2024 Senri Life Science International Symposium

Science of Behaving and Sleeping Brains

Senri Life Science / WPI-IIIS Joint International Symposium

Date : March 1st (Friday), 2024 10:30 – 16:30

Venue : Senri Life Science Center Building 5th floor
"Yuichi Yamamura Memorial Life Hall" /Hybrid

Coordinated by
Masashi Yanagisawa & Takeshi Sakurai

Sponsored by
Senri Life Science Foundation
International Institute for Integrative Sleep Medicine, University of Tsukuba (WPI-IIIS)

Supported by Biocommunity Kansai (BiocK)

2024 Senri Life Science International Symposium

"Science of Behaving and Sleeping Brains"

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10:30 - 10:35 Opening address

Shizuo Akira (President of Senri Life Science Foundation)

10:35 - 10:40 Complimentary address

Noriko Osumi (Vice President, Tohoku University)

Chair: Takeshi Sakurai (WPI-IIIS, University of Tsukuba, Japan)

10:40 - 11:25

Talk 1 Deciphering the mysteries of sleep: toward the neuronal substrate for "sleepiness" ‥2

Masashi Yanagisawa (WPI-IIIS, University of Tsukuba, Japan)

11:25 - 12:10

Talk 2 The human SLEEP puzzle: genes, molecules, and circuits ……6

Ying-Hui Fu (University of California San Francisco, USA)

12:10 - 13:15 Lunch

13:15 - 14:00

Talk 3 Neural mechanisms that control hunger ……8

Zachary Knight

(Howard Hughes Medical Institute, University of California San Francisco, USA)

Chair: Masashi Yanagisawa (WPI-IIIS, University of Tsukuba, Japan)

14:00 - 14:45

Talk 4 Sleeping Brain: Unveiling the Art of Artificial Induction

Takeshi Sakurai (WPI-IIIS, University of Tsukuba, Japan) …… 10

14:45 - 15:00 Coffee break

15:00 - 15:45

Talk 5 Mitochondrial Origins of the Pressure to Sleep

Gero Miesenböck (University of Oxford, UK) …… 12

15:45 - 16:30

Talk 6 Making memories in mice

Sheena Josselyn (The Hospital for Sick Children, University of Toronto, Canada) …… 14

16:30 Closing remarks

Masashi Yanagisawa (WPI-IIIS, University of Tsukuba, Japan)

Described time includes questions and answers.

Introduction
Science of Behaving and Sleeping Brains

Masashi Yanagisawa, MD, PhD

Latest advances in physiological techniques such as neuronal activity imaging/recording and optogenetic manipulations, combined with cutting-edge molecular genetic tools and single-cell omics, have transformed our investigation into the neurobiology of animal behaviors. We are now starting to understand how the brain regulates various behaviors in health and disease. This symposium will discuss several hot topics of basic behavioral neuroscience in organisms ranging from flies to mice to humans. Internationally recognized experts in the field will present their latest work in phenomena ranging from sleeping/waking, hibernating, eating/drinking, to remembering /forgetting.

Talk 1

Deciphering the mysteries of sleep: toward the neuronal substrate for "sleepiness"

Masashi Yanagisawa, MD, PhD

Title:

Director, International Institute for Integrative Sleep Medicine (WPI-IIIS)
University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8575, Japan
Email: yanagisawa.masa.fu@u.tsukuba.ac.jp / Web: wpi-iiis.tsukuba.ac.jp

Professional membership:

American Academy of Sleep Medicine
Japanese Society of Sleep Research, The Japan Neuroscience Society

Education and Professional Appointments:

1984	MD degree from School of Medicine, Faculty of Medicine, The University of Tokyo
1985	M.D. (summa cum laude), 1985, University of Tsukuba
1988	Ph.D. in Medical Sciences, 1988, University of Tsukuba
1988 – 1989	Postdoctoral fellow, Department of Pharmacology, University of Tsukuba
1989 – 1991	Assistant Professor of Pharmacology, University of Tsukuba
1991 – 1991	Assistant Professor of Pharmacology, Kyoto University School of Medicine
1991 – 1996	**Associate Professor of Molecular Genetics, University of Texas Southwestern Medical Center at Dallas (UTSW); Associate Investigator, Howard Hughes Medical Institute (HHMI)**
1996 – 2014	**Professor of Molecular Genetics, UTSW; Investigator, HHMI**
1998 – 2014	The Patrick E. Haggerty Distinguished Chair in Basic Biomedical Science, UTSW
2001 – 2007	Director, Yanagisawa Orphan Receptor Project (JST/ERATO)
2010 – 2014	Professor and Director, FIRST program, University of Tsukuba
2012 – Present	**Director, International Institute for Integrative Sleep Medicine (WPI-IIIS), University of Tsukuba**
2014 – Present	Adjunct Professor of Molecular Genetics, UTSW

Honors/Awards:

2003	**Elected Member, National Academy of Sciences**
2016	Medal with Purple Ribbon, Government of Japan
2017	Erwin Von Bälz Preis, Boehringer Ingelheim
2018	The Asahi Prize, Asahi Shimbun Foundation
2018	The Keio Medical Science Prize, Keio University Medical Science Fund
2019	Takamine Memorial Daiichi Sankyo Prize, Daiichi Sankyo Foundation of Life Science

2019 **Person of Cultural Merit, Government of Japan**
2022 Toshihiko Tokizane Memorial Award, The Japan Neuroscience Society
2023 **Breakthrough Prize in life sciences**
2023 **Clarivate Citation Laureate**

Biographical Narrative:

In 1988, as a graduate student at University of Tsukuba, Yanagisawa discovered endothelin, a potent vasoconstrictor peptide from vascular endothelial cells, which sparked an intense research activity in the field. In the subsequent year, his group identified a G protein-coupled receptor for endothelin, which would become an important drug target; the endothelin receptor antagonist bosentan was approved in 2001 for the treatment of pulmonary hypertension. After moving to University of Texas Southwestern Medical Center at Dallas in 1991 as a young principal investigator, he identified the endothelin-converting enzyme, a metalloprotease that generate the active, mature endothelin peptides. Through gene-targeting experiments in mice, he also discovered in 1994 that the endothelin pathway is essential for embryonic development of certain neural crest derived tissues, and that endothelin-B receptor deficiency causes Hirschsprung disease in mice and humans. In 1996, he initiated a systematic search for endogenous ligands of "orphan" G protein-coupled receptors, which resulted in his 1998 discovery of orexin, a hypothalamic neuropeptide. He then discovered in 1999 that orexin deficiency causes the sleep disorder narcolepsy. This opened up a new avenue in sleep research, and led to a better understanding of sleep/wake switching mechanisms in the brain. The notion that orexin is an important endogenous waking agent led to the development of orexin receptor antagonists as sleep-inducing drug, first of which, suvorexant, was approved in 2014. Recognizing, however, that the fundamental mechanism for sleep homeostasis still remains a mystery, in 2010 he embarked upon a highly ambitious project of polysomnography (EEG/EMG)-based forward genetic screen for sleep/wake abnormalities in chemically mutagenized mouse cohort. This large-scale project is now continuing in Tsukuba, Japan, and has recently led to identification of several new genes and molecular pathways that are importantly involved in the regulation of sleep amounts and the level of sleep need.

Abstract

Although sleep is a ubiquitous behavior in animal species with a nervous system, many aspects in the neurobiology of sleep remain mysterious. Our discovery of orexin, a hypothalamic neuropeptide involved in the maintenance of wakefulness, has triggered intensive research examining the exact role of the orexinergic and other neuronal pathways in the regulation of sleep/wakefulness. Orexin receptor antagonists, which specifically block the endogenous waking system, have been approved as a new drug to treat insomnia. Also, since the sleep disorder narcolepsy-cataplexy is caused by orexin deficiency, orexin receptor agonists are expected to provide mechanistic therapy for the disease; they will likely be also useful for treating excessive sleepiness due to other etiologies.

Even though the executive neurocircuitry and neurochemistry for sleep/wake switching, including the orexinergic system, has been increasingly revealed in recent years, the mechanism for homeostatic regulation of sleep, as well as the neural substrate for "sleepiness" (sleep pressure), remains unknown. To crack open this black box, we have initiated a large-scale forward genetic screen of sleep/wake phenotype in mice based on true somnographic (EEG/EMG) measurements. We have so far screened >10,000 heterozygous ENU-mutagenized founders and established several pedigrees exhibiting heritable and specific sleep/wake abnormalities. By combining linkage analysis and the next-generation whole exome sequencing, we have molecularly identified and verified the causal mutation in several of these pedigrees. Since these dominant mutations cause strong phenotypic traits, we expect that the mutated genes will provide new insights into the elusive pathway regulating sleep/wakefulness. Indeed, through a systematic cross-comparison of the SIK3 Sleepy mutants and sleep-deprived mice, we have found that the cumulative phosphorylation state of a specific set of mostly synaptic proteins may represent the molecular substrate of sleep pressure. We have also found that the neuronal molecular pathway LKB1-SIK3-HDAC4/5 may represent the level of sleep pressure, regulating the amount, depth, and timing of sleep by acting in different brain regions, respectively.

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Talk 2
The human SLEEP puzzle: genes, molecules, and circuits

Ying-Hui Fu, PhD

Title:

Ying-Hui Fu, PhD, Professor of Neurology, University of California San Francisco

Ying-hui.fu@ucsf.edu

Educational Background:

1976 - 1980	National Chung-Hsing University, Taichung, Taiwan, B.S., Food Science
1981 - 1986	Ohio State University, Ph.D., Biochemistry & Molecular Biology
1987 - 1989	Ohio State University, Postdoc, Molecular Biology
1990 - 1992	Baylor College of Medicine, Postdoc, Human Genetics

Profesional History:

1993 - 1995	Scientist, Millennium Pharmaceutical Inc., Boston, MA
1995 - 1997	Senior Scientist, Darwin Molecular Corp., Seattle, WA
1997 - 2002	Associate Professor, Department of Neurobiology, University of Utah, Salt Lake City, UT
2002 - 2006	Associate Professor, Department of Neurology, University of California San Francisco
2006 - Present	Professor, Department of Neurology, University of California San Francisco

Awards and Honors

2006	Sleep Science Award, American Academy of Neurology
2006	Bauer Foundation Colloquium Distinguished Guest, Brandeis University, Boston, MA
2008	Distinguished Guest, Bollum Symposium, University of Minnesota, Minneapolis, MN
2009	Distinguished visiting professorship, Tamkang University, Taiwan
2012	Faculty Research Lecture in Basic Research, UCSF
2012	Presidential Lecture, University of Vermont
2015	TEDx
2018	Member, National Academy of Sciences, USA
2018	Member, Academia Sinica, Taiwan
2018	Member, National Academy of Medicine, USA
2018	Outstanding Alumni Award, Chung-Hsing University, Taiwan
2021	Harvard Medical School Division of Sleep Medicine Prize

Abstract

Sleep occupies a significant portion of our daily lives, yet our understanding of sleep, in general, is minimal. Sleep of sufficient duration, continuity, and intensity is necessary to promote high levels of cognitive performance during the wake period and prevent physiological changes that may predispose individuals to many adverse health outcomes. Sleep insufficiency is prevalent in our society due to the high demand for work, school, and many environmental factors, thus significantly contributing to many health conditions we face. Interestingly, the biological need for sleep varies dramatically among humans. We have identified a group of humans named "Familial Natural Short Sleep (FNSS)" with unusual sleep behaviors and have used human genetics approach to identify many genes/mutations that give them unusual sleep behaviors. Mouse models recapitulate the human condition, and in vitro molecular and neurocircuitry studies offer insight into the underlying mechanisms. Because of sleep's fundamental role in our health, the pathways regulating sleep are intertwined with those regulating other functions. Thus, our method also offers opportunities to investigate how sleep can impact other conditions, including mood, pain, and other disease pathology.

Refernces

1. He Y, Jones CR, Fujiki N, Xu Y, Guo B, Holder J, Nishino S, and Fu Y-H. The transcriptional repressor DEC2 regulates sleep length in mammals. *Science* 2009 325:866.
2. Hirano A, Hsu P-K, Zhang L, Xing L, McMahon T, Yamazaki M, Ptacek LJ, Fu Y-H. DEC2 modulates orexin expression and regulates sleep. *Proc Natl Acad Sci USA*. 2018 *Mar 12*.
3. Shi G, Xing L, Wu D, Jones CR, McMahon T, Chong C, Chen J, Coppola, Geschwind D, Krystal A, Ptáček LJ, Fu Y-H. A rare mutation of β_1-adrenergic receptor affects sleep/wake behaviors. *Neuron* 2019 Sep 25;103(6):1044-1055.
4. Webb JM, Ma M, Yin C, Ptacek LJ, Fu Y-H. An Excitatory peri-Tegmental Reticular Nucleus Circuit for Wake Maintenance. *PNAS* 2022 July 28. DOI:10.1073/pnas.2203266119.

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Talk 3
Neural mechanisms that control hunger

Zachary Knight, PhD

Department of Physiology, UCSF
Rock Hall, Rm 348F
1550 Fourth St.
San Francisco, CA 94158
415 502 2011
zachary.knight@ucsf.edu

Positions

2021–Present	Professor, Department of Physiology, UCSF
2018–Present	Investigator, Howard Hughes Medical Institute
2018–2021	Associate Professor, Department of Physiology, UCSF
2012–2018	Assistant Professor, Department of Physiology, UCSF

Education

2006 Ph.D.	Chemistry and Chemical Biology. University of California, San Francisco
1999 B.A.	Chemistry, magna cum laude. Princeton University

Training

2007–2012	Postdoctoral fellow, Rockefeller University. Advisor: Jeff Friedman, M.D. Ph.D.
2006–2007	Postdoctoral fellow, UCSF. Advisor: Kevan M. Shokat, Ph.D.
2000–2006	Graduate student, UCSF. Advisor: Kevan M. Shokat, Ph.D.

Honors and Awards

2019	Presidential Early Career Award for Scientists and Engineers (PECASE)
2018	Investigator, Howard Hughes Medical Institute
2016	Helmholtz Young Investigator in Diabetes Award
2016	Pathway Accelerator Award – American Diabetes Association
2015	NIH New Innovator Award
2014	Rita Allen Scholar Award
2014	Alfred P. Sloan Foundation Research Fellow in Neuroscience
2013	New York Stem Cell Foundation – Robertson Neuroscience Investigator Award
2013	NARSAD Young Investigator Award
2013	McKnight Technological Innovations in Neuroscience Award
2013	Klingenstein Fellowship Award in the Neurosciences
2013	Program for Breakthrough Biological Research Award - UCSF

2009	NIH Pathway to Independence Award
2007	Life Sciences Research Foundation, Postdoctoral Fellowship
2006	UCSF Krevans Distinguished Dissertation Award
2002	Grand Prize Winner, National Collegiate Inventors Competition
2001	Howard Hughes Medical Institute, Predoctoral Fellowship
2000	ARCS Foundation, Predoctoral Fellowship

Abstract

Hunger is controlled by specialized interoceptive neurons that monitor bodily energy stores. How these cells transform the need for food into the desire to eat is not fully understood. I will describe our studies investigating the mechanisms that regulate hunger circuits in the forebrain. An emerging theme is that these circuits integrate sequential sensory cues arising from inside and outside the body in order to steer the progress of a meal.

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Talk 4
Sleeping Brain: Unveiling the Art of Artificial Induction

Takeshi Sakurai, MD, PhD

Title:

Professor, Institute of Medicine/WPI-IIIS, University of Tsukuba
EMAIL: sakurai.takeshi.gf@u.tsukuba.ac.jp

Educational Background:

1989 Medical Degree
University of Tsukuba, Ibaraki, Japan
1993 PhD (University of Tsukuba)

Professional History:

1993 -	Postdoctoral fellow of Institute of Basic Medical Sciences
1993-	Assistant Professor of Institute of Basic Medical Sciences, University of Tsukuba
1995 -	Postdoctoral fellow HHMI, University of Texas Southwestern Medical Center at Dallas.
1996 -	Assistant Professor of Institute of Basic Medical Sciences, University of Tsukuba
1999 -	Associate Professor, Department of Pharmacology, Institute of Basic Medical Sciences, University of Tsukuba, Japan
2001 -	Group Leader, Yanagisawa Orphan Receptor Project, Exploratory Research or Advanced Technology (ERATO), JST
2007	Professor, Department of Molecular Neuroscience and Integrative physiology, Kanazawa University
2016 – present	Professor, Institute of Medicine/WPI-IIIS, University of Tsukuba

Awards and Honors

2000	Tsukuba Encouragement Prize
2009	Ando Momofuku Prize
2012	65th, Chunichi Bunka Award
2013	Prizes for Science and Technology, the Minister of Education, Culture, Sports, Science and Technology
2018	2nd Shiono Prize
2020	5th Matsuo Prize
2021	32nd Tsukuba Prize

Abstract

Even when referring to a "sleeping brain," it can exhibit activity in various modes. Sleep encompasses both REM and non-REM sleep, with several stages of non-REM sleep. Moreover, certain mammals enter a hibernation state as a form of dormancy, serving as a biological strategy for thermoregulating mammals to adapt to harsh environments. What neural circuits facilitate the expression of these various modes of the "sleeping brain"? Recent advancements in neuroscience have uncovered the complexity of the neural circuits responsible for these switching mechanisms, which are distributed throughout the brain. Additionally, manipulating these elements has the potential to induce sleep or hibernation states. For example, our group recently demonstrated the possibility of inducing a hibernation-like state by manipulating a population of neurons in the hypothalamic preoptic area of mice, a species that typically does not hibernate. We also showed that initiating REM sleep can be achieved by manipulating dopamine signaling in the amygdala. These examples illustrate just a few ways in which "sleeping brains" can be induced by manipulating brain circuits. In the future, manipulating specific neurons in the brain may enable the artificial creation of any desired state in the sleeping brain.

Refernces

1. Hasegawa E, Miyasaka A, Sakurai K, Cherasse Y, Li Y, Sakurai T. Rapid eye movement sleep is initiated by basolateral amygdala dopamine signaling in mice. ***Science***. 2022;375(6584):994-1000.
2. Takahashi, T.M., Sunagawa, G.A., Soya, S., Abe, M., Sakurai, K., Ishikawa, K., Yanagisawa, M., Hama, H., Hasegawa, E., Miyawaki, A., Sakimura, K., Takahashi, M., Sakurai, T. A discrete neuronal circuit induces a hibernation-like state in rodents, ***Nature*** 583, 109–114(2020)

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Talk 5
Mitochondrial Origins of the Pressure to Sleep

Gero Miesenböck, MD

Title:

Waynflete Professor of Physiology
Director, Centre for Neural Circuits and Behaviour
University of Oxford
EMAIL: gero.miesenboeck@cncb.ox.ac.uk

Educational Background:

1993	MD, University of Innsbruck, Austria
1992 – 1998	Postdoctoral Fellow, Memorial Sloan-Kettering Cancer Center

Profesional History:

2011 –	Director, Centre for Neural Circuits and Behaviour, University of Oxford
2007 –	Waynflete Professor of Physiology, University of Oxford
2004 – 2007	Associate Professor of Cell Biology, and of Cellular and Molecular Physiology Yale University School of Medicine
1999 – 2004	Assistant Member and Head, Laboratory of Neural Systems Memorial Sloan-Kettering Cancer Center
1999 – 2004	Assistant Professor of Cell Biology and Genetics, and of Neuroscience Cornell University

Awards and Honors

2023	The Japan Prize
2022	Louisa Gross Horwitz Prize
2020	The Shaw Prize in Life Science and Medicine
2019	Warren Alpert Foundation Prize
2016	The Massry Prize
2016	Member, German Academy of Sciences Leopoldina
2015	BBVA Foundation Frontiers of Knowledge Award in Biomedicine
2015	Fellow of the Royal Society
2015	Heinrich Wieland Prize
2014	Member, Austrian Academy of Sciences
2013	Gabbay Award in Biotechnology and Medicine
2013	The Brain Prize
2012	InBev-Baillet Latour International Health Prize

Abstract

The essential but enigmatic functions of sleep must be reflected in physical changes sensed by the brain's sleep-control systems. In *Drosophila*, a handful of sleep-inducing neurons projecting to the dorsal layers of the fan-shaped body (dFBNs) estimate sleep pressure by monitoring the flow of electrons through their own mitochondria. Sleep loss diverts high-energy electrons from the respiratory chain into uncontrolled side reactions with molecular oxygen, producing reactive oxygen species which fragment the polyunsaturated fatty acyl (PUFA) chains of membrane lipids into short- or medium-chain carbonyls. dFBNs transduce this biochemical signal into sleep in a process that involves an allosteric dialogue between the voltage sensors of the potassium channel Shaker—a critical determinant of dFBN activity—and the active sites of its redox-sensitive ß-subunit Hyperkinetic. The oxidation state of Hyperkinetic's nicotinamide adenine dinucleotide phosphate (NADPH) cofactor changes when PUFA-derived carbonyls abstract an electron pair. $NADP^+$ remains locked in the active site of Kvß until membrane depolarization permits its release and replacement with NADPH. dFBNs use this voltage-gated oxidoreductase cycle to encode their recent lipid peroxidation history in the collective binary states of their Kvß-subunits; this biochemical memory influences—and is erased by—spike discharges driving sleep. The presence of a lipid peroxidation sensor at the core of homeostatic sleep control suggests that sleep protects neuronal membranes against oxidative damage. Sleep, like ageing, may thus be a consequence of aerobic metabolism.

References

1. Donlea, J.M., Pimentel, D., and Miesenböck, G. (2014) Neuronal machinery of sleep homeostasis in Drosophila. Neuron *81*: 860–872.
2. Pimentel, D., Donlea, J.M., Talbot, C.B., Song, S.M., Thurston, A.J.F., and Miesenböck, G. (2016) Operation of a homeostatic sleep switch. Nature *536*: 333–337.
3. Kempf, A., Song, S.M., Talbot, C.B., and Miesenböck, G. (2019) A potassium channel β-subunit couples mitochondrial electron transport to sleep. Nature *568*: 230–234.

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Talk 6
Making memories in mice

Sheena Josselyn, PhD

Title:

Professor, University of Toronto
Senior Scientist, Hospital for Sick Children (Research Institute)
EMAIL: sheena.josselyn@sickkids.ca

Educational Background:

1996 PhD (Psychology, Neuroscience)
University of Toronto, Toronto, Canada
1991 MA (Clinical Psychology)
Queen's University at Kingston, Canada
1989 BA (Psychology)
Queen's University at Kingston, Canada
1987 BScH (Life Sciences)
Queen's University at Kingston, Canada

Professional History:

2003 - Present Senior Scientist, Hospital for Sick Children, Toronto, Canada
2003 - Present Professor, University of Toronto, Toronto, Canada
1998 - 2003 Research Associate, UCLA, Los Angeles, California, USA
1997 - 1998 Post-doctoral Fellow, Yale University, Ct, USA
1996 - 1997 Post-doctoral Fellow, Clarke Institute of Psychiatry (now CAMH), Toronto, Canada

Awards and Honors

2023 The Betty & David Koester Award for Brain Research (University of Zurich)
2022 National Academy of Medicine US
2022 Hughlings Jackson Award Lecturer (McGill)
2021 Andrew Carnegie Prize in Mind and Brain Sciences
2021 Benning Society Lecturer (University of Utah School of Medicine)
2021 Blum Lecturer (UT San Antonio)
2019 UCLA Distinguished Lecture Award
2018 Fellow, Royal Society of Canada (Life Sciences Division)
2018 Pavlovian Society Research Award
2017 Senior Fellow, Massey College (University of Toronto)
2016 - 2021 Senior Fellow, Canadian Institute for Advanced Research (CIFAR)
2016 Brenda Milner Lecturer (University of Lethbridge)

2016	Bryan Kolb Lecture in Behavioural Neuroscience (University of Calgary)
2016-2023	Canada Research Chair (CRC) in Brain and Cognition Tier I
2014	Daniel H. Efron Research Award, American College of Neuropsychopharmacology (ACNP)
2012	Travel award from American College of Neuropsychopharmacology (ACNP)
2009-2014	Canada Research Chair (CRC) in Molecular and Cellular Cognition Tier II (renewal)
2009	Innovations in Psychopharmacology Award, Canadian College of Neuropsychopharmacology (CCNP)
2008-2011	EJLB Scholar

Abstract

Understanding how the brain uses information is a fundamental goal of neuroscience. Several human disorders (ranging from autism spectrum disorder to PTSD to Alzheimer's disease) may stem from disrupted information processing. Therefore, this basic knowledge is not only critical for understanding normal brain function, but also vital for the development of new treatment strategies for these disorders. Memory may be defined as the retention over time of internal representations gained through experience, and the capacity to reconstruct these representations at later times. Long-lasting physical brain changes ('engrams') are thought to encode these internal representations. The concept of a physical memory trace likely originated in ancient Greece, although it wasn't until 1904 that Richard Semon first coined the term 'engram' (Semon, 1904). Despite its long history, finding a specific engram has been challenging, likely because an engram is encoded at multiple levels (epigenetic, synaptic, cell assembly). My lab is interested in understanding how specific neurons are recruited or allocated to an engram (Han et al., 2007; 2009), and how neuronal membership in an engram may change over time or with new experience (Rashid et al., 2016; Josselyn & Tonegawa, 2020). Here I will describe data in our efforts to understand memories in mice.

Refernces

1. R. Semon, *Die Mneme als erhaltendes Prinzip im Wechsel des organischen Geschehens*. W. Engelmann, Ed., (Leipzig, 1904).
2. Han JH, Kushner SA, Yiu AP, Hsiang HL, Buch T, Waisman A, Bontempi B, Neve RL, Frankland PW, **Josselyn SA** (2009). Selective erasure of a fear memory. *Science,* 323, 1492-1496.
3. Han JH, Kushner SA, Yiu AP, Cole CA, Matynia A, Brown RA, Neve R, Guzowski JF, Silva AJ, **Josselyn SA** (2007). Neuronal competition and selection during memory formation. *Science*, 316, 457-460.
4. Rashid AS, Yan C, Mercaldo V, Hsiang HW, Park S, Cole CJ, De Cristofaro A, Yu J, Ramakrishnan C, Lee SY, Deisseroth K, Frankland PW*, **Josselyn SA*** (2016). Competition between engrams influences fear memory formation and recall. *Science,* 353, 383-7.
5. **Josselyn SA** & Tonegawa S (2020). Memory engrams: Recalling the past and imagining the future. *Science*, 367, 6473-6480.

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President of Senri Life Science Foundation

Shizuo Akira

The foundation was established in July 1990, based on the vision of the late Yuichi Yamamura, former Osaka University President, who aimed to make the northern Osaka area, centered around Senri, into a hub for life science. The foundation serves as "the exchange base of wisdom," where life science researchers in industry, academia, and government can freely and openly exchange information and ideas, transcending the boundaries of their respective organizations.

The northern Osaka area hosts a cluster of medical and research institutes such as Osaka University, the National Cerebral and Cardiovascular Center (NCVC), and the National Institutes of Biomedical Innovation, Health and Nutrition (NIBIOHN), as well as research laboratories and factories of pharmaceutical companies. Hubs like Saito Life Science Park, KENTO (Northern Osaka Health and Biomedical Innovation Town), and Nakanoshima (International Hub for Future Medicine) are also being established here.

In this environment, the foundation was accredited as a public interest incorporated foundation in 2010, and has since been further enhancing its role as "the exchange base of wisdom." It has expanded and reinforced its activities across various areas, including cultivating research talent in the field of life sciences, research grants and support, public awareness, and assistance in the practical application of research, all with the goal of promoting cutting-edge and socially beneficial endeavors.

The field of life sciences, which explores the mechanisms of life, encompasses a broad range of academic disciplines. Its outcomes are expected to make significant contributions not only to medical and health, but also to the foundation of human life, including areas such as the environment and food to create a prosperous and happy human society. However, we believe that achieving this requires us to steadfastly accumulate a diverse range of research with a solid foundation in science. The foundation aims to support such research endeavors and widely provide information.

With the spread of the new coronavirus infection from 2020, the nature of our business activities has changed completely. Web-based events have become the primary format, bringing benefits such as increased accessibility for a wider audience, including those from distant locations. As a result, this has contributed to enhancing the foundation's visibility and the satisfaction level of our programs.

On the other hand, there is concern about whether we are fully fulfilling the role of "the exchange base of wisdom" as envisioned by Dr. Yamamura in creating a casual networking place like an "Aka-chochin*" in Senri. In the "With Corona" and "Post Corona" era, even with the hybrid format combining web and on-site components, we are actively exploring program development to create a sense of unity between speakers and audience, and encouraging participation of large audiences at the venue. We aim to continue contributing to society as the exchange of life sciences. We appreciate your ongoing support and cooperation in the foundation's activities.

*Aka-chochin: Japanese traditional pub showing a red lantern(Aka-chochin) in front of it.

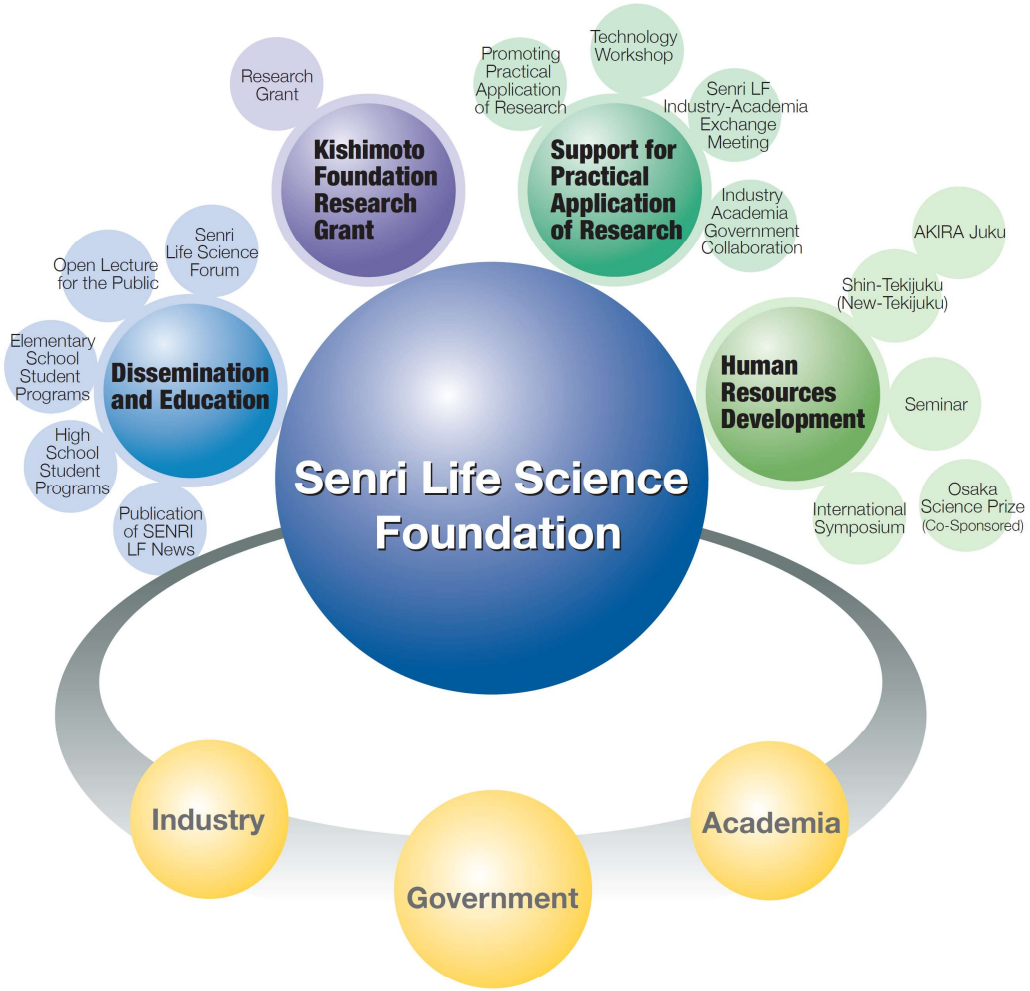
Senri Life Science Foundation
Honorary President,

Tadamitsu Kishimoto

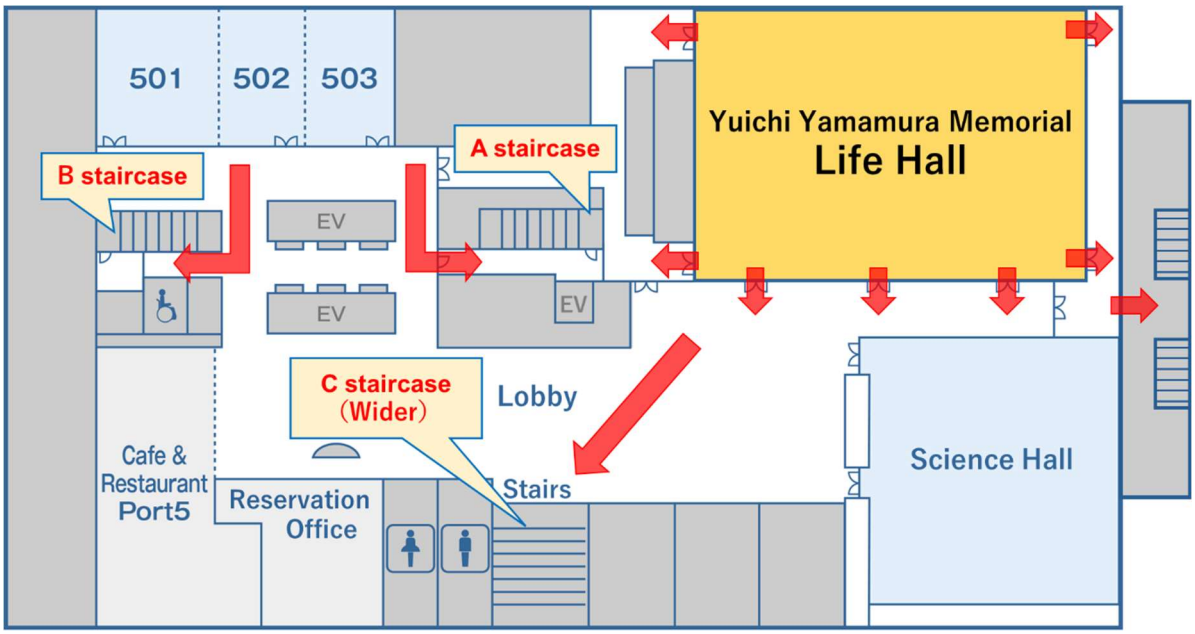
継続が創造を生む

Continuity
Produces
Creativity.

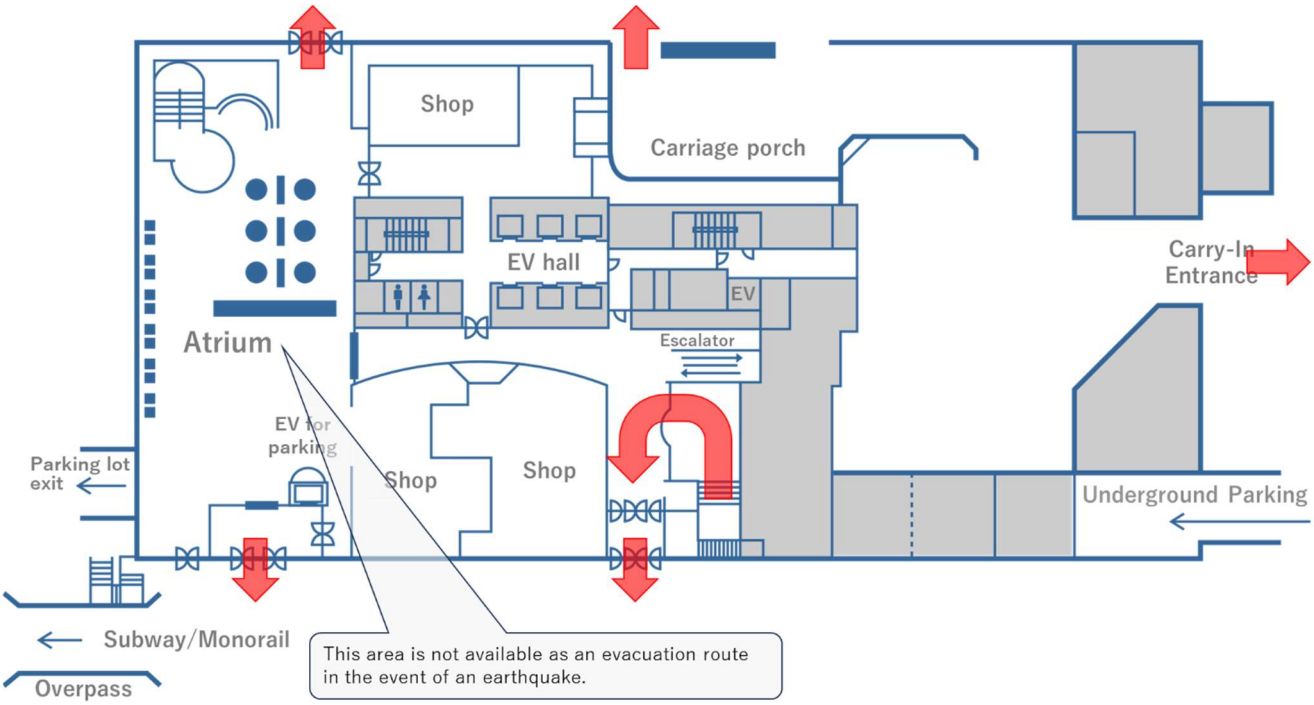
Business Activities



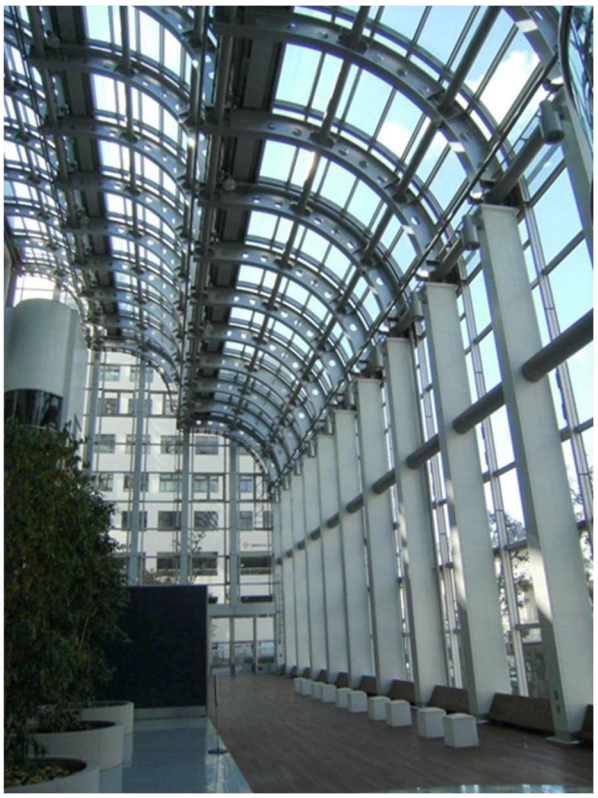
Evacuation routes of the 5th floor



Evacuation routes on the 1st floor



- There is an announce in an emergency. We will provide guidance if evacuation becomes necessary. Please remain at your seat, stay calm, and await instructions from the staff.
- During evacuation, please exit the route indicated by the red arrows.
- Don’t use the elevators.



Senri Life Science Foundation

Level 20, Senri Life Science Center Building
1-4-2, Shinsenri-Higashimachi, Toyonaka-City,
Osaka 560-0082, Japan
Phone: 06-6873-2006,　Fax: 06-6873-2002
E-mail: smp-2022@senri-life.or.jp
URL: https://www.senri-life.or.jp