Highlights of the Year

Research

In 2022, hundreds of scientists working in more than 60 Cold Spring Harbor Laboratory (CSHL) research groups published their findings in the world's major research journals. Their efforts reflect the full spectrum of CSHL's programs in Cancer, Neuroscience, Plant Biology, Quantitative Biology, and Genomics. The following is a sample of this year's important findings.

Breast Cancer's Mini-Me

D. Spector

Organoids are miniature, three-dimensional copies of cancers. They allow scientists to study the basic biology of particular types of tumors and then test specific drugs on those cancers in a dish instead of in a patient. CSHL Professor David Spector and collaborators at CSHL and Northwell Health created a biobank of breast cancer organoids from 87 patient tumor samples. Nearly half the samples were "triple negative," which is an aggressive form of breast cancer. The researchers published their work in *Cancer Research.*

The research team, which plans to expand the biobank to more than 100 patient-derived samples, conducted extensive tests to ensure the organoids had the same characteristics as the tumors when they were in the patient. They tested that the organoids and tumors (1) had similar genetic variation in their DNA; (2) had similar RNA profiles; and (3) produced tumors similar to the patients' tumors when implanted in mice.

Spector's laboratory is testing various treatments to find weaknesses specific to each tumor. They are developing a library of therapeutics known as antisense oligonucleotides to target RNA molecules active in cancer cells, but not in healthy cells. Spector and his team already have 200 potential targets and will prioritize RNA molecules that are made in the largest amounts. Their efforts might one day allow doctors to use organoids in the clinic.

Next Steps for Spinraza®

A. Krainer

In 2016, Spinraza® became a game changer for spinal muscular atrophy (SMA) patients. It was the first FDA-approved treatment for the neurodegenerative disease, which is the leading genetic cause of infant death. The Spinraza® drug was conceived and developed by CSHL Professor Adrian Krainer and his collaborators. More than 11,000 SMA patients have been treated with Spinraza® in more than 50 countries. But Krainer has not stopped there.

His laboratory has been investigating whether Spinraza® could be improved. They discovered that pairing Spinraza® with a second FDA-approved drug called valproic acid (VPA) could boost its therapeutic effects. Spinraza® is a type of molecule called an antisense oligonucleotide (ASO). When mice with SMA were treated with both VPA and a Spinraza®-like ASO used for research, the mice survived longer and had improved muscle function.

Krainer has also been searching for ways ASOs can help treat other disorders. He has zeroed in on cystic fibrosis (CF), in which patients do not make enough of a protein called CFTR. His team discovered how to use ASOs to make more of an imperfect but still functional version of CFTR. Their method improved the function of lung cells. The discovery sets the stage for a new therapeutic approach that may help reduce CF symptoms and improve patient quality of life.

Krainer's discoveries spotlight new ways ASOs can be used to treat diseases. "If more of this type of drug, ASOs, are approved," he says, "I wouldn't be surprised if in the not-so-distant future ASOs become a routine way to make personalized medicines."

Battling Brain Cancer

A. Mills

The brain cancer glioblastoma is a fierce and formidable opponent. Most patients succumb within two years and few make it past five, a statistic that has not improved in decades because of lack of effective treatment options. But now, CSHL Professor Alea Mills and her colleagues have discovered in this deadly cancer a vulnerability, known as BRD8, that may finally lead to new treatment options and better patient outcomes.

The CSHL team recently solved a decades-old mystery surrounding glioblastoma's aggressiveness by linking the BRD8 protein to another protein, named P53. Mills and her team revealed that BRD8 was inappropriately active in glioblastoma, keeping many of P53's critical anticancer defenses at rest. When the researchers inactivated BRD8 via genome editing, P53's "arsenal" suddenly woke up and began blocking tumor growth.

Mills' team implanted tumor cells from glioblastoma patients into mice and watched the tumors grow in the brain. When BRD8 was inactivated, P53 was unlocked—the tumors stopped growing and the mice lived longer. The finding suggests that drugs targeting the heart of BRD8 could work against glioblastoma. Mills hopes her team's discovery will help turn this deadly brain cancer into a treatable disease and, for the first time in a generation, extend the life expectancy of patients who are diagnosed with it.

Immune System Training

T cells are a special class of white blood cells that patrol the body and attack infected or foreign tissue. They learn to distinguish friendly proteins from dangerous ones in an organ called the thymus. However, when T cells mistakenly identify healthy proteins as foreign, it can lead to autoimmune disorders such as multiple sclerosis or diabetes.

H. Meyer

CSHL Fellow Hannah Meyer has discovered how the human thymus generates the list of friendly proteins that T cells should not attack. Her team identified, for the first time, the RNA molecules used to generate this list that protects healthy tissue from T cells. Their discovery may help identify key differences between effective and flawed immune systems and lead to improved autoimmune disorder treatments.

Meyer focuses on the thymus for its role in not just preventing autoimmune diseases but also fighting infections and cancer. She hopes these diseases can be better understood and treated by further exploring the proteins made in the thymus. Meyer's new list has been made available to other researchers via an interactive online database.

Brain Sex Differences Defined

Hundreds of genes in the brain fall under the control of estrogen. Fluctuating levels of the hormone cause shifts in mood, energy balance, and behavior throughout life, in addition to sculpting developing neural circuits early on. These effects occur when activated estrogen receptors sit directly on a cell's DNA to turn genes on or off.

CSHL Assistant Professor Jessica Tollkuhn and her colleagues have been mapping exactly where estrogen receptors latch onto DNA inside mouse brain cells. They have looked at both males and females and compared the brains of adults to the still-developing brains of young pups. In the journal *Nature*, they reported on the hormone receptor's targets and showed that estrogen sets up physical differences in the brains of males and females during development.

J. Tollkuhn

Tollkuhn's team focused on a brain region called the BNST, which is larger in males than females in both mice and humans. They found a host of genes that were under estrogen's control, including many involved in neurodevelopment and neuronal signaling. And although estrogen itself remains in the brain for only a few hours, it seems that the hormone-controlled genes remain active for weeks.

Now that they know what genes estrogen is targeting in the brain, Tollkuhn's team plans to explore exactly how those genes mediate the hormone's diverse effects on brain development, behavior, and disease.

From Smell to Perception


F. Albeanu


A. Koulakov


A. Zador

CSHL investigators Florin Albeanu, Alexei Koulakov, and Anthony Zador have created an extensive new map of the brain's olfactory circuits. Using new DNA-based brain-mapping technologies developed in Zador's lab, called MAPseq and BARseq, the CSHL team traced the paths of thousands of smell-processing neurons within the brain of a single mouse. The new map charts the way sensory information is routed between parts of the brain. These include the olfactory bulb, which receives sensory information from the nose, the primary smell-processing hub called the pyriform cortex, and several other brain regions that receive inputs from the olfactory bulb.

Within the pyriform cortex, the team found that neurons toward the front of the brain had different connectivity patterns than those in the back. "As you move along this axis, you see the neurons' projection pattern gradually changing in terms of how it broadcasts information into other brain regions," Koulakov said. "That is synchronized with the way the olfactory bulb projects to those brain regions, as well as to the same locations within the pyriform cortex."

The olfactory map points toward the existence of different neural circuits dedicated to assessing the identity of a smell, how pleasant it is, where it is coming from, and how to act on it.

Nurturing Brain Connections


L. Van Aelst

Microglia, the immune cells of the brain, are known for eating up unwanted items like germs and debris. Now, CSHL Professor Linda Van Aelst has found that in mice microglia also help neurons grow synapses critical to cognitive functioning.

It was Van Aelst's obsession with a rare type of inhibitory neuron called a chandelier cell that sparked her interest in microglia. Chandelier cells are named for the ornate branching shape of their nerve fibers. These structures make direct contact with the section of a target neuron that sets off its firing: the axonal initial segment (AIS). This unique synapse gives chandelier cells powerful control over the signaling of hundreds of neighboring neurons at once.

Van Aelst's laboratory studied how microglia interact with chandelier cells. They found that microglia wrap their arm-like processes around the synapse-forming structures of a chandelier cell and its target neuron, increasing proper synapse formation. These special embraces were more common in pups and young mice than in adults.

The team then tested what happens when microglia are impaired. "We saw that there were less microglia going to where chandelier cells make contact on the AIS," Van Aelst said. "And we saw that fewer of these synapses formed." Ultimately, she wants to see if microglia could be recruited to help treat neurological disorders.


D. Jackson

Plant Notes to Self

In plants, important messages are packaged into RNA, which is sent from cell to cell. By studying the mustard-like plant *Arabidopsis thaliana*, CSHL Professor David Jackson and his team found that RNA messages need a special protein to escort them where they need to go. Without this escort, cells cannot coordinate and the plant fails to develop properly.

Unlike animal cells, plant cells are surrounded by a rigid cell wall. Messages can cross this wall through tiny holes called plasmodesmata. Jackson's team wondered how the plasmodesmata's gates regulate messaging from one cell to the next. They discovered that RNA signaling relied on a protein called AtRRP44a. Lowering the amount of AtRRP44a slowed the movement of RNA messages; lacking the right messages, the plants failed to develop properly. A protein similar to this escort protein is present in other plants, yeast, and animals. The researchers were able to swap out part of the *Arabidopsis thaliana* signaling system with parts from corn and restore normal development, showing that this signaling system is similar in many kinds of plants.

In a related study published in the journal *Science*, Jackson and collaborators at New York University found that signals transported through these gates can increase the number of cell layers in corn roots, making the plants potentially more resilient to environmental changes.

Finding the Right AI

Artificial intelligence (AI) programs can find patterns in the genome related to disease much faster than humans can. They also spot things that humans miss. Unfortunately, AI's recent popularity surge has led to a bottleneck in innovation.

P. Koo

"It's like the Wild West right now. Everyone's just doing whatever they want," said CSHL Assistant Professor Peter Koo. Just like Frankenstein's monster was a mix of different parts, AI researchers are constantly building new algorithms from various sources. And it's difficult to judge whether their creations will be good or bad. After all, how can scientists judge "good" and "bad" when dealing with computations that are beyond human capabilities?

That's where GOPHER, the Koo laboratory's newest invention, comes in. GOPHER (short for GenOmic Profile-model compreHensive EvaluatoR) is a new method that helps researchers identify the most efficient AI programs to analyze the genome.

GOPHER judges AI programs on several criteria: how well they learn the biology of our genome, how accurately they predict important patterns and features, their ability to handle background noise, and how interpretable their decisions are. GOPHER helped Koo and his team dig up the parts of AI algorithms that drive reliability, performance, and accuracy. The findings help define the key building blocks for constructing the most efficient AI algorithms going forward.

COVID-19 Clinical Trial

A high dose of famotidine, commonly known as Pepcid®, was found to have beneficial effects in adult patients with COVID-19, according to results of an outpatient clinical trial. Patients who took famotidine in this trial experienced a decrease of inflammation within the body and reported earlier alleviation of symptoms. Findings from the trial, led by the Feinstein Institutes for Medical Research at Northwell Health and CSHL, were published in the journal *Gut*.

Famotidine is a safe, low-cost, over-the-counter drug usually used to treat heartburn. People with COVID-19 often get sick because the body's inflammatory response to the virus gets overactivated. This trial confirmed that famotidine leads to earlier resolution of inflammation in patients with COVID-19 and also alleviates symptoms of the disease while the acquisition of immunity against the virus that causes COVID-19 is maintained. Because famotidine does not target the virus directly like vaccines or antiviral medications, it may be a promising potential treatment for patients with COVID-19 and emergent viral variants.

T. Janowitz

"We closely monitored patients in this fully remote clinical trial while protecting their safety and that of health care providers in pandemic conditions," said CSHL Assistant Professor Tobias Janowitz. "We hope that the data we are sharing with this study guide future trials that are necessary to confirm famotidine as a treatment for patients with COVID-19."

Research Faculty

Awards

L. Cheadle

Assistant Professor Lucas Cheadle became CSHL's first recipient of the U.S. National Institutes of Health (NIH) Director's New Innovator Award, which supports early career researchers working on innovative, high-impact projects. He will use the $1.5 million grant to investigate the links between inflammation and autism spectrum disorders. *Diverse: Issues In Higher Education* magazine also named Cheadle an Emerging Scholar. He joins 14 other "40 and under" scholars who have been selected for their significant achievements in academia through research, teaching, and service.

CSHL Fellow Corina Amor Vegas was awarded the NIH Director's Early Independence Award. The grant provides up to $1.25 million over five years. It supports Amor Vegas' investigations into how the aging process is affected by cellular senescence—when cells stop dividing but do not die. She is one of 14 investigators to receive the award this year.

C. Amor Vegas

D. Tuveson

Professor and Cancer Center Director David Tuveson was elected to the National Academy of Medicine (NAM). He was recognized for his pioneering work with cancer organoids—miniature versions of tumors—which led to the development of the first mouse models for two types of pancreatic cancer. Tuveson also earned a 2022 Luminary Award, presented by the Ruesch Center for the Cure of Gastrointestinal Cancers on November 17, World Pancreatic Cancer Day.

Professor and HHMI Investigator Rob Martienssen was elected to the American Academy of Arts and Sciences. He is best known for his groundbreaking work in the field of genetics, including his contributions to defining the role of RNA interference (RNAi) in silencing genes and stabilizing the genome across generations.

R. Martienssen

The Indiana University School of Medicine awarded Professor Adrian Krainer the August M. Watanabe Prize in Translational Research for his revolutionary work on a cellular process called RNA splicing. The Watanabe Prize honors individuals who have transformed scientific discoveries into new therapies for patients.

Assistant Professor Arkarup Banerjee was named a 2022 Searle Scholar to pursue his work on neural circuits for flexible vocal communication. The Searle Scholars Program supports high-risk, high-reward research across a broad range of scientific disciplines, making grants to support recently appointed assistant professors in chemistry and the biomedical sciences.

Assistant Professor and Cancer Center Member Tobias Janowitz received a $25 million grant from Cancer Grand Challenges. He is leading an international, multidisciplinary team to develop new treatments for cachexia. The debilitating disease causes severe weight loss, weakness, and immune suppression in cancer patients. Cancer Grand Challenges is a global funding initiative founded by the NIH's National Cancer Institute and Cancer Research UK.

A. Banerjee

S. Sun

Simón(e) Sun, a postdoc in Associate Professor Jessica Tollkuhn's laboratory, was named a 2022 Leading Edge Fellow for her research on the protein estrogen receptor β and its role in the development and function of the nervous system. Sun is a senior fellow at the Center for Applied Transgender Studies and a vocal advocate for transgender rights. The Leading Edge Fellow program provides women and nonbinary postdocs with a platform to present their work and opportunities for mentorship and career development training from world leaders in biomedical research.

C. Lambert

J.R. Inglis

Charla Lambert, Director of the Office of Diversity, Equity, and Inclusion, was elected as president-elect of the Society for the Advancement of Chicanos/Hispanics and Native Americans in Science, or SACNAS. She will serve as president of SACNAS during its 50th anniversary in 2022.

John R. Inglis, Executive Director of the CSHL Press, was named a fellow of the American Society for Cell Biology. Inglis founded the CSHL Press in 1988. He has expanded its catalog to include approximately 600 monographs, laboratory manuals, and professional handbooks. He has also built a portfolio of nine scientific journals including *Genes & Development* and *Genome Research*, two of the most prominent research journals in genetics. Inglis also co-founded the life sciences preprint server bioRxiv in 2013 and health sciences preprint server medRxiv in 2019.

New Hires/Promotions

Benjamin Cowley, Helen Hou, Gabrielle Pouchelon, and Peter Westcott joined as Assistant Professors. Corina Amor Vegas was named a CSHL Fellow. Lee Hassal was welcomed as a Clinical Fellow. Kyle Daruwalla became a NeuroAI Scholar. Scott Quehl joined as CSHL Chief Financial Officer.

B. Cowley

H. Hou

G. Pouchelon

P. Westcott

L. Hassal

K. Daruwalla

S. Quehl

Semir Beyaz and Lingbo Zhang were promoted to Assistant Professor. Tatiana Engel, Ullas Pedmale, and Jessica Tollkuhn were promoted to Associate Professor.

Scott Lyons and Johannes Yeh were promoted to Research Associate Professor. Paolo Cifani was named Research Associate Professor and Director, CSHL Mass Spectrometry Shared Resource. Erika Tse-Luen Wee was promoted to Director, Microscopy Shared Resource. Pamela Moody was promoted to Director, Flow Cytometry Shared Resource.


S. Beyaz


L. Zhang


T. Engel


U. Pedmale


S. Lyons


J. Yeh


P. Cifani


T.-L. Wee


P. Moody


Z. Lippman

Howard Hughes Medical Institute Investigator and CSHL Professor Zachary Lippman was promoted to Professor and Director of Graduate Studies.

Education Highlights

Meetings & Courses Program

Following two years of virtual programming, the Meetings & Courses Program saw a strong resurgence in 2022. Six meetings—*The Biology of Genomes; Glia in Health and Disease; Genome Engineering: CRISPR Frontiers; Translational Control; Molecular Mechanisms of Neuronal Connectivity, Epigenetics, and Chromatin;* and *Neurodegenerative Diseases: Biology and Therapeutics*—hit the "COVID cap" for in-person attendance.

Also held in 2022 was the much-anticipated *86th Cold Spring Harbor Laboratory Symposium*, which focused on *Genome Stability and Integrity*. This theme had been selected for the 2020 Symposium, but COVID-19 prompted a change of plans. The historic conference expanded on past CSHL symposia that covered genome integrity, the earliest of which dates back to 1951.

GLIA participants on Bungtown Road.

All told, more than 10,000 participants attended CSHL meetings, virtually or in person, in 2022. In-person attendance has now reached prepandemic levels, boding well for 2023. Notably, the hybrid format allowed more attendees from low- and middle-income countries to participate in CSHL's meetings.

At the CSHL campus on Long Island, advanced scientific courses covered an array of topics in molecular biology, neurobiology, structural studies, and bioinformatics, with 590 students attending. Students from underrepresented minority groups accounted for 20% of all U.S. applicants—a figure that has more than doubled over the past decade.

As a final update of note, 2022 Nobel laureate Svante Pääbo has participated extensively in CSHL's educational programs. Pääbo has taken part in at least 43 meetings here, including the *Biology of Genomes* conference, which he organized from 2004 to 2006.

Banbury Center

After COVID caused first-quarter postponements, Banbury resumed a busy schedule in April. Despite the three-month shutdown, the Center hosted 15 Banbury meetings. Participants hailed from six continents, 34 countries, and 33 U.S. states.

Banbury topics in 2022 spanned the range of research, education, and policy issues. Basic science research–focused meetings covered regenerative biology, biostatistics, genomics, and cell death. Translational research topics included disruptive therapeutics, perinatal transmission of Lyme disease, pediatric brain tumors, and the Lustgarten Foundation's scientific meeting. Science education was well represented by meetings on short-format training in the life sciences and the Boehringer Ingelheim Foundation retreat on communicating science. Policy was another major focus, with five meetings covering HIV prevention, deep-seabed mining, agricultural biotechnology, science philanthropy, and human research in spaceflight.

Since 2018, Banbury has instituted efforts to improve the gender diversity of its meetings. Steady improvement has been seen in this area, with 2022 marking the first time in the Center's history that women and nonbinary participants outnumbered men—52% to 48%.

Although Banbury was able to convene in-person meetings in 2022, COVID-related travel restrictions and related issues led the Center to offer a virtual option for eight of its meetings. The hybrid format allowed participation from experts who were not able to travel; however, remote participants were disconnected from informal discussions that are the hallmark of Banbury. The overwhelming sentiment was that hybrid meetings were a necessary evil, but should not continue.

School of Biological Sciences

In August, the School of Biological Sciences (SBS) welcomed its 24th incoming class, comprised of four students from the United States and two from abroad. An additional three students who accepted offers this year deferred to next year. To date, 137 students have received their Ph.D. from the School. Approximately one-third of SBS graduates are in faculty positions, most in tenure-track positions at major U.S. or international research institutions. Current students continue to win prestigious fellowships and awards. This year, two current students received scholarships: Emily Isko was awarded a National Science Foundation Graduate Research Fellowship and Alexa Pagliaro was awarded an NIH Ruth L. Kirschstein National Research Service Award Individual Fellowship.

In 2022, the New England Commission on Higher Education voted to grant CSHL institutional accreditation. This year also marked the last with Professor Alexander Gann as the School's dean. In December, Professor Gann stepped down from the position after 10 years of dedicated service. Professor Zachary Lippman has taken the leadership role at the School, with the title of Director of Graduate Studies.

Finally, the SBS continued to expand its educational offerings beyond doctoral studies in 2022. The summer Undergraduate Research Program (URP) was held in person for its 64th year. Additionally, the School launched a new Postbaccalaureate Research Education Program (PREP), which will welcome its first cohort in June 2023. Each year, CSHL PREP will host four postbaccalaureate students, who will conduct research with CSHL faculty members and attend courses and skills workshops in preparation for graduate school.

DNA Learning Center

The DNA Learning Center (DNALC) enjoyed one of its most successful years to date in 2022. The 2022 summer camp season hosted 1,287 campers—besting the previous attendance record, set in 2018, by 20%. Additionally, visitation to the Dolan DNALC on Long Island recovered to pre–COVID-19 levels. Regeneron DNALC in Westchester continued to bring in students at a rate similar to DNALC West, even while operating at about 50% capacity.

SBS Entering Class of 2022.

High schoolers at DNALC NYC's Genome Science summer camp in July 2022.

The DNA Learning Center NYC at City Tech, opened in Brooklyn in 2021, continues to expand its offerings. DNALC NYC is now home to a world-class permanent exhibition called "What DNA Says about Our Past and Future," which includes eye-catching replicas of Ötzi the Iceman and a Philistine burial.

In 2022, the DNALC awarded 118 week-long scholarships to students from underrepresented minority groups. Notably, DNALC has rekindled a collaboration with Gateway to Higher Education, a program that operates in 11 New York City public high schools. This is expected to help increase attendance at DNALC summer camps in the years ahead.

In addition to having a massive positive impact on the lives of elementary, middle, and high school students who attend its educational programs, the DNALC has employed 363 high school and college students as interns since 1987. Of 312 interns surveyed in 2022, 81% began their internship as high schoolers and 99% went on to a four-year college, with three out of four pursuing degrees in science, technology, engineering, or medicine.

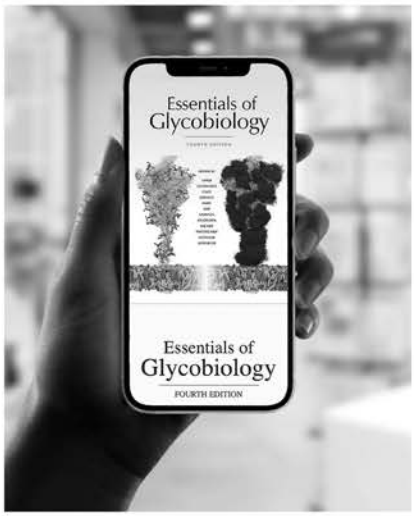
Cold Spring Harbor Laboratory Press

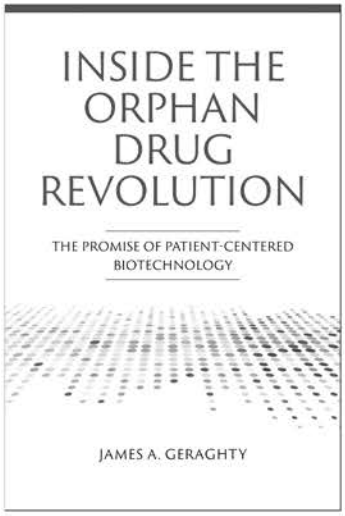
In 2022, CSHL Press continued its progress toward the ambitious goal of making its research journals fully open-access by 2025, in accord with many funders' requirements. Agreements are being made with institutions worldwide that provide reading access to the three highly regarded Press review journals along with free publishing rights in the four research titles.

Bolstering this strategy, online usage of Press journals remained exceptional in 2022. *Cold Spring Harbor Protocols* and *RNA* achieved new milestones in revenue. Judged by citations, *Genes & Development* and *Genome Research* remained in the top tier of research journals in their disciplines and in the top 1% of all 9,600 journals in the Science Citation Index.

The Press published seven new book titles in 2022 on topics that included lung cancer, human genetics, organ regeneration, and sex differences in brain and behavior. The fourth edition of the major reference work *Essentials of Glycobiology* was published in print, in a freely accessible web-based format, and as a sponsored, freely downloadable e-book. James Geraghty's widely praised *Inside the Orphan Drug Revolution: The Promise of Patient-Centered Biotechnology* was a #1 biotechnology seller on Amazon. Book sales, including e-books, benefited from effective direct-to-consumer marketing and order processing through the Press website.

Both the book and journal publishing programs exceeded financial projections, enabling the Press to contribute once again a substantial surplus in support of the Laboratory's operations.





Preprints in Biology and Medicine

A preprint is a research manuscript made freely available by its authors without peer review. The Laboratory's preprint platforms, bioRxiv for biology and medRxiv for health sciences, are free for both authors and readers and are accelerating the pace of biomedical research by transforming how scientific work is shared.

More than 70% of manuscripts first posted on bioRxiv and medRxiv are published in journals, but it may take a year. Meanwhile, the freely accessible preprint can prompt other scientists to build on the results or initiate collaborations and demonstrates the productivity of early-career researchers as they advance in their profession.

In 2022, 35,700 new preprints were posted to bioRxiv, increasing the total to 186,000, and 10,500 new preprints appeared on medRxiv, bringing its total to 40,000. The work of hundreds of thousands of scientists from 190 countries appears on the platforms and is read many million times each month.

In 2020, six-month-old medRxiv rapidly became a vital source of information about all aspects of the pandemic. Pandemic-related preprints fell by 3,000 in 2022, but those on other topics increased by 1,000 as preprints continued to gain acceptance in medicine.

In 2022, both platforms added new features for authors and readers, including the ability to read peer reviews of preprints commissioned by journals and other organizations. The platforms received continued generous multiyear funding from the Chan Zuckerberg Initiative.

Board of Trustees

The 17th annual Double Helix Medals dinner (DHMD) was held on November 9 at the Museum of Natural History in New York City. This year we honored Pfizer Chairman and CEO Dr. Albert Bourla and 2020 Nobel laureate Dr. Jennifer A. Doudna. CBS journalist Lesley Stahl returned to emcee the event, which raised a record $5.8 million for biological research. The gala was chaired by Ms. Jamie Nicholls and Mr. O. Francis Biondi, Ms. Barbara Amonson and Dr. Vincent Della Pietra, Drs. Pamela Hurst-Della Pietra and Stephen Della Pietra, Mr. and Mrs. John M. Desmarais, Ms. Elizabeth McCaul and Mr. Francis Ingrassia, Mr. and Mrs. Jeffrey E. Kelter, Dr. and Mrs. Tomislav Kundic, Mr. and Mrs. Robert D. Lindsay, Ms. Ivana Stolnik-Lourie and Dr. Robert Lourie, Dr. and Mrs. Howard L. Morgan, and Drs. Marilyn and James Simons.

Bruce Stillman and Marilyn Simons with 2022 Double Helix Honorees Albert Bourla and Jennifer Doudna.

Three trustees were elected to the CSHL Board of Trustees this year: Mark L. Claster, Tracy L. Johnson, Ph.D., and Tom Lister. Claster is Founder and Managing Partner of Carl Marks Advisors and the President of Carl Marks Securities. Johnson is Professor of Molecular, Cell and Developmental Biology, Cecilia and Keith Terasaki Presidential Endowed Chair, Howard Hughes Medical Institute Professor, and dean of the Division of Life Sciences at UCLA. Lister is a senior partner and was the co-managing partner of Permira, based in London and New York from 2008 to 2020. He has oversight of the firm's direct lending/credit business, Permira Debt Managers.

M.L. Claster

T.L. Johnson

T. Lister

The Center for Humanities and History of Modern Biology

The Center for Humanities and History of Modern Biology continued its History of Science series with two 2022 meetings.

Fifty Years of Reverse Transcriptase celebrated the discovery of reverse transcriptase 50 years ago as one of the most dramatic findings of the 20th century, for both scientific and nonscientific reasons. The discovery provided instant proof of the previously ridiculed hypothesis that retroviruses replicate through a DNA intermediate, amending a widely held dogma of genetic information flow and establishing a new paradigm of gene transfer. The unique properties of retroviruses also laid the essential technical and conceptual groundwork for defining discoveries to follow—the molecular basis of cancer, the causes of important animal and human diseases, including T-cell lymphoma and AIDS, and the rapid development of antiretroviral drugs in response to the HIV pandemic. The goal of this meeting was to bring together the researchers involved in

Fifty Years of Reverse Transcriptase Group.

these seminal discoveries, to exchange historical information and insights into what made them possible, and to provide a historical archive of a major turning point in the remarkable story of 20th-century biological science. The meeting was organized by John Coffin, Tufts University; Steve Goff, Columbia University; Anna-Maria Skalka, Fox Chase Cancer Center; Steve Hughes, National Cancer Institute; and Hung Fan, University of California, Irvine.

Celebrating the Life and Science of Sydney Brenner was a commemorative symposium about the life of the late irreplaceable and irrepressible Sydney Brenner (January 13, 1927–April 5, 2019). Brenner made countless indelible marks on the development of modern biology. From his long and fruitful collaboration with Francis Crick to crack the genetic code (among so much more), to his co-discovery of messenger RNA; and from his cultivation of the nematode *Caenorhabditis elegans* into a widely used model system, which resulted in his shared 2002 Nobel Prize in

Celebrating the Life and Science of Sydney Brenner Group.

Physiology or Medicine, to his foundational efforts in establishing the Human Genome Organization (HUGO). The meeting, which was originally scheduled for 2020, was organized by Phillip Goelet, Red Abbey, LLC; Jonathan Hodgkin, University of Oxford, UK; Barbara Meyer, HHMI/University of California, Berkeley; Mila Pollock, Cold Spring Harbor Laboratory; and Daniel Rokhsar, University of California, Berkeley.

In collaboration with the City University of New York Graduate Center, the Center for Humanities and History of Modern Biology co-hosed a CITY OF SCIENCE event: Phillip A. Sharp in Conversation with Siddhartha Mukherjee.

Molecular biologist and former CSHL faculty member Phillip A. Sharp received the 1993 Nobel Prize in Physiology or Medicine for his discovery of "split genes," which has been fundamental to medical research on the development of cancer and other diseases. Sharp is an institute professor at MIT and a member of its Department of Biology and Koch Institute for Integrative Cancer Research. He co-founded the biotech companies Biogen and Alnylam Pharmaceuticals.

Siddhartha Mukherjee, the Pulitzer Prize–winning author of *The Emperor of All Maladies: A Biography of Cancer*, is a faculty member at Columbia University Medical Center and a cancer physician and researcher. Mukherjee is also the author of *The Gene: An Intimate History* and the forthcoming *The Song of the Cell: An Exploration of Medicine and the New Human*.

Business Development and Technology Transfer

The life sciences industry faced major challenges in 2022 because of market volatility in the biotech industry, resulting in reduced interest from investors and venture capitalists in funding early-stage drug development companies. The Business Development and Technology Transfer Department pivoted its focus toward rapidly increasing new disclosures from our faculty arising from postpandemic work. We were also able to participate in a nonpharma medical-based nutrition start-up in a difficult market.

Licensing and equity revenue totaled $1.7 million, and CSHL received $0.58 million of patent reimbursement. Sponsored research booked in 2022 grew significantly to $4.1 million from multiple companies.

Early bridging finance will be even more critical to future new company formations and will benefit from the launch of CSHL and Deerfield Management's Harbor Discoveries, a unique research and development collaboration to help bring next-generation therapeutics to market. Under this partnership, Deerfield Management has committed up to $130 million over a decade to provide CSHL scientists with both funding and functional expertise to advance biomedical research.

Infrastructure

The Facilities Department undertook a variety of capital projects and investments to enhance the campus infrastructure and support scientific endeavors.

Renovations were carried out in research spaces located in the McClintock, Axinn, and Freeman buildings to meet the needs of researchers and provide them with state-of-the-art facilities. To facilitate microscopy research, a new darkroom was installed in the Beckman building.

The Delbrück course lab, utilized for educational programs and research, was upgraded to improve the functionality and aesthetics of the lab.

Planning continued for the expansion of facilities on the hillside of the Main Campus. In preparation for this expansion, a temporary parking lot and a new access road off Route 25A were constructed. The development plans include the construction of new laboratory buildings, housing facilities for the Meetings & Courses Program and visiting scientists, and additional campus parking.

In 2022, the restoration of CSHL's iconic 172-year-old seawall was completed, protecting the Laboratory and the Cold Spring Harbor area for years to come.

CSHL's new seawall is two feet taller than its predecessor. It is constructed from the same kind of heavy-duty concrete used in skyscrapers and features a facade comprised of stones from the original seawall built in 1850.

At Uplands Farms, two new high-tech growth chambers were installed. These chambers will provide researchers with highly controlled environments to conduct experiments related to plant growth and agricultural research.

Additional projects included renovations to housing at 1650 Moore's Hill Road, resurfacing the two Main Campus tennis courts, installation of permanent awnings at Bush Hall and Blackford Hall, and structural repairs to the Beckman building parking garage.

The Facilities Department also undertook important maintenance and improvement tasks that included a once-in-a-generation inspection and cleaning of the CSHL sewer force main pipe that runs for 12,915 feet from the on-site CSHL pump station to the Nassau Country sewer. The Department continued programs aimed at modernizing and improving the heating, ventilation, air

Marilyn Simons, Bruce Stillman, New York Lieutenant Governor Antonio Delgado, Empire State Development Chair Kevin Law, and State Senator James Gaughran at the Foundations for the Future groundbreaking.

conditioning, electrical, and plumbing systems throughout the campus facilities. These efforts aim to ensure a comfortable and efficient working environment for researchers and staff while promoting energy efficiency and sustainability.

Community Outreach

COVID-19 health and safety restrictions continued to limit in-person public programming at CSHL facilities. Virtual programming, the CSHL website CSHL.edu, and social media channels continued to grow the institution's engagement with broader scientific and nonscientific audiences.

Looking Forward

We are now building "Foundations for the Future," a campaign approved by the Board of Trustees to expand the Laboratory by approximately seven acres. When completed, the project will add new state-of-the-art labs, offices, and collaboration spaces to support the Laboratory's brain–body and NeuroAI initiatives. Thank you to the Board of Trustees for its forward-looking vision, and to all CSHL faculty, students, and employees for contributing to the success of this institution. With your support, we will continue to advance biology and genetics to benefit mankind.

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