PRESIDENT'S REPORT

On the same day in February 1809, two individuals were born, who, by virtue of their intellect and the course of events, would greatly influence contemporary thinking and establish principles that would be debated long after they were gone. Abraham Lincoln, through skillful political leadership and with sound moral compass, saved the union of the United States and set in motion what would be a longer than expected struggle for equality in America. Charles Darwin expanded on ideas about evolution that emerged in the early part of the 19th century to articulate a revolutionary approach to thinking about how species arise and evolve. In 2009, Cold Spring Harbor Laboratory will take special pride in celebrating the achievements of Charles Darwin, recognizing that our work is connected to his in a direct line of descent, for the very beginnings of the Laboratory can be traced to the scientific urge "to investigate experimentally the origin of species."

Those words were used in a proposal for the construction of a permanent Station for Experimental Evolution at our current location in the early years of the 20th century. The goal was to apply Darwin's theory and test Mendel's laws in animal and plant breeding experiments. When such a Station opened its doors in 1904, thanks to a grant from the Carnegie Institution of Washington, the idea that gave rise to Cold Spring Harbor Laboratory was already 14 years old. At an old fish hatchery on the edge of an intertidal zone, a field station of the Brooklyn Institute of Arts and Sciences had been established in 1890 to study how life, per Darwin's theory, had adapted to fill a diversity of ecological niches.

The Laboratory has itself evolved since its days of affiliation with the Brooklyn Institute and the Carnegie Institution. Although evolution in the natural world is selected from a wide variety of nondirected mutations, in the case of our institution, change has been deeply purposeful. From its beginnings in the observation-based study of evolution, to its focus on genetics under Charles Davenport beginning in 1904, to its historic role in the 1940s and 1950s in incubating molecular genetics and molecular biology under the leadership of the geneticist Milislav Demerec, Cold Spring Harbor Laboratory has taken the lead in setting the agenda for the advancement of biological science.

Progress in science depends on a variety of factors: intellectual and conceptual breakthroughs, technological leaps, firm financial backing, and lots of hard work by scientists who have a passion for what they do. Advances cannot be predicted, and sometimes serendipity is a real factor in our movement forward. But the experience of more than a century demonstrates that the process of discovery is continuous and that it exerts an inexorable force on institutions such as ours to adapt or risk falling away from the leading edge in generating knowledge.

The current phase in our evolution is being given palpable, physical expression in the six new interconnected laboratory buildings that comprise our Hillside Research Complex, now nearly finished. These beautifully conceived and executed structures underlie the future evolution of research at the Laboratory. They announce, first, our intention to build on our expertise in cancer research, an area in which we have earned great respect since 1968, thanks to the vision of James D. Watson. Among the new structures is one that will be home to the CSHL Cancer Center and house important research that investigates the relationship between cancer genetics and therapeutic strategies. An adjacent building will focus on tumor microenvironment and metastasis, both areas that are key to developing new therapeutic strategies.

There are two other messages that these new buildings send regarding CSHL's evolution. One is about how we are adapting to changes in the way science is performed; the other is about how biological science advances along an endless frontier, to use a phrase made famous by Vannevar Bush, the father of modern American public science policy.

No one involved in biological research needs to be reminded of the impact that advances in information technology have had on the pace and nature of the work. Science moves ahead much more rapidly today than it ever has, and in our fields of biology, much of the research is now performed by groups larger than ever before, comprised of members representing a diverse range of fields and disciplines. Multidisciplinary team science has come to dominate the research landscape and CSHL has adapted well to its advent. Our Meetings and Courses and Banbury programs facilitate such an approach to team-based science because CSHL continues to be the crossroads for life scientists across many disciplines, a place of intellectual ferment and vigor at the very center of the action.

The author lists on many of the hundreds of research papers published by our faculty this past year offer evidence of the multidisciplinary richness of the science that we do. CSHL is a place where collegiality thrives, a

fact that many Laboratory visitors comment upon each year. One can see it at the in-house lectures given every week on our campus, and perhaps most vividly at the Friday noontime lectures, which more often than not attract overflow audiences of faculty and postdocs listening intently to results obtained by their neighbors, on topics entirely outside of their own fields of expertise. Regular exposure to the ideas of others is a condition of successful team science at CSHL, and I believe it is at the core of great discoveries.

Carefully planned strategic investments in our research program also aid in realizing potential synergies and in taking advantage of new opportunities, many of them interdisciplinary. Perhaps the most important of our investments this past year involved two new areas of research, in neuroscience and quantitative biology. The neuroscience program is a case study of how disciplines once regarded as distinct from one another yield insights that constitute new sources of institutional strength. For instance, a wholly independent line of work centering on the human genetics of cognitive dysfunction has emerged in our neuroscience effort and is now merging with separate studies on brain anatomy, neuronal development, and behavioral analysis of normal cognition.

Our genetics research, which is already shedding new light on the complex genetic causation of illnesses such as autism, schizophrenia, and bipolar depression, emerged from techniques developed at CSHL to study the genetics of cancer and adds a new dimension to the neuroscience effort at CSHL to understand long-term memory and cognitive processes such as attention, decision making, and working memory. That effort, which will expand into new buildings at the Hillside Research Complex, seeks to understand the structure and function of neural circuits whose activity makes possible complex behaviors and the cellular biology underlying these circuits. It also explores how the brain as an ensemble of circuits responds to external stimuli and how the processing of these stimuli serves as the basis of cognition. What is now particularly pleasing is that the genetics of psychiatric diseases in humans is starting to merge with basic studies on rodent cognition and neuronal development, a program that has been built up over the past five or so years. The genes implicated in autism, schizophrenia, and depression are becoming focal points for understanding what they do in the normal brain and how alterations in these genes affect complex cognitive behaviors.

The latter thrust, in systems neuroscience, is one area in which mathematical and statistical insights are certain to help drive research forward. We are reminded of “the endless frontier”—the startlingly new approaches to science that the human mind continues to generate that exert a kind of positive adaptive pressure. Such adaptation is no more apparent than in the requirement in all our research programs for sophisticated, quantitative analysis of large data sets.

Events in 2008 realized a major step forward with the hiring of the first members of what will be a distinctive feature of the research program at the Laboratory—our new Center for Quantitative Biology. A brainchild of Michael Wigler, it was made possible by forward-looking and sizable grants from the Simons and Starr foundations. The Center will become the home base for outstanding scientists who are primarily focused on mathematical and computational approaches to biology, applying their insights in the formulation of research hypotheses pertinent to all of the areas in which the Laboratory specializes: cancer, neuroscience, and plant biology. One particularly interesting aspect of this area of research that has already emerged from the studies of the center’s first new faculty member, Gurinder (“Mickey”) Atwal, is the quantitative analysis of mutations in the human population, informing us in new ways about the processes of evolution and natural selection.

The Laboratory, then, is succeeding in its missions as it continues to adapt, both proactively and in response to external events. One of the major external events that has already altered our behavior during the last year has been the global crisis in the financial system that clearly will impact our work over the near term. Our significant reliance on fund-raising to support the cutting-edge research of our very productive faculty, including many in the earliest stages of their independent careers, will be a constant challenge.

Ironically, this crisis is occurring at a moment when a new president has been elected, fulfilling the dreams of Abraham Lincoln and all too many who have followed. It is a time of major crisis that rivals some of the most serious in the nation’s history. Fortunately, the new administration has renewed this nation’s commitment to including science in its policy making, while recognizing that science is not the only arbitrator of a vibrant political system.

On a more practical note, the public sector’s commitment to funding scientific research will in part reverse the significant cuts in funding that we have endured during the past seven years. Because it is not possible to predict the course of macroeconomic events any more than discoveries in science, we have already taken strong measures at the Laboratory to trim, save, and conserve wherever possible. But confidence in the future is not out of place with a new federal administration in place, our supporters continuing to recognize the importance of our science, and our scientists continuing to be among the most productive and innovative in their fields of endeavor.