

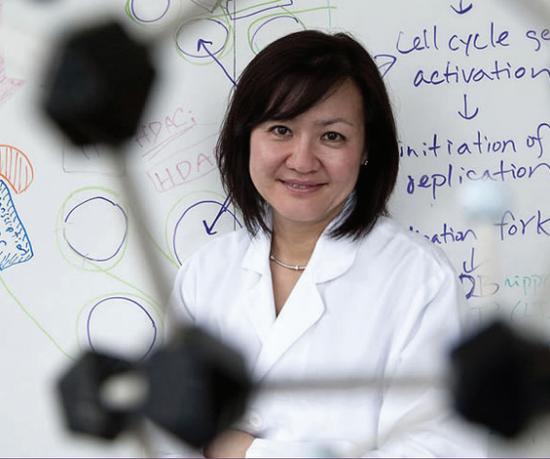
**BASIC
RESEARCH
MATTERS**

Neuroscience News

Winter 2016



**THE PICOWER
INSTITUTE**
FOR LEARNING AND MEMORY



DIRECTOR'S MESSAGE

Dear Friend,

Answers lie in what we don't know. The importance of basic neuroscience research, particularly focused on animal work, is what will lead to new and effective cures for brain illnesses. Crippling diseases like smallpox, polio, and pneumonia are no longer threats because of the fundamental knowledge and groundbreaking results basic research provides. Basic research stimulates new ways of thinking and neuroscience has entered into a golden age of remarkable progress. As technology allows scientists to map the brain from neurons to cognition, it is expected that brain disorders will be better treated if not cured.

In this issue, we're featuring major basic research breakthroughs to better map the brain in three dimensions, new understandings of how synapses encode the information we've learned, and identified brain circuits that store the when and where of our memories.

In other news, I'm thrilled to share that computational neuroscientist and practicing anesthesiologist, Professor Emery Brown, has joined our institute as faculty. Professor Kwanghun Chung was also awarded the distinguished 2015 Packard Fellowship. In addition, we'd like to extend a warm thank you to Robert and Renee Belfer and Jeff and Nancy Halis for their tremendous new support to further translational discoveries on Alzheimer's and brain-aging quests.

Basic research exposes the power of investigation, is the foundation on which applied research is built, and is a prerequisite for innovation. It has the potential to save lives and result in direct and indirect economic impact. We hope you see the value and need for investment in basic neuroscience research and will join us in continuing our tradition of curiosity and seeking answers to questions that will define our future.

LI-HUEI TSAI, DIRECTOR

Basic Research: The Innovation Catalyst to Cure Mental Health

During the 1950s the first generation of psychopharmacological medications transformed the treatment of psychiatric disorders with the development of mood stabilizers, antipsychotics, antidepressants, and anxiolytics. At the time, scientists assumed that chemical imbalance was the culprit to psychiatric illness. Over the past 60 years, neuroscientists now know that the chemical imbalance theory of mental illness is too simplistic.

Trillions of neurons must travel long distances to connect in just the right way for a developing brain to work properly. The intricacies of the brain

are as astonishing as the human mind is complex. Given the vast interconnectivity that underlies our conscious awareness, it is not surprising that brain dysfunction cannot be easily explained by general chemical imbalance. Genetic mutations, stress, and traumas impact the brain that can deteriorate mood and cognitive ability, all of which are due to complex interactions with the person and their environment.

The environmental stressors of living in urban centers further increase psychiatric disorders like depression, schizophrenia, anxiety, and substance abuse. Over half of the world's population now lives in cities, which is predicted to exacerbate the global mental health epidemic as cities contain ever more people. According to the National Institute of Mental Health, the World Health Organization, and the Center for Disease Control, mental health services cost the United States more than \$100 million yearly; there is up to \$44 billion lost in workdays, and global mental health costs will hit \$6 trillion by 2030. Brain dysfunction is the basis of psychiatric disorders and constitutes the greatest global burden on mental health treatment.

Moreover, inadequately sophisticated technologies make the research a costly and lengthy endeavor to pursue and therefore unresponsive of the

IN THIS ISSUE

- 2 Basic Research: The Innovation Catalyst to Cure Mental Health
- 5 Reinventing Anesthesia
- 6 Seeing the Brain in 3D
- 6 Making it Easier to Learn
- 7 Mapping Memory Through Space and Time
- 8 Stimulating Sleep
- 8 Rewards Alter Thoughts and Dreams
- 8 Critical Path to Vision Loss
- 9 Picower News
- 10 Picower Accomplishments
- 11 Picower Events

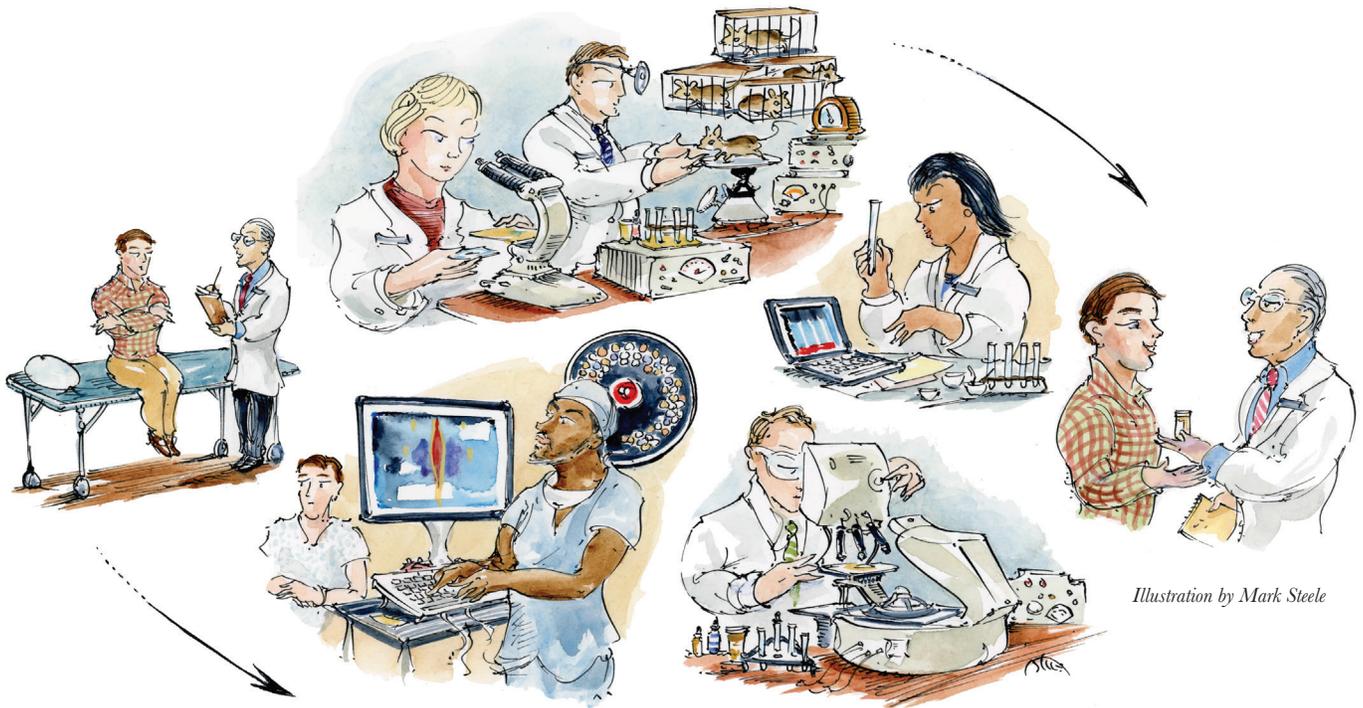


Illustration by Mark Steele

INFLUENCE OF BASIC RESEARCH ON THE CLINIC

Over the past 15 years pharmaceutical giants have shut down or significantly reduced research into psychiatric diseases, largely because of inadequate understanding of brain function and dysfunction.

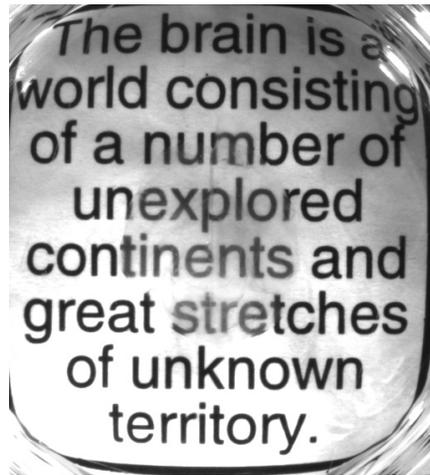
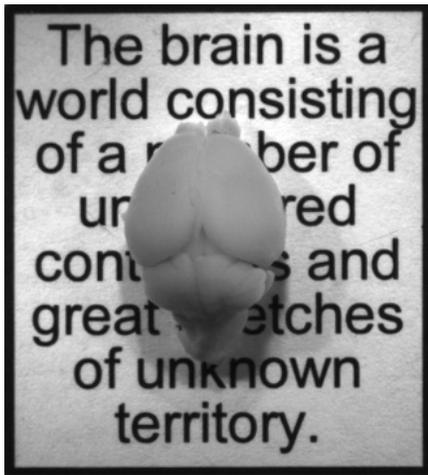
short-term profit models. Today, academic laboratories and their biotech start-up ventures perform the vast majority of basic research and technological development. Thus, placing the lion's share of the burden on under-funded institutions and industries to make the necessary progress for clarifying complicated functions of brain activity that underlie healthy and unhealthy psychological function.

The socio-economic strain of psychopathologies highlights the need for fundamental research, a better understanding of the brain in health and disease, and new models to overturn decades of old assumptions about the chemical imbalance model of mental illness. Now more than ever, basic research will be critical to developing life saving treatments for psychiatric illness mitigating severe economic repercussions, and relieving the mental burden of suffering people. Fundamental neuroscience research has begun creating technologies that peer into brain processing so powerfully that decades of prevailing knowledge on mental illness are starting to overturn. They include new technologies to see, record and control brain function, combined with ways to mutate and fix genes, or to introduce elements of a cell's machinery back into cells. All of which allow us to connect specific brain regions, circuits, cells and molecules to mental health and provide the foundation for future diagnostic approaches and treatment possibilities for psychiatric disorders.

Picower Institute Professor Kwanghun Chung, for example, is a chemical

engineer and neuroscientist who recently gained international recognition for creating a breakthrough technology called CLARITY. CLARITY makes tissue, like the brain, completely see-through. With a clear brain and additional biological techniques, an exceptionally detailed map of neuronal pathways can be made, which had been inaccessible even from our best technologies a few years ago. With this enhanced resolution of brain anatomy, neuroscientists are now able to look for the microscopic differences between healthy and dysfunctional brains. CLARITY further weds basic research to clinical practice, providing new views on biopsied and post-mortem human samples.

This fall, Chung has built on this progress to develop another technology for brain imaging called SWITCH [see more on page 6]. Unlike any other techniques used in neuroscience labs today, SWITCH perhaps has the most direct application to the biomedical field. With SWITCH, neuroscientists and clinicians can rapidly and precisely analyze nearly dozens of chemical reactions suitable to test medications for mental disorders. SWITCH will be used to identify each



(TOP LEFT) A mouse brain before and after (MIDDLE) the use of the revolutionary technique called CLARITY. CLARITY makes the brain transparent, which allows for previously unknown brain circuits to be revealed.

brain region in great detail to understand the locations that exhibit aberrant genetic activity that relates to mental illness. Thus, SWITCH creates a comprehensive brain map like no other, which can detect brain regions that show potential disease. SWITCH is cost-effective, easy to implement, and scalable, making this new technology an incredible tool in understanding human disease from single molecules to the entire brain.

Using technologies effectively to answer critical biomedical questions is the lifeblood of basic neuroscience research and results in discoveries to better understand the brain in sickness and in health. For mental health for example, researchers in the laboratory of **Picower Institute Professor Kay Tye** have made a startling discovery about a brain circuit in relation to stress, reward, and loneliness [see more next issue]. Their work shows that a brain region originally thought to produce and release the neurotransmitter serotonin also releases the neurotransmitter dopamine and that this release of dopamine regulates social isolation. Although this finding may sound surprisingly simple it is a fundamental shift in our understanding of how a neurotransmitter (i.e., dopamine) can alter brain activity depending on which brain region it comes from. The Tye lab findings also connect complex behaviors like loneliness brought about by social isolation to brain networks, which are deeply affected by a particular source of dopamine. Without

breakthrough technologies such research would not be possible and in fact it was not possible just a few years ago.

Professor Kay Tye’s work parallels the overwhelming data that when people are isolated and without a community, mental health declines, which often leads to major depressive disorder or MDD. Treatment of MDD includes counseling and medication like antidepressants that artificially enhance neurotransmitters (e.g., serotonin, dopamine) all throughout the brain. However, antidepressants do not provide relief from MDD in the majority of patients, medications are not specific to brain regions that underlie

different types of mental illness, and they also have serious side effects like weight gain, sedation, and can lead to abnormal behavioral changes. These noted problems are likely due to the oversimplified idea that a chemical imbalance underlies mental illness like MDD. Indeed, research in the Tye lab is overturning decades old assumptions about the chemical imbalance model of mental illness and highlights the need for new direction, insights, and transformative research.

Neuroscience technologies are creating a new era for basic research and one that can usher in a new generation of understanding and treatments to meet the challenges of burgeoning mental illness. There is a pervasive optimism in the field, that with the right investment, basic research and technology development could bring us concrete solutions.

– Joshua Sariñana, PhD



(Right) Picower Institute Professor Kay Tye stands with her postdoctoral researcher Gillian Matthews (Left). Their recent Cell paper identifies the neuronal substrate of loneliness. (Photo by Joshua Sariñana)

Emery N. Brown

Joins the Picower Institute

Reinventing Anesthesia

Dr. Emery Brown, the Edward Hood Taplin Professor of Medical Engineering and Computational Neuroscience in MIT's Department of Brain and Cognitive Sciences, has joined the team of investigators at the Picower Institute for Learning and Memory. He also codirects MIT's Institute for Medical Engineering and Science (IMES) and is a founding investigator in MIT's new Aging Brain Initiative – a faculty driven effort to tackle the scourges of brain aging and cognitive decline, led by Picower Institute director, Li-Huei Tsai.

renowned researchers selected to join the working group tasked with managing President Obama's BRAIN Initiative.

Brown studies the dynamics of the unconscious brain—more specifically, the underlying neural mechanisms of anesthesia drugs. His research shows that the brain's arousal circuits actively oscillate rather than turn off while patients are unconscious under general anesthesia. This disrupts normal communication, making it impossible for information to be transmitted from one brain region

“The doses required to achieve the same anesthetic state in older patients can be as little as half what is needed for younger patients. Explanations for that difference have focused on age-related declines in cardiovascular, respiratory, liver and kidney function, but the primary sites of anesthetic effects are the brain and central nervous system.”

-EMERY BROWN, SCIENCEDAILY

In addition to his work at MIT, Brown is a professor of anesthesiology at Harvard Medical School and a practicing anesthesiologist at Massachusetts General Hospital. He received his undergraduate degree in Applied Mathematics from Harvard College, his MA and PhD degrees in statistics from Harvard University, and his MD from Harvard Medical School. Brown is a member of the National Academy of Medicine, the National Academy of Sciences, the National Academy of Inventors, and the National Academy of Engineering. He was also among several of the nation's

to another. The innovative real-time monitoring technology Brown developed reveals how different anesthesia drugs act in different ways on various brain regions. This insight is driving new anesthetic approaches that target specific parts of the brain with the appropriate drug dose and minimal duration necessary to control unconsciousness and pain, and thereby reduce the side effects associated with existing drugs.

Brown and colleagues also found that the brain's responses to anesthesia change dramatically with age.



Picower Institute Professor Emery Brown. Professor Brown is a world renowned anesthesiologist, neuroscientist, and statistician.

Anesthesia-induced oscillations—brain wave patterns—decay over time and are two to three times smaller in older versus younger adults. Older patients are more likely to experience profoundly deep anesthesia at lower doses. Brown's findings propose age-specific monitoring that will help avoid post-operative cognitive dysfunction and lead to improved safety of general anesthesia for elderly patients.

Brown has also spearheaded research using optogenetics to produce natural sleep patterns. Distinct stages of sleep provide different benefits, but there are no drugs available today that can selectively trigger a specific state, such as REM sleep. Brown says using light to induce more episodes of REM sleep could be useful for enhancing human learning and memory. Brown's collective body of neuroscientific work, to date and in the future, is expected to lead to improved anesthetic drugs as well as new treatments for chronic pain, depression, and insomnia. The Picower Institute community is excited to expand and enhance its collaboration with Brown, whose interests and goals precisely align with Picower's investigations into how experience modifies the brain.

Seeing the Brain in 3D

A new technique can accelerate efforts to map the human brain

Using a single tissue sample, MIT researchers can now label and image the proteins found in each brain cell. “Each cell uses a unique combination of proteins. It’s basically a fingerprint,” says lead researcher **Picower investigator Kwanghun Chung**.

The new technology, known as SWITCH, allows different proteins to be imaged repeatedly in a transparent, three-dimensional structure of preserved brain tissue. The key advance was to devise a method for controlling the chemical reactions required for tissue preservation and labeling.

For the first time, researchers visualized 22 different proteins inside the same human brain slice with the method, which could be scaled up for larger tissue samples and even more proteins. “Now, researchers will be able to investigate the differences between brains from disease models and normal animals, simultaneously looking at potentially dozens of different molecules” instead of looking at those same molecules one at a time among dozens of samples, says graduate student Evan Murray.

The researchers can now also evenly and more rapidly label and image brain



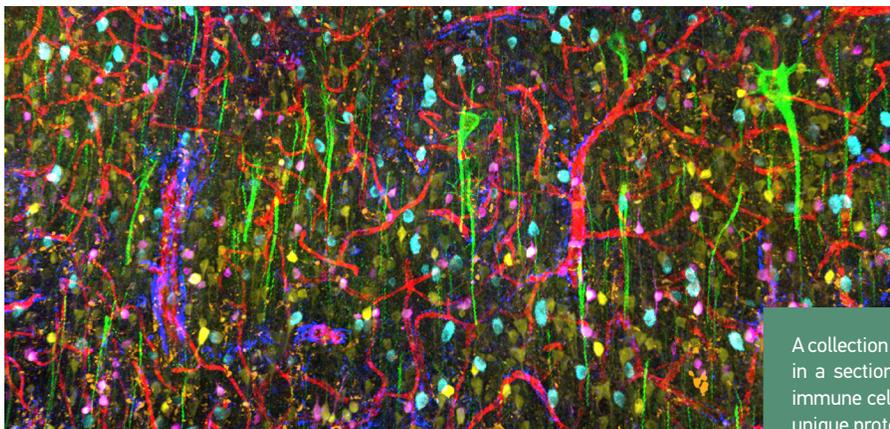
Picower investigator Kwanghun Chung

anatomy such as myelinated fibers that connect different regions of the brain, illuminating fundamental brain connectivity.

Robert Brown, chair of neurology at the University of Massachusetts Medical School, called the new technique “extraordinary,” adding, “It allows one to look for multiple targets simultaneously in the same cell, with three-dimensional resolution, which has not been feasible with previous imaging methods.”

Published in **Cell**

Simple, Scalable Proteomic Imaging for High-Dimensional Profiling of Intact Systems. Evan Murray, Jae Hun Cho, et al. *Cell*. December 3, 2015.

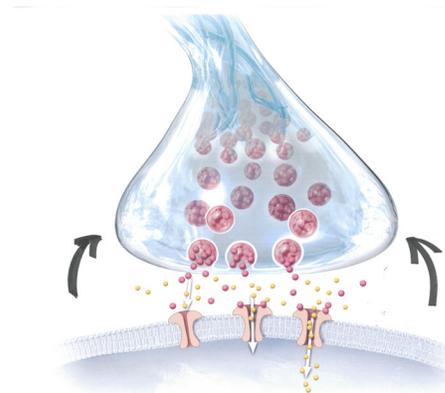


A collection of 22 different proteins illuminate different structures in a section of the brain including different types of neurons, immune cells, blood vessels, and DNA. Each color represents a unique protein.

Making it Easier to Learn

When the brain forms memories or learns a new task, it encodes the new information by tuning connections between neurons, called a synapse. Neuroscientists in **Troy Littleton’s** lab at the Picower Institute of Learning and Memory have discovered a new mechanism that contributes to the strengthening of these synapses.

At each synapse, a presynaptic neuron sends neurotransmitters to one or more postsynaptic receiving cells. Neurotransmitters are contained in round packets called vesicles. Vesicles can release neurotransmitters by an electrical signal or spontaneously (called mini-events). However, it’s not understood how spontaneous release occurs.



A presynaptic neuron terminal (Top) releases neurotransmitters (pink and yellow balls) that activates a postsynaptic neuron (Bottom). The arrows represent a retrograde signal that is sent from the postsynaptic to the presynaptic neuron.

Mapping Memory Through Space & Time

An image of the brain's cortex, which contains island cells (pink round clusters) and interspersed ocean cells (green neurons).

When you remember a particular experience that memory has three critical elements – what, when, and where. It's easier to understand either what, when, or where by itself, but it's much more difficult to understand how they all link together in the brain. In **Picower professor Susumu Tonegawa's** laboratory, neuroscientists have identified a brain circuit that links the when and where components of memory.

The when-and-where-circuit connects the hippocampus, critical for memory formation, and a nearby region called the entorhinal cortex. This when-and-where-circuit separates location and time into two streams of information. Two populations of neurons convey each stream: "ocean cells" and "island cells." Island cells help an animal navigate through

space while ocean cells help it recognize where it is at a given time.

Researchers identified the two cell populations at work when mice were given the task to discriminate between different environments. When the team blocked ocean cell activity, the animals were no longer able to associate a particular environment to foot stimulation. In a different task mice were given a sound cue and then several seconds of silence before receiving foot stimulation. Manipulating the island cells allowed the researchers to lengthen or shorten the time gap between the events for mice to store into memory.

Published in **Neuron**

Entorhinal Cortical Ocean Cells Encode Specific Contexts and Drive Context-Specific Fear Memory. Takashi Kitamura, Chen Sun et al. *Neuron*. September 23, 2015



Picower Institute Professor Susumu Tonegawa

The Littleton lab has shown that the postsynaptic neuron sends a chemical signal backwards to the presynaptic neuron to control spontaneous mini-events. "People have largely ignored these because they only induce a very small amount of activity in the postsynaptic cell," Littleton says. "This mechanism we've uncovered adds to a toolkit that we have for understanding how synapses can change," says senior author Troy Littleton.

Littleton found that these mini-events, previously considered background noise, actually drive physical changes and communication between the presynaptic and postsynaptic neurons. These changes

in communication and physical connections are critical for making new memories. Understanding mini-events could help scientists better understand neurodevelopmental disorders such as autism, in which genetic alterations target synaptic connections and communication.

Published in **Neuron**

Phosphorylation of Complexin by PKA Regulates Activity-Dependent Spontaneous Neurotransmitter Release and Structural Synaptic Plasticity. Richard William Cho, L.K. Buhl et al. *Neuron*. November 18, 2015.



Picower Institute Professor Troy Littleton

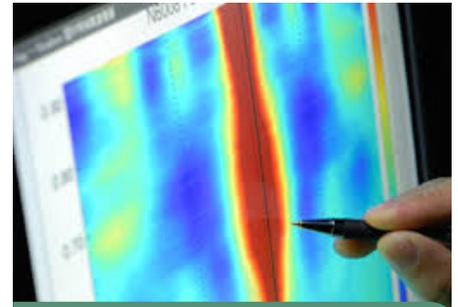
Stimulating **Sleep**

Picower neuroscientists have discovered a brain circuit that can trigger small regions of the brain to fall asleep or become less alert while the rest of the brain remains awake. This circuit originates in a brain structure known as the thalamic reticular nucleus (TRN), which relays signals to the cortex. TRN stimulation induces pockets of the slow oscillating brain waves characteristic of deep sleep. Emery Brown, the Edward Hood Taplin Professor of Medical Engineering and

Computational Neuroscience at MIT and an anesthesiologist at Massachusetts General Hospital, studies these slow waves that also occur during coma and general anesthesia. The TRN may help the brain consolidate new memories by coordinating slow waves between different parts of the brain, allowing them to share information more easily.

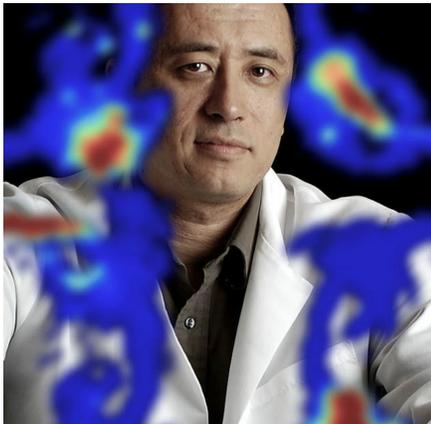
Published in **eLife**

Thalamic reticular nucleus induces fast and local modulation of arousal state. Laura D Lewis, Jakob Voigts, et al., eLife. October 2015



A scientist points to a high intensity portion (red) of a spectrogram, which shows the power of recorded brain frequencies.

Rewards alter **Thoughts** and **Dreams**



Picower Institute Professor Matt Wilson

Picower professor **Matt Wilson's** lab looked at how the hippocampus and the dopamine-generating ventral tegmental area (VTA) coordinate to replay recent experiences. Increased dopamine levels in the brain are associated with the pleasurable feelings of reward. In this study, rats learned to run on a maze for a reward. After learning, when the rats were resting, spatial sequences of the maze were reactivated in the

hippocampus. This reactivation occurred at the same time activity in the VTA increased. However, when the animals slept, the opposite was found. These results suggest that

dopamine neurons relay reward-related signals in concert with reactivation in the hippocampus. The altered reactivation of the hippocampus and VTA sheds light on how rewarding experiences reinforce learning and memory.

Published in **eLife**

VTA neurons coordinate with the hippocampal reactivation of spatial experience. Stephen N Gomperts, Fabian Kloosterman, Matthew A Wilson. eLife. October 2015.

Critical Path to **Vision Loss**

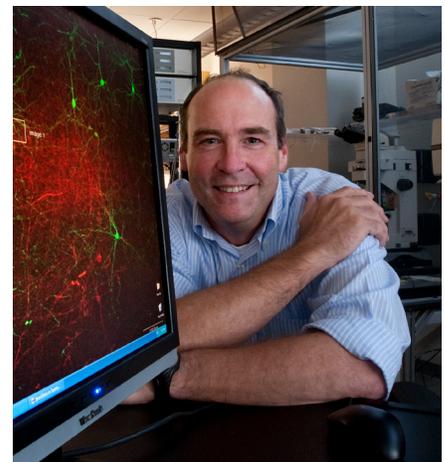
Covering one's eye for several days during a critical developmental period results in impaired vision in that eye. Researchers have tied the vision loss to a weakening of synapses in the visual cortex, but the underlying mechanisms have not been clearly defined. **Mark Bear's** lab looked at the metabotropic glutamate receptor 5 (mGluR5),

because this receptor peaks in activity during the aforementioned developmental period. The researchers found--using a new way to inhibit the neurotransmitter in

living animals--that mGluR5 signaling establishes the biochemical conditions that help set the sensitivity of the developmental period.

Published in **PNAS**

Metabotropic glutamate receptor signaling is required for NMDA receptor-dependent ocular dominance plasticity and LTD in visual cortex. Michael S. Sidorov, Eitan S. Kaplan, et al., PNAS. October 2015



Picower Institute Professor Mark Bear

Accelerating the Search for New **Alzheimer's** Drugs

The Robert A. and Renee E. Belfer Family Foundation has committed an additional \$3.5 million gift to the Neurodegeneration Consortium (NDC), a collaborative enterprise comprised of renowned scientists from the Massachusetts Institute of Technology (MIT), The University of Texas MD Anderson Cancer Center, and Baylor College of Medicine. The Belfer Family Foundation's inaugural \$25 million gift in 2012 and this new funding enable investigation of new ways to slow, stop, or reverse the progression of Alzheimer's and other neurodegenerative diseases.

This new gift extends the NDC program timeline into 2017, expands the scope of MIT's participation in the consortium, and is specifically earmarked to support an additional collaborative project that promises to expedite the transition from research to identification of new targets for drug discovery and development of clinical therapeutic treatments for Alzheimer's disease. The new project will combine the expertise of original NDC member and **MIT professor Li-Huei Tsai**, director of the Picower Institute for Learning and Memory, and new NDC participant and **MIT professor Susan Lindquist** of the Whitehead Institute for Biomedical Research.

"The Belfer Foundation's continuous support has been extremely important for our research endeavors," says Tsai. "The additional funding enables us to combine our strengths and collaborate with our remarkable colleagues at MIT, MD Anderson, and Baylor to pursue research that will rapidly reveal unconventional drug targets and accelerate development of effective treatments for Alzheimer's disease, transforming it from a terminal pandemic into a treatable condition."



Robert A. Belfer and MIT Professor Li-Huei Tsai

The addition of Dr. Lindquist, a highly accomplished geneticist, is expected to broaden the capabilities and perspective of the NDC team. Her work over the past two decades has focused on gaining a better understanding of the genetic mechanisms underlying neurodegenerative diseases. "Alzheimer's is an incredibly complex disease, so it is vitally important to bring together creative experts from a variety of disciplines to collectively generate innovative ideas and approaches to treating and preventing this debilitating and costly disorder affecting more than 40 million people worldwide," observes Lindquist.

Employing a groundbreaking approach involving relatively simplistic yeast cells

that mimic the basic structure and characteristics of sophisticated human neuronal organisms, she examines proteins in the brain that are known to be primary precipitators of dementia. Her current research targets the least understood but most significant genetic risk factor associated with Alzheimer's disease—a variant of apolipoprotein E (APOE).

Lindquist's novel scientific approach and collaboration with Tsai are the foundation of a fascinating new project that synergizes the genetic and molecular expertise of the two MIT principal investigators. Together they will determine how genetic activity alters functionality in both yeast cells and human neuronal systems. Using Lindquist's yeast model, the neuroscientists can quickly identify genetic variants in APOE and the resulting toxic effects that signal neurodegenerative disease. Using stem cells Tsai's team derived from Alzheimer patients, they can leverage tissue engineering technology to create miniature brains and further study the impacts of these APOE modifiers—the potential new targets for drug discovery to treat Alzheimer's disease.

To learn more about this research or to give a gift in support of Alzheimer's research, please contact Dr. Asha Bhakar, abhakar@mit.edu, 617-258-0759.

"By combining Dr. Lindquist's innovative discovery approach, Dr. Tsai's groundbreaking neural model system, and the world-class drug discovery capabilities at MD Anderson, we hope to find a way to reduce the risk for dementia caused by APOE4 and translate that finding to patients as rapidly as possible," explains Jim Ray, head of research for the NDC.

Gift Propels Work on **Aging Brain**

A gift from MIT Corporation member **Jeffrey S. Halis** '76, SM '76 and his wife, **Nancy**, longtime supporters of MIT, will seed the first year of projects at eight labs across MIT associated with the Aging Brain Initiative. The Aging Brain Initiative is a multidisciplinary cross-institutional research effort developed at MIT that brings together Boston's leading aging researchers in neuroscience, biology and bioengineering, chemical engineering, computer science, artificial intelligence, health economics, urban planning and the clinical environment. The Initiative focuses on radically different whole-brain systems approaches along with new types of collaborative perspectives and MIT's commercial resources to tackle the dementias associated with aging. Li-Huei Tsai, lead investigator of the Initiative, says the gift will help ambitious high-risk, high-reward projects move closer to real-world applications.



MIT Corporation member Jeffrey Halis and his wife Nancy.

PICOWER Accomplishments

KWANGHUN (KC) CHUNG has received the **2015 Packard Fellowship for Science and Engineering**. The five-year, \$875,000 grants give emerging young scientists and engineers the freedom to pursue innovative ideas. Chung develops and applies novel technologies for integrative and comprehensive understanding of large-scale biological systems.

EMERY N. BROWN is one of four MIT faculty members to be named **2015 Fellows of the National Academy of Inventors (NAI)**. Brown, the Edward Hood Taplin Professor of Medical Engineering and of Computational Neuroscience in the MIT School of Science and School of Engineering, investigates neural signal processing algorithms and seeks to understand general anesthesia.

MICHELE PIGNATELLI DI SPINAZZOLA and **TAKASHI KITAMURA** of the Tonegawa Lab and **RAM MADABHUSHI** of the Tsai Lab are 2015 Infinite Kilometer Award winners. The Infinite Kilometer Award recognizes the outstanding contributions of postdoctoral researchers and research scientists who routinely work beyond their assigned responsibilities.



Kwanghun (KS) Chung



Emery N. Brown



Michele Pignatelli Di Spinazzola



Takashi Kitamura

Upcoming **Events**

For a list of ongoing scientific lectures, colloquia, and workshops, please go to: picower.mit.edu

NEW INSIGHTS ON EARLY LIFE STRESS AND MENTAL HEALTH

Picower Institute Spring Symposium, May 12th, 2016

Early childhood adversity and the debilitating effects it can have throughout life is a global health problem and the repercussions are far reaching from physical to mental and societal and can include conditions like obesity, asthma, anxiety, addiction, and depression. On May 12th, 2016 the Picower Institute will host a symposium with clinical, community, and basic science talks—a bench to bedside perspective—for a very informative conversation on the varied approaches taken and progress made for interventions to improve early life health.



Speakers include:

JACK SHONKOFF, professor of child health and development at Harvard and chair of the National Scientific Council on the Developing Child

NADINE BURKE HARRIS, founder of the Center for Youth Wellness, which addresses adverse childhood experiences as risk factors for adult diseases, and expert advisor on Hillary Clinton's Too Small to Fail initiative

MICHAEL MEANEY, associate director of Canada's Douglas Research Centre and one of the first researchers to describe how maternal care influences

gene expression of the offspring; in particular genes which regulate responses to stress

V. FAN TAIT, pediatric neurologist and associate executive director of the American Academy of Pediatrics (AAP)

MICHAEL C. LU, associate administrator of maternal and child health of the Health Resources and Services Administration (HRSA) at the U.S. Department of Health and Human Services

GEOFFREY CANADA, educator, social activist and author renowned for his pioneering work helping children and families for more than 30 years through the Harlem Children's Zone

JOHN GABRIELI, MIT cognitive neuroscientist, director of the Athinoula A. Martinos Imaging Center at the McGovern Institute and MIT's Integrated Learning Initiative

DARCY LOWELL, executive director of Child FIRST (Child and Family Interagency, Resource, Support, and Training) and a developmental and behavioral pediatrician in the Department of Pediatrics at Bridgeport Hospital, Yale-New Haven Health System

BRUCE MCEWEN is Head of the Harold and Margaret Milliken Hatch Laboratory of Neuroendocrinology at Rockefeller University and a past president of the

Society for Neuroscience.

ELLEN C. PERRIN'S clinical interests include the management of developmental and behavioral issues in primary care, family stress, chronic health problems and children in non-traditional families

KAY TYE, is a principle investigator at MIT's Picower Institute for Learning and Memory. Her research includes using optogenetics to identify and control connections in the brain that are linked to social behaviors such as reward-seeking and anxiety



Aging Brain Seminar Series

Upcoming Seminars

MORGAN SHENG

Vice president of Genentech
4pm on April 27, 2016

DAVID BENNETT

Director of the Rush Alzheimer's Disease Center
4pm on May 10, 2016

BRUCE YANKER

Professor of genetics and neurology at Harvard Medical School
4pm on Sept. 21, 2016

RUDOLPH TANZI

Professor of Child Neurology and Mental Retardation at Harvard University and Director of the Genetics and Aging Research Unit at Massachusetts General Hospital
4pm on November 30, 2016

BRADLEY HYMAN

Professor of Neurology at Harvard Medical School, Alzheimer's Unit Director at Mass General Institute for Neurodegenerative Disease, and Director of Massachusetts Alzheimer's Disease Research Center, at 4 pm on December 7, 2016

Neuroscience News // Winter 2016



OUR VISION

The Picower Institute is a community of scientists focused on a common question: How is the brain modified by experience?

To answer this question we use multiple levels of analysis, ranging from molecular to behavioral, and exploit the tools of modern molecular biology and genetics to dissect the contributions of specific molecules, synapses, cells and circuits to behavior.

We work to understand the pathophysiological mechanisms underlying complex disorders of the brain that affect emotion and cognition.

SUPPORT THE PICOWER INSTITUTE

For more information on our research or how to make a gift to the Picower Institute for Learning and Memory, please contact: Asha Bhakar, PhD, abhakar@mit.edu, Tel: 617-258-0759.

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EDITORIAL BOARD & CONTRIBUTORS

Asha Bhakar, Erin Edwards, Deborah Haliber, Najat Kessler, Joshua Sariñana, and Veronica Vela.

CONTACT THE PICOWER INSTITUTE

The Picower Institute for Learning and Memory Massachusetts Institute of Technology, 77 Massachusetts Avenue, Building 46, Room 1303, Cambridge, MA 02139-4307, Tel: 617-324-0305 picower.institute

TOP ROW: **Mark F. Bear**, Picower Professor of Neuroscience, Department of Brain and Cognitive Sciences, Investigator, Howard Hughes Medical Institute (HHMI); **Emery Brown**, Edward Hood Taplin Professor of Computational Neuroscience and Health Sciences & Technology, The Picower Institute for Learning and Memory, Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology; **Kwanghun Chung**, Assistant Professor, Departments of Chemical Engineering and Brain and Cognitive Sciences; **Steven Flavell**, Assistant Professor of Neuroscience, The Picower Institute for Learning and Memory, Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology; **Myriam Heiman**, Assistant Professor of Neuroscience, Department of Brain and Cognitive Sciences, Broad Institute core member; **Troy Littleton**, Picower Professor of Biology and Neuroscience, Departments of Biology and Brain and Cognitive Sciences; **Earl Miller**, Picower Professor of Neuroscience, Department of Brain and Cognitive Sciences.

BOTTOM ROW: **Elly Nedivi**, Professor, Departments of Brain and Cognitive Sciences and Biology; **Mriganka Sur**, Paul E. Newton Professor of Neuroscience, Director of The Simons Center for the Social Brain; **Susumu Tonegawa**, Picower Professor of Biology and Neuroscience, Departments of Brain and Cognitive Sciences and Biology, Investigator, Howard Hughes Medical Institute, Investigator and Director of the RIKEN-MIT Center for Neural Circuit Genetics; **Li-Huei Tsai**, Picower Professor of Neuroscience, Department of Brain and Cognitive Sciences, Director, The Picower Institute for Learning and Memory; **Kay Tye**, Assistant Professor of Neuroscience, Department of Brain and Cognitive Sciences; **Matthew Wilson**, Sherman Fairchild Professor in Neurobiology, Departments of Brain and Cognitive Sciences and Biology, Associate Director, The Picower Institute for Learning and Memory; **Weifeng Xu**, Assistant Professor of Neuroscience, Department of Brain and Cognitive Sciences.