IN DEFENSE OF ANIMALS

April 16, 2009

President Barack Obama
The White House
1600 Pennsylvania Avenue NW
Washington, DC 20500

Dear President Obama:

At the onset of World Week for Animals in Laboratories (April 18 – 26, 2009) and a day after millions of hard-working Americans paid their taxes to the federal government, we write to express our concerns about the $10.4 billion given to the National Institutes of Health (NIH) under the American Recovery and Reinvestment Act for 2009. These monies are in addition to the NIH's budget of $30.3 billion for 2009. Without safeguards to ensure that the money is spent judiciously and effectively, this part of the stimulus package will result in a TARP-like scenario – but with potentially graver consequences for human health and long-term U.S.-based biomedical research.

In Defense of Animals (IDA) bases this conclusion on 25 years of experience in a watchdog capacity over the NIH's funding of experiments on animals (which by some estimates accounts for 40 percent of the agency's research budget). Time and time again, we have uncovered wasteful and inhumane animal experiments that were funded by NIH grants for years, sometimes decades, with only the most tenuous claims made to medical breakthroughs. We have come to understand that a "good old boys" network in the peer review system perpetuates the use of outdated animal research methods at the expense of innovative and modern research methodologies that do not involve animals.

This is why we request that the entire $10.4 billion in stimulus funds be directed exclusively toward the funding of non-animal methods. This would include much-needed funding for clinical and community-based prevention and wellness programs.

Funding animal experiments at expense of prevention programs is bad fiscal and health policy

At the White House Forum on Health Reform last month, you stated that prevention is a key component to improving Americans' health. Yet while the stimulus package gives $10.4 billion to a fundamentally flawed oversight and funding system at the NIH, just $650 million of stimulus money is earmarked for addressing chronic disease rates through evidence-based clinical and community-based prevention and wellness strategies at the HHS Prevention and Wellness Fund. Instead, much of the NIH stimulus funding, as well as the NIH's $30.3 billion regular budget, will underwrite outdated animal experiments that search (unsuccessfully) for a magic bullet to cure or ameliorate uniquely human, life-style related illnesses that could be successfully addressed by clinical and community-based prevention and wellness programs.

We believe this approach is poor and health fiscal policy. Indeed, a 2008 report issued by the Trust for America's Health concluded that an investment of just $10 per person annually in programs related to

physical activity, improved nutrition and prevention of smoking could save $16 billion in five years while resulting in healthier Americans.

Wasteful, ridiculous, federally-funded experiments abound

Our long-standing criticisms of the NIH have been substantiated by a compelling body of economic and demographic research that suggest the NIH grant awards system is fundamentally broken, and has a history of oversight problems. The system perpetuates outdated, useless experiments and is rife with malfeasance and misconduct. The research indicates that the doubling of the NIH's budget between 1998 and 2003 is in part responsible for these problems.

We list here condensed summaries of studies that have been supported in part by federal tax dollars:

- Toy preference of juvenile monkeys. (Conclusion: Females prefer plush toys whereas males show a strong preference for wheeled toys).
- Nipple preference in infant monkeys. (Conclusion: Monkeys develop left vs. right nipple preference after 48 hours; siblings preferred the nipple not used by the previous infant.)
- Effect of high fat diets on wakefulness in mice. (Conclusion: High-fat diets make mice fat and sleepy, i.e. increase body weight of mice, but reduce their wakefulness.)
- Effect of stress and isolation on voles. (Conclusion: Prairie voles have less anxiety than meadow voles in response to social isolation and stress-inducing maze activity.)
- Effect of cocaine on Japanese quail. (Conclusion: birds addicted to high doses of cocaine showed increased locomotor activity after suffering withdrawal for 10 days and then being injected with half the high dose of cocaine.)
- Effect of social separation on wound healing in mice. (Conclusion: prolonged separation delays wound healing in monogamous mice, but not in polygynous white-footed mice.)
- Effect of exercise on rat health. (Conclusion: Rats allowed unlimited exercise are healthier than rats prevented from exercising.)
- Binge-like alcohol exposure in 4-9 day old rats (Conclusion: impairs learning ability later.)
- Rats subject to uncontrollable stress developed greater dependence on nicotine.

All but the last of these examples were culled from just three out of the thousands of published scientific journals. Although the federal grants that have supported these studies also have supported many other experiments, we believe these samples illustrate an extremely broad-based problem.

NIH grant award system is fundamentally broken

A "good old boys" network in the NIH's peer review system perpetuates the use of outdated research, much of it involving antiquated and irrelevant animal "models," at the expense of innovative and modern research methods that will advance human health.

This concern is shared by many in the scientific community, as evidenced by an NIH-financed survey of 3,247 NIH-funded researchers. According to results presented at a 2007 international conference on research integrity to foster responsible science, between 59 and 98 percent of early-career and mid-career investigators agreed or strongly agreed with the following statements:

- "The 'peer review' system of evaluating proposals for research grants is, by and large, unfair; it greatly favors members of the 'old boy network.'"

- "The top people in my field are successful because they are more effective at 'working the system' than others."
- "Eminent scientists and scholars are more likely to receive research grants than others who submit proposals of about the same quality."

The fundamental problems at the NIH were further elucidated by a March 2008 study in the prestigious scientific journal *Nature*, which found 22 scientists received 222 grants worth over $170 million from the NIH in 2007. *Nature* reported a climate of "anxiety and fear" where talented young researchers repeatedly have their grant proposals rejected, while the NIH funds significantly more people over age 70 than under age 30. Then-NIH Director Dr. Elias Zerhouni cited the doubling of the NIH budget as a reason for many of the problems with grant funding.

The frustration of these talented young researchers could have long-term, devastating impacts on human health and the viability of U.S. research, since "[H]istory suggests that the most dramatic innovations come from the young." It appears the NIH's systemic problems are already leading to young researchers leaving academia for industry. According to the 2008 article "Be Careful What You Wish For: A Cautionary Tale About Budget Doubling," written by economists from Harvard and the London School of Economics, "In 1980, 22% of [NIH] grants went to researchers 35 or younger, but in 2005, only 3% did. In contrast, the proportion of grants going to scientists 45 and older increased from 22% to 77%, and within the 45 and older group, the largest gainers were scientists aged 55 and older."

The researcher who led the NIH-funded survey, Dr. Brian Martinson – who has received several NIH grants himself – used the term "ageing cash cows" in his 2007 *Nature* article (attached) referring to investigators at universities that depend on NIH grants for indirect costs and funding faculty salaries. He stated that "**Calls for further increases to the NIH budget are a facile response from institutions overly dependent on NIH dollars. But they are an incomplete, and potentially dangerous, answer to the problem of excessive competition."**

Dr. Martinson cites the predictable, deleterious consequences of the NIH budget doubling: in 1998 there were about 19,000 scientists competing for continuation awards; in 2006, there were 34,000. He calls senior researchers who have benefited universities by getting grants – such as the 22 researchers who received over $170 million in 222 grants uncovered by *Nature* – as being on the NIH dole, likening them and their employers to addicts who need the NIH "fix."

Rampant scientific wrongdoing

Dr. Martinson has also published stunning results gleaned from this NIH-funded survey regarding self-reported scientific misbehavior, ranging from falsifying data to using inadequate research designs to using funds from one project to get another done to cutting corners to complete a project. This litany includes 27 separate misbehaviors, and astounding, profoundly disturbing percentages of NIH-funded researchers who actually admit participating in them. Please see the attached table documenting these shocking survey results.

This malfeasance can be attributed in large measure to the woefully deficient oversight of NIH-funded research from the agency itself. Relying on a policy of institutional self-regulation, the agency has historically had a laissez-faire attitude toward both research integrity and animal welfare.

In 2003, the House Committee on Energy and Commerce launched an investigation of the NIH's management and oversight of billions of dollars in taxpayer-funded grants after finding that the agency

had continued to fund a lab – the Coulston Foundation – that had repeatedly violated federal animal welfare and data integrity regulations, commenting that "This incident raises the question whether NIH oversight ensures that its grant funds are properly managed." That investigation was based in large part on information uncovered by IDA.

Another TARP-like Scenario?

Given the structural deficiencies for research funding by NIH and in light of the evidence that past large budget increases have exacerbated these problems, we strongly believe that the multi-billion-dollar giveaway to the NIH under the guise of "stimulus" money is a colossal mistake in the absence of a serious plan for reform. It is a set-up for another TARP-like situation, where taxpayer money disappears without proper oversight and is blatantly misspent by the recipients of the bailout. The NIH's history of woefully deficient oversight heightens these concerns. Previous large funding increases at the NIH have already been attributed as the cause of many of the fundamental problems with the current grant funding system.

Intent of stimulus funding ideal for modern, non-animal research

The challenge areas identified for the NIH stimulus spending – e.g., clinical research, genomics, information processing and stem cell research – are ideal for the funding and expansion of non-animal methods. Increasingly, there is broad acknowledgement among scientists of the superiority of human-based research methods, like clinical research and tissue and organ cultures, which provide fully relevant results and do not suffer from species-specific disparities. The landmark 2007 National Research Council report "*Toxicity Testing in the 21st Century: A Vision and a Strategy*" called for less reliance on animal studies, and a 2008 Memorandum of Understanding between the Environmental Protection Agency and the NIH aims to reduce reliance on animal testing by using the NIH Chemical Genomics Center's high-speed, automated screening robots to test suspected toxic compounds using cells and isolated molecular targets instead of animals. This and other rapidly progressing technological breakthroughs are the future of biomedical research for the 21st century and beyond.

Your new administration has vowed to scrutinize the federal budget to eliminate waste, and you said in your eloquent Inaugural Address that "*The question we ask today is not whether our government is too big or too small, but whether it works….Where the answer is no, programs will end.*"

In these dire economic times, it is essential to eliminate the waste of federal funds on cruel and unnecessary animal experiments, fix the broken research funding system that perpetuates them, and fund programs that will directly improve Americans' health, such as clinical research, prevention, epidemiology, genomics, proteomics, and nanotechnology.

Many thanks for your consideration.

Sincerely,

Elliot Katz, DVM, President

Enclosures (Table of Self-Reported Misbehaviors by NIH-Funded Researchers, 2007 *Nature* article)

Table 2

Numbers and Percentages of 3,247 Early- and Midcareer Scientists Who Reported Having Engaged in One or More of the Behaviors Listed in the Given Category Within the Previous Three Years, 2002*

Category and questionable behaviors within it	No. (%) early-career respondents (No. = 1,479)	No. (%) midcareer respondents (No. = 1,768)
Data	402 (28)	454 (27)
Falsifying or "cooking" research data		
Dropping observations or data points from analyses based on a gut feeling they were inaccurate		
Overlooking others' use of flawed data or questionable interpretation of data		
Failing to present data that contradict one's own previous research		
Methods	529 (37)	684 (40)
Using inadequate or inappropriate research designs		
Inadequate record keeping related to research projects		
Withholding details of methodology or results in papers or proposals		
Policy	640 (45)	722 (43)
Ignoring major aspects of human-subjects requirements		
Circumventing certain minor aspects of human subjects requirements (e.g., related to informed consent, confidentiality, etc.)		
Ignoring minor details of animal care policies		
Ignoring minor details of materials handling policies (biosafety, radioactive materials, etc.)		
Relationships with students, research subjects, or clients that may be interpreted as questionable		
Use of funds	557 (39)	1,215 (72)
Using organizational resources for outside consulting work or other personal purposes		
Using funds from one project to get work done on another project		
Outside influence	392 (27)	893 (53)
Not properly disclosing involvement in firms whose products are based on one's own research		
Unauthorized use of confidential information in connection with one's own research		
Changing the design, methodology or results of a study in response to pressure from a funding source		
Modifying research directions or agendas to fit the priorities of funders		
Peer review	217 (15)	518 (31)
Inappropriate or careless review of papers or proposals		
Providing an overly positive or overly negative letter of recommendation		
Credit	186 (13)	328 (19)
Using another's ideas without obtaining permission or giving due credit		
Inappropriately assigning authorship credit		
Trying to get by on the work of others		
Publishing the same data or results in two or more publications		
Cutting corners	713 (50)	1,112 (66)
Inadequate monitoring of research projects because of work overload		
Cutting corners in a hurry to complete a project		
Signing a form, letter, or report without reading it completely		

* Respondents were from a 2002 national survey of 4,160 early-career and 3,600 midcareer biomedical and social science researchers supported by the NIH. Note that the table presents valid percentages, adjusted for missing values.

had not received separate or integrated training in research ethics. We reiterate that all respondents whom we categorized as not having received ethics training reported so on the survey. It is possible that some of these respondents did not remember their research-ethics training, but this possibility is not encouraging.

In general, respondents who received training in research integrity differed little in their subsequent reported behavior from those with no training in research integrity, at least in the categories of problematic behavior that we examined. It may be that RCR instruction does not typically address these behaviors, though it would seem that an effective research-integrity program would provide some guidance

COMMENTARY

Universities and the money fix

Funding woes plague US biomedical researchers. But calls for more funding ignore the structural problems that push universities to produce too many scientists, argues **Brian C. Martinson**.

Federal funding for biomedical research is a substantial investment in the US science community. Earlier this year, representatives of several major research universities testified before Congress and issued a report arguing that the budget of the National Institutes of Health (NIH) in Bethesda, Maryland, is insufficient to sustain "a strong and vibrant program of basic research"[1]. They pointed to stifling of innovation and damage to the career prospects of young scientists, ultimately warning that there could be a threat to US pre-eminence in biomedical research if Congress does not increase levels of funding for the NIH. Yet, what is it that poses the most potent threat to the future of biomedical research — a lack of resources, or our failure to manage the level of competition for available resources? The answer to this question is vital if society is to gain maximum benefit from the public money invested in biomedical research.

B. MELLOR

There is undeniably excessive competition for NIH grants, and we should all be concerned about the negative effects this may have on the robustness of the research engine; by damping scientists' willingness to pursue high-risk projects; by causing them to spend excessive time in pursuit of funding; or by causing talented individuals to shun research careers. Yet, largely because of the structure of the funding flows between the NIH and the universities, there are few checks in the system to keep competition for grant funding at a healthy level. Thus, calls for further increases in the NIH budget may only make matters worse. In my view, it is time to ask the biggest beneficiaries of NIH largesse — the universities and academic health centres — to find ways to balance supply and demand that better reflect their obligations to researchers and society.

University leaders know that when the money gets tight, it's junior faculty members who feel the pinch. They are less established in their careers, more peripheral to their professions and institutions, and often most dependent on obtaining NIH funding as an implicit or explicit condition of their continued employment. As NIH funding becomes harder for junior researchers to obtain, we might expect them to experience the elevated levels of depression, anxiety and job dissatisfaction documented in a survey[2] of medical faculty members in 2006. We might also expect the greatest effects to be felt by female scientists and those from minority groups, for younger researchers to leave science, and to see somewhat less ethical behaviour among those who stay. The robustness of the research engine must be judged on more than the level of funding or the number of scientists.

The doubling of the NIH budget between 1998 and 2003 was intended to increase success rates in obtaining NIH grants[3], which have been declining since the mid-1970s. Yet, the budget rise did not have its intended effect, and by 2003, grant-application success rates were slightly worse than before. What happened? The budgetary increases were swamped by an equally large escalation in the number of NIH applicants and applications (see graph, overleaf)[4]. In 1998, there were about 19,000 scientists applying for competing awards; in 2006 there were approximately 34,000.

Since the 1970s academic researchers in biomedicine and the institutions that employ them have become increasingly dependent on NIH dollars[5]. The financial reasons for this are simple. The 'direct costs' of NIH grants cover the fixed costs of faculty salaries, whereas 'indirect cost recovery' pays for operational overheads, capital equipment and other expenses. Federal training grants also provide revenue streams for doctoral and postdoctoral training, directly stimulating workforce growth. Even before the doubling in funding, the Bayh–Dole act of 1980 created incentives for universities to grow their NIH workforce by permitting employers to own the inventions their employees created with federal funding.

Ageing cash cows

As dependence on NIH grants has grown, they have also become harder to obtain, especially for junior scientists. The average age at which PhD scientists earn their first independent support from the NIH has increased steadily[6], from 34 in 1970 to 42 in 2006. The situation has certainly been made worse by the flat NIH budget (declining after taking inflation into account) since the end of the doubling initiative. Yet, the excessive demand for NIH funds predates the recently flat budget (see graph, overleaf). Since the early 1980s new investigators have been entering NIH funding at a more rapid rate than experienced investigators have been exiting[4], leading to a population increase.

With academic faculty members seen as revenue generators, they are encouraged in subtle and not-so-subtle ways to expend greater effort on lucrative activities: this has made research a preferred activity over teaching or patient care. It also means they must spend a substantial amount of time writing grants. This arrangement generally works in the universities' favour, but the downsides of the dependence on NIH funding are becoming harder to ignore.

For too long now, financial incentives to the universities have been aligned to promote unlimited growth in the number of

biomedical researchers seeking funding from the federal government, despite the realities of finite resources. Some have suggested that a solution lies in biomedical researchers and universities becoming less dependent on NIH money by finding commercial funding sources and philanthropies[7], but this approach is not without its own risks, and it avoids dealing with the structural arrangements that keep us from applying sound principles of supply and demand to the scientific workforce.

We need to look at both the supply and the demand sides of the NIH funding equation. Most who worry about these issues have focused on the size or distribution of the pool of NIH dollars. Far fewer have given consideration to the size or dynamics of the population of biomedical researchers living on NIH funding. Few have overtly asked the question — are there too many biomedical scientists?

There are insufficient 'feedback loops' linking the production of biomedical researchers to the availability of resources to support them. Instead, the educational system is replete with incentives to generate ever more PhDs and medical doctors. In the short term these arrangements may benefit universities, but in the longer term, such extreme levels of competition for funding are unsustainable. And they may already be doing harm. Difficult funding decisions are increasing ill will, perceptions of injustice, and eroding the bases of ethical behaviour among academics. Some of my own work leads me to believe that the current situation may be adversely affecting the integrity of research[8].

The needle and the damage done

The imbalance between the supply of NIH funding and the potentially unlimited demand for grants threatens the future of US biomedical science. I have argued that because of structural incentives, demand for NIH grants is largely a function of the size of the biomedical workforce. Recent NIH initiatives to increase funding of junior researchers are welcome, and have the best chance of maintaining a pool of new research talent. But without some counterbalance, these initiatives may escalate competition for grants.

B. KRIST/CORBIS

Campus overload: are universities producing too many biomedical scientists?

Calls for further increases to the NIH budget are a facile response from institutions overly dependent on NIH dollars. But they are an incomplete, and potentially dangerous, answer to the problems of excessive competition. And although short-term NIH budget increases to make up for inflation-related declines since 2003 seem reasonable, further increases risk fuelling, rather than reducing, demand. For now, budgetary increases that simply keep pace with inflation would seem prudent, so as not to reactivate the growth impulse. Regrettably, the current imbalance may be addressed only through a reduction in the biomedical workforce; something that already seems to be happening.

"What is needed is not necessarily more people, but more time, space and freedom."

There are two main routes to contraction of the academic workforce today — through tenure failures, and with younger investigators shifting from academia into industry research[8]. This is worrisome for university research in particular because history suggests that the most dramatic innovations come from the young. So is the only solution to force long-time NIH grant getters into retirement? Perhaps not. Universities have benefited handsomely from the efforts of senior faculty members in securing NIH grants during their careers, perhaps those same universities could now return the favour by taking full responsibility for paying these faculty salaries in their later years. This would serve the dual purpose of getting them off the NIH dole, and encouraging them to share their knowledge with their younger colleagues through more teaching.

This won't be easy. Given the levels of dependency on NIH money, it is akin to asking an addict to give up an easy fix. And not all universities will be in financial positions to employ this strategy, but it's difficult to imagine that richer institutions — some of whom acknowledge that their success lies in capturing an increasing share of the NIH pie[9] — could not lead the way in this. Prospective students and their parents may also look favourably on senior faculty members spending more time teaching.

An implicit assumption underpinning the current system of funding is that having more biomedical scientists automatically leads to greater innovation and more breakthroughs. Yet what is needed is not necessarily more people, but more time, space and freedom for existing researchers to ask questions in new ways, to be willing and able to take risks, and to innovate rather than simply writing safe, incremental grants. The excessive competition for NIH funds discourages this kind of risk-taking, and ultimately reduces opportunities for the sort of creative thinking that leads to major scientific breakthroughs. ■

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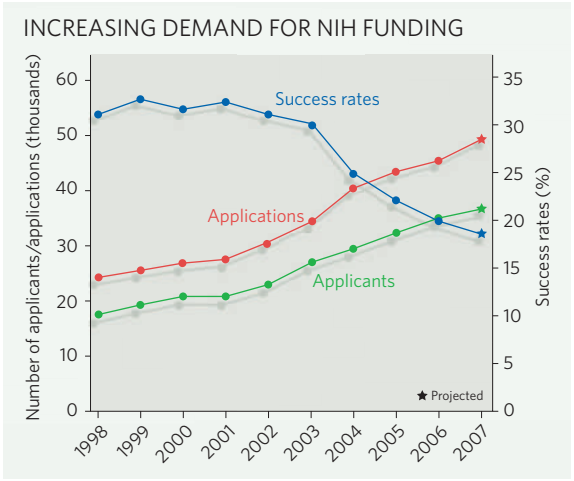
FASEB/NIH/SCIENCE



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