

research. The projects and thinking I have outlined are all essential for our research institution to remain dynamic. At the same time, we must make sure that our scientists are supported to the fullest extent possible and that the research remains of the highest possible quality, in the new academic style.

## HIGHLIGHTS OF THE YEAR

### Research Highlights

#### *Cancer Genetics and Cell Division*

In March, Cold Spring Harbor Laboratory (CSHL) scientists Michael Wigler and Clifford Yen with colleague Ramon Parsons, M.D., Ph.D., of the Herbert Irving Comprehensive Cancer Center and Columbia-Presbyterian Medical Center, announced the discovery of a tumor suppressor gene, which they named PTEN. The gene appears to be altered in a large percentage of brain, breast, and prostate cancers, and evidence suggests that loss

of PTEN affects the way a benign tumor becomes malignant. Unlike mutations of genes such as *hMSH2* and *BRCA1*, which were found in people who have hereditary predispositions to cancer, PTEN was discovered by analyzing the more common sporadic cancers. More than 80% of all cases of cancer are sporadic, meaning that they have no obvious hereditary contribution.

PTEN received its name because of its similarity to phosphatases and tensin. The similarity between PTEN and protein phosphatases, which remove phosphates from proteins, is significant because many oncogenes—genes that help to transform normal cells into cancer cells—encode tyrosine kinases, which add phosphates to proteins. Tensin is part of a complex of proteins that sits below the cell surface and controls cell shape. Thus, PTEN may also be involved in the spread of tumors, by localizing to the cell surface and removing phosphates from key signaling proteins. In a productive collaboration between the Wigler laboratory and

Nicholas Tonks' laboratory at CSHL, the two groups quickly confirmed that PTEN is a phosphatase and have identified proteins with which it interacts. These studies should point to the pathway in which PTEN functions in normal cells and which is altered in tumor cells.

Representational difference analysis (RDA), an advanced genetic technology developed by Mike and Nikolai Lisitsyn, then at CSHL, played a key role in the identification of a PTEN tumor suppressor gene. RDA is a procedure used to analyze the differences between two genomes. (A genome is the entire DNA sequence of an organism.) By comparing DNA from diseased and normal cells from the same person, scientists can use RDA to identify DNA sequences that differ between the cancer cells and normal cells. In the case of PTEN, RDA was used to find unique DNA sequences present in normal tissue but missing in breast cancer. To date, the Wigler lab has located about a dozen genetic loci potentially involved in breast cancer. Each of these discoveries represents a vital step forward in the path to earlier diagnosis and improved treatment for breast cancer patients, and it illustrates the growing realization of the genetic complexity of cancer.

In 1994, to further utilize RDA in the search for cancer-related genes, the Laboratory and Mike formed Amplicon Corporation. In October 1997, the Laboratory announced the acquisition of Amplicon by biotech leader Tularik, Inc. Tularik is the largest privately held biotechnology company in the nation, and its scientists are enthusiastic about continuing



M. Wigler

collaborations with CSHL scientists while using RDA in an extensive cancer research program. Although Tularik, Inc. is located in California, the oncology division of the company will continue to operate on Long Island for at least 5 years and will continue to collaborate with CSHL scientists.

There was good news and bad news from Carol Greider's lab in 1997: The good news was the report of a line of telomerase knock-out mice. The bad news was that Carol left Cold Spring Harbor after 9 years to accept a position as Associate Professor in the Department of Molecular Biology and Genetics at Johns Hopkins University School of medicine in Baltimore, Maryland, to follow her historian husband to his new faculty position at George Washington University.

In October, Carol's group published a report about mice that lack telomerase, an enzyme that she discovered in 1985 and has continued to study. Telomerase is necessary for maintaining chromosome integrity. Several studies have suggested that telomerase also plays a role in cancer and cell senescence. The ends of chromosomes, called telomeres, shorten each time a cell divides. It is thought that when telomeres reach a critically short length, the cell division cycle arrests and cells enter into a senescent state after which they never divide again. Telomerase appears to sustain telomeres against this shortening.

In collaboration with Ron DePinho's lab at Albert Einstein College of Medicine, Carol's group bred a line of mice that lacked the telomerase enzyme. The results showed that mice can survive for six generations without telomerase. The studies also proved telomerase's role in chromosome stability; mice that lacked telomerase showed telomere shortening and loss of telomere function, and they eventually developed chromosomal abnormalities. After five or six generations, telomere loss in mice leads to sterility and loss of cell viability in certain highly proliferative tissues. The work confirms the suspected role for this important enzyme in cell proliferation and demonstrates that when telomeres reach a critically short length, cell and tissue viability are progressively lost. Interestingly, cells that lacked telomerase could still form tumors, demonstrating that telomerase is not essential for tumor formation in mice. As predicted, however, recent results indicate that the rate of tumor formation is lower in mice that lack telomerase. Thus, although telom-



C. Greider



D. Beach, S. Lowe

erase is not essential for the development of cancer, it may play an important role in tumor formation.

Scott Lowe and David Beach made a surprising new discovery about the transformation of normal cells into cancer cells. Usually, most human cells undergo senescence, or permanent cell cycle arrest, after a restricted number of cell divisions. This, in effect, limits the cells' life span. Cancer occurs when cells continue dividing beyond the normal limit or fail to die when they should. In 1981, scientists, including Mike Wigler at CSHL, discovered that a gene called *ras* was involved in some human cancers. This was the first discovery of a human oncogene that was derived from a tumor. In 1983, Earl Ruley—then at CSHL, now at Vanderbilt University School of Medicine—showed that *ras* acts in concert with other oncogenes to cause cancer. It was determined that most of these cooperative oncogenes can independently extend the life span of—or even immortalize—cells. Recently, Scott and David reported the surprising observation that when the oncogenic form of *ras* is overexpressed in normal cells, it immediately induces the same sort of cell senescence that occurs during cell aging. Two other genes, p16 and p53, both extensively studied at CSHL and elsewhere, are necessary for this type of cell cycle arrest. When p53 or p16 are absent from the cell, *ras* now stimulates uncontrolled cell division, rather than cell division arrest. This research provides important information about the multistep nature of cancer and suggests that, in the right context, it may be possible to exploit oncogenes to reverse tumor cell growth.

### **Neuroscience**

In previous reports, CSHL neurobiologist Hollis Cline described the role of the enzyme CaMKII in neuronal development. In 1997, her lab built on its previous discoveries—that expression of CaMKII is involved with neuronal maturation and with the stabilization of synapses, the intricate connections between neurons. Evidence from the Cline lab showed that CaMKII coordinates the development of the physical structure of neurons with the development of their synaptic connections. The normal, gradual increase of CaMKII expression during early brain development correlates with slowed growth rate and increased stabilization of dendrites—the branches through which neurons receive their electrochemical signals. These changes signify neuronal maturity. Holly therefore hypothesized that CaMKII, which is regulated by calcium activity, may represent an activity-dependent mediator of neuronal maturation. Her lab tested this theory by forcing the expression of CaMKII in immature neurons and obtained the exciting result that indeed CaMKII expression suppressed the development of additional, longer dendrites and prompted the stabilization of the existing branches. Thus, it promoted the maturation of neurons during brain development.

Conversely, Holly and research investigator Elly Nedivi showed that a novel protein, CPG15, increases the number of dendritic branches in neurons. Elly isolated the gene for CPG15, which belongs to a group of genes whose expression is elevated by neuronal activity. In addition to inducing neuronal branching, they found that CPG15 also controls the growth of neighboring neurons through an intercellular signaling mechanism. These studies suggest that CPG15 is capable of translating local neuronal activity into structural changes in the brain. This would represent the discovery of a new class of neuronal activity regulated growth factors.

Alcino Silva's lab continues to study the molecular and behavioral functions involved

in learning and memory in mice. In 1997, Alcino tied previous results together through an experiment with collaborator Howard Eichenbaum of Boston University in which he monitored the activity of specific cells in the hippocampus in the brains of living, functioning mice.

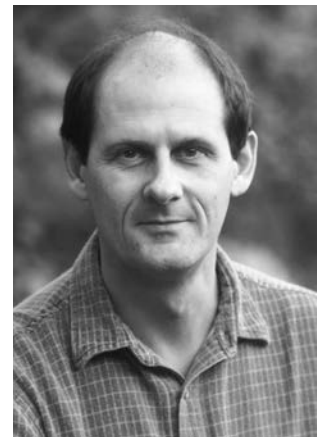
Alcino has been studying “place cells”—specific, identifiable brain cells that fire only when an animal is in a precise place in its environment, a place that the animal’s brain recognizes. These place cells are representative of the “place circuits” that are stimulated as an animal becomes acquainted with a place or area. The establishment of such a series of circuits is called spatial orientation or learning; the mouse recognizes familiar things as it travels about. Alcino tested the function of place cells in two types of mutant mice, each representing a component in learning and memory that Alcino has been studying—the  $\alpha$ CaMKII protein and a CREB protein. Alcino created genetically modified mice that carry a point mutation in a single amino acid of the  $\alpha$ CaMKII protein. Instead of firing at specific times like wild-type cells, place cells in animals with this  $\alpha$ CaMKII mutation fire randomly when they are exposed to familiar and unfamiliar places, which indicates a lack of learning. Mice containing decreased levels of CREB also display this reduced learning, albeit to a lesser degree. Behavioral studies corroborate this finding, as the same mutant mice demonstrate a marked lack of spatial orientation.

In a second set of experiments, Alcino’s lab successfully reversed the learning deficit in mice with the NF1 mutation characteristic of neurofibromatosis type 1. These mice have proven to be a valuable model for the study of this disease. He has confirmed a mechanism that is defective in NF1 mice and has restored the ability of mice to learn by breeding in a second mutation that counteracts the effects of the NF1 mutation. These behavioral studies may suggest targets for the search for treatments of learning deficiencies in children affected by mutations in the neurofibromatosis type 1 gene.

### ***HIV Pathogenesis***

Jacek Skowronski’s studies of HIV pathogenesis have continued to produce new understanding of how the deadly virus commandeers its host cells. Jacek’s laboratory has used genetic techniques to dissect the functions of the Nef protein, the product of the viral gene *nef* that is found in human and simian immunodeficiency viruses (HIV and SIV). Nef is a regulatory protein that is important for efficient viral replication and essential for the development of AIDS in humans and primates. HIVs lacking Nef do not cause AIDS, and thus inhibiting the functions of this protein is a key goal for controlling HIV pathogenesis.

Jacek has shown that Nef possesses multiple independent functions. One role is to control levels of the CD4 protein on the cell surface of CD4<sup>+</sup> T lymphocytes. CD4 is one component of the cell surface receptor for HIV. A second role is to control the levels of cell surface MHC molecules, proteins that play a key role in immune recognition of virus-infected cells. The genetic dissection of the multiple functions of Nef provides a basis for experiments directed toward understanding in detail the molecular mechanisms by which Nef affects the development of AIDS, and such experiments are currently under way in Jacek’s laboratory. In addition, Jacek and his colleagues are collaborating with scientists who study SIV pathogenesis using animal models of AIDS with the goal of developing an HIV vaccine.



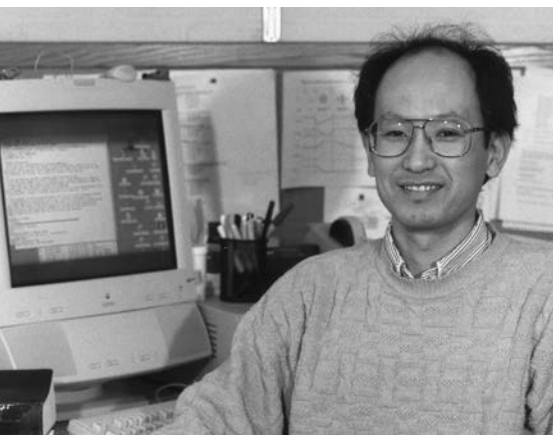
J. Skowronski

### ***Cell Death during Development and Cancer Progression***

In the study of programmed cell death, or apoptosis, Michael Hengartner's lab has made significant progress in identifying the genes involved and their roles. Working with post-doctoral researcher Mona Spector, Michael has continued to gain new information about this process by studying the tiny worm *Caenorhabditis elegans*, an ideal model organism for genetics research. Previously, three genes were known to be essential for properly controlled programmed cell death to take place in *C. elegans*, and two of these genes were known to have counterparts, or homologs, in mammals. Michael and others had shown that CED-3 and CED-4 work in concert to kill unneeded cells, a necessary process cells during normal development, and that CED-9 suppresses this action. If the worm carries a mutation in either CED-3 or CED-4, then this necessary mechanism to rid the body of unwanted cells never takes place, resulting in excess cells in the adult worm. In contrast, if there is a mutation in CED-9, programmed cell death is not controlled and cells die at an abnormally high rate.

Recently, Michael and Mona identified a previously unknown physical interaction between the suppressor of cell death, CED-9, and the activator of cell death, CED-4. They discovered that if the interaction between the two proteins is disrupted, there is a failure to control apoptosis. These and other results suggest that CED-9 works by binding to CED-4 and regulating its activity. The new information begins to suggest how CED-3, 4, and 9 interact to control the process of programmed cell death.

Many drugs for treating cancer kill tumor cells by inducing apoptosis, or programmed cell death, but many tumor cells have mutations that produce resistance to chemotherapy. Yuri Lazebnik and Scott Lowe have been studying the process of cell death in normal and tumor cells and they reported this year that unexpectedly, extracts from drug-resistant tumor cells contain the cell death machinery and the ability to trigger this process. Interestingly, the tumor cells contain an activity that can induce programmed cell death in normal cells, a factor that Yuri and Scott call oncogene-generated activity (OGA). They are pursuing the nature of OGA with the hope that they might be able to stimulate its function in tumor cells that have become resistant to chemotherapy.



T. Hirano

### ***Chromosome Structure***

In another vital area of our research program, Tatsuya Hirano has made significant strides in his studies of chromosome structure and function. DNA in chromosomes exists in a coiled state usually stretched out like a fully extended Slinky (the popular children's toy) within the cell nucleus. Immediately before cell division, the DNA molecules must condense and be packaged into compact rod-shaped structures, like the Slinky retracted into its tightly coiled shape, so that the duplicated chromosomes can be divided evenly into the daughter cells. Unlike the Slinky, however, the packaging of DNA into chromosomes is not a spontaneous process because it requires the assistance of "packaging" proteins. Tatsuya studies the mechanisms of chromosome packaging (or condensation) via a biochemical approach using frog egg extracts and was the first to identify such a "packaging" protein, named condensin (for condensation protein).



In 1997, Tatsuya and his colleagues purified and characterized condensin. They found that condensin contains several highly conserved proteins that induce, in a test tube, remarkable structural changes in DNA called positive supercoiling, which is comparable to the retraction and tight coiling of DNA necessary for cell division. This is the first reported evidence for how this class of proteins actually works. In addition to the condensin protein complex, Tatsuya has shown that another protein complex containing condensin-related proteins exists in cells and is involved in chromosome cohesion, the process by which the two duplicated DNA molecules remain bound to each other prior to their condensation and separation at mitosis. Further understanding of the proteins' control of higher-order chromosome structure will likely reveal more surprises.

### ***Plant Biology***

In plant genetics, the Laboratory's part of the global *Arabidopsis* Sequencing Project continues to go well. Richard McCombie's sequencing expertise and Rob Martienssen's work with the gene traps that he developed with Venkatesan Sundaresan have proved an invaluable contribution not only to the sequencing effort, but also to the determination of gene function. Rob continues to do other plant genetic research as well, and he recently made an important discovery relating to protein transport. Protein translocation is a term used to describe the process of moving proteins across cell membranes. Rob's lab identified a gene, *hcf106*, which produces a membrane protein that is vital to one of three known pathways for protein translocation in maize. Two things about this discovery were especially exciting: (1) This was the first component of the pathway to be identified and (2) the pathway in which this protein is involved was thought to be unique to higher-plant chloroplasts. However, after Rob and his lab cloned and characterized the *hcf106* gene, they found in database searches that homologous genes were present in bacteria! This interesting discovery was made possible by the worldwide bacterial genome sequencing projects and the accessibility of the data in public databases.

### ***Bioinformatics***

The Laboratory's bioinformatics program—the use of computers to analyze, store, and distribute scientific data, a kind of scientific information technology—has continued to evolve. Bioinformatics scientist Michael Zhang has been at CSHL since 1991 and studies DNA sequence pattern recognition. Recently, he was joined by three new computational biologists: Andy Neuwald, Andy Reiner, and Lincoln Stein. Andy Neuwald brings expertise in understanding the relationship between protein sequence and structure. Andy Reiner studies mechanisms for data storage and management, and Lincoln Stein is an expert in genome research and sequencing. In addition to their own research, all are providing valuable contributions to Dick McCombie's DNA sequencing efforts. Tom Marr, a member of the Laboratory's bioinformatics team since 1989, spent 1997 in transition between the Laboratory and Genomica Corporation in Boulder, Colorado. Tom is still involved in research projects here at Cold Spring Harbor, but he is now president and C.E.O. of Genomica.

The goal of the Laboratory's bioinformatics program is to develop and use computerized methods to study biology. As genomic research advances, so too does the need for efficient analysis, reliable storage, and accessibility of data. Genome scientists make up one of the most open group of research scientists today, posting programs and results on searchable Internet sites as soon as they are assembled. The bioinformatics group at

the Laboratory will continue to work on original research and development projects and to collaborate with other Cold Spring Harbor scientists on a wide range of projects.

## **Symposium LXII: Pattern Formation during Development**

One of the great scientific accomplishments of the past decade or so is the recognition that the molecular and cellular mechanisms that guide the patterning of tissues and organs during embryonic development are remarkably similar among different species. What works for flies and frogs also serves humans very well as embryos acquire their form and identity. To celebrate these marvelous discoveries, the 62nd CSH Symposium focused on pattern formation during development, with a particular emphasis on evolutionarily conserved mechanisms and molecules.

When the CSH Symposium was initiated in 1933, the length of each meeting was five summer weeks, and the length of presentations was unlimited. In 1941, director Milislav Demerec saw fit to reduce the duration of the meeting to two weeks; in 1948, he reduced it to eight days. The length of the symposium remained at a week and a day for almost half a century, but in today's fast-paced world, with many two-career families, it has become increasingly difficult for most scientists to be away from home for more than a week. After much careful consideration, the length of the Symposium was reduced to five days in 1997.

The 62nd CSH Symposium, *Pattern Formation during Development*, took place from May 28 to June 2. On Sunday evening, June 1, Sean Carroll, Professor of Molecular Biology, Genetics and Medical Genetics at the University of Wisconsin at Madison, presented the annual Dorcas Cummings lecture for meeting participants and the public. In it, Dr. Carroll presented an audiovisual short course in the development of body parts that was extremely interesting to both the lay and scientific audiences.



Twenty years of splicing: The Toast

## 20 Years of Splicing

On August 23, during the *Eukaryotic mRNA Processing* meeting, the Laboratory held a special historic session and champagne toast to honor the 20th anniversary of the discovery of RNA splicing and split genes. In 1993, the Nobel Prize for Medicine or Physiology was awarded to Rich Roberts and Phil Sharp for their contributions to the discovery of split genes. The discovery—that some regions of a gene, the exons, are transcribed into messenger RNA (mRNA), whereas other regions, the introns, are spliced out—led to the creation of a new field of science, known as RNA splicing.

Phil Sharp and his colleagues in the Nobel Prize-winning work, Sue Berget and Claire Moore, were on hand for the celebration. Thoughtful reflection by James Watson familiarized the largely younger audience with the Nobel selection process, and remarks from Phil and Sue provided a candid perspective on winning a Nobel and the research that contributes to one.

## National Medal of Science

On April 30, 1997, President Bill Clinton announced that Jim Watson had been awarded the National Medal of Science. The presidential honor, administered by the National Science Foundation, is this nation's highest scientific honor. The award was made in recognition of Jim's co-discovery of the structure of DNA in 1953 and for his pioneering role in the establishment of the Human Genome Project, the worldwide effort to map and sequence the human genome. Jim was appointed Associate Director for Human Genome Research of the National Institutes of Health in 1988, and in 1989 he became the first Director of the National Center for Human Genome Research, a position he held



1997 National Medal of Science Award Ceremony  
James D. Watson and President Clinton





Executive's Seminar meeting at Banbury

until 1992. On December 16, 1997, he traveled to Washington, DC, to accept the medal from President Clinton.

## **Banbury Conference Center**

### ***Executives' Seminar Weekend at Banbury Center***

Our close relationship with J.P. Morgan and Co., Inc. continues and has led to their support of the annual Executives' Seminar meeting, Banbury Center's equivalent of the CSH Symposium. To be sure, the scales are different—the Banbury Center is about one-tenth the size of Grace Auditorium—but both meetings, in their different ways, are unique occasions for reviewing the most exciting and interesting biological research. This year, the topic of the Executives' Seminar was *Genetic Engineering*. The coverage was broad. Stanley Cohen (of the famous Cohen-Boyer recombinant DNA discovery) discussed the origins of his work, Jim Wells described the genetic engineering of molecules, Shirley Tilghman and Richard Michelmore discussed the genetic engineering of animals and plants, respectively, and Kay Davies led participants into the world of gene therapy. Of special note was Alan Colman's presentation on the cloning of Dolly the sheep, and on the hope of the biotechnology community for the use of cloning to produce genetically engineered proteins in animals.

### ***Gene Therapy of Duchenne Muscular Dystrophy***

An important function of Banbury Center meetings is to promote research by hosting discussions on important topics. A recent example was the meeting on *Up-regulation of Utrophin Gene Expression*. Kay Davies, of the University of Oxford, has devised a research initiative with the goal of turning on the utrophin protein to take the place of the critical protein—dystrophin—missing in patients with Duchenne muscular dystrophy. With funding from the Oxnard Foundation, we are holding a series of expert meetings to explore the ramifications of this approach, and in February, Banbury Center hosted a meeting that brought together scientists working on Duchenne muscular dystrophy, researchers studying the control of gene expression, and clinical scientists who are using

a gene-reactivation strategy for treating the thalassemias. We will hold further meetings at Banbury so that the expertise and knowledge already gained in other systems can be brought to bear on this debilitating disorder.

### ***The “Post-Genomics” World***

In the past two years, a flood of complete genome sequences has been published, including those of the bacterial “workhorse,” *E. coli*, and of the yeast *Saccharomyces cerevisiae*; the genome sequence of the nematode worm *C. elegans* will be completed in 1998. Knowledge of complete genome sequences will have a profound impact on the way biological research is carried out, and two Banbury Center meetings examined what is to be done in this so-called “post-genomics” world. One meeting—*Integrating Genetic, Biochemical, and Other Data*—discussed how best to make use of all the data on the functions of cells and organisms that have been acquired during the past 100 years, in light of the more recently obtained genome sequences. The goal of this meeting is to produce a “virtual cell” that can be used as a predictive tool.

Physiologists traditionally have used other techniques to study organisms on more of a systems level, and the American Physiological Society is keen to use the tools of genetics to further their research. The meeting *Genomics to Physiology and Beyond* was designed to introduce physiologists to some of the ways in which genomics and the analysis of complex genetic traits might be used to answer the kinds of questions that interest them.

### **Robertson Research Fund**

The Robertson Research Fund has been a continuing source of support for the Laboratory since 1973. Robertson funds supported labs in each of the Laboratory’s primary fields of research: cancer, neurobiology, and plant genetics. Cancer research recipients were Xiaodong Cheng, Ryuji Kobayashi, Yuri Lazebnik, Benjamin Lee, W. Richard McCombie, David Spector, Jacek Skowronski, Nick Tonks, and Rui Ming Xu. In neurobiology, the Robertson Research Fund supported Hollis Cline, Alcino Silva, Tim Tully, Jerry Yin, and Yi Zhong—all of whom have made great strides in understanding the biological basis of learning and memory. In plant research, the fund furthered the studies of Ueli Grossniklaus and Hong Ma. The Robertson Research Fund also helps to support postdoctoral researchers, graduate students, and scientific seminars.

In 1975, the Robertson family established an additional fund, designated for neuroscience, in memory of Marie H. Robertson. In 1997, allocations went to Hollis Cline for her work on neuronal growth and stabilization and to Grigori Enikolopov for his studies of the neurobiology and development of the fruit fly *Drosophila*.

### **Board of Trustees**

Several valued trustees completed their terms in 1997. Scientific trustees Günter Blobel, M.D., Ph.D., Gerald Fink, Ph.D., and Eckhard Wimmer, Ph.D. have departed, as have individual trustees Wendy Russell and Douglas A. (Sandy) Warner III, who is taking the requisite 1-year interval after two successive 3-year terms.

At the close of the 1997 term (February 1998), John Cleary concluded his term as President of the CSHL Association and as Trustee. We are most grateful to John for his outstanding service to the Association and to the Laboratory in general and will continue to seek his valuable advice and guidance. We look forward to working with Vernon Merrill who has now assumed the position of CSHL Association President.

Wendy Russell has been named Honorary Trustee. Wendy began serving on the Board in 1984, has served four 3-year terms, and was Secretary in 1985–1987 and 1992–1997. She has served on the Development, Executive, Finance & Investment, Banbury, Building, and DNALC Committees, as well as the CSHL Association.

Wendy is a superstar in raising financial support for the Laboratory and was instrumental in starting the Corporate Advisory Board (CAB) for the DNA Learning Center. She was also a vital and wonderful part of the Laboratory's initiative to establish on-site child care. Her tireless efforts toward that end, as well as on behalf of the CSHL Association Annual Fund, are deeply appreciated.

The Laboratory's continuing success is due, in large part, to the outstanding leadership and support of the dedicated people who volunteer their time in support of an excellent cause. We offer heartfelt thanks to each of these individuals for their contributions and active participation and look forward to continuing our relationship in the future.

Our new scientific trustees, whose terms became effective in 1997, are Edward Harlow, Ph.D., of Harvard Medical School and Massachusetts General Hospital; John Kuriyan, Ph.D., a prominent X-ray crystallographer studying signal transduction and DNA replication among other things as a Howard Hughes Medical Institute Investigator and Professor at Rockefeller University; and Lorne Mendell, Ph.D., Distinguished Professor and Chairman of the Department of Neurobiology and Behavior at State University of New York (SUNY) Stony Brook and President of the American Society for Neuroscience. Ed Harlow's return to CSHL is particularly meaningful: Ed was on our scientific staff from 1982 to 1991. His demonstration here in 1989 of a relationship between the retinoblastoma (*rb*) oncogene and the E1A tumor suppressor have won him much well-deserved acclaim. Ed studied oncogenes for a decade prior to this important discovery and has had a stellar career in science since. In addition, he is also co-author with David Lane of our very successful laboratory manual *Antibodies*. Ed is currently Professor of Genetics at Harvard Medical School and the Massachusetts General Hospital and Associate Director for Science Policy at the National Cancer Institute. We

are honored and grateful to have the participation of these and other scientists in charting the course for continued scientific success at Cold Spring Harbor.

In November, the Board of Trustees voted to approve the Laboratory's plan to establish a CSHL graduate program. This has allowed us to begin the application process for becoming a degree-granting institution. Our intention is to initiate a small program of approximately five Ph.D. students per year to be run in conjunction with our existing program of graduate education for students of SUNY Stony Brook. The planning and application process is being handled by Assistant Director Winship Herr, who will also be the first Dean of the graduate school.



M.J. Harris

### **A Friend Lost: Mary Jeanne Harris**

In November, we were deeply saddened by the death of a very special friend, Mary Jeanne Harris. Mary Jeanne and her husband Henry U. Harris, Jr., have been members of the CSHL Association since 1980, and over the years, they have been extremely generous in their support of a wide variety of projects at the Laboratory. In 1982, Mary Jeanne joined the Laboratory's Board of Trustees, on which she served for six consecutive years. She served on the Building Committee; the Robertson House Committee, through which she helped to decorate the guest accommodations at the Laboratory's Banbury Center; the DNA Learning Center (DNALC) Committee; and as Vice Chairman of the Education Committee. The Harris' support was instrumental in the establishment of the Laboratory's DNALC in 1988, and in 1991, they funded an architectural study and made the lead gift toward construction of an addition to the DNALC.

Over several terms as a CSHL Association director (1980–1988, 1991–1994, and for a short time in 1997), including a period as Vice Chairman, Mary Jeanne demonstrated a heartfelt interest in education and child care, and a deep concern for the quality of life of Laboratory scientists and their families. She organized and hosted many events designed to make the young families more comfortable in their new surroundings.

Mary Jeanne brought a unique warmth to the projects on which she worked and a determined sensibility to the goals she set. We miss her deeply.

### **CSHL Association**

On February 2, 1997, guest speaker Philip R. Reilly, M.D., Executive Director of the Shriver Center for Mental Retardation in Waltham, Massachusetts, addressed the members of the CSHL Association at their annual meeting. His talk, entitled "Genetics, Ethics, and You," was a thought-provoking analysis of the impact of genetic information on our daily lives. He explored various issues faced by the public as advances in genetics are increasingly applied to health care, including diagnostics and prognostics. Dr. Reilly also examined the possible effects of genetic information on health insurance, life insurance,



CSHL Association Annual Meeting  
J. Cleary and P. Reilly

and employment.

The Association held its annual Major Donor Cocktail party on November 16 in the home of David and Jamie Deming. Association members and scientists shared a relaxed evening of wonderful food and good conversation in the Demings' warm and comfortable home.

## **DNA Learning Center**

We were very pleased to learn that the DNALC has received a 3-year grant of \$820,000 from the Josiah Macy, Jr. Foundation to create an extensive Internet site for public education about genetics. The DNALC's newly created multimedia communications group will first develop *DNA from the Beginning*, an animated "primer" to provide background information on classical genetics, molecular biology, and biochemistry. This will be followed by a *Gene Almanac*, designed to function as an animated "encyclopedia" of genetic disorders featuring detailed information on causative or predisposing genes, DNA diagnosis, and treatments. A 3-year grant of \$335,000 from the Department of Energy enabled the DNALC staff to continue their tradition of nationwide teacher training. *The Science and Issues of Human DNA Polymorphisms* introduces high school biology teachers to a laboratory-based unit on human DNA polymorphisms, which provides a uniquely personal perspective on the science and ELSI aspects of the Human Genome Project. Finally, the DNALC received a 3-year grant of \$600,000 from the National Science Foundation's Advanced Technological Education (ATE) Program to create and disseminate advanced technology units on genomic biology. Operating under a direct congressional mandate, the ATE program aims to ensure U.S. competitiveness in emerging technologies of the 21st century.

## **CSHL Press**

1997 was a year of extensive change for the Press and it ended with much improvement in organizational efficiency, technical expertise, and financial performance.

The Cold Spring Harbor journals, *Genes & Development*, *Genome Research*, and *Learning & Memory* all gained ground in 1997, with record circulation, more published papers, higher impact factors, booming advertising sales, and increased visibility. There were new faces among the principal editors of all three journals, and the scope and the mix of articles in the journals broadened. Most notably, online editions of *Genes & Development* and *Genome Research* were created. These offered the entire contents of each issue via the Internet in a fully searchable format with links to other electronic resources such as Medline. Initially, these editions were made available free of charge, with the intention of providing the electronic subscription only to print subscribers until the impact of this development on the journals' circulation and revenues could be assessed. *Learning & Memory* received a generous grant from the Donaldson Charitable Trust that will support the development of its electronic edition in 1998.

A total of 18 new books were published in 1997, double the previous year's total. They included three of the most complex and colorful volumes ever to originate from the Laboratory: the remarkable laboratory manual *Cells*, by David Spector, Bob Goldman, and Leslie Leinwand; *Retroviruses*, by John Coffin, Steve Hughes, and Harold Varmus, a textbook for a community of scientists and physicians given dramatic prominence by HIV-induced disease; and *Mutants of Maize*, by Gerry Neuffer, Ed Coe, and Sue Wessler,



an encyclopedic account of the extraordinary genetic diversity of corn, which was recognized as one of the three Best Books of the Year in Biology by the American Association of Publishers. These and the other new titles, such as the commanding Symposium volume on nervous system function, combined with the continued strength of classics such as *Molecular Cloning* and *Antibodies* to produce an increase of over 12% in book sales.

## Major Gifts

We have been extremely fortunate over the years in the amount of support the Laboratory receives from the private sector. As federal support now constitutes less than approximately 38% of the Laboratory's budget, contributions from individuals, foundations, and businesses are ever more crucial to the Lab's survival and to the continuation of our scientific mission.

The Laboratory's neuroscience program recently received unparalleled private support. William and Marjorie Matheson, of Mill Neck, New York, and Hobe Sound, Florida, have been members and generous supporters of the CSHL Association since 1989. In 1995, they established the Matheson Fund for Neuroscience with two contributions totaling \$300,000. In 1997, Bill and Marjorie added an unprecedented \$2.8 million to this endowment. The fund's value at year-end was \$3,537,952, after an award of \$121,659 was made to support scientist Grisha Enikolopov and his work on the role of nitric oxide in development. The endowment provides a vital and enduring source of support for our neuroscience program, as its sizable principal, carefully invested, will continue to generate income that may be applied directly to research support without decreasing the balance.

Another very important research project that we likely could not have undertaken without private support was the *Arabidopsis* Sequencing Project. This is an organized, global effort to sequence the entire genome of a flowering plant for the first time in history. Like the Human Genome Project, the *Arabidopsis* Sequencing Project is expected to produce an entire genetic "toolbox" for plants, providing the basis for vast continued discovery as scientists explore the function and manipulation of important genes. We could not have geared up for this project and subsequently qualified for important federal grants without the support of Westvaco Corporation and of Laboratory Board Chairman David L. Luke III. Westvaco provided \$290,000 for the purchase of sequencing equipment, and then subsequently and separately, Mr. Luke made two gifts totaling approximately \$700,000 for additional sequencing equipment and plant research. This roughly million dollar combined investment has enabled CSHL to further secure its place in plant genetics research, a fitting step forward for the Laboratory in light of its long history of plant genetics research. George Schull's demonstration of "hybrid vigor" began CSHL's foray into plant genetics in 1908, and it yielded the sweet corn we eat today, and Barbara McClintock's 1951 description of "transposable elements" in maize, the jumping genes now studied widely in genetics, earned her the 1983 Nobel Prize in Physiology or Medicine.

For 10 years now, Edna Davenport has given generously to the Annual Fund. Her contribution of \$100,000 in 1997—and each of the previous 3 years—typifies her gen-



William and Marjorie Matheson with Liz Watson

erosity toward the Laboratory. These funds help to support young researchers who have not yet secured federal or other grant support, awards that may elude young scientists because they are often dependent on a track record in research.

During the past 8 years, Alan and Edith Seligson have fully supported 15 postdoctoral fellowships. Again in 1997, they gave a 1-year award of \$35,000, this time supporting Howard Fearnhead in Yuri Lazebnik's lab. Howard has done excellent work in his studies on apoptosis, or programmed cell death, a process involved in a variety of diseases including cancer. We are most grateful for the Seligsons' continuing support of our promising young researchers.

Plans for the new Advanced Imaging Facility are well under way and we have received exceptional gifts to that end. Edwin and Nancy Marks gave \$2.5 million through the Marks Family Foundation, and the W.M. Keck Foundation contributed \$2 million. Our good friends George and Mary D. Lindsay gave \$250,000 toward the new initiative, Burroughs Wellcome contributed \$470,800 over 5 years in support of Zachary Mainen, a postdoctoral researcher working with Roberto Malinow and Karel Svoboda on the new two-photon excitation laser scanning imaging. The two-photon imaging technology around which the Advanced Imaging Facility will be built is currently being developed in Karel's temporary lab in the Beckman Neuroscience building.

The capital campaign for the Mary D. Lindsay Child Care Center continued in 1997, and was completed in excess of its \$1 million goal with gifts including \$50,000 from Mr. and Mrs. William R. Miller through the Miller Family Foundation. The DNALC received a most important 3-year grant of \$820,000 from the Josiah Macy, Jr., Foundation to enable them to develop an extensive educational genetics website. Geri Barish and our special friends at *1 in 9: The Long Island Breast Cancer Action Coalition* presented a check for \$75,000 to Mike Wigler's lab in October at their annual black tie dinner dance fundraiser.

In other gifts, the St. Giles Foundation gave \$508,000 to Mike Wigler's lab and to visiting scientist Eli Hatchwell of Southampton University, Wessex Genetics Institute in Southampton, U.K., who came here to apply representational difference analysis to his studies of human genetics. The Sidney Kimmell Foundation for Cancer Research gave \$400,000 to cancer researchers Linda Van Aelst and Scott Lowe. The William and Maude Pritchard Charitable Trust gave \$243,000 in unrestricted funds, which were applied to the high-powered beamline at Brookhaven National Laboratory, a vital off-site tool for our X-ray crystallographers. The Lita Annenberg Hazen Foundation awarded \$200,000 to Karel Svoboda for neuroscience research, and the Pew Charitable Trust gave \$200,000 to research: Recipients included Greg Hannon, Tatsuya Hirano, Yuri Lazebnik, and Yi Zhong. The Alexander and Margaret Stewart Trust gave \$150,000 to support new projects in cancer research, and we are pleased that they have designated CSHL as one of the few cancer centers which they will support. The Oxnard Foundation gave \$120,000 toward muscular dystrophy research; the Oliver S. and Jenny R. Donaldson Trust contributed \$100,000 for sequencing equipment for the McCombie lab; and the V Foundation gave \$100,000 to Linda Van Aelst for her studies on the *ras* pathway. The Helen Hay Whitney Foundation gave \$87,000 to a postdoctoral fellowship for Peiqing Sun in David Beach's lab, and Pioneer Hi-Bred International, Inc., gave \$70,000 toward Ueli Grossniklaus' plant research. Henry Wendt gave \$56,450 for two postdoctoral fellowships in neuroscience: Frances Hannan in Yi Zhong's lab and Peter Krasnov in Grisha Enikolopov's lab. The Goldring Family Foundation gave \$50,000 toward support of two postdoctoral researchers: Bill Henry in Nouria Hernandez's lab and Kaetrin Simpson in

my lab. The Perkin Fund gave \$50,000 to neurobiologist Alcino Silva in support of his work on learning and memory in mice.

We also received two very generous gifts of real estate. Jill Hershey of Laurel Hollow and Bob Garland of Oyster Bay have each gifted their homes to the Laboratory, with each retaining a life estate. Jill and Al Hershey have been a part of the Laboratory for many decades, and Al's death in 1997 was a loss that we shared with Jill. Bob Garland, a good friend to several of our trustees, has been a supporter of the Laboratory since 1990. We are most appreciative of these very generous planned gifts.

## **President's Council**

The President's Council was formed four years ago in an effort to bring together a small group of individuals who have a keen interest in science and the work of CSHL. Through their annual commitment of \$25,000, the members provide support for the Cold Spring Harbor Fellows program. The funding is critical in attracting top-notch young scientists fresh from their Ph.D. studies. It allows them to embark on an independent research career, rather than assisting in the laboratory of an established scientist.

A major feature of the President's Council is its annual meeting that brings together this select group of leaders from business, finance, and science to discuss the latest developments in genetics research and biotechnology. The Council's 1997 meeting, held May 16–17, commenced with lunch on Friday at Ballybung and was followed by thought-provoking lectures by Scott Lowe and Ueli Grossniklaus of CSHL. The keynote speaker, Matt Ridley, of the Evolution and Behavior Research Group, University of Newcastle, England, opened the evening session with his talk on Gender Warfare and Evolution. Saturday's highlights included lectures by Rudi Jaenisch, of the Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology; Suzanne B. Cassidy, of the Center for Human Genetics, Case Western Reserve University; and David Haig, of the Museum of Comparative Zoology, Harvard University. The mix of leaders from the business field and the scientific community evoked interesting insights as well as provocative discussions. The meeting ended on Saturday with the guests gathering once again at Ballybung for a parting luncheon. The following are Members of the President's Council:

Abraham Appel, Appel Consultants  
Peter Bloom, General Atlantic Partners  
James Conneen, A.T. Hudson & Co.  
Michel David-Weill, Lazard Freres & Co.  
Stefan Englehorn  
Leo A. Guthart, ADEMCO  
Charles E. Harris, Harris & Harris Group, Inc.  
Walter B. Kissenger, WBK Associates  
Donald A. Pels, Pelsco, Inc.  
George B. Rathmann, ICOS Corporation  
Hubert J. P. Schoemaker, Centocor, Inc.  
James H. Simons, Renaissance Technologies Corp.  
Sigi Ziering, Diagnostic Products Corporation.



Leland Hartwell and Bruce Stillman

### **Gavin Borden Visiting Fellow**

On May 17, Leland Hartwell, Ph.D., now President of Fred Hutchinson Cancer Research Center, delivered the annual Gavin Borden Lecture. Dr. Hartwell discussed the role of yeast genetics in cancer research as part of the Gavin Borden Visiting Fellowship, named for the late charismatic publisher of scientific textbooks. The annual event was initiated in 1995 in honor of Gavin, who died in 1991 of salivary gland cancer, and in an effort to carry on the mission that was so dear to him: the education of graduate students. With this goal in mind, the annual lecture by an inspiring scientist is directed toward that audience, although it is open to all Laboratory staff. During their a 2-day stay at the Laboratory, Gavin Borden Fellows spend time talking with the graduate students who are currently studying at the Laboratory. Discussions typically involve science, life in science



Child Care Center Dedication

and careers in science.

## **Major Building Projects**

Over the course of 1997, we saw the completion of two very important building projects. The Mary D. Lindsay Child Care Center, which involved extensive renovation of the old De Forest Stables, was readied for its young charges in the late spring. The dedication of the building, which represented the culmination of a decade of effort to secure on-site child care for our employees, was held on Saturday, June 21. Tributes and thanks to Mary Lindsay and the Child Care Capital Campaign Committee were offered by the Laboratory's Director of Public Affairs and Development Susan Cooper, Laboratory President James Watson, and myself. The children of many lab employees, climbing on the colorful geometric playground equipment, made the event complete.

On October 19, we celebrated the completion of the Facilities Department's move to the Richards Building and facilities complex. The Richards Building resulted from the renovation of the old Kurahara house on the west side of Bungtown Road, supplemented by the construction of barns to the east and west of the building. The building was named for long-time director of Buildings and Grounds, Jack Richards, who has now assumed the more focused position of Director of Construction. His projects included major building renovations on a failing campus in the early 1970s, as well as assorted other tasks that fell under his loosely defined job, which in the early days included plowing, mowing, and distributing mail. Jack was responsible for developing a skilled and comprehensive staff of plumbers, carpenters, electricians, and others to serve the Laboratory's growing needs over the years. He also supervised the construction of Ballybung, the President's residence, together with Jim and Liz Watson in 1994. Toasts to Jack were offered by Arthur Brings, Director of Facilities; Raymond Gesteland, former Assistant Director of the Laboratory (1968–1971); contractors Arthur Herman of Herman Development Corporation and George Feraco, Sr. of Abel Grenier Inc. and Feraco Inc.; architect James Childress of Centerbrook, and me.

In 1997, we directed extensive effort toward planning of the Marks Building, which will be home to the new CSHL Advanced Imaging Facility. Centerbrook, the architectural firm recently awarded the American Institute of Architects (AIA) 1998 Architecture Firm Award, the highest honor conferred by the AIA, has been contracted by the Laboratory for this project. Lead architect Bill Grover has been involved in the planning and execution of many building projects at the Laboratory over the years, including Grace Auditorium in 1986; Beckman Neuroscience, Dolan Hall, and Hazen Tower in 1991; and the Watson's residence, Ballybung, in 1994.

The Marks Building will house teaching laboratories, which will further strengthen our educational initiative, and will expand our research initiatives through sophisticated imaging studies of the brain.

## **Undergraduate Research Program (URP)**

In 1997, we received 375 applications—a record number—for the Undergraduate Research Program. The 23 successful candidates, 16 men and 7 women, came from six countries. The program, known as the URP program, was initiated in 1959. Many former URPs have gone on to productive careers in the biological sciences, including David



Baltimore, a member of the first class, who went on to share the 1975 Nobel Prize in Physiology or Medicine. The URP program exposes students to hands-on experimental approaches to science and helps lead them to a greater understanding of the issues involved in biochemistry, genetics, and molecular and cellular biology. Participants live and work at the Laboratory for 10 weeks during the summer, so that they are exposed not only to science in the lab, but also to life as scientists.

A list of the students, their schools, mentors, and research projects may be found in the Undergraduate Research Program Section of this Annual Report. Information about the URP program and its alumni may also be accessed through the Laboratory's web site at: <http://www.cshl.org/URPsite/URP.html>

### **Partners for the Future (PFF)**

Each year since 1990, the Laboratory appeals to every Long Island high school science department chairman for the nomination of one student for participation in CSHL Partners for the Future program. In 1997, we were pleased to increase the number of Partners to six, each of whom spends a minimum of 10 hours per week at the Laboratory in October through March, doing original molecular biology experiments under the guidance of a scientist mentor.

The participants for the 1997–1998 school year (and their scientist mentors) are Aaron Bronfman of Syosset, Cold Spring Harbor High School (Bruce Stillman); Arti Anand of Jericho, Jericho High School (Peter Nestler); Bradley Gottfried of Plainview, Portledge School (John Connolly); Elyse Katz of East Setauket, Ward Melville High School (Hong Ma); Nancy Choi of Woodbury, Syosset High School (Michael Hengartner); and Chian Chuu of Bayville, Locust Valley High School (Michael Regulski). Arti Anand was the second Cablevision Scholar under a special Partners for the Future scholarship offered by Cablevision, the first local business to underwrite a portion of this important educational program.

### **Educational Outreach**

The Laboratory continues to take great pride in its educational outreach programs. We remain committed to the philosophy that it is vital to provide positive scientific experiences for young people in order to pave the way to a scientifically literate, and excited, next generation. The Interschool Exchange program continues to provide tours and meetings for students and parents of local private and public schools.

In 1997, we hosted four West Side School Science Nights: "How to Teach a Mutant Fly" (Tim Tully), "Turning Genes On" (Winship Herr), "You Don't Have to Be a Chicken to Lay an Egg" (Ueli Grossniklaus), and "How to Find a Needle in a Haystack" (Peter Nestler). These programs, initiated through West Side School, are now open to all local elementary students, parents, and teachers.

For high school students, we host a lecture series called Great Moments in Science. This year's talks were about gene transcription (Nouria Hernandez), the three-dimensional structure of proteins (Leemor Joshua-Tor), and brain development (Holly Cline). Students from the East Woods School enjoyed a tour and visit with scientist Roberto

Malinow. The Cold Spring Harbor High School brought their Japanese exchange students for a tour and luncheon for the third consecutive year.

The Laboratory once again participated in Project WISE—Women in Science and Engineering. Orchestrated by SUNY Stony Brook and funded by a grant from the National Science Foundation, the project involves several Long Island institutions—SUNY Stony Brook, CSHL, Brookhaven National Laboratory, and the American Association of University Women—each helping to expose bright young women to the world of science. The program involves female high school students in 9th through 12th grade, and each year the girls participate in research programs at one of the four institutions. In 10th grade, they come to CSHL for a research experience in molecular biology and genetics under the guidance of scientist mentors.

## Community Outreach

Several initiatives through our Department of Development continue to go well. The Next Generation Initiative (NGI) is a series of lectures and tours designed to inspire interest in basic research in people in their 30s and 40s. The Young President's Organization (YPO) provides similar experiences for young leaders of industry and companies, and the Harbor Society is a small group of Laboratory supporters who have contributed to the Laboratory's planned giving program.

For the general public, the Laboratory holds lectures and concerts throughout the year. Jan Witkowski continues to host Lloyd Harbor Seminars at the Banbury Conference Center, and periodically, scientists who are attending scientific conferences at Banbury will deliver a public talk on their area of expertise in Grace Auditorium. In April, Mary-Claire King did just that with her talk, "Breast Cancer Update." Dr. King, professor in the Division of Medical Genetics at the University of Washington in Seattle, was responsible for locating the first breast cancer gene, *BRCA1*; she gave her lecture while participating in *The Biology of BRCA1* meeting at the Banbury Center.

In October, Dr. Svante Paablo, Professor of General Biology at University of Munich, presented a lecture entitled "DNA, Neandertals, and Us." In November, we presented the



Benjamin Loeb (piano) and Allison Charney (soprano)



Top row: Art Brings, Bruce Stillman, Dave Micklos, James Watson, David Beach, Susan Cooper  
Bottom row: Cliff Sutkevich, Patricia Bird, Terri Grodzicker, Elaine Gaveglia, Barbara Terry

third Cold Spring Harbor Laboratory Lyme Disease Forum. Moderators of the discussion were Steven E. Schutzer, M.D., of the New Jersey Medical School Department of Medicine, and John Dunn, Ph.D., of Brookhaven National Laboratory's Department of Biology. The speakers, Patricia K. Coyle, M.D., of the University Hospital at Stony Brook Department of Neurology and Raymond Dattwyler, M.D., of the University Hospital at Stony Brook Department of Allergy and Lyme, discussed current research and clinical treatment of the disease and answered questions from the audience.

## Concerts

In 1997, we hosted seven concerts, each by one or more outstanding young classical musicians. Pianists, violinists, cellists, and sopranos played to audiences of scientists, staff, and neighbors. These concerts began as cultural refreshment for scientists who were at the Laboratory for several days or more attending scientific conferences. The caliber of the musicians has made these concerts an attractive event for our staff and neighbors as well and we have been delighted to provide great musical performances, usually for no charge. Performances in 1997 included: April 26, Alexander Velenzon on violin and Inessa Zaretsky on piano; May 10, pianist Freddy Kempf; May 24, pianist Wendy Chen; June 13, pianist Misha Dichter; August 30, The Laurel Trio with SunghaeAnna Lim on violin, Amy Levine Tsang on cello, and Dena Levine on piano; September 6, pianist Benjamin Loeb and soprano Allison Charney; and on September 20, pianist Jon Klibonoff.

## Long-term Service

A pool-side dinner at Robertson House on June 11 marked the anniversaries of several long-term employees of the Laboratory. Susan Cooper, Director of Public Affairs and Development, and Terri Grodzicker, Assistant Director of Academic Affairs, both cele-

brated their 25-year anniversaries. Over the years, Susan evolved from librarian, to marketing for the CSHL Press, to Director of the Library, then Director of Public Affairs, and finally took on Development as well. Her departure to become Director for Institutional Advancement at the Trudeau Institute in upstate New York (see Changes in Administrative Staff, below) left many holes to be filled at the Laboratory. Terri Grodzicker, who came to Cold Spring Harbor as a scientist in Joe Sambrook's James lab, went on to become a staff scientist and then Assistant Director of Academic Affairs and editor of *Genes & Development*.

Celebrating 15-year anniversaries were investigator David Beach, scientific secretary Patricia Bird, Director of Facilities Art Brings, typesetter Elaine Gaveglia, DNALC Director David Micklos, manager of equipment repair Clifford Sutkevich, and circulation manager Barbara Terry.

### **Changes in Administrative Staff**

In January, Nancy Ford concluded 24 years of dedicated service to the CSHL Press. Nancy was instrumental in developing the publications program, and she worked extremely well with a wide variety of well-respected scientists to create many landmark publications in molecular biology. Her professionalism and dedication were of great value to the Press and the Laboratory for without Nancy many of the distinguished volumes produced by the Press would not have been as great as they are. Nancy's contributions to the Press will long be remembered.

Susan Cooper, Director of Public Affairs, Development, and the Library exceeded her title by a good measure in her role as confidant and friend to many, in particular Jim



Nancy Ford at her retirement luncheon.



Susan Cooper in her CSHL office.

Watson. Her decision to accept the position of Director for Institutional Advancement at the Trudeau Institute came as a great surprise, although it is not difficult to see why Trudeau would have courted her. Susan worked double-time, with unparalleled dedication and true devotion. She arrived here in 1972 as head librarian in the Laboratory's Carnegie Library, and she grew up with the institution, later adding the roles of Director of Public Affairs and then Director of Development. Susan orchestrated and carried out the Lab's spectacular centennial celebration nearly a decade ago, as well as planning ceremonies and booklets for the Lab's many building dedications over the years. She had a remarkable rapport with our friends, neighbors, and supporters, and she helped foster the careers of many of our scientists. Susan's vitality and enthusiasm made the Laboratory an enjoyable and interesting place to work. That she has "left home" to make her mark elsewhere is saddening to many of us, but we wish her and her husband Bob the best and much success.

## **Changes in Scientific Staff**

### **Departures**

Carol Greider moved on to a position as Associate Professor with Johns Hopkins University School of Medicine, Department of Molecular Biology and Genetics, in Baltimore. Carol's work with telomeres and telomerase, the enzyme that regulates their length, earned her much scientific and popular acclaim during her years at Cold Spring Harbor. Carol came to the Laboratory in 1988 as a Cold Spring Harbor Laboratory Fellow after completing her Ph.D. with Elizabeth Blackburn at University of California Berkeley, where Carol discovered telomerase as a graduate student. In 1989, Carol was appointed to the staff of the Laboratory, eventually being appointed full investigator. The move to Maryland has worked well for Carol and her family as her husband, Nathaniel Comfort—former Science Writer at CSHL—simultaneously accepted an assistant professorship at George Washington University, in Washington DC, after completing his Ph.D. in the history of science.

X-ray crystallographer Xiaodong Cheng left for a position with Emory University in Atlanta, Georgia. Xiaodong came to us as a postdoctoral researcher in 1990 and worked for 2 years in Jim Pflugrath's lab. He became a staff member in 1992 and did much ground-breaking work with DNA methyltransferases and methylation during his time here, including the discovery of the phenomenon called "base flipping," whereby a single base turns outward from the DNA helix—in effect opening the DNA at a given point.

Erich Grotewold, who arrived here as a postdoctoral researcher in 1989, left for a position at Ohio State University, in Columbus.

Tom Marr, a member of the Laboratory's bioinformatics team since 1989, has completed the transition from CSHL to president and C.E.O. of Genomica Corporation in Boulder, Colorado.

Joe Colasanti, research investigator who came to do postdoctoral research with Venkatesan Sundaresan in 1988, has gone on to The University of California at Berkeley, Plant Gene Expression Center, as visiting assistant research geneticist.

Masafumi Tanaka, staff investigator who came as a postdoctoral researcher in 1986 and joined the staff in 1988, moved on to Tokai University School of Medicine in Japan.



## Arrivals

Neurobiologist Karel Svoboda joined our scientific staff in June. Karel studied physics at Cornell University and biophysics at Harvard, where he used a technique called laser-optical tweezers to measure the force generated by individual molecular motors. More recently, at Bell Laboratories in New Jersey, he used two-photon excitation laser scanning microscopy to obtain never-before seen images of neurons in living brains. Two-photon excitation laser scanning microscopy is an emerging imaging technology; it utilizes the tremendous concentrations of light achievable with pulsed-laser light sources to “excite” fluorophores by two-photon absorption. Karel is applying his knowledge of this technique to the establishment and further development of a state-of-the-art neural imaging facility at CSHL.

David Jackson arrived in September, after doing postdoctoral research in Sarah Hake’s lab at the Plant Gene Expression Center in Berkeley, California. David is a maize geneticist; he has been using transposons—Barbara McClintock’s jumping genes—to study such phenomena as development of flowering plants, including the formation of leaves from a small group of cells called the meristem. In addition, David is studying intercellular transport, the movement of proteins and other molecules from one plant cell into another.

Andy Neuwald joined us in November, from the National Institutes of Health, National Center for Biotechnology in Bethesda, Maryland. Andy is a computational biologist and is interested in the development and use of statistical and algorithmic methods to classify and model protein domains and is also working on the development of a comprehensive database in which to log the resulting data.

## Promotions

Yi Zhong, a staff member with our neurobiology program since 1992, was promoted to Associate Investigator. Bill Tansey, a postdoctoral researcher in Winship Herr’s lab since 1992, was appointed Assistant Investigator in 1997, and he is now combining two active areas of research, gene transcription and cell cycle control. Doug Conklin, a postdoctoral researcher in David Beach’s lab since 1993, was promoted to the position of Senior Fellow. Postdoctoral researchers Neilay Dedhia from Dick McCombie’s lab, Robert Lucito of Michael Wigler’s lab, and Elly Nedivi of Hollis Cline’s lab were each appointed Research Investigator. Graduate student John Connolly completed his Ph.D. from the Massachusetts Institute of Technology while working in Tim Tully’s lab and is now doing postdoctoral research in the Tully lab.

In addition, two visiting scientists have joined our staff: Clifford Yen and Masaaka Hamaguchi, both of whom were visiting Michael Wigler’s lab, have each been appointed Research Investigator.

## Visiting Scientists

Nine visiting scientists wrapped up their sojourns to CSHL: Aiping Dong, visitor to Xiaodong Cheng’s laboratory, has moved to a position as visiting scientist at Emory University in Atlanta, Georgia; Konstantin Galaktionov, who came from Leningrad, USSR in 1988, left David Beach’s lab to accept an assistant professorship at Baylor College of

Medicine in Houston Texas; and Roberta Maestro, in David Beach's lab since 1995, returned to CRO in Aviano, Italy. Eli Hatchwell, a clinician from Wessex Clinical Genetics Service in Southampton, UK, spent 6 months in Michael Wigler's lab applying RDA to his research and has since returned to the UK. Liam Dolan returned to the John Innes Center in Norwich, UK, from Rob Martienssen's lab, and Ross Bicknell concluded his visit with Ueli Grossniklaus, to return to Crop & Food Research in Christchurch, New Zealand.

Several more visiting scientists have arrived. Jiaxin An, of the China Academy of Space Technology in Beijing and Zuoping Xie of Tsinghua University, also in Beijing, have both come to do research in Yi Zhong's lab. Ming Huang of Otsuka America Pharmaceutical Inc. is visiting Michael Zhang's lab, Nobuhiro Kashige of Fukuoka University, Department of Pharmacological Science in Kukuoka, Japan, is working in Ryuji Kobayashi's lab, and Tatyana Michurina from the Institute of Developmental Biology in Moscow, Russia is visiting Grigori Enikolopov's lab.

### **Postdoctoral Departures**

Stephen Buck, Siyuan Le, Bong-Kyeong Oh, and Michael Rudd moved with Carol Greider to Johns Hopkins University in Baltimore, MD, to continue their postdoctoral studies in her lab, and Maria Blasco, also of Carol's lab, went to a position as Staff Investigator at the Universidad Autonoma De Madrid.

Weimin Gong and Yu Liu transferred with Xiaodong Cheng to Emory University School of Medicine, Atlanta, GA, to continue their postdoctoral studies in his lab, while John Horton went with Xiaodong to Emory to become an Assistant Professor there. Margaret O'Gara and Xujia Zhang of Xiaodong's lab each moved on as well; Margaret accepted a position as scientist with Pfizer Ltd., in Sandwich, UK, and Xujia became a researcher at the Biophysics Institute, in Beijing, China.

From the Stillman lab, Gerhard Cullmann became a Project Leader at Connex, in Germany; Kim Gavin stayed on to become an Editorial Assistant for the CSHL Press; Masumi Hidaka accepted a position as Assistant Professor at the National Institute for Basic Biology in Okazaki, Japan; Masayoshi Iizuka became an Assistant Professor at the National Cancer Center in Tokyo, Japan; and Caroline Mirzayan took a position as Assistant Professor at the University of Aarhus, in Denmark.

From David Beach's lab, Kang Dai accepted a position as scientist with Chiron Company, Walnut Creek, CA; Manuel Serrano went on to become Staff Investigator with Centro Nacional De Biotechnologia in Madrid, Spain; and Amancio Carnero has moved to David's new laboratory at the Institute for Child Health in London.

From Hollis Cline's lab, James Edwards is continuing his postdoctoral studies at Virginia Commonwealth University, in Richmond, VA, and Gang-Yi Wu is doing the same at Stanford University in CA. From Hong Ma's lab, Hai Huang went on to become Professor at Shanghai Center of Life Science in China, and Hua-Ying Fan is continuing postdoctoral studies at New York University Medical Center. From Nick Tonks' lab, Salim Mamajiwalla became a patent agent with Blake, Cassels & Graydon, in Unionville, and Tony Tiganis is now a research officer with St. Vincent's Institute of Medical Research in Victoria, Australia.

From Dick McCombie's lab, Arthur Johnson became Sequencing Facility Director at North Carolina State University, Department of Forest Biology, in Raleigh, NC, while

Muhammad Lodhi accepted a position as senior scientist with Sequana Therapeutics in LaJolla, CA. From the Krainer lab, Javier Caceres went on to become Group Leader at the MRC, Western General Hospital in Edinburgh, Scotland, and David Horowitz became Assistant Professor at the Uniformed Services University of the Health Sciences in Bethesda, MD.

Derek Gordon left Tom Marr's lab to continue postdoctoral studies at Rockefeller University, in New York, NY. Bing Guo went from Kim Arndt's lab to continue postdoctoral research at the Whitehead Institute in Cambridge, MA. Sui Huang left David Spector's lab to accept a position as Assistant Professor at Northwestern University Medical School in Chicago, IL, and Peter Lorenz is continuing postdoctoral research at University of Rostock, Institute of Immunology in Rostock, Germany. Stephen Brand left Mike Mathews' lab to accept a Clinical Research Scientist position with Cato Research in Durham, NC. Thillai Koothan of the Malinow lab is continuing postdoctoral research at the Mayo Clinic in Jacksonville, FL. Patricia Springer of Rob Martienssen's lab is now an Assistant Professor at the University of California, Riverside, and Mee-wa Wong of Nouria Hernandez's lab is now at the University of Texas. Qizhi Wang finished up in Mike Mathews' lab, and Christopher Jones and Gert Bolwig left Tim Tully's lab: Christopher accepted a postdoctoral position at the University of Tennessee and Gert became an Assistant Professor at the Institute of Human Genetics in Denmark.

### **Graduate Student Departures**

Nick Carpino went from Ryuji Kobayashi's lab to do postdoctoral research at St. Jude's Children's Hospital in Memphis, TN, and Chong Huang graduated from Winship Herr's lab and accepted a postdoctoral research position at the Molecular Neurogenetics Unit of Massachusetts General Hospital in Boston, MA.

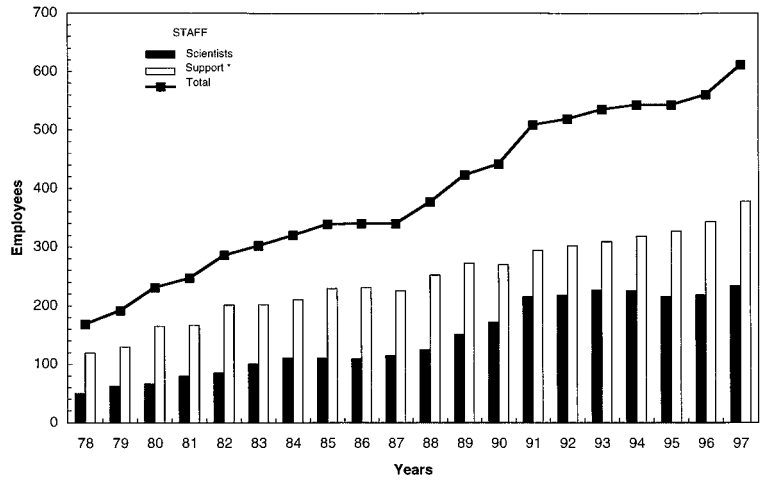
Two graduate students made the transition to medical school and one joined the computer world, Benjamin Lee of Winship's lab is now a medical student at SUNY Stony Brook School of Medicine in NY, and Aneil Shirke of Roberto Malinow's lab is now a medical student at University of Iowa in Iowa City, IA; Jian Sheng of Yi Zhong's lab has become a student in the Computer Department at SUNY Stony Brook.

Doug Mason went to continue graduate studies with Carol Greider at Johns Hopkins School of Medicine.

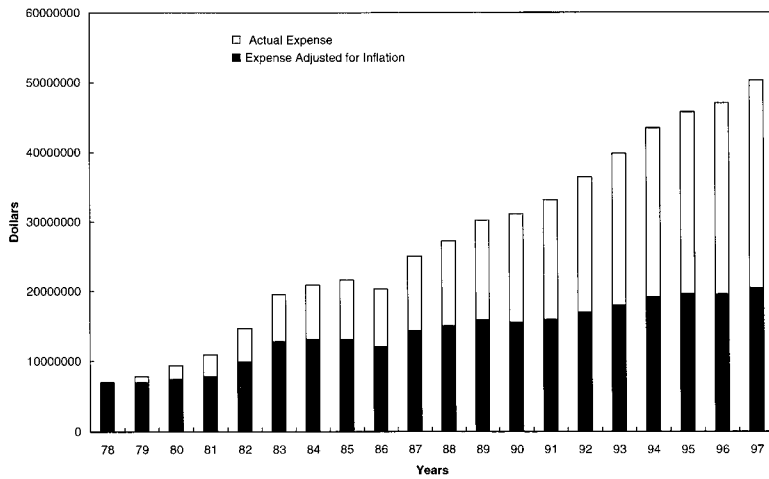
### **A Busy Agenda**

Cold Spring Harbor Laboratory has never rested on its past accomplishments. Throughout the history of the Laboratory, the introduction of new programs such as the scientific meetings in the 1930s, the laboratory courses in the 1940s, the Banbury Conference Center in the 1970s, and the DNA Learning Center in the 1980s has transformed and strengthened the institution. I am pleased that we have a vigorous research agenda and that the educational programs at the Laboratory continue to go from strength to strength. We have chosen to undertake several major initiatives this year: expansion of our research facilities, fostering a local biotechnology industry, and growth of our educational mission by developing a graduate school of biological sciences. Each of these objectives presents a great challenge, but they are all necessary to ensure that Cold

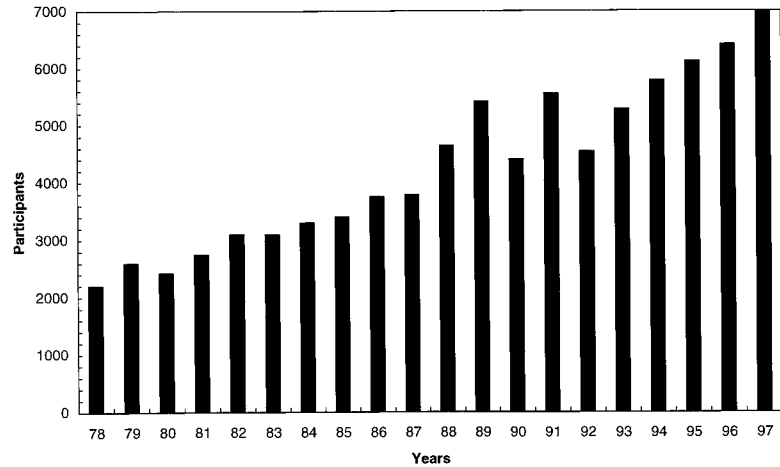
\* Consists of Full time and Part-time Technical Support, Core Services, Publications, Meetings, Library, Public Affairs, Building and Grounds, Administrative Personnel, Banbury Center and DNA Learning Center



### OPERATING EXPENSE



### MEETINGS & COURSE PARTICIPANTS



Spring Harbor Laboratory remains a vital and exciting place to live and work. We have a very busy time ahead, but I am confident that we can efficiently incorporate these new programs into our existing infrastructure while maintaining a high standard of excellence and a leading role in biology and the biomedical sciences.

*April 1998*

**Bruce Stillman**