

HIGHLIGHTS OF THE YEAR

Research

Research performed at CSHL continues to have an extraordinary impact throughout the life sciences, most especially in the areas in which we have chosen to concentrate: cancer biology and genetics, neuroscience, genomics and bioinformatics, and plant genetics. A recent study—Thomson Scientific's *Essential Science Indicators*—placed CSHL in the top 1% of research institutions most frequently cited by scientific research papers. CSHL's scientists collectively ranked in the top 3% of their peer group, a strong indication of their influence on the entire field of molecular biology.

Such statistics are not the only measures of our effectiveness, but they speak unequivocally about the excellence of the research teams we have assembled on our small (although growing) campus. To convey more vividly the remarkable productivity of our programs, just a few of the dozens of important findings reported by CSHL labs during the last year are reviewed here.

Spontaneous Mutations in Autism

This year, a group of CSHL researchers that included Michael Wigler, Jonathan Sebat, and Lakshmi Muthuswamy published a landmark paper shedding light on the causation of autism. To the surprise of many, their work revealed that spontaneous mutations in the genome—gene copy-number variations—are a major cause of the disease. It has long been known that autism, like many other complex neuropsychiatric illnesses, has a strong genetic component. Yet most prior genetic studies have focused on families with more than one autistic child, perhaps skewing our understanding of the importance of inheritance. With generous support from the Simons Foundation, the CSHL team assembled genomic samples from more than 1000 individuals in 264 different families. By characterizing entire families—some with several autistic children and others with only one—and comparing these with controls, the team could determine whether specific sequences in a child's genome were identical to those in their parents' or whether their genomes contained variants that reflected copying errors.



M. Wigler

How common were copy-number variants (CNVs) in autistic children? The results were striking: CNVs proved to be ten times more common in the group representing families with only one autistic child. We now know that spontaneous mutations are a frequent cause of autism, which we can continue to think of as a *genetic* disorder, although not necessarily an *inherited* one. The team of investigators suspect that a higher-resolution analysis of the genome will reveal that as many as half of the autism cases are caused by spontaneous mutations. And they suggest that CNVs are likely to underlie other polygenetic disorders, including schizophrenia. More recently, the Sebat group found tantalizing new evidence that CNVs play a role in that devastating illness.

Pioneering the Small RNA Frontier

Work in Gregory Hannon's lab continues to expand the frontiers of knowledge about small RNAs and how they operate in complex networks to form RNA interference (RNAi) pathways.



G. Hannon

Greg and his team have been involved in this fast-changing area of research from its inception at the beginning of the decade. With the advent of research by Greg, Leemor Joshua-Tor, and other investigators on double-stranded RNAs and a previously unknown cellular machinery that “diced” and “sliced” them into short, single-stranded microRNAs (miRNAs) and short interfering RNAs (siRNAs), a wholly new class of RNA-based gene regulatory molecules came into view.

Greg’s most recent work extends knowledge at the basic science level, while showing experimentally some of the applications that small RNA research is likely to have in years to come. This year, the Hannon lab, in collaboration with Senthil Muthuswamy’s team, demonstrated that by manipulating miRNAs, including the tumor suppressor *let-7*, they could single out and repress stem-like cells in mouse breast tissue that are widely thought to give rise to cancer. Another team led by Greg, and including CSHL investigator Scott Lowe, identified a family of miRNAs (called miR-34) that enable a critical tumor suppressor network called the p53 pathway to fight cancer growth.



S. Muthuswamy

On the basic research front, Greg and colleagues have helped to reveal a new major class of small RNAs, called Piwi-, or piRNAs, which, unlike their small RNA “cousins,” do not appear to arise from double-stranded RNA precursors. But like miRNA and siRNAs, piRNAs guide Argonaute proteins to silencing targets arrayed across the genome, via complementary base pairing. The Piwi clade has been found in mammals and flies; its presence is tightly correlated with the emergence of germ-line cells. Hannon has hypothesized in a recent paper that piRNAs provide a glimpse into the ancestral functions of RNAi, their emergence serving to counter the emergence—eons ago—of genomic parasites that threatened the earliest self-replicating genomes.

Unmasking a “Master” Tumor Suppressor

Naturally occurring tumor suppressive mechanisms have been the focus of work at the Laboratory for many years. This year, Alea Mills and colleagues solved a mystery in this area that has befuddled cancer researchers for decades. It had been known since the 1970s that the short arm of human chromosome 1 was often missing in many kinds of cancers, suggesting that this region contained a “good gene” that prevented tumors from forming. Yet attempts to pinpoint the gene by looking at human tumors turned up empty-handed.

Using an innovative method called chromosome engineering, Mills generated mice that were missing large fragments of DNA identical to the suspect tumor suppressive region in humans. Mice that lacked this region readily developed tumors, whereas mice with an extra copy of this region had excessive tumor suppression that made the cells stop dividing completely. Once they had pinpointed this powerful tumor suppressive region, Mills and her team determined which of the 52 genes in the region was responsible for preventing cancer.



A. Mills

They concluded that it was a gene called *Chd5*, the “master switch” of an extensive tumor suppressor network. When *Chd5* was deleted, the entire network collapsed and prolific cancer resulted. Alea and her team have already found that the gene is commonly deleted in an often fatal brain cancer called glioma, and they are now investigating whether it is responsible for other kinds of human cancers. Future efforts will be focused on exploring anticancer therapies based on modulation of *Chd5* activity.

Reversible Network Effects of Three Lung Cancer Genes

Cancer research that looks at one gene at a time is limited by the growing realization, made possible by the work of Scott Lowe and others, that cancers are often caused by networks of multiple interacting cancer genes. Mutations in these genes are widely thought to determine both response to treatment and clinical outcome in individual cases. This year, Scott Powers and David Mu, with collaborators at Memorial Sloan-Kettering Cancer Center, discovered that interactions of three adjacent genes found on human chromosome 14 can set off a potentially lethal chain of events that results in as many as one fifth of non-small-cell lung cancer cases. The genes—*TTF1*, *NKX2-8*, and *PAX9*—work together to reactivate what appears to be a pattern of gene expression normally present in the fetus, as lung tissue is being formed. Scott and colleagues not only identified the mutation that triggers this abnormal reactivation and demonstrated its causal role in human lung cancer, but also, intriguingly, demonstrated in model systems that by turning these genes off, the cancer can be stopped.



S. Powers

An Online Genome that Illustrates Genomic Variation

It is relevant to note that this year, CSHL launched a Web site enabling the general public to understand visually, as perhaps never before, a key dimension of genetic variation—the level of the single-nucleotide polymorphism, or SNP. With the online posting of Jim Watson's genome, it instantly became possible for anyone, using a plain Web browser, to view places where Watson's sequence is different from the “reference” human genome sequence published by the Human Genome Project. Easy-to-use navigation tools facilitate the viewing of genes and some of the common diseases associated with them.

Fixing an Editing Error to Treat a Neurodegenerative Disease

The process by which genes issue instructions to cells to produce specific proteins in specific amounts is intricate and usually very accurate. In a phase of this process called transcription, itself a marvel of complexity and precision, a strand of RNA is generated, which, in turn, is usually edited before leaving the nucleus to engage the ribosome, the cell's protein factory. Errors in the RNA editing process, called splicing, can lead to abnormal gene expression and in some cases serious disease.

Those suffering from spinal muscular atrophy (SMA), a neurodegenerative disease that is often fatal in children, are the victims of a splicing error about which Adrian Krainer and colleagues have learned a great deal. This year, Adrian's team published results of work that holds genuine promise for SMA patients. The team looked closely at how a mutated version of a gene called *SNM2* is expressed in the illness. In a part of the splicing process involving the precursor of the mature messenger RNA, the team focused on a deleted segment, exon 7, that is linked with the mutated gene's abnormal expression pattern in SMA. Using a class of molecules called antisense oligonucleotides, or ASOs, Adrian's team, in collaboration with a team at Isis Pharmaceuticals, was able to correct the splicing defect in cultured cells gathered from individuals with SMA. They now intend to test this therapeutic approach in mouse models.



A. Krainer

Another phase of the Krainer lab's work, which also has the potential to impact therapeutics, yielded results this year. They established that a splicing factor

called SF2/ASF, which they had previously described, can act to promote cancer. They demonstrated how the SF2/ASF protein, when produced in excess, can cause variations in the splicing patterns of many genes, one of which encodes a protein kinase that regulates cell growth and protein synthesis. A novel variant of this kinase, S6K1, can both cause and maintain cancer in cells.

An Inhibitory Neurotransmitter's Surprising Role in Neural Plasticity

Josh Huang and his team have made substantial progress in recent years in their efforts to characterize cellular and molecular mechanisms underlying the construction and plasticity of GABAergic inhibitory circuits in the mammalian brain. A prominent feature of GABAergic con-



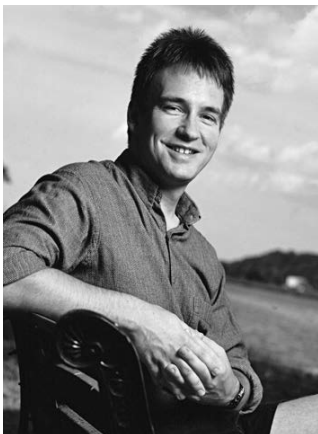
J. Huang

nectivity, which accounts for differential regulation of the input, integration, and output of principal neurons, is the targeting of different classes of inhibitory synapses to neuronal structures including spines, dendrites, somas, and initial axonal segments. This year, they made significant progress on the question of how GABAergic transmission is implicated in the regulation of plasticity, demonstrating how an environmental input can modify GABAergic neural circuitry.

This kind of work has direct implications in neurological and psychiatric illness such as autism and schizophrenia, which involve altered development and function of GABAergic circuits. To the surprise of many in the field, Josh and his team also discovered this year that the inhibitory neurotransmitter GABA itself has a major role in plasticity. They revealed that it serves as a trophic factor, with an impact on signaling that determines whether a synapse will be stable and whether axons will grow or retract.

It is important to mention that the great technical expertise in mouse engineering that makes possible the success of the Huang lab's research program has been recognized by the National Institutes of Health, which has awarded the group a major 5-year grant aimed at the generation of advanced genetic tools for study of the GABAergic system. Because the GABAergic network is very complex and heterogeneous, this will entail the generation of approximately 20 distinct mouse lines for each characteristic cell type.

A Novel Plant Gene That Calibrates Growth to Light



D. Jackson

In recent years, we have learned some surprising things about signaling in plants, including the fact that individual proteins and RNAs can act as the agents of mobile signaling. During 2007, David Jackson and his colleagues discovered a gene whose role in development brings to light a signaling mechanism that is scientifically intriguing and potentially of great commercial value. The gene in question, called *TILLERED1*, encodes a transcription factor that controls the growth of branching in grasses, a process called tillering. This gene, David reports, is particularly interesting because its transcription is calibrated to the sensing of light by the plant. He speculates that sensors in the leaves send signals, via a mechanism the lab is investigating, to the shoot meristem, the compartment within the plant in which stem cells that govern branching reside. Once understood, this signaling mechanism might be mobilized to boost the yield of plants such as switchgrass that are currently being used to make biofuels.

A New Partnership with Industry to Help Feed a Hungry World

To help meet the pressing needs of agriculture at a moment when the world's population is soaring toward the \$7 billion mark, plant scientists at CSHL have joined forces with their counterparts at Pioneer Hi-Bred, the agricultural division of the DuPont Company. In an agreement reached this year that is certain to benefit both organizations, their formidable scientific acumen will be put to the challenge of helping farmers increase crop yields and grow plants specifically engineered to endure environmental stresses while protecting themselves from diseases and pests.

It is a partnership that departs in important ways from past agreements reached between academic research institutions and the private sector, many of which have been quite narrowly conceived. With thanks to John Maroney, Vice President, Technology Transfer, and his staff who worked closely with CSHL scientists, the agreement between CSHL and Pioneer encourages scientists in both organizations to communicate openly and share ideas, information, and research results. Rather than a single project, the teams will collaborate on several interrelated ventures over a 5-year period.

For Pioneer, it is a way to inject intellectual capital into an R&D enterprise that mostly focuses on applied work. For our plant scientists, it is a way to support a significant expansion of basic research while keeping one foot solidly planted in the "actual world," a world that sorely needs innovative solutions if nutritional and energy requirements are to be met in the decades ahead.

Forging a Collaborative to Define the Big Questions in Plant Biology

Just as our campus has served in past years as the setting for historic meetings at which plans were first sketched to sequence the human genome and the first plant genome, so it will witness in the coming months the inaugural meeting of a vitally important research collaborative that aims to define and address "grand challenge questions" in plant biology. CSHL and four research universities, led by the University of Arizona, will share a \$50 million NSF grant over the next 5 years to launch the iPlant Collaborative, which will focus attention on research questions of global significance while at the same time orchestrating the development of an all-encompassing computer- and Internet-based infrastructure that promises to transform the way plant science is done.

Involving Rob Martienssen, Lincoln Stein, Doreen Ware, and Matt Vaughan of CSHL, the initiative's overarching objective is to bring plant science fully into the 21st century, as Rob has put the case, providing the technical and institutional means by which sharing and mutidisciplinarity can fully replace the outmoded single-investigator/single-institution research paradigm. It is a plan to provide plant science and scientists with the means with which to meet the extraordinary challenges to agriculture of the years immediately ahead, implicit in the steady rise in global populations, shrinking ecosystem diversity, and the prospect of significant global climate change.



L. Stein



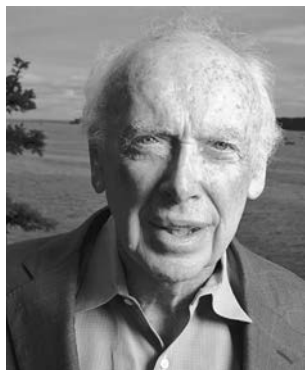
D. Ware

Cold Spring Harbor Laboratory Board of Trustees

The Board of Trustees welcomed two new members at the beginning of the year: CSHL Association President Pien Bosch and American Express Executive Vice President and General Counsel Louise Parent.

We mourned the passing of two Honorary Trustees and long-time friends, Martha Farish Gerry and William E. Murray, Esq. Martha Gerry joined the Board of Trustees of the Laboratory in 1991, serving as Secretary of the Board from 1997 to 2000, and thereafter as an Honorary Trustee. Bill Murray was a member of the Board of Trustees of the Laboratory from 1995, serving as a Trustee until November 2001, and thereafter as an Honorary Trustee.

Many thanks to trustees Jacob Goldfield, Jeff Hawkins, and Douglas Morris, who began terms in 2000 and concluded their service this year. Mr. Goldfield, Managing Director, J. Goldfield & Co., participated in the Finance and Investment Committee from 2001 to 2004, the Investment Committee from 2004 to 2007, the Finance Committee in 2003 and 2005, and the Research Committee from 2004 to 2007. As a Scientific Trustee, Jeff Hawkins, cofounder of Numenta, Inc., served on the Research Committee from 2001 through 2007.



J.D. Watson

In recognition of his outstanding 40-year dedication to Cold Spring Harbor Laboratory, the Board of Trustees appointed James D. Watson Chancellor Emeritus and Oliver Grace Professor of Cancer Research Emeritus. Nobel laureate for the 1953 codiscovery of the double helix structure of DNA, Jim served as director of CSHL from 1968 to 1993, as president from 1994, and then as chancellor from 2003 to 2007.

Under Jim's leadership, CSHL rose to global prominence in cancer research and pioneered a broad range of genetic and biological education programs, including the doctoral program in the school that bears his name, the Watson School of Biological Sciences. He and his wife Liz have made invaluable contributions to this institution in so many ways, ranging from research and education to philanthropy, campus architecture, and art. We look forward to the Watsons' continued participation and support in campus life.

With Pien Bosch as president, the Cold Spring Harbor Laboratory Association (CSHLA) surpassed its 2007 fund-raising goal for the Annual Fund, raising nearly \$1.3 million. Successful events that were organized throughout the year by CSHLA, with able help of our Development and Special Events Departments, included the Annual Meeting, the 9th Annual Jazz at the Lab, the Dorcas Cummings Lecture, a Major Donor Party hosted by Connie and Angelo Silveri, and the Women's Partnership Luncheon. Five new directors were named to the Association this year: Charles B. Goodwin, M.D., Lauryl Palatnick, David Peikon, Freddie Staller, and Fifield Whitman.

Research and Education Management



D.L. Spector

CSHL continues to strengthen the management of our research and education programs, which must evolve constantly to meet the challenges of contemporary science and society. This year, we appointed a new Director of Research, David L. Spector, who for the past two decades has focused his research at CSHL on advancing the ability of biologists to see the processes of transcription and translation in living cells. In addition to continuing to run his own laboratory, David's new charge is to oversee the entire scientific program and staff of more than 400. To support the Director of Research, we created the new position of Director of Research Operations, to which we appointed Sydney Gary, who previously had played a pivotal role as Assistant Director of the Banbury Center.

During the past year, the CSHL Grants Department has been transformed from a service division to a proactive Office of Sponsored Programs (OSP). Under the leadership of Dr.

Walter Goldschmidts, OSP now actively promotes our research and education mission by identifying and matching funding opportunities with CSHL research expertise and needs. A new team approach to facilitating and managing sponsored funding is accomplished by unprecedented collaboration with CSHL investigators, the Director of Research, and other CSHL departments. We have improved support and grant-related counseling for new investigators, enhanced budget monitoring and forecasting, and established a CSHL grant application archive. Grant-writing workshops were hosted throughout the year, and a new OSP intranet Web site with numerous resources available for the CSHL community was launched.

The research management structure was further solidified by three outstanding Program Chairs in our focal research areas: Gregory Hannon, Bioinformatics/Genetics; Scott Lowe, Cancer and Molecular Biology; and Roberto Malinow, Neuroscience.

We also welcomed CSHL professor Leemor Joshua-Tor to a new leadership position as Dean of the Watson School for Biological Sciences (WSBS). Leemor will fuse her award-winning research into the molecular basis of nucleic acid regulatory processes with her expanded responsibilities, which include the doctoral program, the postdoctoral program, joint undergraduate Programs with Stony Brook University, the CSHL Summer Undergraduate Research Program, and the Partners for the Future Program for high school seniors. To provide additional support for the WSBS, the Assistant Dean position was filled by appointment of the former Assistant Director of the Dolan DNA Learning Center, Uwe Hilgert.



S. Lowe



L. Joshua-Tor

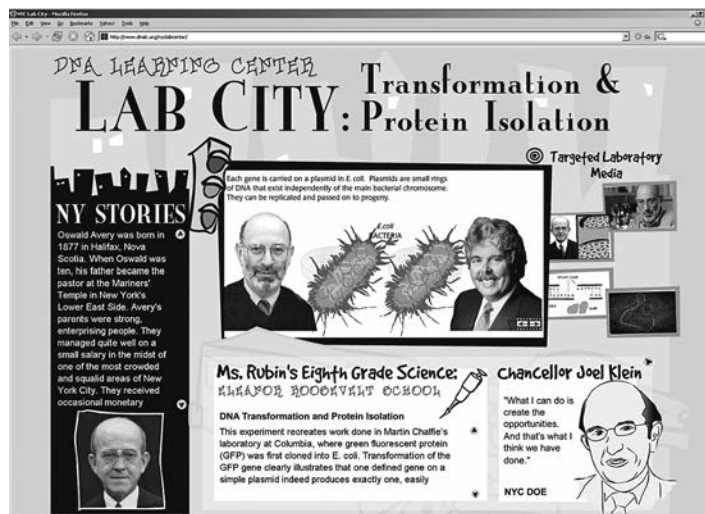
New Markets for CSHL Education Programs

CSHL's program of scientific conferences and courses is one of the most recognized and respected in the biological sciences. Every year, more than 8000 researchers from around the world come to CSHL to participate in a wide range of meetings and courses. We are excited about the progress that David Stewart, Executive Director, Meetings and Courses, and his group have made over the last 2 years to bring a similar meetings and courses program to Asia.

At the end of 2007, we signed an agreement with the Suzhou Industrial Park (SIP), a new high-technology project located west of Shanghai and proximal to the 2500-year-old city of Suzhou. The largest cooperative project between the governments of China and Singapore, the SIP has become one of the fastest growing and most competitive development zones in China. Key to this success is the creation of a high-tech biotechnology and nanotechnology research and education park. As part of the agreement, CSHL will develop and operate an annual series of scientific conferences in a newly constructed complex within the SIP. We plan to open this conference program in 2010.

This year, the Howard Hughes Medical Institute (HHMI), which has supported courses at CSHL for more than 15 years, doubled its funding for the Lab's postgraduate education to \$3 million during the next 4 years.

We are also pleased to be expanding our middle and high school education programs to New York City. Partnering with the New York City Department of Education, the Dolan DNA Learning Center (DNALC) was awarded a 5-year grant of \$750,000 for precollege science education from the HHMI. This will enable CSHL to open a DNA Lab in a Harlem public



The DNALC brings interactive Web-based resources to its hands-on workshops and to teachers and students online

school, where we will train local teachers and give New York City students an opportunity to participate in laboratory DNA experiments.

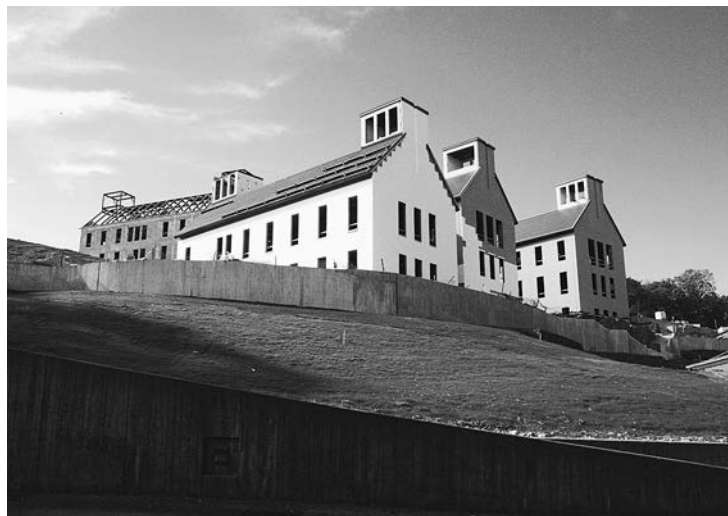
The HHMI-funded program will supplement an existing DNALC “footlocker” program which currently provides training and footlockers full of lab equipment and supplies to 12,000 students in 60 school systems each year on Long Island. In addition, with leadership from DNALC Executive Director David Micklos, the talented DNALC staff began distribution of the world’s first integrated set of RNA interference (RNAi) experiments which use the same technology that won the Nobel Prize in 2006.

Congratulations to Banbury Center staff and its Executive Director Jan Witkowski—who celebrated his 20-year anniversary with CSHL this year—for developing and executing 25 scientific meetings and nine courses on science and public policy. The breadth of topics covered at the Banbury Center is fantastic and this year was no exception. Highlights included “Protecting the Public Trust in Immunization” and “Retreat from Reason,” which discussed how to bring rationality to public discourse.

Hillside Campus Update

Groundbreaking on the Hillside Campus expansion project began in 2005, but this year, we witnessed the most dramatic progress yet in this monumental capital project that will increase our research capacity in cancer, neuroscience, and bioinformatics by nearly 40%. At the beginning of the year, only the foundations for the six-building research complex were in place. By year’s end, all of the internal piping and wiring were installed; the concrete superstructure was complete, exterior block walls were erected, and the roof structure and sheathing were in place, enclosing the buildings and ensuring that interior work continued through the winter months.

All the work on building structures could readily be seen at a glance as it progressed. Much less obvious was the enormous amount of work taking place inside the structures. Electricians and steamfitters worked hard, installing electrical and mechanical systems, including the two high-pressure boilers that will ultimately heat the six-building complex. These two areas were



Current construction of the Hillside Campus

by far the most complex components of the project, and the impressive progress made in these areas is essential to the timely completion of the Hillside Campus.

The final touches were also put on the new chiller plant, and much of the underlying infrastructure—drainage systems, electrical conduit and wiring, water and sewer piping—was installed underground.

The Nassau County Chapter of the New York State Society of Professional Engineers presented CSHL with the Project of the Year Award for the engineering and innovative environmental design of the storm water management system for the Hillside Campus. CSHL was recognized for achieving a balance between development and the environment. The unique and functional storm water management system not only is effective at protecting the surrounding ecosystems, but also provides a visually pleasing backdrop for the Laboratory.

We thank Vice President and Chief Facilities Officer Art Brings and the Facilities Department for all of these great results and the minimal disruption to our daily operations and quality of life on campus as the work has proceeded.

Awards and Honors

CSHL Professor and HHMI Investigator Greg Hannon was honored by two prestigious awards this year: The National Academy of Sciences 2007 Award in Molecular Biology for his extraordinary scientific achievement in molecular biology and The Memorial Sloan-Kettering Cancer Center's 2007 Paul Marks Prize for cancer research.

Two CSHL postdoctoral students from Greg's laboratory received the prestigious Pathway to Independence Award from the National Institutes of Health. With this award, Jose Silva will be able to continue developing highly efficient RNAi libraries. Alexei Aravin's award was from the National Institute of Child Health and Human Development. This is a new NIH program, providing one of the few opportunities for postdoctoral fellows to receive both mentored and independent research support.



G. Hannon

James D. Watson became the first individual to have his genome sequenced. The sequence was completed by collaboration between academic and industrial laboratories using a new rapid DNA sequencing method. Such personalized genome sequences will enable analysis of the details of human genome variation and will prompt needed public discussions about the use of such information.

Our new Dean of the Watson School of Biological Sciences, Leemor Joshua-Tor, was awarded the first Dorothy Crowfoot Hodgkin Award from the Protein Society in recognition of her exceptional contributions in protein science that have profoundly influenced our understanding of biology.



L. Trotman

Lloyd Trotman, who recently joined our faculty, was named a 2007 Rita Allen Foundation Scholar for his work on breast and colon cancer tumors. This program identifies promising leaders in research focused on the development of treatments and cures for cancer, cerebral palsy, or multiple sclerosis.

Lars Zender, a senior clinical postdoctoral fellow at CSHL, was awarded a \$40,000 grant for his seminal contributions in the field of cancer biology and epigenomics. The grant was presented at the second annual "Cracking the Code with the Bear" research symposium sponsored by the Bear Necessities Pediatric Cancer Foundation in Chicago. In addition to Lars, CSHL postdoctoral fellows Danielle Irvine and Julius Brennecke were also selected to present their cancer research from a large pool of outstanding postdoctoral fellows across the country.

I was honored to receive the Curtin Medal for Excellence in Medical Research from the John Curtin School of Medical Research at the Australian National University, where I received my doctorate in 1979. In May, I also received an honorary degree and presented the commencement address at the Long Island University graduation.

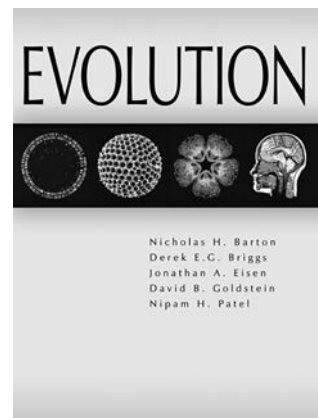
At the 2007 Watson School of Biological Sciences Commencement Convocation on April 22, we conferred the Degree of Doctor of Philosophy to Darren James Burgess, Beth Li-Ju Chen, Catherine Yvonne Cormier, Claudia Edith Feierstein, Tomas Hromadka, Elizabeth Proby Murchison, and Dougal G. R. Tervo. Jonathan See-Ming Kui received the Master of Science degree. The Watson School awarded honorary degrees to Trustee Mary D. Lindsay, former CSHL Director Joseph F. Sambrook, and Nobel Prize winner Sydney Brenner.



Watson School Commencement Convocation. Former CSHL Director J.F. Sambrook receives his honorary degree.

CSHL was ranked among the most published and cited institutions by Thomson Scientific's *Essential Science Indicators*. In addition, *Genes and Development*, a publication of the CSHL Press, ranked sixth in the category of journals that publish high-impact research in molecular biology and genetics.

This fall, the CSHL Press published a groundbreaking textbook, *Evolution* by Nicholas H. Barton, Derek E.G. Briggs, Jonathan A. Eisen, David B. Goldstein, and Nipam H. Patel., which for the first time integrates molecular biology, genome science, and evolutionary biology. CSHL Press Executive Director John Inglis and his staff of nearly 60 continue to innovate, most recently leveraging interactive digital technology. One excellent example of their effort to keep pace with society's increasing use of the Internet, editors at the Press have supplemented the newly released undergraduate *Evolution* textbook with a Web site (which even includes blogs) targeted for teachers and students who have adopted the text.



CSHL Press textbook *Evolution*

For the sixth consecutive year, CSHL received the highest possible rating from Charity Navigator for its financial organizational efficiency and capacity. According to Trent Stamp, President of Charity Navigator, "with only 1% of the charities rated receiving six consecutive four-star Charity Navigator evaluations, Cold Spring Harbor Laboratory outperforms most charities in fiscal responsibility."

The critical job of maintaining the highest standards of financial responsibility is ably performed at CSHL by Lari Russo, Vice President, Finance and Comptroller, and her team. These standards distinguish CSHL as an institution prepared to meet the expectations of public and private donors who demand accountability, transparency, and quantifiable results from their investments in nonprofit organizations.

Development

Under Charlie Prizzi, Vice President, Development, Cold Spring Harbor Laboratory's fund-raising efforts saw much success in 2007. An additional \$20 million was committed to the Hillside Campus Campaign goal of \$200 million. More than \$40 million was raised in unrestricted and program support. On behalf of CSHL, our Board of Trustees, and our Development Department, I would like to acknowledge all those who helped us achieve our goals.

The Cold Spring Harbor Campaign

Capital, Endowment, and New Faculty and Laboratory Investment

We greatly appreciate the major donors who have generously contributed new gifts and pledges of \$100,000 or more to support the Laboratory's Hillside Campus Campaign, including Dr. and Mrs. Bayard D. Clarkson, Mr. and Mrs. John P. Cleary, Mr. and Mrs. John H. Coleman, Mr. and Mrs. Norris Darrell, The Shelby Cullom Davis Foundation, the Estate of Norman Dorf, Empire State Development Corporation (New York State), the William Stamps Farish Fund, the Coleman Fung Foundation, Robert A. Gay, the Harrison Family Foundation, Mary D. Lindsay, Mr. and Mrs. Robert D. Lindsay and Family, the Estate of Elisabeth Sloan Livingston, Mr. and Mrs. David L. Luke III, Mr. and Mrs. Thomas D. McGrath, Jr., Mr. and Mrs. Alan Seligson, The Seraph Foundation, Mr. and Mrs. Theodore R. Stanley, Cynthia R. Stebbins, and the Roy J. Zuckerberg Family Foundation.

Education Programs

New gifts and pledges of \$100,000 or more to support the Watson School of Biological Sciences, the Dolan DNA Learning Center, and other educational initiatives were gratefully received from Edward A. Chernoff, the Annette Kade Charitable Trust, The Jerome L. Greene Foundation, and the Doris M. and Peter S. Tilles Foundation.

Program Support

The Laboratory relies on private funding to maintain its innovative research programs. We appreciate new gifts and pledges of \$100,000 or more from Mr. and Mrs. Donald Everett Axinn, The Mary K. Chapman Foundation, Kathryn Wasserman Davis, Dr. Leo A. Guthart, The Thomas Hartman Foundation for Parkinson's Research, Jo-Ellen and Ira Hazan, The Lita Annenberg Hazen Foundation, Joan's Legacy: The Joan Scarangelo Foundation to Conquer Lung Cancer, The G. Harold and Leila Y. Mathers Charitable Foundation, The Don Monti Memorial Research Foundation, Manyu Ogale, V. Kann Rasmussen Foundation, The Sass Foundation for Medical Research, The Simons Foundation, Mr. and Mrs. Theodore R. Stanley, and the Swartz Foundation.

Breast Cancer Research Support

The Laboratory greatly appreciates the many individuals, foundations, and grassroots groups who provide the funding, outreach, and public awareness essential to maintain our cutting-edge breast cancer research. This year, CSHL was fortunate to receive support from Breast Cancer Awareness Day in memory of Elizabeth McFarland, Breast Cancer Help, The Breast Cancer Research Foundation, Clear Channel Enterprises/WALK 97.5, F.A.C.T. (Find A Cure Today), the Joni Gladowsky Breast Cancer Foundation, Glen Cove Cares, Elaine Hayes Special Effects Salon, Hearts for Cancer, Islip Breast Cancer Coalition, Long Beach Breast Cancer Coalition, Long Island 2-Day Walk To Fight Breast Cancer, L.I.A.B.C. (Long Islanders Against Breast Cancer), Manhasset Women's Coalition Against Breast Cancer, Pam and Pierre Omidyar, Sons of Italy, West Islip Youth Enrichment Services, and the Women's Insurance Network of Long Island.

The Robertson Research Fund

The Robertson Research Fund has been the primary in-house support for CSHL scientists for more than three decades. In 2007, it supported research in the labs of Grigori Enikolopov, Josh Huang, David Jackson, Leemor Joshua-Tor, Adrian Krainer, Rob Martienssen, Bill Tansey, Marja Timmermans, and Anthony Zador. Start-up research support was also provided by the Fund to four new investigators: Hiroyasu Furukawa, Raffaella Sordella, Lloyd Trotman, and Glenn Turner. In addition, the Robertson Research Fund continues to support the annual CSHL In-House Symposium and programs for postdoctoral fellows, graduate students, the laboratory seminar program, and faculty recruitment.

Library and Archives

We broke ground on a renovation and expansion project of the Carnegie Building that will allow CSHL's Library and Archives to serve our rapidly expanding campus and enable the continued collection of important materials in the field of molecular biology, genetics, and



Groundbreaking ceremony for the Library expansion. (Left to right) M. Pollock, W. Szybalski, J. Watson, H. Anand, and B. Stillman

biotechnology. The expansion is supported by CSHL donors, including corporate sponsor Genentech and CSHL alumni scientist and friend Waclaw Szybalski, Ph.D., Professor Emeritus of Oncology, University of Wisconsin-Madison.

The Archives completed a 2-year digitization project supported by the Josiah Macy, Jr. Foundation. A new database now allows us to convert our archival materials into digital format and to provide access through a Web-based interface. The Archives Advisory Committee, led by Nobel laureate and Chairman Rich Roberts, met for the second time since its formation in 2006. The committee decided to host a scientific meeting at CSHL in 2008 on the subject of the history of biotechnology. The Sydney Brenner Scholarship, endowed by Dr. Phillip Goulet, was awarded to noted scientist and biographer in history of science Jim Schwartz for his proposed project on Hermann J. Muller.

This year, we were fortunate to acquire the collection of prominent scientist and longtime CSHL Trustee Norton Zinder. The Medical Research Council donated to the Archives 136 notebooks of important research on *C. elegans* done by Sydney Brenner's laboratory. Under the leadership of Mila Pollock, the Library and Archives looks forward to organizing these new collections, along with contributions from pioneering scientist Charles Weissmann.

The year 2007 also marked the debut of the Library's CSHL Authors' Publications Database. The growing database of CSHL researchers currently contains more than 7500 citations from scientific journals spanning 1892 to the present.

Building Projects

It was another busy year for the CSHL Facilities Department, which undertook many simultaneous building projects during the year. The number, size, and ages of the Laboratory's facilities have necessitated a near-constant cycle of building and renovation.

As mentioned previously, the renovation and expansion of the Carnegie Building began in 2007. This project, scheduled with a very aggressive timetable, is slated for completion by the end of 2008. Not only will the project provide much-needed space in the CSHL Library and Archives, but it will also bring the historically significant structure up to current code and will be completely accessible to those with disabilities. Moreover, it will serve as the home for the new Genentech Center for the History of Molecular Biology and Biotechnology.

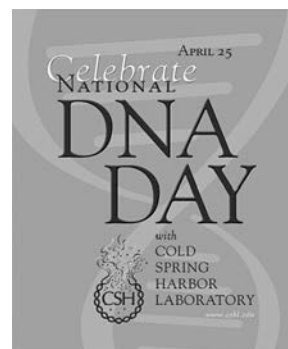
The Laboratory also undertook several projects to shore up the existing campus infrastructure. The last remaining section of high-tension electrical main was replaced, completing a project begun last year. To anticipate future needs, a water main was reinforced and a new gas main was connected to the campus. We also began a multiyear project to replace all building management systems with high-efficiency systems to control the heating and air conditioning. This project is anticipated to reduce power consumption in research buildings by 25% and is expected to lower energy costs by as much as \$500,000 per year.

Other small projects include the renovation of the Darrell House, a single-family property formerly owned by a longtime neighbor of the Laboratory, the late Ms. Susan Rose. This house was renovated into faculty housing and is the last of three houses purchased by the Laboratory that encircle a historic garden designed by Frederick Law Olmstead. The Laboratory also completed the renovations of the James library, updating the room to meet current needs, and completed renovations in the James Laboratory. In 2007, the Laboratory renovated laboratories in Beckman and Delbrück to accommodate newly arriving faculty. The Osterhout house—formerly used as sabbatical housing—was converted to office space to accommodate library staff while construction takes place in the Carnegie Building. The Laboratory also continued its improvement of meeting facilities, building a reception office in Grace and renovating and expanding the nearly 60-year-old restrooms in the Bush Auditorium.

Special Events

National DNA Day

We celebrated the 5th anniversary of the congressionally designated “National DNA Day” on April 25, featuring special laboratory walking tours and festive signage on campus as well as throughout the village of Cold Spring Harbor. In addition to collaboration with the National Institutes of Health, our local partners in this celebration of DNA as part of our history and everyone’s future were the Cold Spring Harbor Library and Environmental Center and the Cold Spring Harbor Main Street Association.



CSHL celebrated National DNA Day April 25

Symposium

The 72nd annual Cold Spring Harbor Symposium celebrated the latest research on “Clocks and Rhythms,” welcoming more than 300 researchers from around the world with wide-ranging specialties in circadian clocks, aging, and developmental biology.

One of the traditional highlights of the Symposium is the Dorcas Cummings Memorial Lecture, this year delivered by Charles A. Czeisler, Ph.D., M.D., the Baldino Professor of Sleep Medicine and the Director of Sleep Medicine at Harvard Medical School, as well as the Chief of the Division of Sleep Medicine at Brigham and Women’s Hospital, Boston.

Jazz at the Lab

The 9th annual *Jazz at the Lab* on April 14 featured the Dena DeRose Trio with special guest Bob Merrill. The event raised more than \$165,000 and was cochaired by CSHLA Directors Suzanne and Michael DiMaio and Maria Brisbane, and Wallace Henderson.

Concert for a Cure for Cancer

Violin prodigy Jourdan Urbach performed a benefit concert and reception on September 30. Proceeds benefited the Lustgarten Foundation for Pancreatic Cancer and CSHL.

Women's Partnership for Science

Nearly 200 women attended the Women's Partnership for Science benefit luncheon, held at the home of Mr. and Mrs. Daniel P. Davison on June 24, to learn about the most recent approaches to personalized treatment for breast cancer. The talk was given in tandem by CSHL investigator Mona Spector, Ph.D, and Jacqueline Bromberg, MD, Ph.D., Memorial Sloan-Kettering Cancer Center.



M. Spector and J. Bromberg

Gavin Borden Visiting Fellows

The 13th Annual Gavin Borden Visiting Fellow Lecture, in memory of the publisher of *Molecular Biology of the Cell*, was presented by Dr. David Baker on October 29.

Groundbreaking for Library and Archives

On October 12, more than 100 friends celebrated the groundbreaking for the renovation and expansion of the Carnegie Building, home to CSHL's Library and Archives and the new Genentech Center for the History of Molecular Biology and Biotechnology. At the podium, with shovels in hand, I was joined by the Mayor of the Village of Laurel Hollow Harvinder (Harry) Anand, Dr. Watson, Library benefactor Wacław Szybalski, and Mila Pollock.

The Double Helix Medals Dinner

The Laboratory held its second Double Helix Medals Dinner on November 8 at the Mandarin Oriental, New York. Medals were presented to David Koch for Corporate Leadership and Richard Axel, M.D., and Michael Wigler, Ph.D., for Scientific Research. This special event, which raised more than \$3 million for CSHL, was cochaired by Ms. Jamie C. Nicholls and Mr. Fran Biondi, Mr. and Mrs. Stephen M. Lessing, Dr. Arthur D. Levinson, Mr. and Mrs. Robert D. Lindsay, Mr. Sean McManus, and Mr. and Mrs. David M. Rubenstein.

Science Soirees

CSHL and The New York Public Library's Science, Industry, and Business Library (SIBL) sponsored a series to help nonscientists better understand the scientific concepts fundamental to understanding



CSHL and New York Public Library
cohosted a public lecture series called
Science Soirées



Double Helix Medals Dinner participants. (Left to right) E. Lauder, D. Koch, A. Hayes-Dale, and J. Koch

health and the well-being of society. According to CSHL researcher Partha Mitra, Crick-Clay Professor of Biomathematics and series moderator, “The idea is to expose nonscientists to fundamental scientific concepts that could affect their lives and provide them with a foundation for informed decisions and further exploration.”

February 1

Tim Tully, Professor, Cold Spring Harbor Laboratory: *The Future of Memory: The Biochemistry of Memory and Its Future Enhancement*.

March 12

Nicholas D. Schiff, Associate Professor and Associate Attending Neurologist, Weill Medical College of Cornell University: *Regaining Consciousness: Recovery from Severe Brain Injury*.

April 9

Jeff Dangl, John N. Couch Distinguished Professor of Biology, The University of North Carolina at Chapel Hill: *Genetically Modified Foods: Revolutions in Plant Science and the Controversies They Spur*.

May 1

Robert L. Kleinberg, Senior Research Scientist and Scientific Advisor, Schlumberger Research: *Energy Sources of the Future: The Arctic National Wildlife Refuge, Global Warming, and National Security*.

June 11

Partha Mitra, Professor, Cold Spring Harbor Laboratory: *Learning to Sing: Birdsong, Baby Talk, and the Origins of Language*.

CSHL Public Lecture Series

March 13

Don Axinn, *What You Always Wanted to Know About Poets' Lives, Their Odd Behavior, and Their Creative Process but Were Afraid to Ask*.

May 15

Gregory Hannon, HHMI Investigator and Professor, Cold Spring Harbor Laboratory: *Recent Progress in Cancer Research*.

June 21

Portia Iversen, Cofounder of the Cure Autism Now Foundation and the Autism Genetic Resource Exchange: *An Evening About Autism*.

September 25

Avner Hershlag, Director of North Shore Hospital's Preimplantation Genetic Diagnosis program: *Custom-made Babies: Fact or Fiction?*

October 23

Robert Malinow, Professor, Cold Spring Harbor Laboratory:
Recent Progress in Neuroscience Research.



R. Malinow

Public Concerts**April 21**

Chu-Fang Huang, piano

April 28

Yousun Chung and Teddy Robie, oboe and piano

May 5

The Parker String Quartet, violins, viola, and cello

May 19

Liza Ferschtman and Inon Barnatan, violin and piano

September 8

Wendy Warner and Irina Nuzova, cello-piano duo

September 29

Peter Orth, piano

October 13

Jean-Frederic Neuburger, piano

Exhibits

Photographer-in-Residence Max S. Gerber exhibited his work in a show titled "Faces of Science," in the Bush Auditorium from July 13 through July 29.

Laboratory Employees**New Staff**

We welcomed Lloyd Trotman as an Assistant Professor in the CSHL Cancer Center, where he will continue to research the role of PTEN "dosage" in breast and colon cancers. Lloyd received his Ph.D. from the University of Zurich and did his postdoctoral fellowship at Memorial Sloan-Kettering Cancer Center. At MSKCC, he and his colleagues found that removal of only one copy of PTEN was sufficient to induce cancer in a mouse model of prostate cancer and that removing both copies prevented the growth of cancer cells.

Dagnia Zeidlickis joined the CSHL staff as Vice President, Communications, with a mission to further our success in educating the general public about CSHL's biomedical research

and education initiatives and accomplishments. Dagnia brings international experience in public and government relations to the Public Affairs Department. Joining her later in the year was Jim Bono, our new Director of Public Affairs. His media experience and understanding of our private and public sector audiences locally and throughout the state will be an asset to our institution.



A. Zador

Promotions

Congratulations to Anthony Zador who was promoted to Professor and Director of the Swartz Center for Computational Neuroscience. We also commend Senthil Muthuswamy who is now Associate Professor, Adam Kepecs who is Assistant Professor, and Matthew Vaughn who was promoted to Research Assistant Professor.

Departures

During the course of the year, several faculty members took on new challenges at other institutions. Lilian Clark, our former Dean of the Watson School of Biological Sciences, became the Executive Director for Research Operations and Funding at Cancer Research U.K. I thank Lilian for the enormous amount of work she did to help establish and eventually run the Watson School. The success of the School is a reflection of her talent and capabilities.

Professor Tasuya Hirano moved to the Riken Discovery Research Institute in Japan. Two CSHL researchers joined Howard Hughes Medical Institute's Janelia Farm: Professor Karel Svoboda, who continues his relationship with CSHL as an adjunct professor; and Associate Professor Dmitri Chklovskii, who also continues here as an adjunct associate professor. Similarly maintaining ties to CSHL, Professor Tim Tully remains an adjunct professor while assuming the new role of Chief Scientific Officer at Dart Neuroscience, a company that he cofounded. Wolfgang Lukowitz is now an adjunct assistant professor at CSHL, with a new position as assistant professor at the University of Georgia in Athens. Michael Myers, who was an assistant professor at CSHL, is now with the International Centre for Genetic Engineering & Biotechnology in Italy.

Community Outreach

CSHL employees continue to actively participate in local and national community service events, including Lab-wide Blood Drives in February, August, and December, the American Cancer Society's Daffodil Days in the spring, and both the John Theissen Children's Foundation Toy Drive and the Suffolk County Toy Drive in December. Every year, CSHL is proud to sponsor the Cold Spring Harbor Library and Environmental Center kickoff festivities for the children's summer reading program.

We also continue to open the CSHL campus to guided walking tours, which are open to the public most weekends from spring through the fall. Thanks to our specially trained team of tour guides, who include CSHL students and postdocs, and the Meetings and Courses team that administers this program. They open our doors to new friends and provide tour participants with hands-on insight into the fantastic campus that we have built.

Looking Forward

2007 was another remarkable year in the history of CSHL. Our research, education, and administrative staff continue to surpass expectations. With Dill Ayres as our Chief Operating Officer, this staff—now more than 1000 strong—put CSHL at the forefront of biomedical science in so many respects. During this year, we have all worked hard to prepare for the future—a future brimming with the potential of more breakthroughs. I appreciate all of the efforts of our employees and thank Katie Raftery, Vice President, Human Resources, and her Department for continuing to help make CSHL such a great place to work.

I often marvel at the fact that despite our long and rich history and despite our significant growth, CSHL remains nimble in its ability not only to react, but also to anticipate change. The world around us is changing fast in so many ways—the economy, the political climate, the physical environment, societal norms. Evolution is a concept that we as scientists embrace. We as an institution have also embraced this concept and are stronger for it. Kudos to the Trustees, faculty, staff, and supporters for your help in making sure that CSHL continues to stay ahead of the curve.

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