ABOUT BCS
RESEARCH
ACADEMICS
PEOPLE

- **Faculty**
- Staff
- Researchers
- Postdocs
- Graduate Students
- Undergrad Students

NEWS & EVENTS
DIVERSITY & OUTREACH
GIVING

BCS Website
BCS People
MIT Wide

SEARCH

People / Faculty

Susumu Tonegawa, Ph.D.
Picower Professor of Biology and Neuroscience
Investigator, Howard Hughes Medical Institute
Director, RIKEN-MIT Center for Neural Circuit Genetics

Department of Biology
Building: 46-5285
Email: tonegawa@mit.edu

Learning and memory are vital for day-to-day living, from finding our way home, to playing tennis, to making a cohesive speech. Many of us have personally witnessed the devastating consequences of memory disorders, such as Alzheimer's and Parkinson's diseases. The main research interest of Professor Susumu Tonegawa's lab is to understand the molecular, cellular, neuronal circuitry, and neural systems mechanisms underlying learning and memory and associated cognitive functions.

Our main approach is to generate conditionally engineered mouse strains in which a specific gene or its protein function is eliminated in a spatially restricted and/or temporally controlled manner in the brain; we then analyze these mice with a series of techniques designed to detect abnormal phenotypes at different levels of complexity from molecules and cells to neuronal circuitries and brain systems to behavior of a whole living animal. These techniques include those of molecular and cell biology, histology and histochemistry, confocal and two-photon laser microscopy, in vitro and in vivo electrophysiology, and behavioral studies. Our goal is to identify a correlate at a particular level of complexity of an event occurring at another level, and eventually establish their cause-consequence relationship from molecules all the way to behavior.

As research targets, we have thus far focused on hippocampus-dependent memory, i.e., memory of events, facts, space, etc. The hippocampus consists of multiple interconnected areas such as area CA1, CA3 and the dentate gyrus (DG), each of which contains a unique set of neurons composing a distinct cellular network. We aim to identify the roles of specific proteins (e.g., NMDA receptors), synaptic plasticity and neural circuitries in each of these areas in different stages of the mnemonic process such as memory acquisition, consolidation and recall. For instance, we have demonstrated that NMDA receptors in a neural circuit in CA3 play a crucial role in both rapid acquisition and recall of an episodic memory.

Another important development in the lab was the identification of genes (calcinearine and PAK kinase) whose reduced activities increased susceptibility to schizophrenia and Fragile X mental retardation, respectively. These discoveries were made by combining the behavioral analysis of genetically engineered mice and/or genetic analysis of DNA from human patients.

More recently, we have invented a novel genetic engineering technology that permits a blockade of synaptic transmission at a specific neural pathway in mice. This general method allows us to identify the function of a particular neural circuit in a specific aspect of cognition and behavior. Currently, this exciting method is being applied to various circuits suspected (but not proven) to be involved in subserving learning and memory. For instance, we have recently demonstrated that the transmission from area CA3 and CA1 plays a crucial role in converting a time-limited memory initially stored in the hippocampus to a long-lasting memory stored in the neo-cortex. We have also shown that reactivation of the hippocampal memory engram during sleep is crucial for this conversion.

We are also developing virus vector-mediated intervention techniques. Their use in combination with transgenic techniques promises a diverse set of experiments that will be highly informative for our understanding of the function of specific neural circuits underlying cognition and behavior of animals in health and under disease conditions.

Liu X, Tonegawa S. Optogenetics 3.0. Cell. 2010 Apr 2;141(1):22-4.

Slutsky I, Abumaria N, Wu LJ, Huang C, Zhang L, Li B, Zhao X, Govindarajan A, Zhao MG, Zhuo M, Tonegawa S, Liu G. Enhancement of learning and memory by elevating brain magnesium. Neuron. 2010 Jan 28;65(2):165-77.

Kamsler A, McHugh TJ, Gerber D, Huang SY, Tonegawa S. Presynaptic m1 muscarinic receptors are necessary for mGluR long-term depression in the hippocampus. Proc Natl Acad Sci U S A. 2010 Jan 26;107(4):1618-23. Epub 2010 Jan 8.

Jinde S, Belforte JE, Yamamoto J, Wilson MA, Tonegawa S, Nakazawa K. Lack of kainic acid-induced gamma oscillations predicts subsequent CA1 excitotoxic cell death. Eur J Neurosci. 2009 Sep;30(6):1036-55. Epub 2009 Sep 4.

Additional Publications

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
77 Massachusetts Ave Cambridge, MA 02139
(tel) 617.258.9344