PRESIDENT'S REPORT

As the year covered by this report came to a close, we reached the end of the new century's opening decade. In the brief interval of 10 years, the American economy soared, crashed, and then soared and crashed again. And yet here at Cold Spring Harbor Laboratory, we remained on a remarkably even keel, blazing a trail forward on multiple fronts. One of the virtues of scientific research is that it does not come to an abrupt halt in hard times. Without a doubt, we are able to do more when all of the economic arrows are pointing upward. But it is a measure of the strength of our institutions that progress in science does not correlate, at least over the short-run, with the condition of the economy.

The challenges posed by the current recession have been by no means trivial. We have made a concerted effort to husband our resources and reduce costs while keeping at full strength the superb faculty and staff that has put us at the leading edge of discovery. Our base of private donors has risen to the occasion, as has the federal government, which wisely set aside additional funds for scientific research as part of a broad economic recovery and revitalization package. Our scientists performed admirably in the ensuring competition for one-time special funding.

The Laboratory has not simply weathered the storm—it has flourished. Our campus has not contracted along with the economy during the last year but rather has grown with our burgeoning research capabilities. The magnificently designed Hillside Laboratory buildings opened in June and provided our faculty with ~40% more space in which to perform their work. We will be adding faculty as funding permits, thereby enhancing our already world-class programs in cancer, neuroscience, and plant genetics research, as well as building a new center of expertise in the field of quantitative biology.

All of this is possible because of groundwork we laid in the first years of the decade. Extensive planning, coupled with both public and private generosity, enabled a plan made in boom times to come to fruition during a trough. Although I am fond of pointing out that science moves inexorably forward, it is important to qualify that science of the caliber performed at Cold Spring Harbor Laboratory is possible only because of careful forethought, periodic assessment of trends in research, and philanthropy that drives innovation.

As I survey the road ahead, I would be remiss if I did not offer some cautionary words. Although academic science has flourished during the past decade, as powerful new technologies have enabled us to reap the fruits of the many genome sequences that have been determined, the private sector has lagged behind. Ever since the technology bubble broke at the beginning of the decade, funds for value-added science have all but disappeared, and in the last few years, venture capital investment in the biomedical sciences has dropped precipitously. By value-added science, I mean the kind of research and development activity that adds commercial value to discoveries made by scientists engaged in basic research. Value-added science was once the purview of early-stage biotechnology companies. In the current environment, however, such companies are not being formed. Compounding the problem, pharmaceutical investment in research has also dropped, owing to the recessionary economy and a reduction in corporate income as major pharmaceuticals have gone off patent.

During the past decade, scientists at Cold Spring Harbor Laboratory have developed a rich collection of technologies for discovery and validation of new therapeutic targets, particularly for cancer. This followed from a deliberate expansion of our research into areas that are closer to the clinic, yet still strongly rooted in basic discovery. In the coming years, we shall increasingly be contributing to knowledge that is of great potential value to projects of national and global import, particularly in health-related sciences. But there are other areas in which biology can make a major impact.

This past year, the National Academy of Sciences Board on Life Sciences, of which I am a member, issued a report from a committee cochaired by Thomas Connelly of DuPont Company and Phillip A. Sharp, CSHL alumnus, MIT professor, and Nobel laureate. The report identified four grand challenges to which 21st-century biology might contribute in major ways: cultivation of food plants that will sustain

the growing global population, development of methods with which to sustain ecosystem function and biodiversity, creation of sustainable and economical alternatives to fossil fuels, and continued progress toward medicines that are increasingly coupled to individual experience and genetics.*

If what the National Academy committee calls the "new biology"—collaborative, multi- and cross-disciplinary science—is to rise to these challenges, I believe we who perform basic science and guide it at the institutional level will have to address one internal challenge and advocate for action on a related, but external, front.

The problem we must address within basic science concerns our relationships, individually and collectively, with private industry. The ability of academia and industry to collaborate has become clouded by controversy arising from recent disclosures of unreported financial arrangements made between private-sector companies, notably large pharmaceutical firms, and a small number of scientists and physicians. What can only be regarded as the undeclared greed of a tiny minority of academic scientists now imperils the health of the research establishment as a whole. Following the uncovering of a few cases in which clinicians received large sums of money from industry, sums deliberately hidden from their academic institutions, and later, from a Congressional investigation of certain medical schools, the entire academic community was tarred with the same brush. Some members of Congress have now caused the National Institutes of Health (NIH) to introduce regulatory reforms that are adding more detailed layers of reporting of conflict of interest. Remarkably, those that violated the previous and reasonable institutional policies have, as far as I know, retained their academic positions. Clearly if the few clinicians who blatantly violated their intuitional policies had been appropriately disciplined, we might have avoided the now more burdensome regulations and scrutiny that have been imposed. It is now the situation that if an academic scientist has a relationship with a company, motives are immediately suspect.

The solution is obvious. Full disclosure must be made by research scientists (and immediate family members) of all external financial arrangements directly pertinent to their work, including ownership of company shares, as well as fees from speaking engagements, board service, and the like. This was the situation in all leading research centers before the recent abuses came to light. Now, reports must be made to the federal government, with clarifying follow-up questions that seem to me to be feeding a bureaucracy and not achieving any real purpose. For example, in advising the National Cancer Institute, I have found the level of disclosure and documentation of personal information required before every meeting to be excessive. I know of senior scientists who have been counseled not to join such advisory committees because of the potential criminal liability that is coupled with the requirements for accuracy of such detailed disclosures. The process has gone too far, as such measures now stand as a disincentive for well-meaning people to provide advice to the scientific community. The mere fact of disclosure—publication over the Internet and in publications—will serve to curtail abuses. Beyond the humiliation that will be visited upon any faculty transgressor, I believe properly documented abuses should be punished by dismissal or by preventing transgressors from applying for public research funds.

At the same time, it is vital that regulators not choke off the vitality of research activity. Overreaction would almost certainly have a harmful impact upon discovery and innovation nationwide. Indeed, there is nothing wrong if basic scientists who make significant discoveries to which commercial value is subsequently added, in the process of translation or commercialization, are able to benefit from their contributions. Appropriately, as is now the case, most of the financial benefits that may derive from commercial research in academia do not go to individual scientists but to the institutions in which they work, so that it can be plowed back into more research. The public interest will in fact be damaged if scientists and institutions are discouraged from thinking about practical applications of their own research.

Those who make discoveries in basic science ought not be prevented or scared away from entering into partnerships with industry. Rather, they should be encouraged to do so, particularly if we are to accomplish the grand challenges that the National Academies report has identified for biology. Collaboration between academia and industry is also needed if we are to fulfill the promise of basic research under way

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today at Cold Spring Harbor Laboratory: cataloging genes and tracing pathways involved in major mental illnesses, as prelude to the development of diagnostics and next-generation treatments; acquiring a much deeper understanding of metastasis in cancer and the means of predicting and circumventing resistance to chemotherapy as a means to identify new therapeutic strategies; laying the groundwork for the therapeutic use of gene-regulating RNA interference; and applying results from experimentation in plant development to processes such as increasing food production and generating biofuels.

We must also advocate for a solution on a second and related front, equally important to ensure the vitality of basic science and its translation to value-added research. Since the steep stock market decline of 2002–2003, private financing for new science-based companies has virtually dried up. Venture capital is not being risked as much as it was in the past, and the market for initial public offerings for companies that do get started has essentially ground to a halt. Such an economic climate has greatly reduced a major source of funding that supported value-added science. One mechanism to overcome the steep decline in small-company formation is for industry and academic interactions to be made more seamless than they are now. It is important that publication of basic research results upon which applied science is necessarily based not be delayed by discussions about intellectual property even before such property has been developed. I suggest that improved interactions between academia and industry may be the only way to benefit from the sizable public funding of research in the United States. Industry must find new ways to develop research interactions with academia that are more open and collaborative, and academic institutions must limit their appetite for financial benefit, a concern that often drives them to extended negotiations about intellectual property and financial reward.

If we are to spur translation of basic biological discoveries, we need to identify better models for academic–industry collaboration. Such measures could include venture capital investment in research within academic institutions so that venture capital does not have to bear the substantial costs associated with establishing a completely independent entity until it is obvious that the research warrants it. Perhaps a review of policies concerning the Small Business Innovation Research (SBIR) grants provided by NIH at the request of Congress will provide funds for new modes of collaboration. These might enable venture capital and government to better collaborate in seeding early-stage value-added research within academia before companies exist.

Alternatively, large existing corporations and academia should discover new ways of interacting. Cold Spring Harbor Laboratory now has an interesting partnership between our plant geneticists and the Pioneer Hi-Bred division of the DuPont Company. This entirely above-board relationship represents the best of two worlds: our basic research and Pioneer's product development engine. Laboratory scientists collaborate with company scientists on research of mutual interest. Our scientists benefit from access to resources that only could be provided within a large corporation, such as the rapid mapping of gene mutations in plants, and company scientists become involved in exciting early-stage research that normally would not be possible if they were left to work on their own within a corporate development environment. Early access to new discoveries should enable Pioneer to capitalize on those ideas, ensuring that there is a path to commercialization for our basic research. We both benefit, as will society, if, for instance, new methods of boosting crop yields are the result. Such arrangements should not be frowned upon as benefiting industry with taxpayer funds, because the United States economy depends on the success of such advancements. Otherwise, we will find that published research from United States–based academic institutions will be commercialized in other countries.

To sum up, scientists must fully and publicly disclose all arrangements from which they stand to benefit, transgressors should lose their jobs or their ability to seek taxpayer-supported research funds, scientists should be able to profit from their inventions, and academia and industry must be encouraged to invent new ways to interact that will ultimately serve the public good.

It would be a supreme irony if Americans regulated themselves out of a world-leadership position in the sciences. Responsibly managed, basic science can and should provide fuel for entrepreneurialism in America, a signature attribute of the nation that links scientific discovery with public benefit.

Bruce Stillman, Ph.D., F.R.S.
President