POLICY FORUM

RESEARCH CAREERS

Improving support for young biomedical scientists

Expand grant programs to encourage innovative research

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Over the past several years, we and others in the biomedical research community have become increasingly concerned that younger scientists are not being adequately supported as independent academic investigators and that, of equal importance, these newly launched investigators are being strongly discouraged from tackling novel scientific problems (*1*–*6*). Both issues can prevent talented trainees from aspiring to careers in biomedical research, despite the extraordinary opportunities offered by new technologies and recent discoveries. We view this situation as an existential threat to our profession, demanding that we urgently confront the underlying problems.

It is widely recognized that career pathways for young scientists have changed dramatically and that over 80% of those who receive biomedical Ph.D.'s today will be employed in positions other than academic faculty (*1*, *5*). The U.S. National Academies of Sciences, Engineering, and Medicine recently released a report that addresses many important aspects of these cultural changes (*7*). Here we focus on the problems faced by those who will renew the ranks of academic research faculty, with proposals that complement the recommendations in that report. Drawing on lessons from Europe and the United States, we propose three steps that could be taken by funding agencies, specifically the U.S. National Institutes of Health (NIH) but also others across the world, to support young investigators in more constructive and effective ways.

THE NATURE OF THE DILEMMA

Major changes have occurred in the demographics of funded biomedical investigators in the United States, with a striking shift of awardees from younger to older scientists. This is evident from the number of those holding NIH R01 grants, the type most often awarded to independent investigators (see the figure, left). The factors responsible for this shift include the aging of the population, the elimination of a mandatory U.S. retirement age, the lengthening of graduate and postdoctoral training, and the often multiyear delay between assuming a faculty position and successfully competing for an NIH grant (*4*, *8*).

A cardinal feature of the shift is a dramatic reduction in NIH-funded investigators under the age of 37 (see the figure, right). Despite a large increase in the NIH budget and number of grants awarded since the early 1980s, there has been a greater than fivefold decrease in the number of investigators aged 36 or younger who hold R01-type grants: from more than 2500 grant holders to fewer than 500. Expressed in terms of NIH dollars, the proportion of all NIH funding awarded to scientists under the age of 36 has dropped from 5.6% in 1980 to 1.3% in 2012 (*1*). Although valuable support from philanthropic organizations is provided to a select set of young investigators, the scale of that support is much too small to compensate for the above changes. Thus, by these measures, the U.S. scientific community is doing a poor job of renewing itself.

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The claim that investigators early in their careers are being discouraged from addressing the most challenging problems in biomedicine rests on less quantitative observations. But in our experience, the next generation of scientists report that the peer-review process for grant applications is perceived to be unduly conservative because of the hypercompetitive grant-funding environment, discouraging them from proposing to conduct highly original work (*7*, *9*). In conversations with trainees and young faculty, we have repeatedly heard that emerging scientists feel compelled to remain well within the bounds of the research that they and their mentors are already pursuing, because obtaining a research grant requires strong preliminary data and a high probability of success.

In addition, many junior and senior scientists operate with the conviction that essential components of the grant-making system, including peer reviewers and agency administrators, currently undervalue research that seeks to decipher the fundamental principles of living systems, in favor of projects with shorter-term objectives that focus directly on human diseases—so-called translational biomedical research. Yet the history of science has repeatedly shown that insightful studies of basic biological mechanisms in easily manipulated model organisms—such as bacteria, yeast, worms, and flies—provide revolutionary insights into life processes. Over the long term, these discoveries contribute to human health in profound ways (*10*).

ADDRESSING THE SITUATION IN THE EUROPEAN UNION AND THE UNITED STATES

Some ideas on how best to fund young scientists have recently come from Europe. In 2007, the European Research Council (ERC) launched its Starting Grants (StG) program, aimed at young scientists from all disciplines who received their Ph.D. within the previous 2 to 7 years. At the same time, the ERC initiated the parallel Advanced Grant program, open to applicants at any career stage, which likewise emphasizes innovative interdisciplinary research. Since then, the ERC has added a third category, the Consolidator Grant award, designed to support investigators who have previously received a single grant, such as a StG award, and are 7 to 12 years post-Ph.D. Importantly, the competitions for the three grant categories are conducted separately, and the awards are supported from three independent budgets (*2*).

This division of careers into three stages has a number of advantages. First and most crucially, investigators conducting their first independent projects and those stabilizing their laboratory programs are competing against scientists at the same career stage, not against senior scientists with longer careers and stronger reputations. Second, different criteria for review can be applied to applicants at different career stages. In this way, the StGs encourage applicants to pursue highly original projects when they start their own laboratories, without requiring extensive preliminary data.

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Competition for these pan-European StGs is held annually, and each of the 100 to 200 successful applicants in the life sciences receives substantial funding, €1.5 million over 5 years. A critical feature of the process is the use of nine review panels, each composed of outstanding scientists coming from a broad range of disciplines and many European countries; this serves to minimize narrow specialization and to focus decisions on the broad implications of the proposals (*2*).

The ERC has recently completed a qualitative evaluation of the outcomes from the first several classes of investigators who completed the full course of funding from the ERC StGs. The results are very encouraging. Of the 199 individuals evaluated, 43 were judged to have produced a "scientific breakthrough," and 99 were thought to have generated a "major advance" (*11*). An ERC StG is now seen as a stamp of quality for a new investigator and his or her institution.

The NIH leadership has also been attentive to these problems. Over the past few decades, the agency has experimented with several programs designed to fund the next generation of biomedical scientists more effectively and at earlier ages (*2*). Some of these experiments, such as the R29 [First Independent Research Support and Transition (FIRST) Award] grant program, were discontinued after unfavorable evaluations that suggested the award stifled new investigators' careers. Other programs, such as the policy initiated in 2008 to raise the success rates of applications from Early Stage Investigators (ESIs; applicants within 10 years of receipt of their Ph.D. or completion of clinical training), have made a difference, and they continue. Additional experiments include the Early Independence (DP5) and the New Innovator (DP2) awards, popular programs that provide only a small number of research grants each year.

To be eligible for a DP2 grant, a scientist must be an ESI and cannot have received a major grant previously. The criteria for selection emphasize imaginative and original scientific goals without a requirement for preliminary results. These DP2 grants are generous with funds and time, providing $300,000 per year in direct research costs for 5 years. In addition, all of the money is provided at the start of the award period, so that expenditures can be tailored to the needs of each investigator (for example, to purchase major equipment). Although nearly 2200 DP2 applications were received in the initial year (2007), the fiscal allocation through the NIH Director's Common Fund allowed only 30 awards to be made. This presumably sent a discouraging signal, because only about 550 applications are now received each year, with 100 finalists selected by a single broad review group. After further evaluation, about 40 to 60 awards are made (*12*).

The NIH has just completed a careful external evaluation of the first three cohorts of DP2 recipients, compared to an equivalent control group, that deemed the program a success. This grant program is supporting "research that is more innovative, risky, and impactful than research that typically is reviewed and funded using the traditional R01 program." In addition, despite concerns that supporting ESIs to pursue highly original research topics might place their careers in jeopardy, the evaluation found that receiving a DP2 award did not hinder a young scientist's career (*13*).

Encouraged by directives in last year's 21st Century Cures Act enacted by Congress and responsive to concerns in the research community, the NIH has announced its intention to enlarge the cohort of young investigators who receive R01-type grants. NIH leadership has provided a list of mechanisms by which individual institutes and centers might increase the number of awards made to younger investigators and reaffirmed the NIH's commitment to improving prospects for ESIs (*3*). That announcement also defined a new category of applicant, the Early Established Investigator (EEI)—a scientist who has received only one R01-type grant and is thus formally analogous to a candidate for the ERC Consolidator Grant. This new NIH policy statement includes a pledge to increase the number of R01-type grants made each year to ESIs and EEIs by a few hundred in each category; however, the precise number of additional awards and the definitions of beneficiaries are still under review (*3*).

THREE SPECIFIC PROPOSALS

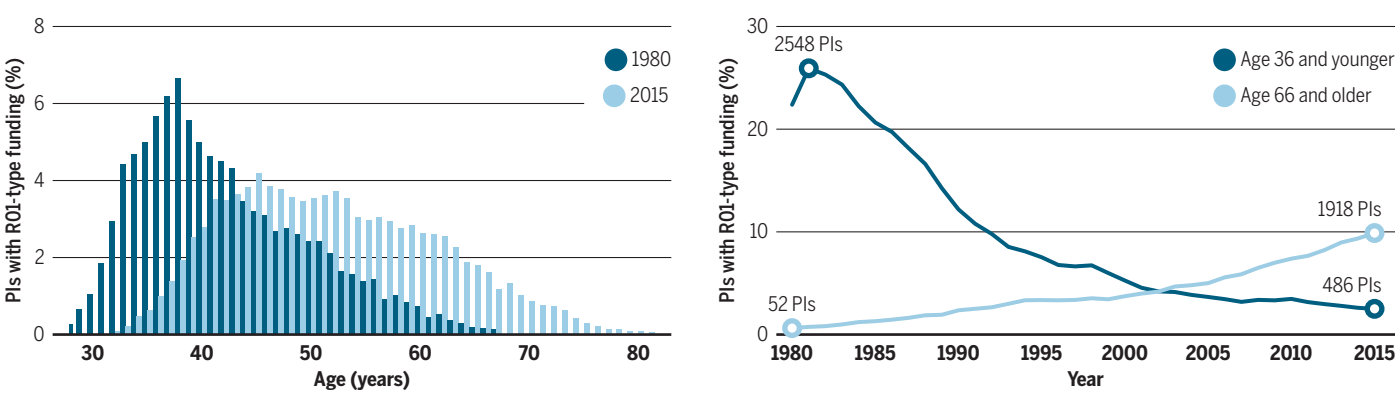
We are encouraged by the continued engagement of NIH leadership with the plight of young investigators. It is in that spirit that we propose three additional steps to enhance opportunities for early stage investigators.

Greatly expand use of the DP2 mechanism

The DP2 award has now been used for a decade and evaluated favorably. We believe it deserves expanded use and propose that the NIH move in a step-wise manner toward providing greater NIH resources to ESIs through this mechanism. In 2016, the NIH funded 908 of the 3937 applications from ESIs for R01-type grants, and the NIH now proposes to award grants to about 1100 ESIs annually (*3*, *14*). We suggest that the NIH move gradually toward making half of those awards (about 550) as DP2 grants. This number would greatly increase the probability that an ESI will explore new approaches to an important biological problem. The NIH

The increasing age of principal investigators funded by the NIH

(Left) The age distribution of NIH R01-type funded principal investigators (PIs) in 1980 and 2015. (Right) The percent of NIH PIs with R01-type funding plotted against year, selecting out older and younger age brackets. R01-type grants are defined as R01, R23, R29, and R37 awards. Data are from files posted for the NIH's Early Stage and Early Established Investigators at https://grants.nih.gov/policy/new_investigators/index.htm (file name "Age of RPG Awardees 1980 to 2015 from SARB File 191-16").



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should, of course, monitor expansion of the program to ensure that the quality of funded applications remains high and to identify any possible bias in making awards. The critical goal is to liberate new independent investigators, as well as the graduate students and postdoctoral fellows who will soon become independent, from the widely perceived tyranny of conventional thinking.

One can question whether a major expansion of the DP2 program would be able to reduce the average age at which new investigators in the United States are funded, given the large backlog of postdocs competing for a limited number of independent positions at U.S. research institutions. In the current funding environment, why would a university hire a scientist proposing to undertake an innovative research program after only a few years of postdoc training, when the institution could hire someone with several more years of training, many more publications, and a plan to continue an already productive research program? We propose that, by providing sufficient funds for new faculty without a preexisting publication record on a proposed research topic, the NIH would free university search committees to think more imaginatively about the type of science and scientists that they want for their institutions.

To encourage this type of hiring, we recommend that the NIH adopt two current practices of the ERC. The first is to allow postdocs to apply for a DP2 award, provided that he or she has secured a faculty position that is conditional on the award decision. This is the case for the ERC StGs, where, in addition, a successful applicant retains the option of shifting institutions after the grant has been awarded. The second is to restrict DP2 grants, over time, to applicants who completed their Ph.D. or clinical training between 2 and 7 years ago, with allowable exceptions, instead of the current 10-year limit. This recommendation recognizes that young investigators will often wait until the end of any eligibility period to apply, so as to expand their prior records. Reducing the number of years of eligibility for DP2 awards would thus encourage two healthy trends: less time in postdoctoral training and earlier research independence.

Much of the recommended expansion of the DP2 program could be accomplished within the NIH Director's Common Fund, which this year totals $588 million, perhaps by not replacing some of its special initiatives when they expire. In addition, the individual institutes should consider funding a greater number of DP2 grants, as an effective way to recruit a new generation of scientists to address institute missions.

Increase the funding of young investigators through requests for applications (RFAs)

It is often underappreciated that NIH institutes and centers issue substantial numbers of R01-type grants to applicants responding to RFAs—"top-down" initiatives, in which institutes identify priority topics to be funded, in contrast to the traditional "bottom-up" investigator-initiated awards. Ideally, RFAs can be used to attract more investigators into fields of research that warrant greater attention because the public health needs are great or because new findings or technologies offer unexpected opportunities for progress. In 2016, the total number of new NIH R01s was 4541; of these, 333 (7.3%) were awarded through an RFA.

We propose that the NIH mandate that a substantial percentage of grants be awarded to ESIs as part of both institute-sponsored RFAs and NIH-wide initiatives, such as the Cancer Moonshot and the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, and that the ESI competition be conducted using the selection criteria already used for DP2 awards. Reserving funds in each case for a separately reviewed, DP2-type competition that stresses experimental originality would both attract new scientists into the targeted field and encourage new approaches to an important problem.

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Experiment with separate competitions for ESIs when awarding traditional investigator-initiated R01 grants

For several years, the NIH has encouraged its institutes to favor ESI applicants when selecting recipients of new grants. This has produced higher success rates for ESIs at some institutes, but it has not achieved a substantial change in workforce demographics (see the figure).

To reach a greater representation of young investigators among grant recipients, we suggest that the NIH experiment with the kind of strategy adopted by the ERC, in which ESIs compete separately for predesignated numbers of R01 awards, rather than against the entire pool of applicants.

An ideal funding program for young biomedical scientists would award enough independent grants to young investigators to inspire the most talented students to aim for scientific careers, while simultaneously encouraging them to attempt to solve important biological problems in new ways. We recognize, as does NIH leadership, that earmarking funds to support more young investigators will come at a cost to older investigators (*3*, *4*). Nevertheless, it is important to make this shift, which we consider essential for the future vitality of biomedical research. If properly implemented, our proposals could substantially increase the number of scientists under 40 years old who receive independent research support, while enhancing the originality of their research. These changes should also find support in Congress, which has repeatedly expressed concern about the status of young investigators. ■

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ACKNOWLEDGMENTS

The proposals in this piece reflect the views of the nonprofit organization Rescuing Biomedical Research, as approved by its Steering Committee (http://rescuingbiomedicalresearch.org/). We thank the Open Philanthropy Project for grant support, as well as numerous colleagues for their feedback on drafts of this manuscript.

10.1126/science.aar8405

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Science **360** (6390), 716-718.
DOI: 10.1126/science.aar8405