Founded in 1890, CSHL is a preeminent international research institution achieving breakthroughs in molecular biology and genetics and enhancing scientific knowledge worldwide.

**FACTS & FIGURES**

- Home to eight Nobel laureates, including Barbara McClintock, discoverer of “jumping genes”
- National Cancer Institute-designated Cancer Center
- Test facility delivers drug candidates to biotech industry
- Incubator for more than 25 biotechnology start-ups
- Highest rating from Charity Navigator

Annual operating budget $180 million
Endowment $600 million
Research laboratories 54
Postdoctoral fellows 150
Graduate students 100
Total employees & students 1,100
Annual Meetings & Courses attendees 12,000
Annual DNA Learning Center program participants 45,000

**EDUCATION**

CSHL is recognized as a pioneer in science education, training professional scientists, students and teachers:

**Watson School of Biological Sciences**: trains the next generation of scientists through an innovative Ph.D. program that fully funds the doctoral research of each student.

**Meetings & Courses Program**: attracts 12,000 scientists annually from around the world to learn the latest technologies and share advances in biological research.

**Banbury Center**: a think-tank that convenes global experts to guide science and public policy.

**DNA Learning Center**: produces web-based multimedia tools, presently delivers 33,000 hands-on learning experiences to middle and high school students each year, and trains teachers; over 643,000 students have been taught since 1988.

**CSHL Press**: publishes authoritative materials for the global scientific community, with journals, books and manuals used in over 2,000 academic institutions worldwide.

**CANCER**

Understanding fundamental cellular processes that are the basis of life, and how they go wrong in cancer. Improving diagnosis and treatment of all major cancers: brain, breast, colon, leukemia, lung, lymphoma, melanoma, ovarian, pancreatic, and prostate.

**GENOMICS & QUANTITATIVE BIOLOGY**

Using cutting-edge technology to read the genome of organisms, tumors, or even single cells. Creating innovative data analysis tools to develop disease diagnostics and therapeutics.

**PLANT BIOLOGY**

Investigating the mechanisms of plant development and genetics. Improving crop yields, increasing biodiversity, and developing biofuels.

**NEUROSCIENCE**

Exploring the brain to identify the neural networks involved in sensory processing, cognition, and decision-making. Providing insight into disorders such as Alzheimer’s, autism, schizophrenia, bipolar disorder and depression.

**RESEARCH FUNDING BY SOURCE**

- **FEDERAL**: 48%
- **PRIVATE**: 29%
- **ENDOWMENT**: 22%
- **CORPORATE**: 1%

In this Faculty Guide, Cold Spring Harbor Laboratory (CSHL) proudly features our primary investigators. The Laboratory’s 125+ years are rich with discoveries in biology and genetics that have had major impacts on society in human health, agricultural production, and the environment. Grounded in basic research, CSHL’s multi-disciplinary approach to cancer, neuroscience, genomics, quantitative biology and plant biology continues to enhance our understanding of life.
2019 CRISPR technology is used to make small changes to regions of DNA adjacent to genes regulating traits important to yield of tomatoes.

2016 FDA approves Spinraza®—a drug based on CSHL insights into alternative RNA splicing—used to treat spinal muscular atrophy (SMA), a childhood neurodegenerative disease.

2016 Clinical Trial initiated on a PP2 inhibitor for treatment of metastatic breast cancer.

2015 FDA approves breast cancer drug that works on cyclin D-dependent kinase, based on CSHL insights into the role of cyclin D in cancer progression.

2014 Toolkit of plant gene variations is developed, allowing breeders to maximize yield of tomato and other crops.

2011 Drug target discovered for lethal form of acute myeloid leukemia (AML).

2011 First genomic profiling of single cancer cells completed.

2007 Exome sequencing developed—the most common tool for identifying genetic mutations in disease.

2007 Link identified between spontaneous genetic mutations and autism.

2002 shRNA technology developed to switch on and off any gene in a cell.

1994 Process of genome replication recreated for first time in test tube.

1992 Damage to ends of chromosomes (telomeres) linked to cell aging.

1988 Cancer-causing genes shown to interact with cancer-suppressing genes, overriding signals that keep cell growth in check.

1982 First human cancer-causing "oncogene" identified.

1977 Discovery that genes can be discontinuous or "split" reveals RNA splicing mechanism, an essential process for editing and communicating genetic information.

1962 DNA revealed as genetic material in bacteriophage.

1951 "Jumping Genes" discovered in plants, proving that genomes are subject to rearrangement.

1945 War-time penicillin production significantly increased by isolation of better strain of penicillium.

1933 Prolactin (a hormone for milk secretion) identified and purified.

1929 ACTH, a key hormone produced by the pituitary gland, is isolated, benefiting Addison disease patients suffering from insufficient steroid production.

1908 Modern agriculture revolutionized by discovery of hybrid vigor in corn.

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PRACTICAL APPLICATIONS OF RESEARCH

Cancers

**BREAST**
Camila dos Santos
Mikala Egeblad
Adrian Krainer
Alexander Krasnitz
David Spector
Bruce Stillman
Nicholas Tonks
Michael Wigler

**CARCINOID TUMORS**
David Tuveson

**ESOPHAGEAL**
W. Richard McCombie

**HOST-TUMOR INTERACTIONS**
Tobias Janowitz

**HUMAN PAPILLOMAVIRUS (HPV) | CERVICAL**
Leemor Joshua-Tor
Anne Stenlund

**LEUKEMIA**
Bruce Stillman
Christopher Vakoc

**LYMPHOMA**
Christopher Vakoc

**MEDULLOBLASTOMA**
Linda Van Aelst

**MELANOMA**
Molly Hammell

**MYELODYSPLASTIC SYNDROME (MDS)**
Lingbo Zhang
Adrian Krainer

**OVARIAN**
Alexander Krasnitz
Nicholas Tonks

**PANCREATIC**
Mikala Egeblad
Douglas Fearon
Je Lee
Darryl Pappin
David Tuveson

**PROSTATE**
Lloyd Trotman
Michael Wigler

**SARCOMA | RHABDOMYOSARCOMA**
Robert Maki
Christopher Vakoc

**ADDITION**
Adam Kepecs

**ALS/LOU GEHRIG’S DISEASE**
Molly Hammell

**ALZHEIMER’S DISEASE**
Hiro Furukawa

**AUTISM**
Josh Huang
Ivan Iossifov
Adam Kepecs
Alexander Krasnitz
Dan Levy
W. Richard McCombie
Alea Mills

**ANEMIA**
Lingbo Zhang

**BIOFUEL**
Robert Martienssen

**CHILD DEVELOPMENT**
Jessica Tollkuhn

**CROP YIELD**
David Jackson
Zachary Lippman

**DIABETES | OBESITY**
Nicholas Tonks

**EEC SYNDROME**
Alea Mills

**GENOMIC TECHNOLOGIES**
Je Lee
W. Richard McCombie

**IMAGING TECHNOLOGIES**
Florin Albeanu
Mikala Egeblad
Pavel Osten
Partha Mitra

**INFERTILITY**
Alea Mills

**STRUCTURAL BIOLOGY**
Hiro Furukawa
Leemor Joshua-Tor

**ADDICTION**
Adam Kepecs

**DEMENTIA/FTD**
Molly Hammell

**DEPRESSION**
Hiro Furukawa
Adam Kepecs
Bo Li
W. Richard McCombie

**PTSD | ANXIETY**
Bo Li

**RETT SYNDROME**
Hiro Furukawa
Josh Huang

**Neuro-related**

**STEPHEN SHEA**
Nicholas Tonks

**SCHIZOPHRENIA**
Hiro Furukawa
Josh Huang
Adam Kepecs
Bo Li
W. Richard McCombie
Pavel Osten

**SPINAL MUSCULAR ATROPHY**
Adrian Krainer

**OTHER**

**ANEMIA**
Lingbo Zhang

**BIOFUEL**
Robert Martienssen

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MEET OUR FACULTY

Florin Albeanu | NEUROSCIENCE
How does the brain encode stimuli from the outside world to give rise to perceptions? What does a smell look like in the brain? The focus of my group is to understand how neural circuits compute sensory-motor transformations across different contexts, senses, and brain states to generate meaningful behaviors.

Gurinder Atwal | QUANTITATIVE BIOLOGY
The biological landscape is made up of millions of variables that interact in complex and often seemingly random ways. I am applying principles from physical and computational sciences to the study of biology to find patterns in these interactions, to obtain insight into population genetics, human evolution, and diseases including cancer.

Semir Beyaz | CANCER
Are you really what you eat? Our goal is to uncover the precise mechanisms that link nutrition to organismal health and disease states at the cellular and molecular level. A particular focus in our lab is to understand how dietary perturbations affect the immune system and contribute to the risk of diseases that are associated with immune dysfunction such as cancer.

Anne Churchland | NEUROSCIENCE
Animals are faced with many decisions. They must integrate information from a variety of sources—sensory inputs like smell and sound as well as memories and innate impulses—to arrive at a single behavioral output. My laboratory investigates the neural circuits that underlie decision-making.

Alexander Dobin | GENOMICS
Next-generation sequencing technologies have revolutionized genetics and molecular biology, enabling quantitative analyses of entire genomes and paving the way for Personalized Medicine. My lab leverages Big Genomic Data and develops statistical methods and computational algorithms to approach problems in precision health, such as genetic and epigenetic mechanisms of cancer development.

Camila dos Santos | CANCER
Among the changes that occur during pregnancy, those affecting the breasts have been found to subsequently modify breast cancer risk. My laboratory investigates how the signals present during pregnancy permanently alter the way gene expression is controlled and how these changes affect normal and malignant mammary development.

Mikala Egeblad | CANCER
Cancer cells are surrounded by immune cells, blood vessels, chemical signals and a support matrix—collectively, the tumor microenvironment. Most micro-environments help tumors grow and metastasize, but some can restrict tumors. My lab studies how to target the bad microenvironments and support the good ones to combat cancer.

Tatiana Engel | NEUROSCIENCE
My lab investigates how perception and cognition arise from changes in neural activity. We develop and apply computational methods to discover dynamic patterns in large-scale neural activity recordings. We then create mathematical models to explain how these activity changes emerge from signaling between neurons, ultimately driving behavior.

Douglas Fearon | CANCER
I’m studying how to harness the power of the immune system to fight cancer. Our underlying premise is that the microenvironment within a tumor suppresses the immune system. We have found a way to eliminate this suppression in the mouse model of pancreatic cancer, which has led to development of a drug for human pancreatic cancer.

Hiro Furukawa | NEUROSCIENCE
The nervous system transmits information by passing chemical signals from one nerve cell to the others. This signal transmission relies on a variety of proteins to receive and transmit the chemical signals. My group studies the structure and function of neurotransmitter receptors and ion channels that regulate fundamental neuronal activities.
MEET OUR FACULTY

Jesse Gillis | GENOMICS
Of the tens of thousands of protein-coding genes in the human genome, only a small portion have an experimentally defined function. For the rest, how can we determine what they do? My lab develops computational predictions based on co-expression networks. We are applying our predictions to understand neuropsychiatric disorders.

Thomas Gingeras | GENOMICS
Only a small portion of the RNAs encoded in any genome are used to make proteins. My lab investigates what these noncoding RNAs (ncRNAs) do within and outside of cells, where regulators of their expression are located in the genome, and how perturbations of ncRNAs and their regulators contribute to disease.

Christopher Hammell | CANCER
As organisms develop, genes turn on and off with a precise order and timing, much like the order and duration of notes in a song. My group uses model organisms to understand the molecules that control the tempo of development. We also study how changes in the timing of gene expression contribute to diseases like cancer.

Molly Hammell | CANCER
To ensure that cells function normally, tens of thousands of genes must be turned on or off together. To do this, regulatory molecules—transcription factors and non-coding RNAs—simultaneously control hundreds of genes. My group studies how the resulting gene networks function and how they can be compromised in human disease.

Josh Huang | NEUROSCIENCE
My lab studies the development and organization of neural circuits in the mouse cerebral cortex. We use an integrated approach to identify neuronal cell types and discover how they interact to process information and guide behavior, focusing on the motor cortex that controls forelimb movement. Our studies of inhibitory interneurons have implications for understanding schizophrenia and autism.

Ivan Iossifov | QUANTITATIVE BIOLOGY
Every gene has a job to do, but genes rarely act alone. Biologists have built models of molecular interaction networks that represent the complex relationships between thousands of different genes. I am using computational approaches to help define these relationships—work that is helping us to understand the causes of common diseases including autism, bipolar disorder and cancer.

David Jackson | PLANT BIOLOGY
My lab studies genes and signals in cells that regulate the growth and shape of plants. We have discovered several genes that control plant architecture by exerting an influence on stem cells. By identifying the genes that control the number of stem cells in corn plants, for example, we’ve discovered a means of boosting the yield of that vital staple.

Tobias Janowitz | CANCER
Cancer is a systemic disease. Using both laboratory and clinical research, my group investigates the connections between metabolism, endocrinology, and immunology to discover how the body’s response to a tumor can be used to improve treatment for patients with cancer.

Leemor Joshua-Tor | CANCER
Our cells depend on thousands of proteins and nucleic acids that function as tiny machines: molecules that build, fold, cut, destroy, and transport all of the molecules essential for life. My group is discovering how these molecular machines work, looking at interactions between individual atoms to understand how they activate gene expression, DNA replication and small RNA biology.

Adam Kepecs | NEUROSCIENCE
My lab studies the neurobiological principles underlying cognition and decision-making. Using state-of-the-art technologies, we interrogate neural circuits in rodents as they perform a task. We validate our findings with analogous tasks in humans. We hope to define the neural circuits underlying decisions that will inform the development of new therapies for psychiatric diseases.
MEET OUR FACULTY

Justin Kinney | QUANTITATIVE BIOLOGY
From regulating gene expression to fighting off pathogens, biology uses DNA sequence information in many different ways. My research combines theory, computation, and experiment in an effort to better understand the quantitative relationships between DNA sequence and biological function. Much of my work is devoted to developing new methods in statistics and machine learning.

Alexei Koulakov | NEUROSCIENCE
The complexity of the mammalian brain challenges our ability to explain it. My group applies methods from mathematics and theoretical physics to understand the brain. We are generating novel ideas about neural computation and brain development, including how neurons process information, how brain networks assemble during development, and how brain architecture evolved to facilitate its function.

Adrian Krainer | CANCER
Our DNA carries the instructions to manufacture all the molecules needed by a cell. After each gene is copied from DNA into RNA, the RNA message is “spliced”—an editing process involving precise cutting and pasting. I am interested in how splicing normally works, how it is altered in genetic diseases and cancer, and how we can correct these defects for therapy.

Alexander Krasnitz | QUANTITATIVE BIOLOGY
Many types of cancer display bewildering intra-tumor heterogeneity on a cellular and molecular level, with aggressive malignant cell populations found alongside normal tissue and infiltrating immune cells. My lab is developing mathematical and statistical tools to disentangle tumor cell population structure, enabling an earlier, more accurate disease diagnosis and better-informed clinical decisions.

Je Lee | CANCER
Cells are amazingly complex, with the ability to sense and to remember timing, location and history. I am exploring how cells store this information, and how their surroundings influence their communication with other cells. I am also developing various imaging and molecular sequencing methods for tracking genes, molecules, and cells to understand how cancer cells arise and evolve.

Bo Li | NEUROSCIENCE
My group studies the neural circuits underlying cognitive function and dysfunction as they relate to anxiety, depression, schizophrenia and autism. We use sophisticated technologies to manipulate specific neural circuits in the rodent brain to determine their role in behavior. We are interested in changes in synaptic strength that may underlie mental disorders.

Zachary Lippman | PLANT BIOLOGY
My research team studies the genes that determine when and where, and thus how many, flowers are produced on plants. Flowers form on branches called inflorescences, which originate from stem cells. By studying the genes that control how stem cells become inflorescences, we are able to manipulate flower production to improve crop yields.

Robert Martienssen | PLANT BIOLOGY
Chromosomes are covered with chemical modifications that help control gene expression. I study this secondary genetic code—the epigenome—and how it is guided by small mobile RNAs in plants and fission yeast. Our discoveries impact plant breeding and human health, and we use this and other genomic information to improve aquatic plants as a source of bioenergy.

MEET OUR FACULTY

Dan Levy | QUANTITATIVE BIOLOGY
We have recently come to appreciate that many unrelated diseases, such as autism, congenital heart disease and cancer, are derived from rare and unique mutations, many of which are not inherited but instead occur spontaneously. I am generating algorithms to analyze massive datasets comprising thousands of affected families to identify disease-causing mutations.

Robert Maki | CANCER
With joint appointments at CSHL and Northwell Health, I am working to expand clinical cancer research at both institutions, to provide new treatments for patients, as well as to gain greater insight into the biology of this complex set of diseases. In my own research, I am collaborating on work in soft-tissue and bone sarcomas to better understand the cancer microenvironment and epigenetics, targeting molecular weaknesses to halt cancer growth.
MEET OUR FACULTY

David McCandlish | QUANTITATIVE BIOLOGY
Some mutations are harmful, but others are benign. How can we predict the effects of mutations, whether they are single mutations or in combination? Using data from experiments that simultaneously measure the effects of thousands of mutations, my group develops computational tools to predict the functional impact of mutations in protein coding sequences.

W. Richard McCombie | GENOMICS
Over the last two decades, revolutionary improvements in DNA sequencing technology have made it faster, more accurate, and much cheaper. We are now able to sequence up to 10 trillion DNA letters in just one month. I harness these technological advances to assemble genomes for a variety of organisms and probe the genetic basis of neurological disorders, including autism and schizophrenia, better understand cancer progression and understand the complex structures of the genomes of higher plants.

Alea Mills | CANCER
Cells employ stringent controls to ensure that genes are turned on and off at the correct time and place. Accurate gene expression relies on several levels of regulation, including how DNA and its associated molecules are packed together. I study the diseases arising from defects in these control systems, such as aging and cancer.

Partha Mitra | NEUROSCIENCE
A theoretical physicist by training, my research is centered around intelligent machines. I do both theoretical and experimental work. The theoretical work is focused on analyzing distributed/networked algorithms in the context of control theory and machine learning, using tools from statistical physics. My lab is involved in brain-wide mesoscale circuit mapping in the mouse as well as in the marmoset. An organizing idea behind my research is that there may be common underlying mathematical principles that constrain evolved biological systems and human-engineered systems.

Pavel Osten | NEUROSCIENCE
To understand what’s going wrong in illnesses like autism and schizophrenia, we need to know more about how neural circuits are connected in the healthy brain. We’ve developed advanced imaging methods to draw the first whole-brain activation map in the mouse. Now we’re applying that technology to study changes in brain activity in mice whose behavior models human autism and schizophrenia.

Darryl Pappin | CANCER
Our genome can encode hundreds of thousands of different proteins, the molecular machines that do the work that is the basis of life. I use proteomics, a combination of protein chemistry, mass spectrometry and informatics, to identify precisely which proteins are present in cells—cells from different tissues, developmental stages, and disease states.

Ullas Pedmale | PLANT BIOLOGY
Unlike animals, plants lack specific organs that see or hear various stimuli, yet, plants are sensitive to their surrounding environment and modify their development according to various external signals. My lab studies how the environment of a plant modulates its growth and development. Understanding environmental control of growth will have far-reaching implications for agriculture, energy production, and many other human activities.

Stephen Shea | NEUROSCIENCE
When confronted with another individual, social animals use multiple sensory inputs—smells, sounds, sights, tastes, touches—to choose an appropriate behavioral response. My group studies how specific brain circuits support these natural communication behaviors and how disruptions in these circuits can lead to inappropriate use of social information, as in Autism Spectrum Disorders.

Jason Sheltzer | CANCER
Nearly all tumors exhibit a condition known as aneuploidy—their cells contain the wrong number of chromosomes. We’re working to understand how aneuploidy impacts cancer progression, in hopes of developing therapies that can specifically eliminate aneuploid cancers while leaving normal cells unharmed.

Adam Siepel | QUANTITATIVE BIOLOGY
I am a computer scientist who is fascinated by the challenge of making sense of vast quantities of genetic data. My research group focuses in particular on questions involving human evolution and transcriptional regulation.
MEET OUR FACULTY

Raffaella Sordella | CANCER
Two challenges in cancer biology guide my work: first, how do tumors become addicted to certain gene products, and second, how do tumors develop resistance to anti-cancer drugs. I focus on the epidermal growth factor receptor (EGFR), which is both addictive when mutated and a common source of drug resistance. We are also identifying new targets for the treatment of lung cancer.

David L. Spector | CANCER
The immense amount of DNA, RNA and proteins that contribute to our genetic programs are precisely organized inside the cell’s nucleus. My group studies how nuclear organization impacts gene regulation, and how misregulation of non-coding RNAs contributes to human diseases such as cancer.

Arne Stenlund | CANCER
Despite the development of preventive vaccines, human papillomaviruses (HPVs) still infect more than five million women each year, significantly increasing their risk of cervical cancer. I am working to identify how HPV multiplies so that we may develop drugs that can defeat the virus once it has infected an individual.

Bruce Stillman | CANCER
Every time a cell divides, it must accurately copy its DNA. With 3 billion “letters” in the human genome, this is no small task. My studies reveal the many steps and molecular actors involved, as well as how errors in DNA replication are involved in diseases that range from cancer to rare genetic disorders.

Jessica Tollkuhn | NEUROSCIENCE
I am interested in how transient events during development program neurons to take on a specific identity and function. More specifically, I am studying how estrogen and testosterone generate sex differences in the brain and behavior.

Nicholas Tonks | CANCER
Cells must constantly react to what is happening around them, adapting to changes in neighboring cells or the environment. I study the signals that cells use to exchange information with their surroundings. Our group is finding drugs that target these signals and thus can treat diabetes, obesity, cancer, and Autism Spectrum Disorders.

Lloyd Trotman | CANCER
We have recently developed the first genetic mouse model for therapy and analysis of metastatic prostate cancer. Now we can test whether and how modern concepts of cancer evolution can outperform the 80-year-old standard of care—hormone deprivation therapy—and turn lethal prostate cancer into a curable disease.

David Tuveson | CANCER
Pancreatic cancer is an extremely lethal malignancy. On average, patients who are diagnosed with pancreatic cancer succumb to the disease within six months. Research is the only way to defeat pancreatic cancer. My lab is making progress toward finding a cure by detecting the disease earlier and designing novel therapeutic approaches.

Christopher Vakoc | CANCER
Cancer cells achieve their pathogenicity by changing which genes are on and off. To maintain these changes in gene expression, cancer cells rely on proteins that interact with DNA or modify chromatin. My group investigates how such factors sustain the aberrant capabilities of cancer cells, thereby identifying new therapeutic targets.

Linda Van Aelst | CANCER
Normal cell function relies on coordinated communication between all the different parts of the cell. These communication signals control what a cell does, what shape it takes, and how it interacts with other cells. I study these signaling networks to understand how they guard against cancer and neurological disorders.
Doreen Ware | GENOMICS
When we think of evolution, we often think about physical changes, like a plant developing broader leaves to collect more solar energy. Such evolution actually occurs within the plant’s DNA. I am using computational analysis and modeling to visualize how plant genomes have evolved over time, particularly those of staple crops. We are learning from this work to improve the range and yield of modern plants.

Michael Wigler | CANCER
Devastating diseases like cancer and autism can be caused by spontaneous changes to our DNA—mutations first appearing in the child, or in our tissues as we age. We are developing methods to discover these changes in individuals, tumors, and even single cells, to promote early detection and treatments.

Anthony Zador | NEUROSCIENCE
My lab studies how circuitry in the brain gives rise to complex behaviors, one of nature’s great mysteries. We study how the auditory cortex processes sound, and how this is interrupted in autism. We also seek to obtain a wiring diagram of the mouse brain at the resolution of individual neurons. Our unusual approach exploits cheap and rapid “next-gen” gene sequencing technology.

Lingbo Zhang | CANCER
My lab focuses on hematopoietic stem and progenitor cells. We utilize both CRISPR/Cas functional genomic and forward chemical genomic approaches to uncover critical genes and small chemical compounds regulating the self-renewal of normal and malignant cells. The ultimate goal of our research is to identify novel therapeutics for treatment-resistant hematopoietic malignancies, including myelo-dysplastic syndrome and acute leukemia, through targeting of novel self-renewal pathways and metabolic vulnerabilities.