

# Can small institutes address some problems facing biomedical researchers?

Michael P. Sheetz

Mechanobiology Institute of Singapore, National University of Singapore, Singapore, 102275; Department of Biological Sciences, Columbia University, New York, NY 10027

**ABSTRACT** At a time of historically low National Institutes of Health funding rates and many problems with the conduct of research (unfunded mandates, disgruntled reviewers, and rampant paranoia), there is a concern that biomedical research as a profession is waning in the United States (see "Rescuing US biomedical research from its systemic flaws" by Alberts and colleagues in the *Proceedings of the National Academy of Sciences*). However, it is wonderful to discover something new and to tackle tough puzzles. If we could focus more of our effort on discussing scientific problems and doing research, then we could be more productive and perhaps happier. One potential solution is to focus efforts on small thematic institutes in the university structure that can provide a stimulating and supportive environment for innovation and exploration. With an open-lab concept, there are economies of scale that can diminish paperwork and costs, while providing greater access to state-of-the-art equipment. Merging multiple disciplines around a common theme can catalyze innovation, and this enables individuals to develop new concepts without giving up the credit they deserve, because it is usually clear who did the work. Small institutes do not solve larger systemic problems but rather enable collective efforts to address the noisome aspects of the system and foster an innovative community effort to address scientific problems.

Being honored to present the Porter Lecture has caused me to reflect on the discussion about the current National Institutes of Health (NIH) funding paradigm and to share a few thoughts. There are a number of concerns about the current system, ranging from the quality of the review of NIH grants to the paranoia that we will get scooped if we share our latest results in a scientific discussion. In addition, there is a major waste of resources on top-down projects to develop huge amounts of data without testing a hypothesis. However, things are not totally terrible. Objectively, the NIH budget is very large, despite the problem of too many scientists vying for a diminishing pot. Worldwide, there are increasing budgets for research, particularly in the East. If we could efficiently deal with some



Michael P. Sheetz

DOI:10.1091/mbc.E14-05-1017

Michael P. Sheetz is the 2014 Porter Lecturer for the American Society for Cell Biology.

Address correspondence to: Michael Sheetz (ms2001@columbia.edu).

Abbreviations used: MBI, Mechanobiology Institute; NIH, National Institutes of Health; PI, principal investigator.

© 2014 Sheetz. This article is distributed by The American Society for Cell Biology under license from the author(s). Two months after publication it is available to the public under an Attribution–Noncommercial–Share Alike 3.0 Unported Creative Commons License (<http://creativecommons.org/licenses/by-nc-sa/3.0>).

"ASCB," "The American Society for Cell Biology," and "Molecular Biology of the Cell" are registered trademarks of The American Society for Cell Biology.

of the increase in regulatory paperwork and break down barriers to sharing technologies across disciplines, then we could spend more time testing new ideas. The Marine Biological Labs provided an open environment for scientific exchange that greatly aided the

discovery of kinesin and the development of in vitro motility assays. Likewise, Bell Labs and the Laboratory of Molecular Biology fostered innovation with a strong emphasis on open scientific discussions and with outstanding facilities. Can this type of environment be developed in a university setting? Together with a strong group of international collaborators, I recently had an opportunity to start a small interdisciplinary institute in Singapore that was associated with the National University of Singapore. With some luck, trial and error, and a lot of hard work by staff and colleagues, we developed a system that may work in the U.S. context. The general concept was to provide excellent facilities for all investigators in an open-lab environment that encouraged open discussion of problems by researchers with different backgrounds.

We started the Mechanobiology Institute (MBI) in 2009 with a block grant covering about two-thirds of projected indirect and direct costs for 10 years (the remainder to come from outside grants). With the help of excellent support staff and the cooperation of all, an open multidisciplinary lab for 200 investigators (about half grad students and postdoctoral fellows) and 15–20 principal investigators (PIs) was operational by the end of year 3. Many of our PIs were initially skeptical about an open lab, but it provided benefits at multiple levels. First and foremost, the students and postdocs liked the open lab. It made collaborations simple, and they had easy access to all the tools and instrumentation. Further, we hired sufficient staff to manage the equipment and to instruct new students and postdocs in its proper use. Lab areas were managed by staff, which helped to keep order and maintain stocks of disposables. Postdocs were recruited by individual PIs, but other PIs were always involved in reviewing candidates. This aided both the selection process and recruitment. To encourage exchanges between groups, we assigned writing desks on a lottery basis. In a short time, these efforts created a sense of community that enabled meaningful scientific discussions on how to solve biological problems. In the current competitive environment, the institute provides an excellent environment for those who buy in.

The major emphasis was to create an environment in which investigators can solve scientific problems—not build lab empires, companies, or clinics. In a recent article in the *Proceedings of the National Academy of Sciences*, Bruce Alberts and colleagues document the increases in regulatory demands, difficulties in raising funds, and the cutthroat competitive environment that has arisen during the recent funding crisis (Alberts et al., 2014). Although some NIH-level solutions exist, and I support many of the measures proposed by Alberts et al., I feel that the most meaningful changes can be made at the level of small institutes of 12–20 PIs. At that level, there is an economy of scale to alleviate regulatory burdens, while maintaining accountability. My assertion is that small institutes in universities can be the most cost-effective way to undertake interdisciplinary research focused on major research problems. In the remainder of this article, I will describe one approach that succeeded in one environment, and I hope that others will be stimulated to improve on our efforts.

### GIVING THE RESEARCHER ACCESS TO THE TOOLS FOR PROOF OF CONCEPT

In designing a multidisciplinary institute, there was a conscious attempt to provide investigators with tools of other disciplines, so they could efficiently test hypotheses. A related issue is that young investigators could rapidly start doing research without a major effort to purchase and set up equipment. Good central facilities were key to providing biologists with the new generation of micro- and nanofabrication tools and physicists with molecular biology reagents and purified proteins for their studies. All were afforded access to the latest

microscopic technologies. To provide a high level service, we hired Ph.D.-level managers for the facilities with sufficient staff to train users and/or provide materials needed with information on the best practices in certain applications. Facilities offered tutorials and regular educational sessions for all investigators. To encourage the facilities to be responsive to the users, we asked that multiple PIs participate in facility management committees. This bottom-up approach has kept the priorities in touch with the user needs. After all, the money spent on the facilities was coming out of our common research funds.

### COPING WITH THE MUNDANE BUT NECESSARY ISSUES

The burden of paperwork for regulations for the responsible conduct of science, effort reporting, conflict of interest, safety training, animal care, and so on all detract from the time that can be spent on research. Most of these tasks can be fulfilled more responsibly by staff (with some PI input) than by individual PIs in separate labs. A team of lab managers was hired to handle such diverse tasks as safety training of new students, assembling best-practices protocols for routine operations (tissue culture, gel electrophoresis, etc.), and stocking disposables for the lab benches. Similarly, the microscope facility staff trained new students/researchers and kept the facility functioning. Microfabrication and cloning were performed by staff after consultation with the faculty and students. This system enabled the PIs, with the assistance of the staff, to satisfy the requirements of safety, basic training, and maintenance with minimal daily input. PIs met regularly with the facility staff to answer questions and assure that things were functioning properly.

### INNOVATION IS OFTEN INTERDISCIPLINARY

There is a lot written about innovation and even more discussion about it. Almost by definition, however, it is a process of unexpected random connections that enable new approaches or insights to solve problems. Those connections need to make sense to someone who can actually test new ideas, often with new tools. To facilitate innovation, it helps to have people with different backgrounds discuss a problem, because they will often benefit from one another's perspective. Such discussions are most fruitful when there are chance encounters over lunch, tea, or beer, as has been proven at Bell Labs, the Laboratory of Molecular Biology, and the European Molecular Biology Laboratory. Open labs lower the energy barriers to meeting people outside your lab, and then the discussions are easier. Small institutes provide good chances to bring together people with vastly different backgrounds and to encourage them to be adventurous. Having resources available also lowers the energy barriers to trying something new. Further, it is useful in institutes to bring in outside experts, because that stimulates everyone. With all of these features in place, innovation relies upon motivated researchers; the PIs need to encourage the pursuit of the unusual as opposed to the expected result. This occurs more often if there are seed funds designated for innovative experiments. Finally, in an interdisciplinary environment, it is usually easy to know who did which part of the work, and credit can be given to the proper person during evaluation for promotion.

### FUNDING OF SMALL INSTITUTES

A major drawback to the formation of small institutes is that they are expensive. However, our analyses show that there are real savings due to the economy of scale. For example, when we added up the cost of the central facilities (microscopy, cloning, microfabrication, computers, and wet lab management plus disposables) and divided it by the number of investigators, we calculated that the central services cost on average about \$15,000 per person per year. With

proper record keeping, these costs can be charged to grants. The overhead costs of facilities (heat, lighting, etc.) and faculty salaries and administrative costs for ordering, employment, and so on are commonly borne by the university. In many cases, those costs are significant and can account for 30–50% of the overall budget. To fund such an institute in the long term, there needs to be outside funding; a figure of 20–30% of the total budget is a common figure in Europe and Asia (more in the United States). A very important part of the budget is an internal seed grant to the PIs that provides funding for innovation and start-up. If PIs can support one to two researchers for innovative projects, then they can develop the successful ideas to the point that they can compete for outside funding. Because these funds are internal, they can be carried over from one year to the next to avoid hurried or wasteful spending at the end of a grant year. For ~20 PIs with an average lab size of approximately eight people, the cost for central facilities and the seed grants is about \$6 million per year after the initial capitalization. This is significant, but it is low compared with the internal budgets of most European and Asian institutes, where the total budget divided by the number of PIs provides an annual cost of \$1.4–2.2 million per PI. If the point of a research institute is to foster innovative research, then flexible research funds are critical for the researchers to be able to take risks.

### MAINTAINING VITALITY IN SMALL INSTITUTES

The Singapore government mandated a major feature of the MBI. Namely, members of the institute are members of departments at the university. This means that there can be fluidity between the departments and the institute. As the directions and the needs of the institute change, the PIs in the institute can change, without loss of tenure. This means that high standards can be maintained without major disruption to either the institute or the faculty member's career.

In regard to evaluating research performance, the stories of Sanger and the long time he spent to develop sequencing technologies serve to remind us that progress is not always measured in regular publications. Similarly, impact factor points don't really correlate with impact when we look back on the initial publications of

many important, novel findings. Thus, it is very difficult to strike a proper balance between accountability and the freedom to try something really new. With a site visit, an outside panel of experts can see the people in context and can better evaluate the performance. Still, no one has a crystal ball that sees into the future, and in the end, some difficult decisions need to be made for the vitality of the institute. In this regard, it is much easier for an administrative panel to move a PI from an institute to a department than from an institute to the street. Dynamics is a critical part of long-term vigor and can help to avoid the feelings of entitlement that sap the energy from many longer-lived institutes. Further, universities need to have teachers, and it is reasonable for young faculty members to have the chance to do research before they take on a large teaching load.

### SUMMARY

No system is perfect, but there are some glaring flaws in the U.S. system that perhaps will mean that other systems will do better in innovation and solving problems in the future. Moving to multidisciplinary institutes in universities can provide a much more efficient approach to research and to innovation. Multidisciplinary institutes also encourage a sharing of ideas and a questioning that is very healthy for the system. New technologies can easily be combined with old problems. Many of the problems in research are best approached with multiple techniques that are seldom done well in one lab. I put this idea forward with the hope that this or an even better idea can help the system to thrive. This is the best occupation in the world despite the current challenges.

### ACKNOWLEDGMENTS

I gratefully acknowledge the helpful comments of Linda Kenney, G.V. Shivashankar, Gareth Jones, and Ronen Zaidel-Bar. This paper was made possible by the generous support of the Singapore Government.

### REFERENCE

Alberts B, Kirschner MW, Tilghman S, Varmus H (2014). Rescuing US biomedical research from its systemic flaws. *Proc Natl Acad Sci USA* 111, E2634.