

A Responsibility to Experiment



NEARLY 10 YEARS AGO, JUST AFTER THE TRUSTEES OF THE Howard Hughes Medical Institute elected me as the Institute's fourth president, I had the opportunity to meet with the staff in the auditorium at our headquarters in Chevy Chase. There was an air of anticipation in the room, one that echoed the excitement I felt on the cusp of my new responsibilities to HHMI.

As a long-time HHMI investigator, I had great appreciation for all that had been accomplished under the leadership of Purnell W. Choppin, the man I was about to succeed. I thought—certainly at the time—that I understood the opportunities ahead. Yet, the journey has been more surprising, fascinating, and demanding than

I ever could have anticipated in May 1999. I know that my successor, Robert Tjian, can look forward to a similarly challenging and rewarding journey during his tenure.

So let's step back briefly to that moment in the auditorium—the scene of so many investigator meetings, the backdrop for the Holiday Lectures on Science, a space now named in memory of HHMI's legendary chief scientific officer, W. Maxwell Cowan. With the benefit of hindsight, the words with which I described HHMI's impact on my own research could just as easily apply to the role of the Institute within the broader scientific community. As I said at the time, "Howard Hughes has allowed us to go into some new

directions that we otherwise wouldn't have been able to. In fact, I think really it is more the other way around. I almost felt a responsibility to go in some new directions because we had the advantage of not having to rely on traditional sources of funding."

The responsibility to experiment has been a recurring theme of the past decade of my leadership. But before I mention a few of the Institute's recent experiments, I need to say that we experiment within the confines of a set of values—including freedom, flexibility, creativity, and integrity—that define HHMI's science-based culture.

These values have never been more important. The public has begun to express deep concern about the loss of objectivity that can occur at the intersection of science and commerce. At HHMI, we have remained tough-minded about Institute policies that reinforce our independence from company-funded research. Also, during this event-filled decade, the nation has twice endured periods of great financial upheaval. With the government's attention focused on issues related to national security, we have seen the impact of continued fiscal and political pressure on federal research agencies, particularly the National Institutes of Health (NIH). HHMI is hardly immune from these currents. Many of

our investigators also conduct research that is supported by the NIH, and they are based at medical schools, research universities, and institutes that are best served by steady year-to-year resources. The Institute's commitment to plan for long-term, consistent funding serves our scientists well.

Given the opportunity to examine our own programs and activities in the light of pressing national needs, I have worked with Peter Bruns to launch several new educational initiatives. The goal has been to expand opportunity in key areas: to promising college students who come from disadvantaged or minority backgrounds, to graduate students who want to study across disciplinary boundaries or to incor-

porate medicine into their Ph.D. studies, to physician-scientists at a variety of career stages who seek to combine research with clinical practice. On the biomedical research front, I first worked with vice presidents Gerry Rubin and David Clayton to expand the cadre of patient-oriented physician-scientists within the ranks of our investigators and later with Jack Dixon to open the investigator selection process to direct application from scientists. We have also taken steps to ensure that the results of our investigators' discoveries will be broadly shared within the scientific community.

One of the Institute's most visible experiments is the Janelia Farm Research Campus, which opened in 2006 along the Potomac River in Ashburn, Virginia. The notion of creating a freestanding campus with a distinct scientific culture arose in conversations I had with my colleagues Gerry Rubin and David Clayton in 1999. We touched on many subjects during those conversations, most notably the HHMI investigator program. That program seemed to be just the right size—a much larger program might have reduced quality and been difficult to manage—so we concluded that additional Institute resources should be invested in a novel direction.

According to our analysis, the research opportunities most

challenged at U.S. academic institutions were in the area of interdisciplinary research—bringing physics, chemistry, computer science, and engineering to bear on problems of biology. By building a research facility without departmental barriers, we thought we could catalyze such collaboration. As we looked for a suitable piece of property, we refined the scientific challenges that an interdisciplinary campus might address. The initial goals of what is now the Janelia Farm Research Campus are to understand the neural circuits that enable complex behavior and to create new imaging and computational technologies. Already, the campus has become a hive of activity for the resident scientists as well as for our



CBS reporter Leslie Stahl visited HHMI headquarters in 2003 to interview Tom Cech for a 60 Minutes story about the Institute.

investigators and their collaborators from around the world. Janelia Farm has added to—rather than subtracted from—the vibrant culture of HHMI’s investigator program and that, for me, is an important touchstone.

One area where HHMI charted an independent course concerns research involving human embryonic stem cells. HHMI enabled its investigators to work outside the constraints of a national policy that limited the stem cell lines that could be used and barred the development of new cell lines in federally funded research. We made our decision in consultation with outside advisors, including ethicists, and with the support of our Trustees. The care with which HHMI proceeded made the initiative no less bold. Our stem cell investigators, who aim to cure some of our most devastating diseases, have established new cell lines and have published important, sometimes surprising, findings on tissue development and regeneration.

Back in the 1980s, HHMI president Donald Fredrickson believed the Institute should locate its headquarters “inside the Beltway” so that it would be proximate to the NIH and the officials (elected and otherwise) who make important decisions about science policy in the United States. The decision to base HHMI in the Washington, D.C., area was prescient and has facilitated my interactions with the National Academy of Sciences, NIH, National Science Foundation, American Association for the Advancement of Science, and the numerous scientific societies headquartered in Washington. Often we find ourselves facing the same issues about biomedical research in the United States. These issues include the challenges early career scientists face and the cumulative effect of conservative funding decisions on innovation in America.

Last year, the Institute launched a new open-application competition to identify talented researchers at the very beginning

of their independent careers, between years two and six of their first academic appointments. We’re betting that unfettered financial support to these Early Career Scientists, coupled with the new interactions they’ll forge as part of the HHMI community, will have a big impact on their ability to develop full-fledged research programs.

This issue of the *HHMI Bulletin* highlights another response by HHMI to the current research environment. Jack Dixon, our chief scientific officer, has led the creation of the Collaborative Innovation Awards. Using HHMI investigators as the nucleus, we challenged them to assemble teams of scientists to tackle transformational research projects that are too big or too risky for any single laboratory to handle. If a quarter of these efforts succeed, HHMI will have done something worthwhile. That’s the whole point: we don’t want to be assured that these teams of scientists will solve the problem; we do want to ensure that they have the means to explore big questions.

As I prepare to return to my laboratory at the University of Colorado at Boulder—to focus more on some scientific questions of my own—I am deeply conscious of the fact that the Institute’s successes of the past decade reflect the contributions made by HHMI employees

around the country, the members of the Medical Advisory Board and other advisory groups, and, most particularly, the Trustees. Led by Hanna H. Gray, the Trustees have ensured that HHMI remains true to its mission as a medical research organization and lives up to the highest standards of excellence. Thank you for the privilege of leading this great organization.



Tom Cech presided over the 2003 groundbreaking of the Janelia Farm Research Campus. Since its 2006 opening, he has been a regular visitor for science meetings, workshops, and public lectures.

Thomas R. Cech