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National Institute for Physiological Sciences

National Institutes of Natural Sciences









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Goals for the NIPS

Physiology is the study of human beings and life. The NIPS offers various types of the most advanced research devices and places for research using them to researchers belonging to universities and other research institutes on a nationwide basis, as the promotion of joint usage research with other research institutes, including national, public, and private universities throughout Japan, is one of its core duties. In the NIPS, researchers with diverse backgrounds, belonging to it or universities or other research institutes, perform their research activities daily while desiring to promptly utilize the outcomes of their studies for social benefit and to elucidate the science of life.

Summary

Physiology

Physiology is the study of the functions and mechanisms of living organisms. "Living organisms" refer to all living matter, including the human body. "Functions" refer to the biological functions of an individual, as well as those of its components (molecules, cells, tissues, and organs) and those needed when multiple individuals lead social lives,



including morphological and psychological events. In short, physiology aims to elucidate biological functions by clarifying mechanisms at the levels of molecules, cells, organs, and individuals, and integrate them as a system; therefore, physiology is also integrated biology. As one of the domains targeted for the Nobel Prizes is "physiology or medicine", it is an important academic discipline providing a basis for all life sciences, including medicine.

Roles of the National Institute for Physiological Sciences (NIPS)

1. Leading physiological research

The first duty of the National Institute for Physiological Sciences (NIPS) is to: continuously conduct high-quality studies on a global basis to examine living organisms at the levels of molecules, cells, tissues, organs, systems, and individuals; organically integrate the outcomes of such studies; and clarify biological functions and mechanisms.

2. Providing a basis for research on physiology

Its second duty is to: offer our most advanced research facilities, equipment, databases, techniques, and conference halls to domestic and international research institutes, including national, public, and private universities throughout Japan, as a joint usage research institute; and promote joint usage research by organizing diverse events, such as study seminars and symposiums, as a basis for domestic and international research communities.

3. Training researchers

The NIPS provides 5-year comprehensive doctoral programs for the Department of Physiological Sciences, School of Life Science at the Graduate University for Advanced Studies. It also contributes to the nurturing of physiologists who globally expand their activities through training courses, lectures on various topics, and symposiums for students and young researchers belonging to other research institutes. The development of human resources supporting research on physiology in- and outside Japan is the third duty of the NIPS.

Message from the Director-General



NABEKURA, Junichi, M.D., Ph.D.

National Institute for Physiological Sciences (NIPS) promotes cutting-edge research to understand the mechanism of human body function from molecules/ cells to organs/ individuals, and also to the level of sociality. We also conduct joint research with world-wide researchers and educate young researchers.

In recent years, medical and biological research has achieved great progress in analysis of constituent molecules and disease-causing genes based on genetic information due to the rapid development of genome analysis. The importance of these factors and the causative genes of pathological conditions have



been clarified by manipulating the expression and activity of each factor to capture changes in the functions of cells, organs, and individuals. On the other hand, many factors are intricately interconnected in vivo. To maintain human function, how many factors interact to maintain the functions of organs, and how organs communicate each other still remain to be elucidated. For example, the brain is involved in complex functions such as sensation and movement, sleep and eating, memory and emotion, and even social behavior, but also communicates with various organs to maintain individual homeostasis. However, their communication still remained to be elucidated. Heart beats without rest for nearly 100 years without cell regeneration. The body is still full of mystery.

Recent research tends to focus on studying pathological conditions and etiology. On the other hand, what is "normal" ?; no answer has been found for this question. Living body/organs/cells constantly fluctuate to maintains their homeostasis. National Institute for Physiological Sciences conducts research on the mechanism to maintain body homeostasis from the perspective of molecules, cells, tissues, organs, and whole body for the purpose of understanding their integration beyond their layers. In order to support a wide range of research fields, we introduce the cutting-edge experimental equipment and technologies. In particular, in addition to state-of-the-art measuring instruments such as advanced electron microscopes, laser optical microscopes, electrophysiological devices, cerebral magnetic field measuring devices, and ultra-high magnetic field magnetic resonance devices, gene manipulating technology using genetically modified animals and viruses. We also aim to establish analysis technology for large-scale data. As Inter-University Research Organization, we provide these advanced experimental equipment and technologication, we provide these advanced experimental equipment and technology for large-scale data.

NIPS also focuses on educating young researchers. Many domestic and foreign graduate students study at NIPS, one of the foundation organization of the Graduated University for Advanced Studies/SOKENDAI. We also accept the graduate students enrolled in other universities. Young researchers are engaged in research in the free atmosphere characteristic of our institute. Mechanism of the body is one of the most mysterious wonders and receives the most curiosity in society. In addition, their collapse could lead to the illness. To understand "Normal/homeostasis" will lead to the establishment of treatment for illness and appropriate prevention methods, which could make a significant contribution to society.

Please visit to NIPS and conduct fruitful collaboration with us.

Organization of the Institute

National Institutes of Natural Sciences

National Astronomical Observatory of Japan Management Council National Institute for Fusion Science President Board of Directors National Institute for Basic Biology Educational and Research Council National Institute for Physiological Sciences Institute for Molecular Science - Division of Biophysics & Neurobiology - Department of Molecular & CellularPhysiology Division of Membrane Physiology Division of Neural Development & Regeneration Division of Cell Structure Division of Cell Signaling - Department of Homeostatic Regulation Division of Cardiocirculatory Signaling - Division of Endocrinology & Metabolism Division of Ultrastructural Research Division of Cerebral Circuitry Division of Homeostatic Development - Department of Fundamental Neuroscience National Institute for Division of Visual Information Processing **Physiological Sciences** Division of Biophotonics Division of Behavioral Development Division of System Neurophysiology - Department of System Neuroscience Division of Neural Dynamics - Division of Cerebral Integration Section of Collaboration Promotion Section of Advanced Research Support Center for Research Collaboration Section of NBR Project Section of Visiting Collaborative Research Project Section of International Collaborative Research Project * Section of Brain Structure Information Section of Multiphoton Neuroimaging - Supportive Center for Brain Research Section of Electron Microscopy Section of Brain Function Information Section of Instrumental Design Section of Viral Vector Development Section of Mammalian Transgenesis - Center for Genetic Analysis of Behavior Section of Behavioral Patterns - Section of Metabolic Physiology Section of Research Archives - Center for Communication Networks Section of Physiology & Medicine Education - Section of Network Management Section of Health & Safety Management Technical Division *Adjunctive divisions/sections ★Exploratory Research Center on Life and Living Systems **Okazaki Research Facilities** Research Center for Computational Science stitute for Basic Biology stitute for Physiological Sciences Center for Animal Resources and Collaborative Study

Inter-University Research Institute Corporation National Institutes of Natural Sciences (NINS)

- Center for Radioisotope Facilities

Division of Coordinator for Animal Experimentation

Inter-university research institute corporations are Japan's original and high-level research institutes managed by research communities. In such institutes, which have been organized as bases to offer places for joint usage and research to researchers throughout Japan, pioneering researchers are engaged in collaborative research activities, with the aim of developing new academic fields. The National Institutes of Natural Sciences (NINS) consist of 5 inter-university research institutes: the National Astronomical Observatory of Japan (NAOJ), National Institute for Fusion Science (NIFS), National Institute for Basic Biology (NIBB), National Institute for Physiological Sciences (NIPS), and Institute for Molecular Science (IMS).

National Institute for Physiological Sciences (NIPS)

The National Institute for Physiological Sciences (NIPS) is a research institute dedicated to studying human body functions, such as those of the brain, through collaboration with universities, and training young researchers as future physiologists. It is also a unique inter-university research institute corporation for basic human physiology research and education in Japan. Man is a "thinking reed", thanks to his well-developed brain. In the NIPS, diverse studies are currently being conducted to examine the brain as the central system of the human body.

Research Departments



Division of Biophysics and Neurobiology

Professor KUBO, Yoshihiro

Structure-function relationship and regulation mechanisms of ion channels and receptors

The aim of our research is to elucidate the functioning mechanisms of ion channels and receptors. Toward the aim, we focus on the structure-function relationship, dynamic structural rearrangements and situation dependent regulation mechanisms of membrane proteins. We utilize *in vitro* expression systems such as Xenopus oocytes and HEK293 cells which enable solid and precise biophysical analyses by purely reconstituting the target molecules. We conduct research by combined techniques of (1) molecular biology to isolate cDNA and introduce mutations, (2) electrophysiology such as two electrode voltage-clamp, gating current analyses and patch-clamp, (3) optophysiology such as FRET analyses to detect structural rearrangements, voltage clamp fluorometry, and single molecule imaging for subunit counting. We also perform research using gene targeted mice to identify the distribution, molecular/cellular function and behavioral roles of orphan metabotropic receptors.



Simultaneous recordings of voltage-gated K⁺ channel current and its structural rearrangements by voltage-clamp fluorometry using Xenopus oocytes.



Division of Membrane Physology

Professor FUKATA, Masaki

Fundamental mechanisms for synaptic transmission and synaptic disorders

We will elucidate the core regulatory mechanisms for synaptic transmission and finally address the fundamental question, "How does our brain physiologically function and how is the system disrupted in brain diseases?". We have focused on the regulatory mechanisms for AMPA-type glutamate receptor (AMPAR) as AMPAR plays a central role in learning and memory formation. Based on our specific and quantitative biochemical methods, we discovered two types of AMPAR regulatory proteins: the DHHC palmitoylating enzymes and the epilepsy-related ligand/receptor, LGI1/ADAM22. So far, we have elucidated the physiological functions of these two AMPAR regulatory proteins and the implication in the pathogenesis of brain diseases such as epilepsy and limbic encephalitis, by developing new methods to screen the palmitoyl enzyme-substrate pairs and to specifically visualize the palmitoylated protein, and by integrating many methods such as super-resolution imaging, mouse genetics, and electrophysiology. We will elucidate the molecular basis in which these AMPAR regulatory proteins regulate synaptic plasticity and cognitive functions of mouse and human brains using the following our developed or cutting-edge approaches and resources.

- 1) Analyses of in vivo protein-protein interactions
- 2) Screening of palmitoylating enzyme library
- 3) Live cell imaging with palmitoylated protein-specific probes
- 4) Observation of synapses with super-resolution microscopy
- 5) Mouse models of human epilepsy with the LGI1 mutation



Figure (A) Two unique AMPA receptor regulatory proteins: DHHC palmitoylating enzymes and the epilepsy-related ligand/receptor, LGI1 and ADAM22. (B) Discovery of novel postsynaptic nanodomains by palmitoylated PSD-95-specific probe and super-resolution microscopy: a synaptic DHHC protein locally regulates the formation and reorganization of nanodomains



Division of Cell Structure

Professor FURUSE, Mikio

Molecular basis of the regulation of epithelial barrier function and paracellular transport

The epithelium maintains the fluid environment of each body compartment not only by transporting various substances selectively but also by working as a diffusion barrier. To elucidate the mechanism underlying these roles of the epithelium, we have been clarifying the molecular basis of cell-cell junctions that directly contribute to the epithelial barrier function and passive transport of solutes through the paracellular pathway. By combinining molecular biological, morphological and physiological analyses, the following research projects are ongoing.

 Analyses of the function and behavior of claudin family proteins, major structural components of tight junctions.
Molecular dissection of tricellular tight junctions.

3) Analyses of the regulatory mechanism of cell-cell junction formation by using Drosophila genetics.

4) Response of epithelial barrier function to environmental changes.



Freeze-fracture replica of tricellular tight junctions (left) and a model of the molecular organization of tricellular tight junctions (right).



Division of Cell Signaling

Professor TOMINAGA, Makoto

Clarifying the Functions of Thermosensitive TRP Channels

It was little known until recently how temperature is detected although we survive by sensing a wide rage of ambient temperatures. Capsaicin receptor TRPV1 is the first molecule involved in temperature sensation, and now there are nine ion channels belonging to the TRP ion channel super family. These thermosensitive TRP channels not only sense noxious temperature and chemical stimuli in the sensory nerve endings but also are involved in the various physiological functions including

ambient skin temperature detection, regulation of skin barrier function, detection of mechanical stimulation in bladder and intestine, regulation of taste sensation, insulin secretion from pancreas, regulation of immune cell function and regulation of neural excitability in the central nervous system under the body temperature conditions. Thus, most of the cells in our body which are not exposed to the dynamic temperature changes survive by detecting temperature around the cells.



Research Departments



Division of Cardiocirculatory Signaling

Professor NISHIDA, Motohiro

Elucidation of biological functions using multilevel techniques to evaluate cardiovascular functions and its clinical application

Our cardiocirculatory function is mainly controlled by muscular organs composed of striated muscles (heart and skeletal muscles) and smooth muscle (blood vessels). Our group aims to elucidate the molecular mechanisms underlying transition of the muscles from adaptation to maladaptation against environmental stress (mainly hemodynamic load) multi-level techniques to evaluate cardiovascular functions (in vivo and in vitro), and work toward practical application (e.g., drug discovery and fostering). We also investigate the mechanism of muscle repair and regeneration, and aim to develop a novel therapeutic strategy for refractory diseases. In addition, we address the inclusive research to elucidate the mechanism underlying maintenance and transfiguration of cardiocirculatory homeostasis via multi-organ interactions by combining non-invasive measuring methodologies of motor functions and those cardiovascular functions.



Figure. Measuring systems for cardiovascualr functions and summary of our research using these systems



Division of Endocrinology and Metabolism

Professor MINOKOSHI, Yasuhiko

The central regulation of whole body energy metabolim

The animal body has an integrated-regulatory system for "homeostasis" that maintains a normal, constant internal state by responding to changes in both the external and internal environments. Within the central nervous system, the hypothalamus is a crucial center that regulates the homeostatic activities by integrating autonomic nervous system, endocrine system and immune function. This division is investigating the role of hypothalamus in body energy balance, especially regulatory mechanisms for food preference, taste modification and metabolic control of skeletal muscle and adipose tissues in mammals.



Fig. Discovery of neurons that induce selection of carbohydrate over fat. AMP kinase-regulated CRH (corticotropin-releasing hormone) neurons in the PVH is necessary and sufficient to induce selection of carbohydrate over fat after fasting.



Division of Homeostatic Development

Director-General NABEKURA, Junichi

Functional regulation of the neural circuits remodeling in development and recovery. – Physiological role of the glial cells –

Our research focuses on studying the long term plasticity of neuronal circuits/synapses in physiological/ pathophysiological brain. We mainly employ various electrophysiological techniques and in vivo imaging with 2photon excitation microscopy to visualize the morphology and function of neurons in combination with





gene manipulation and optogenetics.

Recent topic is to elucidate the physiological function of glial cells; microglia and astrocyte. We are focusing particularly on interaction between glia cells and neuronal circuits. Our research has identified the contribution of microglia to neuronal formation in developing brain and to modulation of neuronal/synaptic activity. We are also interested in the role of astrocyte in pathophysiological brain, such as chronic pain

Glia (microglia) could regulate the number of synapses by promoting their formation and eliminating them in developing and mature brain.



Division of Visual Information Processing

YOSHIMURA, Yumiko

The mechanisms of information processing in sensory cortex and the experience-dependent regulation of that processing.

Professor

In order to elucidate how specific neural circuits in the brain are established during development and how these circuits contribute to the sensory information processing, we are studying the following 3 issues using rodent sensory cortex.

1. The mechanisms that establish fine-scale networks in visual cortex and the role of these networks in visual information processing

2. Cell-lineage dependent establishment of neural connections and visual responsiveness in visual cortex

3. Activity-dependent synaptic plasticity and the experience-dependent plasticity of visual responses

To this end, we are analyzing the visual responses of cortical neurons using multi-channel electrodes or calcium imaging with 2-photon microscopy, the properties of neural circuits with a combination of laser scanning photostimulation and whole-cell recording methods in brain slice preparations, and the neural connections morphologically using modern virus tracers.



The cross-correlation analysis of photostimulation-evoked EPSCs in synaptically connected pairs in visual cortical slices.



Division of Biophotonics

Professor NEMOTO, Tomomi

Innovative bioimaging for physiological functions and biological rhythms by utilizing cutting-edge technologies of non-linear optics, materials, and laser

We explore innovative bio-imaging methodologies and applications for life- and medical sciences by utilizing cutting-edge technologies of laser, optical, and materials. Primarily, we are developing two-photon microscopy for realizing invasive fast and super-resolution observations and manipulations in living biospecimens. We hope that such visualization technologies elucidate the emergence and molecular basis of neural activities, including biological rhythms. Recently, for high-speed threedimensional imaging, a multipoint scanning two-photon microscope has been developed to realize molecular orientation imaging in a living body by ellipsometry. Also, we have succeeded in visualization analysis of the neural activity in the deep brain of the living mouse and quantitative analysis of Ca2+-dependent exocytosis in secretory glands. Besides, we are conducting multifunctional imaging analysis of the circadian clock at the center of the circadian clock, optical imaging analysis of the circadian clock of intracellular organelles, and in vivo optical measurement of the circadian clock. We are also promoting the application of various animal models, cancer and diabetes models, and physiological functions in plant cells.





Division of Behavioral Development

Professor ISODA, Masaki

System-level understanding of social cognitive function

There has been a rapid progress in the study of social brain function. In this field called social neuroscience, studies on human subjects are surely indispensable, as they can tell us about our social mind most directly. Yet research using other animal species, especially nonhuman primates, are also crucial, as it allows us to monitor neural activities at multiple levels ranging from single neurons to global neural networks and additionally to employ various causal approaches via intervention, thereby complementing data in humans. To probe the neural basis of the self, others and their interactions at the system level, our laboratory applies cutting-edge techniques, such as multi-site/multi-electrode neural recordings, pathway-selective intervention, and 7-T MRI, to macaques performing various social cognitive tasks.



Neural activities are recorded from multiple brain regions using multi-contact electrodes with high spatiotemporal resolutions.



Division of System Neurophysiology

Professor NAMBU, Atsushi

Mechanism of voluntary movements and pathophysiology of movement disorders

The brain areas, such as the cerebral cortex, basal ganglia and cerebellum, play a major role in controlling voluntary movements. On the other hand, malfunctions of these structures result in movement disorders, such as Parkinson's disease and dystonia. The major goal of our research project is to elucidate the mechanisms underlying higher motor functions and the pathophysiology of movement disorders. To explore such intricate brain functions, we apply a wide range of neurophysiological and neuroanatomical techniques to rodents and subhuman primates, such as macaques and marmosets. The current topics under study are as follows:

1)Elucidation of information flows through the neuronal networks by electrophysiological and anatomical methods.

2) Understanding the mechanism how the brain controls voluntary movements and higher brain functions by electrophysiological recordings of neuronal activity from animals performing motor tasks, combined with local injection of neuronal blockers, optogenetics or chemogenetics.

3) Elucidation of the pathophysiology of movement disorders by applying electrophysiological methods to animal models.



Cortical stimulation of the face, hand and foot areas in the motor cortices of monkeys induced responses in the subthalamic nucleus (STN) and the internal (GPi) and external (GPe) segments of the globus pallidus, and revealed somatotopic maps of these structures. These maps contribute to stereotactic surgery, such as deep brain stimulation (DBS), for Parkinson's disease.



Division of Neural Dynamics

Professor KITAJO, Keiichi

Functional roles of neural dynamics

We investigate the functional roles of a variety of nonlinear neural dynamics such as oscillations, synchrony in brain information processing from a computational neuroscience perspective based on dynamical systems theory. We deal with EEG (electroencephalography), ECoG (electrocorticography), MEG (magnetoencephalography), and fMRI (functional magnetic resonance imaging) data in humans while subjects are engaged in cognitive tasks, at rest, or during noninvasive brain stimulation such as TMS (transcranial magnetic stimulation). We analyze the data, and we try to understand the neural dynamics by mathematical modeling based on nonlinear dynamical systems theory, signal processing theory, information theory, network analysis, and statistical machine learning methods. We also analyze clinical data obtained from collaborators and try to understand clinical symptoms in terms of altered neural dynamics. Moreover, we try to investigate the relationships between neural dynamics and phenomena in different layers such as autonomic nervous activity and excitation/inhibition balance in neural circuits for the integrative understanding of functional roles of neural dynamics.



We record brain activity, analyze the data, and do mathematical modelling to understand and predict a new phenomenon.

Research Departments



Division of Cerebral Integration

Professor SADATO, Norihiro

Exploring neural substrates of human cognition by functional MRI

The goal of Division of Cerebral Integration is to understand the physiology of human voluntary movement and other mental processing including language using noninvasive functional neuroimaging technique, mainly fMRI. In particular, understanding of the mechanisms of plastic change in the human brain accompanied by learning, sensory deafferentation, and development of social cognition is the main focus of our research activities. Multimodality approach including EEG, MEG, TMS, and NIR are considered when appropriate. To explore the neural mechanism of real-time social interaction, hyper-scanning fMRI (3T) and 7TMRI will be applied.



Brain areas commonly activated by social and monetary rewards. Why are we nice to others? One answer provided by social psychologists is because it pays off. A social psychological theory stated that we do something nice to others for a good reputation or social approval just like we work for salary. Although this theory assumed that social reward of a good reputation has the same reward value as money, it was unknown whether it recruits the same reward circuitry as money in human brain. In this study, we found neural evidence that perceiving one's good reputation formed by others activated the striatum, the brain's reward system, in a similar manner to monetary reward. Considering a pivotal role played by a good reputation in social interactions, this study provides an important first step toward neural explanation for our everyday social behaviors.





SONG, Chihong

Section of Electron Microscopy

1. What are you doing (researching) at NIPS?

My research is in the field of structural biology using electron microscopy. The purpose of my research is to reveal the relationship between structures and functions in biological materials at molecular and organelle levels. For this purpose, I use several electron microscopes (Cryo-EM, High voltage-EM and Serial block facing-SEM etc.), and develop techniques of electron microscopy and image processing. Structural information obtained by electron microscopy helps to understand the mechanisms of physiological phenomena.

Why are you working at NIPS? (Why did you choose NIPS?)
I have been studying in Japan since I was a student. During my graduate school years, I conducted collaborative

research with NIPS using an electron microscope. NIPS is composed of the best experts with state-of-the-art equipment. Recently, electron microscopy technology has become more advanced and is becoming one of the most important technology in the field of structural biology. I have also chosen NIPS to gain expertise in this field of research. I hope my research through NIPS will contribute to society.

3. What are the good points about NIPS?

The NIPS has the best conditions for research. With world-class professors, researchers, equipment, and skilled technicians, NIPS is leading research around the world. The NIPS is located in the same research complex as IMS, and NIBB, making it easier to collaborate research. During my four years at NIPS, I have been working with researchers from IMS and NIBB, and it has broadened my views greatly. NIPS also has the advantage of convenient transportation. Because it was geographically convenient, located in the central Japan, it makes it possible to do joint research with institutions anywhere in the country.



DEROUICHE Sandra Project Assistant Professor

Division of Cell Signaling

①. What are you doing (researching) at NIPS?

My research interest is on thermosensitive Transient Receptor Potential (TRP) ion channels and how they regulate physiological functions. I am currently investigating two different topics related to temperature: how it can modulate the sweat gland cells secretion as well as how it affects microglial cells movement within the brain, through the activity of TRP channels. For this purpose, I am using both in vitro and in vivo approaches and combine multidisciplinary techniques such as patch-clamp, calcium imaging, immunostaining, two-photon imaging and mouse behavior experiments.

②. Why are you working at NIPS? (Why did you choose NIPS?) During my PhD in France, I was working on TRP channels' involvement in prostate carcinogenesis. While writing my defense manuscript I read many papers on the subject of TRP channels and I found several high quality papers from Prof. Tominaga and his team. I was really attracted by their research topics and methodologies, and this is how I came to know about NIPS and its highly praised scientists and facilities.

3. What are the good points about NIPS?

NIPS is a great working environment for many reasons. It offers the possibility to use cutting-edge equipment and technics in a peaceful setting. I also really appreciate the openness of the different teams and their willingness to collaborate between each other. If you come upon a theoretical or practical difficulty in your research project, there is a great chance that someone in NIPS is familiar with this field and can help you overcome this problem. International collaborations are also encouraged and allows you to broaden your knowledge and network. Finally, there is a friendly atmosphere in NIPS that makes everyone comfortable and allows foreign researchers to enjoy their stay here.



01

Center for Collaborative Research

Director Professor KUBO, Yoshihiro

The "Center for Collaborative Research" established in April 2016 plays critical roles in the promotion of various collaborative research activities, including inter-university research, advanced bio-imaging support, supply and management of monkeys for experiments, and domestic as well as international research collaborations. It consists of 5 sections of Collaboration Promotion, Advanced Research Support, National Bio-Resource (NBR) Project, Visiting Collaborative Research Project and International Collaborative Research Project.

(1) As a mission of the inter-university research institute, NIPS promotes and conducts collaborative researches. The "Collaboration Promotion" section is in charge of facilitation of joint researches utilizing the facilities of NIPS. It responds to inquiries about available research facilities and laboratories suitable to achieve research aims, and also coordinates the joint research. Thus, it serves as a sort of "concierge" of joint research with NIPS. (2) NIPS, in cooperation with NIBB, started "Supporting Platform for Advanced Bio-Imaging" project supported by JSPS KAKENHI grant in April 2016. In this framework, the "Advanced Research Support" section serves to promote support for advanced imaging techniques using optical microscope, electron microscope and fMRI. Another activity of this section is to support "The Next Generation Brain Research" Project. It is to organize a symposium of wide-ranged brain science researchers including the ones belonging to MEXT priority research areas. (3) The "National Bio-Resource (NBR) Project" section had been in charge of the activity of NIPS to supply monkeys for research experiments. In 2017, the primary responsible role of NBR Project was transferred from NIPS to the Primate Research Center in Kyoto University. NIPS will continue to cooperatively contribute to the activity of NBR Project including the maintenance and management of monkeys. (4) The aim of the "Visiting Collaborative Research Project" section is to facilitate collaborative researches with researchers staying in NIPS using a sabbatical leave. (5) The "International Collaborative Research Project" section is a laboratory run by a visiting professor from abroad who stays for a significantly long time in NIPS. From 2017, Professor Denis Le Bihan (Former Director of NeuroSpin in France) is serving as a P.I.



Supportive Center for Brain Research

Director Professor ISODA, Masaki

The Supportive Center for Brain Research consists of five sections (Sections of Brain Structure Information, Brain Function Information, Multiphoton Neuroimaging, Electron Microscopy, and Instrumental Design) and provides their specialized and large-scale equipment for use in collaborative studies. Here we introduce the activities of three sections.

(1) The Section of Brain Structure Information has carried out three-dimensional structural analysis of biological samples at nanometer scales through single particle analysis, tomographic analysis, and crystal analysis using the state-of-the-art electron microscopes (high-voltage TEM, phase contrast cryoEM, and serial block-face SEM; Figure 1). The major research targets are large protein complexes, membrane proteins, viruses, bacteria, cell organelles such as mitochondria, and synapses. We also develop novel image processing procedures for structural analyses.

(2) The section of Multiphoton Neuroimaging utilizes the state-of-the-art two-photon fluorescence microscopes and two-photon fluorescence lifetime imaging microscopes for in-vivo imaging of the brain of living mice and the signal transduction at synapses (Figure 2). By combining these techniques with optical manipulation techniques such as an optogenetic approach, we aim to understand physiological functions crucial for vital activity, such as the mechanism of memory in the brain.

(3) The section of Brain Function Information aims to clarify the mapping between structure and function of the brain by using high-field magnetic resonance imaging (MRI, 3T and 7T) in humans and nonhuman primates. We actively promote collaborative studies ranging from basic research on and development of MRIs to clinical applications. We aim at establishing standards for MRI procedures, including safety protocols, novel applications, and quantitative analyses of MR images. We are now trying to develop algorithms to mathematically and statistically handle a vast amount of image data.

Brain science is one of the hottest research fields worldwide, and recent progress in this field is surprisingly





Figure 1. Asymmetric binding

architectures of the activation factors on 20S proteasome revealed by electron tomography and single particle analysis (Kumoi et al., PLOS ONE 8: e60294, 2013). Scale bar, 10 nm.



Figure 2. Imaging biochemical reaction in a single synapse by 2-photon fluorescence lifetime imaging microscopy. The arrowhead indicates the activation of Cdc42 after glutamate uncaging stimulation.

Phase encoding task manufacture, and 20th



Figure 3. Functional MRI using 7 T machine. Somatotopic representation of the left fingers mapped onto the cortical surface of an individual with spatial resolution of $1 \times 1 \times 1$ mm.

03

Center for Genetic Analysis of Behavior

Fig 1

Director Professor TOMINAGA, Makoto

Section of Mammalian Transgenesis

Services offered by Laboratory for Transgenesis include generating transgenic rodents (mouse and rat) by pronuclear microinjection of foreign DNA and generating knockout (KO)/knock-in (KI) rodents by new genome-editing tools using zinc finger nucleases (ZFNs), TAL effector nucleases (TALENs) or the clustered regularly interspaced short palindromic repeat/Cas9 (CRISPR/Cas9). In addition, embryonic stem (ES) and induced pluripotent stem (iPS) cells established in rats can be utilized for researches in regenerative medicine. Production of cloned rats by somatic cell nuclear transplantation is a challenging subject.

Section of Behavior Patterns

Since 99% of mouse genes have homologous in humans, a large-scale project that is aimed to encompass knockouts of every gene in mice is in progress. Approximately 80% of all genes are expressed in brain and, to investigate their function in individual organisms, we should investigate their functions in the brain. We can identify the genes that have a significant impact on the brain functions efficiently by examining the final output level of gene function in the brain, that is, behavior. The influence of a given gene on a specific behavior can be determined by conducting the behavioral analysis of mutant mice lacking that gene. The test comprehensive behavioral battery covers sensori-motor functions, emotion, learning and memory, attention and so on. So far, we obtained behavioral data from 75 strains. In those mice strains, we found some models of psychiatric disorders.

Section of Metabolic Physiology

A Rosa26-tdTomato KI rat offspring derived from the gene-modified rat ES cells.



Heat map showing behavioral phenotypes of genetically engineered mice. Each column represents the strain of genetically-engineered mice that has been analyzed. Each row represents a category of behavior assessed by comprehensive behavior test battery. Colors represent an increase (red) or decrease (green) in a comparison between the wild-type and mutant strains.

This section analyzes the in vivo neuronal and metabolic activity in mice and rats which were modified their related genes and exposed with various environmental conditions. This section has been opened for the collaboratory use of researchers all over Japan since April, 2011. This section examines the following subjects:

- 1) Single unit recording from motor related brain regions in awake state.
- Regional neural activity detected as intrinsic signals with taking the advantage of light fluorescent dynamics of flavin or hemoglobin.
- 3) Energy intake and expenditure in free-moving animals.
- 4) Body temperature, heart rate and blood pressure in free-moving animals.
- 5) Non-invasive echo-graphic imaging of tissue structurefunction relationships (liver, kidney and blood vessels),
 4-dimensional changes in cardiac functions, and capillary blood flow (brain and umbilical cord) using anesthetized mice.
- 6) Mouse temperature preference assay with thermal gradient ring.



ARCO system: measurement of whole body energy metabolism by mass spectrometorical analysis of respiratory gas exchange

Center for Animal Resources and Collaborative Study

Director Professor MINOKOSHI, Yasuhiko

 $\bigcirc 4$

Experimental animals are relevant to human health and contribute meaningfully to medical advances such as providing better support for the life science research and the development of medical technology. To perform a highly reproducible animal experiment, it is necessary to maintain high standards of experimental animals. In order to achieve this aim, the experimental animal facilities have to control the uniformly breeding environment all year round, provide husbandry to experimental animals in a clean state without pathogenic microbial contamination (specific pathogen-free: SPF).

The Center for Animal Resources and Collaborative Study is one of the top-class experimental animal centers in Japan. The center was reorganized from the Center for Experimental Animals in FY2019 to further enhance collaborative study based on animal research as a common facility of the interuniversity institutes. In the terrestrial and aquatic animal sections, multiple species including mouse, rat, marmoset, macaque, fish, and amphibians are maintained and supplied for experimentation. The principal responsibilities of the center include (1) the appropriate breeding of rodents and other experimental animals, (2) embryo transfer and cryopreservation for genetically modified mouse lines, (3) development and refinement of diagnostic testing methods, microbial containment, and disease prevention strategies, (4) provision of information related to the techniques of animal experimentation as well as promotion of education and awareness with regard to ethical considerations and regulations related to the study of experimental animals, (5) enhancement and support of collaborative animal research involving domestic and foreign researchers. The new building in "Myodaiji" area, which is equipped with the state-of-the art system and experimental rooms for collaboration studies, will start operation in October, 2020. We are capable of supplying high quality animal care and resources to reach the best research achievements in the world.





Individually ventilated cage system

05

Research Center for Computational Science

Research Center for Computational Science, it was established the computer center of IMS in 1977, primarily provides an opportunity for large scale computation in molecular science which could not be carried out at regional university computer centers. Further, the Center is supporting experimental data collection and analysis, developed and maintained the program library and database in molecular science, basic biology and physiological sciences.



Computer Cluster Fujitsu PRIMERGY RX300S7 Specificatons: 126.9TFlops, 5472cores, 342nodes, 43.7TB memory



Computer Cluster Fujitsu PRIMERGY CX2550M1 Specificatons: 302.8TFlops, 7280cores, 260nodes, 33.2TB memory

06

Center for Radioisotpe Facilities

The Center for Radioisotope Facilities promotes research works using radioisotopes for three institutes in the Okazaki campus. The center educates researchers for their safe and efficient experiments and strictly controls the use of radioisotopes to ensure the safe handling.



Radioisotope laboratory Radioisotope experiments in the controlled area for research using radioactive materials.



Monitoring system for the safe use of radioisotopes

Exploratory Research Center on Life and Living Systems



What is life? The Exploratory Research Center on Life and Living Systems (ExCELLS) aims to achieve a comprehensive understanding of living systems beyond reductionism by utilizing large-scale data analyses and synthetic biology approaches. For this purpose, ExCELLS develops novel approaches for observing biological entities, deciphering hidden information, and creating living systems to improve understanding of their nature. Moreover, ExCELLS promotes collaborative, interdisciplinary research involving investigators who explore organisms living in extreme environments and provides a unique platform for cross-disciplinary research in an interuniversity, collaborative environment, using the "Observe, Read, and Create" approach. Furthermore, for developing a strong research and innovation base, ExCELLS enlightens young people to become the next generation scientists. To achieve our aims, we would like to expand our international collaborative network.

ExCELLS consists of Department of Creative Research and Section for Exploration of Life in Extreme Environments.

Department of Creative Research develops novel approaches for "Observe, Read, and Create", and aims to achieve a comprehensive understanding of living systems. Section for Exploration of Life in Extreme Environments explores living systems in extreme environments to elucidate original modes of living and adaptation strategies of organisms.

"Observe"

To develop innovative methods for observing dynamic behaviors of biomolecules in situ and for visualizing changes in quantities of various physical components in complex living systems

"Read"

To develop theoretical and computational approaches to decode, interpret, and predict biological patterns from varying data

"Create"

To understand the design principles of dynamically ordering, and robust systems in varying environment by creating experimental and computational living systems



The National Institute for Physiological Sciences (NIPS) as an inter-university joint usage institute corporation is conducting diverse (general and planned) joint research projects and joint usage experiments using various types of large-scale equipment through collaboration with researchers belonging to universities throughout Japan and national or public research institutes.

Large facilities and equipments for cooperative studies

As a mission to be the inter-university research institute, NIPS conducts joint studies with researchers from domestic or foreign universities and other research institutes. NIPS provides specialized equipment, large-scale equipment, and research facilities, and develops new equipment for morphological and functional 4D imaging s of various organs such as the brain.

Magnetic Resonance Imaging System (MRI:3tesla,7tesla)

MRI is an imaging technique that utilizes the nuclear magnetic resonance of the hydrogen atom. Not only to image the anatomical details of the brain, but MRI also allows exploring the neural substrates of human cognitive function by the visualization of the task-related changes in regional cerebral blood flow (functional MRI). For over a decade, we have been working on 3T MRI to investigate higher brain function of a human (The first 3T machine installed in 2000 was shutdown in 2018). To simultaneously measure the neural activities of two participants during their social



interaction, we have recently installed dual functional MRI system with two 3T MRI. Furthermore, ultra-high field (7T) MRI system has been installed. In 2016 and 2017, cooperative study projects using 7T machine were performed for the purpose of technical assessment and development. As we have confirmed stable operation in 2018, it is being fully provided for cooperative studies.

Phase Contrast Electron Cryomicroscopy

Phase contrast electron cryomicroscopy is an electron microscope developed for observing close-to-life state biological samples with a combination of rapid freezing and ice embedding sample preparation methods. Biological specimens up to 200 nm thicknesses can be observed with high-resolution and high-contrast. Ultrastructure analyses of protein molecules, viruses, bacteria, cultured cells and frozen tissue sections are performed with this novel microscopic system.



Serial Block-Face Scanning Electron Microscope (SBF-SEM)

Serial block-face scanning electron microscope (SBF-SEM) is an advanced 3-D nano-imaging equipment. Two different types of SBF-SEM are available; high-resolution and wide-area types. Resin-embedded biological specimens are sliced by a diamond knife equipped inside the chamber, and the block-face images are acquired by scanning electron microscopy (SEM). 3-D structures of the specimens are finally reconstructed from the acquired serial block-face images. 3-D structures of large biological specimens like a brain tissue can be visualized at the resolution of several nanometers.



Multiphoton excitation microscopy

Phase contrast electron cryomicroscopy is an electron microscope developed for observing close-to-life state biological samples with a combination of rapid freezing and ice embedding sample preparation methods. Biological specimens up to 200 nm thicknesses can be observed with high-resolution and high-contrast. Ultrastructure analyses of protein molecules, viruses, bacteria, cultured cells and frozen tissue sections are performed with this novel microscopic system.



Analytical equipment for in vivo neuronal, metabolic and physiological parameters in mice and rats

We analyze the following physiological parameters in mice and rats:

1) Single unit recording from motor-related brain regions in the awake state, 2) Regional neural activity detected as intrinsic signals with taking the advantage of light fluorescent dynamics of flavin or hemoglobin, 3) Energy intake and expenditure in free-moving animals, 4) Body temperature, heart rate and blood pressure in free-moving animals, 5) Non-invasive echo-graphic imaging of tissue structure-function relationships (liver, kidney and blood vessels), 4-dimensional changes in cardiac functions, and capillary blood flow (brain and umbilical cord) using anesthetized mice, 6) Mouse temperature preference assay with thermal gradient ring.



Magnetoencephalography (MEG)

Magnetoencephalography (MEG) has a potential to measure brain activities with better temporal and spatial resolution in milliseconds and millimeter, respectively, compared with other methods such as functional magnetic resonance imaging. Event-related magnetic fields following various kinds of sensory stimulation are mainly analyzed. Also, background brain activities (brain waves) in various conditions can be analyzed.





Young Fostering

One of the missions of NIPS is fostering young researchers who could lead science of Japan in the future.

What is SOKENDAI?

The Graduate University of Advanced Studies, SOKENDAI is a graduate school which educates students in the institutes belonging to the Inter-University Research Institute Corporation where students are exposed to the leading edge of science and become scientists having sophisticated expertise, a wide perspective and an ability to explore the novel scientific research. NIPS is in charge of Department of Physiological Sciences which forms School of Life Science with Departments of Basic Biology (National Institute of Basic Biology) and Genetics (National Institute of Genetics).

A lot of researchers are working on brain and neuroscience in NIPS and NIPS is one of a few strong education bases where students can learn a wide rage of brain science. Because brain science is really interdisciplinary, students entering Department of Physiological Sciences have various backgrounds not only of scientific research fields such as medicine, science, technology and agriculture but also of cultural sciences. In order to further enhance the interdisciplinary education of brain science, Department of Physiological Sciences is carrying out a Brain Science Joint Program with other Departments related to brain science research using a remote lecture system.

In addition, School of Life Science Retreat is held once a year with students and teachers belonging to the three Departments in School of Life Science and Department of Evolutionary Studies of Biosystems in which people improve mutual understanding through oral and poster presentations.



Collaborative Researcher

In addition to the SOKENDAI students, graduate students from universities of all over the country are working in NIPS.

Young Fostering & Career Paths

It is an important function for NIPS to foster prestigious researchers in the field of physiological sciences and to supply them to universities and research institutes all over the country, and indeed, a lot of excellent researchers from NIPS are successfully working inside and outside the country. In addition, NIPS supports especially young researchers by providing original research grants.





Misbah Rashid

Graduate Student

1. What are you doing (researching) at NIPS?

I am trying to ameliorate the symptoms of obesity in high fat diet induced obese mice by activating steroidogenic factor 1 (SF1) expressing neurons in the ventromedial hypothalamus (VMH). SF1 neurons play a crucial role in energy metabolism and feeding regulation. Therefore, I am interested to target this population of neurons. By chemogenetic technology DREADD, I activate SF1 neurons for long-term and check the effects on body weight, food and energy metabolism.

2. Why did you choose SOKENDAI (NIPS)?

With my passion to help the humanity, I found NIPS as a best place to accomplish my dreams. Because it exactly matches with my field of interest. I was interested in exploring underlying mechanisms that may help to treat obesity and related metabolic problems like diabetes. Fortunately, I found both my field of interest and opportunity to do research with the world-class renowned professors under one roof. The highly supportive environment and serenity of the place made it more attractive to me.

3. What are the good points about NIPS?

This reputed institute provides very professional, beneficial, friendly and supportive atmosphere. Faculty members are really kind, patient and expert in their areas of research. NIPS give you freedom to formulate your research question. This institute also offers the opportunity to travel internationally to collaborate and expand the knowledge with foreign research institutes. Moreover, counselling is provided on individual basis to students to take care of their mental health, living issues and problems related to research and studies. NIPS provides cheap and fully furnished lodging facility for the foreigner researchers. I found NIPS as a leading platform that nourishing the scientific society by making the superlative scientists in every field of science.



Deveci Aykut Graduate Student

1. What are you doing (researching) at NIPS?

My research topic is about molecular and cellular physiology of ion channels. I am particularly interested by Transient Receptor Potential Melastastin 2 (TRPM2), a calcium-permeable, non-selective cation channel which exhibits heat sensitivity. It acts as a biosensor of oxidative and osmotic stresses under physiologic and pathologic conditions. Moreover, it is also highly expressed in the brain, similarly to calcium-activated Potassium Channels (IKCa and BKCa) which is one of my interest too. Consequently, my aim is to find the relationship between these two types of channels in neuronal cells or microglial cells.

Futhermore, about 20-25% of brain volume is occupied by extracellular matrix (ECM). The composition and integrity of the brain's ECM regulate tissue diffusion properties and are essential determinants of neural plasticity, e.g. via regulating volume transmission of neuromodulators. This is why I would also like to investigate if an enriched environment of ECM can impact TRPM2-IKCa signaling pathway.

2. Why did you choose SOKENDAI (NIPS)?

The main reason why I am a student of National Institute for Physiological Sciences (NIPS) is due to my research field which is focused on Ion Channels. There are world-class research teams in NIPS that can help me during my PhD and give me suggestions for the progress of my project. I was accepted in the Iab of Prof. Tominaga, who is a world famous professor working on ion channels. And I believe that his Iab is the best place for my young scientist life in order to acquire new knowledge, skills and experiences.

3. What are the good points about NIPS?

First of all, NIPS is located in Okazaki which is a really nice place, where everyone can live in peace and calm. It is also really well organized. Staff members, labs, both scientific staff and technical departments are professional.

Secondly, NIPS has cutting-edge equipment and devices in order to perform several experiments in diverse fields of research. There are also many opportunities for collaboration inside NIPS labs or internationally. This allows to develop new ideas.

And finally NIPS offers many job opportunities after the PhD program. This helps the young scientists to enter in the researcher life more easily.



Research communities

The NIPS also functions as a base for research communities. It is currently developing systems to provide researchers throughout Japan and the general public with information more actively.

Japan-U.S Brain Research Cooperative Program

Japan-U.S. Science and Technology Cooperation Program has been implemented since 1979 under the treaty concluded between the governments of two countries, of which "Brain Research" Division was commenced in the year 2000. National Institute for Physiological Sciences from Japanese side and National Institute of Neurological Disorders and Stroke (NINDS), a sub-organ of NIH, from the U.S. support the cooperative projects of researchers of both countries as the responsible agency. The activities are classified into 1) Researchers dispatched to the US, 2) Group joint study project, and 3) Information exchange seminars. The recruitment is made by publicly announcing through the home page and academic journals.



National BioResource Project "Japanese Macaques"

National BioResource Project (NBRP) "Japanese Macaques" aims at establishing a system to collect, maintain, and supply Japanese macaque monkeys (macaca fuscata) as essential bioresource for life science researches on the national scale. Macaca fuscata has high cognitive abilities and is an essential animal model for higher brain function studies in Japan. NIPS promotes NBRP "Japanese Macaques" with Primate Research Institute, Kyoto University, the headquarter.





International research collaboration

The NIPS has reached agreements for academic exchange with NeuroSpin (France), Tubingen University, Center for Integrative Neuroscience (Germany), McGill University (Canada), University of New South Wales Sydney (Australia), Chulalongkorn University, Faculty for Pharmaceutical Sciences (Thailand), Korea University, College of Medicine & College of Dentistry (Korea) and Yonsei University, College of Medicine (Korea). It organizes joint symposium and performs collaborative research including exchange of researchers.

In 2014, the NIPS established "Section of International Collaborative Research Project" in "Center for Research

Collaboration". It invites a distinguished foreign adjunct professor to run the section as a P.I. Dr. Le Bihan, a former director of Neurospin, is currently running the lab to promote research on human brain imaging using the 11.7 Tesla Magnetic Resonance Imaging instrument.

The NIPS also promotes collaborative research with many other oversea institutions and universities. It also welcomes internship students and accepts graduate students from Asian and other countries.



Joint workshop of NIPS and McGill University (Nov, 2019; Montreal, Canada)

Study seminars

The NIPS organizes more than 20 study seminars annually for researchers belonging to universities throughout Japan to participate in discussions on important topics. Up to the present, a total of approximately 1,000 researchers have participated in such events. Unlike academic meetings, these seminars enable researchers to thoroughly discuss important research topics in relatively small groups within sufficient time frames, consequently contributing to the development of new research areas and formation of new research groups.



NIPS international symposium and NIPS international workshop

We organize NIPS international symposium and workshop every year inviting cutting-edge researchers from abroad. Okazaki Conference Center and accommodation facilities support institutional activities.



Public relations activities

One of the missions of National Institute for Physiological Sciences is to disclose and return research results to the public. In cooperation with the Okazaki City Board of Education and the Health Center, MEXT(the Ministry of Education, Culture, Sports, Science and Technology), the Japan Science and Technology Agency, the Brain Century Promotion Conference, and The Physiological Society of Japan, we are engaged in a wide range of public relations activities including visiting lectures and lectures for citizens. We also have Public Open Day every 3 years.

Development of science teaching materials

We are developing a variety of scientific learning materials to enjoy learning how the body works. In particular, we are focusing on the development of digital educational materials using smartphones and tablets.

[Brain Responder]

An application that can measure the response time to visual, auditory, and tactile stimuli.

[Brain KARUTA]

It is an application software that uses AR (Augmented Reality) to show which brain is which animal's by holding a tablet camera over pictures of various mammalian brains. You can also hear the voices of animals.

[KARADA Scope]

It is another AR application software that you can feel like observing your digestive organs, brain, bones, etc. by seeing your body through the tablet camera.

Common Facilities in Okazaki

Okazaki Conference Center

Okazaki Conference Center was founded on February,1996 to promote international and domestic conferenceprogram of research and education.

- Ohsumi Conference Hall(capacity of 208)
- Conferece Room A (capacity of 112)
- Conferece Room B(2 rooms, capacity of 50 each)

Accommodation

The lodging houses (Mishima Lodge and Myodaiji Lodge) are provided for guests, both foreign and domestic, for the common use of the three Institutes (NIPS, NIBB and IMS).

The lodging capacities are as follows :		Single Room	Twin Room	Family Room
	Mishima Lodge	60	14	12
	Myodaiji Lodge	14	-	3

The Sakura Nursery School

The Sakura nursery school is the institutional child care facility established for supporting both research and child-rearing.

The school accept a child from the 57th day of after the birth, and is supporting a researcher's smooth return to research activity.

• Age : From the 57th day of after the birth to 3 years old

- Capacity : 18 persons
- Use candidate : The officers, reserchers, visiting researchers, graduate students at Okazaki three institutes
- Opening day : From Monday to Friday
- Opening time : From 8:00 to 19:00 (maximum extension 20:00)
- Childcare form : Regular childcare, temporary child care





Myodaiji Lodge





Location of Institute -

(http://www.nips.ac.jp/eng/profile/access.html)



Central Japan International Airport (Centrair. NGO)

From Central Japan International Airport

By train

Take the Meitetsu train from Central Japan International Airport to Higashi Okazaki Station. NIPS is a 7-minute walk up the hill on the south side of the station.

From New Tokyo International Airport (Narita Airport)

A) By plane (*Recommended)

Transfer to Central Japan International Airport

B) By train

Take the JR Narita Express airport shuttle train from Narita to Tokyo Station (approximately 60 minutes) and change trains to the Tokaido shinkansen (bullet train).

At Toyohashi JR Station (approximately 2.5 hours from Tokyo), change trains to the Meitetsu Line's Limited Express train bound for Gifu. Get off at Higashi Okazaki Station (approximately 20 minutes from Toyohashi). Turn left (south) at the ticket gate and exit the station. NIPS is a 7-minute walk up the hill.





Myodaiji Area

From the south exit of Higashi-Okazaki station. About 7 min. on foot.

Yamate Area

From the south exit of Higashi-Okazaki station.

- By taxi : About 7 min.
- By bus : Take Tatsumigaoka-jyunkan, which departs from No11 bus station, and get off at Tatsumi-kita-1chome (about 6min), and walk to the east for about 3min..
- On foot : About 20 min.



