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24th Surugadai International Symposium
1st CURE International Symposium on Multilayered Stress Diseases
JOINT SYMPOSIUM

From Mechanosensing to Stress Responses: Deciphering Biological Regulation Across Molecular, Cellular, and Organismal Scales

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Director's Greeting



Prof. Takehiko Sasaki, Ph.D.
Director
Medical Research Laboratory
Institute of Integrated Research
Institute of Science Tokyo, Japan

It is my great privilege to welcome you to the 24th Surugadai International Symposium, hosted by the Medical Research Laboratory of the Institute of Science Tokyo. Our laboratory has convened this symposium for more than two decades, serving as a platform for sustained scientific exchange and interdisciplinary collaboration. This year opens a new chapter, as the symposium is held jointly with the 1st CURE International Symposium on Multilayered Stress Diseases.

Last year, under the theme "Transforming Life Sciences through Robotic Automation and Artificial Intelligence," we examined how emerging technologies are changing the way research is conducted. This year, we turn to a fundamental question of biology itself: how living systems sense and respond to stress. Our theme, "From Mechanosensing to Stress Responses: Deciphering Biological Regulation Across Molecular, Cellular, and Organismal Scales," reflects the recognition that stress, whether a physical force acting on a membrane channel or a psychosocial burden on an individual, operates at every level of biological organization, and that the responses it evokes shape health and disease.

This perspective lies at the heart of the "Multilayered Stress Diseases" project, selected in fiscal year 2023 for the Coalition of Universities for Research Excellence (CURE) Program of the Ministry of Education, Culture, Sports, Science and Technology (MEXT). Building on our role as a Joint Usage/Research Center, and in partnership with the Tokyo Metropolitan Institute of Medical Science and the National Center of Neurology and Psychiatry, we are developing an interdisciplinary hub that integrates the basic medical and life sciences with psychiatry and psychology, with the aim of overcoming stress-related intractable diseases.

The program embodies this multilayered view. The first session addresses mechanical stress, from the gating of mechanosensitive channels to tissue mechanics and physical performance. The second moves to the brain and mind, covering the neural mechanisms of emotion and social behavior, stress in mental illness, recovery from stroke, and a novel mode of synaptic transmission. We are honored to welcome the distinguished invited speakers joining us this year. I also extend my sincere appreciation to the organizing committee and to our colleagues in the CURE project.

I sincerely hope that this symposium will provide all participants with new insights, foster meaningful scholarly dialogue, and promote further collaboration.

24th
Surugadai International Symposium

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1st
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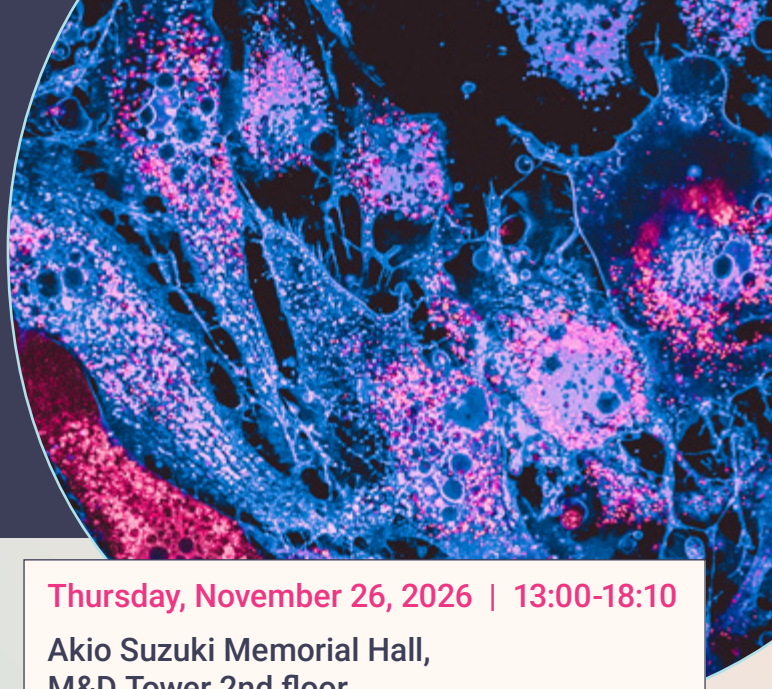
JOINT SYMPOSIUM



From Mechanosensing to Stress Responses: Deciphering Biological Regulation Across Molecular, Cellular, and Organismal Scales

Thursday, November 26, 2026 | 13:00-18:10

Akio Suzuki Memorial Hall,
M&D Tower 2nd floor,
Institute of Science Tokyo

1-5-45 Yushima, Bunkyo-ku, Tokyo, Japan

13:00—13:05 OPENING REMARKS

Dr. Takehiko Sasaki *(Director, Medical Research Laboratory, Institute of Science Tokyo)*

Moderated by Dr. Fumika Koyano *(Institute of Science Tokyo)*

13:05—15:20 SESSION 1

Chaired by Drs. Katsumori Segawa and Toshiro Moroishi *(Institute of Science Tokyo)*

13:05—13:50 KEYNOTE LECTURE 1

Structural Choreography and Mechanogating of PIEZO Channels

Dr. Bailong Xiao *(Tsinghua University)*

13:50—14:20 TALK 1

Activation Mechanisms of TMEM63B, a Mechanosensitive Lipid Scramblase

Dr. Yugo Miyata *(Institute of Science Tokyo)*

14:20—14:50 TALK 2

Dynamic Tissue Mechanics across Life Stages

Dr. Fumiko Toyoshima *(Institute of Science Tokyo)*

14:50—15:20 TALK 3

Born to Move: Mechanotransduction and the Biology of Athletic Giftedness

Dr. Hiroshi Asahara *(Institute of Science Tokyo)*

15:20—15:50 COFFEE BREAK

15:50—18:05 SESSION 2

Chaired by Drs. Shusaku Uchida and Hiroki Shiwaku *(Institute of Science Tokyo)*

15:50—16:35 KEYNOTE LECTURE 2

From Pecking Order to Ketamine: Neural Mechanism of Emotion and Social Behavior

Dr. Hailan Hu *(Zhejiang University School of Medicine)*

16:35—17:05 TALK 4

Neuro-Immuno-Metabolic Mechanisms of Stress in Mental Illness

Dr. Tomoyuki Furuyashiki *(Institute of Science Tokyo)*

17:05—17:35 TALK 5

Sustaining Microglial Reparative Function Enhances Stroke Recovery

Dr. Jun Tsuyama *(Institute of Science Tokyo)*

17:35—18:05 TALK 6

The Channel Synapse: From Discovery to Biological Function

Dr. Akiyuki Taruno *(Kyoto University)*

18:05—18:10 CLOSING REMARKS

Dr. Katsumori Segawa *(Institute of Science Tokyo)*

Jointly organized by: The 24th Surugadai International Symposium Organizing Committee and the CURE Multilayered Stress Diseases

CURE: Coalition of Universities for Research Excellence Program, MEXT Promotion of Development of a Joint Usage/Research System Project

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Session 1　13:05-13:50　Keynote Lecture 1

Structural choreography and mechano-gating of PIEZO channels

Dr. Bailong Xiao

Tsinghua University

Abstract

PIEZO1 and PIEZO2 were identified by Patapoutian and colleagues as bona fide mechanically activated cation channels. PIEZO1 broadly regulates the development and function of the cardiovascular, skeletal, immune and nervous systems, while PIEZO2 mediates the sense of gentle touch, proprioception, interoception, and tactile pain. Using a combination of cryo-EM structure determination, mutagenesis, electrophysiology, mouse genetics, and pharmacology, our research aims to systematically understand how PIEZO channels effectively convert piconewton-scale forces into selective cation permeation. In this talk, I will present our current understanding of PIEZOs, with particular focus on their unique structural designs, physical principles, structural dynamics underlying the activation and inactivation process, which may enable them to serve as versatile and professional mechanosensors.

Keyword

PIEZO1, PIEZO2, Mechanogating, Structure



Short biography

Dr. Bailong Xiao is a tenured Professor at the School of Pharmaceutical Sciences at Tsinghua University, a New Cornerstone Investigator, and a Principal Investigator at the Tsinghua-Peking Center for Life Sciences, the IDG/McGovern Institute for Brain Research, and the Beijing Frontier Research Center for Biological Structure. He received his B.S. degree from Sun Yat-Sen University (China) in 2001 and completed his Ph.D. at the University of Calgary (Canada) from 2001 to 2006 under the

supervision of Dr. Wayne Chen, focusing on the structure-function relationship of the cardiac ryanodine receptor. From 2007 to 2012, he conducted postdoctoral training with Dr. Ardem Patapoutian (2021 Nobel Laureate) at the Scripps Research Institute (USA), where he contributed to the establishment of the mechanically activated PIEZO channel family. In 2013, Dr. Xiao joined the School of Pharmaceutical Sciences at Tsinghua University as an Assistant Professor. Since then, he has established a multidisciplinary research program aimed at advancing the understanding of the structure-function relationships and physiological and pharmacological regulation of PIEZO channels. His key contributions include determining the cryo-EM structures of PIEZO channels in detergents or liposome membranes and elucidating their unique structural design and curvature-based gating dynamics, which enable their versatile mechanotransduction functions across a wide range of physiological and pathophysiological processes. Dr. Xiao's work has received broad recognition. Notably, his research has been cited by the 2021 Nobel Assembly in Physiology or Medicine to describe the discovery and study of PIEZO channels, and has also been referenced in the textbooks Principles of Neural Science (6th ed., 2021), edited by Nobel Laureate Dr. Eric Kandel, and Principles of Neurobiology (2nd ed., 2021), edited by Dr. Liqun Luo.

Specialty and present interests

1. Identification and characterization of novel mechanically activated ion channels and regulators;

2. Structure-function and drug discovery of PIEZO channels.

References

1. Structure and Mechanogating Mechanism of the Piezo1 Channel. ***Nature*** 2018 Feb 22;554(7693):487-492. doi: 10.1038/nature25743.

2. Structure and mechanogating of the mammalian tactile channel PIEZO2. ***Nature*** 2019 Sep;573(7773):225-229. doi: 10.1038/s41586-019-1505-8.

3. Deformation and curvature-gating of the PIEZO1 channel in lipid membranes. ***Nature*** 2022 Apr;604(7905):377-383. doi: 10.1038/s41586-022-04574-8.

4. Spring-like mechanics enable rapid inactivation and stochastic single-channel gating of the mechanically activated PIEZO channel. ***Cell Rep*** 2025 Dec 23;44(12):116615.doi: 10.1016/j.celrep.2025.

5. Structural conservation and ion selectivity adaptation of the mechanically activated PIEZO channel. ***Neuron*** March 30, 2026

Session 1　13:50-14:20　Talk 1

Activation Mechanisms of TMEM63B, a Mechanosensitive Lipid Scramblase

Dr. Yugo Miyata

Institute of Science Tokyo

Abstract

The plasma membrane is a lipid bilayer with different phospholipid compositions in its inner and outer layers. For example, phosphatidylserine is largely restricted to the inner layer, whereas phosphatidylcholine is enriched in the outer layer. Maintaining this asymmetry and changing it when needed are important for cell function and tissue homeostasis. However, the mechanisms regulating phosphatidylcholine distribution between the two layers were poorly understood.

To identify proteins involved in this regulation, we performed a genome-wide CRISPR screen and identified TMEM63B as a candidate regulator. Subsequent functional analyses revealed that TMEM63B acts as a scramblase, translocating phospholipids in both directions between the two layers. This scrambling activity was induced by treatments that alter membrane thickness or curvature. These responses suggest that TMEM63B acts as a membrane sensor, coupling changes in membrane physical properties to phospholipid scrambling.

We next performed cryo-EM structural analysis of TMEM63B to identify its phospholipid translocation pathway. Comparison of the closed and open conformations, together with functional analyses of mutants, revealed a membrane-facing cleft that serves as a phospholipid translocation pathway in the open state. The structures also provided clues to how membrane changes might regulate this pathway. We found two distinctive intracellular “hook regions” that are likely to be partially embedded in the membrane. Mass spectrometry also detected palmitoylated cysteine residues in these regions. Palmitoylation generally promotes membrane association, suggesting that these hook regions may interact with the membrane and thereby contribute to sensing changes in its physical properties. Substitution of the cysteine clusters in either hook abolished stimulus-induced scrambling activity in cells, despite preserved plasma membrane localization. These results support a role for the palmitoylated hook regions in membrane sensing.

The open-state structure was obtained using a Fab fragment of a monoclonal antibody that stabilizes the open conformation. We hypothesized that the antibody-binding region might regulate the transition between open and closed states. We mapped the binding site to the C-terminal tail and found that deleting a nearby segment or substituting a key amino acid caused scrambling without membrane stimulation. Thus, the C-terminal tail normally acts as an autoinhibitory region that suppresses TMEM63B activity. In this talk, I will discuss membrane sensing and activity regulation by the intracellular regions of TMEM63B, along with structural insights into the underlying mechanisms.

Keyword

TMEM63B; Lipid scramblase; Palmitoylation; Mechanosensitivity; Autoinhibition



Short biography

Yugo Miyata is a Lecturer at Institute of Science Tokyo and a JST FOREST Researcher. He received his Ph.D. from Osaka University in 2011 for his research on metabolic syndrome. At Tokyo Institute of Technology and later at the National Agriculture and Food Research Organization (NARO), he studied a midge that can survive complete drying. His research has been driven by an interest in physiological phenomena and their underlying mechanisms, with a current focus on membrane lipid asymmetry and scramblase regulation.

Specialty and present interests

Lipid biology, with interests in membrane transport, homeostasis, and their physiological significance.

References

1. Miyata Y, Takahashi K, Lee Y, et al. Membrane structure-responsive lipid scrambling by TMEM63B to control plasma membrane lipid distribution. Nature Structural & Molecular Biology. 2025;32:185-198. doi:10.1038/s41594-024-01411-6.

2. Nishimura M, Miyata Y, Shiraki Y, et al. Autoinhibition of the mechanosensitive lipid scramblase TMEM63B by its C-terminal tail. Journal of Biological Chemistry. 2026;302:113223. doi:10.1016/j.jbc.2026.113223.

3. Miyata Y, Nishimura M, Nagata A, et al. Membrane structure-responsive lipid scramblase activity of the TMEM63/OSCA family. FEBS Letters. 2025;599:656-666. doi:10.1002/1873-3468.15084.

Session 1　14:20-14:50　Talk 2

Dynamic Tissue Mechanics across Life Stages

Dr. Fumiko Toyoshima

Institute of Science Tokyo

Abstract

Tissues continuously remodel their architecture and function in response to physiological changes throughout life. Tissue mechanical properties, including stiffness and tension, play critical roles in regulating cellular behavior and tissue remodeling. However, how these mechanical properties change across life stages and contribute to tissue adaptation and homeostasis remains poorly understood.

The skin provides an excellent model for investigating these questions, as it undergoes extensive remodeling during different life stages, including pregnancy and aging. Our studies have revealed that dermal mechanical properties influence epidermal cell behavior through mechanical-to-chemical signal conversion. In particular, we identified a distinct population of dermal fibroblasts that remodels the extracellular matrix and promotes epidermal proliferation in response to pregnancy-associated skin expansion. In contrast, age-associated changes in dermal stiffness and tissue architecture are linked to altered epidermal cell dynamics.

In this talk, I will discuss how dynamic changes in tissue mechanics regulate epithelial–mesenchymal interactions and contribute to skin remodeling across different life stages, with a particular focus on pregnancy and aging.

Keyword

Tissue stiffness, organ remodeling, skin, pregnancy, aging



Short biography

Dr.Toyoshima is a professor of the Department of Homeostatic Medicine at Institute of Science Tokyo. She received her Ph.D. in Biophysics from the Kyoto University and completed postdoctoral training at Kyoto University before joining the faculty at Institute of Life and Medical Science at Kyoto University prior to her current position at Institute of Science Tokyo.

Specialty and present interests

Dr. Toyoshima research centers around defining the mechanisms that control organ remodeling across life stages in adulthood, particularly focus on how alterations in mesenchymal mechanics control epithelial cell behavior.

References

1. Kobayashi, Y., Sunadome, K., Maki, K., Fukunaga, H., Matsubara, H., Ohkubo, S., Maki, R., Yoshikawa, M., Tata, A., Tata, P.R., Matsumoto K., Adachi, T., Iwaki, M., Yamamoto, T., Toyoshima, F. Distinct dermal fibroblasts direct mechano-chemical signaling to the epidermis during pregnancy. bioRxiv. (2025)

2. Ichijo R, Maki K, Kabata M, Murata T, Nagasaka A, Ishihara S, Haga H, Honda T, Adachi T, Yamamoto T, Toyoshima F. Vasculature atrophy causes a stiffened microenvironment that augments epidermal stem cell differentiation in aged skin. Nat. Aging 2, 592-600 (2022).

3. Ichijo R, Kabata M, Kidoya H, Muramatsu F, Ishibashi R, Abe K, Tsutsui K, Kubo H, Iizuka Y, Kitano S, Miyachi H, Kubota Y, Fujiwara H, Sada A, Yamamoto T, Toyoshima F. Vasculature-driven stem cell population coordinates tissue scaling in dynamic organs. Sci. Adv. 7, ea2575 (2021).

4. Ichijo, R., Kobayashi, H., Yoneda, S., Iizuka, Y., Kubo, H., Matsumura, S., Kitano, S., Miyachi, H., Honda, T., and Toyoshima, F. Tbx3-dependent amplifying stem cell progeny drives interfollicular epidermal expansion during pregnancy and regeneration. Nat. Commun. 8, 508 (2017)

Session 1　14:50-15:20　Talk 3

From sprinters to arthritis: what human genetic variation reveals about how tissues sense force and keep their identity

Dr. Hiroshi Asahara

Department of Systems BioMedicine, Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, Tokyo, Japan

Abstract

Why can some people run faster than others, and why do some joints wear out while others last a lifetime? Both questions ask how tissues sense mechanical force and maintain their identity, and human genetic variation offers a natural experiment to answer them.

At one end of this spectrum, we found that the mechanosensitive ion channel PIEZO1 is a key force sensor in tendon. Mice carrying a gain-of-function Piezo1 mutation developed stronger tendons and jumped higher, and a human PIEZO1 gain-of-function variant was enriched in elite Jamaican sprinters. A single genetic change that tunes how cells feel force appears to shape athletic performance.

At the other end, osteoarthritis (OA), the most common joint disease, affects hundreds of millions of people and still lacks disease-modifying therapy. Genome-wide association studies (GWAS) have mapped around 100 OA risk loci, yet most lie in non-coding regions, and the genes and tissues they act on remain largely unknown. In collaboration with Scripps Research, we mapped expression quantitative trait loci (eQTL) across multiple tissues of the human knee, including cartilage, meniscus, synovium, ligament and tendon, from the same donors. Integrating these maps with OA GWAS revealed that many risk variants act not only in cartilage but also in meniscus, ligament and tendon, suggesting that OA is a disease of the joint as a whole organ. We are now testing candidate variants with massively parallel reporter assays and CRISPR-based screens in primary human cells to move from risk loci to causal genes.

Bridging these two extremes is a more basic question: what makes a tissue what it is? Using EMBRYS, a whole-mount in situ hybridization atlas of about 1,600 transcription factors in mouse embryos, we identified Mohawk (Mkx) as a master regulator of tendon and ligament whose expression is induced by mechanical loading. The MKX-PIEZO1 axis thus links developmental programs, mechanical signals and tissue maintenance, and offers a target for drugs that strengthen tissues.

In this talk, I will use the contrast between sprinters and arthritis to show how developmental biology, mechanobiology and human genetics can be combined to understand how tissues sense force, maintain their identity and fail in disease.

Keyword

tissue identity; mechanosensing; PIEZO1; osteoarthritis GWAS; eQTL



References

1. https://www.summitpharma.co.jp/japanese/service/products/autiv/
2. https://kachaka.life/
3. Avinash Ummadisingu, Jongkeum Choi, Koki Yamane, Shimpei Masuda, Naoki Fukaya, Kuniyuki Takahashi, "**SAID-NeRF: Segmentation-AIDed NeRF for Depth Completion of Transparent Objects,**" IROS2024
4. Naoki Fukaya, Koki Yamane, Shimpei Masuda, Avinash Ummadisingu, Shin-ichi Maeda, Kuniyuki Takahashi: "**Four-Axis Adaptive Fingers Hand for Object Insertion: FAAF Hand**," IROS2024
5. Kuniyuki Takahashi, Shimpei Masuda, Tadahiro Taniguchi: "**Stable Object Placing using Curl and Diff Features of Vision-based Tactile Sensors,**" IROS2024

Session 2 15:50-16:35 Keynote Lecture 2

From pecking order to ketamine - Neural mechanisms of social and emotional behaviors

Dr. Hailan Hu

Zhejiang University

Abstract

Our understanding of the brain has advanced in successive waves—from how we perceive the external world, to how we learn and remember, and now increasingly to the neural basis of our inner mental life. Emotion is central to this inner world: it shapes our decisions and behavior, while itself being profoundly influenced by social experience and our relationships with others. Disturbances in these processes can contribute to psychiatric disorders such as depression.

Our laboratory studies how emotion, social behavior, and mental illness are linked at the level of brain circuits. I will first discuss how pathological burst firing in the lateral habenula, the brain's antireward center, can drive depressive-like states, and how ketamine rapidly suppresses this abnormal activity to produce antidepressant effects. I will then turn to social competition and hierarchy, examining the neural basis of the "winner effect" and how changes in social status can reshape emotional state and brain circuits, including mechanisms that may contribute to depression. Finally, I will discuss how these insights can be used to identify additional molecular and cellular targets that converge on pathological habenula bursting, opening new possibilities for rapid-acting antidepressant therapies.

Together, these studies illustrate how internal brain dynamics and social experience interact to shape emotion and behavior, and how understanding these interactions may reveal new principles for treating psychiatric disorders.

Keyword

Emotion, social hierarchy, depression, winner effect, social stress

Short biography

Hailan Hu is Professor and Director of School of Brain Science and Brain Medicine at Zhejiang University. She received a BA in Biochemistry from Beijing University and a PhD in neuroscience (with Corey Goodman) from UC Berkeley. After a postdoc training with Roberto Malinow at CSHL, she joined the faculty of Institute of Neuroscience, Chinese Academy of Sciences. Since 2015, she has been professor at Zhejiang University. Her laboratory seeks to understand how emotional and social behaviors are encoded and regulated in the brain, with a main focus on the neural circuitry underlying depression and social dominance. Her team has identified the neural mechanism underlying the winner effect, by which individuals increase their chance of winning after previous victories. Her recent work has uncovered a new model to explain the etiology of depression and the rapid antidepressant actions of

ketamine, involving NMDA receptor-dependent burst activity of lateral habenular neurons. Her work has led to the identification of several molecular targets for developing new antidepressant drugs. She is a recipient of the IBRO-Kemali International Prize and the L'Oreal-UNESCO for Women in Science International award.

Specialty and present interests

Neural mechanism of depression and rapid antidepressants

References

2024 Chen M, Ma S, Liu H, Dong Y, Tang J, Ni Z, Tan Y, Duan C, Li H, Huang H, Li Y, Cao X, Lingle CJ, Yang Y, Hu H**.** Brain-region-specific Action of Ketamine as Rapid Antidepressant. *Science*, 385(6709) eado7010.

2023 Fan Z, Chang J, Liang Y, Zhu H, Zhang C, Zheng D, Wang J, Xu Y, Li Q, Hu H. Neural Mechanism Underlying Depressive-Like State Associated with Social Status Loss. *Cell*, 186: 560-576.

2023 Ma S*, Chen M*, Jiang Y, Xiang X, Wang S, Wu Z, Li S, Cui Y, Wang J, Zhu Y, Zhang Y, Ma H, Duan S, Li H, Yang Y, Lingle CJ, Hu H. Sustained antidepressant effect of ketamine through NMDAR trapping in the LHb. *Nature*, 622:802.

2018 Yang Y*, Cui Y*, Sang K*, Dong Y*, Ni Z, Ma S, Hu H. Ketamine blocks bursting in the lateral habenula to rapidly relieve depression. *Nature*, 554: 317-22.

2018 Cui Y, Yang Y, Ni Z, Dong Y, Sang K, Cai G, Foncelle A, Ma S, Sang K, Tang S, Li Y, Shen Y, Berry H, Wu S, Hu H. Astroglial Kir4.1 in the lateral habenula drives neuronal bursts in depression. *Nature*, 554: 323-27.

Session 2　16:35-17:05　Talk 4

Neuro-Immuno-Metabolic Mechanisms of Stress in Mental Illness

Dr. Tomoyuki Furuyashiki

Institute of Science Tokyo

Abstract

Stress increases the risk of mental disorders, including depression. Clinical studies have identified inflammatory changes in the brain and peripheral blood of patients with depression, including unmedicated individuals. However, how stress-induced inflammation interacts with neuronal function to reshape neural circuits remains poorly understood.
Using mouse models of social stress, we have demonstrated contrasting effects of acute and chronic stress on prefrontal neuronal plasticity. Acute stress enhances dopaminergic signaling, promotes dendritic growth, and increases stress resilience. In contrast, chronic stress activates microglia through innate immune receptors, suppresses prefrontal dopaminergic responses, induces dendritic retraction, and promotes behavioral alterations. Chronic stress also mobilizes bone marrow-derived neutrophils and monocytes, implicating peripheral inflammation in stress-related behavioral changes.
To investigate underlying mechanisms, we performed transcriptomic and epigenomic analyses of microglia isolated from multiple brain regions under different stress conditions. These studies revealed that glucocorticoid receptor signaling sensitizes microglia to acute and chronic social stress in stress-susceptible mice, whereas chronic stress activates microglia through TLR2/4 signaling, contributing to behavioral alterations. In addition, three-dimensional electron microscopy, multi-omics analyses, and genetic manipulations revealed that chronic stress alters central metabolic pathways at prefrontal cortical synapses. These metabolic changes may interact with microglial responses to influence neuronal structure and function.
We are extending these findings through single-cell multi-omics and spatial omics analyses to characterize cell-type-specific molecular changes and their spatial organization in the stressed brain. In parallel, whole-brain imaging is being used to map functional and structural remodeling of neural circuits across widespread brain regions following stress-induced inflammatory and metabolic responses. Integrating these approaches may reveal how neuroinflammation and synaptic metabolic alterations contribute to brain-wide circuit remodeling and stress susceptibility.

In this presentation, I will discuss our latest findings on neuroimmune and metabolic mechanisms of stress-induced neural circuit remodeling and their implications for understanding and developing treatments for stress-related disorders.

Keyword

Social stress; Neuroinflammation; Microglia; Synaptic metabolism; Neural circuit remodeling



Short biography

Tomoyuki Furuyashiki is Professor and Chair of the Department of Pharmacology at the Graduate School of Medical and Dental Sciences, Institute of Science Tokyo, and Professor Emeritus of Kobe University. He received his M.D. in 1997 and Ph.D. in 2001 from Kyoto University. Following research appointments at Kyoto University and Johns Hopkins University, he served as Professor and Chair of Pharmacology at Kobe University from 2014 to 2025 before assuming his current position.
His research focuses on the neural and immune mechanisms underlying stress responses, particularly how neuroinflammation and neuroplasticity influence emotional and cognitive functions. His work aims to clarify the biological basis of stress susceptibility and resilience and inform approaches to stress-related psychiatric disorders.

He serves as President of the Japanese Pharmacological Society and Vice-Chairperson of Section II of the Science Council of Japan. His honors include the CINP Brain Health Research Award (2024), the AsCNP Science Award (2025), and the Setsuro Ebashi Award from the Japanese Pharmacological Society (2026).

Specialty

Neuropsychopharmacology

present interests

Neuro-immuno-metabolic mechanisms underlying stress susceptibility and resilience, with particular emphasis on neuroinflammation, neuroplasticity, and brain-periphery interactions. Current research examines how acute and chronic stress alter emotional and cognitive functions by integrating behavioral analyses, neural circuit approaches, and molecular profiling, including single-cell and spatial omics. The ultimate goal is to identify mechanisms and therapeutic targets for stress-related psychiatric disorders.

References

Shinohara R et al. Dopamine D1 receptor subtype mediates acute stress-induced dendritic growth in excitatory neurons of the medial prefrontal cortex and contributes to suppression of stress susceptibility in mice. *Molecular Psychiatry*. 2018;23(8):1717–1730.
Nie X et al. The innate immune receptors TLR2/4 mediate repeated social defeat stress-induced social avoidance through prefrontal microglial activation. *Neuron*. 2018;99(3):464–479.e7.
Ishikawa Y et al. Repeated social defeat stress induces neutrophil mobilization in mice: maintenance after cessation of stress and strain-dependent difference in response. *British Journal of Pharmacology*. 2021;178(4):827–844.
Okuda Y et al. The activation of the piriform cortex to lateral septum pathway during chronic social defeat stress is crucial for the induction of behavioral disturbance in mice. *Neuropsychopharmacology*. 2025;50(5):828–840.
Yamada R et al. Synaptic mitochondrial oxidative stress contributes to individual variability in age-related cognitive inflexibility in mice. *Aging Cell*. 2026;25(9):e70716.

Session 2　17:05-17:35　Talk 5

Sustaining microglial reparative function enhances stroke recovery

Dr. Jun Tsuyama

Department of Neuroinflammation and Repair, Medical Research Laboratory, Institute of Science Tokyo

Abstract

Neurological symptoms after brain injury can remain as lifelong detrimental sequelae since most spontaneous brain recovery disappears within a few months after brain injury. However, cellular and molecular mechanisms that diminish spontaneous brain functional recovery remain unknown. Microglia play an essential role in recovery processes after brain injury. Insulin-like growth factor 1 (IGF1) is a representative neurotrophic factor produced by post-stroke microglia that promotes synaptogenesis and remyelination.

Depletion of IGF1-expressing cells after stroke impaired spontaneous neurological recovery in mice, supporting the importance of these cells during the recovery phase. We discovered by cellular fate analysis that reparative microglia persisted in the post-stroke brain even after losing their reparative function. Using *Igf1*-CreER mice with a lineage reporter and an *Igf1*-Egfp transgene, we distinguished microglia that retained IGF1 expression from those that had lost it. We identified 391 recovery phase-associated genes in IGF1-expressing microglia and found that their expression progressively decreased after stroke.

Through epigenetic analysis, ZFP384 was identified as a pivotal transcriptional regulator that diminished recovery phase-associated gene expression in reparative microglia, turning them into dysfunctional cells that lost reparative functions. Microglia-specific deletion of *Zfp384* maintained recovery phase-associated gene expression and improved neurological recovery after stroke. Mechanistically, ZFP384 disrupted YY1-mediated chromatin interactions that were necessary for the expression of these genes in microglia.

Antisense oligonucleotides targeting *Zfp384* sustained the broad range of neural repair effects of microglia and enhanced stroke recovery, even in the chronic phase of ischemic stroke recovery. ASO-*Zfp384* was administered into the lateral ventricle of mice after stroke and improved neurological recovery even when treatment began on day 29 after stroke onset. Histological analyses showed enhanced synaptogenesis and remyelination after ASO-*Zfp384* treatment. In post-mortem brain tissue from patients with ischemic stroke, ZFP384 expression was inversely correlated with IGF1 expression in the peri-infarct region. Thus, therapeutics that prevent myeloid reparative immunity from losing its beneficial functions sustain brain functional recovery.

Keyword

Microglia; Ischemic stroke; ZFP384; Chromatin regulation; Antisense oligonucleotides



Short biography

Jun Tsuyama works in the Department of Neuroinflammation and Repair at the Medical Research Laboratory, Institute of Science Tokyo. He received his Ph.D. in Medicine from Keio University in 2015. He worked at the Tokyo Metropolitan Institute of Medical Science from 2017 to 2023 and joined Tokyo Medical and Dental University in April 2023, which became part of the Institute of Science Tokyo in October 2024. His research focuses on microglial regulation of brain repair and therapeutic approaches to sustain functional recovery after stroke.

Specialty and present interests:

Neuroinflammation and brain repair; microglial cell states; single-cell transcriptomics and epigenomics; antisense oligonucleotide approaches to stroke recovery.

References

1. Tsuyama J, et al. Sustaining microglial reparative function enhances stroke recovery. *Nature* 655:447–457 (2026). https://doi.org/10.1038/s41586-026-10480-0

2. Nakamura A, et al. PLA2G2E-mediated lipid metabolism triggers brain-autonomous neural repair after ischemic stroke. *Neuron* 111:2995–3010.e9 (2023). https://doi.org/10.1016/j.neuron.2023.06.024

3. Tsuyama J, et al. Pivotal role of innate myeloid cells in cerebral post-ischemic sterile inflammation. *Seminars in Immunopathology* 40:523–538 (2018). https://doi.org/10.1007/s00281-018-0707-8

Session 2　17:35-18:05　Talk 6

The Channel Synapse: From Discovery to Biological Function

Dr. Akiyuki Taruno

Department of Cellular and Molecular Physiology, Graduate School of Medicine, Kyoto University

Abstract

Chemical neurotransmission is a fundamental mechanism of neural communication, traditionally mediated by Ca^{2+}-dependent exocytosis of synaptic vesicles. However, it has long been known that taste receptor cells in taste buds lack synaptic vesicles, yet still transmit gustatory signals to afferent neurons. We discovered a unique synaptic mechanism in these cells—termed the channel synapse—in which neurotransmitter (ATP) release is mediated not by vesicular fusion, but through the ion-conducting pore of a voltage-gated channel complex, CALHM1/3. Structurally, the channel synapse is defined by a tripartite architecture comprising a presynaptic mitochondrion or endoplasmic reticulum, a CALHM1/3-enriched presynaptic membrane, and a closely apposed postsynaptic afferent nerve terminal. In the first part of my talk, I will review the discovery, structural organization, and physiological roles of the channel synapse in the mammalian gustatory system[1-4].

The second part will highlight our recent findings that extend the concept of channel synapses beyond the tongue[5]. Using a whole-body screen for CALHM1/3 expression in mice combined with single-cell transcriptomics, we identified novel chemosensory epithelial cells in the throat that form channel synapses with vagal sensory neurons. These cells express GPCRs for noxious chemicals, T2Rs, and mediate airway-protective reflexes: swallowing via hypopharyngeal taste buds and coughing via laryngeal tuft cells. These reflexes were abolished in *Calhm3* knockout mice and could be artificially triggered by optogenetic stimulation of these cells. Moreover, exposure to aeroallergens sensitized the cough reflex in a CALHM3-dependent manner. These findings identify these chemosensory epithelial cells with channel synapses as previously unrecognized end organs of airway protective reflexes and as sites of reflex hypersensitivity, underscoring the broader significance of the channel synapse in sensory physiology and host defense.

Keyword

Taste, Cough, Swallow, Synapse, Ion Channel



Short biography

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Specialty and present interests

Physiology, Biophysics, Chemosensory neuroscience

References

1. Nature 495; 223-226, 2013.

2. Neuron 98; 547-561, 2018.

3. Sci Adv 6; eaba8105, 2020.

4. Neuron 106; 816-829, 2020.

5. Cell 188:2687-2704, 2025.