Science and technology consortia in U.S. biomedical research: A paradigm shift in response to unsustainable academic growth

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Modern-day bioscientific research is now at an economic crossroads. Specifically, the past 30 years have brought extraordinary advancements in biomedical knowledge, initiating the era of "personalized medicine", therapies tailored specifically to individual patients' genomic, epigenomic, and transcriptomic profiles, discovery of drugs based on computational analyses of massive datasets, and systems pharmacology (optimizing dosing and detection of adverse drug events). These have resulted in an exponential increase in our understanding of biological processes at the molecular, cellular, and organismal levels. Overall U.S. life expectancy (at birth) has risen from 74.7 years in 1985 to 78.7 years in 2010. Concurrently, the U.S. infant mortality rate declined by 42%, while mortality from heart disease and cancer decreased by 53% and 20%, respectively.[1]

Despite these monumental advances, the traditional manner in which biomedical research is conducted in the United States is no longer sustainable. A recent perspective by Alberts et al., entitled "Rescuing U.S. biomedical research from its systemic flaws", contends that our current system is based on the presumption of perpetual growth, and that the negative consequences of this ideology have been realized only recently [1].

The belief in perpetual growth was in part fueled by a doubling of the budget of the National Institutes of Health (NIH) from 1998 to 2003 [2]. Since 2003, however, increasing demand for research monies (i.e. the Biomedical Research and Development Price Index, BRDPI) [3] has overwhelmed supply. During the past decade, the BRDPI has outpaced the rate of general inflation (i.e. the "gross domestic product price index", GDPPI, Fig. 1A), because of expansions in research personnel, university "indirect cost" rates, and technological advances. In BRDPI-adjusted dollars, the 2014 NIH budget fell 25% since 2003 [3] (Fig. 1B). As a result, the number of R01 grants (the most common project-funding mechanism) awarded by the NIH fell from 7430, in 2003, to 3902, in 2013 (a 47% decrease), while the number of research program project grants (RPGs) decreased from 10,393 to 8310 [3] (Fig. 1C). Despite this precipitous drop in awards, total applications have increased, resulting in success rates for RPGs, competitively renewed R01s, and first-time R01s to drop from, respectively, 25.3%, 24.1%, and 21.0%, in 2003, to 14.6%, 14.3%, and 13.4%, in 2013 (Fig. 1D). While the BRDPI was a modest 1.3% in 2012, it is expected to rise from 1.9%, in 2014, and to 3.3%, in 2019, again significantly outpacing general inflation (Fig. 1A) [3].

One consequence of the belief in continuous growth [1] was a steady increase in PhD awardees. During the same approximate time period of NIH budget stagnation (actually inflation-

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Abbreviations:
BRDPI, biomedical research and development price index; **GDPPI,** gross domestic product price index; **RPG,** research project grant.

[1] http://www.infoplease.com/ipa/A0110390.html

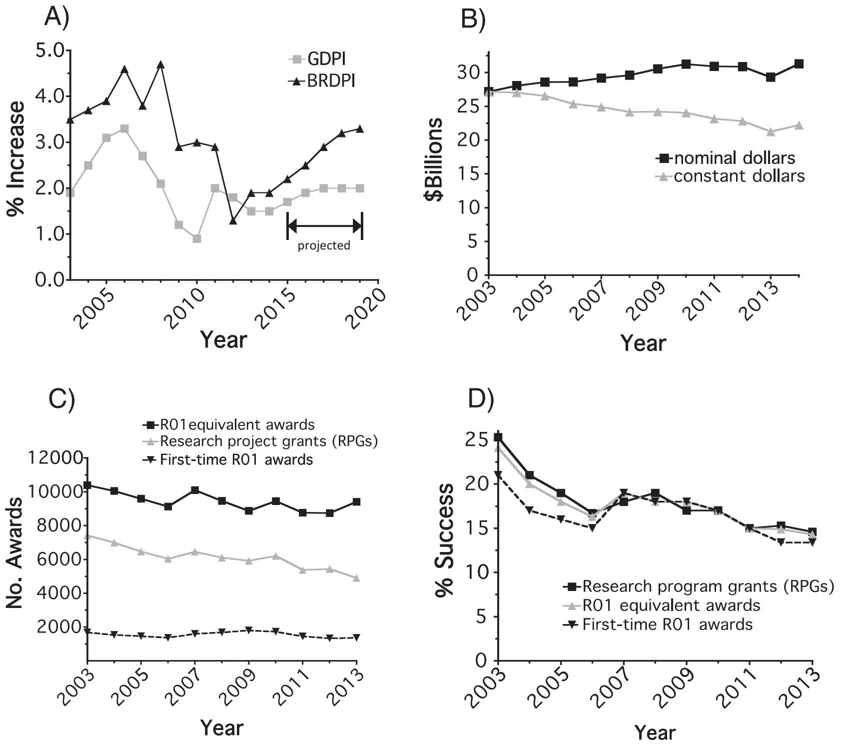

Figure 1. A: Annual rates of the gross domestic price index (GDPI, the general measure of consumer inflation) and the biomedical research domestic price index (BRDPI, the annual increase in cost of performing biomedical research). Years 2015–2020, projected values. **B:** Annual NIH budget from 2003 to 2013, in nominal (unadjusted) and constant (BRDPI-adjusted) dollars. **C:** Annual number of three types of NIH research awards from 2003 to 2013. **D:** Annual success rates for the same three research award types from 2003 to 2013.

adjusted decline), from 2001 to 2011, the number of life science PhD awards increased by ~30% [4]. Because low-wage PhD and postdoctoral trainees have traditionally served to generate laboratory data vital for research publications and funding proposals, there has been little incentive to reduce their numbers. Additionally, recent surveys of university professors aged 49–67, found that 74–85% had already not, or had no plans to retire by age 65 [4]. Consequently, newly trained scientists enter an oversaturated labor market where supply largely exceeds demand, often preventing even the brightest of these individuals from securing independent academic research positions (<15% of doctorates 6 years after obtaining their PhDs) [4]. As a result, many of these well-qualified persons remain in training positions, unable to expand upon their own promising scientific ideas. Of medical school faculty growth from 2001 to 2011, 70% was for non-tenure track positions [2]. Even for those able to secure independent faculty positions, the number of first-time R01 awards has remained consistently low, the average age of first-time R01 awardees rising from 34, in 1970, to 42.6, in 2007 [2].

A primary consequence of this fallacy of perpetual growth in biomedical research is, according to Alberts et al., a hypercompetitive climate that is counterproductive to sustaining high quality science [1]. Increased competitiveness for funding, in which the gap between demand and supply continues to widen, has had several negative consequences. The time-sensitive pressure to publish can diminish the rigor of experimental design and reproducibility and promote a "quantity over quality" mindset. Investigators are also hesitant to propose "high-risk" investigations of fundamental, evolutionarily conserved processes in favor of established concepts more likely to succeed within the constraints of a limited timeline and budget. In parallel, reports of failures to prove a hypothesis (i.e. presentations of unglamorous negative results) have decreased, in nearly 25 years, from 30% to less than 14% of original research publications, despite the considerable importance of postulate testing [5]. A direct result is that recent examinations of preclinical cancer findings discovered reproducibility rates of less than 50% [6]. The same group found that 21 irreproducible studies, published in upper-tier journals, continued to be heavily cited in later publications, suggesting a persistence of flawed conclusions that may corrupt subsequent clinical trial success rates [6].

Taken together, decreased NIH grant success rates, scarcity of academic positions, and a hypercompetitive and risk-averse research climate has effectively disengaged many highly trained and imaginative scientists. Many of these scientists were trained using public funding, thus representing a poor return-on-investment of human capital. Viable alternative approaches are needed to reengage displaced biomedical scientists and infuse new ideas and energy into the biomedical research community.

To address the imbalance between research workforce supply versus demand and increase scientific quality, several proposals have been set forth. One is to limit the number of PhD and postdoctoral trainees, and encourage the hiring and retention of "staff scientists", i.e. non-trainee MS or PhD awardees having greater autonomy and research administrative capability [1]. Another proposal is to encourage local institutional support for new infrastructure and faculty wages by capping academic institution "indirect costs" and the percentage of allowable faculty salary support from grants [1]. A third recommendation is to prohibit predoctoral student support from investigator grants and shifting support to training grants or competitive fellowships [2]. Another movement, including the recent NIH Broadening Experiences in Scientific Training (BEST) initiative, is to train PhD students for non-academic research careers, including those in the biotechnology, pharmaceutical, and government sectors. All of these proposals would serve ultimately to reduce the supply of incoming scientists and rebalance the workforce.

Changes to the current funding system have also been proposed, including limiting the trend of renewing large program grants (at times, for decades) to specific groups, and offering long-term awards to encourage basic research (similar to the model of the Howard Hughes Medical Institute, HHMI) [1]. The 2004 development of the NIH Director's "High-Risk/High-Reward" Pioneer program was similar in scope and proved as efficacious as the HHMI program. That program was part of a greater NIH initiative, the "Roadmap for Medical Research" (a.k.a. "Common Fund", https://commonfund.nih.gov) that funded 21 exploratory interdisciplinary centers to promote "team science" investigation of complex biological questions. Notable successes of the Roadmap were the development of large public datasets, innovative tools and technologies, and cross-discipline student and postdoctoral training [7]. One study also found that the number of publications by interdisciplinary groups exceeded those resulting from equal numbers of individual funding awards [8]. However, the 2% annual funding for the Roadmap initiative fell short of its 5% allocation goal and, in some cases, created unsustainable new transdisciplines [7].

Various recommendations have also been made to increase scientific quality. One is to encourage articles examining the reproducibility of previously published studies. To discourage data "cherry picking", decreased statistical rigor, and cutting corners (all contributors to irreproducibility), an interesting proposal is journal acceptance of a study *before* its performance (regardless of outcome). This is largely aimed at increasing the translational success rates of compounds found preclinically promising [6]. Advocacy has also increased for alternative measures of research success ("altmetrics"), such as contribution of public datasets, software developments, and blog entries; to that end, the National Science Foundation now requests grant applicants to list "research products" rather than "research publications" [9]. Another approach, albeit controversial, is the emergence of journals practicing "post-publication" peer review. These journals are a subset of "open access", web-based publications disseminated freely, that allow all readers, rather than a few reviewers, to evaluate study quality. Such a process could effectively increase scrutiny and reduce journal retractions of articles accepted for publication via the traditional "prepublication" review process [9]. However, while all these proposals would enhance scientific rigor and improve the availability of academic positions over time, they fail to address the immediate problem of how to reengage scientists displaced or disheartened by the current research climate.

As mentioned above, the supply/demand imbalance of academic positions has motivated many PhDs to pursue non-academic careers [4]. Alternatively, however, a distinct number of individuals desire to continue pursuing specific aspects of academia, including originality of ideas, critical thinking, and independent research, without a traditional academic affiliation [10]. These persons include those displaced by the academic job market and those who freely leave academia due to institutional dissatisfaction, geographical constraints, family matters, and time limitations. While these "independent scholars" have been present now for several decades, they have largely remained unorganized, performing their work remotely (largely from their homes) [10].

The downsides of independent scholarship are obvious: low pay, isolation from like-minded colleagues, and considerable skepticism of their work by university-affiliated faculty. Some organizations have arisen to support these individuals. The first of these, the National Coalition of Independent Scholars (NCIS), founded in 1989, was composed largely of historians [10]. Another group, Hidden Scholars, founded in 2012 as a support and networking group for part-time academicians and adjunct faculty in New England, began to include some "hard" scientists [10].

As more and more biomedical scientists exit the academic workforce, scholarly associations now include a large number of highly trained researchers. Through their academic experiences, many of these researchers have enlisted former co-workers with existing institutional affiliations. This unique pairing of academic and non-academic minds allows for the possibility of research consortia ("team science") in which multi-institutional and independent researchers can collaborate to solve complex problems. The Ronin Institute, Harvard's SBGrid Consortium, and the Complex Biological Systems Alliance are examples of established independent virtual platforms aimed at providing their members highly collaborative research environments that include access to academic journals, high-performance computing, advanced analytical tools, and discussion forums. A concept that has been developed for expediting biotechnology "start ups", i.e. "incubators" for laboratory space rental, could also be parlayed for non-profit use by research consortium members. Such incubators exist nationwide, usually in association with major universities, and receive start-up financial support provided from local economic development agencies.

Research consortia may also strive to raise private funding from intellectual property licensing and commercialization, venture capital investment, grants, and endowment monies for their members and partners. Non-profit status also provides members an alternative affiliation for seeking public funding [10]. This approach is quite similar to the NIH Roadmap's "team science" concept mentioned above [8], with the exception that the collaborative alliance is formed prior to petition for research monies. Such team science-based models could help alleviate the current "all or nothing" method of allocating funds to single laboratory groups, and counter the current hyper-competitive climate increasingly viewed as detrimental to scientific pursuit. Continued expansion of research consortia could reengage disenfranchised scientists and introduce novel ideas and approaches to publically funded projects. As many of these independent researchers were trained using public funds [2], research consortia could effectively increase the return-on-investment of postgraduate education.

In summary, while the problems facing U.S. biomedical research are formidable, many innovative recommendations, by leaders from all sectors of the research community, have been set forth to "right the ship" [1]. Biomedical research consortia are a particularly attractive means to tackle the challenges facing the scientific community. Scholarly consortia could enhance research participation and leverage the skills of diverse, highly trained and dedicated scientists toward non-traditional research. As such, research consortia could play an important part in fulfilling the NIH's mission of "seeking fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability".

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