

**Urgent needs that a new director of NIH must heed to (8 point formula):**

Over the last 8 years NIH has become more driven by politics, more controlled by top administrators, and diminished resources for sustaining the research efforts of the US biomedical community. The details of the devolution remain complicated and will not be discussed here. It should, however, be emphasized that these negative trends were facilitated by the disinterest of the administration in the main product of NIH, namely fundamental medical research, and perhaps best gauged by continued efforts to deny any substantial funding increases to NIH for 8 years. Therefore, there is a sense of real urgency regarding the preservation of the fundamental values of an institution that has funded and thus directly nurtured and produced the world's best medical science. As other countries copy the values of NIH and attempt to create similar institutions, the best and most successful is in danger of being slowly dismantled.

The history of NIH attests to the success of individual investigator initiated research, and this point has been commented on repeatedly in the past. The individual R01 research conducted in individual research labs (both large and small) has and continues to be the most innovative and fruitful approach in developing new understanding in biomedical research (neither the scientific nor bureaucratic branches of NIH contest this claim). Recently, a long list of other funding mechanisms was created (blueprint, transformative, training, & others) and the relative quantity of funds siphoned away from R01-s remains unknown to the public and to the medical research community. In this realm there are very simple steps that can be taken and these will have a profound influence on NIH: **1) financial transparency:** It is amazing that the public dollars dedicated to NIH are not visible to the public or to the scientific community. The NIH administration posts only very minimal information regarding distribution of resources. Somewhere within NIH this information is available and it should be available to the public. We all need to know the exact distribution of resources, not only in disease category, but also the breakdown of the resources in specific research topics, in specific universities and scientists, as well as the type of grant mechanisms. **2) Strengthening the emphasis on investigator-initiated science, and especially the young scientist:** The simplest approach in this regard would be to insure that some fixed amount of the NIH research budget (e.g. > 80%) be dedicated to R01 funding. Although the last administration insisted that they attempted to protect R01 funding, one remains skeptical as long as the details of the NIH budget are not fully disclosed. It should be mentioned that NIH has recognized the plight of the young scientist in times where funding levels have plummeted and they need to be commended for taking steps to help new investigators by imposing lower funding thresholds for this group (around 20% cutoff). Given that the majority of these young investigators enter tenure track positions at universities where very rigorous competition and evaluation takes place, the threshold for funding new investigators can be further lowered especially for tenure track new first time applications (maybe a threshold closer to about 50%).

The bedrock mechanism upon which funding of R01 applications has traditionally been decided on is the peer scientific review conducted in Study Sessions, where priority scores are supposed to indicate a judgment as to the merit of an application and hence its funding priority. With essentially zero additional funding in the last 8 years this process has been direly tested and shown weaknesses (reviewers being frustrated as they attempt to discriminate between the best 5-10% of the applications, and NIH administrators being frustrated by their inability to recruit the most qualified scientists to participate in the reviews). Here NIH seems to have decided to down grade the review process (the latest idea is that only 2 cycles of reviews are accepted in applications), which by default strengthens administrative decisions (more influenced by political winds) and in many instances NIH seems to over ride the reviewers decisions and fund grants with lower priority scores (i.e. choose to fund a worse application based on institutional priorities). The funding decision process remains obscure and unavailable to the public and to the research community. Here too transparency would go a long way in dispelling these mysteries. The latter requires precisely stated set of rules regarding the decision making process for awarding funds, that is: **3) decision-making transparency.** The selections of reviewers and council members are often arbitrary and non-transparent, with no objective evaluation of performance. A second approach to strengthen and rationalize grant application assessment would be **4) to engage the medical/scientific community in a bottom-up**



manner, where the scientists and medical professionals take direct responsibility for selecting/nominating and then monitoring the performance of reviewers. At the moment, reviewers are selected by NIH staff. The scientific community should be encouraged to take ownership of this process, nominate reviewers through scientific societies or other professional organizations, and then evaluate their performance using objective criteria in a structured assessment of the outcomes of grants that are funded based on the recommendations of specific reviewers. The reviewers in such a process could be compensated by the provision of small grants to enhance their research, as well as earn the respect of their societies by being selected based on a merit system.

Research is the act of exploring uncharted territories of thought. Yet, with limited budgets the grant dollars tend to be so tight that even in successful labs there are few financial resources to explore new ideas/directions. **5) To foster new directions of research perhaps every R01 should include innovation funds** (e.g. an additional ~10% of the budget), which are expected to be used for explorative research.

The last administration of NIH emphasized translational research as well as funding for training students/post-doctoral fellows/clinical scientists and helping universities setup core facilities. The imposition of translational requirements (mandating inclusion of clinical trials or study of human samples) often conflicts with the scientific priorities of individual investigators, and falsely provides the notion of accelerating development of ideas into the clinical realm when not all of the requirements of scientific rigor have been met. Additionally, these mechanisms frequently do not provide sufficient funds for scientifically valid translational studies, a famous example being the SPORC programs of the NCI. Thus relatively large amounts are set aside for programs that are sometimes artificially forced to “translate”. The right balance of basic and translational research is predicated on the presence of basic findings that beg translation. Allowing scientists and clinicians to set the agenda for translation is more likely to produce science that demands translation. For the most part, the rewards of translating from lab to clinic are large enough in our society that scientists will actively seek out translational opportunities; when they do, the funds awarded need to be large enough to enable fruitful clinical developments. Therefore, **6) the number of translational awards can be decreased, yet the actual dollars per project should be increased.**

The NIH funds used for student training and for building core facilities are in many ways commendable given the lack of resources for such programs. The graduate student is both the main workhorse for generating new research as well as the future independent researcher/scientist. His/her participation in R01 funded milieu is fundamental for both the lab and for the participant. From this perspective training grants seem far too restricted mechanism for nurturing graduate students. To further empower R01 funded researchers and encourage graduate student participation in it, graduate students who join a lab with R01 funding should receive full stipend coverage directly from NIH, preferably with minimal or no review process, that is: **7) streamline graduate student funding (rather than the cumbersome NRSA program) and link it to R01 funded labs.**

Historically NIH has been the beacon of advancement of our understanding of our selves and the use of science to improve human health and well being. Generations of bright minds have been inspired to dedicate their lives to this process, giving up lucrative careers in private medicine and industry. The hope is to restructure NIH to regain this lure and guarantee that the best minds flock back into the field and participate in charting the future health of mankind. The state of biomedical research is at a very exciting point. There are tremendous new possibilities and opportunities for solving many of the health issues of mankind. These all require expansion of the medical science community that can only be achieved by increased funds. As Obama’s campaign has already promised to double the budget of NIH over the next 10 years, **8) a commitment for steady increase in funding NIH** (10-20% increase in the budget every year over the next 10 years) would provide the resources to implement points 1-7, inspire a whole new generation of medical scientists, and insure that the US biomedical research remains at the forefront of advancing understanding and thus also improving human health.



Formulated by Professor A. Vania Apkarian, in consultation with professors Haldar, Khan, and V.A. Apkarian. Due to the short notice this paper is being submitted directly to the Obama Transition Team focused on the National Institutes of Health. We will also circulate the paper to our peers and seek their endorsements.

Sincerely,

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