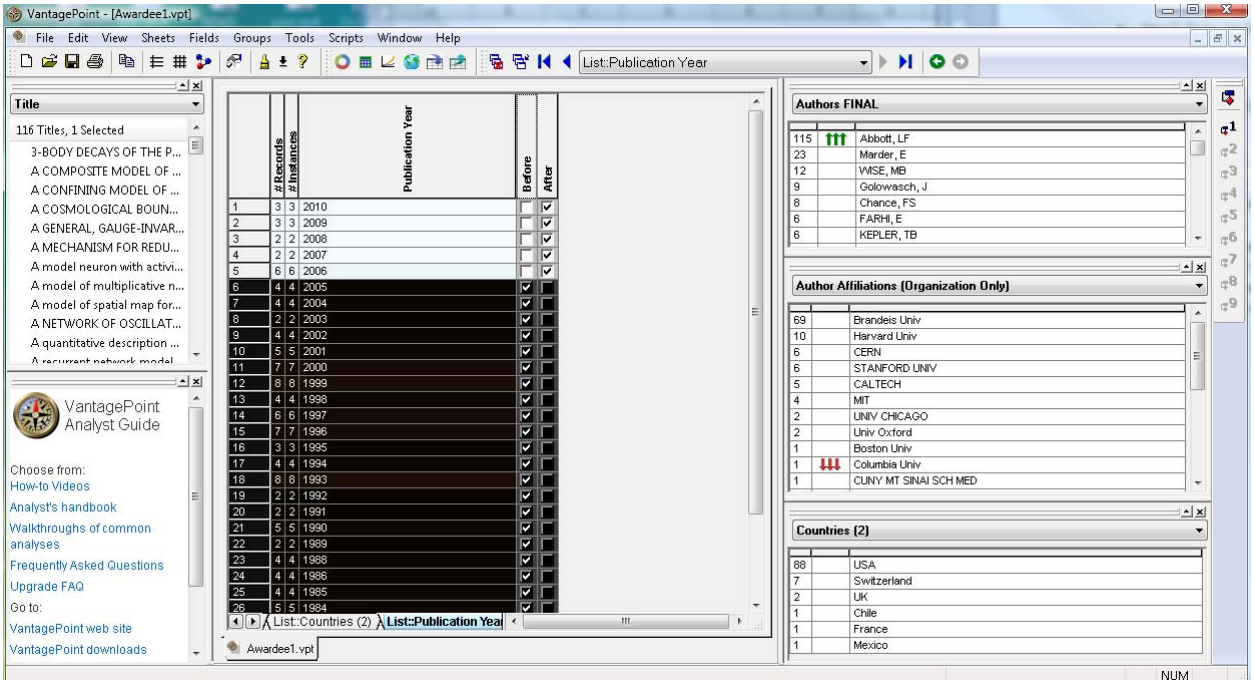


Figure H-7. Detailed Windows and Before and After Groups in Publication Year Field in VantagePoint

FIELD 4: Cited Journals and Interdisciplinarity Calculations [TOTAL TIME: 20-30 Minutes]

You will be creating new fields: "Cited SC FINAL" and creating two subsets of the data in new VantagePoint files "Before" and "After".

35. Open the provided spreadsheet with WOS Journals matched to WOS Subject Categories (WOS SC-Journals spreadsheet).

36. Clean the Cited Journals Field - Under Tools>Thesaurus editor…; open the most up-to-date Journal-Subject Category (J-SC) thesaurus, and select the field "Cited Journals".

    a. Apply the thesaurus and check the Un-Matched Terms.

    b. Use the WOS SC-Journals spreadsheet to lookup the individual journals and check to see (1) if the journal is indexed in WOS; (2) if it is, then to edit the

thesaurus by dragging the journal to the subject categories that are linked to the journal. Save.

Note: There may be multiple subject categories for the journal, so make sure to drop the journal into each one of the subject categories in the second window of the thesaurus editor.

Note: The WOS SC-Journals spreadsheet may have variations of the journal name so make sure to search variations of the journal or use wildcard notation when searching for the journal name.

37. Once satisfied with the editing, use the J-SC thesaurus on the Cited Journal Field. IMPORTANT: check "Allow Multiple Matches". Specify the new field as "Cited SC RunJ-SC.the" Confirm that the thesaurus has not left out journals with high frequency (number of publications). If you need to make further changes—use the thesaurus editor (Step 2). If you are satisfied with the changes, then rename the field as "**Cited SC FINAL"**.

Note: As a general rule of thumb, journals that are Un-Matched Terms in the J-SC thesaurus and with at least 5 publications should be searched in the WOS SC-Journals spreadsheet.

38. Subset the file/data to calculate the Integration Score for "Before" and "After" publications:
    a. Open the Publication Year list and highlight the "Before" labeled grouping (this will highlight all cells for years grouped as "Before.")
    b. Go to File-Create Sub-dataset to create a new VantagePoint file with only the highlighted cells.
        1) Make sure in the Create Sub-dataset window that Selection is selected. Select Ok. (Figure H-8)
        2) Save the file as the "STPICode_Before" (e.g., Awardee1_Before)
    c. Create a new VantagePoint file for the "After" labeled grouping in the Publication Year list in a similar manner and save as "STPICode_After" (e.g., Awardee1_After).

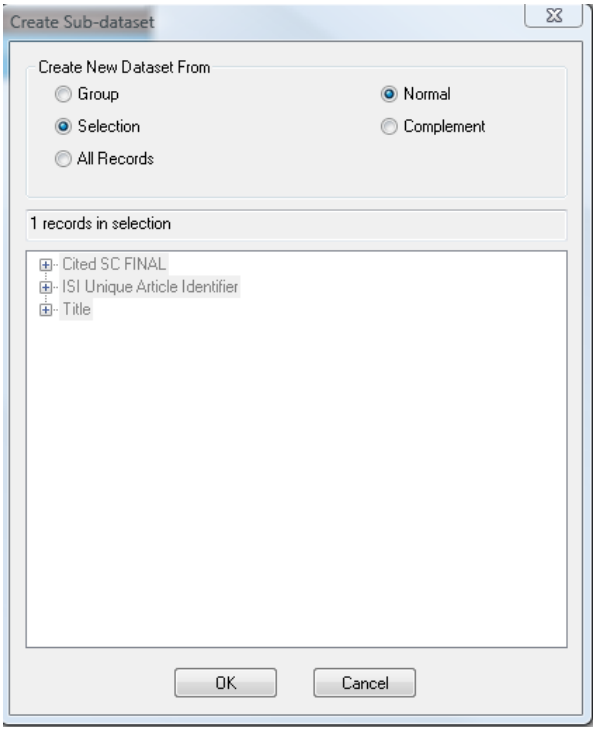


Figure H-8. Create Sub-dataset Window in VantagePoint

39. For each of the new "Before" and "After" VantagePoint files, calculate the Integration Score using the Calculate Integration v3.vpm Script (Scripts>Run Script…). When calculating the Integration Score, you will be prompted to enter:
    a. "Author": enter the "File Name" field.
    b. "Subject Category": enter the "Cited SC FINAL" field.
    c. "Cited Subject Category": also enter the "Cited SC FINAL" field.
40. The Integration Scores will show up in an excel file that is opened by the script; record this data for the "before" and "after" periods.

Data Compilation

To create the final publication data spreadsheet, the study team compiled variables from the citation report data, VantagePoint field export, SCImago Journal Rank (SJR), PubMed, and the NIH's Query/View/Report database. For each publication record, the team collected the following information for analysis: publication title, authors, publication year, journal, citations accumulated each year from 1980 to 2011, document type, WOS category, and SJR.

The team merged the researcher-level, grant-level, and "top five" publication records into a single file using a rough title match and removed duplicate records. Additional data-cleaning steps were performed. The team then checked that publication records were appropriately marked as researcher level and grant level; for instance, the author field for researcher-level publications needed to have the author's last name, and the grant-level publications needed to be published after the year of award but before 2012, and be a research article (as opposed to a review, editorial material, etc.). The team matched the correct SJRs to journal names using a combination of automated methods and by hand. Where systematic errors in the data were found for individuals or grants, all publications associated with that individual or grant were removed, and the publication data were downloaded and cleaned again. Once the data were corrected in the spreadsheet, the corresponding researcher-level and grant-level VantagePoint files were edited so that the data were consistent across all interfaces.

Appendix I
Statistical Details

Basic Model

The model is discussed in terms of impact, but the same structure was used for both impact and innovativeness. The basic structure of the model is adapted from Johnson and Albert (1999).

Assume that each packet has an underlying impact that can be measured. Let μ_i denote the impact of packet i. Further assume that the packet impacts are independent. To establish a scale for impact, assume that $\mu_i \sim \text{Normal}(0, 1)$.

Assume also that the expert has some "measurement error" (σ_k^2) when evaluating the impact of packet i. Let t_{ik} denote the perceived impact of packet i by expert k and assume that $t_{ik} \sim \text{Normal}(\mu_i, \sigma_k^2)$. Neither μ_i nor t_{ik} are observed. Instead, assume that the expert discretizes his individual impact scale, and the observation is which "bin" contains the assessed impact. For each expert, let γ_{kl} denote the bin cutoffs for expert k. Take the leftmost cutoff (l = 6) as negative infinity and the rightmost cutoff (l = 1) as positive infinity. The other bin cutoffs are assumed to be ordered. This notation is displayed in Figure I-1. The expert would assess the packet as a 2.

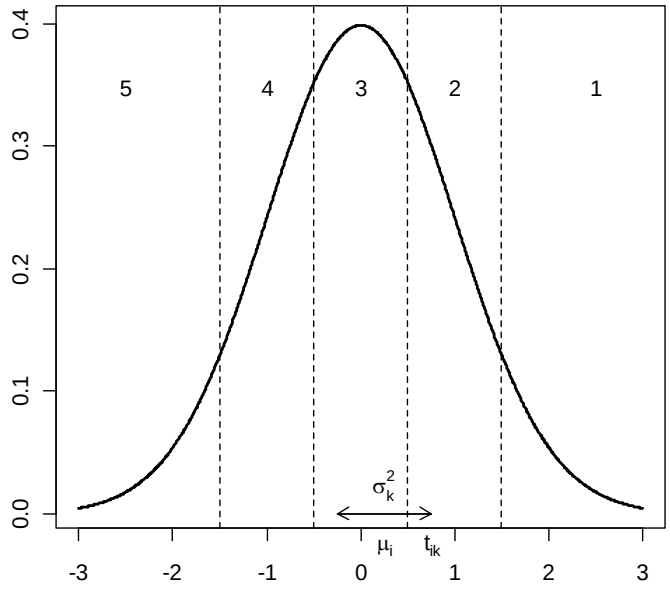


Figure I-1. Bayesian Ordinal Data Model

A similar structure is used for papers. Let z_{ij} denote the impact of paper j from packet i. Assume that paper rankings are distributed around the packet ranking, so $z_{ij} \sim \text{Normal}(\mu_i, \tau_i^2)$. Let ρ_{ijk} denote the assessed impact of paper j from packet i by expert k. Further assume that the expert k has some "measurement error" when evaluating the impact of paper j from packet i, so $\rho_{ijk} \sim \text{Normal}(z_{ij}, \omega_k^2)$.

The rating for each packet i by expert k has likelihood $\Phi(\gamma_k, \mu_i, \sigma_k^2) - \Phi(\gamma_{k-1}, \mu_i, \sigma_k^2)$, where Φ denotes the standard normal cumulative distribution function. The rating of each paper j from packet i by expert k has likelihood $\Phi(\gamma_k, z_{ij}, \omega_k^2) - \Phi(\gamma_{k-1}, z_{ij}, \omega_k^2)$.

The model was fit using a Bayesian approach, which requires prior distributions to be specified for each parameter. The γ must be ordered, but otherwise a non-informative (flat) prior distribution is used. InverseGamma(10, 3) distributions are used for the variance parameters σ_k^2, ω_k^2, and τ_i^2.

The model was also fit using standard Markov chain Monte Carlo techniques. The figures in Chapters 2 and 5 are normalized so that the estimated impact and innovation ranged between 0 and 1; the figures in this appendix are on the original Normal(0, 1) scale.

Regression Model

Covariates were added to the model to identify which variables are predictive of the underlying packet or paper impact as assessed by the experts. The response variable ("true" packet or paper impact), however, is unobserved. The model estimates impact from the expert-rating data, and the variability inherent in the estimate must be accounted for to fit the regression model. In addition, the observations are not independent: the assumption is that the packet ratings are informative about the paper ratings and vice versa. Consequently, the estimates are somewhat different from the ordinary least squares estimates.

Modify the model above by assuming that the expected value for packet impact (μ_i) is $X_i\beta$, where X_i is a vector of observed packet or investigator characteristics. In particular, consider granting mechanism (NDPA, R01, HHMI), number of pre-award citations for the PI, SCImago Institutions Ranking (SIR) for the PI at time of award, number of pre-award publications for the PI, PI h-index at time of award, years since degree, receipt of early career award, and, for the R01 awards, total direct costs. A description of these variables is found in Chapter 2, Section A.

Assume that the expected value for paper impact (z_{ij}) is $\mu_i + W_i\delta$, where W_i is a vector of observed paper characteristics. In particular, consider journal impact factor, whether the paper is a review paper, and total citations through 2011. These variables are also described in Chapter 2, Section A.

To complete the Bayesian specification, choose prior distributions for the parameters β and δ. To keep the correct marginal distribution for the μ_i, assume that

$$\beta \mid \mu, \nu \sim \text{Normal}((X^TX)^{-1}X^T\mu, \nu^2(X^TX)^{-1})$$

and

$$\nu \sim \text{InverseGamma}(0.5(\text{number of grants} - \text{number of covariates}), 0.5*(\mu - X\beta)^T(\mu - X\beta)).$$

The analysis uses a flat, non-informative prior distribution for δ.

Results

There is no expectation that the regression models will be a good surrogate for the expert ratings: it is unlikely that simply knowing the grant mechanism, characteristics of the PI, and the journal where the paper appears will fully characterize its impact or innovativeness. Table I-1 summarizes the estimated regression coefficients for impact. A normalized variable has had its mean subtracted and is divided by the standard deviation so that the covariate has mean 0 and variance 1.

Table I-1. Regression Results for Impact

Level	Metric	Estimate	90% Credible Interval	Probability $\beta < 0$
PI-Level	NDPA	0.69	(–0.21, 1.6)	0.10
	Matched R01	–1.3	(–2.6, 0.0041)	0.95
	HHMI	1.0	(0.17, 1.9)	0.024
	Pre-Award citations (normalized)	0.39	(0.039, 0.74)	0.034
	SCImago Institutions Ranking	–0.0012	(–0.0035, 0.0010)	0.82
	Pre-award publications	–0.000094	(–0.0092, 0.0091)	0.51
	H-index at award	–0.020	(–0.061, 0.022)	0.78
	Years since degree	–0.0016	(–0.046, 0.043)	0.53
	Early career award	0.20	(–0.26, 0.67)	0.24
	Direct Costs ($M)	0.88	(–0.14, 1.92)	0.078
Paper-Level	Journal impact factor (normalized)	0.44	(0.34, 0.55)	0.00
	Review paper	–0.88	(–0.21, –0.53)	1.0
	Total citations (normalized)	0.16	(0.056, 0.27)	0.0068

The linear model is:

predicted packet impact = 0.69*(Is NDPA?) – 1.3*(Is Matched R01?) + 1.0*(Is HHMI?)
+ 0.39*(normalized pre-award citations) – 0.0012*(SCImago Institutions Ranking)
– 0.000094*(pre-award publications) –0.020*(h-index at award)
– 0.0016*(years since degree) + 0.20*(early career award?)
+ 0.88(direct costs in $M)

predicted paper impact = predicted packet impact + 0.44*(normalized journal impact factor)
– 0.88*(review paper?) + 0.16*(normalized total citations through 2011)

The correlation between the expert-estimated "true" impact for packets and the regression model is 0.64. The correlation between the expert-estimated "true" impact for papers and the regression model is 0.66. See Figure I-2.

Table I-2 summarizes the estimated regression coefficients for innovation. The linear model is:

predicted packet impact = 0.95*(Is NDPA?) – 0.19*(Is Matched R01?) + 0.98*(Is HHMI?)
+ 0.42*(normalized pre-award citations) – 0.0024*(SCImago Institutions Ranking) – 0.00095*(pre-award publications) –0.018*(h-index at award)
– 0.0099*(years since degree) + 0.089*(early career award?)
+ 0.11(direct costs in $M)

predicted paper impact = predicted packet impact + 0.34*(normalized journal impact factor)
– 1.6*(review paper?) + 0.018*(normalized total citations through 2011)

The correlation between the expert-estimated "true" innovation for packets and the regression model is 0.56. The correlation between the expert-estimated "true" innovation for papers and the regression model is 0.55. See Figure I-3.

The study team conducted a preliminary analysis of an additional covariate: the number of grants cited on each publication. The team had data on 200 of the 500 "top five" papers from NDPA and the matched R01s. The analysis suggested that having additional grants cited on the paper increases both impact and innovation.

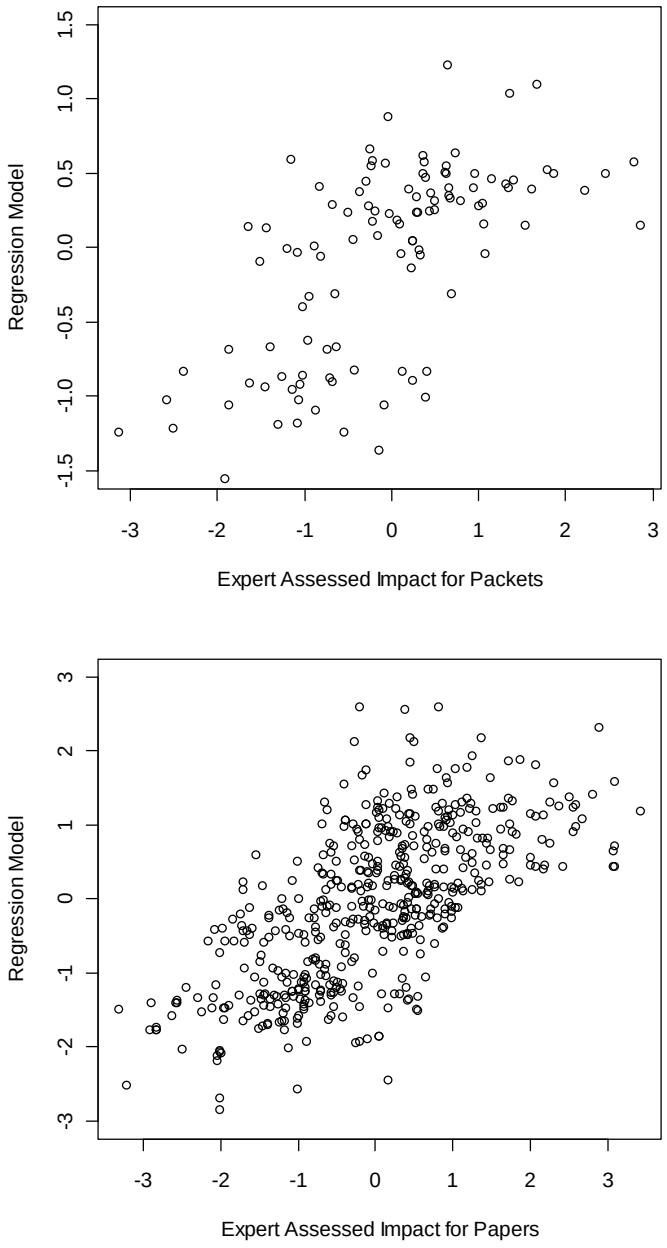
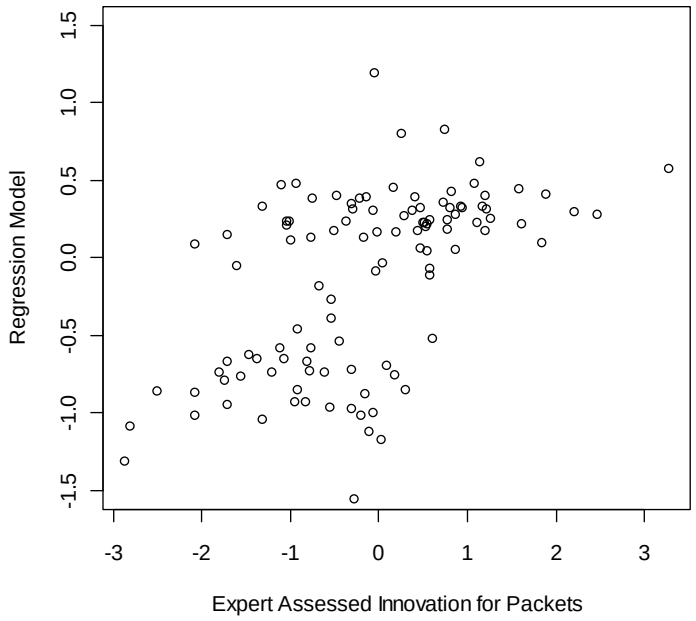


Figure I-2. Regression Models for Impact

Table I-2. Regression Results for Innovation

		Estimate	90% Credible Interval	Probability $\beta < 0$
PI-Level	**NDPA**	0.95	(0.020, 1.9)	0.047
	Matched R01	–0.19	(–1.6, 1.2)	0.59
	HHMI	0.98	(0.085, 1.9)	0.036
	Pre-Award citations (normalized)	0.42	(0.041, 0.79)	0.035
	SCImago Institutions Rank	–0.0024	(–0.0048, 0.000080)	0.94
	Pre-award publications	–0.00095	(–0.010, 0.0086)	0.57
	H-index at award	–0.018	(–0.063,.026)	0.75
	Years since degree	–0.0099	(–0.057, 0.038)	0.63
	Early career award	0.089	(–0.39, 0.57)	0.38
	Direct Costs ($M)	0.11	(–0.97, 1.2)	0.44
Paper-Level	Journal impact factor (normalized)	0.34	(0.25, 0.44)	0
	Review paper	–1.6	(–2.0, –1.2)	1.0
	Total citations (normalized)	–0.018	(–0.11,0.08)	0.61



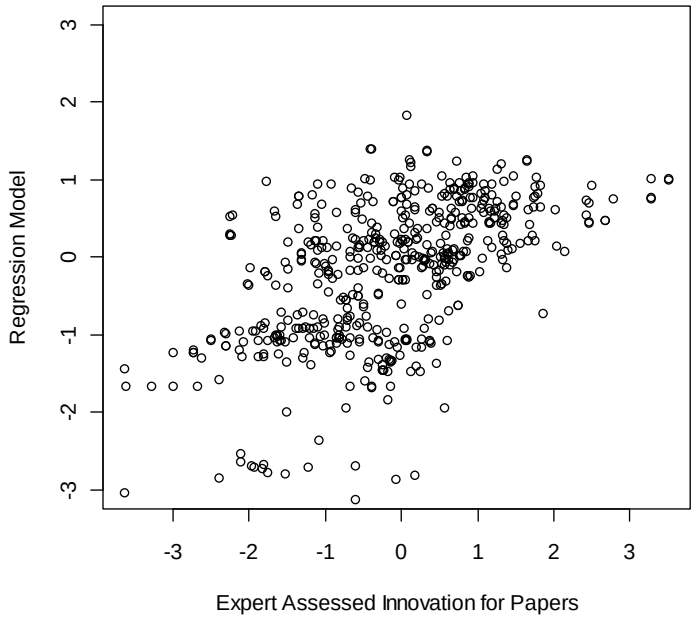


Figure I-3. Regression Models for Innovation

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Abbreviations

CAREER	Faculty Early Career Development
eSPA	electronic Scientific Portfolio Assistant
FY	fiscal year
HHMI	Howard Hughes Medical Institute
ICs	Institutes and Centers (of the NIH)
ISI	Institute for Scientific Information
JIF	Journal Impact Factor
M	million
NCI	National Cancer Institute
NCRR	National Center for Research Resources
NDPA	NIH Director's Pioneer Award
NEI	National Eye Institute
NHLBI	National Heart, Lung, and Blood Institute
NIA	National Institute on Aging
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
NIDA	National Institute of Drug Abuse
NIDCD	National Institute of Deafness and Other Communication Disorders
NIDCR	National Institute Institutes of Dental and Craniofacial Research
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIH	National Institutes of Health
NIMH	National Institute of Mental Health
NINDS	National Institute of Neurological Disorders and Stroke
NSF	National Science Foundation
NYI	NSF Young Investigator Program
PECASE	Presidential Early Career Award for Scientists and Engineers
PFF	Presidential Faculty Fellows Program
PI	Principal Investigator
PYI	Presidential Young Investigator award
QVR	Query/View/Response
SC	subject category

SIR	SCImago Institutions Ranking
SJR	SCImago Journal Rank
SPIRES	Scientific Publication Information Retrieval and Evaluation System
STPI	Science and Technology Policy Institute
WOS	Web of Science

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14. ABSTRACT

This evaluation addressed two primary study questions: To what extent does the research supported by the NDPA program produce unusually high impact, and to what extent are the research approaches used by the NDPA awards highly innovative? Using complementary methods (bibliometric analysis and expert review), the study team compared outcomes for five groups: a matched set of National Institutes of Health Research Project Grant Program (R01) grants, principal investigators on the same R01 grants, random R01 portfolios that received comparable amounts of funding to the NDPA portfolio, a group of Howard Hughes Medical Institute (HHMI) investigators, and a group of NDPA finalists. The STPI study team found that the Pioneers performed as well as or better than the matched R01 principal investigators and NDPA finalists; the Pioneer portfolio performed as well as or better than the random R01 portfolios on bibliometric measures of impact; and the HHMI investigators scored as well as or better than the Pioneers on all metrics of interest.

15. SUBJECT TERMS

transformative research, outcome evaluation, high-risk high-reward research, comparison groups, observational study, quasi-experimental design evaluation

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