


A Vision and Pathway for NIH

Recommendations for
the New Administration

NOVEMBER 2016





A Vision and Pathway for NIH

Recommendations for
the New Administration

REPORT BRIEF

To the Transition Team:

We are pleased to present *A Vision and Pathway for NIH*, offering recommendations for your administration that would further advance the National Institutes of Health, the world's leading biomedical research and health agency. The goal of this report is to better align NIH organization and policies with present and future strategies to achieve the greatest impact in research and training, improve health, and combat disease.

The report was created by an *ad hoc* working group whose members understand the opportunities and challenges presented by today's dynamic research and health enterprise—an enterprise that has produced remarkable advances. The group's members also have management experience, some within NIH itself, and appreciate the ways that large bureaucracies can both enable and inhibit progress.

Achieving the vision and pathway envisioned here will require the appointment of a wise and bold Director who respects NIH's foundation of excellence while leading the agency toward changes in particular policies and longstanding practices that extend across the spectrum of NIH activity. In this report, we describe a pathway to identifying such a leader. While the group did not attempt to raise every relevant matter, we believe that attending to the examples raised here would have broad positive impact.

Acknowledging present realities, the recommendations herein are feasible and actionable without substantial new costs; indeed, they might reduce costs, while enriching public benefit and addressing national priorities.

Working Group Members

Keith R. Yamamoto, PhD (Chair)

Vice Chancellor for Science Policy and Strategy, University of California, San Francisco (UCSF); Director, Precision Medicine, UCSF; Vice Dean for Research, UCSF School of Medicine; Professor, Cellular and Molecular Pharmacology, UCSF; National Academy of Sciences; National Academy of Medicine

Bonnie L. Bassler, PhD

Howard Hughes Medical Institute Investigator; Squibb Professor in Molecular Biology; Princeton University; National Academy of Sciences; National Academy of Medicine

Tom Cech, PhD

Distinguished Professor of Chemistry and Biochemistry, University of Colorado Boulder; Former President of the Howard Hughes Medical Institute; National Academy of Sciences; National Academy of Medicine; National Medal of Science; Nobel Laureate, Chemistry 1989

R. Alta Charo, JD

Warren P. Knowles Professor of Law and Bioethics; University of Wisconsin Law School; National Academy of Medicine

Mark Fishman, MD

Professor, Harvard Department of Stem Cell and Regenerative Biology; Former President, Novartis Institutes for BioMedical Research; National Academy of Medicine

H. Robert Horvitz, PhD

David H. Koch Professor of Biology; Massachusetts Institute of Technology (MIT); National Academy of Sciences; National Academy of Medicine; Nobel Laureate, Physiology or Medicine 2002

Steven Hyman, MD

Director of the Stanley Center for Psychiatric Research at Broad Institute, MIT and Harvard; Former Director of the National Institute of Mental Health; National Academy of Medicine

Story Landis, PhD

Former Director of the National Institute of Neurological Disorders and Stroke (NINDS); National Academy of Medicine

Philippa Marrack, PhD

Senior Faculty Member in the Integrated Department of Immunology at National Jewish Health; Professor of Biochemistry and Molecular Biology, Immunology, and Medicine, University of Colorado Health Sciences Center, Denver; National Academy of Sciences

Shirley Tilghman, PhD

President Emerita/Professor of Molecular Biology, Princeton University; National Academy of Sciences; National Academy of Medicine

Harold E. Varmus, MD

Lewis Thomas University Professor of Medicine, Weill Cornell Medicine; Former Director of the NIH; Former Director of the National Cancer Institute; National Academy of Sciences; National Academy of Medicine; National Medal of Science; Nobel Laureate, Physiology or Medicine 1989

Elias Zerhouni, MD

President, Global R&D, Sanofi; Former Director of the NIH; National Academy of Engineering; National Academy of Medicine

Affiliate Advisors**Margaret Anderson**

Executive Director, FasterCures

India Hook-Barnard, PhD

Director of Research Strategy; Associate Director, Precision Medicine, University of California, San Francisco

Lynn Marquis

Director, Coalition for the Life Sciences

Michael Stebbins, PhD

Vice President of Science and Technology, the Laura and John Arnold Foundation

Mary Woolley

President, Research!America; National Academy of Medicine

The Laura and John Arnold Foundation (LJAF) provided funding for this report. The analysis and recommendations are the authors' alone and do not necessarily represent the views of LJAF.



TABLE OF CONTENTS

Preface and Committee Roster	iii
Executive Summary	1
1. Research: Driving Innovation and Discovery	6
Visions	
Recommended Pathways	
2. Training: Preparing the Next Generation	12
Visions	
Recommended Pathways	
3. Administration and Operations: Maximizing Opportunity	16
Visions	
Recommended Pathways	
4. Appointment of the NIH Director	22
Recommended Pathways	
Characteristics of Candidates	
Queries for Candidates	
Acknowledgments	26
About the Laura and John Arnold Foundation, the Coalition for the Life Sciences, FasterCures, and Research!America	

EXECUTIVE SUMMARY

A Vision and Pathway for NIH

The National Institutes of Health (NIH) is charged with providing leadership and support for innovative research that reveals mechanisms and modulators of biological processes, applying that knowledge to improve prevention, diagnosis, treatment and cure of human diseases, and enhancing the nation's health and economic well-being.

To accomplish these grand goals, NIH disperses its funds to support research, researchers, research facilities and trainees in some 2,500 universities, medical schools, research institutes, companies and nonprofits, and indirectly to a myriad of suppliers and service agencies, spread across virtually every congressional district. The impact of NIH's work has made the U.S. pre-eminent in biomedical and health research for seven decades, and the NIH has repeatedly been characterized in the Congressional Record and in public discourse as "the crown jewel of the federal government." Fundamental discoveries are the lifeblood of the NIH, and, not infrequently, are serendipitous observations rendered significant by brilliant researchers. These discoveries are creating remarkable opportunities to attack even complex disorders, including cancer and neurological diseases, at their mechanistic root; enabling researchers to find cures rather than merely ameliorate symptoms. Powerful technologies, such as genome editing and cryo-electron microscopy, continue to open new wide avenues of discovery and improvement of health. Thus, despite enduring an extended funding stasis, the biomedical research and health community are poised to make striking new progress.

With health, healthcare costs, and infectious threats all major concerns for Americans, the new Administration would be wise to demonstrate that further strengthening NIH is one of its priorities. To help inform the Administration, an *ad hoc* working group of scientists and policy experts presents a vision for research, health, and

The first 100 days

Among this report's primary recommendations, several represent visible opportunities for the Administration, in its first 100 days, to drive progress and build upon NIH's successes through progressive transformative policymaking.

1. Appoint NIH Director who will identify and act upon goals and approaches such as those set forth here.
2. Convene a Strength in Science Task Force, composed of stakeholders from government, industry, academia, philanthropy, and the public/patient community, and charged with identifying actions that ensure continued U.S. pre-eminence in scientific research and innovation.
3. Provide sustainability and enable bold strategies, invite NIH to prepare and submit to Congress a rolling five-year professional judgment budget.
4. Encourage joint-institute and trans-NIH research, increase the Common Fund to 5% of the NIH research allocation and specify that most of the funds support such integrated investigations.

healthcare made possible by past and current NIH-supported discoveries, as well as pathway to achieving that vision. Both the vision and pathway compel certain changes in policies and practices across three components of NIH activity: its research enterprise, its training mandate, and its overall administration and operations. It is the anticipation of the committee that these actionable changes would reduce overall costs while addressing national priorities. To this end, the committee has outlined the three following categories as a vision for what change at the NIH should look like to optimize our research potential: Research, Training, and Administration and Operations.

Research

- Recommit NIH to funding fundamental discovery.
 - Ensure that at least 55-60% of NIH's research portfolio supports fundamental discovery
 - Develop a mechanism to ensure that earmarked and targeted funding programs encourage and support research at the highest level of excellence
 - Charge a task force with setting priorities among fundamental, translational, clinical and social/behavioral/population research

- Revise the grant application review process to reward bold ideas, creative risks and innovative approaches.
 - Engage highly respected generalists in each area for study section membership
 - Obtain external technical advice as needed without requiring *ad hoc* study section members
 - Reconfigure study section topics, focusing on biological processes and new technologies
- Provide stable and predictable funding to enable scientists to pursue transformative research.
 - Prepare and negotiate rolling five-year professional judgment budgets
 - Develop funding mechanisms that support common research goals for multiple institutes
 - Develop NIH-wide, 7-10 year, investigator-focused grant mechanism for top researchers

Training

- Transform the training of scientists and physician researchers to prepare them for 21st century science.
 - Promote development of transdisciplinary, quantitative, team-based active learning curricula
 - Periodically convene leaders of these curricula to share best practices and to rigorously evaluate the programs
- Support a much greater proportion of trainees under individual fellowships and training grants.
 - Have a task force plan a shift in support toward training grants and fellowships
 - Begin shift in Year 2, likely with institution-specific time course; include support for non-citizen trainees in training grants and fellowships
- Ensure that the NIH-trained workforce is fluent in the public context of science.
 - Develop programs to educate trainees in the public context of science

- Require all students at institutions holding training grants to complete training in the public context of science

Administration and Operations

- Free scientists to focus on advancing science by streamlining the rules for research protections and the processes for grant applications.
 - Reduce regulatory and administrative burdens
 - Harmonize common grant mechanisms across NIH; periodically adjust fixed-budget mechanisms for inflation
 - Develop NIH-wide mechanisms to consolidate multiple grants and to provide long-term support for most-accomplished researchers
- Transform NIH organization and operations to align with, inspire and better enable the best science.
 - Expand inter-institute collaborative programs and restructure CSR study sections
 - Consider changing Institute and Center (IC) organizational structure
- Achieve the full potential of the Intramural Research Program and Clinical Center.
 - Ease federal bureaucratic restrictions; create NIH special pay statute
 - Consider transforming IRP into an incubator for early stage investigators
 - Address financial and organizational issues in the Clinical Center

Appointment of the NIH Director

In practice, it will be the NIH Director and his/her deputies and close advisors who must weigh and implement these recommendations. However, it is important that the new Administration understand opportunities to advance research and health, and recognize that achieving these advances requires revising current NIH policies and practices.

- **Characteristics and queries**

The working group suggests that the Administration assess the views of its NIH Director candidates on the matters and issues that are the basis of the recommendations presented here. The working group recommends that the new Administration promptly undertake a systematic search for a highly qualified director, and describes here the characteristics that define his/her qualifications, and offers a list of topics and questions that might be used to inform a search committee.

Opportunity for the New Administration

With this vision and pathway, the Administration can seize an opportunity to shape NIH, this crown jewel of the federal government, in ways that will maintain U.S. scientific pre-eminence, while making NIH more effective and efficient in improving the health and well-being of Americans.

1. RESEARCH: DRIVING INNOVATION AND DISCOVERY

Vision 1.1. Recommit NIH to its imperative to foster and fund fundamental discovery.

Most new medicines and advances in health stem from fundamental understandings of biology. The paths from biological discovery to novel drug or diagnostic, to preventive therapy or behavioral guidelines, are not direct, and typically take decades to be realized. This is evidenced, for example, by the timeline that connects understanding the genes that drive development of the fruit fly to their practical embodiment as some of the most prominent targets for cancer drugs. Distinct scientific communities blaze the jagged trail from idea to new therapies; untargeted, paradigm-shifting discoveries (so-called “basic research”), and disease connections are most commonly realized by scientists in academia or other non-profit research institutions, while conversion of those findings into products is typically performed by scientists in the business sector. U.S. biotechnology has led the world in productivity and economic impact, capitalizing on the proximity of scientists and science entrepreneurs who forge links between curious discoveries and management or prevention of disease.

In recent decades, this separation of research loci has sharpened, with fundamental discoveries occurring in the publically funded academic sector, while development and application are pursued in the private sector. Global markets, competition, and stockholder impatience increasingly mandate that industry focus its resources narrowly. However,

*Industry cannot support a robust discovery endeavor, public funds from the federal government **must** support it; there is no Plan B!*

not only applied research, but continued progress in understanding, preventing, treating and curing disease, depends on a continuous influx of fundamental discoveries. Because industry *cannot* support a robust discovery endeavor, public funds from the federal government *must* support it; there is no Plan B! Hence, it is a concern that NIH appears to be leaning more toward application, and shifting away from its historical Office of Management and Budget guidance that it fund basic research as >55% of its portfolio, and even further from the 60:25:15 distribution for basic:translational:clinical research established in 2003 by NIH Director Elias Zerhouni.

Another trend, earmarked or targeted funding, also threatens NIH's ability to achieve its imperative to support basic research. Clearly, well-conceived, broadly scoped "Grand Challenge"-type goals, such as sequencing the human genome and achieving precision medicine, can expand fields, invite fundamental discovery, inspire transformative technologies, and advance knowledge. However, narrow legislative earmarks, and an increase in narrowly scoped targeted projects conceived, reviewed, and funded by individual NIH institutes, can erode funding for unscripted basic research that delivers breakthroughs essential for the health of the nation.

Although the 60:25:15 standard is a useful benchmark, there have been no attempts to define an optimal distribution of resources to basic, translational and clinical research, or to include a distinct social/behavioral/population research sector. A systematic analysis to define such an optimum and assess its dynamics may inform policy and facilitate progress.

Recommended Pathways

1.1.1 The NIH Director should re-emphasize an imperative for public funding of fundamental science, and ensure that the NIH research portfolio prioritizes funding of such research, consistent with its historical 55-60% standard.

1.1.2 The NIH Director should ensure that proposals for targeted projects are developed in consultation with, and rigorously evaluated by, *ad hoc* working groups of scientists expert in the field. The Director should put in place mechanisms to evaluate the impact of earmarked funds on the NIH portfolio and on the health of the nation.

1.1.3 The Administration should create a Strength in Science Task Force, composed of stakeholders from government, academia, industry, NGOs, philanthropy, and the patient/public community, to define an optimal distribution of support for different types of NIH research, and consider other high-level matters that seek to ensure continued U.S. pre-eminence in scientific research and innovation.

Vision 1.2. Revise the grant application review process to better reward bold ideas, creative risks and innovative approaches.

Merit review by peer researchers is deservedly regarded as the best approach for allocation of research funds; the outcomes of its judgments have been outstanding. Nevertheless, NIH peer review is challenged in three areas.

First, peer review is inherently conservative, favoring proposals that support prevailing paradigms, focus on hypotheses that extend those paradigms, and seem most likely to yield anticipated results. Acknowledging these properties, peer review should be bolstered by mechanisms that identify and promote proposals of two distinct types: those that advance, in bold leaps rather than incremental steps, the boundaries of knowledge and understanding of biological processes, and approaches to combatting disease; and those that lack explicit hypotheses, and instead invent transformative technologies to enable detection, analysis, or determination at new breadth or depth. Peer review must recognize, and not penalize, the inherent risk of these two types of projects, embracing the higher chance of failure embodied in bold goals. In recent years, as grant proposal success rates have fallen, peer review has become increasingly risk-averse, promoting projects with high feasibility but incremental impact, and withholding support for creation of new technologies not grounded in traditional hypotheses.

Second, the growing transdisciplinarity of biomedical research complicates the logistics of NIH peer review. Addressing a problem with multiple experimental approaches and methodologies increases the potential for significant outcomes, but makes it hard to ensure all the needed technical expertise is present for a given study section meeting. Currently, NIH invites relevant technical experts as one-time study section members. Unfortunately, this practice is problematic:

e.g., government policy requires that the *ad hoc* invitees score every application to be considered by the study section, not just those for which their technical advice was requested, even though they are unlikely to be familiar with the area of study; in addition, development of a coherent peer review culture among the chartered members is disrupted by the *ad hoc* members, disincentivizing participation in the peer review process by the best scientists.

Finally, many study sections on the current NIH Center for Scientific Review (CSR) roster focus on particular disorders or organs rather than the underlying biological processes and mechanisms, despite frequent revelations that defects in a given biological process serve as the basis for multiple apparently unrelated disorders, and therapies effective for one indication may ameliorate symptoms of another disease for which there is no known treatment. Identification of these mechanistic commonalities, as well as spread of best research practices, new technologies, and experimental systems across studies of a wide range of specific disorders would be greatly facilitated by appropriate realignment of study section topics.

Recommended Pathways

1.2.1 CSR should limit meeting participation to chartered members, selected as highly respected generalists in each designated area of study. In this setting, such generalists would be motivated to participate in peer review, and would recognize and reward bold and disruptive proposals that could strongly advance a broad area of study, rather than those that contribute incrementally to a subspecialty. This reconfiguration would rebuild a peer review culture that motivates the best scientists to participate.

1.2.2 CSR should adopt a mechanism to obtain focused technical advice as needed, without requiring *ad hoc* reviewers to participate in the study section meetings.

1.2.3 Study section topics should be reorganized to align peer review with the transdisciplinary, trans-disease, integrated approaches that will characterize much of the most important research. In practice, this effort would shift study section foci toward biological processes and machineries, and toward creation of new technologies that empower description, analysis, manipulation, and prediction of those processes.

Vision 1.3. Provide stable and predictable funding to enable scientists to pursue transformative research.

The progression of fundamental discovery is extended, nonlinear, and not easily aligned with the single-year federal budget.

Indeed, for precisely this reason, NIH research grants are typically awarded for four or more years.

This allows researchers to plan ambitious research programs, which over time may yield transformational discoveries.

However, this funding is not guaranteed; both NIH and individual investigators are

obligated, in effect, to place wagers on the outcomes of federal budget negotiations

for all but the first year of every research award.

When those bets are lost, due to stagnant, or even decreased, funding levels, ongoing research is compromised, and future proposals become increasingly conservative, to the detriment of breakthroughs and impact. Despite remarkable opportunities for scientific and medical advances, the unreliable funding atmosphere jeopardizes top researchers and discourages the best aspiring trainees from even entering the field. This erodes U.S. primacy in the science enterprise, as well as the health and well-being of the nation. The NIH budget needs sufficient sustainability and predictability to allow responsible planning to foster and nurture outstanding research and training, and progress against disease.

NIH and individual investigators are obligated, in effect, to place wagers on the outcomes of federal budget negotiations...

When those bets are lost, due to stagnant or even decreased funding levels, ongoing research is compromised.

Recommended Pathways

1.3.1 NIH should prepare rolling five-year, professional judgment budgets, which present projected needs and opportunities, for direct transmission to Congress. Annual professional judgment budgets have been used in certain high priority areas as designated by Congress, e.g., cancer, HIV/AIDS and Alzheimer's, but not for NIH overall and not in a multi-year configuration.


1.3.2 To promote inter-IC cooperative and integrative research, as well as novel trans-NIH initiatives, 5% of the research budget should be allocated to the Common Fund, with the increase over current levels dedicated specifically to programs that address common research interests of multiple institutes. The Director would be aided in developing and adjudicating these programs by an advisory committee that includes both intramural and extramural scientists.

1.3.3 The NIH Director should create an NIH-wide competitive grant mechanism to provide long-term (7-10 year) support for its most highly accomplished investigators, analogous to the 10-year Merit Award offered by some Institutes to more junior investigators. This investigator-based (as opposed to project-based) statement of confidence and trust will enable transformative research, while reducing uncertainty and administrative burden for the investigator, his/her institution, and NIH.

2. TRAINING: PREPARING THE NEXT GENERATION

Vision 2.1 Transform the training of our scientists and physician researchers to prepare them for 21st century science.

Many of the most pressing problems facing humanity are biological at their core: health, food, energy, the environment. New global threats to human health have emerged, e.g., antibiotic resistance in Zika, Ebola and other infectious diseases, and we need scientists who can combat them. If these global challenges are to be addressed, the U.S. needs a generation of biologists who are trained broadly as well as deeply, and who have the necessary interdisciplinary talents to move their research into the 21st century.



The NIH can rightfully celebrate its long-standing leadership in training future biomedical scientists.

The NIH can rightfully celebrate its long-standing leadership in training future biomedical scientists. Nonetheless, science itself is at an inflection point, and the training landscape needs to change accordingly for two reasons: cross-disciplinary science, underpinned by quantitative approaches, is now essential and transformative for solving the most challenging biomedical questions; and big datasets and systems-level analyses can deliver information at scales never before contemplated, although progressing from information gathering to meaningful understanding remains a challenge.

There is an urgent need for scientists who are highly skilled in these new disciplines, who couple that expertise with a vision to solve problems of extreme magnitude, and who can work hand-in-hand with policymakers to enact solutions. These cross-disciplinary opportunities combined with the potential to address biomedical

problems of global significance have transformed the training needs for scientists in our society. NIH training mechanisms, which have changed only modestly over the past few decades, need to be revitalized to meet those needs.

Recommended Pathways

2.1.1 The NIH Director should establish a competitive grant mechanism, analogous to the Broadening Experiences in Scientific Training Awards, to incentivize, implement, and disseminate approaches to curriculum development, training, and transdisciplinary, quantitative, team-based active learning that meet the needs for future research.

2.1.2 NIH should serve a convening function, periodically bringing together leaders of the grant mechanism described above to share information during the award period, define practices to be adopted or adapted nationally, regionally or institution-specifically, and obtain an expert evaluation of the value of the grant mechanism and its outcomes after completion of the award.

Vision 2.2 Support a substantially greater proportion of trainees under individual fellowships and training grants.

Most graduate students and postdoctoral trainees are supported largely by research grants that fund the research of their mentors (principal investigators), and to a lesser extent by teaching assistantships that provide undergraduate instruction for their host institutions while working to advance their mentors' research. Training support for the next generation of biomedical scientists should begin to shift away from the research projects on which they work, and more toward the trainees themselves, allowing them greater independence and control over their research and career direction. In contrast to research grant funding, which is evaluated exclusively on productivity, dedicated funding for training is much more comprehensive, incorporating foundational course work, training in research skills, development of scientific communication skills, training in the ethical conduct of research, and exposure to a range of health-science career options.

Two predominant mechanisms for dedicated training support are individual fellowships, awarded competitively to the trainees themselves, and training grants, which provide funds to institutions in support of cohorts of trainees. Training grants have the positive ancillary feature of integrating faculty investigators into partnerships that commonly span departments and disciplines. Looking forward, an important goal is to substantially broaden availability of training vehicles that are decoupled from research funding, that build strong conceptual foundations for insightful problem-solving and expansive skill-building, and career development opportunities. In addition, inclusion of non-citizen trainees in these training grant and fellowship programs is essential for continued international leadership in biomedicine.

Importantly, implementation of these substantial shifts in the funding of trainees has complex implications for institutions, which currently have wide-ranging differential access to such awards and related resources, and could create or exacerbate inequities unless very thoughtfully developed.

Recommended Pathways

2.2.1 The NIH Director should create a task force to devise a plan within the first six months of the Administration to substantially shift the funding for trainees from research awards to individual fellowships and training grants. The task force must consider how such a shift would affect the full spectrum of training institutions, and how potential negative effects could be mitigated.

2.2.2 Deliver actionable recommendations on the trainee funding shift plan during the Director's first year, and begin implementation of the shift in funding in Year 2; include support for non-citizen trainees in the training grant and fellowship programs.

Vision 2.3 Ensure that the NIH-trained workforce is fluent in the public context of science.

Even as new discoveries and technologies are transforming research, health, and healthcare, trainees engaged in biomedical discovery research are rarely exposed to the public context of their work. It is essential that those who are creating these transformations be well versed in engaging and communicating with the public that has funded their investigations. Neither the work nor those who are doing it should remain opaque to our citizenry.

To bridge this gap in understanding and shared engagement, future biomedical scientists and physician scientists alike must be prepared to articulate to the public and its elected representatives the immediate and potential future impact of their work. Such training involves exposure to and expertise in science communication (including the role of media), as well as social, economic, ethical, political, and global issues, and an understanding of the roles of advocacy, patient groups and other NGOs, industry, and government agencies. As noted above, ensuring that many or most trainees receive appropriate mentoring in this space will likely require shifting support for most trainees away from research grants and onto training grants and fellowships.

Recommended Pathways

2.3.1 The NIH Director should establish a competitive grant mechanism to develop and evaluate ways to best educate biomedical graduate and postdoctoral trainees in the public context of science.

2.3.2 The NIH Director should mandate that all students and postdocs at institutions holding NIH training grants receive training in the public context of science, based on the effective training approaches developed in 2.3.1.

3. ADMINISTRATION AND OPERATIONS: MAXIMIZING OPPORTUNITY

Vision 3.1 Free scientists to focus on advancing science by streamlining the rules for research protections and the processes for grant applications.

In “*Optimizing the Nation’s Investment in Academic Research: A New Regulatory Framework for the 21st Century*,” the National Academies of Sciences, Engineering and Medicine Committee on Federal Research Regulations and Reporting Requirements noted that overlapping and inconsistent federal regulations hinder research productivity across the government-academia partnership. Examples given included important matters such as protection of human subjects and experimental animals. As a result, investigator time and institutional funds are increasingly expended on compliance infrastructure instead of research and training. The report recommends specific remedies, such as: reduce, streamline and harmonize reporting, assurances and verifications across agencies; simplify research grant applications, requiring only information essential for review of scientific merit; and request information needed for funding only from those selected for support.

In addition, the time that biomedical scientists spend writing, revising, and reviewing grant proposals could be reduced by shortening the time from application submission to receipt of funds, increasing the fixed budgets of grant mechanisms such as the modular R01 and the R21 (set in 1998 and 2003, respectively), consolidating the funding of individual scientists with multiple NIH grants, and creating an NIH-wide seven to 10 year award for highly accomplished investigators (see *Recommended Pathway 1.3.3*). Finally, harmonization of common research, training and career development grant mechanisms across NIH would simplify investigator choices and reduce NIH administrative costs.

Recommended Pathways

3.1.1 The new Administration and Congress should select relevant recommendations from the National Academies' Committee on Federal Research Regulations and Reporting Requirements report, "*Optimizing the Nation's Investment in Academic Research: A New Regulatory Framework for the 21st Century*," to reduce administrative burden on investigators, grantee institutions and NIH itself.

3.1.2 The NIH Director should declare common grant mechanisms to be NIH-wide, requiring harmonization and adoption of standardized application and funding guidelines across the institutes; grant mechanisms with fixed budgets should be adjusted for inflation every three years.

3.1.3 The NIH Director should develop NIH-wide programs that motivate investigators with multiple NIH grants to consolidate their funding, and competitively award highly accomplished investigators increased duration of funding (seven to 10 years).

Vision 3.2 Transform NIH organization and operations to align with, inspire, and better enable the best science.

Twenty-first century biomedical research is increasingly a transdisciplinary, quantitative endeavor, adopting precision medicine approaches that integrate and analyze massive sets of diverse data, finding and linking patterns and correlations from biological molecules, experimental organisms, individual people, and human populations. A growing cohort of patients, as well as healthy people, are collecting and contributing data and seeking to engage actively in the research process. Biological mechanisms and processes discovered in one disease are commonly found to be relevant for others.

Contrary to these dynamic integrative forces, the NIH has long been divided into 24 ICs, with separate budgets and administrations, each organizing, funding and overseeing research



Twenty-first century
biomedical research
is increasingly
transdisciplinary.

and training centered around a particular organ system, a set of diseases, and/or a research area. While the contributions of each are justifiably recognized and respected by patients, advocates, and scientists, there is a striking mismatch between modern biomedical science and the established NIH structure. Mergers or reorganization of NIH institutes have been suggested but not implemented, likely due to logistical and political complexity. Nevertheless, the increasing divergence between the structure of NIH and the convergence of the sciences across disease areas makes an evaluation of isolated organ- and disease-focused institutes now an imperative.

One encouraging development is that NIH directors have, over the past decade, implemented and incentivized functional changes under the Common Fund, Neuroscience Blueprint, and BRAIN Initiative to identify and address major scientific challenges that span institutes and disciplines, significantly accelerating progress. In these programs, cross-cutting and potentially transformative projects are led by two or more institute directors and managed by program staff from multiple institutes. An additional change that would promote cross-disciplinary and integrative science is reorganization of the study section roster in the Center for Scientific Review (see also *Vision 1.2* and *Recommended Pathway 1.2.3*), moving away from organs and disorders in favor of biological processes and machines, as well as new technologies.

Recommended Pathways

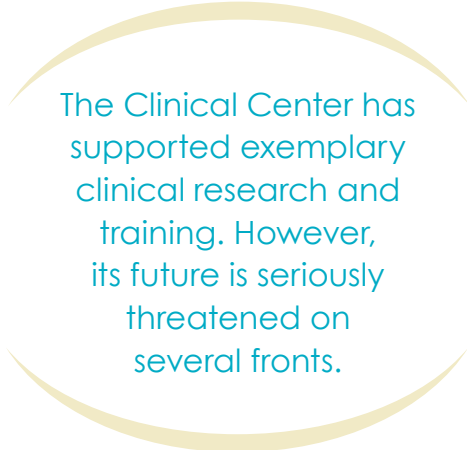
3.2.1 The NIH Director should build upon the success of inter-institute collaborative programs within the Common Fund and BRAIN Initiative, exploiting a dedicated increase in the Common Fund budget (see *Recommended Pathway 1.3.2*) to expand them broadly across biological mechanisms, research disciplines and diseases, and adopt recommendation 1.2.3 to reconfigure the CSR study section roster, placing greater focus on biological mechanisms and processes, as well as new technologies.

3.2.2 The NIH Director should name a working group that includes basic, clinical, and population scientists, as well as patient advocates, to define and consider the implications and impacts of modifying the NIH IC organizational structure. Specifically, the group should complete a formal analysis within the next two years to consider

how NIH should be structured to better reflect and enable modern biomedical science and to reduce barriers that impede progress.

Vision 3.3 Achieve the full potential of the Intramural Research Program and Clinical Center.

The NIH Intramural Research Program (IRP), which includes the Clinical Center, supports research, training, and career development, functioning as a distinctive ecosystem in which investigators undertake innovative research projects with long-term stable funding within a research environment that brings together investigators from multiple fields. The IRP provides a compelling example of NIH research inside the beltway, visible to Congress and policymakers, and serves as a special research site and a national resource.



The Clinical Center has supported exemplary clinical research and training. However, its future is seriously threatened on several fronts.

The contributions of the IRP to the biomedical research enterprise could be enhanced by implementing policies to make it more nimble, cutting edge, and competitive:

- Federal restrictions affecting personnel, compensation, contracting, and travel should be addressed, as they impede scientific progress, limit IRP efficiency and effectiveness, and reduce its competitiveness for outstanding investigators.
- IRP investigators in good standing who depart to extramural institutions should be provided with three to five years of transitional support, consistent with policies for NIH Lasker fellows and HHMI Janelia Farm group leaders.
- With bureaucratic concerns adequately addressed as above, and a favorable transition policy in place, the IRP could be converted into a premier “incubator” for exceptional early stage investigators, from which they could launch bold research programs with ~7 years of unrestricted funding, free of non-research academic responsibilities (analogous to current Stadtman Fellows), after which

they would be expected to depart to extramural positions (as at certain premier science centers such as the European Molecular Biology Laboratory and the Max Planck Institutes). Of course, the IRP would continue to host a proportion of tenured established investigators, recruited from intramural and extramural ranks, but incubator-investigators would typically depart, rather than expect to advance to a permanent appointment. This scheme would provide a continuous influx of exciting investigators, ensuring a healthy turnover of personnel while retaining the very best.

- The 23 intramural programs should be consolidated into a smaller number with coherent themes and integrated space, recruitment, and shared resources that reflect the conduct of modern science. The Porter Neuroscience Center, housing investigators from eight ICs, provides precedent for assigning space by research foci rather than institute affiliation. Program integration would be further advanced if control over budget, appointments, and/or review were delegated to the consolidated units.

The Clinical Center has been a centerpiece of the IRP for decades, supporting exemplary clinical research and training. Currently, however, its future is seriously threatened on several fronts. First, the Clinical Center budget resides within the overall IRP budget, which has declined in real dollars in recent years, with no provision to keep pace with the rising costs of healthcare and clinical research. Second, recruitment of outstanding clinical trainees and tenure-track investigators has been compromised by federal bureaucratic burdens and by concerns about difficulties for investigators returning to academia. Third, the volume of activity in the Clinical Center has declined, reflecting the national trend toward conducting clinical research in outpatient settings, the greater cost of clinical research relative to laboratory research, and difficulty in recruiting new investigators. Finally, the organizational structure of the Clinical Center should be updated to enable its central role in the IRP and its expected contributions nationally in infectious diseases, vaccine development, cancer immunotherapy, and other critical areas.

Recommended Pathways

3.3.1 The NIH Director and the Department of Health and Human Services should work with Congress in the first year to revise a range of policies, such as those affecting personnel, travel, and contracting to more closely align with research universities and medical schools, and to create an NIH-specific “special pay statute” that would provide compensation parity with academic institutions.

3.3.2 The NIH Director should develop and support IRP standards and policies that ensure a continuously creative, vibrant, and impactful research environment, and that promote scientific and personnel flexibility and healthy turnover. Configuration of the IRP as an incubator for exceptional early-stage investigators is one actionable approach.

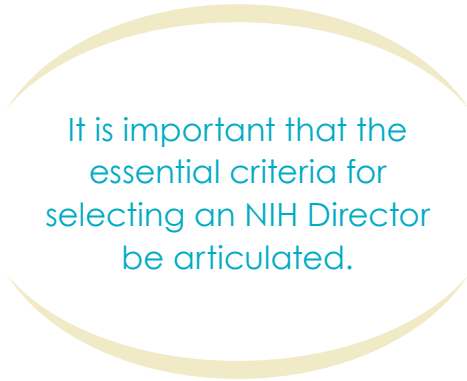
3.3.3 The NIH Director must address expeditiously four related challenge areas currently facing the Clinical Center to ensure that its future contributions are not irrevocably compromised: develop a new governance structure advised by external experts in administration of clinical research and delivery; change the funding model to support from general funds, responsive to variable research activity and to elevating fixed costs; improve recruitment of clinical scientists, highlighting advantages and importance of that career track, and offering loan repayments and other incentives; increase clinical activity by partnering with area academic health centers, and promoting intramural and extramural collaborations.

4. APPOINTMENT OF THE NIH DIRECTOR

In accord with historical tradition and good institutional practices, the new Administration will likely search for a new NIH Director; the working group considers this the highest priority among its recommendations. We urge that a systematic search for a highly qualified person be initiated as early as possible following the election, recognizing the essential role of the director in developing the recommended pathways above, and the complexities of identifying and appointing the best possible person.

Recommended Pathways

4.1 Characteristics of Candidates. It is important that the essential criteria for selecting an NIH Director be articulated. Our group offers the following characteristics as qualifications for the position: an outstanding record of scientific accomplishment in one or multiple areas of biomedical research, likely evidenced by election to one or more of the National Academies, high ranking positions at respected institutions, and/or the award of major prizes; an appreciation of the importance of other areas of medical research; a strong reputation for integrity and good character, with a history of public service; excellent knowledge of the NIH and its activities, usually based on participation in the affairs of the NIH as a grantee, reviewer, consultant, or employee; an ability to represent the NIH with clarity and conviction to other members of the U.S. government, the scientific community, and the public; and a high level of interest in leading the NIH in a fashion that will enhance the agency's performance. Traditionally, the NIH Director has always held an M.D. degree, and it is essential that the Director have wide knowledge about medicine, but we do not view the M.D. degree as an essential attribute.



It is important that the essential criteria for selecting an NIH Director be articulated.

4.2 Queries for Candidates. Many of the qualities that would be sought in candidates for NIH Director can be discerned by having a search committee ask questions that reveal a candidate's knowledge and attitudes about the agency. We offer below a list of topics and questions that members of a search committee might pursue during the interview process:

Motivations. Why would you want to become the Director of the NIH? What are your aspirations and major plans for the agency?

Views of the agency overall. What are the two or three strongest and weakest aspects of the NIH as it currently operates?

The climate for federally supported science. Federal funding of all fields of science has not fared very well in recent years. How do you account for this problem? What do you see as the major consequences? What would you aim to do—other than argue for more funds—to ameliorate the problems?

The NIH budget. What do you think are the best arguments to present to leaders of the new Administration or to congressional appropriators for enhancing the NIH budget? What are your goals for its budgetary future?

The Common Fund. The NIH Reauthorization Bill of 2006 created the Common Fund to provide the NIH Director with a greater hand in guiding program development across the institutes and centers. How well do you think the Common Fund mechanism has worked? What would you do, if anything, to improve it?

Open science. In recent years, there has been increasing interest in sharing the results of publicly funded science through the creation of shared data repositories, public digital libraries, open access journals, and pre-print servers. What is your view of these developments? How would you grow such efforts?

Scientific initiatives. The NIH grant system is best known for investigator-initiated R01 awards, but significant funding is also allocated to contracts, training, and cooperative agreements. In addition, specific research programs are often initiated by Institute leaders, the Administration, or Congress. What is your view of those other approaches to NIH-supported science? Is the balance among them right? Are any of the current Administration's

initiatives on precision medicine, Alzheimer's disease, cancer (Vice President Biden's Cancer Moonshot), or neuroscience (BRAIN) in need of adjustment?

The Intramural Program. About 11% of the NIH budget supports the Intramural Research Program (IRP). What are your views about the size, direction, function, and quality of the IRP? What kinds of changes do you think are desirable?

The Clinical Center. The Clinical Research Center on the NIH campus has been a major feature of the IRP for several decades and is housed in an impressive new facility, but it is confronting several problems: fiscal shortfalls, declining patient census, inefficient recruitment of new clinical investigators, and procedural deficiencies. What is your view of these problems and what do you think should be done?

Peer review. NIH-based systems for review of grant applications are a persistent target for concern, especially when success rates for applicants are low. What do you think are the major deficiencies in the review process as practiced by the Center for Scientific Review or by individual institutes? How would you go about repairing them?

General directions of biomedical research. As the world's largest funder of biomedical research, NIH is widely emulated, and its practices are intensively debated. What are your views of the current distribution of NIH's resources for fundamental, translational, and clinical research? Or of the need for additional resources for studies of prevention, behavior, public health, global health, implementation science, complementary medical practices, and other topics judged by some to be under-supported? Do other portions of the NIH research portfolio need more or less support in the next five to 10 years?

Recruitment of NIH leaders. A major responsibility of the NIH Director is the hiring of individuals to occupy major positions in the Director's Office and to serve as Directors of Institutes and Centers. What kinds of approaches do you favor for these recruitments? What qualities do you look for in such searches? What do you see as the advantages and disadvantages of such positions and how would you try to overcome the shortcomings?

Research integrity and reproducibility. NIH-sponsored research has been criticized frequently in the past few years for lapses in accuracy and even integrity. How do you view these criticisms? What do you think are the underlying causes? What kinds of remedies do you envision?

Training. Several profound questions have been raised about the way in which biomedical scientists are trained in the U.S.: Are we training too many people for too few academic positions? Why are trainees becoming independent scientists at such an advanced age? Do trainees get an accurate picture of the available employment opportunities? Why do so few trainees come from the underrepresented minority sectors of our increasingly diverse population? Which of these do you see as central issues? What are your responses to them? What steps do you think might be taken to improve the situation?

Workforce demographics. What do you think of the demographics of the scientific workforce? At issue are disparities among racial and ethnic groups and gender, and the increasing average age at which scientists receive their first independent grant. What are your views? What policy changes would you recommend?

Multidisciplinary science. Biological sciences increasingly depend on multidisciplinary strategies including physical and information sciences. Is NIH in need of change to address these trends? If so, what would you do to encourage and enable such changes?

Miscellany. The NIH directorship is a complex job with deep responsibilities. Are there aspects of the position that worry you? Are there parts of the job that we haven't asked about that you would like to discuss? Are there reasons that you might not want to accept the position if asked?

ACKNOWLEDGMENTS

The Coalition for the Life Sciences (CLS) is an alliance of professional organizations working together to foster public policies that advance basic biological research and its applications in medicine and other fields. The issues addressed by the CLS include science education, professional training, and the funding, management, and oversight of scientific work, especially by the federal government.



FasterCures, a D.C.-based center of the Milken Institute, is driven by a singular goal – to save lives by speeding up and improving the medical research system. We focus on cutting through the roadblocks that slow medical progress by spurring cross-sector collaboration, cultivating a culture of innovation, and engaging patients as partners. *FasterCures* works across sectors and diseases to accelerate the process by which great advances in science and technology are turned into meaningful medical solutions for patients. Our programs identify what's working and what isn't across the research ecosystem, and share that knowledge so that every sector – and every patient – can benefit.



Research!America is the nation's largest 501(c)(3) dedicated to making research to improve health a higher national priority. R!A's public opinion data, advocacy programs, and publications reach the public and decision makers to help advance medical, health and scientific research. We urge Congress and the Administration to increase funding for the National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), Agency for Healthcare Research and Quality (AHRQ), Food and Drug Administration (FDA) and National Science Foundation (NSF) at levels that keep pace with scientific opportunity. We advocate for a legislative and regulatory



climate that fosters public and private sector innovation. The alliance is comprised of stakeholders across the research ecosystem: academia, industry, patient advocacy organizations, scientific societies, academic health centers, independent research institutes, and foundations.



