HIGHLIGHTS OF THE YEAR

Research

Cancer

Liver cancer is the fifth most frequent neoplasm worldwide. However, owing to the lack of effective treatment options, it is the third leading cause of cancer deaths. By generating tumors in laboratory mice that mimic human liver cancer and by comparing the DNA of mouse and human tumors, researchers at CSHL have identified two genes that are likely to have a role in this form of cancer. The study also establishes an efficient and adaptable method for exploring the biology of liver cancer, for validating potential therapeutic targets, and for testing new treatments.

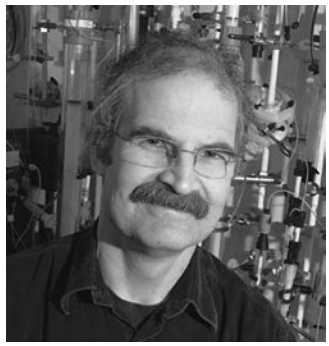
To gain a better understanding of the molecular causes of liver cancer, the researchers (see below) devised a strategy for genetically engineering liver stem cells, harvested from mouse embryos, and subsequently transplanting the cells into adult mice. Following transplantation, the cells can become part of the recipient mouse's liver.

The scientists engineered the liver stem cells to mimic the genetic lesions that are known to occur in human liver and other cancers (namely, deletion of the *p53* gene and activation of the *myc* gene). Transplanted cells lacking the *p53* gene and bearing an activated version of the *myc* gene rapidly gave rise to aggressive, invasive liver tumors. Scanning the DNA of these tumors revealed that a specific segment of mouse chromosome 9 was amplified—or present in excess copies—compared to the DNA of healthy mouse liver cells. Because this segment of mouse DNA carried several genes, the researchers turned to the human genome to help them narrow down which gene (or genes, as it turned out) was the culprit in liver cancer. In parallel with their analysis of the mouse liver tumors, they scanned the DNA of human liver and other tumors. Remarkably, they found that a region of human chromosome 11 that is evolutionarily related to the segment of mouse chromosome 9 was amplified in several of the human tumors.

Additional experiments revealed that two genes—*Yap* and *cIAP1*—were both consistently overexpressed in both mouse and human tumors. Thus, when produced at abnormally high levels, proteins encoded by the *Yap* and *cIAP1* genes contribute significantly to human liver and other cancers. Therefore, these proteins and others in the pathways they control are attractive candidates for the development of novel cancer therapies.

The study involved scientists from five institutions in Europe, Asia, Australia, and the United States and five research groups at CSHL led by Scott Lowe, Mike Wigler, Greg Hannon, Rob Lucito, and Scott Powers.

In some cases, the fusion of human cells is a normal process that leads, for instance, to the formation of muscle and bone. Seemingly innocuous infections by common viruses can also cause cells in our bodies to fuse. Such fused or "hybrid" cells are widely considered to be harmless because they are generally believed to die and be cleared from the body without consequences to our health. This view of cells fused by viruses as being harmless may need to be revised, and revised dramatically. According to a recent study led by Yuri Lazebnik and postdoctoral fellow Dominik Duelli, cell fusion triggered by common viral infections may be a significant factor in the development of human cancer.



Y. Lazebnik

The idea that aberrations in the number or structure of human chromosomes can spur tumor formation is more than a century old. Such aberra-

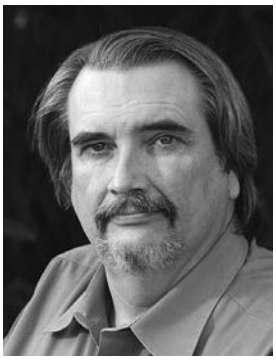
tions—known collectively as "aneuploidy"—arise in two principal ways: as a consequence of abnormal cell division or as a result of cell fusion. In both cases, aneuploid cells have an abnormal genetic makeup (e.g., too few or too many copies of a particular chromosome or chromosome segment) and they frequently die. But not always.

Researchers have long known that cancer cells—very much alive—are often aneuploid. Whether aneuploidy is a cause or a consequence of a cancerous state is still being debated. But in any case, given that cell fusion causes aneuploidy and that aneuploidy may cause cancer, it follows that cell fusion may cause cancer. This is where "innocuous" viral infections come in.

Dominik and Yuri first observed that cultured human cells are fused through the action of a particular virus (Mason-Pfizer monkey virus [MPMV], one among many "fusogenic" viruses). As expected, the resulting hybrid cells are aneuploid and fail to grow. However, the researchers next showed that if one of the cell fusion partners is engineered to carry a particular mutation in an oncogene or a tumor suppressor gene, then a significant number of the resulting hybrid cells grow land are thus potentially cancerous. Yuri's group is currently exploring whether such proliferating fused cells are produced by viral infections in animal models. If they are, then the work of sorting out which of the many known fusogenic viruses might contribute to human cancer will likely begin in many laboratories.

Genomics and Bioinformatics

Rice feeds more than half of the world's human population. Estimates indicate that the rice crop yields will need to be increased by about 30% over the next two decades to meet a projected increase in demand.



W.R. McCombie

W. Richard McCombie, his CSHL colleagues, and other members of the 10-nation International Rice Genome Sequencing Project have reported a highly accurate, "finished" DNA sequence of the entire rice genome. The complete rice genome sequence—which reveals some 38,000 genes on the 12 chromosomes of rice—provides the raw material for many studies aimed at improving the agricultural yield of the world's most important food source. Moreover, because the rice genome is closely related to that of other major cereal grasses (including corn, wheat, barley, rye, sorghum, and millet), the complete rice genome sequence is an extraordinarily useful resource for identifying genes of interest in a group of crop plants that collectively supply two thirds of humanity's food supply.

The study revealed thousands of genetic markers in the rice genome that are of immediate use to plant breeders and others working to improve rice agriculture. It also generated the first finished genome sequence of any crop plant, making rice a powerful model for how to use genome sequence information to improve many other aspects of agriculture. The finished rice genome sequence builds upon draft sequences previously published by the private companies Monsanto and Syngenta. As such, it is an excellent example of a successful public-private partnership that saved the public consortium both time and money.

By enabling scientists to identify genes that underlie agriculturally important traits, a draft of the rice genome sequence released by the public consortium in 2002 has already spurred both biotechnological and conventional plant-breeding approaches to increasing rice yields. The new, finished rice genome sequence has the potential to accelerate those efforts. The availability of the sequence should greatly speed the hunt for genes that increase yield, protect against disease and pests, and improve other traits of rice and several other cereal crops.

Plant Molecular Genetics

Although most people probably do not give too much thought to leaves, they are in fact crucial light-harvesting and gas-exchange organs, without which agriculture as we know it, not to mention life on Earth itself, would be very different.

To the naked eye, the top and bottom surfaces of leaves look rather similar. Closer inspection reveals that they are highly specialized regions that arise through a complex series of molecular events. Marja Timmermans has recently made a number of important discoveries concerning these events and how they instruct unspecialized stem cells to form the specialized top (light-harvesting) and bottom (gas-exchanging) surfaces of leaves.

M. Timmermans

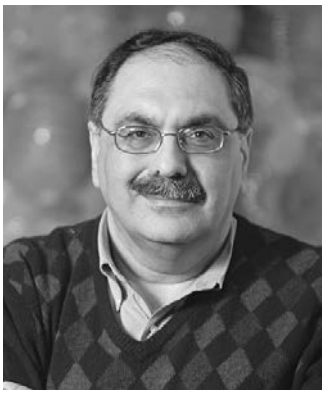
One of Marja's projects explores the role of a gene called *leafbladeless1* in plant development. Corn plants with a normal *leafbladeless1* gene develop broad, flat leaves with distinct top and bottom surfaces, as usual. In contrast, mutant plants lacking a functional *leafbladeless1* gene develop long, threadlike leaves that are "all bottom, no top." This means that the *leafbladeless1* gene is somehow required to specify the formation of top surfaces of leaves. To find out how, in parallel with other experiments (see below), Marja and her colleagues, including postdoctoral fellow Fabio Nogueira, isolated the *leafbladeless1* gene. They discovered that *leafbladeless1* is similar to another gene with a known role in generating biologically powerful snippets of RNA called "*trans*-acting small interfering RNAs" (ta-siRNAs). This is clue #1, i.e., *leafbladeless1* specifies "top" by promoting ta-siRNA formation. Clue #2 came from examining a different sort of small regulatory RNA called "microRNA166" (miR166). Marja's group had previously shown that in normal plants, miR166 is present in the cells that generate the bottom surfaces of leaves but is absent from adjacent cells that generate the top surfaces of leaves. In short, miR166 means "bottom."

If ta-siRNAs mean "top" and miR166 means "bottom," then what might ta-siRNAs and miR166 mean to each other? Does one control the other? Marja and her colleagues answered this question by determining whether the pattern of miR166 expression is altered in plants (*leafbladeless1* mutants) that lack ta-siRNAs. The result (clue #3 and a major discovery): In the absence of ta-siRNAs, miR166 is present both in its usual "bottom" cells *and* in the cells that normally generate the top surfaces of leaves. This is consistent with the idea that in normal plants, ta-siRNA activity blocks miR166 expression in the "top" cells. It also explains why the leaves of *leafbladeless1* mutants are "all bottom, no top." In such mutants, the "bottom promoting" activity of miR166 is abnormally present in the "top" cells and transforms the fate of those cells from top to bottom.

Through the work of other scientists, including some of CSHL's own (Greg Hannon, Leemor Joshua-Tor, Rob Martienssen), small RNAs akin to miR166 and ta-siRNAs have recently been shown to have important roles in the biology of many organisms, including humans. Therefore, the discovery by Marja and her colleagues that the opposing activity of two small RNAs can control major developmental events in plants establishes a paradigm that is likely to have broad implications for the biological and biomedical sciences.

Neuroscience

CSHL neuroscientist Grigori (Grisha) Enikolopov and his colleagues have identified which cell type among several different kinds of neural precursor cells in the brain is the sole target of the widely prescribed antidepressant Prozac. This discovery might enable a new generation



G. Enikolopov

of more specific treatments for depression, with fewer side effects, to be developed. It also lays the foundation for many studies of the factors that control how, when, and where new neurons are generated from stem cells in the brain. Such work could eventually lead to cell replacement therapies for neurodegenerative and other brain disorders including Alzheimer's and Parkinson's disease.

It has been known for some years that Prozac (fluoxetine) is likely to relieve the symptoms of depression by somehow causing more neurons to be present in a particular region of the brain (the "dentate gyrus"). But the origins of these neurons, and how Prozac promotes their existence, have been a mystery. Until now. By profiling the telltale marker proteins produced by different kinds of cells in the brains of adult mice, Grisha's group—spearheaded by postdoctoral fellow Juan Manuel Encinas—first defined discrete steps in the complex process, called neurogenesis, that converts unspecialized stem cells into mature, specialized neurons.

Next, knowing that Prozac treatment somehow increases the number of neurons in the brain, the researchers tested which step in the neurogenesis pathway might be stimulated by Prozac. They found that Prozac treatment specifically stimulates the generation of a kind of cells they dubbed "amplifying neural progenitors" or ANPs—the second step in the neurogenesis pathway from stem cells to mature neurons.

To address the controversy surrounding the use of Prozac in children and in pregnant women, Grisha's group is currently testing the effects of the drug on brain neurogenesis in juvenile and pregnant mice. The results of those experiments should provide valuable information for assessing the possible effects of Prozac and related drugs on fetal and adolescent brain development. The researchers are also using the tools they have developed to explore whether other treatments for depression, including other drugs and deep brain stimulation, act in the same way as Prozac or in different ways. In addition, they are screening for new drugs that stimulate ANP cells to multiply and thus expand the production of brain neurons for the treatment of neurodegenerative diseases.

Z. Mainen

It is a classic upper-middle-class dilemma: Should we buy a perfect second home in an area that takes hours to get to or should we settle for something closer but not as nice? In the rodent world, an equivalent decision-making situation might be, "Was the food I liked better down this alley or over there?"

By discovering that particular rat brain neurons combine or "integrate" dissimilar pieces of information (e.g., location vs. reward), Zach Mainen and his colleagues have begun to learn how the brain controls decision-making and goal-oriented behaviors. Examples of these include foraging and navigation in animals and in humans, whether to buy a particular second home or, in general, whether to favor a long-term benefit over immediate gratification.

Zach's recent study represents the first time that brain neurons have been shown to integrate spatial and reward information. Its results contrast with a previous "pure economic" view that neurons in the orbitofrontal cortex (OFC) are involved solely in assessing value. Moreover, the study has implications for understanding pathological states in humans that affect decision-making, motivation, and emotions such as addiction, depression, obsessive-compulsive disorder, autism, and other disorders of thought or mood.

The research was spearheaded by graduate student Claudia Feierstein, who recorded the activity of OFC neurons while rats performed an odor discrimination task that they had previously learned to accomplish. In the task, the animal receives a test odor ("A" or "B") by pok-

ing its nose into a centrally located odor port. Next, the animal chooses odor A or odor B as being the same as the test odor by poking its nose into a choice port located to its right (odor A) or left (odor B). If the animal chooses correctly, it receives a reward (a drop of water). As expected, many of the OFC neurons actively signaled "I'm getting a reward" when the animal moved right or left, i.e., toward odor A or odor B. Surprisingly, however, several of the neurons signaled "I'm getting the reward to my right," whereas several others signaled "I'm getting the reward to my left."

One of Zach's next steps will be to examine what happens in the brain while the animals are first learning to recognize new odors. Through this work, the researchers hope to gain a greater understanding of learning and memory as well as the neural basis of perception, motivation, decision-making, and other aspects of behavior.

Cold Spring Harbor Laboratory Board of Trustees

The Board of Trustees was pleased this year to welcome four new members: John C. Phelan, Managing Partner and cofounder of MSD Capital, L.P.; Jamie C. Nicholls, recently a General Partner and currently a Limited Partner at Forstman Little & Co.; Donald Everett Axinn, writer, respected investor and builder in the New York area, and committed public servant; and Landon Clay, Managing Member of East Hill Management Company.

Concluding their terms as Trustees this year were Arthur M. Spiro and Susan Lee Lindquist. Mr. Spiro was first elected to the Board in November 1999 and was then reelected to a second term in 2002. He was active on several committees, including Audit, Executive, and Woodbury Genome Research Center, and he served for 6 years as the Chairman of the Dolan DNA Learning Center Committee. Dr. Lindquist was elected to the Board in 2002 and brought her expertise to bear on the Tenure and Appointments Committee throughout her term.

We said a sad goodbye to Wendy Vander Poel Russell, Honorary Trustee, who passed away in March, 2006. Mrs. Russell was an active member of the Board of Trustees since 1984, serving as Secretary from 1985 to 1987 and from 1992 to 1997. A legendary fundraiser, her pet project at the Laboratory was the Dolan DNA Learning Center, and she was instrumental in the establishment of its Corporate Advisory Board.

The Cold Spring Harbor Laboratory Association (CSHLA) raised a total of $1,155,000 this year under the leadership of Association president Joe Donohue. We say thanks to Mr. Donahue who served his second term as president in 2006, doing double duty while also serving as a Trustee of the Board. New Directors in 2006 included Joe Amelia, Suzanne DiMaio, Nancy Edsparr, Larry Gellman, M.D., and Scott J. Ratner, M.D.

Hillside Campus Dedication

The Hillside Campus Cornerstone Dedication Ceremony on October 15 marked the transition from constructing the infrastructure for new facilities to construction of the facilities themselves. Much of the work done this year has been groundwork for the construction of six buildings dedicated to scientific disciplines that fulfill the core research mission:

- The David H. Koch Building
- The DeMatteis Family Building
- The William L. and Marjorie A. Matheson Building

- The Leslie and Jean Quick Building
- The Donald Everett Axinn Building
- The Wendt Family Building

The bright, crisp afternoon of the ceremony brought dozens of well-wishers, including CSHL faculty, staff, dignitaries, and most importantly the donors and their families whose names will grace these facilities. Once complete, the Laboratory's research space will increase by nearly 40%.

The festive day included a solemn note with fond memories of Jean Quick who passed away earlier this year after naming the Leslie and Jean Quick Building for Cancer Research after her late husband and CSHL Trustee Leslie C. Quick, Jr. Long-time residents of Laurel Hollow and neighbors of the Laboratory, their legacy at CSHL lives on through their gifts and the continued involvement of the family.

In planning for the Hillside Campus, CSHL has worked to be environmentally and aesthetically sensitive to the unique environment of Cold Spring Harbor. The new facilities have been designed to encourage efficiency and easy communication between buildings and scientists. Together, they will function as an academic village at the southern end of the campus, stylistically within the broader village of science that now exists.

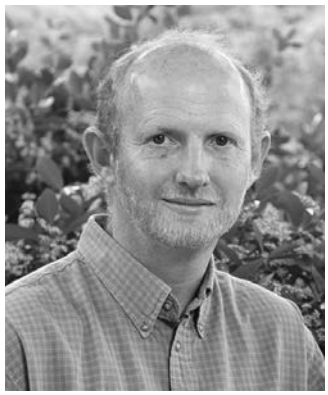
Much of the infrastructure work completed this year consisted of ensuring adequate storm water drainage for the previously wooded site. Rather than employ the conventional approach of installing an enormous quantity of dry wells to accommodate storm water, our civil engineers adopted an ingenious approach: They designed water quality rain gardens and bioretention ponds to collect and treat storm water runoff before it enters the harbor. This approach not only provides an environmentally sound means of treating storm water, but also creates additional naturalized water features on the campus, adding beauty and a wildlife habitat.

Hillside Campus Dedication Ceremony

Awards and Honors

Rob Martienssen was elected a Fellow of the Royal Society, distinguished for fundamental discoveries on the epigenetic mechanisms that regulate transposon silencing, gene control, and stem cell function in plants. He was also noted by the Royal Society as a major contributor to sequencing the genome of *Arabidopsis*, the first plant genome sequence completed. This is one of the highest honors that can be accorded a scientist, and CSHL now adds Martienssen to its list of previously elected fellows: Jim Watson, Nick Tonks, and myself.

The Leukemia & Lymphoma Society selected Bill Tansey as one of five researchers to receive its prestigious Stohllman Scholar Award, recognizing his outstanding contributions to the advancement of blood cancer research. The focus of his work is a protein, Myc, known to contribute to the growth of leukemia and lymphoma cancer cells.



R. Martienssen

Sandra J. Kuhlman and Eleonore Real each received the National Alliance for Research on Schizophrenia and Depression Young Investigator Award. Sandra is studying in an animal model the role GABAergic synapses in the prefrontal cortex have in memory impairment in people with schizophrenia. Eleonore is working on glutamate receptor trafficking and synaptic plasticity, since glutamate abnormalities have been implicated in psychotic disorders.

CSHL Fellow Ira Hall received a 2006 Burroughs Wellcome Fund Career Award in the Biomedical Sciences. This award provides early-career biomedical researchers with funding over a 5-year period to foster their development and help them make the critical transition to independent investigators. Ira is using DNA microarray technology to explore DNA copy-number fluctuations and epigenetic inheritance in the mouse, an important model system for many diseases including cancer.

Thomson-ISI added the CSHL Press journal *Genes & Development* to its "Top 10 Scientific Journals in All Areas" list for the decade 1995–2005. Edited by Terri Grodzicker, this journal presents research papers of broad general interest and biological signficance in molecular biology, molecular genetics, and related fields. Thomson-ISI provides a service that measures the impact of some 7 million papers published in 11,000+ journals in 22 major scientific fields.

Inside Cancer—a comprehensive, user-friendly Web guide to cancer biology created by the BioMedia Group of CSHL's Dolan DNA Learning Center—was selected as an official "Site of the Day" by Adobe Systems Incorporated, joining the ranks of other winners that included Nike, Cartier, and Bentley Motors.

A publication by Leemor Joshua-Tor and her colleagues Niraj Tolia, Fabiola Rivas, and Greg Hannon was selected as the "New Hot Paper" by Thomson Scientific's Essential Science Indicators. "Purified Argonaute2 and an siRNA form recombinant human RISC" won this distinction by virtue of it being cited more frequently than 99.9% of all other studies in numerous journals surveyed.

CSHL was selected to be part of a consortium that will benefit from a $100 million grant from the Starr Foundation. CSHL, The Broad Institute of MIT and Harvard, Memorial Sloan-Kettering Cancer Center, The Rockefeller University, and Weill Cornell Medical College will collaborate on research aimed at understanding cancer at its most fundamental levels and at developing new approaches to the prevention, diagnosis, and treatment of many forms of the disease.

Starr Cancer Consortium members (*left to right*) A.M. Grotto, Jr., E. Lander, M. Greenberg, H. Varmus, B. Stillman, F. Davis

D. Spector

David Spector will lead CSHL's involvement in the establishment of the Nanomedicine Center for Nucleoprotein Machines. The National Institutes of Health awarded a $10 million grant to CSHL, the California Institute of Technology, Emory University, Georgia Institute of Technology, The German Cancer Research Center, the Medical College of Georgia, Massachusetts Institute of Technology, and the New York University Medical Center. The focus of the center will be to understand the molecular machines that enable cells to detect and repair damaged DNA. David was also the first recipient of the Winship Herr Award for Excellence and Creativity in Teaching in the Watson School of Biological Sciences.

CSHL President Bruce Stillman was honored by the Society of Surgical Oncology, receiving the American Cancer Society Basic Science Award and Lecture.

Development

This year has proven to be another year of successful fund-raising at Cold Spring Harbor Laboratory. Our most generous donors have provided much needed support to both capital and research projects as well as our endowment.

Cold Spring Harbor Campaign

Capital

The following major donors have generously contributed new gifts and pledges of $100,000 or more to support the Laboratory's Hillside Campus expansion project: Mr. and Mrs. Donald Everett Axinn, David H. Koch Charitable Trust, Mary D. Lindsay, and The Perkin Fund.

Faculty Recruitment Support and Equipment

We gratefully acknowledge support of $100,000 or more from Mr. and Mrs. Landon T. Clay, Mr. and Mrs. Norris Darrell, The Shelby Cullom Davis Foundation, The Coleman Fung Foundation, Jeff Hawkins and Janet Strauss, Jamie Nicholls and Fran Biondi, The Robertson Foundation, Dr. and Mrs. James Stone, and The Roy J. Zuckerberg Family Foundation.

Watson School of Biological Sciences

Support of the Dean's Chair, fellowships, and lectureships enable the Watson School to continue to grow and influence the field of biological sciences. We appreciate new gifts and pledges of $100,000 or more this year by Mr. Michel David-Weill, Mr. Curt Engelhorn, and Mr. and Mrs. Robert D. Lindsay and Family.

Dolan DNA Learning Center

New gifts and pledges to support the Dolan DNA Learning Center endowment were gratefully received from The Lessing Family Foundation and the OSI Pharmaceuticals Foundation.

Carnegie Library

The Genentech Center for Molecular Biology and Biotechnology was established with a generous gift from Genentech. Other supporters of $100,000 or more include the New York State Office of Parks and Historic Preservation and Dr. Norton Zinder (see the Chancellor's Report).

Program Support

Private funding is essential to maintain the Laboratory's innovative research programs. We appreciate new gifts and pledges of $100,000 or more from the following donors: an anonymous donor, Mr. and Mrs. Donald Everett Axinn, Ms. Kathryn Wasserman Davis, The DeMatteis Family Foundation, Mr. and Mrs. Leo A. Guthart, The Thomas Hartman Foundation for Parkinson's Research, Jo-Ellen and Ira Hazan, The Lita Annenberg Hazen Foundation, Hope for Depression Foundation, The Keck Foundation, The Miracle Foundation, The Don Monti Memorial Research Foundation, and Pam and Pierre Omidyar.

Robertson Research Fund

The primary in-house support for our scientists for more than three decades, the Robertson Research Fund in 2006 supported research in the labs of Alexei Koulakov, Cordula Schulz, Leemor Joshua-Tor, Rui-Ming Xu, Wolfgang Lukowitz, Rob Martienssen, Marja Timmermans, and David Jackson. Start-up research support was also provided by the Fund to two new investigators: Glenn Turner and Hiroyasu Furukawa. In addition, the Robertson Research Fund continues to support the annual CSHL In-House Symposium and our programs for postdoctoral fellows, graduate students, the laboratory seminar program, and faculty recruitment.

Breast Cancer Research Support

The Laboratory greatly appreciates the many supporters of our breast cancer research program. This includes several local grassroots groups that provide not only much needed funds, but also public awareness and outreach. This year, we were fortunate to receive support from Breast Cancer Awareness Day in memory of Elizabeth McFarland, Breast Cancer HELP, Glen Cove Cares, The Breast Cancer Research Foundation, the Cold Spring Harbor Main Street Association, Find A Cure Today (F.A.C.T.), Mr. and Mrs. Richard Gordon, Long Island 2-Day Walk, Long Islanders Against Breast Cancer (L.I.A.B.C.), the Manhasset Women's Coalition Against Breast Cancer, the Pierre and Pam Omidyar Fund, the Judi Shesh Memorial Foundation, the Waldbaum Foundation, the West Islip Breast Cancer Coalition for Long Island, the Women's Insurance Network of Long Island, and the Clear Channel/WALK for Women Breast Cancer Fund.

Building Projects

The year 2006 was a busy one for the Facilities Department, with multiple simultaneous construction projects being undertaken in addition to the work on the Hillside Campus.

The James Laboratory renovation—a multiyear project in which nearly the entire building has been reconstructed to meet modern needs—continued from 2005, with only one laboratory and two offices remaining to be completed in 2007. The replacement of the Grace Auditorium bluestone patio, begun in the fall of the previous year, was completed in time for the meeting and course season, and the groundwater-cooled chiller plant that was to service the Grace and Harris Buildings was completed, meeting the increased cooling demand with greater efficiency. This also paved the way for the complete renovation of the Harris Building mechanical systems, which, when completed in 2007, will increase the building's capacity by more than 40%. Additionally, the Demerec Building chiller, running above its design capacity and beyond its useful life, was replaced with a new unit of increased capacity and far greater efficiency.

2006 also saw a continuation of the Laboratory's program to upgrade and improve its residential properties. The final Hooper apartment, the remaining two Firehouse apartments, and the Rose cottage were all renovated during this year. Additionally, the caretaker quarters of the Robertson House—previously composed of two cramped rooms—were expanded and renovated into a comfortable apartment for the live-in caretaker.

Other small projects include those in support of meetings, courses, and special events. Restrooms in Grace were enlarged to accommodate the increased size of meetings. Power and lighting were improved in the Bush Auditorium, and offices were constructed in Blackford Hall to accommodate the increased size of the events planning staff.

Less visible, but equally as important, several key infrastructure projects were completed as well. Several sections of the Laboratory's underground high-voltage power mains were replaced. Underground fiber optic network cables were extended to areas not previously serviced. And the Laboratory's water main was extended both to accommodate future expansion into the Upper Campus and to connect to residential properties at the north end of the campus, which were previously fed by well water. Two highly visible infrastructure projects are the curbing and stabilizing of the Davenport lawn parking lot and a major drainage project intended to divert the stream running through the campus around the foundations of the Demerec Laboratory during 100-year floods, two of which occurred within a single month the previous year.

Special Events

Symposium

The 71st Symposium—"Regulatory RNAs"—once again included the annual Dorcas Cummings Lecture. Ron Pasterk's outstanding lecture on "The Emerging World of Small RNAs" was presented to a mixed audience of scientists and lay friends and neighbors of the Laboratory. Following the lecture, more than 20 of our neighbors graciously opened their homes and hosted dinner parties for Symposium participants and Laboratory friends alike.

Gavin Borden Visiting Fellows

The 12th Annual Gavin Borden Visiting Fellow Lecture—in memory of the publisher of *Molecular Biology of the Cell*—was held on Tuesday, May 9. Dr. Michael Levine, Professor of Molecular and Cell Biology at the University of California, Berkeley, presented the lecture entitled "Gene Networks for Fly Gastrulation and Heart Formation in Sea Squirts."

Delbrück 100th Birthday Celebration

On August 26 and 27, the Laboratory commemorated the centennial of the birth of Max Delbrück (September 4, 1906). Delbrück, who frequently visited during the 1940s through the 1960s, was a scientific leader who conducted breakthrough research and began Cold Spring Harbor Laboratory's Phage Course. With Salvador Luria and Alfred Hershey, he founded the "Phage Group" to research bacteriophage (viruses that attack bacteria) in order to understand the nature of the gene, work for which the three shared the Nobel Prize in 1969.

The meeting brought together several of Delbrück's colleagues, students, friends, and family members to share stories and discuss his contributions to 20th century science. The 2-day conference included talks by Ernst Peter Fischer, Delbrück's former student and biographer; Matt Meselson, who conducted experiments that helped show how DNA replicates; and Delbrück's longtime collaborator, Gunther Stent; among others. The meeting continued with a symposium on current research related to topics that had interested Delbrück, concluding with a review of the burgeoning area of Systems Biology by Lee Hood, a longtime colleague of Delbrück's.

The First Double Helix Medal

The Laboratory held its inaugural Double Helix Medal Dinner on November 9 at the Mandarin Oriental, New York. Medals were presented to Muhammad Ali for his public campaign against Parkinson's disease; to Suzanne and Bob Wright (NBC Universal) for their work in bringing attention to autism through Autism Speaks; and to Nobel laureate and former CSHL faculty member Phillip Sharp for his lifelong contributions to biomedical research leading to a deeper understanding of cancer and other genetic diseases. This special event, which raised nearly $2.5 million for the Laboratory, was cochaired by CSHL Trustees Tom Quick, David Rubenstein, and Roy Zuckerberg and NBC Universal President, Jeff Zucker.

Double Helix Medal

Public Lectures

The CSHL Cultural Series is a tradition in which an eclectic mix of artists, writers, and scientists present lectures, concerts, and exhibits that provide compelling glimpses of how we experience, discover, live in, and make sense of our world. Open to the public, the aim of the Cultural Series is to stimulate, inspire, and entertain.

S. Lowe

March 14
Simon Baron-Cohen, Professor of Developmental Psychopathology at University of Cambridge and Director of the Austism Research Centre in Cambridge: *Seeking the Cause of Autism*.

April 25
Scott Lowe, HHMI Investigator/Professor, Cold Spring Harbor Laboratory: *Recent Progress in Cancer Research*.

May 16
Irene Pepperberg, Adjunct Associate Professor, Brandeis University; Research Associate, Harvard University; Leader, The Alex Foundation: *In Search of King Solomon's Ring: Cognitive and Communicative Abilities of Grey Parrots*.

M. Ridley

June 13
Matt Ridley, F.R.S., Visiting Professor, Watson School of Biological Sciences: *Francis Crick: Discoverer of the Genetic Code*.

September 12
Jeffrey Friedman, HHMI Investigator/Professor, The Rockefeller University: *Leptin and the Biological Basis of Obesity*.

September 26
Paul Liam Harrison, artist-in-residence, Human Genome Organization: *Pertaining to Origins: Organization of Form and Function*.

J. Friedman

October 24
Tim Tully, St. Giles Professor of Neuroscience, Cold Spring Harbor Laboratory: *Recent Progress in Neuroscience Research*.

Public Concerts

March 18
Alexandre Pirojenko, piano

March 25
Rui Shi and Chris Gaudi, piano and oboe

April 29
Martin Kasik, piano

May 6
Asmira Woodward-Page, violin

May 20
Gleb Ivanov, piano

August 26
Julie Albers, cello

September 2
Orion Weiss, piano

September 16
Efe Baltacigil, cello

September 30
Wonny Song, piano

O. Weiss

W. Song

Jupiter String Quartet

October 14
Thomas Meglioranza, baritone

November 18
Daniel Phillips, violin

December 2
Jupiter String Quartet

Exhibits

The 2005 Photographer-in-Residence Ryan Brenizer exhibited his works in Bush Auditorium throughout the month of July. The photographs of many CSHL researchers were captured during his residency the previous summer.

Paul Liam Harrison, Artist and Printmaker, exhibited his work in a show entitled "Pertaining to Origins," held in the Racker Room of Blackford Hall from September 26 through October 1.

Laboratory Employees

New Staff

Glenn Turner joined the faculty in the winter of 2006 to study the association between smell and taste; for example, how the brain encodes the association between spoiled milk and the memory of that awful taste. He is using the fruit fly's association between a given odor and a bitter taste along with the electrophysiology techniques that he developed at the California Institute of Technology (CalTech) and the powerful ability to manipulate genes in the fruit fly using molecular genetics. Turner did postdoctoral research in Dr. Gilles Laurent's laboratory at CalTech, where he collaborated on a method to measure electrical activity and hence the activity of neurons in the fruit fly brain. Using this technology, he found that olfactory information is represented in an area of the fruit fly brain called the mushroom body that is essential for learning and memory.

Hiro Furukawa, who joined the faculty of CSHL in December 2006, is interested in the connection between the NMDA receptors and proteins involved in Alzheimer's disease. His research both as a graduate student in Dr. Tatsuya Haga's laboratory at The University of Tokyo and as a postdoctoral fellow in Dr. Eric Gouaux's laboratory at the Vollum Institute at Columbia University focused on understanding how these neurotransmitter receptors work. He is studying γ-secretase, which cuts amyloid precursor protein into a plaque-forming γ-amyloid fragment found in Alzheimer's patients and may affect neuronal activity by associating with NMDA receptors. Understanding these interactions may aide in defining targets for developing new drugs to treat Alzheimer's disease.

A new faculty member as of September, Raffaella Sordella is interested in exploring the molecular mechanism of why particular mutations in the oncogene called epidermal growth factor receptor (EGF-R) result in cancer cell addiction, and why other EGF-R mutations are resistant to the drug *Iressa*. Continuing the work that she did at Massachusetts General Hospital Cancer Center as a postdoctoral fellow, she hopes to identify other cellular components to which cancer cells become addicted that potentially can be targeted by cancer therapies. Sordella received her Ph.D. from Turin University, Italy, where she worked with Dr. Paolo Comoglio studying the role of growth factor receptors in cancer development.

Dr. Walter Goldschmidts joined the laboratory as the Executive Director of Sponsored Programs, bringing extensive federal and private sector management and research funding experience to our campus. In this newly created role, his Department facilitates new and continuing sponsored research initiatives to promote the research, education, and scholarly mission of the Laboratory and its investigators.

Promotions

Congratulations to David Jackson and Linda Van Aelst who were both promoted to Professor.

Departures

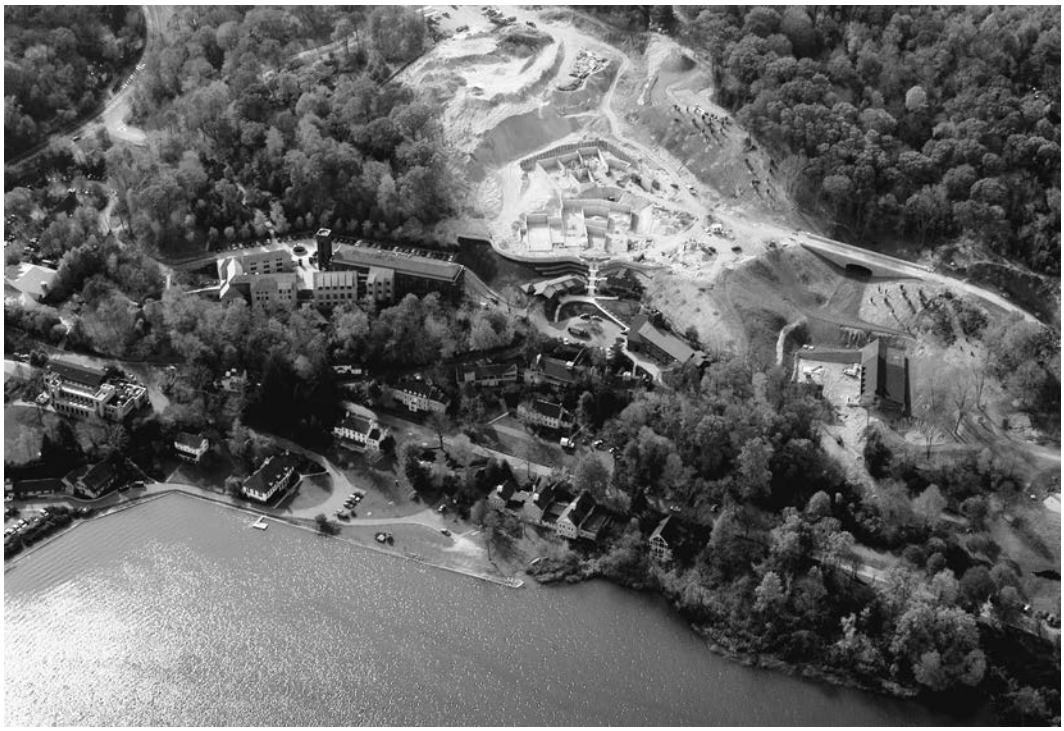
During the course of the year, several faculty took on new challenges at other institutions. Associate Professor Carlos Brody moved to Princeton University, but we are pleased to have him continue at CSHL as an Adjust Professor. Eli Hatchwell moved further east on Long Island to Stony Brook University, and Andrew Neuwald began a faculty appointment at The Instititute for Genomic Research (TIGR).

Jeff Picarello, the Director of Public Affairs for Cold Spring Harbor Laboratory and former managing editor of the Annual Report, took a position with Edelman Public Relations.

Peter Sherwood, who was the Director of Research Communications and Editor-in-Chief of the Harbor Transcript, moved on to Hofstra University.

We are saddened by the passing of Teresa Haire, a talented graduate student in Senthil Muthuswamy's laboratory. Several events were held to celebrate Teresa's life, and a fund has been established in her honor to support graduate student education at the Watson School of Biological Sciences.

The CSHL community also mourned the death of Enrique (Henry) Cepero, a postdoctoral fellow in Scott Lowe's laboratory who had battled cancer for three years. He is survived by his wife Jennifer and two newborn daughters, for whom college funds were established by friends here.



Hillside Campus expansion

Community Outreach

Cold Spring Harbor Laboratory participated in a number of community outreach events, including the sixth annual Pancreatic Cancer Walk at Old Westbury Gardens; the Long Island 2-Day Walk to Fight Breast Cancer; the Long Island Prom Boutique; the Long Island Cares Food Drive; and numerous activities to support the Ronald McDonald House at Schneider Children's Hospital in New Hyde Park.

Looking Forward

The year 2006 was one that propelled Cold Spring Harbor Laboratory forward. The foundations for the future were firmly set this year. Structurally, we moved mountains to set the cornerstone for the Hillside Campus expansion whose buildings will proudly bear the names of some of our most generous supporters. We celebrated the history and legacy of our Long Island campus with yet another successful symposium and numerous other concerts and lectures. The Double Helix Medal begins a new legacy that received national recognition for CSHL's dedication to raising awareness about the importance of genetics research for improving the health of people everywhere. The year 2006 should inspire us all to continue to move forward and realize the full potential of this institution. Thanks to our Trustees, our faculty and staff, and to our supporters for making this possible.

Bruce Stillman, Ph.D., F.R.S.
President