PRESIDENT'S REPORT

From the eastern shore of Cold Spring Harbor and many vantage points on our beautiful campus, the emergence of a cluster of new buildings is now obvious. This exciting expansion of our research facilities flows naturally from the success of our current research and makes real a long-held dream.

A decade ago, the village of Laurel Hollow redefined our campus as a scientific and research zone distinct from its residential areas. Soon thereafter, the Board of Trustees initiated a strategic review of future use of the Laboratory's 113-acre main campus. This review determined that any future development would take place at the south end of the campus, close to existing buildings, to encourage scientific collaboration. By the fall of 2001, our Connecticut-based architectural firm, Centerbrook, had completed a vision for campus expansion that made efficient use of available space while retaining the "village of science" style that has come to define Cold Spring Harbor Laboratory. Now, because of the ingenuity of the Laboratory's recent science, our need for such expansion is very pressing.

The dramatic success of our Cancer Center offers opportunities to turn our attention to novel therapeutic and diagnostic approaches for controlling human cancer. In recent years, our research staff has begun collaborating with clinicians in many cancer centers worldwide. A number of new technologies developed at the Laboratory offer novel approaches to investigating diagnoses and treatments. One new technology is the RNAi library developed in Greg Hannon's laboratory, which makes it possible to turn off the expression of every human gene and thus identify those that, when inhibited, cause tumor regression or enhance the effects of chemotherapy. This approach will accelerate the rate of discovery of new molecular targets for drugs that fight cancer.

A new effort in human genetics by Michael Wigler's research group, in collaboration with Robert Lucito, uses newly developed, powerful techniques for identifying the number of copies of genes that exist in each individual. Classical Mendelian genetics have taught us that we all have two copies of most of our genes, but in 2004, Wigler, Jonathan Sebat, and colleagues discovered that this idea is too simplistic. In our individual genomes, we all have either missing genes or extra copies of genes, and the particular genes affected vary. This new aspect of human genetic variation, referred to as copy-number polymorphism (CNP), has important implications. One is that CNP may contribute to an individual's vulnerability to disease, an insight that has given fresh impetus to research on the genetics of autism, schizophrenia, and neurodegenerative Parkinson's disease. Another is that CNP may influence cancer cells. Cancer results from accumulated mutations in an individual's DNA and many of these mutations are copy-number variations. Using the new technology, such variations can now be quickly detected by scanning DNA taken directly from a tumor itself. This information will help physicians to identify the cellular origin of a tumor and decide on appropriate therapy, and help scientists to identify potential therapeutic targets.

Identifying potential targets is immensely valuable, but validating them as effective is still a major challenge. One approach has been to study hard-to-cure cancers in mice, cancers that attempt to mimic the genetics of human cancer cells and also reflect the clinical experience with human tumors. Laboratory scientist Scott Lowe has been a leader in this area, pioneering new work on leukemias, lymphomas, and liver carcinomas. Lowe has developed techniques for creating tumors in mice that contain combinations of genes that cause human cancers. This approach permits the discovery of new cancer-causing genes as well as the testing of novel therapeutic strategies. For example, Lowe and Hannon have collaborated with Scott Powers to block tumor growth using RNAi molecules directed against cancer-producing genes. Such mouse models are potentially powerful because anticancer drugs can be tested and validated in many combinations, something that is very difficult to achieve in human clinical studies.

The Laboratory's development of these technologies, coupled with our strong program in understanding the biology of cancer, has fashioned a new path for cancer therapy research. Technology development has also opened additional possibilities in neuroscience.

The current neuroscience program began at CSHL in the early 1990s. From an initial focus on the genetics of learning and memory in the fruit fly by Tim Tully and colleagues, it expanded to similar studies in rodents. Underlying learning and memory are processes that mold and strengthen

synaptic connections among neurons. These processes are being studied in several laboratories here at Cold Spring Harbor and the need to observe them at work in living animals led to the construction of the Marks Building to house a new program in innovative, high-resolution brain imaging. The success of this program created the need for computational studies of complex imaging data and for modelling the way in which neuronal networks in the brain respond to external stimuli. From this basis, our neuroscience research has grown to embrace investigations at a systems level into how the brain handles the immensely complex processes of normal cognition, such as decision-making and attention. This cutting-edge initiative, pioneered by Zach Mainen, Tony Zador, and Carlos Brody, will, I expect, eventually mesh with the new studies on the genetics of human cognitive dysfunction. Our 15-year-old neuroscience research program has been remarkably successful and now needs space to grow even further.

A third area of research that has prospered at Cold Spring Harbor and elsewhere over the last decade is bioinformatics. It is no longer possible to keep track of all the data and information published in biology. As a result, new science has emerged that employs practioners with backgrounds in biology, medicine, physics, computer science, and mathematics who use computers as their workbench. Scientists at Cold Spring Harbor, such as Lincoln Stein, have been instrumental in this revolutionary approach, developing, for example, methods to manage and analyze the huge amounts of data that have emerged from worldwide genome-sequencing. From their work on our campus have emerged databases revealing new knowledge of human genetic variation and of the evolutionary history of humanity. But these scientists are housed in converted apartments normally used to accommodate visitors to our campus; new facilities are required to maintain and expand this exciting and important area of research.

In addition to new research facilities, we also need permanent housing for our highly successful Watson School of Biological Sciences, as well as more on-campus accommodation and facilities for the approximately 8000 yearly visitors to our meetings and courses programs. We also believe there is an opportunity to establish a unique center for the history of molecular biology and biotechnology. Many of the important advances in molecular biology can be traced to the courses, meetings, and research that took place at Cold Spring Harbor from the late 1940s onward, and the Laboratory is thus a natural location for the archives of the founders of these fields. Mila Pollock, our energetic, enthusiastic librarian and archivist, has begun a number of new initiatives such as oral history, Web-based memory boards, and collections of archive materials that have enhanced our already rich collections. Short- and long-term development of these resources will not only benefit our graduate students, but also provide valuable reference material for scholars pondering the future of genetics and biotechnology.

The needs, opportunities, and initiatives outlined here have prompted a clever and sensitively constructed master plan (page 3) that shows how Cold Spring Harbor Laboratory will respond. Our vision, however, is tempered by the reality of the substantial financial resources required to achieve it, so the plan will be executed in phases, the first being the completion of research facilities close to the existing buildings.

Site preparation for the research buildings that is now so visible was approved about 1 year ago by the Village of Laurel Hollow, and during that process, local residents were informed via a series of meetings and mailings. Installation of the infrastructure for the entire site will be complete by summer 2006 and construction of six new research buildings (100,000 sq. ft.) will proceed shortly thereafter, with the aim of completion at the close of 2008 or early 2009. Extensive landscaping and some reforestation of the disrupted areas of the campus will begin in spring 2006.

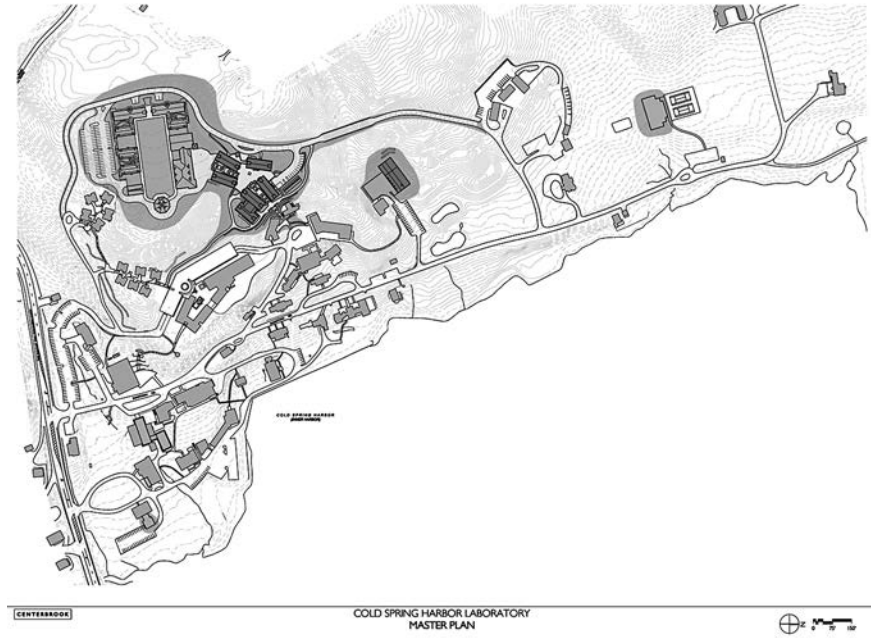
From the initial planning stages, through discussions with the Village and interactions with the architects, to the beginning of construction, the huge and complex needs of this unprecedented project have been addressed with extraordinary efforts from our administration and faculty and, in particular, the dedication, energy, and attention to detail of Art Brings, our Chief Facilities Officer. Without his hard work, this project would not be where it is today.

Throughout its history, Cold Spring Harbor Laboratory has expanded in response to significant advances in biological and biomedical research. This is such a moment. Our long-held dream is becoming reality and the opportunity to do even more exceptional research is energizing the faculty and support staff as never before. We have much to discover.

Existing conditions of the construction site

The Hillside Campus

The figure above shows the existing campus buildings. Route 25A and our southern boundary is on the left. The figure at right shows the new buildings in the master plan, shaded in light gray. Those planned as part of phase 1 are shown in dark gray: a series of six research buildings and a supporting mechanical building.



Plan of proposed modifications