

PRESIDENT'S REPORT

In 2015, Cold Spring Harbor Laboratory marks the 125th anniversary of its founding. In 1890, our institutional ancestor, The Biological Laboratory, brought together a small group of biology teachers. A pristine tidal estuary off the Long Island Sound provided these men and women with a living laboratory in which to explore the principles of Darwinian evolution. This was, in retrospect, a wonderful anticipation of the “hands-on” principle of learning by doing that the contemporary DNA Learning Center (DNALC) has spread far and wide. Our institutional DNA also reflects an investment made in the first years of the twentieth century by the Carnegie Institution of Washington. It breathed life into a Field Station for evolutionary studies at Cold Spring Harbor, merging Gregor Mendel’s ideas on inheritable traits with Charles Darwin’s explanation of natural selection. Housed in the structure we now call the Carnegie Building, the Field Station conducted experiments inspired by the re-discovery of Mendel’s research on quantitative traits that he first presented exactly 150 years ago.

I would like to take the occasion of our quasiquicentennial not only to remember our rich history, but to look forward. The contemporary Laboratory is the product of an evolutionary process in which major capabilities have been continuously added—particularly since 1968, the year Jim Watson was named Director. For friends and supporters of the Laboratory, I want to start by reflecting on what I think is most extraordinary about what we are today and then suggest how this informs the path we intend to take in the years ahead, indicating the critical role of the Laboratory’s new **Capital Campaign**.

I cannot think of a contemporary institution, anywhere in the world, that does what Cold Spring Harbor Laboratory does. It is an institution like no other. We are not only a research institution of the highest caliber, we are also a major innovator in biology education. Dr. Francis Collins, one of the prime movers in the Human Genome Project and for the last 5 years the Director of the National Institutes of Health, had it right when he noted some years ago that “Cold Spring Harbor has placed itself at the center of great science *and* great education.”

The educational part of our mission, a legacy of our earliest days, is indeed singular. Our campus is a crossroads of professional activity in the biomedical and life sciences. That reputation reflects the richness of our Meetings program, which brings nearly 9000 scientists to Bungtown Road each year and another 3000 to our meetings center in Suzhou, China. In the lobby of Grace Auditorium between meeting sessions, you are likely to see distinguished professors mixing with postdoctoral fellows and graduate students, an experience I encountered when, as a second-year graduate student, I was fortunate to speak at the Symposium celebrating the 25th anniversary of the discovery of the double helix structure. There is a kind of intellectual quickening that occurs in these situations that is priceless. The same can be said for what happens among those who participate in the over two dozen professional Courses we offer annually, which collectively serve to advance the entire field’s capabilities in the latest technologies and methods.

The impact of our educational program further reflects the excellence of our “think-tank”-inspired programs at Banbury Center and the wide-ranging efforts of the Cold Spring Harbor Laboratory Press to publish high-impact research journals as well as lab handbooks and monographs on important subjects across the biological sciences. All this activity probably qualifies our educational program as unusual, particularly for a research laboratory. But there are two critical components I have not yet mentioned. One is the DNA Learning Center. Its prodigious efforts over a quarter-century have brought the insight and plain fun of hands-on biological experimentation to hundreds of thousands of Long Island youths, most of them of middle- and high-school age, as well as thousands of their teachers. The DNALC also has educated millions globally, both

at centers established in many countries and through over two dozen educational websites that travel everywhere, instantly and for free, via the Internet.

The other critical component is our bold experiment in graduate education, the Watson School of Biological Sciences. Now in its 16th year, the school has performed as well as we had hoped in the 1990s. Watson School students, along with students from nearby Stony Brook University and nearly 200 postdoctoral fellows, add vibrancy to life on our campus. It is the combined breadth of our educational and basic research activities that makes Cold Spring Harbor Laboratory different. The graduate education program complements the long-standing advanced courses that we teach for scientists who come to learn new techniques and approaches to a field of science.

How do we sustain and expand upon the excellence I have just described? We may be a singular kind of place, but we are facing the same challenges that other institutions face. Never in my 20-year tenure in guiding our science have we been in an environment in which securing operational funds has been more challenging, mostly because of the dramatic reductions in federal funding of science—particularly of fundamental discovery science. In support of both our educational and research missions, therefore, the Laboratory is embarking on a “125th Capital Campaign.” It is one that looks to the future and seeks to secure the means that will enable us to continue playing the wide-ranging, truly unique role that I have described. The fact is that if Cold Spring Harbor is to remain “a Lab like no other,” it will have to significantly add to its endowment. Our goal for the Campaign is to raise at least \$250 million.

Some \$50 million of this sum will enable our extraordinary educational offerings to continue to thrive. About \$13 million will endow student fellowships at the Watson School. These are critical in sustaining one of the school's key innovations. Every student accepted for the program knows that he or she, or their research mentor, is not going to have to worry about securing funds to support their stipend. Our primary goal is to bring the best students here and provide them the freedom to blossom as future leaders in the field. The Meetings and Courses Program will also benefit from an initial endowment because the pressures on federal funding no longer make it obvious that we should receive support for training scientists. As we note each year in this report, the excellence of our program has critically depended on corporate donations. Those funds have declined, in part because of business consolidation among companies but also because of diminished corporate and federal investments in education—hence the need for private support to sustain these highly influential courses. Another portion of the educational endowment will help provide much-needed funds for the DNA Learning Center, including our plans to build a flagship site in Manhattan that will directly serve students in the nation's largest public school system. I can think of no more important investment in America's future.

The bulk of the Capital Campaign—some \$200 million—will endow research at Cold Spring Harbor Laboratory, the excellence of which is the bedrock of our reputation. Two factors make the success of the Campaign essential. First, the cost of doing research has skyrocketed since the dawn of the genome era. Genome science is powerful, but costly to do—and those costs have risen steadily at a rate significantly exceeding that of inflation. As the pie chart on this page indicates, only about 40% of the Laboratory's research operating budget is now supported by federal grants. Even as the government's contribution has declined over the last decade, a second factor has come into play. Today, the amount of money an investigator can expect to receive from a typical “modular” government grant is frozen at \$250,000. If these grants had kept up with inflation in recent years, they would now amount to \$340,000. Our investigators are receiving less money to perform work that costs much more to do. This is seriously eroding the ability of scientists at CSHL and elsewhere to plan ambitious and innovative programs of research. But we are not throwing our hands up in exasperation. Instead, we are seeking help from nongovernmental sources—private individuals, foundations, enlightened corporations—to endow operations critical for Cold Spring Harbor Laboratory's continuing leadership in discovery science.

In research, the Capital Campaign will endow programs that are a critical part of our ongoing Cancer Therapeutics Initiative (CTI), as well as the President's Fund that will support the most basic science and the infrastructure to enable innovation. The CTI represents our effort to identify targets for better cancer drugs. For decades, CSHL has been a world leader in developing tools and methods to characterize the genetic changes that are among cancer's hallmarks. Our understanding of cancer genetics and the interaction between cancer cells and the surrounding tissue cells now provides us with a realistic chance to reduce certain forms of cancer to at least chronic illnesses, manageable over long periods of time, if not attain true cures. Technologies developed at CSHL have made it possible to compare the genomic properties of cancerous versus healthy cells; to model human cancers with remarkable fidelity in mice; and to shut off genes one by one in animal models to dissect genetic and biochemical pathways that drive cancers. We are now at an inflection point. Our next step—and one of the key goals of the Capital Campaign—is to integrate cancer genetics with cancer cell metabolism and whole-organism physiology.

Our new thrust recognizes the importance of thinking about human health in organismal terms. By this I mean understanding disease—cancer, but other diseases as well—not just in terms of what goes wrong in specific cells or tissues, but in terms of the functioning of the entire human system. The biology of the whole affects what diseases we get. One example is the immune system. We are learning, through the work of faculty members including Mikala Egeblad, Douglas Fearon, and David Tuveson, about how stromal tissue—the environment in which cancers develop and thrive—interacts with tumors to affect their course. Nicholas Tonks is exploring the relationship between metabolism and cancer. His recent work provides insights into linkages between the biology of nutrition and disease. Obesity is a state that has broad impacts on the human system; it plays a role in causing diseases, including cancer. Aging affects the entire human system; its processes impact disease susceptibility. Our scientists now have clues that other changes over the life span, for instance, pregnancy, appear to alter disease susceptibility, in this case for breast cancer. What causes ductal-cell precursors in breast tissue to be differentially responsive to oncogenesis—but only if a woman has had a baby before a certain age? How is this effect sustained over many years?

Funds raised through the Capital Campaign will support our exploration of these kinds of questions. We will renovate the Demerec Laboratory, a research building dating from the 1950s where four Nobel laureates have worked, to provide state-of-the-art facilities supporting a Center for Therapeutics Research. As part of this new initiative, we will integrate studies on cancer metabolism and nutrition into CSHL's already strong cancer program. Building on our ability to examine cancer cells and tissue at the single-cell level and employing advanced genomics developed here, the new core facilities will enable our scientists to identify metabolic and oxidative vulnerabilities of cancers that have heretofore remained resistant to therapy.

The Capital Campaign will also add to the capabilities of our Preclinical Experimental Therapeutics (PET^x) facility, which will open on our Woodbury campus in 2015. We hope that PET^x will enable Cold Spring Harbor Laboratory to deliver well-validated drug candidates to industry. The PET^x facility encompasses two core facilities. One enables us to conduct drug testing in animal models for cancer that recapitulate cancer in patients. In particular, we look forward to testing novel drug combinations in these models, which is hard to do in human trials. The other core function in the PET^x facility is advanced imaging. Our scientists will be able to look in real time at the progression of different cancers, particularly cancers being treated with experimental therapeutics. We want to assess not only whether particular drugs are working in our models, but also how they are working. About 40 years of fundamental cancer research has brought us to the stage where rational approaches to cancer therapy are now possible. I look forward to the day, in the not-too-distant future, when our neuroscientists will likewise apply their knowledge of how the brain works to use the PET^x facility to advance treatments of the numerous neurological and psychiatric disorders.

Cold Spring Harbor Laboratory has had a very important impact on science over its 125-year history. The mix of basic research and education comes together in a model that is well proven. The Capital Campaign will ensure that the Laboratory continues to be an innovator and a world leader in fundamental discovery science—which is critical to our future, even in times of restricted federal support of such science. I hope you will support it.

Bruce Stillman, Ph.D., F.R.S.
President and Chief Executive Officer