A Message From Our President

The events of the past few years have made clear that knowledge coming from fundamental research is essential to solve the ills that afflict us and to advance our economy. As we look to the future, CSHL has identified specific areas of study that will be crucial for the betterment of human health including Alzheimer's disease, mental illness, and cancer through a whole-body perspective and improving artificial intelligence by understanding brain circuits. Our $350 million Foundations for the Future Campaign seeks to raise vital support for these transformative programs by adding new research space, recruiting faculty and providing research endowment funds.

Scientific research is not done in isolation and a major and fundamental part of our expansion is CSHL's Meetings and Courses program. Scientists from throughout the world gather at CSHL to explore the latest research and to learn from each other. This globally-renowned program has contributed to many great successes in science including the Human Genome Project.

Biology and genetics research has thrived at CSHL for over 130 years. Our cross-disciplinary, highly collaborative environment has encouraged ambitious science, resulting in a long history of impactful discoveries. Funding from private, visionary philanthropy has been essential — ambitious but high risk science is not well served by Federal grant mechanisms. Philanthropic support has not only made this innovative research possible but it has also allowed it to happen much faster.

While we cannot predict the future, we must prepare for it. An investment in CSHL's research and educational programs will help to ensure that science is ready to tackle whatever the future holds.

~ Bruce Stillman

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Foundations For the Future

LET'S BUILD IT TOGETHER

CSH Cold Spring Harbor Laboratory

Leadership Matters when Charting New Frontiers

Cold Spring Harbor Laboratory (CSHL) is an outstanding research and innovative educational institution. Supporting CSHL is important because we need basic science research to advance our knowledge. Most of us see the end product of scientific research, but it is that fundamental understanding, those breakthroughs, that make the difference.

I have seen firsthand the impact that CSHL research has made on autism. Whether it be for the betterment of patients with Alzheimer's disease, depression, bipolar disorder or anxiety, there is so much potential in understanding how the brain works.

We are the guardians of this institution and we will continue to foster CSHL so that future generations will have better lives and a bright future. I am very proud to be associated with an institution that is making such a difference in the world.

Marilyn Simons, CSHL Board Chair

Biology is the science that is determining the future of humankind. From fundamental molecular biology and genetics, to understanding cognition and the brain and then curing diseases—it seems to me that we are standing on the shores of a gigantic ocean of discoveries to come.

CSHL is a special place where research is purposely unfettered, collaboration is encouraged and there is a recognition of the importance of translating fundamental research into clinical applications, directly helping patients.

This is the most exciting aspect of our Foundations for the Future Campaign, blending fundamental discovery research, such as the study of neuroscience, along with more applied research into cancer, Alzheimer's and other diseases. Support of CSHL means support for basic knowledge, to improve, and even save lives.

Robert Lourie, Campaign Chair

World Leader in Genetics and Molecular Biology

- Founded 1890 – Birthplace of Molecular Biology
- 1st institution in the country to conduct genetics research
- 8 Nobel Prize Winners
- Focus on Young Scientists, No Tenure
- Prestigious National Cancer Institute designation since 1987
- Human Genome Project Planned at CSHL
- Ranked #1 in the world for Global Scientific impact by the respected journal Nature

Pictured above: Foundations for the Future expansion rendering.

Scientific Innovation in a Beautiful Setting

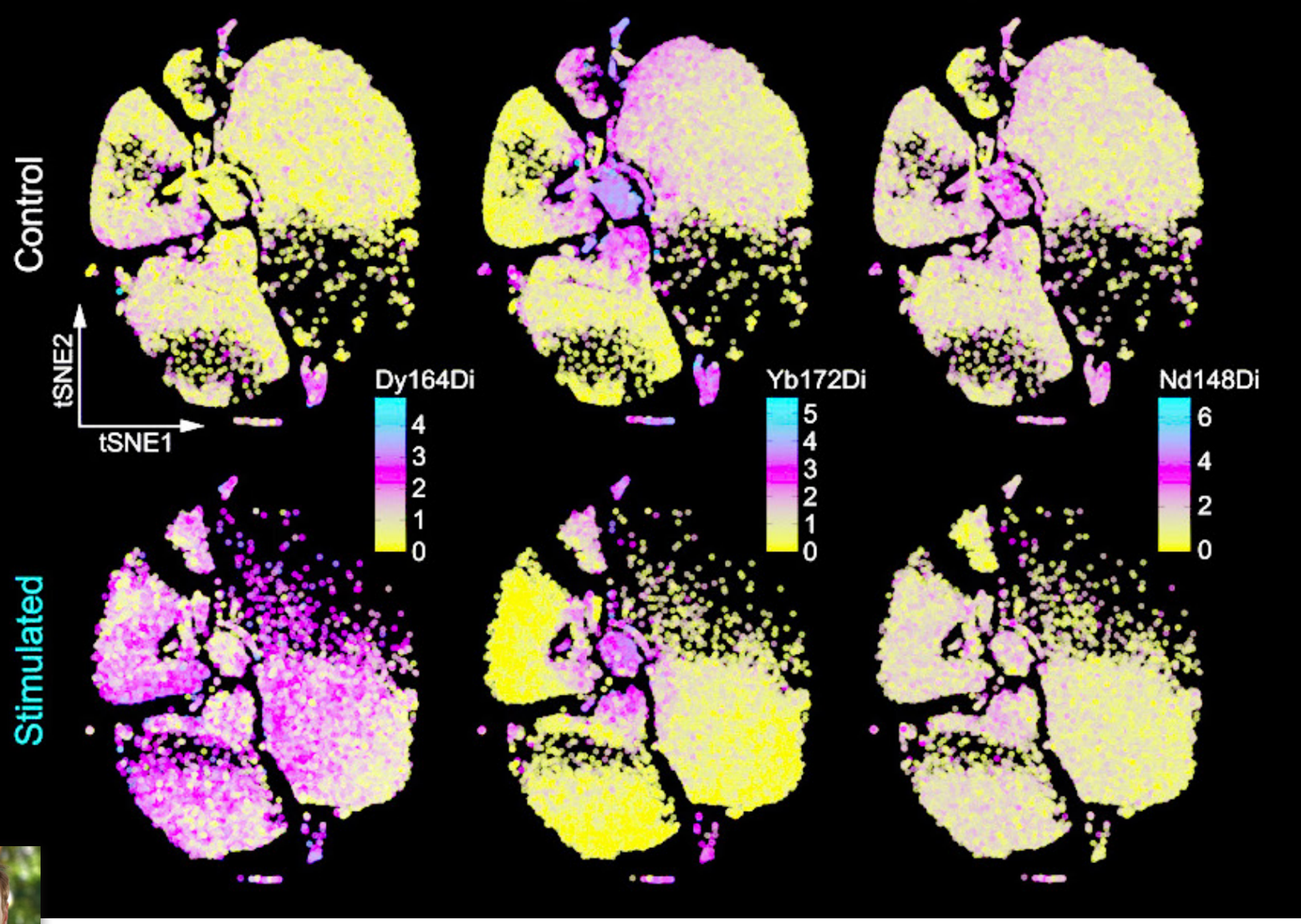
CSHL is one of the world's leading centers for biomedical research. For over 130 years, our scientists have made many significant discoveries that have advanced knowledge and brought about a deep understanding in areas as diverse as cancer, identifying the first cancer gene, uncovering genetic changes that give rise to autism, the functioning of the brain, and mathematical approaches to biology. CSHL was the site of the initial discussions leading to the Human Genome Project, the Innocence Project and the BRAIN initiative, all of which have had a transformative impact on science and society.

A key component of CSHL's worldwide influence is its role as a global hub for the exchange and critical assessment of research. The advanced training course programs have taught many of today's leading scientists new experimental techniques, while the scientific conferences have been the venue for the announcement of ground-breaking research. The combination of research of the highest level and communication among the world's scientists make CSHL a unique and collaborative institution.

The initiatives described here present an integrated approach that builds on CSHL's strengths, its world-class research and the essential part it plays in communicating the fruits of discovery. The research programs are directed at some of the most challenging problems facing society, including tackling Alzheimer's and Parkinson's disease, the impact of cancer on our body's physiology, advancing artificial intelligence (AI) by building on understanding of how our natural intelligence develops, and on Quantitative Biology, developing new mathematical and computational approaches essential for progress. Enhancing CSHL's mission to promote research worldwide through our meetings is an essential part of this initiative.

I have been associated with meetings and courses at CSHL for over 50 years. It is hard to think of any intellectual site that has had a greater impact on the growth of neuroscience.

~ Eric Kandel, 2000 Nobel Prize

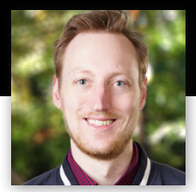


Brain-Body

Cancer has been the subject of intensive research for over a century and while there have been some spectacular successes, it remains the second deadliest killer in the USA. It is clear that a revolutionary new approach is needed. To focus solely on the cancer cell or tumor does not tell us about the many diverse symptoms a cancer patient suffers.

We are exploring a neglected facet of cancer, that a tumor has body-wide impact on the patient, affecting many organ systems simultaneously. Additionally, there are reciprocal interactions between tumors with the tumor-bearing host; in breast cancer, disturbed sleep patterns have been linked to hormones that control wake and sleep phases, and in clinical studies of patients with breast cancer, disturbed sleep patterns have been linked to worsened outcome.

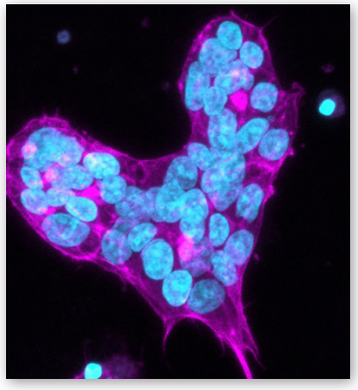
Pictured above: Active "insomnia" neurons suppress immune system impairing its anti-cancer protection, Borniger lab.



Jeremy Borniger
An entire new field is emerging to understand the interplay between cancer, the brain and the body. Trained as a neuroscientist, Jeremy's research into sleep/wake cycles in the brain led him to question why cancer patients have unusual sleep patterns, not to mention changes in appetite, circadian rhythms, cognitive function, and pain, which reduce odds of survival. Jeremy aims to uncover mechanistic interactions between the brain and cancer that drive these phenomena.

Our scientists are investigating these interactions by focusing on three specific areas: the interaction of the tumor and the host neuro-endocrine system; the interaction of the tumor with the host immune system; and the interaction of the tumor and the host microbiome, the bacteria that colonize our bodies.

Our approach of hypothesis-driven experimentation using animal models combined with validation in samples from patients, will generate large data sets that will be analyzed to reveal the interconnectivity of the complex whole-body response pattern to cancer. The results will feed into CSHL's highly translational clinical research program, leading, we believe, to new treatment strategies for cancer patients.



Semir Beyaz uses organoids, 3-D human organ-like structures, to study how nutrition and obesity affect cancer risk. Pictured is an organoid of a very aggressive human cancer from the uterus, the organ with the highest risk of developing cancer in obese women.

Cold Spring Harbor is a mecca. People go to CSHL almost as a religious experience. It's a center for scientific research and it's a world center for communicating science.

~ Bob Horvitz, 2002 Nobel Prize

NeuroAI

While we have invested extraordinary resources in exploring the wonders of the external universe, there is an even more wondrous and unexplored internal universe - the human brain.

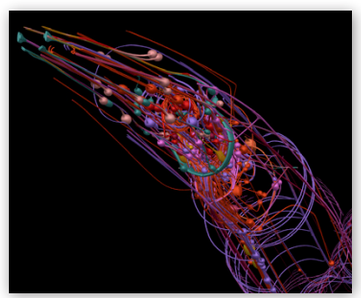
One approach to understanding how our intelligence arises is to model the brain, an approach made possible by recent startling advances in the power of artificial neural networks in computer science. However, even though artificial intelligence (AI) systems can beat human beings at chess and Go, they cannot approach the abilities of simple animals. Behaviors that seem effortless to the ant turn out to be deceptively challenging and out of the reach of even the most powerful AI system.

Pictured above: Color patterns visualize sets of genes lighting up in a brain section, Zador lab BARseq2 technology.

Tony Zador
Exploring the brain like a modern day Magellan, Tony Zador has charted new territory by spearheading technologies that map the activation of thousands of neuronal networks. Tony harnessed the power and scale of DNA sequencing technology and applied it to uncover the roadmap to the billions of neurons in the brain, and how this signaling could go awry in disease. Exploring another great frontier, Tony and his colleagues are utilizing his expertise in neuroscience to circumnavigate discoveries in artificial intelligence or NeuroAI.

There is growing skepticism that simply scaling up current systems will suffice to match the intelligence of a mouse, let alone that of a human being. Instead, we propose that neuroscience will provide the crucial insights essential for the next generation of AI, and that these insights will come from examining the profound ways in which animal brains differ in their operation from artificial neural networks. Recognition of these differences might lead to new artificial systems (NeuroAI) that interact more effectively and efficiently with the real world, and which learn more quickly and robustly.

CSHL's strengths in neurobiology, innovative computational systems and circuit neuroscience, combined with the skills of our scientists in the Simons Center for Quantitative Biology, puts CSHL in an ideal position to develop the new field of NeuroAI.



CSHL NeuroAI Scholar Nikhil Bhattasali develops an algorithm that figures out on its own how to make a digital worm swim using only about two dozen artificial neurons to calculate motions.

I came to Cold Spring Harbor Laboratory as a young postdoc and found an extraordinary research community. The highest level of research combined with access to all the meetings and courses, made CSHL the perfect place for me and many other young scientists.

~ *Carol Greider, 2009 Nobel Prize*

Alzheimer's Disease

Alzheimer's disease (AD) is a devastating disorder, robbing loved ones of their memories and their life. The molecular pathology of AD has been studied for many years and abnormal structures – amyloid plaques and neurofibrillary tangles – and the proteins they contain — have been identified in brain cells. However, despite immense effort, this knowledge has not led to effective therapies. New approaches and strategies are needed and the CSHL Alzheimer's Disease Program proposes a three-pronged approach to developing therapeutics based on discoveries made by our scientists.

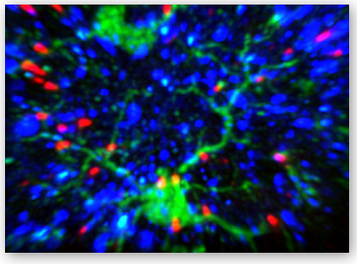
The first is focused on two proteins which our scientists have been investigating and are promising therapeutic targets for AD. We have shown that inhibiting an intracellular signaling protein ameliorates the memory deficits in a mouse model of AD and the Program will continue to optimize such inhibitors. The second class of proteins are receptors involved in communications between nerve cells. Here, we will enhance the activity of those receptors that are protective and inhibit those that promote neurodegeneration.

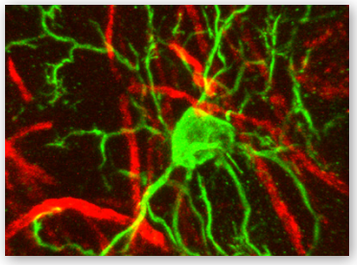
The second approach will explore the neglected role in AD of microglia, the immune cells of the brain. The goal is to identify molecular changes in these cells before symptoms are evident, providing new targets for therapies.

In the third approach we will study an unexplained feature of AD, namely that women are at a significantly increased risk of AD. Estrogen is neuroprotective and, having identified estrogen receptors in the brain, we will study the molecular changes in the brain brought about by the decline in estrogen as women age, revealing new therapeutic targets.

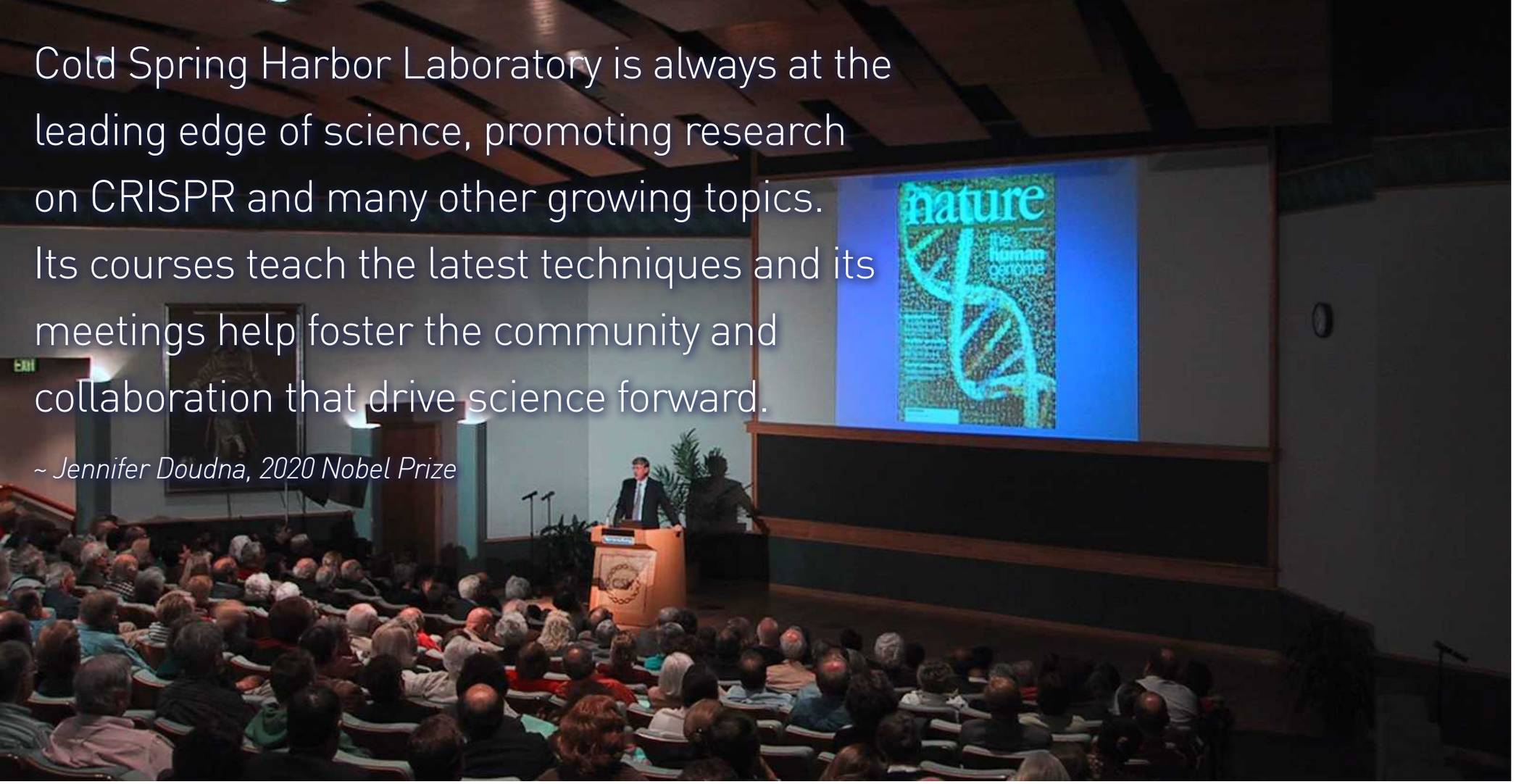
Jessica Tollkuhn
Intractable diseases like Alzheimer's require new thinking and approaches. Jessica Tollkuhn studies diseases that have sex-specific biases and was intrigued by the fact that two-thirds of all Alzheimer's patients are women. Last year, Jessica and her collaborators had a groundbreaking discovery, the first group in the world to find genes in the brain directly regulated by estrogen receptors. With this important breakthrough, Jessica hopes to find new estrogen targeted therapies to benefit women with Alzheimer's disease.

Pictured above: Estrogen responsive genes glow red in mouse brain, Tollkuhn lab.





Lucas Cheadle is investigating microglia, the brain's immune cells (shown in green) and how they transition from supporting connections between neurons to deconstructing them, leading to cognitive decline in Alzheimer's disease.



Cold Spring Harbor Laboratory is always at the leading edge of science, promoting research on CRISPR and many other growing topics. Its courses teach the latest techniques and its meetings help foster the community and collaboration that drive science forward.

~ Jennifer Doudna, 2020 Nobel Prize

Meetings and Courses

CSHL is a unique institution combining its world-class research with its role as a global hub for the exchange and critical assessment of research findings and advanced training of the next generation of scientists. CSHL's meetings program began in 1933 followed by the first advanced course in 1945. Both programs continue to the present day, with 45 meetings and over 35 courses annually (attracting more than 12,000 participants). The meetings have been the venue for the announcement of many important findings, including in 1953 the first public presentation of the double helical structure of DNA. It is a measure of the esteem in which the meetings are held that over 100 Nobel laureates have participated in them. Just as importantly, the meetings prioritize the participation of young scientists, many of whom give their first scientific talk at a CSHL meeting.

The CSHL Courses are famed for providing intensive training in the latest experimental techniques, such as CRISPR, often taught by the scientists who developed them. Students in the courses range from graduate students learning techniques that they will employ for their PhD research, to senior scientists wanting to change fields. Ten course alumni have gone on to win Nobel Prizes, and several credit the courses they took at CSHL with their future success. CSH Asia, based in Suzhou, China, and now in its second decade of operation, provides similar scientific exchange and training programs to connect the rapidly growing Asia-Pacific biomedical research community.

Pictured above: Francis Collins discusses the societal impact of the Human Genome Project, 2003 CSH Symposium.

Since 1933, important advances in biology have been announced, debated, and distilled at the CSH Symposia. Scientists discuss unpublished research at the 2019 Symposium on RNA Control & Regulation.

The informal interactions between meeting participants and between course students are essential to the success of these programs. Much can be said and learned in casual conversations outside the lecture hall or laboratory, especially by young scientists who are able to establish connections with senior colleagues. However, many participants miss out on these interactions because they are obliged to stay in remote locations far from the CSHL campus. We intend to significantly improve and expand the conference center infrastructure on campus, so that many more scientists can stay on-site, within walking distance of all conference facilities.

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