20

20TH ANNIVERSARY REPORT

Kavli Institute *for* Neuroscience *at* Yale

We aim to *understand* **how genes, molecules, cells, and neural circuits interact to give rise to brain development and behavior, and to** *apply this knowledge* **to** *advance* **treatments for brain disorders.**

OUR MISSION

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Message from the director

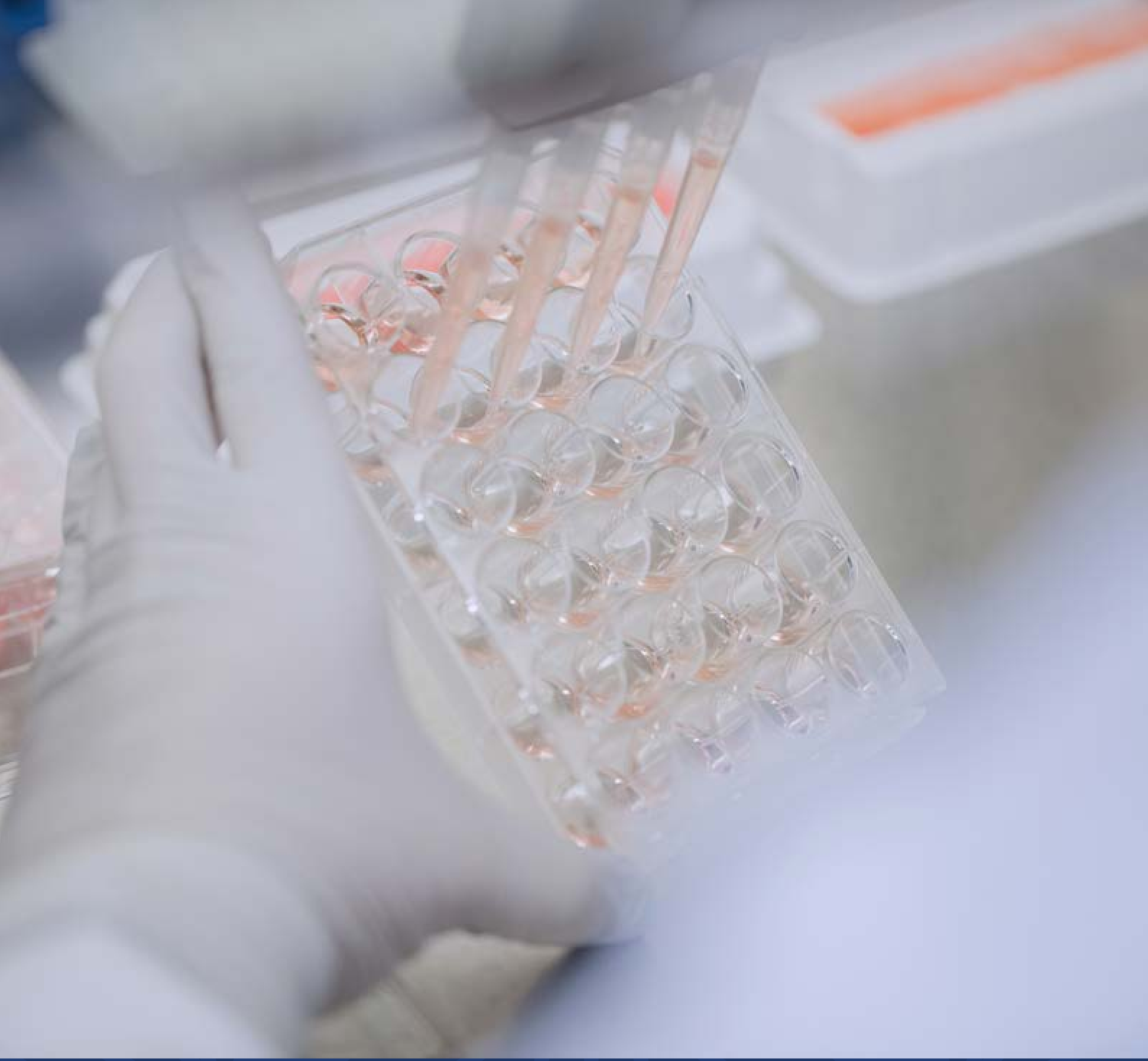
I am delighted to have the opportunity to present the significant progress made through the Kavli Institute for Neuroscience at Yale since its creation in 2004. Over the past 20 years, the Institute has empowered hundreds of researchers across departments to push the boundaries of neuroscience, leading to impactful discoveries. The generosity of the Kavli Foundation has enabled the Institute to serve as a catalyst, advancing interdisciplinary research and technology development, supporting a diverse research community, and promoting exchanges with the international neuroscience community.

This report highlights the initiatives the Kavli Institute has established to foster excellence in neuroscience research. Those efforts include:

- Supporting cutting-edge research with emphasis on interdisciplinary collaborations
- Organizing workshops and symposia on emerging topics that bring together local and global scientists
- Sponsoring distinguished lectures on research that enriches the neuroscience community
- Supporting the career development of trainees through fellowships, awards, training workshops and networking events that promote the exchange of ideas
- Cultivating a diverse community and supporting trainees from historically underrepresented groups
- Establishing and supporting core facilities that enable access to advanced technologies
- Collaborating with other Kavli Institutes and other institutions to promote innovative research, technology development, and professional training opportunities
- Promoting outreach and scientific communication with the public at large

Reflecting on what we have accomplished together throughout the years, we are proud of our community, their work, innovation, and dedication. It is truly a privilege to continue pursuing the Institute's endeavor—for two more decades and beyond—and we look forward to facilitating more breakthroughs. We are very grateful for the longstanding support of the Kavli Foundation, making it possible to fulfill our vision for a transformative and collaborative neuroscience research environment at Yale.

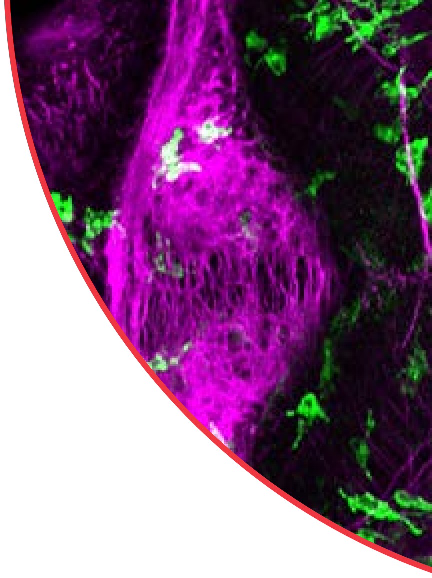
Stephen Strittmatter
Director

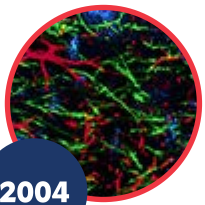


Institute Milestones and Discoveries

The Kavli Institute supports all areas of neuroscience at Yale, from molecular, cellular, systems, computational, developmental, translational, and human neuroscience. This following section, far from being a comprehensive list of contributions, highlights a select few impactful discoveries from the past 20 years.

Timeline and milestones





2004

Creation of the Kavli Institute for Neuroscience, directed by Pasko Rakic

First “Kavli Research initiatives” grant

First Kavli Distinguished Lecture

2008

Pasko Rakic awarded the Kavli Prize in Neuroscience

2009

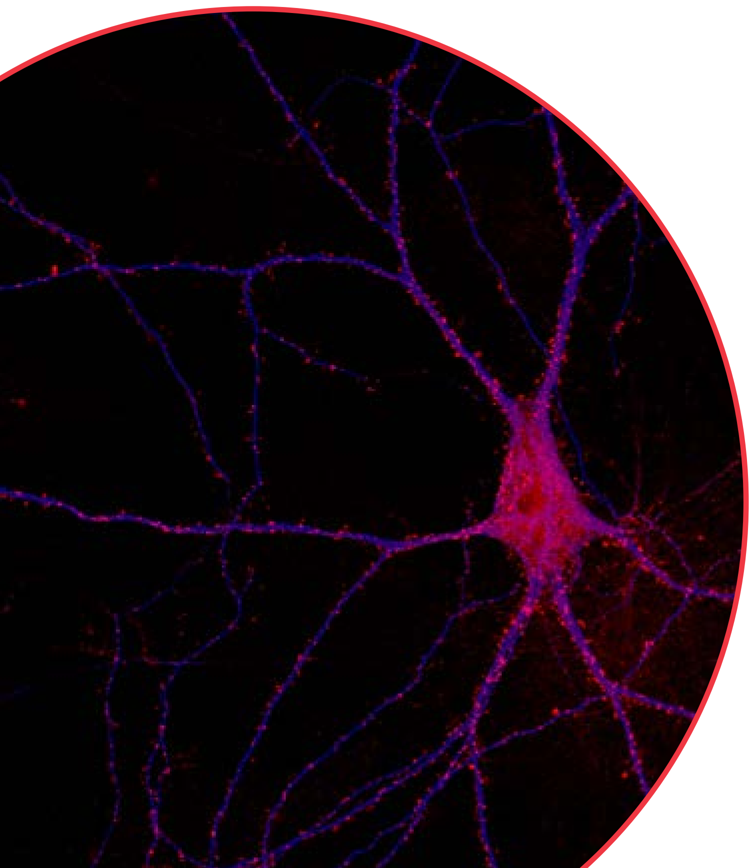
First Kavli Workshop

2010

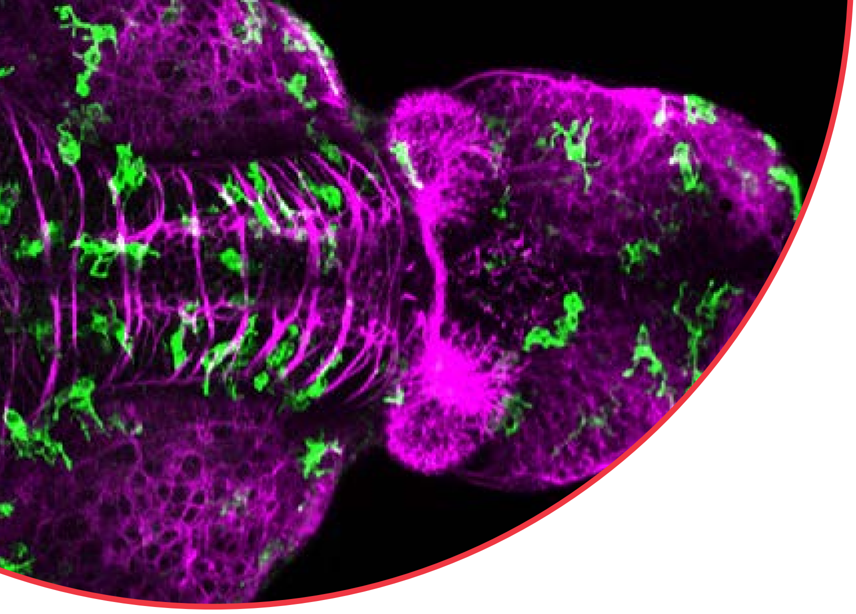
James Rothman awarded the Kavli Prize in Neuroscience

2011

First support of graduate students “Kavli Scholar”



Cultured rat neuron expressing a YFP-intrabody labeling endogenous postsynaptic Homer red and immunostained for dendritic MAP2. Credit: Dhrubajyoti Chowdhury, Biederer lab



Whole brain of a larval zebrafish mutant of the autism gene, DYRK1A, immunostained for microglia (green) and acetylated tubulin (magenta). Credit: Hellen Weinschutz Mendes and Sarah E. Fitzpatrick, Hoffman lab

2015

Pietro De Camilli becomes director

First Kavli Networking Hour

2017

Establishment of the Neurotechnology Core

First Kavli Symposium

2018

First Kavli Postdoctoral Fellowship

2019

Establishment of the Rodent Behavior Analysis Core

2021

First Kavli Postdoctoral Fellowship for Academic Diversity

2022

Stephen Strittmatter becomes director

First Kavli Community Lunch

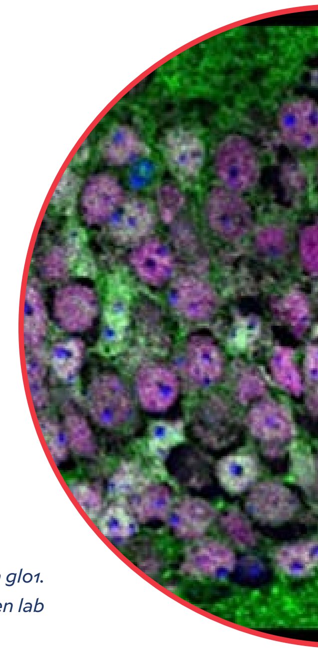
First Kavli Postdoc Series event

2023

First postdoctoral fellow integrating the steering committee

2024

Celebrating 20 years!



Mouse dentate gyrus labeled with glo1. Credit: Elizabeth Woo, Arnsten lab

24 Departments

Neuroscience

Neurology

Neurosurgery

Cellular and Molecular Physiology

Cell Biology

Psychiatry

Psychology

Comparative Medicine

Chemistry

Genetics

Biomedical Engineering

Child Study Center

Molecular Biophysics & Biochemistry

Molecular, Cellular, & Developmental Biology

Marketing

Physics

Ophthalmology

Mathematics

Computer Science

Endocrinology

Cardiology

Obstetrics, Gynecology and Reproductive Sciences

Pediatrics

Pharmacology

From Cortical Development, to Cortical Function, to Visual Science

Cortical development has been at the heart our Kavli Institute since its launch. The work of Pasko Rakic, Dorys McConnell Duberg Professor of Neuroscience, founding chair of the department of neurobiology and inaugural director of the Kavli Institute for Neuroscience, led to advances in the understanding of the origins of neuronal subtypes in the cerebral cortex. Among his many notable discoveries that have shaped our understanding of cortical development, he established that cortical neurons originate in the subventricular zone rather than being generated in the cortex. He hypothesized that cells in the developing cerebral cortex are created at the base of each cortical column, with each new cell migrating past its predecessors. He was awarded the 2008 Kavli Prize in Neuroscience "for discoveries on the developmental and functional logic of neuronal circuits."

The remarkable cognitive abilities of our brains are among the most distinctive features that make us human. Though we now understand that the evolution of these abilities is correlated with the expansion of the prefrontal cortex, our understanding of how the brain has changed in the human lineage remains incomplete. The lab of Nenad Sestan, Harvey and Kate Cushing Professor of Neuroscience, professor of comparative medicine, of genetics, and of psychiatry, has made momentous advances to uncover evolutionarily conserved developmental mechanisms, primate and human-specific features of brain development, and human neurodevelopmental disorders. They have pioneered and leveraged next-generation sequencing to characterize brain development across species. Moreover, their groundbreaking genomic analyses have unveiled conserved and species-specific cell types and molecular processes in prefrontal neural cells, including a uniquely human type of cortical microglia, absent in closely related primates.

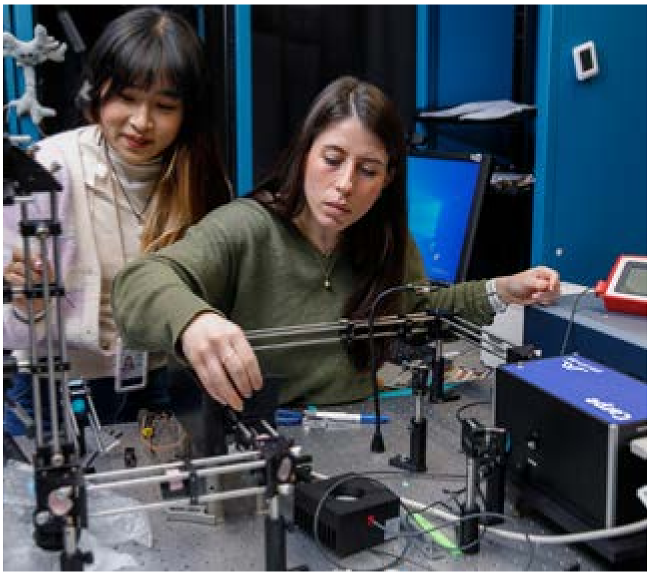
To better understand the evolutionary processes that have driven the elaboration of the human cerebral cortex, James Noonan, Albert E. Kent Professor of Genetics and professor of neuroscience, and his team have pioneered methods to characterize gene regulatory elements that have a potential role in encoding human-specific functions. Their work led to the discovery of thousands of promoters and enhancers that have gained activity during human neocortical development. Notably, they have demonstrated that a major gene linked to autism, CHD8, directly regulates other autism-associated genes during neurodevelopment, providing an entry point for deciphering gene regulatory networks contributing to autism risk.

The prefrontal cortical (PFC) circuits are essential for higher cognitive functions. Research in the lab of Amy Arnsten, Albert E. Kent Professor of Neuroscience and professor of psychology, has uncovered the molecular and cellular events in the dorsolateral PFC that subserve working memory, attention regulation, and executive functions. Their work has led to the development of the a2-adrenergic agonist guanfacine for the treatment of PFC disorders such as attention deficit disorder (FDA-approved) and post-traumatic stress disorder in children. Guanfacine is also being tested for the treatment of delirium and most recently the "brain fog" symptoms of long COVID.

Activity in cortical circuits varies depending on an animal's behavioral state (e.g., sleeping *vs* waking), but little is known about the transition between distinct waking states (e.g., quiescent *vs* active). One of the projects led in the lab of Jessica Cardin, professor of neuroscience, has examined the visual cortex to understand the flexibility of sensory processing. For the first time, the team was able to separate the roles of arousal and locomotion in regulating visual cortex activity and showed that arousal modulates cortical visual encoding. These findings reveal complex elements that contribute to the functional flexibility of cortical circuits.

The balance between excitation and inhibition is important for brain function. In the cortex, this balance is mediated by excitatory glutamatergic pyramidal neurons and inhibitory GABAergic interneurons. Inhibitory neurons are very diverse, and each subtype is thought to have a different function in local circuits. The lab of Michael Higley, professor of neuroscience, of biomedical engineering, and of psychiatry, investigates the localized actions of GABAergic inhibition in pyramidal cell dendrites. The team showed that a subset of interneurons mediates dendritic inhibition that could be compartmentalized within single spines, spatially constraining the functional spread of inhibition. The lab's findings provide a better understanding of synaptic inhibition, which, because GABA signaling is perturbed in neuropsychiatric disorders, could help inform treatments.

With visual information everywhere, how does our visual system decide what is relevant and what is noise? Using experimental methods and computational modeling, the lab of Anirvan Nandy, assistant professor of neuroscience, aims to understand how neurons in different layers of the neocortex orchestrate perception, attention, and social cognition. The team recently focused on saccades, eye movements that transition a gaze from one point to another. Their work has shed light on the mechanisms of saccadic suppression, the temporary reduction in visual sensitivity during a saccade that serves to blunt our perception of this motion.

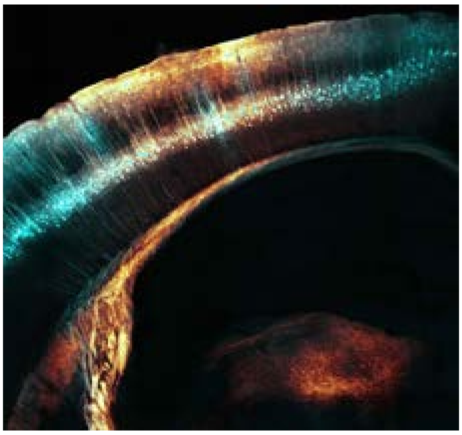


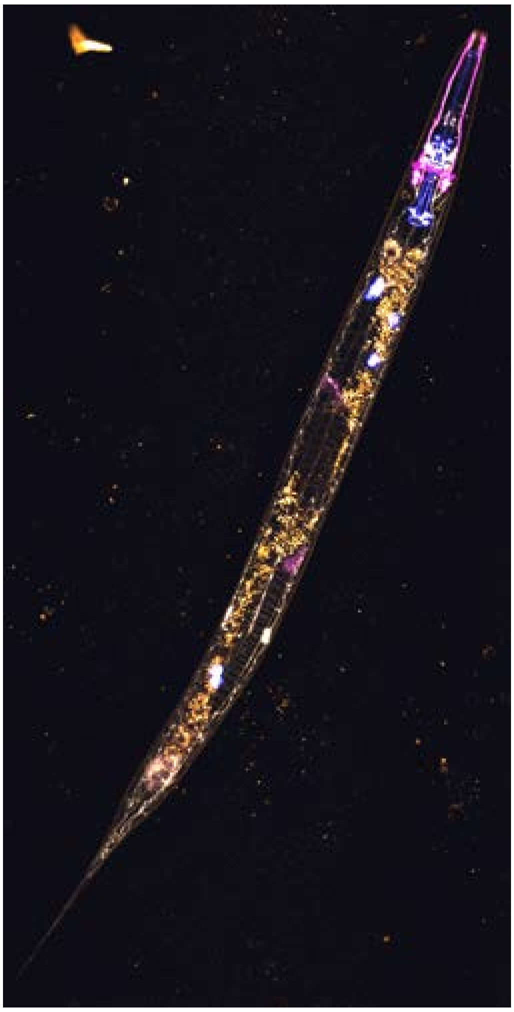
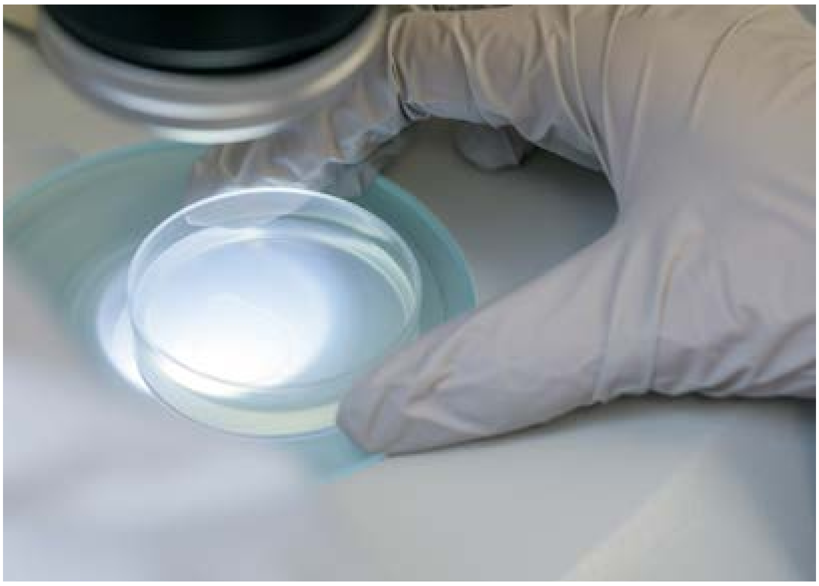
Jenny Yue and Rachel Oren, Cardin lab

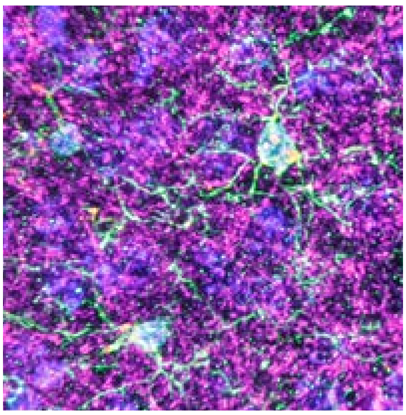
Neuronal activity during development helps circuits to mature. However, how can visual circuits be shaped by neuronal activity even before any visual experience? The lab of Michael Crair, William Ziegler III Professor of Neuroscience, professor of ophthalmology and visual science, and Vice Provost for Research, develops and employs advanced imaging techniques to examine the mechanisms of brain circuit development. The team has made fundamental contributions in this field, notably by demonstrating the existence of waves of spontaneous retinal activity that propagate throughout the entire visual system before eye opening.

One visual pathway goes from the retina to the visual cortex via the thalamus, but more information is required to understand the role the thalamus plays in modulating visual information. The lab of Liang Liang, assistant professor of neuroscience, integrates their newly developed imaging technologies to dissect the functional organization of synapses in the thalamus at an unprecedented spatiotemporal resolution, providing insights into computation occurring along the retino-thalamo-cortical visual pathway. A new collaborative study between the Liang and Crair labs focused on the effect of spontaneous activity on axon refinement during development. Their study revealed that the degree of synchronization of spontaneous activity patterns predicts where an axon branch is added or eliminated, confirming the colloquial "cells that fire together, wire together" and "out of sync, lose your link."





From top to bottom and left to right: Kavli postdoctoral fellows and graduate students, Lim lab, Strittmatter lab, Grutzendler lab, iPSC neurocore, Yogev lab, Hammarlund lab, Snell lab, Favuzzi lab.

Cellular Neurobiology, Neurodegeneration, and Repair

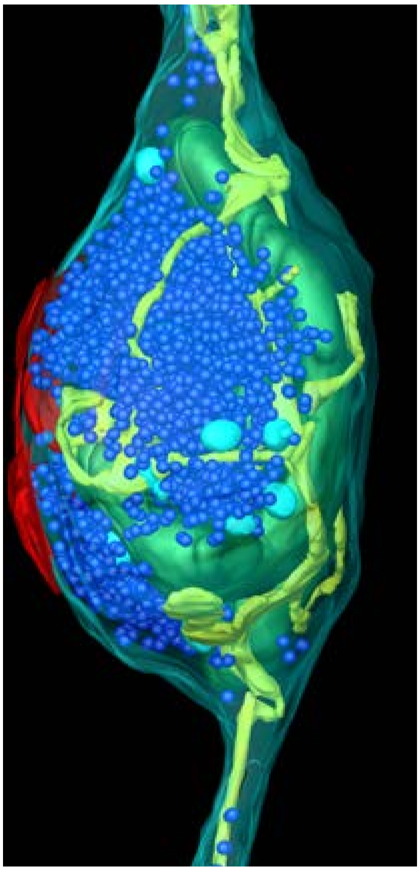
Many neuroscience laboratories at Yale are interested in understanding the fundamental mysteries of the nervous system at the cellular level. Neurotransmission by glutamate, a major excitatory neurotransmitter in the brain, is very quick and clearly essential for brain function; however, the modulation of brain function underlying learning and memory may happen in seconds or over many hours. The lab of Susumu Tomita, professor of cellular and molecular physiology and of neuroscience, aims to uncover how the modulation of synaptic transmission supports complex brain functions. The team has found a molecule that is crucial to long-term potentiation, revealing a new key mediator of learning and memory.

But how are synapses assembled in living animals to produce behaviors and store memories? The lab of Daniel Colón-Ramos, Dorys McConnell Duberg Professor of Neuroscience and professor of cell biology, uses the microscopic worm *C. elegans* to identify the mechanisms of synapse formation *in vivo* and how they change due to behavior and learning. Recently, the team used a new fluorescent biosensor to map the metabolic activity of each neuron of *C. elegans*, unraveling how living organisms distribute the energy needed throughout the body at a cellular resolution.

How do single molecules contribute to behavior? The lab of Marina Picciotto, Charles B. G. Murphy Professor of Psychiatry and professor in the Child Study Center, of neuroscience and of pharmacology, and deputy director of the Kavli Institute, integrates studies at the cellular, molecular, and systems levels to understand the role of the neuromodulator acetylcholine in behavior and its plasticity - specifically related to nicotine addiction. The team has made important contributions to the field by shedding light on neuronal pathways encoding reward, the role of chronic stress in maladaptive behaviors, and the mechanisms of nicotine's effects on food intake. For example, the Picciotto lab has recently shown that in the basolateral amygdala - a brain region necessary for learning that previously neutral cues can predict punishment or reward - acetylcholine release improved the learning of a cue-reward association.

Neurons are highly polarized cells with axons that can reach a meter long in humans. While their shape is critical for their function, little is known about the cell biology of their structure. The lab of Shaul Yogev, associate professor of neuroscience and of cell biology, aims to understand how the neuronal cytoskeleton is established and how it supports polarized traffic to maintain synapses over the lifetime of a neuron. Using *C. elegans* as a model, the team has revealed insights into the mechanisms of axonal transport, a process that delivers proteins and membranes from their site of synthesis in the cell body to axons and dendrites. Recently, members of the Yogev lab overcame previous technical limitations and revealed two distinct mechanisms of slow transport of spectrin, an important cytoskeleton protein needed to prevent neuron degeneration.

Neurodegenerative diseases such as Parkinson's disease (PD), Alzheimer's disease (AD), ataxia, or amyotrophic lateral sclerosis (ALS) affect millions of people worldwide. At Yale, several labs are investigating the molecular and cellular mechanisms of neurodegeneration. The lab of Pietro De Camilli, John Klingenstein Professor of Neuroscience and professor of cell biology, focuses on the mechanisms of the dynamics and traffic of intracellular membranes. Founding director of the Yale Program in Cellular Neuroscience, Neurodegeneration and Repair (CNNR) since 2005, chair of the Department of Neuroscience from 2015 to 2021, and director of the Kavli Institute for Neuroscience from 2015 to 2022, De Camilli made a tremendous impact on the neuroscience community at Yale and beyond.



3D reconstruction of a presynaptic nerve terminal. Credit: Yumei Wu, De Camilli lab

Chengye Feng and Susie Kim, Hammarlund lab

His lab's significant discoveries include a delineation of the biochemistry and ultrastructure of the endocytic machinery and the regulatory roles of special cell membrane phospholipids called phosphoinositides. Their recent work shed light on the human VPS13 genes, a family of genes for which mutations result in neurological disorders like PD. They showed that the VPS13 protein transports lipids between the endoplasmic reticulum and other organelles, implicating that defects in lipid dynamics could play an important role in the clinical manifestations of patients with VPS13 mutations.

Among other organelles, lysosomes are critical for a neuron to survive, as they clear cellular waste, though their dysfunction contributes to the development of neurodegenerative diseases. Understanding lysosome function and how it adapts to cellular needs is one of the goals of the lab of Shawn Ferguson, associate professor of cell biology and of neuroscience. The team has uncovered transcription factors that could regulate the stimulation of genes for lysosome biogenesis by matching lysosome capacity to cellular demands.

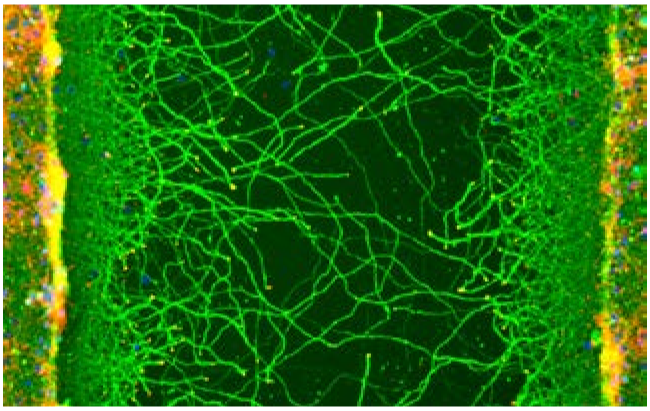
An early event in neurodegeneration is synaptic dysfunction, so it is critical to understand how synapses are normally maintained and how disruptions in these processes result in neurodegenerative disorders. The lab of Sreeganga Chandra, associate professor of neuroscience and of neurology is investigating these processes to better understand disease initiation and inform the development of potential treatments. Their recent work showed that local synaptic protein homeostasis mechanisms are essential for maintaining the structure and functionality of synapses - mechanisms that are disrupted in late-onset neurodegenerative diseases. A collaborative study with the lab of Charles Greer, professor of neurosurgery and of neuroscience, aimed at deciphering the biological mechanism behind the loss of smell - a common, but less studied symptom of PD - revealed reduced neurogenesis in the olfactory bulb.

Amyloid-ß (Aß) oligomers are potent toxins that target the synapse and can trigger symptoms of Alzheimer's Disease (AD). The research of Stephen Strittmatter, Vincent Coates Professor of Neurology, professor and chair of neuroscience and Kavli Institute director, has provided the first mechanistic understanding of how Aß oligomers impair neuronal function. The team built upon these findings to develop disease-modifying therapies, some of which are currently in clinical trials.

Aß plaques are surrounded by microglia, the resident immune cells of the nervous system, but little is known about their function. The lab of Jaime Grutzendler, Dr. Harry M. Zimmerman and Dr. Nicholas and Viola Spinelli Professor of Neurology and professor of neuroscience, showed that microglia constitute a neuroprotective barrier with a profound impact on plaque composition and toxicity. Leveraging their own advances in imaging, they discovered the cellular mechanisms underlying microglia's ability to envelop amyloid deposits.

Spinocerebellar ataxias are a family of neurodegenerative diseases that share similar clinical manifestations but have distinct genetic causes. The lab of Janghoo Lim, associate professor of genetics and of neuroscience, aims to characterize the mechanisms of spinocerebellar ataxia type 1 (SCA1) and translate these findings into therapy development. Leveraging omics approaches, the team revealed both conserved and distinct molecular mechanisms across brain regions in SCA1, providing insights into the pathogenesis of the disorder.

Both ALS and frontotemporal dementia (FTD) are neurodegenerative diseases that are linked to the expansion of nucleotide repeats in the genome. The lab of Junjie Guo, assistant professor of neuroscience, works at the frontiers of neuroscience and RNA biology to understand mRNA translation and how its dysregulation leads to nucleotide repeat expansion disorders. Their work demonstrated that in healthy cells, misprocessed RNAs are degraded quickly before they can accumulate. However, in ALS and FTD, the polypeptides produced by the repeats inhibit this degradation pathway, causing neurotoxicity.



Cerebral cortex neurons were cultured and then their axons were severed mechanically. Over a week, axon regeneration into the region of trauma is apparent. Green, ßIII tubulin; Red, filamentous actin. Credit: Yuichi Sekine, Strittmatter lab

Unlike peripheral nerves, neurons in the central nervous system don't regenerate after injury. What gives a neuron the ability to regenerate its axon? The lab of Marc Hammarlund, professor of neuroscience and of genetics, studies the cell biology of neurons *in vivo*, and how neurons prevent degeneration, repair injury, and maintain circuit function. Using powerful genetic tools available in *C. elegans*, the team identified several novel signaling pathways that regulate axon regeneration, providing insights into the treatment of neurological injury and disease.

Technical Developments For Scientific Advancements

Researchers never run out of questions. But sometimes, the technology necessary to answer them doesn't exist yet. Making possible what was previously untestable is a major goal of the lab of Joerg Bewersdorf, Harvey and Kate Cushing Professor of Cell Biology, professor of biomedical engineering and of physics. The team accelerates scientific progress through the development of optical super-resolution microscopy techniques and applies them to investigate cellular structures that are inaccessible to conventional microscopy. Previously limited to seeing a handful of tagged molecules at a time, they recently developed new imaging probes that transiently bind to a target, switching rapidly from one target to the next. This method enables to visualize a virtually unlimited number of subcellular elements, allowing them to get the cell's big picture.

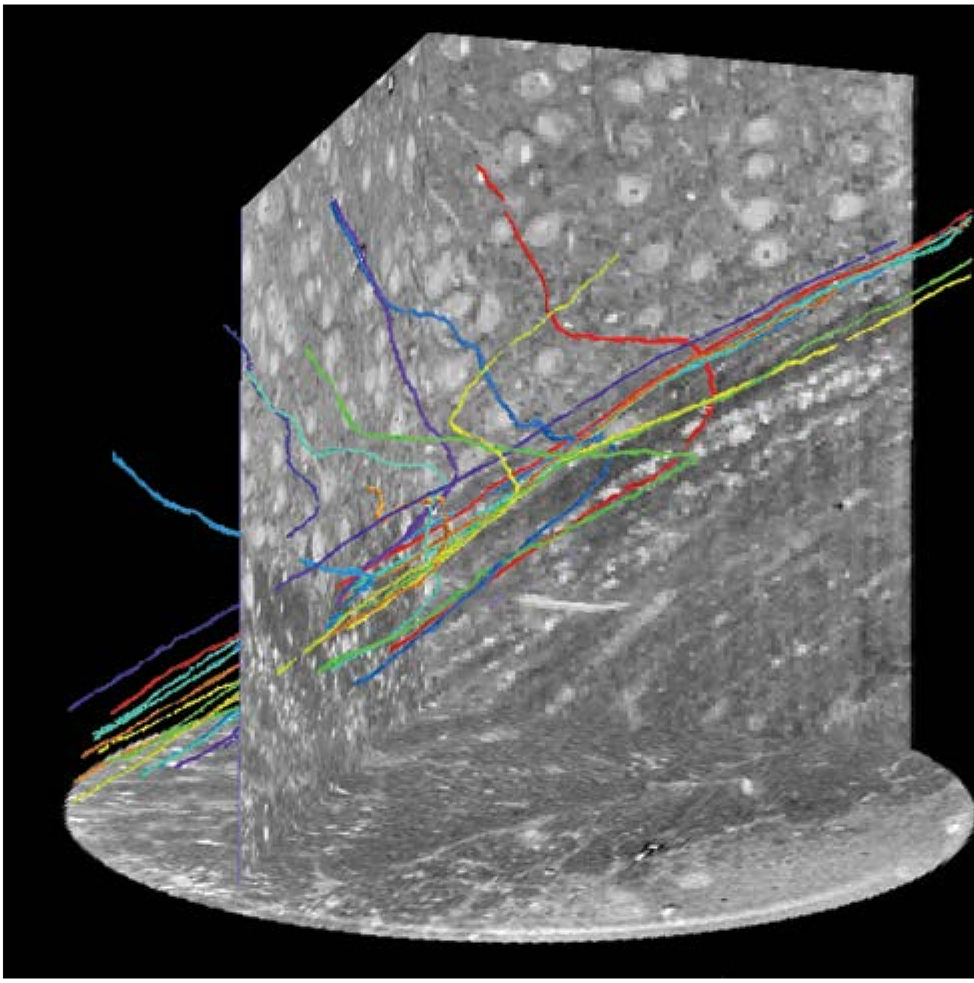
Monitoring brain activity at various scales, from synapses to circuits, is now common though collecting information at all scales at once is not trivial. Together, the Cardin, Crair, and Higley labs developed a novel *in vivo* imaging strategy that pairs wide-field mesoscopic microscopy - in which activity across the entire cortical surface can be monitored in the awake, behaving mouse - with simultaneous 2-photon imaging to reveal large-scale network connectivity of single cortical neurons. With the addition of Todd Constable, professor of radiology and biomedical imaging and of neurosurgery, D. S. Fahmeed Hyder, professor of radiology and biomedical imaging and of biomedical engineering, and Evelyn Lake, associate professor of radiology and biomedical imaging, the interdisciplinary team developed a tool bridging the microscopic (single-cell) and the macroscopic (whole-brain) by combining calcium imaging and functional magnetic resonance imaging (fMRI). This revolutionary method allows for brain activity tracking across modalities, taking advantage of each method's strengths. This project is further described in the "Enabling cutting-edge experiments" section of this report.

Seeding Interdisciplinary Research

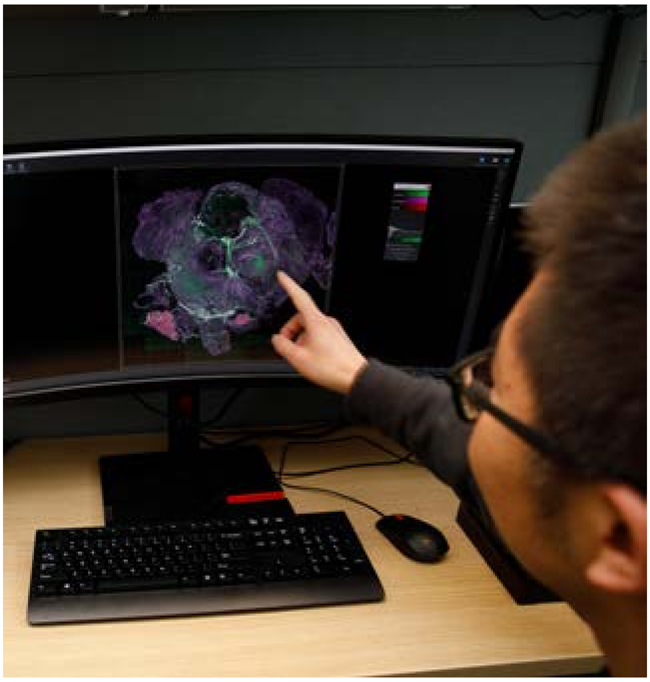
The Kavli Institute supports neuroscience research at Yale through multiple funding mechanisms, including faculty collaborative grants (Innovative Research Awards, Innovative Teams Awards), and postdoctoral awards and fellowships (Postdoctoral Fellowships, Postdoctoral Awards for Academic Diversity). Through these awards, the Institute supports collaborative and cutting-edge research in various fields of neuroscience, as well as the career development of trainees. For each funding mechanism, an ad-hoc committee of scientists reviews and selects proposed projects to support, in alignment with the Institute's mission.

The **Kavli Innovative Research Awards** are granted to faculty and interdisciplinary collaborative teams pursuing innovative, early-stage neuroscience research, enabling them to test bold, new ideas. To date, over 50 projects have been funded through this initiative, supporting high-impact research and collaborations across multiple departments at Yale.

The **Kavli Innovative Teams Awards**, newly launched, support cutting-edge research that assembles research teams with long-term goals of solving major issues in neuroscience. Many crucial questions in neuroscience can be solved only by creating teams of skilled researchers using multiple established techniques to achieve progress where no one laboratory can succeed alone. Awarded innovative teams tackle established questions that will seed future large-scale program grant applications.



Visualization of cortical white matter axons leaving a tract to innervate the cortical neuropil, segmented from X-ray Nano-Holography data. Credit: Kavli awardee Aaron Kuan, Kuan lab



Kavli postdoctoral fellow Qiancheng Zhao, Chang lab

The **Kavli Postdoctoral Fellowships** are competitively awarded to outstanding postdoctoral associates working at the interface of neuroscience and other disciplines under the joint supervision of mentors with different areas of expertise.

The **Kavli Postdoctoral Awards for Academic Diversity** support exceptional scholars who bring a diversity of perspectives, identities, and backgrounds to academic research, including those from groups that are historically underrepresented in the sciences.

4
grant mechanisms

60
faculty awards

14
postdoc fellowships

7
postdoc awards for academic diversity

81
total grants and fellowships

71
labs supported by the Kavli cores

500+
papers acknowledging Kavli Institute support

Catalyzing Impact through Focused Research Funding

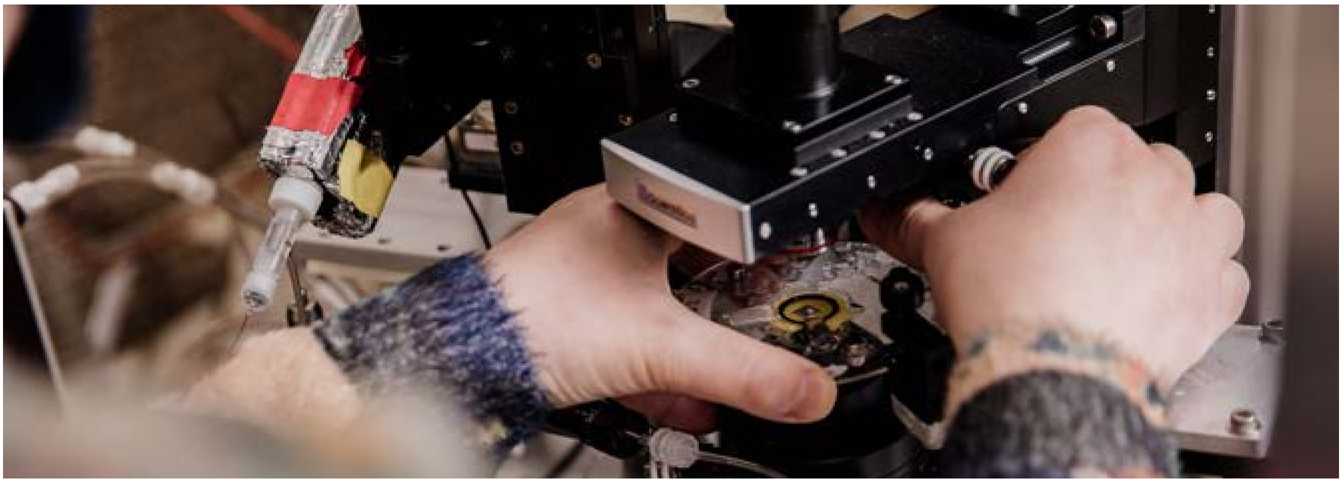
Kavli postdoctoral fellow I-Uen (Yvonne) Hsu, Chang lab

RUI CHANG

Assistant professor of neuroscience and of cellular & molecular physiology

The Chang lab's research focuses on interoception - the body's ability to sense changes within itself. The process of interoception depends on the vagus nerve, which acts as a communication line, sending signals from respiratory, cardiovascular, gastrointestinal, endocrine, and immune systems into the brainstem. This vagal interoception system is essential for survival, but how this communication line works is unclear. Work led by Qiancheng Zhao (2018 Kavli Postdoctoral Fellowship, Chang and Young labs) describes how vagal sensory neurons code these signals with high precision.

Continued support to the Chang Lab through a Kavli Innovative Award (2019, Rui Chang and Le Zhang) enabled the development of a novel projection neuron profiling strategy, called high-throughput Single-Neuron transcriptome Analysis based on Projections (SNAP-seq). The team used large-scale single-cell profiling of vagal sensory neurons and calcium imaging-guided spatial transcriptomics to show that these cells code three dimensions of an interoceptive signal, including the visceral organ (where along the body rostral-caudal axis), the tissue layer (where along the surface-lumen axis of organs), and the stimulus modality (e.g., stretch or chemical challenges). Now an assistant professor at the Baylor College of Medicine, Dr. Zhao is continuing his research on the neurobiology of interoception. More recent work led by I-Uen (Yvonne) Hsu (2021 Kavli Postdoctoral Fellowship, Chang, Young, and Zhang labs) is examining the organizational differences between the enteric nervous system and the intrinsic cardiac nervous system. Understanding these mechanisms of the heart-brain axis will pave the way to new treatment approaches, such as controlling hypertension by targeting "the little brain of the heart".



Gizem Sancer, Jeanne lab

JAMES JEANNE

Assistant professor of neuroscience

Have you noticed how the smell of delicious food has a very different impact on you whether you are hungry or full? A key function of the brain is to evaluate incoming sensory information in the context of immediate internal needs. Under different motivational states—such as hunger—the same sensory input is perceived and acted upon differently. The neural mechanism behind this modulation of information interpretation is still unknown. The lab of James Jeanne aims to understand how behavioral flexibility arises from neural circuit flexibility at the level of synaptic function. A Kavli Innovative Award (2019, James Jeanne and John Carlson) allowed the team to shed light on the anatomical basis of synaptic function. Taking advantage of the emergence of whole-brain connectomics of electron microscopy (EM), the Jeanne lab explored reconstructed maps of synapses in *Drosophila melanogaster* and noted that many connected neurons have a single synapse, whereas others can have hundreds. To examine the functional significance of this diversity, the lab aimed to link *Drosophila* anatomy (i.e., connectomics via electron microscopy) with physiology (a measure of synapse strength). This work revealed a linear correlation between the number of synapses and the connection weight, concluding that much of the connection strength can be explained by EM data. Understanding the relationship between connectivity and activity will enable more biologically relevant functional predictions from the connectome.

ELENA GRACHEVA

Associate professor of neuroscience and of cellular & molecular physiology

The lab of Elena Gracheva is interested in somatosensation (all the sensory inputs received by the skin) and thermoregulation, and particularly how the somatosensory and thermoregulatory systems adapt to the environmental and behavioral needs of an organism. To examine these systems, her lab takes advantage of the process of hibernation in thirteen-lined ground squirrels. These tiny mammals spend about 7 months in torpor, during which they experience plummeting heart, respiratory, and overall metabolic rates. Every few weeks, the animals return to an active-like state (called interbout arousal, or IBA) for about 24-48 hours. Surprisingly, squirrels do not eat and demonstrate little interest in food during these periods despite winter-long starvation – a phenomenon known as hibernation anorexia. Work led by Sarah Mohr (a 2019–2020 Kavli graduate student) sought to understand hibernation anorexia by comparing squirrels in the active season to squirrels during IBA periods. Her efforts showed that hibernating squirrels exhibit reversible resistance to the appetite-stimulating hormone ghrelin and reduced signaling by the satiety hormone leptin. Their findings support that this hormone sensitivity change is due to a deficiency in the thyroid hormone triiodothyronine in the hypothalamus, while thyroid function is preserved peripherally. In this study, Maryann Platt (2022 Kavli Postdoctoral Fellowship, Gracheva and Eichmann labs) confirmed that the observed ghrelin insensitivity was not due to a change in permeability of the blood-brain barrier (BBB). In an independent project, Dr. Platt is currently deciphering how the BBB adapts to such low temperatures during hibernation, which could provide insights into possible neuroprotective strategies for therapeutic use.

iPSC neurocore

FLORA VACCARINO

Harris Professor in the Child Study Center and professor of neuroscience

Flora Vaccarino studies mammalian brain development. As pioneers in the field of 3D brain organoids, her team has generated an extensive collection of induced pluripotent stem cell (iPSC) lines derived from patients with autism spectrum disorder (ASD), which could be essential for personalized medicine. With support from the Kavli Institute, the Vaccarino lab has recently focused on engineering brain organoids using gradients of signaling molecules present in the developing body, creating a reproducible topography of cell identities and mimicking more closely human early neural development (2020 Kavli Innovative Award, Flora Vaccarino & Andre Levchenko). Her lab is also studying cell lineages in human development. Somatic mosaicism, the accumulation of mutations in cellular genomes after fertilization, has known biological consequences and is a potential source of differences in developmental trajectories between individuals. Dr. Vaccarino's lab used deep sequencing technologies of genomes of clonal iPSC lines to quantify somatic mosaicism in many human cell types and tissues, including the human developing brain, and revealed unequal contributions of daughter cells during development. Their studies have paved the way for comprehensive and large-scale analyses of early lineages and understanding their role in human health and disease.

ELLEN HOFFMAN

Associate professor in the Child Study Center and of neuroscience

Over the years, researchers have identified many genes that are strongly associated with autism spectrum disorder (ASD), but it remains unclear whether these "risk genes" are part of common biological pathways. The lab of Ellen Hoffman aims to identify these convergent mechanisms, which could reveal molecular targets with therapeutic potential. With Kavli support (2017 Kavli Innovative Award, Ellen Hoffman and Michael Higley), the team developed a whole-brain mapping protocol that allows for high-throughput analysis, visualization, and quantification of larval zebrafish brain phenotypes. By combining this whole-brain mapping tool with automated behavioral assays, the Hoffman lab uncovered that mutations in 10 ASD risk genes have converging effects: they impact basic arousal and sensory processing behaviors, brain size, and activity in the developing zebrafish brain. Using RNA sequencing on the two mutant lines showing the strongest phenotypes, the team also reported dopaminergic and neuroimmune dysfunction. This convergence of behavioral features can be leveraged to identify potential pharmacological targets, which the lab is now addressing through drug screening. Currently, Priyanka Jamadagni (2022 Kavli Postdoctoral Fellowship, Hoffman and Girgenti labs) is expanding the Hoffman lab's research focus to include genes that are believed to be drivers of post-traumatic stress disorder (PTSD). Through the Fellowship, she aims to expand our understanding of whole-brain circuitry in the context of neurodevelopmental disorders.

A Powerful and Inspiring Community

Fostering community is at the heart of the Kavli Institute. Since its founding, the Kavli Institute has worked to build bridges across the Yale campus, bringing together scientists from traditionally separate academic departments, schools, and disciplines. In addition to funding collaborative research projects and supporting promising scientists, the Institute offers different opportunities to interact with peers—including scholars inside and outside the neuroscience community.

Community

The **Kavli Networking Hour** provides a monthly forum for the Yale neuroscience community to meet with colleagues and informally discuss their research.

The **Kavli Community Lunch** is a monthly lunch for all Kavli-supported students and postdocs, past and present, on the first Friday of each month. They are a way of connecting, getting to know other Kavli trainees and scholars, and encouraging informal peer mentoring.

Kavli Networking Hour

150+ faculty affiliates

7 postdocs for academic diversity

14 postdoctoral fellows

37 graduate students

12 undergraduate thesis awards

34 SYNAPSES speakers

15 SURF students

Fostering the Next Generation

The Kavli Postdoctoral Fellowships were established in 2018.
Discover some of the outstanding postdoctoral fellows' research journeys below.

HURIYE ATILGAN

2018, Labs of Alex Kwan and Ifat Levy

After a PhD in the lab of Jennifer Bizley at University College London studying ferrets, Huriye Atilgan joined the lab of Alex Kwan in the Department of Psychiatry in 2017. Her Kavli project focused on the neural correlates of value-based decision-making, for which she combined state-of-the-art computational, behavioral, and imaging methods in mice. "During this fellowship, I learned behavior modeling, which was a turning point in my career. It is amazing to be able to model mouse behavior with high accuracy using a few mathematical equations based on previous choices." Dr. Atilgan is now working on the functional role of the claustrum in value-decision-making as a Wellcome Trust Sir Henry Fellow at the University of Oxford, UK.

TAL YATZIV

2022, Labs of Helena Rutherford and Philip Corlett

During her postdoctoral training in the Before and After Baby Lab in the Child Study Center, Tal Yatziv worked on the mechanisms of adaptive caregiving, assessing parents' biases in processing infant affective facial expressions. She used a measure of cortical activity time-locked onto stimulus presentation - called event-related potentials - and computational modeling to examine how parents' biases shape the way they detect, understand, and respond to their infant's needs and internal state, as well as how these processes evolve from pregnancy to postpartum. This Kavli project "has been invaluable in jump-starting [her] line of research on biases in processing infant-related information" and enabled her to extend her training in using electroencephalography (EEG) to study responsivity to infant affective expressions in pregnancy. Dr. Yatziv is now a lecturer in the Department of Psychology at Ben-Gurion University of the Negev in Israel, where she directs the Minds Interacting N' Developing (MIND) Lab.

XIZE XU

2023, Labs of Monika Jadi and Anirvan Nandy

Xize Xu comes to Yale with a background in applied mathematics and uses theory, simulation, and analysis of neural data to uncover how population dynamics enable computations in the visual cortex. In his Kavli-supported postdoctoral research, he employs both mechanistic and statistical circuit-level models to explore the mechanisms of visual crowding, a ubiquitous phenomenon in peripheral vision that severely degrades our ability to identify objects in clutter. Specifically, Dr. Xu investigates how crowding stimuli and their spatial configuration influence interactions of neuronal ensembles in the macaque visual cortex. Collaborating closely with the Nandy lab, which collects high-density electrophysiological data, allows him to test his models rigorously. Dr. Xu's Kavli project promises to significantly advance our understanding of the cortical circuits involved in visual processing.

KAVLI POSTDOC SERIES

Supported by a special Kavli Foundation grant, the **Kavli Postdoc Series** brings together Yale neuroscience postdoctoral fellows, regardless of their department affiliation, for scientific discussions, career development activities, and community building. Through presentations, hands-on workshops, and discussions, this series aims to foster a sense of community and encourage peer support, accountability, and collaboration. So far, this series has covered science communication and online presence, how to manage difficult conversations, and how to present a chalk talk during a faculty job interview. During the **Chalk Talk** event, postdocs heard a chalk talk demonstration by a recently appointed assistant professor in neuroscience, learned the best practices for delivering a chalk talk, and gained understanding of what the audience expects during the chalk talk part of faculty interviews. Select participants had the opportunity to practice in front of an audience of peers and faculty members, who asked questions and gave feedback. The event was organized for the first time in March 2022, and was so successful that the event became annual. So far, the initiative has brought together over 25 faculty members from different neuroscience fields at Yale, trained close to 200 postdocs across 19 departments, and allowed 22 postdocs to practice their chalk talk.

GRADUATE SUPPORT

The **Kavli Fellows Education Fund** provides support to a select group of incoming graduate students in the Interdepartmental Neuroscience Program (INP), in recognition of their outstanding academic record and exceptional promise as a scholar. Nominated by the INP admission committee, Kavli-supported graduate students receive a stipend supplement (Kavli Awardees) and research funds (Kavli Scholars), and are invited to participate in special events organized by the Institute, including the annual dinner reception of the Kavli Distinguished Lecture and the monthly Kavli Community Lunch.

UNDERGRADUATE PRIZE

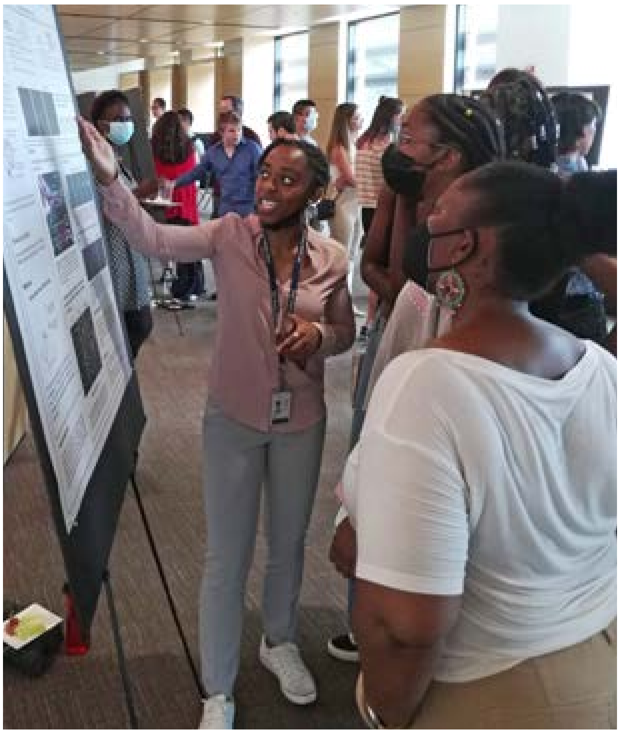
Each year since the Neuroscience major was founded, the Kavli Institute for Neuroscience at Yale has awarded the **Kavli Undergraduate Thesis Prize** to two graduating seniors. These two Neuroscience seniors, chosen by a small committee convened by the major specifically for this award, are selected based on their senior research, their poster presentation, and grades in the major.

Kavli Postdoc Series: mock chalk talk by Vidyadhara D J, Chandra lab

Diversity, Equity, Inclusion, and Belonging

SURF

Since 2022, the Kavli Institute has partnered with the Yale Summer Undergraduate Research Fellowship (SURF) Program to bring a group of undergraduates to Yale each summer to explore what a PhD could offer them. Kavli-supported SURF program participants get immersed in a neuroscience research laboratory and learn many useful skills such as presenting their research effectively, developing a proposal, and writing a paper. They end the experience by attending the Leadership Alliance National Symposium.



SURF program student Sapphire Moore

POSTDOCTORAL AWARD FOR ACADEMIC DIVERSITY

Initiated in 2021, the Kavli Postdoctoral Award for Academic Diversity has supported groundbreaking research projects led by exceptional scholars who bring a diversity of perspectives, identities, and backgrounds to academic research, including those from groups that are historically underrepresented in the sciences.

Rafael Perez, Picciotto lab

"I am especially grateful for all the opportunities I had access to. The Kavli funding allowed me to present my work at multiple international conferences, build my skillsets, and expand my scientific network."

— Elvisha Dhamala

Elvisha Dhamala
2021, Lab of Avram Holmes

Elvisha Dhamala is the inaugural awardee of the Kavli Postdoctoral Award for Academic Diversity. Her project focused on characterizing sex differences in the neurobiological underpinnings of behavioral phenotypes. She developed expertise in brain-based predictive modeling, a machine learning framework that allows to capture robust and reliable associations between brain-derived measures and behavioral phenotypes. She recently demonstrated that sex and gender have unique influences on functional brain networks. Because social identities (e.g., sex, gender, race, ethnicity, socioeconomic status) influence brain and behavior, she believes that aspects of biomedical research such as participant recruitment, data acquisition, and data analysis can be improved to facilitate more inclusive analyses across populations with intersectional identities. Dr. Dhamala is currently an assistant professor at Feinstein Institutes for Medical Research, where her lab studies the influences of sex and gender on neurobiology and behavior across healthy and psychiatric populations.

Rafael Perez
2022, Lab of Marina Picciotto

Rafael Perez's work focuses on determining the brain regions that mediate how contextual cues modify opioid analgesic tolerance. Over the award period, he has identified cortical regions and cell populations that play critical roles in the formation and retention of contextual opioid tolerance. His findings became the basis of a successful K99 application, bringing him one step closer to achieving his dream of establishing a lab to research novel treatment options for drug use disorders while training the next generation of diverse scientists. His work aims to deepen our understanding of the factors controlling analgesic tolerance, which will inform the development of treatments to prevent use escalation while minimizing pain. Dr. Perez is the first postdoctoral scholar to integrate the Kavli steering committee, allowing him to shape the Institute's direction. Being a Kavli awardee brought him training, mentoring, and leadership opportunities.

Clíona Kelly
2024, Lab of Helena Rutherford

Clíona Kelly is a cognitive neuroscientist who pioneered the combination of electroencephalography (EEG) with virtual reality to observe oscillatory changes in a dynamic and naturalistic environment. Her postdoctoral project investigates the mother-infant interaction, focusing on the role of eye gaze in how mothers respond to their infant cues. Dr. Kelly co-founded Black In Neuro, a 501c3 non-profit that highlights Black neuroscientists globally. Since her Kavli award, she has been inducted into the Edward Bouchet Graduate Honor Society, a society that recognizes outstanding scholars for their academic excellence and distinguished outreach contributions. Passionate about engaging the public in science, it is important to her that the research conducted is representative and appropriately disseminated within the local New Haven community. Dr. Kelly has recently been awarded the prestigious Yale School of Medicine Science Fellowship, supporting her transition to faculty. In this position, she will continue to develop her research combining neuroimaging with augmented, mixed, and virtual realities.

Tristan Geiller and Heather Snell

"The series gave me a confidence boost."

— Heather Snell

SYNAPSES

SYNAPSES (Seminars at Yale Neuroscience: Advanced Postdoc Extramural Series) is a seminar series that brings outstanding postdoctoral researchers from across the globe to Yale to share the most recent results in rapidly developing areas of neuroscience. The series, co-sponsored by the Department of Neuroscience, is led by a committee of postdoctoral researchers.

Among the many rising neuroscientists who visited Yale through SYNAPSES, two postdoctoral scholars came back in another capacity - and shared how the program made a difference in their careers. In January 2021, Tristan Geiller, then at Columbia University, presented his postdoctoral work on place cell dynamics in the hippocampus to the Neuroscience community. He received valuable feedback on his presentation, which made his job talks more accessible to non-experts. "I enjoyed meeting the faculty in the department, learning about their research, and establishing contacts before entering the job market. This experience provided a great opportunity to broaden my network and talk to new people whom I later met during my interview." A year later, Heather Snell, a postdoctoral fellow at Albert Einstein College of Medicine at the time, shared her work focused on stress and caffeine-induced motor dysfunction in a mouse model of episodic ataxia type 2. As a result of a one-on-one meeting, Dr. Snell initiated a collaboration with a Yale faculty. She also mentioned how being selected in this competitive program reassured her on her ability to secure a faculty position: "The series gave me a confidence boost. It helped me change my perception of myself". Both Drs. Geiller and Snell successfully applied to the 2023 faculty search in the Department of Neuroscience, and started as assistant professors in January 2024.

Building Crucial Infrastructure

A key component of the Kavli Institute for Neuroscience's vision is to ensure that the most exciting science can be delivered to a broader audience to increase its impact. The Institute supports several scholarly activities each year to help its members and affiliates share their research breakthroughs with the community, and for them to hear from and interact with world leaders in the field of neuroscience.

Sharing Groundbreaking Science

Kavli Symposia are public events that gather international experts to discuss developing topics in neuroscience.

Kavli Workshops address emerging themes in neuroscience with talks by leading researchers at Yale. These events aim to bring together Yale scientists at all levels working on a similar research topic, in order to increase the potential for collaboration across departments. The Kavli workshops usually feature an external speaker, and for the past few years, they have also included talks given by Yale trainees and a panel discussion.

16
Kavli workshops

16
Kavli distinguished lectures

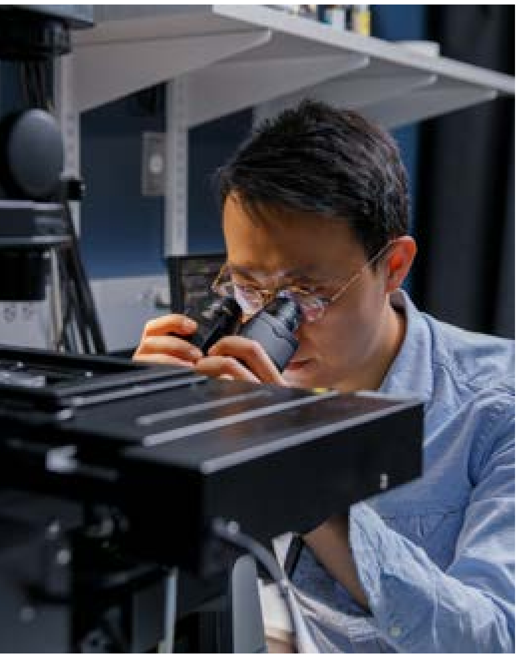
3
cores

- * 2023 Social Behaviors
- * 2022 Spatial Transcriptomics
- * 2021 Neuromodulation
- * 2020 Generation and Analysis of Complex Data in Neuroscience
- * 2018 Molecular Mechanisms of Neurodegeneration
- * 2018 Single Cell Genomics in Neuroscience
- * 2017 Neural Mechanisms of Attention and Awareness
- * 2016 Genome Editing
- * 2014 Multicellular Monitoring and Manipulation
- * 2012 Potential of Induced Pluripotent Stem Cells
- * 2012 Optogenetics
- * 2012 Molecular Genetics
- * 2011 Emerging Techniques in Neural Circuit Analysis
- * 2010 Development, Structure, and Function of Neuronal Networks
- * 2009 Molecular Aspects of Neural Development
- * 2009 Cortical Mechanisms of Decision Making

Once a year, the **Kavli Distinguished Lecture** brings to Yale a preeminent neuroscience investigator to share important ideas and developments emerging in the field.

The Kavli Institute also provides support to the Department of Neuroscience seminar series, the Department of Neuroscience annual retreat, the Goldman-Rakic Lecture in Cognitive Neuroscience Research, the Yale Neuroscience's National Postdoctoral Appreciation Week, and the Yale Postgraduate Trainee Symposium. Furthermore, the Institute also sponsors community events such as Yale's Brain Education Day, which provides grade school students with hands-on opportunities to learn and explore different aspects of neuroscience.

Erin Schuman, Kavli Distinguished Lecture 2023



Peng Xu, De Camilli lab, using one of the microscopes from the core facility

Enabling Cutting-Edge Experiments

In addition to funding targeted research projects, the Kavli Institute enables access to advanced technologies for all Yale neuroscientists by establishing and supporting shared facilities, such as the Rodent Behavioral Analysis Core and the Neurotechnology Core, and by providing support to Neuroscience microscopy facilities.

The **Rodent Behavioral Analysis Core** provides dedicated space and specialized equipment for targeted phenotyping of motor, sensory, and cognitive behaviors in rodent models. Co-directed by Susumu and Megumi Tomita, the core regularly expands the available equipment based on feedback from current and prospective users.

The **Neurotechnology Core** provides customized engineering solutions and training to expand research capabilities in the Yale neuroscience community. The state-of-the-art facility enables the design and fabrication of electronic, mechanical, and optical devices and their interfaces. Joel Greenwood, director, and Paul Shamble, neurotechnology engineer, support the development of novel scientific instrumentation and provide training and consultation on design, fabrication, and purchasing decisions, for scientists to overcome technical barriers to cutting-edge neuroscience research.

Among all Neurotechnology Core projects, two are highlighted on the following page.

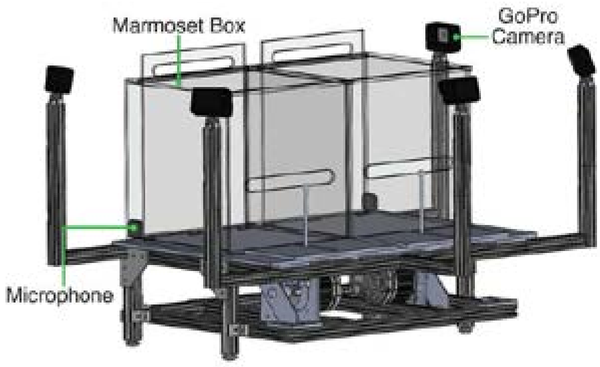
Neurotechnology Core Facility

DUAL IMAGING

Work in the lab of Evelyn Lake centers around dual imaging, a novel, custom-built imaging system for mice that allows for the simultaneous collection of high-resolution MRI data and fluorescence-based optical imagery. This innovative system makes addressing an exciting range of scientific questions possible, but is technically difficult to design, as it requires the creation of a fully MRI-compatible microscope—a setup free of any magnetic materials that can also operate within the extreme spatial constraints of a high-power, small-animal MRI. The Neurotechnology Core designed and produced many parts of this system. First, the team imagined and built an adjustable mouse bed for animal restraint, and glass headplates for clear optical windows for brain imaging - all without metal. Next, they overcame a major challenge: holding the mouse bed stable inside the bore of the MRI. To achieve this, they developed a hydraulic system that uses standard 50mL syringes to create and apply pressure. Modifying standard syringes for this purpose keeps the initial and maintenance cost of this solution low. Recently, the team created a new optical system using lasers instead of LEDs as a light source, enabling more advanced multi-wavelength data collection. The Neurotechnology Core has greatly improved the functionality of the system, and plan to make those designs widely available via publication with the Lake lab.

ADVANCED TOOLS FOR MARMOSET RESEARCH

Marmosets are small primates that share significant social cognition similarities to humans, making them a great model organism to study naturalistic social behavior and its underlying neural mechanisms. Recently, the labs of Anirvan Nandy, and Steve Chang collaborated with the Kavli Neurotechnology Core to develop a novel apparatus to study cooperative behaviors in marmosets. This apparatus, named Marmoset Apparatus for Automated Pulling (MarmoAAP), bridges the gap between ethologically relevant animal behavior studies and neural investigations. The Kavli Neurotechnology Core worked closely with Olivia Meisner, lead author of the study, to build this sophisticated tool with custom-designed components and force sensors. The result is an automated, programmable, and high-throughput apparatus leading to detailed readouts—an important advancement for the study of complex behaviors in marmosets.



Model of the marmoset pulling apparatus showing its layout, transparent testing boxes, frame structure, video cameras, and microphones. Credit: Olivia Meisner, Nandy lab

Leadership

Past leadership

Pasko Rakic
Founding director

Pietro De Camilli
Director

Candace Bichsel
Managing director

Current leadership

Stephen Strittmatter
Director

Marina Picciotto
Deputy director

Pauline Charbogne
Managing director

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Richard Lifton

David McCormick

David Hafler

John Krystal

Tamas Horvath

Arthur Horwich

Jess Cardin

John Carlson

Nenad Sestan

Susumu Tomita

Steve Chang

Current steering committee members

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Flora Vaccarino

Michael Higley

Damon Clark

Shawn Ferguson

Anirvan Nandy

Angeliki Louvi

Elena Gracheva

Ellen Hoffman

Rafael Perez

Past *ex officio*

Carolyn W. Slayman

Patty Pedersen

Current *ex officio*

Tony Koleske

Tammy Wu

Daniel Bennett

Looking forward

The first 20 years of the Kavli Institute for Neuroscience have enabled progress in neuroscience at large, accelerating impact in the fields of neurodegeneration, cortical circuits, technology development, and many more. We are deeply grateful for the support and generosity of the Kavli Foundation and of its visionary founder, Fred Kavli (1927-2013), who trusted Yale to grow into one of the leading institutions in neuroscience research, when the Department of Neurobiology - that would then become Neuroscience - was still in its infancy. We are profoundly appreciative of the diverse community of scholars that compose the Kavli Institute. These researchers are highly committed to scientific excellence, working every day on expanding the boundaries of neuroscience knowledge and mentoring the next generation of scientists. With their curiosity, creativity, and collegiality, they make doing research at Yale productive and exciting, but also fulfilling and enjoyable. We would like to thank our committee members for shaping our direction, and all the behind-the-scenes team members who support the finance, administration, communication, and overall organization of our Institute.

While this document highlights a few of the many advances in Neuroscience through the Kavli Institute at Yale, the knowledge gained has generated many additional questions about brain function – questions that we could not imagine asking 20 years ago. We anticipate further accelerating progress for neuroscience, and look forward to a continued leading role for the research supported by the Kavli Institute for Neuroscience at Yale.

Pauline Charbogne
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