Research

The year 2012 was another superb one for research at Cold Spring Harbor Laboratory. Here, we provide details of a handful of significant investigations that led during the year to published results in major scientific journals. These are suggestive of the breadth of activity at the Laboratory, as more than 600 scientists and technicians in 52 labs extend our knowledge of cancer cell biology and genetics, as well as cancer treatments; critical circuits and biochemical pathways in the brain that go awry in psychiatric as well as neurodevelopmental and neurodegenerative disorders; and genes and their pathways in plants that will help boost crop yields and extend range. The influence of CSHL faculty publications continues to be extraordinary; once again we were independently rated Number 1 in impact on molecular biology and genetics, worldwide.

Pfizer

DuPont Pioneer

The value of the Laboratory's research is gaining broader recognition outside the academic community. 2012 was marked by the announcement of collaborative agreements with two companies at the top of the Fortune 500, DuPont and Pfizer Inc. CSHL's plant biologists are working with scientists at leading seed producer DuPont Pioneer to better understand the genetic processes that control growth and development. This work is already providing a basis for new ways of boosting plant yields and for extending the range of key food crops. Pharmaceutical giant Pfizer is teaming with our researchers to develop technology for a next-generation library of human short hairpin RNAs (shRNAs). These tiny molecules, which can turn genes on and off by engaging a biological mechanism called RNA interference, are extremely useful in the identification of novel targets for anticancer drugs.

Decision-Making Abilities in Response to Multiple Sensory Cues Are Similar in Rodents and Humans

The ability of humans to make decisions in the most efficient and unbiased way based on perceptual information, for example, from auditory and visual cues, is well documented. Assistant Professor Anne Churchland published work this year showing that other mammals, in this case rodents, perform equally well in similar tests. Rats were trained through receiving rewards to respond to visual cues via the appearance of a white light on an LED screen and auditory cues through a speaker, either separately or in tandem. The results of the tests with rats were compared to similar stimuli presented to humans, with some additional features added that mimicked a real-life situation. Both humans and rats made accurate decisions in response to these combined, multisensory stimuli that were close to optimal based on a statistical prediction. By varying the time between the visual and auditory cues, the team was also able to show that the brain processes each cue in parallel, before fusing them together at a later stage in order to make a decision. These results suggest decision-making processes are evolutionarily conserved and provide a basis for researchers to use rodents as an animal model to study decision making in humans.

A. Churchland

Live-Imaging Microscopy Offers Insights into Modulation of Tumor Response during Therapy

M. Egeblad

Assistant Professor Mikala Egeblad and her team are experts in live-imaging microscopy. This technique was instrumental to a study they published this year showing how cancer cells in mouse tumors and the noncancerous "stromal" cells around them (the tumor microenvironment) respond during chemotherapeutic treatment with the drug doxorubicin. They were able to watch as the tumor and the surrounding tissue changed before, during,

and after drug administration. What they saw in the resulting time-lapse movies was that there is regulation of the permeability, or leakiness, of the blood vessels that wind through and around the tumor, which impacts the local recruitment of inflammatory cells. Resistance to doxorubicin correlated with intermediate-stage tumor development and the relative permeability of the blood vessels supplying the tumor. In mice lacking the gene for a protein involved in regulating blood vessel permeability, matrix-metalloproteinase-9 (MMP9), blood vessels were leakier and mice responded better to doxorubicin. The response was also improved when mice were lacking a gene, *CCR2*, important in the recruitment of inflammatory cells. Mikala's live-imaging techniques point to the possibility of boosting therapy responses using additional targeted factors.

T. Gingeras

Massive Analysis of the Human Transcriptome Suggests Redefining the Gene

Professor Thomas Gingeras and colleagues, including Professor Greg Hannon, published a comprehensive analysis of the messages, or transcripts, produced across the complete genome of human cells. The study was part of the latest coordinated release of data from the Encyclopedia of DNA Elements, or ENCODE, consortium. The new data show that up to three-quarters of the genome is capable of being transcribed and that much of nonprotein-coding RNA is organized in a way that indicates it may be functional, i.e., it may perform biochemical actions, and that smaller functional RNA transcripts can reside within longer transcripts, being released as longer ones are chopped up or "processed." Given the large amount of the genome that is transcribed, and the nested organization of many nonprotein-coding RNAs, the perceived boundaries between genes are shrinking and even overlapping. These observations challenge the previous understanding of what discrete unit makes up a gene and raises the implication that disease-associated mutations may lie in functional nonprotein-coding RNA transcribed from what was once thought to be "spacer" regions of DNA between genes.

G. Hannon

Origin and Migration of Powerful Cortical Inhibitory Cells Determined

Chandelier cells are powerful inhibitors of the excitatory impulses from the pyramidal neurons of the brain's cortex. One chandelier cell makes contact, through chemical junctions known as synapses, with up to 500 pyramidal neurons. Thus, they are critical for managing information flow in the brain. But the origins of chandelier cells had remained enigmatic until a study by Professor Josh Huang and colleagues was published this year. Using new technologies to mark and trace migrating neural cell progenitors, they located the starting place for chandelier cells in a previously unrecognized portion of the developing embryonic mouse brain they dubbed the VGZ (ventral germinal zone). In addition, they identified a gene that is switched on at the birth of a chandelier cell called *Nkx2.1*, the product of which is a transcription factor important to other inhibitory neurons. Josh's team found that after birth, chandelier cells take a stereotypical route of migration into the cortex, where they set up residence at very specific sites in cortical layers 2, 5, and 6. Since it is already known that the number and connective density of chandelier cells is reduced in schizophrenia, work on the developing brain and how its circuits are put together has important implications for disease research.

J. Huang

Proteins Involved in Small RNA Biogenesis and Function

Two proteins important in the biogenesis of gene-regulating small RNAs were the subject of new publications in 2012 stemming from collaborative work between the groups of HHMI Investigators and CSHL Professors Leemor Joshua-Tor and Gregory Hannon. One paper detailed the

L. Joshua-Tor

structure of human Argonaute-2 (Ago2) protein bound to a microRNA (miRNA) guide. The structure revealed a remarkable evolutionary conservation also seen in an archebacteria protein the teams had previously determined, especially in regions important for target recognition and activity of the protein. Structure-based understanding of how the structure is stabilized, now clear, could be important for designing therapeutic small RNAs exploiting this mechanism or for blocking Argonaute activity. A second study published this year involved the biochemical characterization of a protein known as Zucchini, which had been thought to be involved in cleaving phospholipid molecules. However, previous work in the Joshua-Tor and Hannon labs had implicated it in the biogenesis of genome-protecting PIWI-interacting RNAs (piRNAs) found in cells of the germline—sperm and eggs. Their new results show that the mouse version of Zucchini, mZuc, does not have phospholipase activity, but in fact acts as a nuclease—it cuts nucleic acid chains. Structural analysis reveals that the shape of the catalytic binding site is consistent with that of a nuclease. Thus, the evidence implies the Zucchini protein is involved in reducing long precursor RNAs to short piRNAs in germline cells.

A Genetic Check in the Molecular Clock That Controls Timing of Tomato Plant Flower Production

The timing of flowering in plants is important for their successful reproduction. It helps attract pollinators such as bees. Variations in this timing can affect flower, fruit, and seed production, and consequently agricultural yield. Assistant Professor Zach Lippman and his team have previously shown that, in addition to external factors such as light and temperature, there is a molecular clock in the tomato plant responsible for controlling timing of flowering. In new research published this year, they showed that a gene called *Terminating Flower*, or *TMF*, is responsible for acting as a check on this clock, preventing it from running too fast. Mutations in *TMF* result in the reproductive shoots, or inflorescences, of the tomato plant producing just a single flower. This is due to the plant proceeding to flower while still in the vegetative state, the phase in which leaves are still being made. When normal *TMF* is present, the tomato plant produces its characteristic multiflowered inflorescences. Thus, *TMF* is responsible for coordinating and synchronizing the tightly controlled process of flowering by gently slowing down. The important implication is that the genetic control of flowering in plants such as tomato can be manipulated in agricultural crops to improve yield.

Z. Lippman

Toward the First Vertebrate Whole-Brain Image Map

Professor Partha Mitra and colleagues are working toward constructing a whole-brain wiring diagram of the mouse. Earlier this year, they released the first set of gigapixel (1 billion-pixel) images from the project (http://mouse.brainarchitecture.org). The current data set is close to 1 petabyte in size (uncompressed). To visualize the brain, the team labeled neuronal pathways with tracers, cut 20-μm-thick slices from "front" to "back," and then imaged each slice. Using a semiautomated, quality-controlled, light-microscopy-based assembly, they captured ~500 images per brain. These were then arranged to present viewers with a unique journey through a three-dimensional model of the mouse brain, along the neuronal pathways that represent the inputs and outputs of given brain regions. The images were produced at the intermediate, or "mesoscopic," scale of detail, i.e., between the extremely fine detail of electron microscopy and the macroscopic scale of MRI-based imaging. At the mesoscopic scale, Partha's team expects to produce a stereotypical map of neuronal connections, i.e., connections that are similar between individuals and genetically determined in a species-specific manner.

P. Mitra

A Protein That Has a Central Role in Cortical Progenitor Cell Fate

Professor Linda Van Aelst and colleagues have identified a protein key in determining whether cortical progenitor cells will proliferate, make progenitor cells, or differentiate and turn into mature cells. The progenitor cells are known as radial glial cells (RGCs), whereas the mature cells are pyramidal neurons, excitatory nerve cells found in the brain's cortex. The protein Linda's group shows to be central in regulating RGC proliferation and differentiation is called DOCK7. It previously had been shown by the Van Aelst lab to be highly expressed in the hippocampus and cortex of the developing rodent brain, controlling the formation of axons. Now they show that when DOCK7 is silenced in developing mouse embryos, RGCs remain in their progenitor state, but when overexpressed, RGCs differentiate prematurely. These two processes must be finely balanced for proper cortical development, and DOCK7 is the key protein in maintaining this balance. The team found that DOCK7 antagonizes the growth of microtubules through an interaction with a protein called TACC3, thus affecting the movement of the nucleus within the cell. This study illuminates a process central to cortical development and may also help further our understanding of abnormal brain development in conditions such as microencephaly, which is characterized by small brain size.

L. Van Aelst

Genome Analyses of Two Major Agricultural Crops Pave Way for Higher Yields

This year, Cold Spring Harbor Laboratory researchers were at the forefront of two ambitious projects to study the complete genomes of two of the so-called big three agricultural crops: maize, better known as corn, and bread wheat. Associate Professor Doreen Ware and colleagues provided the most comprehensive analysis of maize to date. They analyzed genetic structure and the relationships and sequential ordering of individual genes in more than 100 varieties of wild and domesticated corn. This revealed tremendous variation among varieties, including genome size variation of up to 25%, indicating that the evolution of maize is still ongoing. They were also able to identify hundreds of genes that had a role in the domestication of wild corn and discovered that breeding efforts focused on selecting for hybrid vigor, a phenomenon first described by CSHL plant geneticist George Schull in 1908, were important in this process. The consortium of scientists involved was also able to expand upon a previous study in which they identified more than 1 million genetic markers.

D. Ware

Professor W. Richard McCombie's team was involved in a huge and complex technical analysis of the genome of bread wheat. The challenge was that the bread wheat genome's 17 billion DNA "letters," or nucleotides, are spread across six copies of each of its seven chromosomes and up to 80% consists of repeat sequences. The team overcame this using next-generation sequencing techniques in which the DNA was randomly broken up into smaller pieces and assembled for analysis by identifying the overlapping ends. They were then compared to known sequences from a range of grasses, including rice and barley. The analysis revealed 94,000 to 96,000 genes, a large number of gene fragments, and 132,000 SNPs (single-nucleotide polymorphisms). This suggests that bread wheat underwent rapid and significant changes during the process of domestication. In both maize and bread wheat, newly identified structural variations and expanded gene families are implicated in many traits important for crop growth and survival, providing an important framework within which to significantly improve breeding efforts.

W.R. McCombie

A Striking Link between the Fragile-X Gene Product and Autism Mutations

Continuing his laboratory's important investigations of the role in autism causation played by spontaneously occurring, or *de novo,* gene mutations, Professor Mike Wigler and colleagues

M. Wigler

published results this year that revealed an interesting linkage with genes implicated in Fragile-X syndrome. The most common cause of inherited intellectual disability, Fragile X is also counted among the autism spectrum disorders (ASDs) due to the co-occurrence of autism-like symptoms in some patients. It occurs when a gene called *FMR1* fails to direct nerve cells to manufacture a protein called FMRP. Mike's team demonstrated, with help from Ivan Iossifov and other computational biologists at the Laboratory, that ~20% of the genes found to be disturbed in a sample of 343 autistic children appear to be regulated by the FMRP protein. The team finds that small de novo mutations—as small as a single DNA letter or areas of small insertions or deletions of genetic material up to 15 letters in length—could be traced in the majority of small children with ASD to the father's germ cells (sperm) and that their occurrence correlated directly with the father's age, older dads being more likely to contribute sperm that will result in a child with small autism-related de novo mutations. As Wigler points out, because of research connecting FMRP to neuroplasticity—the sensitization and desensitization of nerve cells to repetitive inputs—the new results indicate a possible convergence of mechanisms in autism.

Using DNA Barcodes and Gene Sequencing to Map Circuits in the Brain

A multiyear project conceived by Professor Tony Zador that in 2011 earned him a prestigious National Institutes of Health (NIH) "Transformative Research" grant this year yielded its first results. The project seeks to develop a novel method to map circuits and pathways throughout the mammalian brain at extremely fine resolution, that of individual neurons and their estimated one trillion synaptic connections. Zador and colleagues propose to use high-throughput DNA sequencing, which is both inexpensive and fast, to probe the connectivity of neural circuits at single-neuron resolution. As set forth in a provocative paper, Tony and colleagues introduce a technique they called BOINC, an acronym for the barcoding of individual neuronal connections. Now in proof-of-concept testing, BOINC is designed to provide immediate insight into the computations that a neural circuit performs. It consists of three steps: (1) neurons are labeled with a specific DNA "barcode;" (2) barcodes are exchanged among neurons connected across synapses, by exploiting a deactivated virus that can move genetic material across these gaps; and (3) barcodes from connected neurons are joined to make single pieces of DNA, which can then be read by DNA sequencers. A full set of such sequences would be analyzed computationally to reveal the synaptic wiring diagram of a whole mouse brain. It is a bold idea, and the Zador lab will soon be able to report on its success in realizing it.

A. Zador

A Cancer Target That May Also Be Important in Alzheimer's Disease

Professor Yi Zhong and colleagues obtained intriguing results this year in their continuing efforts to identify targets for treating Alzheimer's disease and other neurodegenerative illnesses. Using the fly brain as a model, Yi had previously studied memory loss associated with the expression in brain cells of a peptide called amyloid β-42 (Aβ-42), found in human brain plaques. Yi's flies express the human *Aβ-42* gene and suffer memory deficiencies analogous to those seen in patients. In new experiments, Yi's team demonstrated that enhanced activation in brain cells of the epidermal growth factor receptor, or EGFR, exacerbated memory loss in the Aβ-42 fruit fly model. EGFR overexpression is a defining feature of certain cancers, notably a subset of lung cancers, which can be temporarily reversed with targeted EGFR inhibitors. Yi's team showed that EGFR overexpression in fly neurons correlates with severity of memory loss in Aβ-42-expressing flies. The team dosed the flies with EGFR inhibitors over a week's time, and behavioral tests showed that this prevented memory loss. The results were confirmed in mouse models of Alzheimer's also based on

Y. Zhong

the human *Aβ-42* gene. Other members of Yi's team, working in a parallel but separate process, also identified EGFR as an Alzheimer's drug target, around the same time. That team was testing a library of 2000 synthetic compounds for activity against Aβ-induced memory loss in fruit fly models. Of these, 45 showed positive results after two months of dosing, and three of these, tested in vitro, specifically prevented Aβ-42 from activating human EGFR.

Cold Spring Harbor Laboratory Board of Trustees

New York Governor Andrew Cuomo said it best when he visited the campus in October: "[For] what it does for the soul, the people it gives hope to, Cold Spring Harbor has always been synonymous with accomplishing the impossible." We do this at all levels of the institution, starting with the Board of Trustees.

A. Cuomo and B. Stillman

Led by Chairman Jamie Nicholls, we are attracting leaders of the highest caliber to our governance bodies. The board welcomed Charles "Casey" Cogut, senior corporate partner at Simpson Thacher & Bartlett LLP, with expertise in M&A, private equity, and governance.

Re-elected to the board for an additional 4-year term were Dr. David Botstein, Jacob Goldfield, Leo A. Guthart, Thomas D. Lehrman, Dr. Charles L. Sawyers, Dr. Marilyn H. Simons, Dr. James M. Stone, Paul J. Taubman, and Roy J. Zuckerberg. Officer elections continued the terms of Chairman Nicholls, Vice Chairs Robert D. Lindsay and Marilyn H. Simons, Dr. Leo A. Guthart, Bruce Stillman, Ph.D., and W. Dillaway Ayres. Paul J. Taubman replaced Edward Travaglianti as Secretary.

C. Cogut

Many thanks to our friends who are retiring trustees, having served on the board and numerous committees from 2004 to 2012: Stephen Lessing, Andrew Solomon, and Dr. Jerome Swartz.

We mourned the passing of former CSHL trustees Townsend Knight, Robert Van Cleef Lindsay, and John J. Phelan. Rod was one of the founding members of the contemporary Laboratory, serving from 1959 to 1965. Townie served from 1973 to 1995, when he was named Honorary Trustee. John served two terms from 1992 to 1999.

Development

With the help of our board, CSHL capped another year of record-breaking success in fundraising with an Annual Fund total of $6.6 million raised. The 7th Double Helix Medals Dinner Gala raised $3.7 million and honored Parkinson's disease research activist Michael J. Fox, Apple Chairman Art Levinson, and philanthropist Mary Lindsay, who is also a CSHL Honorary Trustee.

Double Helix Medal winners M.J. Fox, M. Lindsay, and A. Levinson

In the community, the Cold Spring Harbor Laboratory Association made many new friends by organizing events that included a music, art, and food festival called Labapalooza; the 11th Women's Partnership Luncheon featuring Professor Michael Wigler (who spoke about single-cell sequencing in cancer research); and the annual President's Council retreat, which focused

Women's Partnership for Science Luncheon

A. Solomon, G. Welch, and B. Stillman

this year on the topic of medical ethics. CSHL Director of Research David L. Spector and Associate Professor Lloyd Trotman headed the agenda, which also included DNA Learning Center Executive Director David Micklos. CSHL Trustee Andrew Solomon, acclaimed writer on politics, culture, and society, discussed his new book, *Far From the Tree*. Other guest speakers included Drs. Gilbert Welch of Dartmouth, Jeffrey Berger of Stony Brook University, and Hans Sauer of the Biotech Industry Organization.

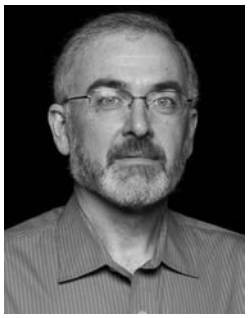
Of course, doing the impossible would not even be imaginable without private philanthropic support. In 2012, CSHL was grateful for new major gifts from (in alphabetical order) an anonymous donor, Jamie Nicholls and Fran Biondi, Mr. and Mrs. David Boies, Charitable Lead Annuity Trust under the Will of Louis Feil, Laurie J. Landeau Foundation, Mr. and Mrs. Robert D. Lindsay and Family, the Lustgarten Foundation, the Simons Foundation, and Dr. and Mrs. James M. Stone.

Research Faculty

There is no clearer evidence of our ability to achieve what our Governor called "the impossible" than the research accomplishments of our faculty. Many are individually recognized each year by competitive awards and academic honors.

Professor and Howard Hughes Medical Investigator Greg Hannon was elected to the U.S. National Academy of Sciences, which ranks among the highest honors conferred upon scientists in America. Dr. Hannon, a molecular biologist, is recognized the world over as among the foremost authorities on small RNA biology and RNA interference. RNAi, as it is known among scientists, is a natural cellular mechanism implicated in genome defense, in which small RNA molecules act to regulate gene expression. It has been exploited by scientists led by Greg and colleagues for many extremely valuable purposes, including hunting for cancer genes, stopping viral infections, and, most recently, treating diseases in clinical trials.

The AAAS council elected Professor and Howard Hughes Investigator Leemor Joshua-Tor a 2012 AAAS Fellow, recognizing her contributions to the field of nucleic acid enzymes, particularly


A. Krainer


N. Tonks


C. Vakoc


F. Albeanu

in the fields of RNA interference and DNA replication. Leemor's laboratory studies the molecular basis of cell regulatory processes, using the tools of structural biology and biochemistry to examine proteins and protein complexes associated with these processes. Her efforts largely center on nucleic acid regulation, including the process of RNA interference and DNA replication initiation in papillomaviruses.

Professor Adrian Krainer received a MERIT AWARD (Method to Extend Research in Time) from the National Institute of General Medical Sciences. This award rewards highly productive scientists by extending funding for an existing research project grant. Adrian is a leader in the field of RNA splicing, which has significant implications for many human genetic diseases because a high proportion of disease-causing mutations affect messenger RNA (mRNA) splicing and stability. mRNAs are the coded instructions copied from the genetic material that direct cells to manufacture specific proteins. Adrian's current research will result in a better understanding of which mutations cause defective gene expression, and precisely how they do so. Already, his research has guided the development of a drug to treat a fatal childhood disease called spinal muscular atrophy (SMA). Clinical trials to test this drug were begun in 2012.

Professor Nicholas Tonks was named Vallee Visiting Professor by the Bert L. and N. Kuggie Vallee Foundation. This honor is conferred upon those who have demonstrated a record of exceptional creativity, originality, and leadership and sustained success at an elite level. A biochemist and molecular biologist, Nick is well known for having laid the foundations for the identification and functional characterization of a superfamily of 107 regulatory enzymes called protein tyrosine phosphatases, or PTPs. Protein phosphatases recognize phosphorylated amino acid residues and function to remove them; their action is thus complementary to the class of protein kinases, which add phosphate groups to amino acid residues. Together, they play crucial roles in signal transduction pathways.

Anne Churchland received the McKnight Foundation Scholar award supporting neuroscience research. This award addresses a basic problem which, when solved, could immediately and significantly impact clinical issues. Anne plans to use the award to study the neural circuits underlying a process known as multisensory decision making—the integration of information from individual senses such as seeing, hearing, and touch to make more accurate decisions. Anne was also selected for the Janett Rosenberg Trubatch Career Development Award, which rewards promise and achievement in the field of neuroscience for early-career professionals.

Assistant Professor Christopher Vakoc received the "A" award for pediatric leukemia research, one of only four to receive this honor from Alex's Lemonade Stand Foundation. He will work on a project entitled "BET bromodomain inhibition as epigenetic therapy in pediatric leukemia." Chris was also named a "V Scholar," one of 17 of the "best and brightest" cancer researchers, by the V Foundation. His project is entitled "Therapeutic targeting of the Polycomb complex PRC2 in acute myeloid leukemia."

Florin Albeanu was named a Pew Scholar in Biomedical Sciences. Florin, who came to CSHL as a Fellow in late 2008 and was appointed a member of the faculty in 2011, studies how the brain

C. Hammell

encodes stimuli from the outside world, within and across sensory modalities, to generate specific perceptions that, in turn, trigger complex behaviors. He is interested in how the brain is shaped by sensory experience and what modifications occur in neuronal circuits that allow us to learn and remember.

Christopher Hammell was named a Rita Allen Foundation Scholar. As part of the cancer research program, Dr. Hammell is interested in understanding the gene regulatory process that gives rise to normal development in animals as well as alterations in these processes that give rise to diseases such as cancer. Chris also received the special honor of being named the Milton E. Cassel Scholar, a tribute to the memory of a longtime president of the foundation.

CSHL once again teamed up with the National Institutes of Health (NIH) to host a regional conference on funding opportunities and research priorities in the neurosciences. Heading up the agenda were Dr. Thomas Insel, Director of the National Institute of Mental Health; Dr. Robert Finkelstein, Director, Division of Extramural Research at the National Institute of Neurological Disorders and Stroke (NINDS), and Dr. Alan L. Willard, Deputy Director of NINDS. Supported by the Alfred P. Sloan Foundation and organized by the CSHL Office of Sponsored Programs, CSHL faculty members Florin Albeanu, Anne Churchland, and Steve Shea facilitated the discussions with faculty from Columbia, SUNY Stony Brook, New York University, and the Massachusetts Institute of Technology (MIT).

The laboratories of CSHL's 52 principal investigators are supported by an active community of postdoctoral fellows, this year numbering nearly 160. The Postdoc Liaison Committee was created to give the postdoctoral community a formal organization through which to pursue its own agenda of enhancing the postdoctoral education experience at CSHL. Headed by an elected group of six, they are the primary organizers of the twice-yearly postdoctoral collaboration and networking retreats.

Some of committee's most successful activities include initiation of a career development series in which faculty members educate postdocs on "real-life" topics such as how to negotiate for a startup package after landing a faculty position or how to hire staff of a new lab. The newly formed Bioscience Enterprise Club, which welcomes postdocs, graduate students, and the CSHL campus community at large, is off to a great start providing opportunities to learn about

Postdoc Symposium

nontraditional science careers, develop entrepreneurial skills, and network with professionals in the biotech industry, clinical research, intellectual property law and tech transfer, consulting, science education, policy, and administration.

New Faculty

CSHL continues its historic commitment to attracting and promoting world-class research faculty. According to Director of Research David L. Spector, who heads the institution's faculty recruitment efforts, "in the last year, we have strategically invested in research faculty who are at the forefront of cancer therapeutics, genomics of human disease, human genetics, computational biology, and bioinformatics. We look forward to the significant impact that we know these exceptional scientists will have in shaping the future of biomedical research."

D. Tuveson

David Tuveson, M.D., Ph.D., was appointed Professor and Deputy Director of the CSHL Cancer Center. Dave obtained a bachelor's degree in chemistry at MIT, followed by M.D. and Ph.D. degrees at Johns Hopkins. After obtaining a faculty position at the University of Pennsylvania, he moved to the University of Cambridge, England, to develop preclinical and clinical therapeutic strategies. CSHL recruited Dave to direct the Cancer Therapeutics Initiative (CTI). He serves simultaneously as Director of Research for the Lustgarten Foundation, the nation's largest private foundation dedicated to funding pancreatic cancer research. Together with the Lustgarten Foundation, CSHL announced the opening of the Lustgarten Foundation Pancreatic Cancer Research Laboratory located on our Hillside Campus. This laboratory will focus exclusively on pancreatic cancer research, with initial studies centered on early detection, drug development, and drug delivery.

Dave's team investigates fundamental aspects of cancer biology and applies this knowledge to the development of new therapeutic and diagnostic strategies. His lab developed the first mouse models of pancreatic ductal adenocarcinoma (PDAC), which have been instrumental in the discovery of biomarkers of early disease. They also identified pathways and druggable targets involved in the initiation, progression, and metastasis of PDAC and developed new therapeutic strategies. Following the observation made in his lab that PDAC tumors contain a deficient and compressed vasculature, which limits therapeutic drug delivery and therefore efficacy, Dave has uncovered several methods to correct or target these vascular deficits and promote drug response. This work has led to the initiation of several clinical trials. At CSHL, he will continue the search for new vulnerabilities in PDAC neoplastic cells and the tumor surroundings, called the microenvironment. His team will evaluate candidate drug targets in an advanced therapeutics testing facility being developed as part of the CTI. He aims to translate his preclinical results into the design of pivotal investigational clinical studies.

G.J. Lyon

Another scientist-clinician whom we added to the faculty this year is Assistant Professor Gholson J. Lyon, M.D., Ph.D. Gholson received a B.A. in biochemistry from Dartmouth College and shortly thereafter completed an M.Phil. in genetics at Christ's College, University of Cambridge, England. He has a Ph.D. from Rockefeller University in chemical biology and an M.D. from Weill Cornell Medical College. Gholson is affiliated with the Utah Foundation for Biomedical Research.

Here, Gholson focuses on analyzing human genetic variation and its role in severe neuropsychiatric disorders. He does so by studying large groups of related individuals living in the same geographic location. The Lyon lab is using sequencing of whole genomes and of the exome—the small portion of the genome that encodes proteins—to find mutations that distinguish disease syndromes, in populations from Utah and elsewhere. Gholson is interested in the discovery of families with rare diseases and/or increased prevalence for syndromes such as Tourette syndrome, ADHD, obsessive-compulsive disorder (OCD), intellectual disability, autism, and schizophrenia.

J. Gillis

Joining CSHL as an assistant professor is Jesse Gillis, Ph.D. He holds a B.S. in biophysics from the University of Toronto, where he also earned both an M.S. and a Ph.D. in Neuroscience. He was recruited to CSHL from the University of British Columbia, where he did a postdoctoral fellowship at the Centre for High-Throughput Biology.

The Gillis laboratory is working to understand how genes interact and how this relates to gene function and the effect on disease. Using computational biology, he is interpreting the functions of genes in the context of the networks they form, with data derived from gene association studies.

Promotions

Congratulations to Alexei Koulakov, who was promoted to professor. Alexei came to CSHL in 2003 from the University of Utah, where he was an assistant professor in the department of Physics. He received his Ph.D. from the University of Minnesota and was a postdoctoral fellow at the Salk Institute. Alex is interested in computational and theoretical neuroscience and is probing neural circuits to understand the mechanisms of neural computation, the means by which vast networks of nerve cells in the brain encode and are able to understand messages.

Glenn Turner and Lloyd Trotman were promoted this year to associate professor. Lloyd came to CSHL as an assistant professor in 2007, after a postdoctoral research fellowship at Memorial Sloan-Kettering Cancer Center. Glenn joined CSHL in 2006 as an assistant professor, having received his Ph.D. and performing postdoctoral research at California Institute of Technology.

Promoted this year to assistant professor were Molly C. Hammell, who, in addition to contributing her expertise in computational biology to many ongoing research collaborations among CSHL labs, has been manager of the CSHL Cancer Center's Bioinformatics Shared Resource since 2010; Ivan Iossifov, who began at the Laboratory in 2008 as a Quantitative Biology Fellow; and Dan Levy, who joined Mike Wigler's lab as a postdoctoral fellow in 2007 and was then promoted to senior computer scientist.

Isabel Aznarez Da Silva, who works in the laboratory of Adrian Krainer, and Camila Dos Santos, who works in Gregory Hannon's lab, were promoted to research investigators.

2012 WSBS Doctoral graduates F. Rollins, K. Honegger, E. Nakasone, P. Finigan, and Z. Wang

Departures

Assistant Professor Rob Lucito is currently Assistant Professor of Science Education at Hofstra North Shore LIJ School of Medicine and remains associated with CSHL as an adjunct professor.

Education Programs

The Watson School of Biological Sciences (WSBS) celebrated its 9th graduating class, awarding Ph.D.s to Patrick Finigan, Kyle Honegger, Elizabeth Nakasone, Frederick Rollins, and Zhenxun Wang.

This year's Honorary Degree recipient was Sir Kenneth Murray, who was knighted by the Queen of England in 1993 for his discovery of hepatitis B antigens. His long list of achievements includes developing a life-saving hepatitis vaccine, starting the first European biotech company, and creating the Darwin Trust to support biological scientists from


K. Murray

less affluent parts of the world. We were saddened to hear that Dr. Murray passed away before this Annual Report went to print.

In August, WSBS opened its doors to the 14th incoming class of nine students: Nitin Singh Chouhan, William Donovan, Talitha Forcier, Yu-Jui (Ray) Ho, Irene Liao, Paul Masset, Annabel Romero Hernandez, and Abram Santana. These new degree candidates come to us from the United States, France, India, Mexico, and Taiwan.

The WSBS now counts 54 Ph.D. graduates who are thriving in the "outside world." They continue to publish in top journals and secure prestigious independent positions, fellowships, and awards. Eleven of our graduates have secured tenure-track faculty positions, and, as such, they are now receiving federal grants and publishing papers as independent researchers.

Current students continue to win prestigious fellowships and prizes. In 2012, Colleen Carlston was selected into the National Science Foundation's East Asia and Pacific Summer Institutes for U.S. Program. In addition, she received a National Science Foundation Graduate Research Fellowship. John Sheppard also was awarded a National Science Foundation Graduate Research Fellowship and received a National Defense Science & Engineering Graduate Fellowship from the Department of Defense. Melanie Eckersley-Maslin was awarded a Keystone Symposium Travel Fellowship. She was also awarded an American Society for Cell Biology Travel Fellowship to attend the annual conference. WSBS students have published more than 210 papers to date, many in the most prestigious journals.

The National Institutes of Health's National Institute for General Medical Studies renewed the School's Training Grant for a period of 5 years. Despite very tight funding, the NIH recognized the outstanding achievements of the program, the students, and the faculty in the funding of this award. The training grant funds six students and also serves as an endorsement of the School's excellence.

The annual Gavin Borden Visiting Fellow Lecture "Electron transfer in times of stress: New roles for redox active antibiotics," was presented on April 23 by Dianne K. Newman, Ph.D., Professor of Geobiology and Howard Hughes Medical Institute Investigator at the California Institute of Technology.

Twenty-six undergraduates (selected from 884 applicants, the largest pool to date) from around the United States as well Canada, Switzerland, Ireland, and the United Kingdom formed the 53rd cohort of the Undergraduate Research Program (URP). This year's URP Faculty Directors were Anne Churchland and Michael Schatz. The historic 10-week program for undergraduate students convenes in the summer, and it provides some of the finest college students a priceless opportunity to conduct sophisticated research at the side of a CSHL investigator.

Under the direction of Professor David Jackson, the Partners for the Future Program for high school seniors attracts the best and brightest aspiring scientists to an average of about a dozen of our labs each year. Established by Dr. James Watson in 1990, the program provides an opportunity for gifted Long Island high school students to have hands-on experience in biomedical research.

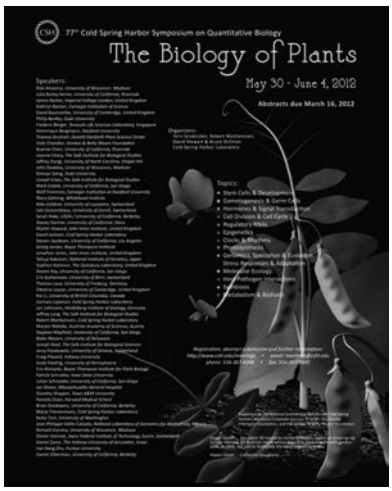
In August, Leemor Joshua-Tor stepped down as Dean of the WSBS after 5 years of outstanding leadership. As the third leader of a school known as one of the nation's most innovative Ph.D.-granting programs, Leemor advanced the curriculum in significant ways, including the addition of timely courses in quantitative biology, physical biology, and imaging. She has also served during her term as a member of the Biomedical Workforce Task Force of the U.S. National Institutes of Health, which recently issued recommendations to support a future sustainable biomedical research infrastructure. A structural biologist who began her career at CSHL in 1995, Leemor is an Investigator of the Howard Hughes Medical Institute. She has made seminal contributions to the understanding of how RNA interference works to silence gene expression and has advanced new therapeutic options for combating papillomavirus, which causes cervical cancer. She continues her

53rd Undergraduate Research Program

research at the Laboratory, studying the molecular basis of cell regulatory processes using the tools of structural biology and biochemistry.

Thank you to Adrian Krainer and Linda Van Aelst, who served as interim deans for the remainder of the year. I was pleased to announce the selection of Alexander A.F. Gann as the new dean, effective January 2013.

We recruited Dean Gann from the CSHL Press, where he served as Editorial Director. At the Press since 1999, he has produced publications ranging from textbooks for undergraduate and graduate education to laboratory manuals and books on the history of science. Alex is a co-author of *Molecular Biology of the Gene,* now in its 6th edition, and of the recently released *Annotated Double Helix,* a new edition of James D. Watson's autobiographical classic. Alex received his Ph.D. from the University of Edinburgh, Scotland, in 1989, after which he continued his postdoctoral training at Harvard and University College, London, and lectured at Lancaster University. A longtime member of the WSBS faculty, he brings a unique combination of inside perspective and broad understanding of the impact of the digital and genomic revolutions upon higher education and the biological sciences.



77th CSH Symposium

Meetings and Courses Program

The CSHL meetings program attracted strong attendance with more than 7100 meeting participants and almost 1300 course participants (trainees, teaching and support faculty). The Cold Spring Harbor Asia program, including 18 conferences and one summer school, has to date attracted more than 3000 participants. This brings the anticipated year-end total for both U.S.- and China-based programs to nearly 11,400.

Our flagship meeting, the Cold Spring Harbor Symposium, focused in 2012 on plant biology for the first time in the 77-year history of the series. Given the importance of plant research in such vital fields as epigenetics and evolution, plants naturally have been discussed at many prior symposia. This year, however, they occupied center stage, with a stellar list of presenters that included four CSHL faculty members.

The year saw the introduction of two new meetings, *Regulatory and Noncoding RNAs* and *Epigenetics and Chromatin,* which drew strong attendance and featured a high proportion of unpublished research. We anticipate these meetings will each become regular biennial series. Two existing meetings were merged in 2012, as well: *Personal Genomes* and *Pharmacogenomics* were combined as *Personal Genomics and Medical Genomes*.

Just how robust our programs are, and how loyal are our attending scientists, was demonstrated when Hurricane Sandy powered up the East Coast at the end of October. Four courses were then due to end and a meeting and a course were due to begin the day of the storm's local landfall, October 30. We made great efforts to accommodate our guests, mostly helping them arrange for departures. But a hearty core group of about 65 braved the elements and held a 2-day version of their scheduled meeting on *Nuclear Receptors and Disease*.

Courses

The CSHL Courses program benefited greatly in 2012 from the opening of the completely rebuilt Hershey Building on the main campus. This fully modern and architecturally striking 18,000-square-foot facility was finished in time to host more than 10 of our annual courses, including a successful new course on *Single-Cell Analysis* and a new *Workshop on Cognitive Aging*. Covering a diverse range of topics in molecular biology, neurobiology, structural studies, and bioinformatics, the courses teach advanced students the latest innovations that can be applied immediately to their research. Instructors are drawn to teach at Cold Spring Harbor from universities, medical schools, research institutes, and companies worldwide.

The Hershey Building was rededicated June 8 in a ceremony that highlighted the history and future of scientific research and education at the Laboratory. Named for the late Dr. Alfred Hershey, a Nobel laureate and CSHL scientist, the new facility was made possible by a $15 million grant provided in 2008 by the Howard Hughes Medical Institute (HHMI).

The new facility allows for a 25% increase in course offerings and participants, including a number of new courses in computational approaches to biological questions. Courses such as *Computational and Comparative Genomics* and *Computational Neuroscience: Vision*, both offered this year, put a new emphasis on the computational aspects of biology, including mathematics, statistics, and computer science.

Harry Anand, mayor of the Village of Laurel Hollow, commended CSHL at the Hershey rededication ceremony, noting the Laboratory's continuing commitment to designing and building facilities that enhance the natural beauty of the local landscape. James Childress, partner of Centerbrook Architects and Planners, led the effort to design a completely new building to replace the original Hershey Building, which was erected in 1979. Other speakers at the rededication were Dr. James D. Watson and Dr. Jack Dixon, Vice President and Chief Scientific Officer of HHMI.

The ceremony also honored beloved CSHL course instructors Dr. Gordon Sato, for whom a new Flow Cytometry Laboratory has been named, and Dr. Mark J. Zoller, whose name now graces one of the facility's modern teaching laboratories. In attendance were Dr. Sato; Dr. Zoller's widow, Ms. Karen Zoller; Senator Carl Marcellino; CSHL Board Chairman Jamie Nicholls; and fellow trustees, faculty, employees, and friends of the Laboratory.

Suzhou Conference Center

Now in its third year of operation, the Cold Spring Harbor Asia (CSHA) program, under the direction of Dr. Maoyen Chi, is headquartered at the Suzhou Dushu Lake Conference Center, a purpose-built academic conference center on the outskirts of old Suzhou,

within a high-technology suburb (SIP). The scientific program includes large symposia and meetings, training workshops and Banbury-style discussion meetings. CSHA is a wholly owned subsidiary of CSHL and is not beholden to outside partners in terms of our scientific programming. The 50% growth in meeting attendance between the first and third year of operations bodes well for the future.

Banbury Center

In its 35th year of operations, Banbury Center continued to have an active role in the Laboratory's educational mission. At the beginning of the year, the Conference Room underwent a major renovation. By autumn, it was the turn of Sammis Hall, which had gone largely untouched since its opening in 1981. These efforts ensure that participants in our programs have the fully modern and up-to-date accommodations that they expect.

Despite the renovation work, Banbury's facilities were used intensively throughout the year, hosting 18 meetings as well as six lecture courses and two Watson School courses. CSHL postdocs came on two occasions for a retreat and the Robertson family came for their annual meeting. As usual, CSHL is happy to help our neighbors; this year, the Cold Spring Harbor School District board twice used the Banbury Center facilities.

We welcomed back the Boehringer Ingelheim Foundation, which, for several years, has brought its fellows for training in writing papers and giving talks. The National Institute for Mental Health returned for its Brain Camp, providing the brightest clinical fellows to high-level neuroscientists, encouraging them to think of taking up research. For the second year, Carl Cohen of Science Management Associates taught a "Leadership in Bioscience" workshop.

Banbury Center's first meeting on patenting was held 30 years ago, just 2 years after the 1980 *Chakrabarty* case (which declared that a modified microbe was patentable). In 2012, the question of patents was brought into sharp focus by the recent Myriad Genetics case involving patents covering the *BRCA* genes. The meeting, *Patenting Genes: New Developments, New Questions*, discussed this and other unresolved issues.

DNA Learning Center

DNA Learning Center (DNALC) Executive Director David Micklos received the 2012 Elizabeth W. Jones Award for Excellence in Education from the Genetics Society of America. David was recognized for bringing "the excitement of DNA science into the educational curriculum for thousands of students, high school teachers, and undergraduate faculty."

Urban Barcode Project grand prize winners

On June 6, nine finalist teams of high school students representing eight public high schools, plus home schooling, from all of the five boroughs of New York City, presented their submissions to the first-ever NYC Urban Barcode Project competition. They were selected from more than 200 students on 75 teams, whose research posters were judged by conservation and genetic biologists and education experts. For most students, it was their first independent research project. Twenty-six percent of contestants were African American or Latino, groups that are underrepresented in science.

New York City institutions, including the American Museum of Natural History, Genspace, New York Botanical Garden, Brooklyn Bridge Park, and the

Rockefeller University, partnered with the DNALC to provide facilities and mentoring to the student teams. Developed and executed by the DNALC with funding from the Alfred P. Sloan Foundation, the Urban Barcode Project was the first large-scale attempt to use barcoding projects to encourage students to explore the urban environment beyond their doorsteps.

It was the biggest summer yet of DNA camps: 1000 5th- to 12th-grade students attended 53 weeks of camps conducted by the Dolan DNALC, DNALC *West,* Stony Brook University, and Brookhaven National Laboratory, the Trinity School, and at the Chapin School in Manhattan. Students from Beijing High School 166 also attended 3 weeks of camps on bacterial genetics, human genomics, and DNA barcoding.

During the summer, the DNALC also extended its NYC *Urban Barcode Project* to the study of biodiversity in the unique glacial landscapes of Long Island. Six student workshops, *Barcoding Biodiversity,* explored the intertidal zone adjacent to the main campus. Naturalist photographer David Liittschwager joined the first workshop, instructing in his methods for examining and photographing life in a one-cubic foot sample, which he published in the February 2010 issue of *National Geographic*. Seventy-seven students collected and processed more than 300 samples, resulting in 165 high-quality DNA barcodes.

DNALC staff continued in 2012 to provide essential support for the National Science Foundation (NSF)-funded *iPlant* Collaborative project, which seeks to develop a national cyberinfrastructure needed for data-heavy 21st-century plant research. As the *iPlant* infrastructure has expanded to support animal genomics research too, the DNALC's *DNA Subway* website has been upgraded to support student projects using animal species. Total visits to the site grew 40% in 2012, to more than 33,000.

This was but a fraction of the more than 4.2 million visits to the 22 DNALC websites in 2012, a figure to which is added 865,000 visits to the DNALC YouTube channel; and 568,000 downloads of the *3D Brain*, *Weed to Wonder,* and *Gene Screen* phone apps, to gauge DNALC's total cyber-impact for the year—more than 5.6 million visits!

In 2012, the team also executed a successful renovation of the museum exhibit at the Dolan DNALC. A fourth teaching laboratory and prep area was added, the lunchroom was enlarged, the basement prep laboratory was renovated, and storage and display spaces were reorganized. The exhibit is evolving into one based on human ancestry. One part will have the theme of "Becoming Human," treating our ancient history and evolution, and the other "Being Human," representing where we are today and comparing characteristics of modern populations.

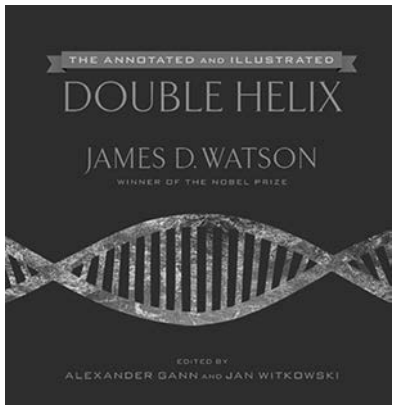
CSHL Press

In 2012, the CSHL Press continued to publish seven journals and added 12 new print and five new electronic titles to its list of 180 print books and 18 online books.

The most recent impact factor analysis continues to rank our journals *Genes & Development* and *Genome Research* at the top of their disciplines; *Genome Research* reached a new high of 13.608, after 4 years of consecutive increases, and now ranks #2 in genetics and #2 in biotechnology. *Genes & Development* currently ranks #2 in developmental biology and #3 in genetics. In 2012, CSHL journal articles were electronically downloaded a remarkable 10 million times, and 38,000 books were shipped to 150 countries.

The first and flagship journal, *Genes & Development*, marked its 25th Anniversary this year. In celebration of this anniversary, the Genetics Society of Great Britain, one of the founders along with CSHL, held its annual autumn meeting in honor of the journal. The 2-day meeting, titled At the Cutting Edge of Molecular Biology: 25 Years of *Genes & Development*, was held November 7–8 at the Royal Society (London). The meeting brought together distinguished scientists from across the biological sciences, focusing on issues such as chromatin, epigenetics,

CSH Perspectives in Biology



The Double Helix

gene regulation, replication, checkpoints and DNA repair, RNA function and control, development, stem cells, and diseases such as cancer, representing the broad scope of science covered by the journal.

In its second year of sales, the review journal *Cold Spring Harbor Perspectives in Biology* continues to increase notably in revenue and usage. The concept of a "new type of review journal" with subject collections that build monthly has been well received, as has its consistent editorial excellence. It received its first impact factor this year. The newest review journal, *Cold Spring Harbor Perspectives in Medicine*, completed its first year of publication with exceptional usage of collections about HIV, Alzheimer's, Parkinson's, and addiction.

New print books and five new e-books included *Genome Science*, a new and long-awaited collection of laboratory exercises by the teaching staff at the DNA Learning Center. In June, a new edition of the laboratory manual *Molecular Cloning* was published. Long established as the gold standard for molecular biology techniques, and by far the most successful book ever published by the Press, with more than 200,000 copies sold, this new edition was a complete revision by authors Joe Sambrook and Michael Green, assisted by a dozen expert contributors. A classic of a different sort also reappeared, co-published by the Press and Simon & Schuster: James Watson's 1968 autobiographical account of the discovery of the structure of DNA, *The Double Helix*, which was named during the year as one of the Library of Congress's 88 "Books that Shaped America." CSHL Professors Alex Gann and Jan Witkowski illustrated and annotated the text with footnotes, photos, correspondence, and other documents that placed this most famous account of scientific discovery in its social, intellectual, and historical context.

Library and Archives

On April 1–3, Library and Archives Department Executive Director Ludmila Pollock and colleagues from Rockefeller University, Memorial Sloan-Kettering Cancer Center, and the Marine Biological Laboratory hosted a meeting at the Banbury Center called "Envisioning the Future of Research Libraries." It brought together the top leaders of scientific research libraries from the United States, United Kingdom, Germany, and France, with a goal of constructing a model for the future (circa 2020) scientific research library.

In 2009, CSHL and the Wellcome Trust initiated a project to create an International Catalog for the History of the Human Genome Project (HGP). On May 3–5, an international meeting about the History of the HGP was held at the Banbury Center, where discussion centered on how to best present the history to different audiences, including scholarly researchers. Phase 1 of this project, which includes identifying all of the potential collections, creating a new, open-access database, and carrying out a pilot project, will be completed in 2013.

Millions of primary-source documents telling the amazing story of the biological revolutions of the 1950s and 1960s are now freely available on the World Wide Web thanks to an effort led by the Wellcome Library of Great Britain. Entitled *Codebreakers: Makers of Modern Genetics*, the resource provides public access to first-hand notes, letters, sketches, lectures, photographs, and essays from those responsible for uncovering the structure of DNA. CSHL's Library and Archives collections, which include the papers of Nobel laureates James Watson and Sydney Brenner among others, are a key source for *Codebreakers*. CSHL was very happy to participate in the project with

partners Churchill Archives Centre Cambridge, the University of Glasgow, King's College London, and University College London.

Infrastructure Projects

Hurricane Recovery

The Laboratory's preparations for Hurricane Sandy were extensive, and apart from an extended power outage that the Laboratory's staffs managed with emergency power, the campus emerged relatively unscathed. There was, however, some damage. The Laboratory has dealt with 40–60 fallen mature trees and the Robertson House slate roof required significant repair, and due to the storm surge, post-storm repairs were required to the mechanical systems of the low-lying Jones Laboratory.

Airslie Renovations

The Laboratory undertook extensive interior renovations to the house, modernizing the kitchen and service areas to accommodate the numerous development activities undertaken at the President's house while maintaining a livable private residence.

Wawepex Alterations

The Office of Sponsored Programs—tasked with an ever-increasing workload—was overcrowded in the circa 1830 Wawepex Building. Interior renovations were completed to provide additional workspace for the department's staff.

Sammis Hall Renovations

Built in 1981, Sammis Hall has housed Meeting and Course participants for more than two decades. New carpet, furnishings, fixtures, and systems were installed to meet contemporary expectations.

Blackford Exterior Renovations

The circa 1905 Blackford Hall has been in continuous operation for more than a century and structural cracks and spalling in the poured concrete structure were evident. It was necessary to repair and stabilize the building to prevent further decay. Of particular concern was preserving the historic nature of the building while conserving the relatively thin four-inch-thick concrete walls. The project was completed with the building remaining in full operation.

Receiving Building

Construction of the new Hershey Building required that the receiving and mail-room facilities be relocated. These functions were temporarily housed in a trailer on-site until the new Receiving Building could be constructed. The 1500-square foot structure was sited close to Route 25A to limit truck traffic on campus and was designed to appear as a complementary outbuilding of the historic Davenport House nearby.

Hershey Building Completion

After 2 years of construction, the Hershey Building was completed in the second quarter of 2012 and hosted courses for the summer. At the same time, both the Flow Cytometry and Microcopy facilities moved their operations into the building.

Community Outreach

On October 5, members of the Long Island Regional Economic Development Council accompanied New York Governor Andrew Cuomo and Lieutenant Governor Robert Duffy to tour the

Receiving building

Hershey building

Hillside laboratory of Professor David Tuveson, one of our latest recruits and a distinguished pancreatic cancer researcher who is also the Deputy Director of CSHL's Cancer Center.

Drs. Tuveson and Stillman briefed the dignitaries on CSHL's new Cancer Therapeutics Initiative, which New York State is helping to fund by seeding the construction of a new Advanced Drug Testing Facility located at the Woodbury Genome Center. The central idea in our Cancer Therapeutic Initiative is to create a translational pipeline that will enable us to help develop a new generation of cancer drugs that will be more effective and less toxic than those currently in use. Another objective is to significantly reduce the time it takes to identify and test candidate drugs, to accelerate their path to the clinic.

Stuart Rabinowitz, President of Hofstra University, and Kevin Law, President and CEO of the Long Island Association, both co-chairs of the Long Island Regional Economic Development Council, highlighted the importance of public support for cutting-edge science in driving economic development of the region and in providing new high-quality jobs. The Governor's next stop that day was the Broad Hollow Bioscience Park, an incubator facility that CSHL helped to found and where CSHL spin-off biotech companies have made their start.

CSHL is pleased to join with Brookhaven National Laboratory, SUNY Stony Brook, Hofstra University, and North Shore LIJ in Accelerate Long Island, an initiative to expand on the success of the Broad Hollow Science Park and strengthen the bioscience economy of Long Island.

Governor Cuomo (*center*) tours Hillside Laboratory

R.J. Duffy, W.D. Ayers, Jr., and B. Stillman

The Governor's visit came just a month after the visit of Lieutenant Governor Duffy, who chairs the state's regional economic development councils. "This is a great intersection of public health and economic development," said Mr. Duffy of CSHL. "This is a jewel in New York State and to see the brain power and expertise we have here makes us all very proud."

As I have already mentioned in brief, thanks to well-laid preparation plans and hard work—not to mention some luck associated with the outgoing tide—the Lab was able to ride out Hurricane Sandy at the end of October. By moving equipment and data storage to higher ground, bringing up elevators, sandbagging, and using diesel-powered backup generators for electricity, all essential scientific operations continued through the storm and in its aftermath. Even attendees of the Nuclear Receptors and Disease meeting continued undaunted, producing a defiant slogan that attendees and the Lab community will long remember: "Science vs. Sandy. . .Science Wins!"

Our preparedness allowed us to help our neighbors. We were in constant contact with the leadership of Laurel Hollow village, firefighters, police, friends, and residents, who benefitted from our food services, WiFi access, and warm spaces. CSHL even hosted TV coverage of the 2012 Presidential Election in Grace Auditorium, for CSHL families as well as community residents who were still without power more than a week after the storm.

A special thank you to those on our campus who helped us all weather the storm, in particular: Art Brings, Peter Stahl, Gerry Holler, Lisa Bianco, Culinary Services staff led by Jim Hope, Payroll staff led by Lari Russo and Damian Desiderio, IT staff led by Sean Kelly, and the Meetings and Courses team with David Stewart, Maureen Morrow, and Andrea Newell. Above all, a warm thank you to COO Dill Ayres, who spent many a sleepless night on watch in his office.

The year was a big one for CSHL in social media. The Laboratory's Twitter following grew to 2500 and friends on Facebook surpassed 1000. The monthly e-mail newsletter we fondly call the Netletter continues to attract new subscribers—more than 7000 by year end—and we consistently outperform other newsletters based on how many of our subscribers actually read the

Meeting attendees defy Hurricane Sandy

R. Martienssen

M. Schatz

stories we deliver. The CSHL blog, Labdish, grew too, and we now host guest bloggers who represent the CSHL campus community from grad students to professors. Thanks, Michael Schatz, Anne Churchland, Clare Rebbeck, Antoine Molaro. Hats off to CSHL faculty who are active in social media, promoting their own ideas and providing perspectives on the latest developments in biology and genetics.

Adding to our public lecture series, both on our own campus and in other venues, are appearances by faculty on the World Wide Web. You can visit www.bigthink.com to watch professors Rob Martienssen and Michael Schatz explain how they're applying their research to solve some very big problems. Rob describes how he's using the principles of epigenetics that his group has uncovered to "persuade" a tiny weed to produce biofuel. Mike talks about his efforts to modify Google's "secret sauce" to manage the DNA data deluge brought on by the revolution in genome sequencing.

We also launched the *Harbor Transcript* interactive iPad app this year, enriching the print version with additional multimedia content. We encourage you to download the *HT* and other apps produced by the DNA Learning Center for free.

Harbor Transcript iPad App

While active in the global arena, we also pursue many local community outreach opportunities. In addition to tours that are conducted for participants in the CSHL Meetings and Courses program, more than 600 "nonscientific" guests participated in the CSHL Walking Tour program, visiting the campus from near and far, including Singapore, Italy, Japan, and China. The success of the program is largely due to the enthusiasm of guides, who this year totaled 13 graduate students and postdocs.

The Laboratory collaborated again with the Cold Spring Harbor Village Main Street Association to celebrate DNA Day on April 21–22 with a scavenger hunt that led participants to the Cold Spring Harbor Library, the Cold Spring Harbor Whaling Museum, the Firehouse Museum, and our own DNA Learning Center. DNA Day is celebrated across the country, with educational events sponsored by the National Human Genome Research Institute (NHGRI), a part of the National Institutes of Health. The day commemorates the completion of the Human Genome Project in April 2003, and the discovery of DNA's double helix, events closely tied to the Laboratory.

2012 Long Island 2-Day Walk

On April 17–18, first graders from local public and private schools Goosehill Primary and Friends Academy came to main campus for a special science fair. At each of six "experiment" stations, the children learned about scientific principles (from non-Newtonian fluid dynamics to cell structure to brain anatomy!) through hands-on activities and instruction conceived, planned, and led by 10 WSBS graduate students and four DNALC instructors. About 140 students, accompanied by 15 teachers and 120 parents, participated during the 2 days.

On August 8, CSHL and 13 local breast cancer organizations received checks from funds raised by the 2012 Long Island 2-Day Walk To Fight Breast Cancer. CSHL actively participates in the event, which attracted more than 400 participants. Each year, LI2DAY earmarks $15,000 for six scholarships that are awarded to local high school seniors with a parent or guardian who has been affected by breast cancer. Thanks to the CSHL volunteers who head

R. Sordella

up the LI2DAY Scholarship Committee. To date, $120,000 has been granted in LI2DAY Scholarships.

Associate Professor Raffaella Sordella participated in the Nassau Suffolk County Swim Across America event, swimming one mile to raise money for cancer research. We salute Raffaella's commitment.

Our employees lent a helping hand to the community in many ways. On campus, we conducted a blood drive in August, collecting 28 pints. CSHL also participated in Daffodil Days for the American Cancer Society. Members of our scientific community volunteer in many local elementary, middle, and high school science fairs.

CSHL Public Lectures

March 14–Alea Mills, Ph.D., CSHL Professor: *Where Will the Future of Genetic Technology Take Us?* Hosted by The Secret Science Club, Brooklyn, New York.

April 16–Brian Skotko, M.D., M.P.P., Board-certified medical geneticist at Children's Hospital Boston, Massachusetts General Hospital, Brigham & Women's Hospital, and Dana Farber Cancer Institute; Instructor, Children's Hospital Boston, Harvard Medical School, Boston, Massachusetts: *Keeping Children and Adolescents with Down Syndrome Healthy: Medical Updates for Physicians, Parents, and Educators*. Co-sponsored by CSHL and Down Syndrome Connection of Long Island.

A. Mills

April 19–David Spector, Ph.D., CSHL Professor and Director of Research: *The Laboratory @ Your Library: Discussion of "The Immortal Life of Henrietta Lacks*." Hosted by the Cold Spring Harbor Library, Cold Spring Harbor, New York.

June 26–W. Richard McCombie, Ph.D., Professor, CSHL and Director, CSHL Stanley Institute for Cognitive Genomics; **Diane Esposito, Ph.D.**, Research Investigator/Research Compliance Specialist, Cold Spring Harbor Laboratory; **Kenneth Offit, M.D., M.P.H.**, Chief, Clinical Genetics Service, Memorial Sloan-Kettering Cancer Center; **Kasmintan Schrader, M.B.B.S.**, Research Fellow, Cancer Biology and Genetics Program, Memorial Sloan-Kettering Cancer Center; **Peter K. Gregersen, M.D.**, Center Head, Robert S. Boas Center for Genomics and Human Genetics, The Feinstein Institute for Medical Research: *Follow Your Genes—Decision Making and Your Personal Genome.* Co-sponsored by CSHL, Bank of America-Merrill Lynch, North Shore-LIJ, and St. Johnland Nursing Center.

July 11–David Liittschwager, Photographer, *National Geographic* and Guest Instructor, DNALC Summer Camp: *A World in One Cubic Foot: Portraits of Diversity*.

November 18–David Spector, Ph.D., CSHL Professor and Director of Research: *Henrietta Lacks and HeLa Cells: Impact on Biological Research and Informed Consent*.

CSHL Public Concerts

March 23:	Charlie Albright, Piano
April 13:	Mischa Bouvier, Baritone (w/piano)
April 27:	Louis Schwizgebel, Piano
May 18:	Michael Brown, Piano
August 17:	Southampton Festival Chamber Orchestra
September 7:	Benjamin Beilman, Violin (w/piano)
September 21:	Narek Arutyunian, Clarinet (w/piano)
October 12:	Sarah Wolfson, Soprano (w/piano)

Looking Forward

Thanks to the entire CSHL community for a remarkable year. The institution continues to set world standards in biological and genetic research and education and that is the result of hard work and dedication on the part of our board, faculty, students, and staff. On behalf of CSHL, I thank our generous donors for allowing the best and brightest scientific minds to push the boundaries of research in cancer, neuroscience, plant genetics, genomics, and quantitative biology.

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