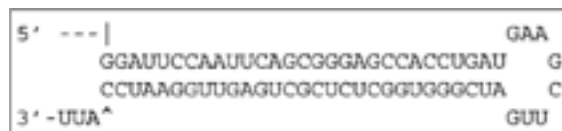


# Highlights of the Year

## Technology Transfer

Cold Spring Harbor Laboratory (CSHL) is engaged in technology transfer as one way of delivering important discoveries to the public. We continue to ramp up institutional support to CSHL scientists in partnering with companies, investors, and others to achieve their research-related objectives and add value to the basic research that is the bedrock of science at Cold Spring Harbor. Our success can be measured in terms of dollars, transactions, and relationships, but most importantly how these efforts eventually translate into applications that benefit society. In 2014, CSHL had 561 active patent cases in progress for 133 technologies and 1627 active technology transfer agreements. Net licensing revenue totaled \$3,866,042. The return on commercialization efforts is reinvested in research and innovation at CSHL.

In June, CSHL announced the settlement of a long-running malpractice suit against law firm Ropes & Gray and attorney Matthew P. Vincent just days before the case was to go to a jury in Massachusetts state court. Malpractice impeded the timely issuance of a CSHL patent on short-hairpin RNAs (shRNAs). These are engineered molecules that allow researchers to turn off expression of virtually any target gene or combination of genes in human and other mammalian cells. The shRNA technology at issue was developed by Professor and Howard Hughes Medical Institute Investigator Gregory Hannon, Ph.D. It represents a considerable advance over other technologies, including the RNA interference technology developed by Nobel Prize winners Drs. Andrew Fire and Craig Mello. The Hannon shRNA technology has had a powerful impact across academic and industry medical research, including its use to identify new drug targets and therapies for cancer.

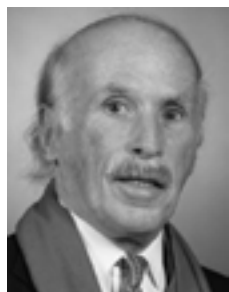


shRNA, named for its hairpin shape

Ultimately patented by CSHL in 2012 while the Laboratory simultaneously pursued the malpractice suit, the proprietary shRNA technology is now a widely used biomedical research tool in cancer research and drug development. Many companies have already signed licenses for this technology with CSHL, and the Laboratory is pursuing additional licensing opportunities.

## Cold Spring Harbor Laboratory Board of Trustees

The CSHL Board of Trustees elects members whose academic and professional accomplishments reach beyond the boundaries of science, providing well-informed governance in an increasingly complex fiscal and regulatory environment. The Board welcomed Lalit Bahl, Ph.D., of Renaissance Technologies Corporation, David M. Knott of Knott Partners, and Elizabeth McCaul of Promontory Financial Group.



D. Knott

The Board congratulated retiring member Thomas Lehrman, who served from 2008 to 2014 and was active on the Planning, Investment, and Academic Affairs committees.

James H. Simons was elected Honorary Trustee. Jim is the founder of Renaissance Technologies and Chairman of the Simons Foundation. He and his wife, Marilyn, who serves as Vice Chairman of the CSHL Board of Trustees, are leaders in private funding of basic research at CSHL and throughout the country.

Trustees, faculty, students, and employees mourned the passing of long-time friends, former CSHL Chairman and Honorary Trustee David Luke and his wife Fanny.



L. Bahl



E. McCaul



B. Stillman and Double Helix Medal winners M. Meselson, M. Thomas, and A. Solomon

With support from the CSHL Association, the Corporate Advisory Board, foundations, and individuals, CSHL raised more than \$6.6 million for the CSHL Annual Fund, which provides unrestricted support for research and education. The 9th Double Helix Medals Dinner, honoring Matthew Meselson, Marlo Thomas, and former CSHL trustee Andrew Solomon, raised a record \$4 million. Through his award-winning writings and lectures, Andrew has promoted awareness and understanding of mental illness, including a number of disorders that have a genetic basis and are under active investigation at the Laboratory. Dr. Meselson is a legendary geneticist whose landmark experiment in 1958 with Franklin Stahl revealed critical aspects of DNA replication, essentially proving Jim Watson and Francis Crick's hypothesis as to how the double helix of DNA is copied. Marlo Thomas has raised the visibility of research in health care as National Outreach Director for St. Jude Children's Research Hospital, spearheading national campaigns in support of the hospital's mission to advance cures and prevent catastrophic pediatric diseases through research and treatment. In 1962, Marlo's father, Danny Thomas, founded St. Jude Children's Hospital in Memphis, Tennessee.

With generous support from Jim and Marilyn Simons, we established the Simons Center for Quantitative Biology in 2009. The Center brings together experts in applied mathematics, computer science, physics, and engineering to further basic research and investigation into illnesses including cancer, autism, bipolar disorder, and depression. Thanks to Jim and Marilyn, this year we were able to recruit computational biologist Adam Siepel from Cornell University to be the inaugural Chair of the Simons Center.



Jim and Marilyn Simons

We are grateful to all major donors who in 2014 supported research and education programs at the Laboratory. The Stanley Medical Research Institute contributed \$10 million to support the Laboratory's Stanley Institute for Cognitive Genomics. The G. Harold and Leila Y. Mathers Foundation continued its support of neuroscience research to map the mouse brain.

A gift from the Seraph Foundation will help support the Laboratory's new state-of-the-art Genetic Screening Facility, named for John and Edna Davenport. The New York State Empire State Development Corporation awarded CSHL \$1.5 million to equip a

Center for Metabolomics, where researchers will assess cell metabolism and oxidative vulnerabilities to develop new small-molecule inhibitors for treating cancers, autism, diabetes, and orphan diseases.

The Lustgarten Foundation contributed \$5 million to support pancreatic cancer researcher Douglas Fearon, M.D., who was recruited from the University of Cambridge, U.K., to continue his work on harnessing the immune system to fight cancer. This support is in addition to a similar amount that was previously given by the Lustgarten Foundation to support pancreas cancer research in David Tuveson's laboratory.

The year's outstanding additions to our Board, scientific staff, and community of supporters all bode well for a future of discovery and teaching innovation. All help CSHL maintain its leadership position in both research and education in biology and the life sciences.

## Research Faculty

### *Awards*

The National Science Foundation (NSF) awarded Early Concept Grants for Exploratory Research (EAGER) to Assistant Professor Florin Albeanu and Professor Partha Mitra, who are working to develop new technologies that will provide insight into the structure and operation of neural circuits and address how complex behaviors emerge from them. The awards are part of President Barack Obama's multiyear BRAIN Initiative that aims to answer fundamental questions about how the brain works.

The National Science Foundation (NSF) selected Assistant Professor Michael Schatz to receive its prestigious CAREER Award. The Faculty Early Career Development Program is targeted for teacher-scholars who are most effective in integrating research and education. Mike was one of a small group selected from among more than 200 young scientists who were under consideration.

Assistant Professor Molly Hammell was one of seven 2014 Rita Allen Scholars. The award supports promising early-career investigators, and Molly received the Foundation's highest honor: designation as the Milton E. Cassel Scholar, which pays tribute to a long-time president of the Rita Allen Foundation.

Assistant Professor Anne Churchland was named a Pew Scholar in the Biomedical Sciences by the Pew Charitable Trusts. She also received a Klingenstein-Simons Fellowship in the Neurosciences from the Simons Foundation and the Esther A. and Joseph Klingenstein Fund.

Associate Professor Mikala Egeblad won an Era of Hope Scholar Award from the United States Department of Defense (DoD) Breast Cancer Research Program. This prestigious award supports early-career scientists who have demonstrated extraordinary creativity, vision, and leadership potential within the field of breast cancer research. Mikala is one of only two recipients of the award this year.

EMBO, founded 50 years ago as the European Molecular Biology Organization, elected Professor David L. Spector, Ph.D., to its ranks. David, who is CSHL's Director of Research, is one of 50 outstanding researchers in the life sciences newly elected to membership. He was also elected to the American Academy of Arts and Sciences, joining some of the world's most accomplished leaders from academia, business, public affairs, the humanities, and the arts.

The Pershing Square Sohn Cancer Research Alliance honored Lloyd Trotman, Associate Professor, with one of six prizes for Young Investigators in Cancer Research. The prize seeks to fuel innovative scientific discoveries in the search for a cure.

I was honored to be selected as the 2014 recipient of the Herbert Tabor Research Award from the American Society for Biochemistry and Molecular Biology (ASBMB). The award is given for excellence in biological chemistry and molecular biology and for contributions to the community of scientists. It was my pleasure to give the opening lecture at this year's ASBMB Annual meeting in San Diego, CA, in April.



D. Fearon



A. Siepel



J. Lee



J. Tolkuhn

### ***New Faculty***

Professor Douglas Fearon, who received his M.D. from Johns Hopkins University School of Medicine in 1968, joined us from the University of Cambridge to further study the interaction between the immune system and tumors. With support from the Lustgarten Foundation, Doug's goal is to develop an immunotherapy to treat cancer.

Thanks to the Simons Foundation, we welcomed Adam Siepel, Ph.D., Professor and Chair of the Simons Center for Quantitative Biology. Adam was previously Associate Professor at Cornell University, focused on comparative genomics and the development of statistical methods and software tools to identify evolutionarily conserved sequences and the complex processes by which genomes evolve over time. Dr. Siepel attended graduate school in computer science, receiving an M.S. from the University of New Mexico (2001) and a Ph.D. from the University of California, Santa Cruz (2005).

Je H. Lee, with an M.D., Ph.D. from Tufts School of Medicine (2002), is an Assistant Professor, joining CSHL from George Church's laboratory at Harvard Medical School. Je studies how cells sense and remember timing, location, and history and how their surroundings influence their signals with other cells. He also develops imaging and molecular sequencing technologies for tracking genes, molecules, and cells.

A neuroscientist from the University of California, San Francisco, Assistant Professor Jessica Tolkuhn, received her Ph.D. from the University of California, San Diego, in 2006 and is studying how estrogen and testosterone generate sex differences in the brain and behavior.

### ***Promotions***

Congratulations to newly promoted Associate Professors Anne Churchland, Mikala Egeblad, and Michael Schatz. Justin Kinney was named Assistant Professor, being promoted from his previous position of CSHL Quantitative Biology Fellow.

### **Education Programs**

#### ***Banbury Center***

More than 500 people took part in 16 by-invitation meetings at the Banbury Center this year. The meetings included two that involved families of people affected by serious illnesses. *Eliminating the Stigma of Mental Illness* was devoted to mobilization of a plan conceived by the foundation BringChange2Mind, spearheaded by the actress Glenn Close, whose sister and nephew have bipolar disorder.

*Rhabdomyosarcoma: A Critical Review* brought together world experts on this common, often fatal, soft-tissue sarcoma that afflicts children. In this meeting, too, urgency to initiate a course of action was spurred by advocacy on the part of affected families. The meeting resulted in the publication of a white paper outlining future research directions and marked the start of the



Eliminating the Stigma of Mental Illness Meeting. Glenn Close models Stigmasucks jacket.



Hands-on biology at the DNALC

Laboratory's Sarcoma Research Project, funded by local, family-based nonprofit organizations to support targeted research on specific sarcomas.

Other important Banbury meetings in 2014 included *Connections and Communications in the Brain*; *Defeating Ovarian Cancer*; *The Immune System and Cancer*; *Interpreting Personal Genomes*; *Reactive Oxygen Species in Biology and Cancer*; and *Epigenetics and Agriculture*.

Unusually, in addition to the Rhabdomyosarcoma White Paper, this year's Banbury meetings gave rise to two published papers, one on adolescent mental health (published in *Science*), the other on redefining the privacy of genomic data (published in *PloS Biology*).

### DNA Learning Center

Operations of the DNALC in 2014 brought an additional 19,300 local students on field trips to the Cold Spring Harbor, Lake Success, and Harlem, New York, locations. An additional 9000 students were reached through in-school instruction by DNALC staff. During the summer months, 60 week-long biology and genetics summer camps were held in Cold Spring Harbor and eight other locations in the tristate area, involving 1300 students.

The Urban Barcode Project, in its third year, enjoyed continued success, with 145 students presenting posters and talks at the American Museum of Natural History in the spring. The Urban Barcode Research Program, supported by the Pinkerton Foundation, made possible an extraordinary opportunity for 38 students from the New York area to take part in summer barcoding workshops followed up with 100+ hours of research time spent with mentor-scientists at the Museum, CUNY, Columbia University, and the New York Botanical Garden. A new *Barcode Long Island* program was initiated.

The DNALC's worldwide reach via the Internet was reflected in record-setting numbers: more than 5.2 million visits to 22 DNALC websites; 875,000 views of DNALC YouTube videos; and 668,000 downloads of popular *3D Brain*, *Weed to Wonder*, and *Gene Screen* apps. Total multimedia visits numbered 6.75 million, up 7.7% over the prior year.

### Meetings and Courses Program

In 2014, just less than 7000 scientists attended meetings held on the main campus. Attendance at each meeting ranged from 100 participants to more than 500, and more



2014 Meetings and Courses

than half of attendees are either graduate students or postdoctoral researchers. Nearly one-third of the attendees come from nations other than the United States. The Cold Spring Harbor Asia program, now in its fifth year, included 20 conferences and one summer school in 2014 and attracted more than 3400 participants.

2014 saw the continuation of many successful annual and biennial meetings and the introduction of several new ones: *Avian Model Systems*; *the PARP Family & Friends*; and *Biological Data Science*. The Courses program, meanwhile, drew about 600 trainees, including advanced graduate students, postdoctoral researchers, and faculty. A new offering in 2014 focused on the *Genetics and Neurobiology of Language*, and this meeting will be held biennially.

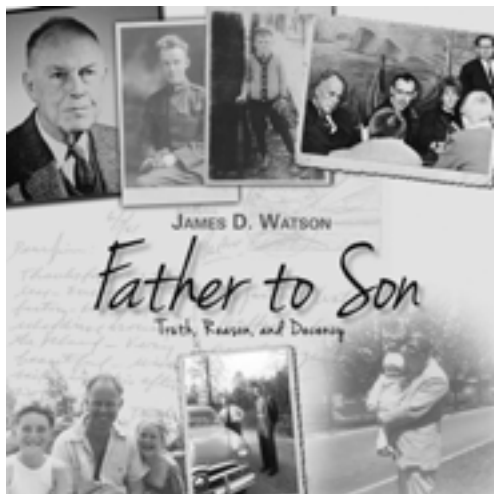
Strong backing of the Howard Hughes Medical Institute continues to sustain the Courses program. Courses also draw essential support from the National Institutes of Health and the National Science Foundation, and they rely on equipment and reagents loaned or donated by many companies. These partnerships enable CSHL to consistently offer training in the latest technologies.

### ***Cold Spring Harbor Laboratory Press***

2014 was another successful year for the Press. It maintained an output of high-quality publications, made a substantial financial contribution to the Laboratory, introduced a promising new service, and laid the groundwork for a new research journal. Subscription and advertising revenue streams for its four research journals were stable or higher. *Genes & Development* and *Genome Research* remain two of the world's four most highly cited genetics journals. There was strong growth for the newer journals, *Protocols*, *Perspectives in Biology*, and *Perspectives in Medicine*, each of which represents a strategic online transformation of print manuals and monographs. Total downloads of Press journal articles worldwide reached a record level of 13 million.

Although only a year old, the preprint service bioRxiv made a significant mark. More than 1000 draft research papers in 25 subject categories were posted, and authors received much feedback through on-site comments, social media, and private email. More than 300 of the posted preprints have now been published, in over 100 journals.

The Press also published 21 new book titles in 2014, including Jim Watson's family memoir *Father to Son*.



J. Watson's family memoir.

### ***Watson School of Biological Sciences***

The Watson School welcomed its 16th incoming class and graduated its 11th class. The achievements of the graduate program continued to grow. The quality of scientific publications produced by school's students remained highly impressive. Watson School students continued to graduate considerably faster than students in comparable Ph.D.-granting institutions and demonstrated an ability to secure excellent jobs. Nineteen WSBS graduates, or 27% of all graduates, have thus far secured tenure-track faculty positions, an impressive record since the first graduates only left Cold Spring Harbor Laboratory in 2004.

Eleven WSBS students were awarded Ph.D. degrees, bringing the total since the school's inception to 71. We were pleased to award an Honorary Doctor of Science degree to Richard Burgess of the University of Wisconsin, Madison, who taught the protein biochemistry course here for many years and who has made major contributions to understanding gene transcription. During the year, scientific papers published by students of the school appeared in major journals, bringing

the cumulative total of publications to nearly 300. Current and former students won prestigious and highly competitive scholarships and fellowships, as in past years.

In August, the WSBS welcomed nine new students. Members of the Class of 2014 were selected from among 276 applicants and represent the United States, Canada, Germany, India, Lithuania, and the United Kingdom. Other new graduate students entered as visitors from other institutions, including seven from Long Island's Stony Brook University. Current visitors hail from more distant institutions, including Cornell University and several from China, Germany, and France, among others.



WSBS class of 2014

During the summer, undergraduates from across the United States, as well as Austria, Bulgaria, Canada, Greece, Mexico, Singapore, Syria, and the United Kingdom, took up residence at CSHL to take part in the historic Undergraduate Research Program. These “URPs” (chosen from among 819 applicants!) had the remarkable opportunity to perform advanced research in the laboratory of a CSHL faculty member.

### *Library and Archives*

The Library and Archives organized a meeting in Grace Auditorium entitled “The History of mRNA” as part of a series held jointly with the Meetings and Courses division. This meeting brought together pioneers in the field of RNA biology, including Jim Watson and Sydney Brenner—who were co-discoverers of messenger RNA (mRNA)—and those involved in the discovery of long heteronuclear RNA (hnRNA) and RNA splicing, which resulted in a Nobel Prize to former CSHL scientists Richard Roberts and Phillip Sharp. The meeting also included talks by contemporary scientists studying mRNA processing, splicing, and translation. This meeting is part of a series on the history of molecular biology and genetics held here each year.

### **Infrastructure**

#### *Preclinical Experimental Therapeutics Facility (PET<sup>x</sup>)*

Construction on the 8000-square-foot addition to the Woodbury Genome Center that will open in 2015 as the Preclinical Experimental Therapeutics Facility (PET<sup>x</sup>) began in late 2013 and was delayed by a particularly harsh winter. When completed, the facility will house state-of-the-art imaging equipment and a dedicated staff to allow for the discovery and development of novel therapeutics and diagnostics strategies. Equipment will include non-invasive imaging such as PET/CT, ultrasound, and optical imaging equipment. The facility will have two surgical suites, necropsy rooms, a pharmacy, and a diagnostic clinical laboratory.



Preclinical Experimental Therapeutics Facility

**Nicholls Biondi Hall**

At the beginning of the year, we broke ground for construction of Nicholls Biondi Hall, a 2000-square-foot poster pavilion space to enhance the Meetings and Courses Program and provide additional configurable space for conferences and seminars. The new building opened in June 2015, looking eastward over a great lawn bounded by the Carnegie Building and the recently constructed



Nicholls Biondi Hall

Hershey Laboratory. The 1904 Carnegie Building that was originally built as a laboratory building and now houses our Library and Archives as a bookend to the new Hall.

The Laboratory this year also dealt with two significant catastrophic system failures. One was the aging, 20-year old McClintock Laboratory chiller plant. Replacement of similarly aging systems have been scheduled beginning in early 2015. Another major event was flooding of the Hershey Laboratory caused by record low temperatures that contributed to the freezing of a fire sprinkler line. Tens of thousands of gallons of water cascaded across the second floor of the building down to the floor below, causing major

damage to the Flow Cytometry and Microscopy facilities and the total loss of a laser confocal microscope. Luckily, the Facilities Department responded immediately and the building was quickly dewatered. Flood damage was repaired and new equipment was procured in less than 60 days.

**Community Outreach****Public Lectures**

**March 11**—**Mikala Egeblad, Ph.D.**, Assistant Professor, Cold Spring Harbor Laboratory; **Nicholas K. Tonks, Ph.D., F.R.S.**, Professor, Cold Spring Harbor Laboratory; **Lora R. Weiselberg, M.D.**, Clinical Associate Professor, Hofstra, North Shore–LIJ School of Medicine. Lecture: “Cold Spring Harbor Laboratory Breast Cancer Research Update.”

**March 28**—**Siddhartha Mukherjee**, author, *The Emperor of All Maladies: A Biography of Cancer*, 2014 Roy J. Zuckerman Lecture.

**April 8**—**Craig Garner, Ph.D.**, Professor, Department of Psychiatry and Behavioral Sciences Stanford University, Co-director Stanford Center for Research and Treatment of Down syndrome. Lecture: “Developing Therapies to Improve Cognitive Abilities of Individuals with Down Syndrome.”

**June 18**—**Michael Schatz, Ph.D.**, Assistant Professor, Simons Center for Quantitative Biology at Cold Spring Harbor Laboratory. Lecture: “Big Data: How Biological Data Science Can Improve Our Health, Foods, and Energy.”

**June 24**—**Michael Ronemus, Ph.D.**, Research Assistant Professor Cold Spring Harbor Laboratory; **Rebecca Sachs, Ph.D.**, Staff Psychologist, Fay J. Linder Center for Autism and Developmental Disabilities. Lecture: “Understanding Autism Spectrum Disorder: Focus on the Facts.”

**October 23**—**Bruce Adolphe**, composer and Resident Lecturer and Director of Family Concerts for the Chamber Music Society of Lincoln Center; **Alexis Gambis, Ph.D.**, founder, Science Films. Lecture: “Creativity in Music, Film, and Neuroscience.”



Roy J. Zuckerman Lecture





C. Albright

**November 4**—Lynn Pasquerella, Ph.D., President, Mount Holyoke College. Lecture: 2014 Lorraine Grace Lecture on societal issues of biomedical research: “Is Death Un-American?”

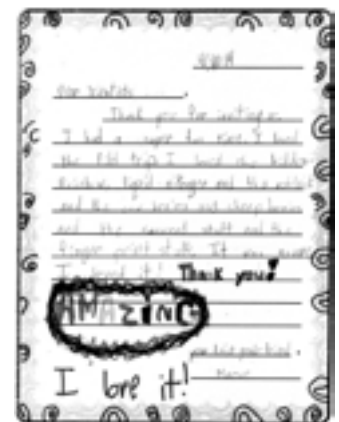
### *Public Concerts*

- March 21:** Igor Lovchinsky, piano  
**April 25:** Cicely Parnas, cello  
**May 2:** Jerome Lowenthal, piano  
**May 16:** Ken Noda with Anthony Kalil, piano with tenor  
**August 15:** Charlie Albright, piano  
**September 12:** Ji, piano  
**September 19:** Yun-Chin Zhou, piano  
**October 2:** Andrey Tchekmazov, cello  
**October 10:** Einav Yarden, piano  
**March 27, 2015:** Martin Kasik, Piano  
**April 17, 2015:** Jiayin Shen and Alan Woo, piano duo  
**May 1, 2015:** Julia Bullock, soprano  
**May 15, 2015:** Trio Solisti, violin, cello, and piano

We thank our team of enthusiastic graduate students and postdoctoral fellows who staff CSHL’s public tour program. They conducted 57 campus tours for more than 800 participants during the course of the year.

Local families enjoyed a day exploring the history of Cold Spring Harbor Village and DNA on April 26 as part of the DNA Day Scavenger Hunt. Local institutions including the Cold Spring Harbor Library, the Cold Spring Harbor Whaling Museum, the Firehouse Museum, and CSHL’s DNA Learning Center took part. DNA Day is celebrated across the country, commemorating the completion of the Human Genome Project in April 2003 and the discovery of the DNA double helix by Chancellor Emeritus James D. Watson and Francis Crick.

In April, first graders from Goosehill Primary and Friends Academy participated in a science fair on the CSHL campus. With graduate students and DNA Learning Center instructors manning interactive stations, more than 100 local children, teachers, and parents explored the brain, seaweed, rainbows, and their own fingerprints.



Thank you from student visitor



Hour of Code @ CSHL

In December, Maria Nattestad, a WSBS Graduate Student, led a community event called “Hour of Code.” Part of a global effort to introduce children to computer coding at early ages, the event brought local families to the Laboratory. Maria also leads a “Girls Who Code” club for girls in grades 7–12 together with the DNA Learning Center Assistant Director Amanda McBrien.

Congressman Steve Israel (D-NY) joined CSHL in congratulating Long Island high school students recognized as Intel Science Prize Semifinalists. Two of the 40 local semifinalists were part of CSHL’s Partners for the Future Program, working in the laboratories of Mikala Egeblad and Leemor Joshua-Tor.

CSHL participated in the 11th Long Island 2-Day Walk that raised more than \$22,800 for breast cancer in the lab of Mikala Egeblad, whose research is aimed at developing new strategies to treat breast cancer. Rather than attacking tumor cells directly, Mikala’s group is investigating whether it is possible to target immune cells in the tumor microenvironment that act to promote cancer metastasis and suppress the response to chemotherapy.

The LI2DAY Walk also awards six \$2500 scholarships to Long Island high school seniors who have a parent or guardian with breast or other women’s cancer. CSHL is proud to participate in the scholarship committee.

Interacting with the public through lectures, tours, and special events is important in our efforts to raise visibility about the significance of basic research and science education. The understanding and support of the general public is critical to CSHL and other independent research institutions that rely on taxpayer funding and private philanthropic giving. We continue to expand our efforts to communicate with the public through use of the latest digital technologies. Follow us on Facebook and Twitter!

## Looking Forward

We look forward to our 125th anniversary year and the future beyond it with excitement and optimism, poised for even bigger breakthroughs that will undoubtedly change the world for the better.

**Bruce Stillman, Ph.D., F.R.S.**  
*President and Chief Executive Officer*