

HIGHLIGHTS OF THE YEAR

Research Highlights

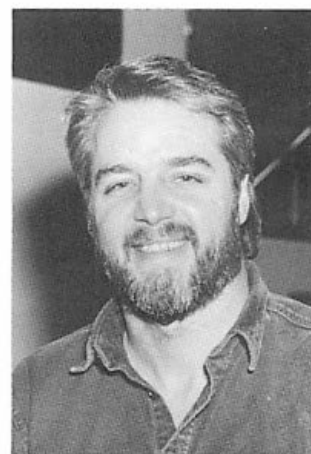
Cold Spring Harbor Laboratory research focuses on three major areas: cancer, neurobiology, and plant genetics. In 1995, all three areas saw exciting progress. Our neurobiology program had a banner year with tremendous breakthroughs in understanding the genetic basis of learning and memory. Senior Staff Scientist Tim Tully came to Cold Spring Harbor in 1991 concurrent with the dedication of the Beckman neuroscience building. He brought with him fruit flies and the training apparatus he had developed for them.

Tully is a behavioral geneticist and performs behavioral experiments on the fruit fly *Drosophila*. Using a Pavlovian approach, he and his colleagues train the fruit flies to avoid a particular odor by associating it with an electrical shock. With the help of an outstanding research technician, Maria Del Vecchio, Tully found that normal wild-type fruit flies require ten training sessions with rest intervals in order to learn an associative learning task and to produce maximum long-term memory. Additional training sessions provide no additional benefit to long-term memory. In contrast, repeated sessions without rest intervals (massed training) produced no long-term memory. Thus, like humans, *Drosophila* remembers best when a task is learned over a period of time as opposed to learning a task crammed into one intense training session, which produces little, if any, long-term memory. By comparing the results of experiments using genetically altered fruit flies with those done using normal wild-type flies, Tully and his colleagues have associated differences in learning patterns with genetic mutations, tracking down the genes and proteins critical to the learning process.

While Tully is training fruit flies, Senior Staff Investigator Alcino Silva is one floor below in Beckman doing similar studies with mice. Silva began by studying the effects of mutations in mice on learning and memory. His work focuses on the function of the hippocampus, a region of the brain that is critical to the formation of new memories in mice and humans. He first studied how removal of the gene that produces an enzyme called CaMKII affects learning and memory in mice. Alcino uses a standardized test known as the Morris Water Maze to test learning in mice.

In the Morris Water Maze, the mice are placed in a tank of cloudy water, where a platform is hidden somewhere just below the surface. Initially, the mice do not know where the platform is, but eventually they learn with the help of a flag on the platform and large geometric shapes on the walls that serve as orientation markers, or landmarks. Both normal mice and mice lacking the CaMKII gene soon learn to find the platform easily by swimming to the flag. When the flag is removed, however, the normal mice continue to swim directly to the platform following clues from the orientation markers, whereas the mice with the CaMKII gene deleted swim aimlessly about, having failed to retain the spatial orientation necessary to remember where the platform is located. Subsequent experiments to test visual impairment, decreased motivation, and other possible effects of the CaMKII deletion proved that in every other way these mutant mice are normal—only their ability to learn how to follow the orientation markers is apparently severely impaired.

These parallel studies on flies and mice have converged on the importance of



Tim Tully



Alcino Silva



Jerry Lin



David Beach



Carol Greider

a protein called CREB, which regulates gene transcription. Tully, his associate Jerry Yin, and Silva have discovered that the CREB gene has a critical role in the formation of long-term memory in both flies and mice.

Jerry Yin, a Senior Staff Investigator, studies the genetic components of learning and memory. In collaboration with Jonathan Wallach, a graduate student in the lab of Chip Quinn at the Massachusetts Institute of Technology, Jerry discovered that the CREB gene produces two proteins, an activator and repressor. Tully and Yin blocked the activity of the CREB protein in the fruit flies by stimulating the repressor form using a genetic tool known as a heat shock promoter. By attaching the heat shock promoter to the CREB repressor, and then raising the flies' body temperature by warming the chamber in which they are trained, they were able to block the activity of CREB in the fly. To study CREB in mice, Silva obtained mice from Günther Schutz in Heidelberg that lacked the CREB gene. Experiments by both Cold Spring Harbor groups—using flies and mice—yielded the same results: CREB-impaired organisms have short-term memory intact, whereas the formation of long-term memory is impeded.

In 1995, a series of experiments by Tully and Yin produced an unprecedented result. Although in the earlier experiments they along with Alcino Silva were able to prevent learning by inhibiting the activity of the CREB protein, last year they asked whether increasing the activity of CREB would improve memory, a much more difficult experimental result to achieve. Again, using the heat shock promoter, Tully and Yin hyperstimulated the activator form of CREB. In doing so, they were able to produce *instant* long-term memory in fruit flies after only one exposure to a given task!

The generation of such "photographic" memory has not yet been accomplished in mammals—Silva does not have the luxury of using a heat shock promoter in his mice. Mice do have such a genetic switch, as do humans, but as warm-blooded creatures, they are only mildly susceptible to changes in body temperature based on changes in the atmosphere. However, as the research progresses and scientists look for other genetic tricks that might be utilized in mammals, we look forward to achieving even greater understanding of learning and memory—knowledge that may lay the groundwork for treatment of learning disabilities, Alzheimer's disease, trauma, and other disorders.

As exciting as the Cold Spring Harbor neurobiology program is, there remains an unfaltering dedication here to basic cancer research. David Beach's lab continues to make progress in studies of cell cycle control. Recent work in his lab further elucidated the role of three genes that encode related regulatory proteins that are similar to the yeast CDC25 protein, two of which—CDC25A and CDC25B—have been implicated in breast cancer. Overexpression of one or both is seen in 70% of breast cancer tumors. Work on this very promising area of cancer research is ongoing and promises to bring new light to the search for effective breast cancer treatment.

Carol Greider studies telomerase, an enzyme that she discovered 10 years ago, while a graduate student with Elizabeth Blackburn at the University of California, Berkeley. Since that time, continued research has shown that telomeres, the ends of chromosomes, are normally shortened with each replication cycle in cells that ultimately die. Telomerase maintains the length of the chromosome's ends and when absent in unicellular organisms causes them to senesce. Interestingly, telomerase is found in approximately 90% of tumor cells but not in most normal cells. 1995 was a year of extraordinary progress in the search for greater understanding of this immortalizing and potentially oncogenic enzyme.



N. Lisitsyn, M. Wigler



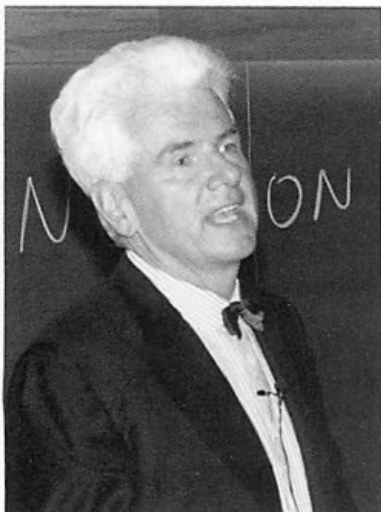
V. Sundaresan, U. Grossniklaus, R. Martienssen

Early in the year, Greider along with Kathleen Collins and Ryuji Kobayashi purified essential protein components of the telomerase enzyme and cloned their corresponding genes. Months later, Greider, in collaboration with researchers at Geron Corporation in Menlo Park, California, cloned the RNA component of human telomerase, termed hTR. Maria Blasco of Greider's lab cloned the telomerase RNA component found in mice, an accomplishment that will allow direct experimental testing of the role of telomerase in normal mammalian development and cancer. Greider and associates also succeeded in expressing a complementary RNA strand, which latches on to the active telomerase RNA, thereby inhibiting the telomerase activity and allowing the shortening of telomeres and ultimate cell death. We hope to know soon whether telomerase might represent an ideal target for anti-cancer drugs.

Michael Wigler and Nikolai Lisitsyn recently developed a technique for gene-finding that has led not only to significant discoveries in their own lab, but also to discoveries nationwide by assorted researchers in various fields. Representational Difference Analysis, or RDA, is a high-tech method of comparing the DNA of healthy tissue with that of diseased tissue. RDA has been used in the Wigler lab and elsewhere to locate mutations in cancer cells from the breast, kidney, bladder, lung, colon, skin (melanomas), and brain (neuroblastomas). RDA has also enabled researchers at Columbia University to identify a virus suspected of causing Kaposi's sarcoma in AIDS patients, scientists at Abbott Laboratories to identify three previously unknown hepatitis viruses, and researchers at Pathogenesis to identify a form of human herpesvirus that may be associated with multiple sclerosis. RDA was also successfully employed by researchers at Johns Hopkins to screen for mutations in pancreatic cancer. The technique was granted a patent by year end and is considered to be a most promising tool in the fight against cancer and infectious disease.

Our plant genetics program, which carries on the Nobel prize-winning work of the late Barbara McClintock, made great strides as well in 1995. Plant geneticists Rob Martienssen and Venkatesan Sundaresan and their colleagues developed a powerful new system for identifying genes involved in plant growth and development. The system utilizes McClintock's maize transposable elements and is being used to generate a large collection of *Arabidopsis* plants, each carrying a transposon tag integrated into or near a different plant gene. This system facilitated identification of the *prolifera* gene, a homolog of yeast and mammalian genes that regulate DNA replication.

With strong progress in neurobiology, cancer, and plant genetics, we now look forward to an equally exciting 1996.



Günter Blobel

Symposium LX: Protein Kinesis

This year's annual CSH Symposium on Quantitative Biology marked the event's 60th anniversary. The topic of discussion for 7 days in early June was Protein Kinesis: The Dynamics of Protein Trafficking and Stability. Günter Blobel, of the Howard Hughes Medical Institute and Rockefeller University and a CSHL trustee, delivered the annual Dorcas Cummings lecture entitled "How Proteins Find Their Addresses in Cells." Dr. Blobel presented a clear overview of the complex system of traffic and transit of proteins within cells, drawing analogies including molecules as cars and microtubules as tracks and describing the types of information encoded in the amino acid sequence of each protein. Dr. Blobel's talk was followed by the traditional Symposium dinner parties in the homes of local Laboratory supporters. At the close of the Symposium, George E. Palade, Nobel prize winner in 1974 for his work on the structural organization of the cell, delivered the summary.

At this year's Symposium, we inaugurated the Reginald G. Harris Lecture in honor of the former director of the Laboratory who initiated the Cold Spring Harbor Symposium in 1933. Harris recognized the need to bring biologists together to discuss their science and to provide a forum for making biology more rigorous; hence, the name "Cold Spring Harbor Symposia on Quantitative Biology." We were pleased to have Dr. Randy Schekman, University of California at Berkeley, present the first Reginald Harris Lecture.

Banbury Conference Center

The J.P. Morgan Executives' Meeting. It is hard to believe that 1995 marked the tenth year of our program designed for the senior executives of pharmaceutical and biotechnology companies. Initiated in 1986, these meetings have achieved a remarkable reputation for combining the best in modern research with the best from the business world. That this has been so is due in large part to our succession of sponsors—first Shearson-Lehman Brothers, then Baring Brothers, and now J.P. Morgan Co. This year's meeting was entitled Infectious Diseases: Ancient Plagues, New Epidemics and covered topics ranging from a history of epidemics to the ways in which X-ray crystallography is being used to understand immunological responses to viruses. A highlight of the meeting was the presentation by Ham Smith on the rapid sequencing of the complete genomes of *Hemophilus influenzae* (1.6 million base pairs) and *Mycoplasma genitalium* (0.6 million bases pairs). This served to show how far we have come since the first meeting on "The Genetic Knowledge of Man" in 1986. At that meeting, Lee Hood talked of his work on sequencing the whole of the HLA region, a project that was at the outer limits of what was then possible. Since we have come so far in ten years, who can tell what might be the subject of our twentieth meeting?

Meetings on Breast Cancer. Two meetings at Banbury Center exemplified our commitment to understanding and using our knowledge of the genetic causes of breast cancer. The first meeting was a joint venture of the Banbury and DNA Learning Centers to provide a forum for members of Long Island's 1 in 9 Breast Cancer Action Coalition to learn in more depth about molecular genetics and cancer. In addition to talks on the fundamentals of genetics from Mark Bloom, Dave Micklos, and Jan Witkowski, there were talks by invited speakers such as Elizabeth Claus of Yale University School of Medicine and experiments at the DNA Learning Center. The second meeting, Molecular Diagnostics of Breast

Cancer, brought together the world's leading breast cancer epidemiologists and molecular geneticists to examine the implications of the cloning of the BRCA1 breast cancer gene (an event that was followed, some two months after the meeting, by the isolation of the BRCA2 gene).

Duchenne Muscular Dystrophy. In 1980, we held a meeting at Banbury Center to examine how the then new advances in molecular human genetics could be applied to what was perceived at that time as the most intractable of the human inherited disorders. Six years later, the gene was cloned, and 15 years later, we were able to hold an open meeting in Grace Auditorium to discuss the various approaches to therapy.

The meeting was intended to provide an opportunity for parents of affected children to hear from key researchers, including Gordon Foulkes, Chief Scientific Officer of Oncogene Science, Inc. The Laboratory has been working with Oncogene Science in utilizing a new strategy in the search for compounds that will turn on a gene that may replace the one damaged in Duchenne muscular dystrophy. We cannot tell how likely success will be, but all avenues must be explored to find a treatment for this terrible disease.

50 Years of Phage

This year marked the fiftieth anniversary of phage research at Cold Spring Harbor. It was in the summer of 1945 that the first course on bacteriophage research was introduced here by Max Delbrück. An annual phage meeting ensued, commencing in 1947 in Nashville, Tennessee, and moving to Cold Spring Harbor in 1950, where it was wisely scheduled to dovetail with the phage course, encouraging course participants to stay on and attend the meeting. The course ran through 1970, after which it evolved into what is today called the ABG course, for advanced bacterial genetics, and the meeting has been at the Laboratory every year since 1950, with the exception of one. The meeting in August was both a celebration of the rich history of phage research and a forum for the presentation of new advances building upon the foundation of knowledge laid here so many years ago. Participants shared memories and data and many younger attendees



François Jacob, Gunther Stent, Marilyn Zinder

were excited to become acquainted with people whose names they knew from the classic papers.

Notable participants included Wacław Szybalski, Evelyn Witkin, Gunther Stent, François Jacob, Franklin Stahl, Takashi Yura, Rollin Hotchkiss, Norton Zinder, Charles Yanofsky, Dale Kaiser, Boris Magasanik, and Gisela Mosig; it was especially delightful to welcome back the witty and charming Manny Delbrück. The meeting was enriched by historic displays of abstracts dating back to the 1950s, photographs, and memorabilia. As the days passed, a sign-in book for reminiscences was filled with insights from phage participants old and new, creating a wonderful new artifact for the Cold Spring Harbor phage collection. By all accounts, the event was a great scientific, historic, and social success.

Fifth Anniversary of the Human Genome Project

In November, 1995, the Human Genome Project celebrated its fifth anniversary. In honor of this milestone, a group known as The Genome Action Coalition (TGAC) sponsored the First Annual James Watson Lecture and Awards Ceremony at the National Academy of Sciences in Washington D.C.

TGAC is a voluntary association of more than 70 patient advocacy groups, professional organizations, and biotechnology and pharmaceutical companies who have pledged their support to this important project through its completion. In recognition of my role (J.D.W.) as the first director of the National Center for Human Genome Research at the National Institutes of Health, I delivered the introduction and opening remarks. Dr. Francis Collins, its current director, then gave an update on the status of the progress of genome mapping and sequencing. The featured speaker for the afternoon was Senator Mark Hatfield of Oregon, the Chairman of the Senate Appropriations Committee and one of the leading congressional advocates of biomedical research. Senator Hatfield spoke about the relationship between groundbreaking genetics research and public policy.

The event was also honored by the attendance of Secretary Donna Shalala of the Department of Health and Human Services, who was awarded the TGAC National Policy Leadership Award, and Senator Pete Domenici of New Mexico, Senator Tom Harkin of Iowa, and Congressman John Edward Porter of Illinois, who received TGAC Congressional Awards for their support of basic research.



Thomas Jessell

Board of Trustees

In 1995 the Board of Trustees nominated and elected three new members: William E. Murray, Whitney D. Pidot, and Lola N. Grace.

Mr. Murray is an attorney in private practice specializing in estates and trust. Bill has been a friend to the Laboratory for many years—he assisted in establishing the Samuel Freeman Computer Laboratory (1985), the Neuroscience Center (1988), and the Samuel Freeman Laboratory of Cancer Cell Biology (1989).

Mr. Pidot is an attorney in corporate law, currently a partner at the firm Shearman & Sterling in New York City. Mr. Pidot is a long-time neighbor of the Laboratory residing in nearby Locust Valley.

Mrs. Grace is a managing director of Sterling Grace Capital Management in New York and is a director of the Society of Memorial Sloan-Kettering. Lola and her husband John are part of an outstanding family of Laboratory supporters. The late Oliver Grace, John's father, and his wife Lorraine have been true friends of

the Laboratory for many years; in 1984, they gave funds toward the construction of Grace Auditorium, allowing the Laboratory to create an exceptional forum for world-renowned scientific meetings, and in 1987, they established the Oliver Grace Chair for Cancer Research which I (J.D.W.) am privileged to hold.

Thomas Jessell completed his six-year term on the Board this year. Dr. Jessell, a former instructor of Cold Spring Harbor neuroscience courses, continues his studies on developmental neurobiology at Columbia University and was recently elected a Fellow of the Royal Society. We wish him the best in his future endeavors.

Townsend J. Knight, Esq., completed his most recent term on the Board and has been named an Honorary Trustee. Townie is a descendant of John D. Jones, founder of the Biological Laboratory at Cold Spring Harbor in 1890 and of the Wawepex Society, an organization established to administer the family's philanthropic interests. Among the family's charitable ventures were the donation of land and monies that were used to establish the first research laboratory at Cold Spring Harbor (known now as Jones Laboratory) built in 1893 and the establishment of the Knight Trust. Townie has served on the Board for many years (1971–1975, 1982–1995), and his continuing presence as an honorary trustee will provide us with invaluable advice and counseling.



Townsend J. Knight, Esq.

Trustee Receives Lasker Award

Scientific trustee Don Wiley, Ph.D., of Harvard University, received the 1995 Albert Lasker Medical Research Award for distinguished contributions to biomedical research. Dr. Wiley, professor of biochemistry and biophysics at Harvard University, was recognized for his revolutionizing work in immunology.

Robertson Research Fund

A tradition of giving was established by the Robertson family of Lloyd Harbor back in 1973, when Charles Robertson gifted nearly \$8 million to the Laboratory to create the Robertson Research Fund. At that time, he also initiated the transfer of the Robertson property on Banbury Lane, now the site of our Banbury Conference Center, and a fund for its maintenance. Then, two years later in 1975, the Banbury Fund—the Robertson family's private foundation—established the Marie H. Robertson Memorial Fund to support neuroscience research at Cold Spring Harbor. Its availability soon after allowed the establishment of year-round research in leech neurobiology by Birgit Zipser in the newly renovated Jones Laboratory.

In 1995, the Robertson Research Fund—its value now up to \$56 million—distributed \$1.6 million to basic research at Cold Spring Harbor, supporting 16 staff scientists; CSH fellow Scott Lowe, who works in James Laboratory on apoptosis and cancer therapy; postdoctoral fellow Chantal Autexier, who studies telomeres (the ends of chromosomes) in Carol Greider's lab; and graduate student Shirley Pinto, who is studying the *latheo* gene, implicated in learning and memory in *Drosophila*, in Tim Tully's lab. The Marie Robertson Memorial Fund also supported research into the genetic basis of learning and memory in *Drosophila* in the Tully lab, including support for postdoctoral researcher Michael Regulski, and in mice in Alcino Silva's lab, including support for postdoctoral researcher Yoon H. Cho.

Major Gifts

We are again grateful for the strong support of our Trustees, interested individuals, foundations, corporations, and other charitable organizations. A major priority this year was the proposed acquisition of the beautiful Friends World College property in Lloyd Harbor. Through the generosity of our trustees, the Dolan Family Foundation, Thomas Saunders, David Luke, Edwin Marks, John Reese, an anonymous donor, and the William Stamps Farish Foundation, we received pledges in excess of \$3 million toward the purchase. In consideration of concerns voiced by a group of community members, we have withdrawn our application for the use of the Friends World College campus from the Village of Lloyd Harbor and, with our Board of Trustees, are discussing alternative projects to meet the needs for administrative and editorial space and additional scientist housing. We deeply appreciate the support of our friends at a time when we hoped to preserve the lovely 30-acre estate while fulfilling pressing needs of the Laboratory.

Our Undergraduate Research Program (URP) received important additions to its endowment with gifts of \$100,000 from The Garfield Foundation; \$100,000 from the estate of Joan Redmond Read; \$60,000 from our friend and colleague Bentley Glass; \$40,620 from the Burroughs Wellcome Fund, proceeds of \$51,000 from the wonderfully warm and well-received concert given by Flicka von Stade and Friends in the spring, and \$7,500 from Jephson Educational Trust.

The Laboratory science programs were well supported during the year with a gift of \$290,000 from Westvaco for the plant genetics program; \$150,000 from the McKnight Endowment for Science and one of \$120,000 from the John Merck Fund, both for Dr. Alcino Silva's lab; \$150,000 from the Prichard Trust for scientific equipment; \$100,000 from the Glaxo Research Institute and \$75,000 from Alan and Edith Seligson, each toward postdoctoral research fellowships; \$45,000 from 1 in 9: Long Island Breast Cancer Coalition for Dr. Mike Wigler's lab for cancer research, especially breast cancer; \$30,000 from the Goldring Family Foundation for postdoctoral support in Dr. Bruce Stillman's lab; \$20,000 from the Irving A. Hansen Memorial Fund; \$20,000 from Arrow Electronics for equipment; \$15,000 from the Lauri Strauss Leukemia Foundation for Dr. Nick Tonks; \$15,000 from Mrs. Oliver R. Grace for equipment; \$10,000 from the Dextra Baldwin McGonagle Foundation and \$10,000 from the Edward S. Moore Foundation for scientific equipment.

A most gracious gift was made by the Olin family in the form of three magnificent sculptures. Gerry and Sue Lin have been generous supporters of the Laboratory and recently, after the death of Sue's father, William Cohen, the Olins had to handle the distribution of his estate. Located on Mr. Cohen's property in Sands Point were original works of art ranging in height from 6 feet to 12 feet tall. The Olins were interested in placing these large sculptures in an appropriate environment and chose to offer them to the Laboratory to be placed on our beautiful grounds.

A cor-ten steel sculpture called *Profile/Canto #1*, by Ernest Trova—an imposing 8 feet high and 12 feet across—was relocated to the field on Bungtown Road across from the Yellow House. *Draco*, a gray Vermont marble piece by Kenneth Campbell now stands on the lawn of Ballybung while a second Campbell piece, twice the height at 12 feet and crafted of white marble, named *Pyramus and Thisbe*, stands just outside the north door of the Beckman Neuroscience Center. The campus has been both enriched and beautified with the addition of these one-of-a-kind heirlooms.



James D. Watson,
Sue Olin, and Gerald Olin

Our endowment funds fared well, led by a gift of \$150,000 from Bill and Marjorie Matheson for the Matheson Fund; \$50,000 from the Banbury Fund for the Robertson Chair; and an addition of \$74,000 to the Harrison Chair.

Support for research into the causes of Duchenne muscular dystrophy continued, with a contribution of \$52,000 from John Cleary. The DNA Learning Center received a grant of \$50,000 from Genentech to help in the construction of the new Cellarium exhibit and the Barker Welfare Foundation provided \$15,000 for program support.

The companies contributing to the Cold Spring Harbor Corporate Sponsor Program continue to provide a very substantial underpinning of the meetings program in Grace Auditorium and at the Banbury Center. Full acknowledgment of their generosity can be found in the Finance Section.

DNA Learning Center

Story of a Gene opened in May. The first exhibition to be developed in-house at the DNA Learning Center (DNALC), it traces the story of human growth hormone (HGH), an ideal case study in modern human genetics. HGH affects an obvious physical trait (height), its physiology and cell biology are well understood, and it was one of the first human therapeutics produced by recombinant DNA. The backdrop for the exhibit is the remarkable Cellarium, a room-size mural depicting the expression of the hormone within a single pituitary cell. Interactive exhibits challenge visitors to consider the parameters of human growth and the physical effects of growth hormone, as well as the controversial use of growth hormone to improve lifestyle for humans and milk production in dairy cows. November saw the publication of *Laboratory DNA Science*, a college-level course in recombinant DNA techniques developed by Learning Center staff members Mark Bloom and Dave Micklos, in collaboration with Cold Spring Harbor alumnus Greg Freyer of Columbia University.

The DNALC continues to play a unique part in promoting genetics education. In 1995, no fewer than 8,000 students and teachers came to the DNALC for hands-on DNA workshops and an additional 10,000 visitors saw the exhibits Story of a Gene and Long Island Discovery.

Scientists Recognized

Our reputation as an institution staffed by the best and the brightest is frequently reinforced by recognition in the form of awards to our scientists. This year, two Cold Spring Harbor scientists received major prizes: Michael Hengartner received the first annual Pharmacia Biotech & Science Prize for Young Scientists. Sponsored by *Science*, the journal of the American Association for the Advancement of Science, the award recognizes outstanding molecular biologists early in their careers. The grant of \$20,000 was formally presented at a ceremony in Sweden and recognized the excellence of Michael's Ph.D. thesis on apoptosis, or programmed cell death, which was completed while he was a graduate student at the Massachusetts Institute of Technology.

Carol Greider was honored by the American Society for Cell Biology, with the presentation of the first annual Glenn Foundation Award at the ASCEB's 35th annual Symposium in December. The \$5,000 grant is in recognition of Greider's work on telomerase, a protein implicated in extending the lives of cancer cells indefinitely.



Michael Hengartner

CSHL Press

Twenty new books were published, plus a new videotape set and an audio tape/CD. The total titles in print now number more than 220. The most successful new title was *PCR Primer*, a laboratory manual on amplification techniques, which sold more than 2,500 copies when released in the last quarter of the year. Also notable were four other lab manuals developed from practical courses taught at the Laboratory and two scholarly monographs edited with colleagues by two of the Laboratory's senior scientists: *Telomeres*, assembled by Carol Greider and Elizabeth Blackburn, and *Translational Control*, edited by Michael Mathews with John Hershey and Nahum Sonnenberg. A special reprint of François Jacob's autobiography *The Statue Within* was published to coincide with the fiftieth anniversary of the Laboratory's bacteriophage course.

The journal program continued to expand in scope and frequency. The successful five-year old bimonthly methods journal *PCR Methods and Applications* evolved into the monthly research journal *Genome Research*. The print issues were supplemented with information such as video clips made available through the journal's World Wide Web site, the first use of the Internet in this way by a science journal. *Genes & Development* consolidated its position in the top ten of the world's biology journals with another successful year editorially, increased circulation, and an increasingly important contribution to the financial performance of the Press.

The first issue of the annual directory, *The Lab Manual Source Book*, contained information from more than 600 suppliers about 15,000 products used in laboratory work with genes, cells, and proteins. It was distributed to 40,000 scientists worldwide. In addition, an interactive database, BioSupplyNet, was created on the World Wide Web to allow scientists rapid access to more detailed information about available products and their sources of supply.

CSHL Association

The annual meeting of the CSHL Association began with lunch at Ballybung on February 5 and was followed by a special lecture by Rich Roberts, the Laboratory's most recent Nobel Laureate. Roberts, who won the highest award of science in 1993, spoke to the audience of directors and friends of the Laboratory about his work on RNA splicing and about the extraordinary festivities associated with the Nobel prize ceremony in Stockholm, Sweden.

Joan Pesek, Associate Director for the annual fund, left the Association after nearly nine years; we will miss her enthusiastic participation. Jean Schwind, former grants assistant here at the Laboratory, has stepped into the position and is effectively handling the many facets of Association fund-raising.

One of the goals of the Association is to reach out to a new generation of supporters for basic research. Toward this end, the Association has initiated the Next Generation Outreach Program, a lecture series designed to stimulate the interest of a generation of 30–40-year-old community members and to bring the importance of basic research home to the audience. In the first lecture, Tim Tully discussed breakthrough discoveries in learning and memory and their implications for humans. The second lecture included Carol Greider, who discussed the importance of fellowships on the path to independent research, and Winship Herr, who discussed educational programs at the Laboratory. In the third lecture, Michael Wigler addressed what is probably the most prevalent question about basic research today: What kind of progress are we making in cancer research?

The final lecture featured David Micklos of the DNA Learning Center, who discussed personal and social implications of reading DNA.

The Association has an outstanding history of support of science and education here at the Laboratory, support that has played a crucial part in fostering our research, especially that of our young scientists. We are sure that through this outreach we will inspire participation by the next generation.

President's Council

The President's Council was formed in an effort to bring together a small group of individuals with a keen interest in science and the work of Cold Spring Harbor Laboratory. 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 young scientists fresh from their Ph.D. studies. It allows them the opportunity to pursue their own research, rather than assisting in the laboratory of an established scientist.

A major feature of the Council is an annual meeting to bring together this select group of leaders from business, finance, and science to discuss the latest developments in genetic research and biotechnology. The Council's first meeting, held May 12-13, began with lunch at Ballybung for Council members and their guests. Senior Scientist Adrian Krainer and CSH fellow Ueli Grossniklaus spoke to the group about the importance of the Cold Spring Harbor Fellows program in allowing scientists to do unrestricted independent research. The discussion at the meeting focused on the Societal Implications of Modern Human Genetics. The mix of minds of leaders in the business world and scientific community evoked provocative discussion as to the implications and issues that are coming to the forefront as our knowledge of the genetics of human behavior increases. The keynote speaker, Dr. Nancy Wexler, Columbia University College of Physicians & Surgeons, opened the meeting on Friday evening with her talk on The Promise and Perils of Human Genetics. A panel discussion was held on Saturday morning to discuss the ethical, legal, and social issues arising from our increasing genetic knowledge. Leading the discussion were Dr. Tom Bouchard, University of Minnesota; Dr. Tom Caskey, Merck & Co. Inc.; Dr. Tom Murray, Case Western Reserve University School of Medicine; and Dr. Norton Zinder,



President's Council

Rockefeller University. The day and the meeting ended with the guests gathering once again at Ballybung for a parting luncheon.

Founding members of the President's Council include Abraham Appel, Appel Consultants; Michel David-Weill, Lazard Freres & Co.; Frederick Frank, Lehman Brothers, Inc.; Leo A. Guthart, ADEMO; Charles E. Harris, Harris & Harris Group, Inc.; Walter B. Kissenger, Long Island Research Institute; David Mahoney, The Charles A. Dana Foundation; Donald A. Pels, Pelsco, Inc.; George B. Rathmann, ICOS Corporation; Frank E. Richardson, Wesray Capital Corporation; Hubert J.P. Schoemaker, Centocor, Inc.; James H. Simons, Renaissance Technologies Corp.; George Soros, The Soros Foundations; Margo Walker, Citivilla Properties; and Sigi Ziering, Diagnostic Products Corporation.

Special Events/Fundraisers

On March 25, Flicka von Stade and Friends charmed and entertained a packed house in Grace Auditorium for a second time. The very talented and equally beautiful diva strayed from her operatic style, performing a spectacular blend of ethnic folk songs, bluesy jazz, a little ragtime, and several rearrangements of classics by Bach and Schubert. Accompanied by Bill Crofut on banjo and vocals, Chris Brubeck on bass and trombone, and Joel Brown on guitar, Flicka raised additional funds for the Frederica von Stade Endowment, a fund that will provide an annual fellowship for our Undergraduate Research Program.

In June, 1 in 9: The Long Island Breast Cancer Action Coalition held their second annual Michael Scott Barish Sand Soccer Tournament in Long Beach. In October, several Lab members were invited to participate in 1 in 9's first annual Governor's Dinner Dance at the Seawane Club in Hewlett Harbor. Proceeds of the outdoor sporting event and the black-tie gala attended by Governor George and Libby Pataki were donated to the Laboratory in support of Michael Wigler's lab and the Human Cancer Fund. In a public ceremony in November, 1 in 9 presented the Laboratory with a check for \$45,000, more than doubling their initial grant to us in 1994 in support of Dr. Wigler's cancer research.

In September, CSHL Association director Carol Large coordinated a new event at Cold Spring Harbor: the Old Westbury Gardens Tree Symposium. Sponsored by the Westvaco Corporation, the event was conceived by Carol and organized in cooperation with Old Westbury Gardens and the Cornell Cooperative Extension of Nassau County. Horticulturists, gardeners, and other lovers of things green were drawn to Grace Auditorium to hear a day-long forum where horticulturists, landscape designers, and plantsmen presented, discussed, and debated their views on the present and future use of trees in the landscape. Participants included noted author Professor Michael Dirr of the University of Georgia and Robert Halpern of the Wildlife Conservation Society. The benefit raised nearly \$8,000 for the CSHL Association which supports scientific research by supporting research fellows.

A most rewarding cultural event is our Young Artist Concert series. Young classical musicians, many of whom have played to audiences around the world, perform in Grace Auditorium during our scientific meetings. Melvin Chen and Alexis Pia Gerlach performed in April at the Cytoskeleton meeting, on piano and cello, respectively. In May, Todd Palmer played clarinet and Margaret Kampmeier played piano before an audience of scientists interested in RNA processing. Respite from transcription factor studies in September was provided by Catherine Cho and Benjamin Loeb on violin and piano. Violinist Dmitri Berlinsky



Carol Large

and pianist Elena Baksht, both natives of Russia, provided melodic entertainment for the DNA replication crowd gathered at the Laboratory later in September with pieces from Ravel, Tchaikovsky, and Franck.

Some of the Young Artists performances are organized through Young Concert Artists, Inc. (YCA), a management company; others are privately sponsored. All are conducted free of charge for the scientists working at and visiting Cold Spring Harbor Laboratory. The Laboratory's long-time friend Roger H. Samet graciously sponsored the Chen/Gerlach performance, and Dr. Mark Ptashne, moved by an earlier YCA performance, donated \$5,000 through the D'Egville Foundation to provide support for the promotion of young artists and was the sponsor for the Cho/Loeb concert.

Family Spirit

The events that contribute to the Laboratory's family atmosphere spanned the year. The Easter Egg Hunt returned to Airlie lawn this past spring, sending children with baskets scampering about in search of brightly colored eggs. The summer brought the annual July Staff Picnic, which took place on one of the notoriously hot, over-100° days. Well-attended by staff, family, and friends, the harbor beach was the most popular place to be, second only to the shade beneath the trees along the shore.

Laurie Landeau, our long-time friend and former trustee, held her annual August beach party for the scientific staff at her still wonderfully undeveloped Eaton Neck property. In the cold of winter, children of Laboratory staff attended the annual Christmas party replete with gifts for every child, and food and drink for everyone. Afterward, the crowd gathered around the Christmas tree on Bungtown Road for caroling and the tree lighting. Carolers were distracted from the cold by the smooth sounds of the American Concert Band, a five-piece brass ensemble well-versed in the traditional songs of the season.

The Lab Makes History

In a satisfying culmination of 25 years of historic preservation here at Cold Spring Harbor, the Laboratory was honored in June with a certificate proclaiming its historic significance at both the state and national levels. Thanks to the tireless efforts of Liz Watson and her dedication to the architectural and historical integrity of each building on the grounds of the Laboratory, we have succeeded in earning a place on the New York State and National Registers of Historic Places (NRHP).

The nomination to the Register of Historic Places was initially inspired by the magnificent and historically true restoration in 1980 of Davenport House—the pumpkin-colored Victorian house built in 1884 that faces Route 25A at the entrance to the Laboratory. As Liz assembled the NRHP proposal, it became clear that virtually all of our buildings were historically significant: Airlie House, built in 1806 for Major William Jones; Davenport Laboratory (now Delbrück Laboratory), built in 1926 and subsequently named for Nobel prize winner Max Delbrück who established the famous "phage course" at Cold Spring Harbor; our grants and development building, Wawepex, built in ca. 1825 during the whaling era and named for the Indian word for "at the good little watering place." Indeed, the land itself, including the field on which Barbara McClintock grew the corn



Liz Watson, Bernadette Castro

used in her Nobel prize-winning work, earned a place on the National Register, as did the Cold Spring Harbor Fish Hatchery, established in 1887.

The designation celebrates not only the historic scientific and cultural significance of the Laboratory, its grounds, and the Fish Hatchery, but also the dedicated efforts of Liz and of Jack Richards of our Buildings & Grounds Department, who supervised much of the restorative construction. Bernadette Castro, Commissioner of New York State Department of Parks, Recreation, and Historic Preservation, presented a beautifully framed certificate to Liz at a breakfast ceremony in Blackford Hall on June 2. Among those in attendance from the Laboratory were Dr. Bruce Stillman, Director; Morgan Browne, Administrative Director; Dr. Winship Herr, Assistant Director; Arthur Brings, Director of Facilities; Susan Cooper, Director of Public Affairs and Development; Nathaniel Comfort, Science Writer who supplied the written documentation necessary for the nomination; and Jack Richards. Representing the CSH Fish Hatchery were Norman Soule, Director, and his wife Mary Ann and board members Mary Jo Hossfeld, Richard Cohen, George Dennis, Carol Dubois, Chris Nuccio, Muffy Osterhus, Mark Trotter, and Charles Holcomb. In addition, Allison Hain of School District 2 and Laurie Hempton, Historic Preservation Field Representative for the New York State Office of Parks, Recreation, and Historic Preservation (who worked so diligently with Liz to bring the project to fruition), were on hand to celebrate the designation.



Elizabeth Borden

Gavin Borden Lecture

Our graduate students are a vital part of Cold Spring Harbor Laboratory, both for their research and for the vitality they bring. This year, the Laboratory instituted a new event to honor a friend to science and the Laboratory and to acknowledge the role of the graduate students. The Gavin Borden graduate student seminar and lecture was named for the energetic and charismatic publisher of *The Molecular Biology of the Cell* (MBC) who died in 1994 of cancer.



Bruce Stillman (Left) and Bruce Alberts (center) at the Gavin Borden Lecture

The program opened on March 9 with a lecture by one of the six authors of *Molecular Biology*, Bruce Alberts, President of the National Academy of Sciences and Professor of Biochemistry and Biophysics at the University of California. The lecture, geared toward graduate students—Borden's target audience as a writer—was entitled "Avoiding a Train Wreck: What Happens When RNA Polymerase and DNA Polymerase Collide." After the lecture, there was a reception for Dr. Alberts, and then he and the graduate students had dinner together.

The following day, Dr. Alberts met individually with me (B.S.) and Assistant Director Winship Herr, and senior scientists Carol Greider, Michael Wigler, Nick Tonks, and Tim Tully. After a lunch with members of the scientific staff, Dr. Alberts met with all of the graduate students for an informal discussion. Topics discussed included the varied careers that young scientists can consider. Dr. Alberts' visit ended with supper at Ballybung with the Watsons. The education of graduate students was a mission dear to Gavin Borden's heart and the Laboratory proudly and enthusiastically supports that important charge.

Funding for the creation of the Gavin Borden Lecture series was provided by Gavin's widow Elizabeth Borden, myself (J.D.W.) and Liz, Dr. Bruce Alberts, and Robert Winthrop.

Undergraduate Research Program (URP)

The Undergraduate Research Program at Cold Spring Harbor Laboratory provides an opportunity for college undergraduate students to participate in active research projects under the supervision of Laboratory staff scientists. Since the inception of the URP program in 1959, 440 students have participated in the course and many have gone on to productive careers in biological science.

The URP seeks to provide not only a greater understanding of the fundamental principles of biology, but also an increased awareness of experimental approaches to science and a deeper understanding of the major issues in the fields of genetics and molecular and cell biology. The participants also garner a personal acquaintance with research, research workers, and centers for study.

This year, 22 students were selected from more than 280 applicants. Support for the URP was provided by Bio-Rad Laboratories, Burroughs-Wellcome Fund, C. Bliss Memorial Fund, The Garfield Internship, Hanson Industries, Jephson Educational Trust, Libby Internship, National Science Foundation, Phillips Petroleum Foundation, Inc., Powers Foundation, William Shakespeare Internship, and the Frederica von Stade Internship. (For a list of these students by name and university, see the URP Section in this Annual Report.)

Partners for the Future

In a mission to open Laboratory doors to an ever younger audience, the Laboratory has solicited nominations from all Long Island high schools each year since 1990. The Partners for the Future program is now in its sixth year, and once again, we have five talented high school students doing original research in the laboratories of staff scientists. The five students chosen to participate in the program come to the Laboratory each day after school, October through March, and do original experiments under the guidance of a scientist mentor. The culmination of the program is an oral presentation by the students in which they present the results of their months of study to an audience of proud parents, teachers, and mentors.

The 1995–1996 Partners, their schools, and mentors are Hayley Solomon of Plainedge High School with Dr. James Dezazzo; Danielle Cain of Sachem High School in Lake Ronkonkoma with Dr. Michael Regulski; Ilana Kurshan of Huntington High School with Dr. Venkatesan Sundaresan; Dominik Rosa of Commack High School with Dr. Hong Ma; and Elizabeth Tegins of St. Anthony's High School in South Huntington with Dr. Kim Arndt.

Project WISE

In an effort to encourage bright young women to enter into the fascinating world of science and technology, the Laboratory has entered into a program with the State University of New York, Stony Brook, called Project WISE (Women in Science and Engineering). Stony Brook recruited our participation, as well as that of Brookhaven National Laboratory and the American Association of University Women, in this program designed to expose high school girls to the sciences. Mary Horton of our Grants Department orchestrated our involvement, which included sponsoring two trips to the DNA Learning Center. On the first trip, the students used restriction enzymes to cut DNA from bacteriophage λ and then analyzed the fragments, all under the guidance of Laboratory scientist Diane Esposito.

On the second trip to the Learning Center, each young woman isolated a sample of her own DNA and fingerprinted it using the automated polymerase chain reaction (PCR). In addition to the DNA Learning Center workshops, the participants had dinner with and visited the laboratories of six Laboratory scientist mentors: Hollis Cline, Carol Greider, Ann Sutton, Roberto Malinow, Luis Peña, and John Horton. Each student participates for four years—9th through 12th grade. The Laboratory will, each year, instruct the 10th graders in molecular biology and genetics, offering a foundation upon which they can build a future in technology and the sciences.



*Top row: James D. Watson, Mike Riggs, Bruce Stillman
Middle row: Madeline Wisnewski, Linda Rodgers, Annette Kirk
Front row: Marlene Rubino, Andrea Stephenson, Georgia Binns*

Long-term Service

Nine Laboratory employees celebrated long-term service anniversaries this year. Madeline Wisnewski, scientific secretary, celebrated her 25th year with us. Madeline joined us in 1970 and has worked in various offices throughout the Laboratory, including as secretary to Dr. Watson, before landing in Demerec Laboratory where she works with Drs. Helfman, Greider, and Spector. Vincent Carey, grounds foreman, and Robert McGuirk, senior laboratory technician, both celebrated their 20-year milestones. Fifteen-year honorees included Michael Riggs, laboratory technician, and Linda Rodgers, research associate, members of Michael Wigler's lab; Bruce Fahlbusch, buyer for the Buildings & Grounds Department; Georgia Binns, research associate in Ryuji Kobayashi's lab; Marlene Rubino, administrative assistant in Environmental Health & Safety; and Andrea Stephenson, now meetings administrator.

Changes in Administrative Staff

This was a year of transition for the Laboratory's computer department. Fred Stelabotte, former Computer Systems Manager, left us to take a position with the Avis Corporation. Jerry Latter, former manager of the Quest Protein Database, was appointed Director of the Information Services Department (ISD) and charged with improving and restructuring the Laboratory's use and support of computers. Latter is orchestrating improvements in the staffing, networking, and approach to troubleshooting for the extensive network of hardware and software of some 560 employees who use a variety of computing systems.

The Buildings & Grounds (B&G) Department has undergone administrative changes as well. Jack Richards retired from his position as Director of B&G, but he remains active in architectural and construction projects. Jack was convinced to join the Laboratory in 1969 after bidding on the renovation of the James Laboratory Annex. Over the years, he has played a valuable part in consulting

with architects and supervising construction and renovation; his attention to detail and quality workmanship during the preservation of many Laboratory buildings was without question a factor in the Laboratory's successful nomination to the State and National Registers of Historic Places. As Jack would tell it, however, it was the construction of the wastewater treatment plant in the 1970s that presented the greatest challenge. That facility, planned and constructed under his direction, maintained a perfect record for meeting health department standards during its years of operation and is among the most attractive settings on the harbor. It is with great pleasure that we acknowledge Jack's extraordinary contributions by naming the future B&G building in his honor.

Art Brings has stepped into the Director's position, managing the staff of 80 who comprise B&G, Environmental Health and Safety, Security, and the Harris Animal Facility. It is a credit to Jack and Art that we have maintained and beautified the grounds and buildings, continually striving to provide not only a pleasant, but also a healthy and safe working environment for all members of the Laboratory staff.

Changes in Scientific Staff

Each year, the Laboratory is infused with fresh new intellect ranging from bright and enthusiastic graduate students and postdoctoral researchers to experienced senior staff scientists. At the same time, we inevitably see the departure of others.

Dan Marshak, a protein chemist who was a part of the Laboratory for 10 years, went on to a position with Osiris Therapeutics, Inc. in Baltimore, Maryland, where we wish him all the best. Nikolai Lisitsyn, Senior Staff Investigator and codeveloper of a powerful new technique for genetic research known as Representation Difference Analysis (RDA) with Michael Wigler, has accepted a position as assistant professor at the University of Pennsylvania, School of Medicine in Philadelphia and Hiroyuki Nawa, Senior Staff Investigator interested in mechanisms of neuronal communication, accepted a professorship at Niigata University in Japan. Harriet Feilotter, Staff Investigator with us since 1990, was an integral part of the Dana Consortium—the Laboratory's collaboration with researchers at Johns Hopkins and Stanford University established to identify genetic components of manic depressive disorder. Harriet has moved to Queen's University in Ontario as a research associate.

Several staff associates have accepted positions elsewhere and have departed Cold Spring Harbor: William I. Chang left the Marr lab to accept a position as Senior Software Engineer at Infoseek Corporation in Mountainview, California; Mi Sha left the Roberts lab to a position as staff scientist at the Genetic Institute in Cambridge, Massachusetts; Ann Sutton departed from the Arndt lab to accept a visiting professorship at SUNY, Stony Brook; Xu Duffy from the Wigler lab went to a research scientist position at North Shore University Hospital here on Long Island; and Michael White moved to the University of Texas Southwestern Medical Center in Dallas, as an assistant professor. Computer scientist Marty Hiller left the Marr lab this year to fill the same position with Millenium Pharmaceuticals in Cambridge, Massachusetts, and Howard Hughes Medical Institute associate Hui Zhang left the Beach lab to become a lecturer at Yale University School of Medicine.

Five visiting scientists completed their stays at the Laboratory in 1995. Young-Seuk Bae returned to Kyungpook National University in South Korea from the

Marshak lab; Doug Demetrick returned to Foothills Medical Center at University of Calgary in Canada from the Beach lab; Carina Dennis left the Helfman lab to return to the Ph.D. program at Oxford University in the United Kingdom; Boris Kuzin returned to the Russian Academy of Science in Moscow from the lab of Grigori Enikolopov; and Peter Barker departed from the Wigler lab.

Two special visitors to the Laboratory, Jonathan Montague and Greg Jeffries, have returned to the United Kingdom. Both graduates of Eton College in Windsor came to Cold Spring Harbor to study with our scientists for one year before proceeding on to university life. Jonathan studied plant genetics in Rob Martienssen's lab and has gone on to begin his studies at Oxford University. Greg worked with Michael Hengartner on studies of programmed cell death in *C. elegans* and is now attending Cambridge University. It was our pleasure to host Jonathan and Greg, and we wish them well in their studies.

New Staff Members

More than 30 new postdoctoral researchers and 20 graduate students joined the Laboratory this year. Tatsuya Hirano joined us as a Senior Staff Investigator, after 6 years at the University of California, San Francisco, studying chromosomal dynamics. Leemor Joshua-Tor also signed on as a Senior Staff Investigator; she arrived from Caltech in Pasadena to join our Keck Structural Biology Laboratory. Peter Nestler made the short trip from Columbia University in New York to join us as a Staff Investigator. Peter will be working on combinatorial chemistry.

We have several new visiting scientists this year: Benjamin Horwitz came from Israel to work on plant genetics in the lab of Hong Ma; Isabelle Jupin arrived from the Institut Jacques Monod University in France to work with Linda Van Aelst on viral/host interactions in viral RNA replication; Leslie Kerrigan came up from Osiris Therapeutics in Baltimore to work in Dan Marshak's lab with Timothy Connolly, who was here on sabbatical; Boris Kuzin from the Russian Academy of Science in Moscow is studying the role of nitric oxide in *Drosophila* development in Grigori Enikolopov's lab; Roberta Maestro has come to the lab of David Beach from CRO Avino in Italy to study the p53 gene and apoptosis; R. Sanders Williams came on sabbatical leave from University of Texas, Southwestern Medical Center to work in the Stillman lab on regulation of DNA replication; and De Ye from the Biotechnology Institute in University Park, Pennsylvania, joined Venkatesan Sundaresan's lab and is working on embryogenesis in *Arabidopsis*.

Promotions

Several staff members were recognized this year with promotions. Two scientists, Tim Tully, Cold Spring Harbor Laboratory's *Drosophila* learning and memory expert, and plant geneticist Rob Martienssen were promoted from Senior Staff Investigator to Senior Scientist. Staff Investigators Michael Hengartner and Yi Zhong—both having arrived fresh out of graduate school—were promoted to Senior Staff Investigator positions. Michael will continue to study apoptosis, and Yi will focus on neural development and learning and memory. Joseph Colasanti, a postdoctoral researcher in Venkatesan Sundaresan's lab, and Michael White, a postdoc in the Wigler lab, were both appointed Staff Associates. Shou Waga, a postdoc in the Stillman lab who studies mechanisms and regulation of eukaryotic DNA replication, was promoted to Staff Investigator.

Postdoctoral Departures

Masahiro Akiyama left Bruce Stillman's lab for an associate professor position at the Nara Institute of Science and Technology in Japan; Zoltan Asztalos went from Tim Tully's lab to a scientist position with ERATO, the Yamamoto Behavioral Genes Project in Tokyo; Wei Guo left David Helfman's lab to continue postdoctoral research at the Scripps Research Institute in San Diego; Chang-Deok Han went from a postdoctoral position with Rob Martienssen to a position as a research scientist at the Gysong-Song National University in Korea; Keiko Mizuno left Hiruyuki Nawa's lab; Piruz Nahreini went from Mike Mathews' lab to a Scientist II position at Ribozyme Pharmaceuticals Inc., in Colorado; and Catherine Weiss left Hong Ma's lab to be a research biologist at American Cyanamid, Agriculture Research Division. David Beach's lab saw the departure of three postdoctoral researchers: Scott Davey to an assistant professorship at Queen's University, Cancer Treatment and Research Foundation in Ontario; Taekook Kim to a research associate position at Harvard University, Molecular and Cellular Biology Department; and Brad Nefsky to continue his postdoctoral research elsewhere. Ariel Avilion and Kathleen Collins both left Carol Greider's lab—Avilion to do her postdoctoral research in Robin Lovell-Badge's laboratory at the MRC in London and Collins to an assistant professorship at the University of California, Berkeley, Department of Molecular and Cell Biology. Nick Tonks said good-bye to Susann Brady-Kalnay, who left to become an assistant professor at Case Western Reserve University in Cleveland, and to Hong Sun, who is now assistant professor at Yale University, Department of Genetics. Yoon Cho left Alcino Silva's lab to do additional postdoctoral research at the Center for Behavioral Neuroscience at SUNY Stony Brook and Bruno Frenguelli left the Malinow lab to continue his postdoctoral research at the University of Bristol, Anatomy Department in the United Kingdom. Kim Arndt bade farewell to Cecilia Devlin, who is continuing her postdoctoral research in Akron, Ohio, and to Fong C. Lin, who is doing the same at New England Biolabs in Beverly, Massachusetts. Doris Germain from Bruce Futcher's lab is continuing her postdoctoral research at the Peter MacCallum Cancer Institute in Melbourne, Australia. Dorre Grueneberg followed Michael Gilman to Ariad Pharmaceuticals in Cambridge, Massachusetts, and Henry Sadowski accepted a position as assistant professor at Mt. Sinai School of Medicine, Biochemistry Department, in New York. Louis A. Peña and Christian van den Bos left Dan Marshak's lab—Peña to become a research associate professor at Memorial Sloan-Kettering Cancer Center, Rockefeller Research Laboratory in New York, and van den Bos to accept a staff scientist position at Osiris Therapeutics, Inc. in Baltimore.

Graduate Students

Ann Ryan and Ken Simon left the Gilman lab to continue their graduate studies at Ariad Pharmaceuticals, and Terrance Vale left the Beach lab and Yaolin Wang left the Zhong lab each to do the same—Vale at the University of Texas Southwest Medical Center and Wang at University of Kansas.

Many of our researchers obtained their degrees and made the transition from graduate student to postdoc. David Casso, of David Beach's lab, went on to do postdoctoral research at the University of California, San Francisco, and Sonja Witte went from the Cline lab to do the same at Massachusetts College of Pharmacology at Quincy College. Michele Cleary, of Winship Herr's lab, will be

going on to postdoctoral work at Shirley Tilghman's lab at Princeton University, but for the time being has remained at Cold Spring Harbor, working for the journal *Genes & Development* in an editorial capacity, assisting Dr. Watson with revisions of his book *Molecular Biology of the Gene*, and continuing to do research in the Herr lab. Cynthia Sadowski of Nouria Hernandez's lab earned her degree and will be leaving to do postdoctoral research at New York University in February 1996. Nick Chester, from the Marshak lab will be doing his postdoctoral research at the Howard Hughes Medical Research Institute, Department of Genetics at Harvard University; Yuliang Ma from Mike Mathews' lab went on to the University of California at San Diego; Robert Mihalik from Tim Tully's lab is doing postdoctoral research at University of Pittsburgh; and Tao Zhong of Kim Arndt's lab went on to Massachusetts General Hospital. Maureen Barr left the Wigler lab to do her postdoctoral research at the California Institute of Technology and George Tokiwa left Bruce Futcher's lab to do postdoctoral research at New York University Medical Center. Patricia (Beth) Elliott has entered into the plant breeding business here on Long Island.

Planning our Entry into the 21st Century

In this report, we see the research made possible by the great burst of building activities that were planned in the last decade (1980–1989) of the Laboratory's first century. It was the creation of the Walter Page Laboratory (1987) and the acquisition of our Uplands Farm Experimental Station (1984) that allow us an international role in plant genomics and developmental biology. And only through the 1991 completion of our Beckman Laboratory did we have the capability of being a world leader in how genes control the acquisition of memory. By our imaginative expansion (1993) of McClintock Laboratory, we have remained at the center of cell cycle research with its vast potential for the eventual control of cancers. The new space so provided let us also create the Lita Annenberg Hazen Genome Center.

Now we must initiate a new set of planning initiatives to ensure that we enter the 21st century with the facilities needed for continued innovation. At this year's annual November meeting of our Board of Trustees, we set up four new committees to make recommendations during 1996 as to how best to ensure our continued leadership roles. One, headed by me (B.S.), is looking into the future of neurobiology, in particular, how we should exploit further our research on learning and memory in flies and mice to encompass the problem of human memory and learning. The second committee, headed by Winship Herr, will look into the Laboratory's future role in graduate education. We now have 51 graduate students doing their Ph.D. thesis requirements here, almost all enrolled in graduate programs at SUNY, Stony Brook. The question we need to ask is whether the ever-increasing size of our graduate training program might demand our becoming a degree-granting institute. Our third committee is looking into the question of whether the Laboratory should be more pro-active in the commercial exploitation of research done here at Cold Spring Harbor. During the past decade, some ten biotechnology companies have been developed using ideas and technologies generated here. Only two, however, Protein Databases and Oncogene Science, are located here on Long Island. Now a committee, headed by John Maroney, is asking whether future laboratory inventions would more likely stay on Long Island if we help bring into existence a nearby biotechnology-oriented industrial park.

Lastly, we have set up a committee to look into how we should house our growing numbers of graduate students and postdoctoral fellows. Neither of these categories of younger scientists receives salaries commensurate with the relatively high cost of housing on the north shore of Long Island. To plan how to respond, Morgan Browne heads a committee that is looking into ways to generate nearby housing units. All of these groups are to report to the Board of Trustees at our 1996 annual November meeting.

During 1996, we will thus be very future-oriented. In this way, we will continue to promote the world of biology that still has so much to offer to human society.

April 30, 1996

Bruce Stillman, *Director*

James D. Watson, *President*