Supercharging Biomedical Science at the National Institutes of Health

Andrew “Sosa” Sosanya

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Summary

For decades, the National Institutes of Health (NIH) has been the patron of groundbreaking biomedical research in the United States. NIH has paved the way for life-saving gene therapies, cancer treatments, and most recently, mRNA vaccines. More than 80% of NIH’s $42 billion budget supports extramural research, including nearly 50,000 grants disbursed to more than 300,000 researchers.

But NIH has grown incremental in its funding decisions. The result is a U.S. biomedical-research enterprise discouraged from engaging in the risk-taking and experimentation needed to foster scientific breakthroughs. To maximize returns on its massive R&D budget, NIH should consider the following actions:

- Form a “Science of Science Funding” Working Group based out of the Advisory Committee to (1) evaluate NIH’s existing funding mechanisms, and (2) pilot several (three to five) novel funding mechanisms. The Working Group should also suggest a structure for evaluating novel funding mechanisms through Randomized Control Trials (RCTs), and should recommend ways in which the NIH can expand its capacity for policy evaluation.

- By Fiscal Year 2025, aim to fund one high-risk, high-reward research proposal for every 20 R01 grants awarded by NIH—instead of the one per 100 that it awards today.

- Explicitly dedicate 5% of its extramural research funding to early-career researchers—including new faculty and postdoctoral researchers—and evaluate those researchers’ proposals separately from the larger proposal pool.

Challenge and Opportunity

Each year, federal science agencies allocate billions of dollars to launch new research initiatives and to create novel grant mechanisms. But an embarrassingly tiny amount is invested into discerning which funding policies work well. Despite having the requisite data, methods, and technology, science agencies such as NIH do not subject science-funding policies to nearly the same rigor as the funded science itself.

Another problem plaguing science funding at NIH is that it is difficult for scientists to secure funding for risky but potentially transformative work. When NIH’s peer-review process was designed more than half a century ago, over half of grant applications to the agency were funded. NIH’s proposal-success rate has dropped to 15% today. Even credible researchers must submit an ever-growing number of proposals in order to have a reasonable chance of securing funding. The result is that scientists spend almost half of their working time on average writing grants—time that could otherwise be spent conducting research and training other scientists. Our nation has created a federally funded research ecosystem that makes scientists beg, fight, and rewrite to do the work they’ve spent years training to do.
Compounding the problem is the fact that fewer and fewer early-career researchers are getting adequate support to do their work. Indeed, it takes fewer years to become an experienced surgeon than it does to launch a biomedical research career and obtain a first R01 grant from NIH (the average age of R01 grantees in 2020 was 44 years). When we place hurdles in front of young scientists, we lose out on empowering them at a particularly innovative career stage. Limited access to funding early on hampstrings the ability of early-career scientists to set up labs, tackle interesting ideas, and train the next generation. And the early careers of young scientists are often judged by their publishing records, which has the pernicious effect of guiding young scientists to propose safe research that will easily pass peer review.

A scientific ecosystem that incentivizes incrementalism instead of impact discourages scientists from bringing their best, most creative ideas to the table—an effect multiplied for women and underrepresented minorities. The risky research underpinning mRNA vaccines would struggle to be funded under today's peer-review system. To catalyze groundbreaking biomedical research—and lead the way for other federal science-funding agencies to follow suit—NIH should reconsider how it funds research, what it funds, and who it funds. The Plan of Action presented below includes recommendations aligned with each of these policy questions.

Plan of Action

**Recommendation 1. Diversify and assess NIH's grant-funding mechanisms.**

In 2020, privately funded COVID “Fast Grants” accelerated pandemic science by allocating over $50 million in grants awarded within 48 hours of proposal receipt. In a world where grant proposals typically take months to prepare and months more to receive a decision, Fast Grants offered a welcome departure from the norm. The success of Fast Grants signals that federal research funders like the NIH can and must adopt faster, more flexible approaches to scientific grantmaking—an approach that improves productivity and impact by getting scientists the resources they need when they need them.

While Fast Grants have received a great deal of attention for their novelty and usefulness during a crisis, it’s unclear whether the wealth of experimental funding approaches that the NIH has tried—such as its R21 grant for developmental research, or its K99 grant for on-ramping postdoctoral researchers to traditional R01 grant funding—have positively impacted scientific productivity. Indeed, NIH has never rigorously assessed the efficacy of these approaches. NIH must institute mechanisms for evaluating the success of funding experiments to understand how to optimize its resources and stretch R&D dollars as far as possible.


2 Other factors that can impede weigh against young scientists—such as the increase in longer training periods and the increasingly arduous, resource-scare path into faculty positions. See A Generation at Risk: Young Investigators and the Future of the Biomedical Workforce by Ronald J. Daniels.
As such, **the NIH Director should establish a “Science of Science Funding” Working Group within the NIH’s Advisory Committee to the Director.** The Working Group should be tasked with (1) evaluating the efficacy of existing funding mechanisms at the NIH and, (2) piloting three to five experimental funding mechanisms. The Working Group should also suggest a structure for evaluating existing and novel funding mechanisms through Randomized Control Trials (RCTs), and should recommend ways in which the NIH can expand its capacity for policy evaluation (see FAQ for more on RCTs).

**Novel funding mechanisms that the Working Group could consider include:**

- Establishing a “fast-grant” funding track that awards select grants to scientists within weeks, not months, of proposal submission.
- Funding grant lotteries that select a small percentage of pre-screened and well-qualified grant applications at random for funding.
- Creating a public-private “marketplace of funders” (comprising non-NIH grantmakers such as the Howard Hughes Medical Institute or the Gates Foundation) to which researchers can opt into having their grant proposal automatically submitted if not funded by the NIH.
- Awarding large (on the order of $5–15 million) project grants designed to support focused research organizations in developing a fundamental tool, platform technology, scientific dataset, or a refined process or resource that would dramatically accelerate progress in the biomedical field.
- Eliminating grant deadlines. In the last five years, the National Science Foundation (NSF) removed proposal deadlines from several of its directorates. NSF concluded that the policy change gave investigators more time to build strong collaborations and to think more creatively without the pressure and burden of a deadline, leading to an improved quantity of high-quality proposals. NIH should consider doing the same.
- Leveraging artificial intelligence to help identify high-impact research and guide funding decisions. While computers should not make funding decisions alone, data-driven algorithms can help grantmakers identify promising proposals and can help policymakers determine how to structure and where to focus calls for funding.

This Working Group should be chaired by the incoming Director of Extramural Research and should include other NIH leaders (such as the Director of the Office of Strategic Coordination and the Director of the Office of Research Reporting and Analysis) as participants. The Working Group should also include members from other federal science agencies such as NSF and NASA. The Working Group should include and/or consult with diverse faculty at all career stages as well. Buy-in from the NIH Director will be crucial for this group to enact transformative change.
Lastly, the working group should seek to open up NIH up to outside evaluation by the public. Full access to grantmaking data and the corresponding outcomes could unlock transformative insights that holistically uplift the biomedical community. While NIH has a better track record of data sharing than some other science-funding agencies, there is still a long way to go. One key step is putting data on grant applicants in an open-access database (with privacy-preserving properties) so that it can be analyzed and merged with other relevant datasets, informing decision-making. Opening up data on grant applicants and their outcomes also supports external evaluation—paving the way for other groups to augment NIH evaluations conducted internally, as well as helping keep the NIH accountable for its programmatic outcomes.

**Recommendation 2. Foster a culture of scientific risk-taking by funding more high-risk, high-reward grants.**

Uncertainty is a hallmark of breakthrough scientific discovery. The research that led to rapid development of mRNA COVID vaccines, for instance, would have struggled to get funded through traditional funding channels. NIH has taken some admirable steps to encourage risk-taking. Since 2004, NIH has rolled out a set of High-Risk, High-Reward (HRHR) grant-funding mechanisms (Table 1). The agency’s evaluations have found that its HRHR grants have led to increased scientific productivity relative to other grant types. Yet HRHR grants account for a vanishingly small percentage of NIH’s extramural R&D funding. Only 85 HRHR grants were awarded in all of 2020, compared to 7,767 standard R01 grants awarded in the same year. Such disproportionate allocation of funds to safe and incremental research largely yields safe and incremental results. Additionally, it should be noted that designating specific programs “high-risk, high-reward” does not necessarily guarantee that those programs are funding high-risk, high-reward research in reality.

### Table 1: NIH’s High-Risk, High Reward Grant Mechanisms and its flagship R01 grant.

<table>
<thead>
<tr>
<th>Award</th>
<th>Purpose</th>
<th>Funding Amount</th>
<th># Awarded in 2020</th>
</tr>
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<tbody>
<tr>
<td>New Innovator Award</td>
<td>For exceptionally creative early-career scientists proposing innovative, high-impact projects.</td>
<td>$1.5M/5 yrs</td>
<td>53</td>
</tr>
<tr>
<td>Pioneer Award</td>
<td>For individuals of exceptional creativity proposing pioneering approaches, at all career stages</td>
<td>$3.5M/5 yrs</td>
<td>10</td>
</tr>
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3 R01 grants are awarded to mature research projects that are hypothesis-driven and have generated strong preliminary data. R01s provide up to five years of support per project.
Transformative Research Award  | For individuals or teams proposing transformative research that may require very large budgets | No cap | 9
---|---|---|---
Early Independence Award  | For outstanding junior scientists wishing to “skip the postdoc” and immediately begin independent research | $250K/yr | 12
R01 Investigator (NIH’s flagship Grant)  | For mature research projects that are hypothesis-driven with strong preliminary data | $250K/yr | 7,767

It is time for the NIH to actively foster a culture of scientific risk-taking. The agency can do this by balancing funding relatively predictable projects with projects that are riskier but have the potential to deliver greater returns.

Specifically, NIH should:

- **Strive to shift its HRHR to R01 ratio from 1:100 to 1:20 by FY 2025.** Like an investor who mixes reliable blue-chips with riskier growth stocks, NIH should take a portfolio-based approach to balancing lower- and higher-risk research. One HRHR domain that NIH could focus on is increasing investments in developing platform technologies, such as advanced equipment, data-analysis tools, and specialized analysis techniques that support biomedical advances broadly (See FAQ for more on platform technologies). Multiple NIH-funded Nobel Prize winners have won the award for platform technologies (including CRISPR-Cas9, cryo-electron microscopy, and phage display) that have fundamentally shifted the way scientists approach problem solving. Without investing deeply in platform technologies, our nation risks continuing its piecemeal approach to solving pressing challenges.

- **Experiment with a new exploratory HRHR grant.** This grant could combine the best features of the MERIT (R37) and Pioneer Award mechanisms, using a set of evaluation criteria that emphasize risk-taking rather than robust preliminary results. The grant would include a time horizon of 8–10 years, with an intermediary review after five years. The grant would also include a renewal mechanism that incentivizes awardees to conduct revolutionary work in their fields, and would be subject to rigorous evaluation. This type of grant would take on a more exploratory and curiosity-driven flavor than the solutions-oriented research—research directed at solving a practical problem—that would be funded under the forthcoming Advanced Research Projects Agency-Health.

- **Revisit high-variance proposal evaluations and explore a “golden ticket” model of proposal evaluation.** NIH’s peer-review process for grant proposals typically averages evaluation scores—a choice that drives award decisions towards
consensus but creates bias against riskier proposals. Riskier proposals are more likely to garner negative reviews because “they don’t fit neatly within established scientific paradigms” that the peer-review process favors. One way to identify and capture HRHR research through traditional funding channels is to identify grants that have high variance in evaluator scores—an indicator of healthy disagreement. Another option is for NIH to experiment with a “golden-ticket” model wherein a proposal can be greenlighted under peer review if a single reviewer strongly advocates for it. To avoid abuse, golden tickets should be allocated in limited numbers among reviewers, commensurate with the funding payline for a study section. The selection process for NIH’s Transformative Research Award serves as a precedent for this model, which NIH policymakers can build upon and should be pilot in other grant programs.

- **Pilot post-award project management for 100 funded high-risk research proposals.** Post-award program management (PPM) is a practice wherein funders are involved choosing collaborators, determining intermediate milestones, and conducting ongoing monitoring. If a project is not meeting milestones, the funders may choose to terminate it early. When combined with high upfront risk tolerance, PPM can ensure that public research dollars are being well spent. PPM also allows funders to shape scientists’ research trajectories by choosing whether and how to conduct reviews for grant renewal, and the extent to which to reward risk-taking as part of intermediate evaluations.

**Recommendation 3. Better support early-career scientists.**

NIH can supercharge the biomedical R&D ecosystem by better embracing newer investigators bringing bold, fresh approaches to science. In recent years, NIH allocated seven times more R01 funding to scientists who are older than 65 years old than it did to scientists under 35. The average age of R01 grantees in 2020 was 44 years. In other words, it takes fewer years to become an experienced surgeon than it does to launch a biomedical research career and obtain a first R01 grant. This paradigm leaves promising early-career researchers scrambling for alternative funding sources, or causes them to change careers entirely. Postdoctoral researchers in particular struggle to have their ideas funded.

NIH has attempted to alleviate funding disparities through some grants—R00, R03, K76, K99, etc.—targeted at younger scientists. However, these grants do not provide a clear onramp to NIH’s “bread and butter” R01 grants.

**NIH should better support early-career researchers by:**

- **Explicitly dedicating 5% of its extramural research funding to young researchers**, including new faculty and postdoctoral researchers. Evaluation of grant proposals from these researchers should be separated from the larger application pool. By providing a dedicated funding pathway for early-career scientists, NIH will ensure a healthy pipeline of talent and ideas. While the success of funding earmarked for specific groups can’t be rigorously evaluated
through an RCT, NIH should still create a set of metrics to evaluate whether dedicated funding is working as intended to boost retention and creativity in the federally funded biomedical ecosystem.

- **Expand funding for young researchers from underrepresented backgrounds.** For instance, NIH could create a “Scientists of the Future” grant program that provides support for promising underrepresented scientists at the postdoctoral level. The Hanna H. Gray Fellows Program at the Howard Hughes Medical Institute could act as a model for such a program.

- **Experiment with non-traditional metrics in peer-review processes.** One reason that older scientists tend to receive more grants is that the peer-review process places emphasis on previous citations (or a derivative thereof, such as the h-index) as a predictor of success. This hurts the chances for younger investigators, who have had less time to publish. NIH should therefore instruct peer-review panels to also consider other indicators of merit, such as:

  - Whether an applicant has developed a key dataset or tool that dramatically advances their field.
  
  - Whether an applicant holds patents for inventions and/or has substantially commercialized prior research.
  
  - The broader impacts of the proposed work. For instance, the NIH could follow the NSF in incorporating a Broader Impacts criterion into its grant-review processes.

  - **Make funded principal investigators (PIs) accountable for training outcomes.** Improving training outcomes is holistically beneficial for the U.S. research ecosystem, but there is little data on the availability of training and mentorship opportunities, or on how effective the opportunities that do exist are. Moreover, PIs have few incentives to invest in training and mentorship. NIH currently has a set of institutional training grant programs that are subject to evaluations, but they are few and far between and not nearly comprehensive enough to meaningfully help the thousands of NIH-funded scientists in training. NIH can act to remedy these problems by embedding training and mentorship into the evaluation criteria for the agency’s flagship R01 grants.

**Conclusion**

NIH funding forms the backbone of the American biomedical research enterprise. But if the NIH does not diversify its approach to research funding, progress in the field will stagnate. Any renewed commitment to biomedical innovation demands that NIH reconsider how it funds research, what it funds, and who it funds—and to rigorously evaluate its funding processes as well.
The federal government spent about $160 billion on scientific R&D in 2021. It is shocking that it doesn’t routinely seek to optimize how those dollars are spent. While this memo focuses on the NIH, the analysis and recommendations contained herein are broadly applicable to other federal agencies with large extramural R&D funding operations, including the National Science Foundation; the Departments of Defense, Agriculture, NASA, Commerce; and others. Increasing funding for science is a necessary but not sufficient part of catalyzing scientific progress. The other side of the coin is ensuring that research dollars are being spent effectively and optimizing return on investment.

**Frequently Asked Questions**

1. **Are Randomized Controlled Trials (RCTs) the only way for the NIH to effectively evaluate funding mechanisms?**

To really understand what works and what doesn’t, NIH must consider how to evaluate the success of existing and novel funding mechanisms. MIT economist Pierre Azoulay suggests that the NIH can systematically build out a knowledge base of what funding mechanisms are effective by “turning the scientific method on itself” using RCTs, the “gold standard” of evaluation methods. NIH could likely launch a suite of RCTs that would evaluate multiple funding mechanisms at scale with minimal disruption for around $250,000 per year for five years—a small investment relative to the value of knowing what types of funding work.

RCTs can be easier to implement than is often thought. That said, NIH would be wise to couple RCTs with less ambitious mechanisms for evaluating funding mechanisms, such as a two-step approach that filters out clearly sub-par applicants and then applies narrower criteria based on the remaining pool to filter a second time for the most competitive or prioritized applicants. Even just collecting and comparing data on NIH grant applicants—data such as education level, career stage, and prior funding history—would provide insight into whether different funding interventions are affecting the composition of the applicant pool.

2. **How would the proposed “Science of Science Funding” Working Group differ from the ACD Working Group on High-Risk, High-Reward Programs?**

The ACD Working Group on HRHR programs reviewed “the effectiveness of distinct NIH HRHR research programs that emphasize exceptional innovation.” This working group only focused on evaluating a couple of HRHR programs, which form a trivial portion of grantmaking compared to the rest of the extramural NIH funding apparatus. The Science of Science Funding Working Group would (i) build NIH’s capacity to evaluate the efficacy of different funding mechanisms, and (ii) oversee implementation of several (three to five) experimental funding mechanisms or substantial modifications to existing mechanisms.

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4 For more on this topic, see *Why Government Needs More Randomized Controlled Trials: Refuting the Myths* from the Arnold Foundation.
3. How would the “Science of Science Funding” Working Group differ from the Science of Science Policy Approach to Analyzing and Innovating the Biomedical Research Enterprise (SCISIPBIO) Active Awards, jointly hosted by the NSF and the NIH?

SCISIPBIO isn’t focused on systematic change in the biomedical innovation ecosystem. Instead, it is a curiosity-driven grant program for individual PIs to conduct “science of science policy” research. NIH can build on SCISIPBIO to advance rigorous evaluation of science funding internally and agency-wide.

4. Isn’t the NIH one of the government’s premier research institutions? Is it really doing such a bad job funding research?

NIH funding certainly supports an extensive body of high-quality, high-impact work. But just because something is performing acceptably doesn’t mean that there are not still improvements to be made. As outlined in this memo, there is good reason to believe that static funding practices are preventing the NIH from maximizing returns on its investments in biomedical research. NIH is the nation’s crown jewel of biomedical research. We should seek to polish it to its fullest shine.

5. What are platform technologies?

Platform technologies are tools, techniques, and instruments that are applicable to many areas of research, enabling novel approaches for scientific investigation that were not previously possible. Platform technologies often generate orders-of-magnitude improvements over current abilities in fundamental aspects such as accuracy, precision, resolution, throughput, flexibility, breadth of application, costs of construction or operation, or user-friendliness. The following are examples of platform technologies:

- Polymerase chain reaction (PCR)
- CRISPR-Cas9
- Cryo-electron microscopy
- Phage display
- Charge-coupled device (CCD) sensor
- Fourier transforms
- AFM/SFM (atomic force microscopy/scanning force microscopy)

There has been an appetite to fund more platform technologies. The recently announced ARPA-H seeks to achieve medical breakthroughs and directly impact clinical care by building new platform technologies. During the Obama Administration, the White House Office of Science and Technology Policy (OSTP)
hosted a platform technologies ideation contest. Although multiple NIH-funded Nobel Prize winners have won the award for platform technologies that have fundamentally shifted the way scientists approach problem solving, not enough emphasis is placed on development of such technologies. Without investing deeply in platform technologies, our nation risks continuing its piecemeal approach to solving pressing challenges.
About the Author

Andrew “Sosa” Sosanya is a technologist who is passionate about exploring the impacts of technology and innovation on our society. Currently, he works a machine-learning engineer and founder of the nonprofit “Builders of Tomorrow”, a community of technologists focused on building public goods. Previously, he worked as a Policy Analyst for the Day One Project, where he built a platform for science and tech policy ideas. At the Day One Project, Sosa helped develop ambitious and actionable policy ideas on issues such as reforming the $700B+ defense budget, electrifying the aviation ecosystem, and training diverse scientists.

Prior to the Day One Project, Sosa worked as an avid researcher, studying topics in physics, artificial intelligence, and national security. In 2020, his senior thesis on the rise of autonomous weapons and militarized AI won Dartmouth’s Chase Peace Prize and was subsequently published in the Peace Review Journal of Social Justice. In 2018, Sosa was an Astrophysics Fellow in Caltech’s NASA NuStar Group, researching ultra-bright neutron stars. Sosa graduated from Dartmouth College in 2020 with an honors B.A. in Physics & Government modified with Computer Science. Sosa is active on Twitter at @sosanyo.

About the Day One Project

The Federation of American Scientists’ Day One Project is dedicated to democratizing the policymaking process by working with new and expert voices across the science and technology community, helping to develop actionable policies that can improve the lives of all Americans. For more about the Day One Project, visit dayoneproject.org.