

Highlights of the Year

Research

Hundreds of scientists working in Cold Spring Harbor Laboratory's 59 laboratory groups contributed to research that in 2020 was published in the world's major research journals. Their efforts reflect the full spectrum of this institution's scientific activity in Cancer, Neuroscience, Plant Biology, Quantitative Biology, and Genomics. The following is a sampling of this year's important findings.

Reward and Punishment

CSHL scientists discovered neurons in the mouse brain that help an animal learn to avoid negative experiences. The cells reside in the region that regulates motivations for behavior.

Previously, this part of the brain, known as the striosome, was thought to support our ability to learn from positive reinforcement and seek out rewards. The discovery that the same region also contributes to negative-reinforcement learning means that the striosome is a complex motivation-processing hub. Understanding its function is critical, says CSHL professor Bo Li, who led the study, because motivation processing is impaired in people with certain mental illnesses.

The cells of the striosome are defined by the chemicals they produce rather than any anatomical boundaries, which makes it difficult to study their function. Li's team identified a gene in mice called *Tshz1*. Not all neurons use that gene, so they could trace the subpopulation of neurons within the striosome that do use it. The tag allowed researchers to manipulate the cells and monitor their activity in mice.

Their experiments, done in collaboration with other CSHL scientists and researchers at Stanford University and the Howard Hughes Medical Institute's Janelia Research Campus, revealed that mice need *Tshz1*-expressing cells in the striosome to learn to associate places or sounds with an unpleasant experience. Surprisingly, those cells played no role in the animals' reward learning, a function that falls to other neurons within the striosome.

Ultimately, Li hopes, deciphering how the brain processes motivation will allow researchers to address motivation impairment in mental illness and develop better treatments.



B. Li

Painting the Brain with DNA

Neuroscientists need anatomical maps to understand how information flows within the brain, and CSHL researchers found an efficient way to do it. "Charting the cellular connections between different parts of the brain—the connectome—can help reveal how the nervous system processes information," says Longwen Huang, a postdoctoral researcher in CSHL Professor Anthony Zador's laboratory. Traditionally, creating these maps has been expensive and time-consuming.

Older methods trace neuronal pathways through their tangled connectome with a limited palette of fluorescent labels. To generate a brain-wide map, injections of fluorescent dyes must be done hundreds of times, using new research animals each time.

The method developed in the Zador lab, called brain-wide individual animal connectome sequencing (BRICseq), takes a different approach. They no longer label brain regions and their projections using fluorescent dyes: they label them using nucleotide sequences. Combining the four letters of the DNA code into short "barcodes" generates a virtually infinite



A. Zador

number of labels that can distinguish one cell from another. After labeling, researchers use DNA sequencing to analyze brain tissue segments, interpreting each recurring barcode as a signal of a cellular connection. Now, they can label a massive amount of neurons and brain regions per animal.

The research team, including former graduate student Justus Kebschull, who worked with Huang to develop the technique, reports that BRICseq accurately maps region-to-region connectivity in the brains of mice. They say the approach could be adaptable to other organisms.

Worry Yourself Awake

Scientists at CSHL and Stanford University pinpointed the circuit in the brain responsible for sleepless nights in times of stress. Their study, done in mice, ties the same neuronal connections that trigger insomnia to stress-induced weakening of the immune system.

The study connects and explains two familiar problems, says CSHL Assistant Professor Jeremy Borniger. Many people are familiar with stress-induced insomnia. In the clinical world, doctors observe that chronically stressed patients typically do worse with various treatments and diseases.

Like many aspects of the body's stress response, these effects are thought to be driven by the stress hormone cortisol. Working in the Stanford laboratory of Luis de Lecea, the research team found a direct connection between stress-sensitive neurons in the brain that trigger cortisol's release and nearby neurons that promote insomnia.

In mice, they found that signals from the hormone-releasing brain cells have a substantial effect on the insomnia-inducing neurons. Interfering with that connection enabled mice to sleep peacefully even after being exposed to a stressful situation, whereas artificial stimulation of the stress-sensitive cells instantly roused slumbering animals. Even very weak stimulation of the circuit would awaken the mice.

The same connection also has a potent effect on the immune system. Stress disrupts certain immune cells in the blood, as well as signaling pathways inside them. The team was able to recreate these changes simply by stimulating the same neuronal connections that link stress to insomnia.

Understanding this complex circuitry opens the door to a deeper understanding of the consequences of stress for both the healthy and the sick.

Brain Immune Cells

Immune cells play an unexpected role in fine-tuning the brain's neural circuits. These cells, known as microglia, not only protect the brain from infection and inflammation, they also help physically sculpt circuits in the developing brain. New research demonstrates that microglia also direct neurons to modify their own connectivity in response to sensory cues.

By birth, the architecture and wiring of the brain is mostly but not completely set. As an animal interacts with its surroundings, some neuronal connections are eliminated, whereas others are strengthened. Robust sensory experience is required for these connections to form properly.

CSHL Assistant Professor Lucas Cheadle and colleagues monitored the connections between neurons, called synapses, in a visual processing circuit in the brains of mice. Young mice need visual input at the right time to develop brain pathways related to vision. But if the mice lack visual input for a critical period, the circuits sprout too many synapses and the mice end up with abnormal connections. The team found that the circuits relied on microglia, which, with the right visual stimuli, signaled nearby neurons to prune some of the synapses.

This impact on neural connectivity represents a new role for microglia in the healthy brain and could help explain why the cells have been implicated in autism and other neurodevelopmental disorders.



J. Borniger



L. Cheadle

Cheadle will continue to investigate this interaction in more depth, tracing the molecular signals that lead to synapse disassembly as well as the changes that take place within microglia in response to environmental cues.

One-Two Cancer Punch

A team led by CSHL scientists Tobias Janowitz and Douglas Fearon, with Duncan Jodrell at the Cancer Research UK Cambridge Institute and Centre, University of Cambridge, reported on a clinical trial of a drug to expand the use of immunotherapy to more types of cancer. This study included clinical collaborators at Weill Cornell Medicine.

Immunotherapy drugs—in particular, a class called checkpoint inhibitors—leverage the body's own immune system to attack cancer cells, but the treatment does not work well on some kinds of cancers. Generally, checkpoint inhibitors work best on cancers with high levels of genetic mutation. The researchers thought cells with fewer mutations could suppress immune cells and keep them out of the tumor.

In this clinical trial, the research team interrupted the immunosuppressive pathway with a drug called plerixafor. The drug was administered continuously by I.V. for one week to 24 patients with either pancreatic cancer or colorectal cancer that had a low tumor mutational burden.

When the team analyzed patient samples, they found that critical immune cells had infiltrated the tumors during the time patients received plerixafor. The finding was encouraging because the team detected changes that have also been observed in patients whose cancers responded well to checkpoint inhibitors.

A larger clinical trial based on this study will test the effects of combining plerixafor with an approved checkpoint inhibitor.



T. Janowitz



D. Fearon

Pregnancy versus Cancer

Getting pregnant before the age of 25 reduces the risk of breast cancer by >30%. CSHL Assistant Professor Camila dos Santos discovered that in mice, breast cells do two things to protect themselves from cancer: they turn off a potent cancer gene called *cMYC*, and they keep breast cells suspended in a state of “presenescence,” a moment in the cell’s life cycle between dying, living, and potential cancer.

dos Santos says this is a rare example of a normal developmental process—pregnancy—inhibiting interaction with a cancer-promoting gene. She and her team are currently working with human breast tissue organoids to see if human cells act like those in mice. She is also transplanting mouse cells altered by pregnancy into mice that have never been pregnant to see whether the altered cells change nonpregnant ones. Pregnancy turns off the deadly *cMYC* gene by tucking it away in its chromosome and making it hard to turn on again. At the same time, another set of genes that promotes senescence is activated. Senescent cells are in a gray zone—not growing or dying. Depending on how the cells are pushed, they can either stay senescent, die, or turn into cancer cells. Cells repeat the pattern, turning on and off sections of the DNA in subsequent pregnancies.

These findings suggest new drug targets and better ways to identify risk before a tumor develops. For example, dos Santos and other researchers are exploring whether puberty or aging can prevent cancer the same way pregnancy does.



C. dos Santos

Stop Cancer from Moving

CSHL researchers found a new way to stop metastatic breast cancer cells in their tracks. CSHL Professor and Director of Research David Spector and his team disrupted filaments and contacts needed for cancer cells to crawl through the body, confining them



D. Spector

to their original tumor. The same strategy could be used to stop breast cancer spread in human patients.

In 2016, Spector and colleagues identified dozens of RNA strands that were more prevalent in breast cancer cells than in noncancerous cells of the same type. These long RNAs do not encode proteins, but are important for regulating cellular processes. Recently, the team investigated how one of these, Mammary Tumor-Associated RNA 25 (MaTAR25), impacted breast cancer cells' behavior in mice.

Kung-Chi Chang, a graduate student in Spector's laboratory, showed that MaTAR25 increases cancer cell growth and metastasis. MaTAR25 turns up use of the *tensin1* gene. The tensin1 protein helps connect the cell's internal skeleton—cytoskeleton—to its surroundings, like sticky pads on the ends of a gecko's feet. When the researchers eliminated MaTAR25, the sticky pads and stiff cytoskeleton dispersed, and the cells could not move. They designed an RNA that binds to MaTAR25 (an antisense RNA) and targets it for destruction. When injected into the bloodstream of mice, the antisense RNA reached tumor cells, decreased MaTAR25, and reduced metastases.

Spector's team found an analogous RNA in human breast cancer patients that is associated with aggressive disease. The scientists are now investigating whether an antisense RNA that targets the human version of MaTAR25 can interfere with tumor growth and metastases in patient-derived breast cancer models.

When You Do Not Know

Brain researchers are using machine learning to understand how the brain's very complicated neural networks process information. CSHL Assistant Professor Tatiana Engel and postdoctoral researcher Mikhail Genkin have some advice for those researchers: Just because the computer gives you a good predictive model does not mean it has described the system accurately.



T. Engel

Their research concerns a type of machine learning known as flexible modeling, which gives users the freedom to explore a wide range of possibilities without formulating specific hypotheses beforehand. Engel's lab has turned to such models to investigate how signaling in the brain gives rise to decision-making.

It is possible to make good predictions using wrong assumptions, Engel said, pointing to Ptolemy's model of the solar system. That ancient model could predict movements in the sky of planets and the Sun accurately, but his model placed the Earth in the center of the solar system, not the Sun.

If a model of the solar system could predict things so well and yet still be so wrong, how could Engel and Genkin be sure their model of neuronal decision-making reflected the truth? They tried fitting models to many data sets. The best models were those that were most consistent across multiple data sets. Although their approach will not work for all situations, Engel hopes that computational biologists will find more ways to test whether their models reflect underlying reality accurately.

Our Inner Heart



H. Meyer

Early in development, the human heart grows an intricate network of muscle fibers—called trabeculae—that form geometric patterns on the heart's inner surface. These are thought to help oxygenate the developing embryonic and fetal heart, but their function in adults has remained an unsolved puzzle. CSHL Fellow Hannah Meyer, along with an international team of researchers, used artificial intelligence to analyze 25,000 magnetic resonance imaging (MRI) scans of the heart, along with associated heart morphology and genetic data. The study reveals how trabeculae work, develop, and can influence heart disease.

The research suggests that the rough surface of the heart ventricles allows blood to flow more efficiently during each heartbeat, just like the dimples on a golf ball reduce air resistance and help the ball travel farther. The study highlights six regions in human DNA that affect how the fractal patterns in these muscle fibers develop. Intriguingly, the researchers found that two of these regions also regulate the branching of nerve cells, suggesting a similar mechanism may be at work in the developing brain.

The researchers discovered that the shape of trabeculae affects the heart's performance, suggesting a potential link to heart disease. To confirm this, they analyzed genetic data from 50,000 patients and found that different fractal patterns in these muscle fibers affected the risk of developing heart failure.

This project included collaborators at EMBL's European Bioinformatics Institute, the MRC London Institute of Medical Sciences, Heidelberg University, and the Politecnico di Milano. Further research on trabeculae may help scientists better understand how common heart diseases develop and explore new approaches to treatment.

Birds of a Feather

Like a modern-day Charles Darwin, CSHL Professor Adam Siepel and collaborators at Cornell University and the Herzliya Interdisciplinary Center in Israel are studying evolution in a related group of birds, the finch-like capuchino seedeaters of South America. Their studies are deepening our understanding of the forces that drive evolution.

Capuchino seedeaters have diversified from their common ancestor relatively recently. Each species has characteristic plumage and its own song. Differences are caused by lots of variations in only a few dozen hotspots in otherwise remarkably similar genomes. These small genetic "islands of differentiation" distinguish species early in their evolutionary split from one another.

Previously, Leo Campagna and Irby Lovette at Cornell determined that many of these islands affected pigment production genes. Siepel's group collaborated with Campagna and Lovette to identify additional differentiation sites and investigate their causes. Computational tools developed in Siepel's laboratory allowed his team, led by postdoctoral researcher Hussein Hejase, to compare the genomes of 60 birds from five species. They found that most of the islands of differentiation that separate today's seedeater species arose because of a form of rapid evolutionary change called selective sweeps. In this case, most changes are due to soft selective sweeps: existing variants in the population are enriched because of selective pressure—like changes of environment, a new predator, or a new food source. Siepel thinks sexual selection may also be a cause.

Siepel said that even quite striking islands of genetic differentiation can be explained by soft sweeps acting separately on newly emerging species.



A. Siepel

Research Faculty

Awards

The George W. Bush Presidential Center ranked Cold Spring Harbor Laboratory (CSHL) #1 for Patent Citations on a per capita basis among research and healthcare institutions for the productivity impact of its innovations on the U.S. economy and society.

Innovations like SPINRAZA®, the antisense oligonucleotide approved in 2016 by the FDA for spinal muscular atrophy, continue to benefit society. Professor Adrian R. Krainer received numerous accolades for work on RNA splicing and SPINRAZA®, including election to the National Academy of Sciences, the Ross Prize in Molecular Medicine, and the Innovators in Science Award.



A. Krainer



B. Stillman



R. Martienssen



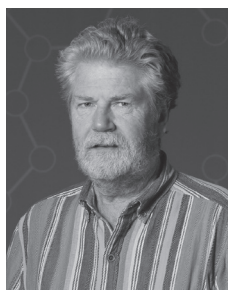
L. Joshua-Tor



Z. Lippman



D. Tuveson



D. Stewart



J. Williams

I was awarded the Dr. H.P. Heineken Prize for Biochemistry and Biophysics from the Royal Netherlands Academy of Arts and Sciences for my research on the way DNA is copied in eukaryotic cells.

Professor and Howard Hughes Medical Institute (HHMI) Investigator Rob Martienssen received the Royal Society Darwin Medal for defining the role of RNA interference in silencing genes and stabilizing the genome across generations.

Professor and HHMI Investigator Leemor Joshua-Tor was named a 2021 Fellow of the Biophysical Society for her work on the molecular basis of nucleic acid regulatory processes.

Professor and HHMI Investigator Zachary Lippman won the National Academy of Sciences Prize in Food and Agriculture Sciences for genetic studies on developing hardier crop breeds. He was also awarded the American Society for Plant Biology Charles Albert Shull Award.

Cancer Center Director David Tuveson was elected President of the American Association for Cancer Research (AACR); he and cancer geneticist Professor Michael Wigler were elected Fellows of the AACR Academy.

Historically hands-on programs were recognized for their innovations, especially during the pandemic. Meetings & Courses Program Executive Director David Stewart was elected an American Association for the Advancement of Science Fellow.

Jason Williams, Assistant Director of External Collaborations of the DNA Learning Center, won in the National Science Foundation 2026 Idea Machine Competition; he was also named a Kavli Frontiers of Science Fellow.

New Hires/Promotions

CSHL welcomed John Moses, its first chemistry professor, along with four assistant professors: neuroscientists Arkarup Banerjee, Jeremy Borniger, and Lucas Cheadle and cancer biologist Michael Lukey.

Strengthening the Laboratory's strategic affiliation with Northwell Health System, the Northwell Health Cancer Institute's Vice President and Chief Scientific Officer Jeff Boyd joined the CSHL faculty.



J. Moses



A. Banerjee



M. Lukey



J. Boyd

Education Highlights

Meetings & Courses Program

Because of the COVID-19 pandemic, no in-person meetings or courses were possible since March. Meetings quickly pivoted to a virtual format. The result was an expansion in the number and diversity of participants. More than 15,000 people participated, including more women, young investigators, and underrepresented minorities than in previous years. They attended from more than 80 countries, compared to 50 countries in the prior year. A series of three Rapid Research Reports conferences on COVID-19/SARS-CoV-2 were held from June to August, attracting nearly 500 people per conference. The fourth meeting in the series was hosted by CSH Asia in November.

The Cold Spring Harbor Asia Program in Suzhou/China suspended in-person operations in January because of COVID-19. Virtual conferences were offered later in the year, including the COVID meeting and another on single-cell genomics.

At the CSHL campus on Long Island, advanced scientific courses were offered in condensed virtual formats, including courses on ion channels, pancreatic cancer, proteomics, scientific writing, and sequencing technologies and bioinformatics analysis.



Virtual presentation

The 85th Cold Spring Harbor Laboratory Symposium was postponed until 2021.

The 2020 Nobel Prize in Chemistry laureate, Jennifer Doudna, has spoken at five Symposia (including the 2019 Dorcas Cummings lecture), many other meetings, and the crystallography course. In 2015, she was the founding organizer of the annual CRISPR meeting, which has become a central platform connecting basic and applied scientists working in the field. In previous years it attracted about 400 scientists to campus, but this year it connected a virtual community of about 750 participants from around the world.

Banbury Center

During a challenging year, the Banbury Center was able to welcome four groups to the estate before COVID-19 took hold, including a strategy meeting for a new education and mentorship program for women and minority senior scientists, an analysis of the profession of science communication and relevant gaps in training and degree programs, a critical look at gaps in precision medicine, and an examination of copper as a therapeutic target in cancer.

The Center was closed to in-person gatherings in March, and after careful consideration of virtual options, it was decided to postpone the 14 remaining meetings scheduled for 2020. The key arguments against virtual Banbury meetings were the loss of informal engagement opportunities and limited ability to ensure confidentiality with the remote format. Although scheduled meetings were not made virtual, we organized three additional virtual convenings tackling digital mental health, therapeutic targets for COVID-19, and deep-sea mining.

Despite the near shutdown of meetings, three papers were published as a result of prior Banbury meetings. Participants in the 2019 Cancer Fibroblasts & Therapies meeting collaborated on a framework, and published in *Nature Reviews Cancer*. Recommendations from 2019's Computational Psychiatry meeting were published in *Biological Psychiatry*. Finally, The Nervous System in Cancer participants produced a "Roadmap for the Emerging Field of Cancer Neuroscience," published in *Cell*.

With the suspension of in-person meetings and courses at the main campus and the Banbury Center, we took the opportunity to renovate Bush Hall; the outside of Blackford Hall; the 11 cabins, converting them to year-round accommodation; and Sammis Hall at Banbury.



Participants in a Banbury meeting returning to the conference room during a meeting conducted before the COVID-19 pandemic



Graduate students enjoying a meal together

School of Biological Sciences

The 22nd incoming class comprised two U.S. and seven international students. During the pandemic the students initially quarantined for two weeks and then moved into student housing to act as a single household. This allowed them to take the majority of their courses in person and on time.

Through 2020 the program counts 118 Ph.D. graduates. Thirty-five graduates have secured tenure-track faculty positions and two others are in independent research positions within academia. Twelve have been promoted to associate professor and two are full professors. Other graduates are in influential positions in administration, publishing, consulting, and industry.

Current students and alumni continue to win prestigious fellowships, awards, and prizes. This year, current student Danielle Ciren was awarded a Graduate Scholarship from the Natural Sciences and Engineering Research Council of Canada (NSERC), and Alexandra Nowlan was awarded a Trainee Professional Development Award from the Society for Neuroscience. To date, the students' Ph.D. research has resulted in nearly 500 publications.

Students in the 61st Undergraduate Research Program could not come to CSHL labs for hands-on research during the pandemic, whereas the Partners for the Future Program for high school students was conducted virtually.

DNA Learning Center

In February, construction began on the DNA Learning Center NYC in Brooklyn, New York. Hosted by the New York City College of Technology (City Tech), the 17,500-square-foot space will provide easy access to students and teachers throughout New York City. This project builds on the success of the Harlem DNA Lab, established in 2008 to extend the DNA Learning Center's (DNALC) services to underrepresented minorities and disadvantaged students in New York City. The Brooklyn center will also be the Genomics Hub of the InnovATE^{BIO} National Biotechnology Education Center, funded by the National Science Foundation's (NSF) Advanced Technological Education (ATE) program to support biotechnician training at two-year colleges. Under this program, the DNALC will provide course-based undergraduate research experiences (CUREs) and help launch a two-year biotech program at City Tech.



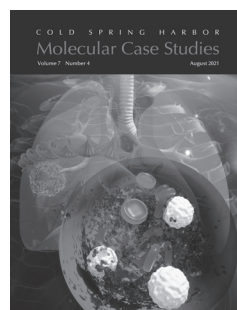
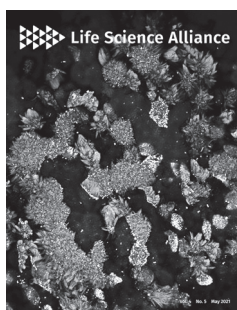
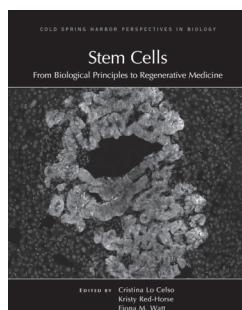
Hands-on learning went virtual.

With funding from the NSF, National Institutes of Health (NIH), and the Simons and Pinkerton Foundations, the DNALC continued to support authentic research by 458 citizen scientists, high schoolers, and college students. They studied biodiversity using DNA barcoding and metabarcoding, including a campaign to identify and track ant species across the United States.

The COVID-19 pandemic challenged the DNALC'S hands-on learning model and forced a shift to remote learning. On March 20, the DNALC launched "DNALC Live," posting more than 120 live events and videos to YouTube to stand in for laboratory field trips. An animation explaining RNA-based testing for COVID-19 was frequently accessed. Over the ensuing two-month quarantine, YouTube views more than doubled, and new subscribers and watch time more than tripled. The DNALC also pivoted to virtual instruction supported by "at-home" kits, with 484 students attending virtual camps in the summer and 2,673 attending virtual field trips in the fall.

Cold Spring Harbor Laboratory Press

CSHL Press publishes nine journals and 275 books. In 2020, despite the pandemic challenges and working from home, its staff produced all journal issues on time, added eight new books, and enabled the Press to make its largest ever financial contribution to the Laboratory. For more than a decade, the four long-established research journals, *G&D*, *Genome Research*, *RNA*, and *Learning & Memory*, have combined subscription access with open access for individual papers paid for by authors or their funders. A transition toward full open access began with a first institutional



consortium financial contract to support free reading and publishing for the institutions' faculty members. Further contracts are in negotiation, with the goal of eliminating subscriptions for all four journals within five years. The two newest research journals, *Cold Spring Harbor Molecular Case Studies* and *Life Science Alliance*, were launched as open access. Both had increased submissions in 2020. The three review journals, *CSH Protocols*, *CSH Perspectives in Biology*, and *CSH Perspectives in Medicine*, will remain subscription-based. Online usage of Press journals remained strong, with a 5% increase to more than 19.8 million article downloads in the year.

COVID-19 hastened the shift to online delivery of books and e-books, and direct sales through the Press website accounted for 25% of all book sales. The best sellers were John Hawkins' biography, *Conscience and Courage: How Visionary CEO Henri Termeer Built a Biotech Giant and Pioneered the Rare Disease Industry*, and Carl and Suzanne Cohen's *Lab Dynamics: Management and Leadership Skills for Scientists*.

Preprints in Biology and Medicine

A preprint is a research manuscript distributed by its authors before publication in a journal. The Laboratory has two preprint servers, bioRxiv for life sciences, launched in November 2013, and medRxiv for health sciences, launched in June 2019 in partnership with Yale University and BMJ, the global health information provider. In 2020, bioRxiv posted more than 38,000 preprints, 13% more than in the previous year. The entire repository of 107,000 manuscripts had 87 million page views and 33 million article downloads. Having posted 900 preprints in its first six months, medRxiv posted 14,000 in 2020. Its content had 61 million page views and 27 million article downloads in 2020.

Both platforms were among the world's most important channels of research on SARS-CoV-2 and COVID-19. Pandemic preprints were 68% of medRxiv's content, cited 70,000 times in journal papers, and covered in 30,000 news stories. The platforms distributed more than 12,000 pandemic-related preprints on topics as diverse as the virus's genome sequence, the spike protein's structure, potential intracellular drug targets, clinical trials of therapeutics, vaccine development and efficacy, serological tests, and viral variants.

To help medRxiv manage the deluge of submissions, the Chan Zuckerberg Initiative generously provided a \$2 million grant in June, enabling the addition of three staff members to the content, product, and development teams that support the servers. These teams and the founders showed unyielding dedication to the urgency of information sharing at a time when the world needed scientific insights into a health crisis as never before.



CHAN
ZUCKERBERG
INITIATIVE

Board of Trustees

We are grateful to supporters who contributed a record \$8 million to CSHL in 2020. The 15th Double Helix Medals, which was a virtual event this year, raised \$4.4 million. It was chaired by Ms. Jamie C. Nicholls and Mr. O. Francis Biondi, Jr., Drs. Marilyn and James Simons, Mr. and Mrs. Robert D. Lindsay, and Mr. and Mrs. Paul Taubman. Host Lesley Stahl explored COVID-19 with George Yancopoulos, a CSHL trustee and the founding scientist, president, and chief scientific officer of Regeneron. "CSHL is one of the most unique science environments in the world, bringing people together," Yancopoulos said. It is clear to me that the staggering effects of COVID-19 compelled CSHL scientists to join together with the scientific community and apply our expertise.



G. Yancopoulos

Library and Archives

A new initiative is the Center for Humanities & History of Modern Biology within the CSHL Archives. It received a grant from the National Endowment for the Humanities to support "Oral



The 2016 HIV/AIDS research history conference.

Histories of Biology, Medicine, and Pandemic Response,” including the creation of annotated transcripts of the 2016 HIV/AIDS research history conference held at CSHL. Readers can follow the expert talks, including links to the literature and highlighted scientists. Library and Archives Executive Director Mila Pollock describes the history of the HIV/AIDS crisis as a “mirror to what’s happened today.”

Business Development & Technology Transfer

The Business Development & Technology Transfer team was impacted dramatically by slowing of scientific work at CSHL and external investment in new initiatives being delayed because of the pandemic. However, the focus on faculty projects to address COVID-19 and our investment in building industry relationships enabled us to push ahead with multiple high-value deals during the year.

Licensing and equity revenue received totaled \$3.2 million and was supplemented by \$0.45 million in patent expense reimbursement. Sponsored research funding more than doubled to \$1.3 million negotiated under agreements managed by the team.

Positioning around “Business and Innovation,” the department continues working to partner scientists with companies and investors, bringing CSHL discoveries to the public domain through intellectual property and licensing know-how, industry (as well as academic) collaborative research, and new ventures. As a result, in 2020, major new companies were formed utilizing CSHL technology including Cajal Neuroscience (Tony Zador) and Mestag Therapeutics (David Tuveson).



**Mestag
Therapeutics™**

Infrastructure

We expanded research facilities at the Woodbury Genome Center, building a new 2,200-square-foot facility to cultivate small, functional organoids for cancer research and clinical applications. The facility is funded by TD Bank, Wasily Family Foundation, and F.M. Kirby Foundation, and received a multiyear operating grant from the Fidelity Foundation.

A new 2,500-square-foot greenhouse was also completed at the Woodbury Genome Center in June 2020.

In the Demerec Laboratory, the 2,500-square-foot laboratory of chemist John Moses was completed and occupied in November.

Additional postdoc office space, two conference rooms, and collaboration space in the Marks Annex were completed and operational in July.



Greenhouse at the Woodbury Genome Center

Construction began on the DNA Learning Center at City Tech, in collaboration with the City University of New York. The 17,500-square-foot facility is in the Pearl building at the CUNY City Tech campus in Brooklyn. Construction activities will continue into mid 2021. Programs at the new facility begin in 2021.

We embarked on a project to revitalize the 11 cabins on the main campus that house Meetings & Courses visitors. Renovation planning and design activities began in late 2020 and construction activities will begin mid 2021, with completion toward the end of 2021.

Looking to the future, we began planning a project to expand the facilities on the hillside of the main campus. The initial plans call for new laboratory buildings, housing for Meetings & Courses and other scientific visitors, and additional campus parking.

Airslie House renovations were completed in July 2020.

The Laboratory also continued its program of modernizing and improving the heating, ventilation, air conditioning, electrical, and plumbing systems throughout its facilities.

Community Outreach

CSHL Public Presentations

January 6: Screening and discussion at Cinema Arts Centre in Huntington Co.; *Jim Allison—Breakthrough*; postscreening discussion with **Bruce Stillman, Ph.D.**, President & CEO, Cold Spring Harbor Laboratory; co-presented by Cold Spring Harbor Laboratory and Cinema Arts Centre as a Science on Screen event.

May 27 (Virtual Event): **Siddhartha Mukherjee** discusses *The Gene: An Intimate History* in conversation with **Matthew Cobb**; moderated by **Richard Sever, Ph.D.**; presented by the Center for Humanities and the History of Modern Biology at Cold Spring Harbor Laboratory.

June 19 (Virtual Event): Nobel laureate **Richard Roberts**, “Why you should love GMOs”; followed by a discussion with Professor **Pamela Ronald** from UC Davis; moderated by **Rob Martienssen, Ph.D.**; presented by the Center for Humanities and the History of Modern Biology at Cold Spring Harbor Laboratory.

July 24 (Virtual Event): Live @ the Lab with **David Tuveson, M.D., Ph.D.**; moderated by **Rebecca Leshan, Ph.D.**

August 17 (Virtual Event): Panel discussion: Human Nature, with **Jennifer Doudna, Ph.D.**, biochemist and leading genomics researcher; **Alta Charo**, bioethicist; **Zachary Lippman, Ph.D.**, CSHL plant biologist; and **Elliot Kirschner**, Executive producer and moderator.



October 1 (Virtual Event): Live @ the Lab with **Partha Mitra, Ph.D.**; moderated by **Eliene Augenbraun, Ph.D.**

November 2 (Virtual Event): Live @ the Lab with **Patricia Churchland** about her book, *Social Conscience*; moderated by CSHL President, **Bruce Stillman, Ph.D.**; 2020 Lorraine Grace lecture-ship on societal issues of biomedical research.

November 18 (Virtual Event): Live @ the Lab with **Camila dos Santos, Ph.D.**; moderated by **Phil Renna**.

CSHL Public Concerts

The annual program was canceled because of the pandemic.

Science Walking Tour Program

Our graduate student tour guides led five group tours (81 guests) before we suspended the public tour program because of the pandemic.



Looking Forward

For the third year in a row, CSHL was ranked by *Newsday* as one of Long Island's Top Workplaces. The anonymous employee surveys of employers across Long Island were analyzed by a third party.

Thank you to our faculty, students, and employees who kept our campus community safe and productive during the COVID-19 pandemic. I am optimistic about the future and the Laboratory's ability to thrive as we emerge from this global health crisis and make progress on preparedness for future challenges. With your support, we will continue to advance biology and genetics to benefit mankind.

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