

Call for Joint Research Project Proposals FY 2024

National Institute for Physiological Sciences

National Institutes of Natural Sciences

1. Joint research projects to be proposed

- (1) General collaborative project
- (2) Planned collaborative project (NIPS)

Themes:

- (i) Ultrastructure analysis of biological specimens by cutting-edge electron microscopy
- (ii) Functional and morphological analyses of cells and tissues by multi-photon excitation microscopy
- (iii) Development and supply of viral vectors and gene-transfer to primates
- (iv) Multi-dimensional fluorescence imaging analysis with a multi-point scanning microscope
- (v) Elucidation of the pathology of mental/neurological diseases by analyzing neural activity dynamics
- (vi) Visualization of white matter fiber bundles and brain microstructure by analyzing brain imaging data

- (3) Planned collaborative project (Center for Animal Resources and Collaborative Study)

Themes:

- (i) Production of animal models
- (ii) Analysis of behavior and physiological functions of mice and rats
 - (A) Evaluation of behaviors related to emotions, learning, and memories, and analyses of neural and muscular activities
 - (B) Non-invasive 4D cardiac function and capillary blood flow ultrasound imaging in mice
 - (C) Functional analysis of neuroimmune interactions in mouse models of diseases
 - (D) Multicellular activity measurement and manipulation in vivo
 - (E) Physiological measurements and analysis in vivo
- (iii) Behavioral and neural activity analysis of macaque monkeys

*Some of the planned collaborative projects of the Center for Animal Resources and Collaborative Study (hereinafter referred to as the “Animal Resource Center”) were conducted as planned collaborative projects at NIPS until fiscal year (FY) 2021 and have been transferred to the Animal Resource Center.

- (4) NIPS Research Meeting
- (5) NIPS International Workshop
- (6) Cooperative study by functional imaging

2. Research Term

April 1st, 2024, to March 31st, 2025

3. Eligibility

A person who is a researcher at a research institution, such as a university or a national or public research institute, or who is recognized by the Director-General of NIPS as having equivalent research capabilities.

4. How to apply

Proposals for joint research projects must be submitted to NIPS online using the Natural Science Collaborative Research Management System (NOUS). NOUS can be accessed from the login page (<https://nous.nins.jp/user/signin>).

Before submitting the proposal, anyone wishing to apply must consult with a professor, associate professor, or equivalent, belonging to the Division most relevant to the intended research, to discuss details such as the research theme, research plan, visit term, and required expenses, etc.

The names, persons in charge, research outlines, and contact information of Departments, Divisions, and Sections of NIPS are as shown in the Annex 1.

Please do not hesitate to contact the Section of Collaboration Promotion of NIPS for help (e.g., if you cannot find a NIPS laboratory that will accept your proposal).

<Support Desk for Collaboration Promotion (for both NIPS and the Animal Resource Center)>

Section of Collaboration Promotion of NIPS, NINS

TEL: +81-564-55-7722

e-mail: collabo@nips.ac.jp

URL: https://www.nips.ac.jp/collabo/researcher_poster.html

The NOUS (NINS Open Use System) is an online integrated project management system for joint research and joint use projects hosted by NINS. It covers all of procedures from submission, examination, and adoption of research proposals to reporting, publication, and analysis of project outcomes (the NOUS is a system shared among NINS member organizations, including NIPS and the Animal Resource Center).

*Submission of a supervisor's approval document was mandatory until FY 2021, but beginning in FY 2022 it is no longer required because the application to be submitted online will require you to declare that you have your supervisor's approval. Please note that an application for an ongoing project still requires your supervisor's approval each year.

Please be careful not to miss the application deadline, because the approval process at your institution may take some time.

5. Deadline for proposals

17:00 Friday, December 8, 2023

Some proposals not submitted by this deadline may be accepted at a later date. Please submit each proposal at least 1 month before the scheduled start of the proposed project.

As a general rule, if a proposal is not submitted by the deadline but is accepted at a later date, reimbursement of travel expenses and research expenses will not be provided.

Also, please be aware that in some cases it may not be possible to decide whether or not to accept or reject a proposal by the planned start date due to our review schedule.

6. Determination of proposal acceptance

The Director-General of NIPS will accept proposals based on reviews of proposed projects by the Advisory Committee for Research and Management of NIPS and the Steering Committee of the Animal Resource Center.

7. Date of decision regarding proposal acceptance

Around March 2024.

8. Collaborative researchers

If a proposed joint research project is successfully accepted, both the representative researcher and co-researcher(s) will carry out the accepted project as Collaborative Researchers (Article 2, item 1 of the NIPS Regulations for Visiting Researchers).

Pursuant to article 3 of the above Regulations, Collaborative Researchers can use research equipment at NIPS that is allowed for use by joint research projects and the Animal Resource Center, where experimental animals are bred and stored.

When visiting the Institute as a Collaborative Researcher, Travel expenses will be covered by NIPS (Article 4 of the same Regulations). For more details, please refer to item 9 (Travel expenses).

NIPS Regulations for Visiting Researchers (Japanese only): <https://www.nips.ac.jp/profile/9-16seikisoku16.pdf>

9. Travel expenses

Travel expenses will be reimbursed, after a review process, pursuant to the NINS Regulations for Travel Expenses within the budget.

When an undergraduate student who visits NIPS is accompanied by or is under the direction of a supervisor who is a co-researcher of a joint research project with NIPS, the travel expenses for the student may also be reimbursed.

*No additional budget will be assigned after the proposal acceptance procedure is completed.

*Due to budget constraints, daily allowances and/or accommodation expenses may be reduced or not paid.

*If you have any inquiries about travel expenses, please see the contact information shown in item 24 (Contact for inquiries).

10. Research expenses

Research expenses will be borne by NIPS as allowed by its budget (Research expenses must not be used outside of NIPS). If you have any inquiries about research expenses, please see the contact information shown in item 24 (Contact for inquiries).

11. Certificate application for individuals working with radiation

If your project involves the use of radioisotopes at NIPS, after its acceptance it will require registration procedures for individuals who will be working with radiation.

12. Gene recombination experiments

If your project involves gene recombination experiments at NIPS, after its acceptance it will require approval by the NIPS Recombinant DNA Experiments Safety Committee.

13. Animal experiments

If your project involves animal experiments at NIPS, after its acceptance it will require approval by the President of NINS once the project proposal is reviewed by the Institutional Animal Care and Use Committee of National Institutes of Natural Sciences. Projects involving mice or rats are required to use specific pathogen-free (SPF) animals.

14. Any projects involving human subjects or specimens obtained from human bodies

If your project involves physiological research on human subjects or specimens obtained from human bodies, or if it involves related fields at NIPS, approval must be obtained from the ethics committee of your institution before the project proposal is submitted to NIPS.

If the project is approved, it will also require the approval of the Ethics Committee for Human Research of National Institutes of Natural Sciences.

Furthermore, if the proposed project uses the magnetic resonance imaging (MRI) apparatus (3-T, 7-T) for humans, the approval of both the NIPS MRI Safety Committee and the Ethics Committee for Human Research of National Institutes of Natural Sciences.

Finally, if a project is classified as “clinical research” by the Ethical Guidelines for Medical and Biological Research Involving Human Subjects issued by the Ministry of Health, Labour, and Welfare of Japan, please consult with a NIPS researcher in advance.

15. Human genome or gene analysis research

In the case of collaborative projects or experiments involving human genome / gene analysis experiments at NIPS, approval by the Ethics Committee for Human Research of National Institutes of Natural Sciences will be required after approval.

16. Japan-U.S. Brain Research Cooperative Program

Projects that have been successfully adopted for the Japan–U.S. Science and Technology Cooperation Program, for which NIPS serves as a contact (<http://www.nips.ac.jp/jusnou/>), will be given priority upon claim.

17. Submission of Joint Research Implementation Report

After the research term ends, a Joint Research Implementation Report that is prepared using the prescribed format must be submitted via NOUS within 30 days of the termination date. For research meetings and international workshop, an implementation report is required to be submitted promptly after the event is closed.

Please be aware that information such as the title of the research project and the affiliations, positions, and names of the representative researcher, co-researchers, and NIPS research meeting participants may be publicized through various public relations activities of NIPS and through the Joint Research Implementation Report. Please ensure that all co-researchers and research meeting participants consent to such information being made public once the project has been accepted.

If consent is not obtained, you will be required to submit a separate report (for publication) with such information blacked out, in addition to the prescribed Joint Research Implementation Report.

18. Clarification of supports by NIPS

If you publish any outcome of the proposed joint research in academic papers, please be sure to clearly **indicate in the Acknowledgments** that the work was performed as joint research hosted by NIPS or the Animal Resource Center.

Example (for NIPS): “This study was supported by the Joint Research Program (XXNIPSYYY) of the National Institute for Physiological Sciences.”

Example (for Animal Resource Center): “This study was supported by the Joint Research Program (XXNIPSYYY) of the Center for Animal Resources and Collaborative Study of NINS.”

* Please replace "XXNIPSYYY" with the project number, which will be provided in the application document and the notification of the results of the proposal review.

19. Handling of intellectual property rights

The basic policy on the intellectual property rights will be handled pursuant to the National Institutes of Natural Sciences Intellectual Property Policy.

Attribution of patent rights and other relevant rights shall be discussed separately.

National Institutes of Natural Sciences Intellectual Property Policy
(Japanese only):https://www.nins.jp/open/post_13.html

20. Hotel accommodations

We have accommodations for use by researchers, specifically an Okazaki facility for facilitating joint research.

21. Promotion of gender equality

NIPS actively promotes gender equality. Please consider this when planning and conducting any collaborative project with us.

22. Personal information

The personal information provided in proposals will be used only for the purpose of selecting successful projects and for administrative procedures involving NOUS.

Please be aware that the name and affiliation of the representative researcher, the project title, and other related information pertaining to each successful project will be published on the NIPS website and in the NIPS Handbook.

For handling of personal information related to Joint Research Implementation Reports, please see item 17 above (Submission of Joint Research Implementation Report).

23. Childcare support

(1) On-site childcare facility

Depending on availability, researchers who participate in NIPS joint research projects can use our onsite childcare facility.

(2) Childcare support system

Researchers who participate in NIPS joint research projects can use our childcare support system, in which NIPS provides reimbursement for a portion of childcare expenses such as daycare, babysitting, and care for sick children.

(3) Support scheme for researchers who travel with their children

Co-researchers and other researchers who participate in NIPS joint research projects can use our travel expenses support scheme whereby NIPS partially supports travel expenses when researchers are accompanied by any of their children during travel made for the purpose of conducting the project.

For more details on (1) through (3), please refer to the NIPS website

(Japanese only): https://www.nips.ac.jp/collabo/child_rearing_support.html

24. Contact for inquiries

■ General matters regarding joint research (incl. expenses and intellectual properties) / NOUS / Hotel accommodation or Okazaki Conference Center usage

38 Nishigo-naka Myodaiji, Okazaki, Aichi, 444-8585, Japan

Joint Research Section of the International Research Cooperation Division, General Affairs Department, Okazaki Administration Center, the National Institutes of Natural Sciences

TEL: 81(Japan)-564-55-7133; Fax: 81(Japan)-564-55-7119; E-mail: r7133@orion.ac.jp



<<Access>>

From areas around Tokyo

Take JR Shinkansen to Toyohashi Station

Take Meitetsu Nagoya Honsen Line from Toyohashi Station to Higashi-Okazaki Station (about 20 min with a Limited Express train)

From areas around Osaka

Take JR Shinkansen or Kintetsu Line to Nagoya Station

Take Meitetsu Nagoya Honsen Line from Nagoya Station to Higashi-Okazaki Station (about 30 min with a Limited Express train)

7-minute walk from the south exit of Higashi-Okazaki Station (Meitetsu Line).

For more details, please refer to the NIPS website (<https://www.nips.ac.jp/eng/profile/access.html>).

Details of the Call for Proposals

I. General collaborative projects

1) Outline:

A general collaborative project is a project on a research theme proposed by a representative researcher and conducted by multiple researchers. The representative researcher must be a researcher (or the equivalent) who does not belong to NIPS, and at least one or more NIPS professors or associate professors must participate in each project.

2) Other:

No project can be conducted for over 5 years on the same research theme. When making an application for ongoing projects, please indicate the updates from the previous year's proposal in your application.

II. Planned collaborative projects (NIPS)

1) Outline:

Planned collaborative projects are conducted on research themes designated by NIPS and are listed below.

Themes

(i) Ultrastructure analysis of biological specimens by cutting-edge electron microscopy

Using the most advanced cryo-electron microscopy techniques, such as those involving the phase-contrast method, we perform single-particle analysis of proteins and tomographic analysis of cells. We also use microtome-integrated scanning electron microscopy to reconstruct the three-dimensional ultrastructure model of specimens at a resolution of dozens of nanometers.

(Person in charge) Project Prof. MURATA (Division of Structural Biology), Prof. FURUSE (Division of Cell Structure), and Adjunct Prof. OHNO (Division of Ultrastructural Research)

(ii) Functional and morphological analyses of cells and tissues by multi-photon excitation microscopy

We perform intracellular signal transduction and functional analysis of cell morphology in vivo and in vitro using fluorescence microscopy with two-photon excitation or fluorescence resonance energy transfer (FRET).

(Person in charge) Assoc. Prof. MURAKOSHI (Section of Multiphoton Neuroimaging) and Assoc. Prof. NARUSHIMA (Division of Homeostatic Development)

(iii) Development and supply of viral vectors and gene transfer to primates

In recent years, the performance of viral vectors has improved as a gene transfer technique in the central nervous systems of mice, rats, primates and the like. The Section of Viral Vector Development of the Supportive Center for Brain Research has developed novel high-frequency conventional lentiviral vectors and various serotypes of adeno-associated viral vectors that can

be manipulated in a pathway-selective manner. The various viral vectors we have developed are and will continue to be used in projects. Furthermore, in order to clarify higher brain function, we will use viral vectors to introduce genes into primates such as macaques and marmosets to perform morphological, physiological, and behavioral analysis.

(Person in charge) Assoc. Prof. KOBAYASHI (Section of Viral Vector Development): preparation and provision of viral vectors

Prof. ISODA (Division of Behavioral Development): gene transfer into primates

(iv) Multi-dimensional fluorescence imaging analysis with a multi-point scanning microscope

We conduct joint research with our original multi-point scanning confocal/two-photon microscope. In particular, we quantitatively visualize and analyze various cell physiological functions, including circadian rhythms, with high-speed 3D, ultra-long-term, multicolor, and super-resolution observations.

(Person in charge) Prof. NEMOTO (Division of Biophotonics)

(v) Elucidation of the pathology of mental/neurological diseases by analysis of neural activity dynamics

We study the relationship between human and animal neural activity dynamics and the pathology of various mental and neurological diseases by combining unit recording, local field potentials (LFPs), electrocorticography (ECoG), scalp electroencephalography (scalp EEG), functional magnetic resonance imaging (fMRI), and magnetoencephalography (MEG) in a multi-layered manner. In particular, we analyze neural activity dynamics such as vibration, synchronization, and fluctuation from the perspective of nonlinear dynamics and computational theory.

(Person in charge) Prof. KITAJO (Division of Neural Dynamics)

(vi) Visualization of white matter fiber bundles and brain microstructure by analyzing brain imaging data

We conduct collaborative research to visualize microstructures in white matter fiber bundles, cortical gray matter regions, and neuronal nuclei by analyzing human or animal brain structural images acquired using MRI and other techniques

(Person in charge) Prof. TAKEMURA (Division of Sensory and Cognitive Brain Mapping)

2) Contact person: Before submitting any proposal, please consult with NIPS members indicated above according to your interest.

3) Others: No project can be conducted for over 5 years on the same research theme. When making an application for ongoing projects, please indicate the updates from the previous year's proposal in your application.

III. Planned collaborative projects (Animal Resource Center)

1) Overview

Planned collaborative projects are conducted on research themes designated by the Animal Resource Center and are listed below. Accepted projects will be conducted at the Animal Resource Center facilities.

(Themes)

(i) Production of animal models

We produce genetically modified rats and mice and develop model animals that are useful for physiological and neuroscience experiments.

Please note that as a general rule, the animals produced by these collaborative projects must be preserved as public bioresources, and details regarding the animals must be available to the public. Please therefore deposit produced animals in the National BioResource Project (rats: Institute of Laboratory Animals Graduate School of Medicine, Kyoto University; mice: Riken BioResource Research Center) within 3 years after completion of the project.

(Person in charge) Prof. NISHIJIMA (Section for development of advanced animal models, Animal Resource Center, Section of Multilayer Physiology, Center for Genetic Analysis of Behavior)

(Note) Until FY 2021, this theme was conducted at NIPS as a joint research theme titled "Physiological and neuroscientific analysis of genetically modified model animals."

(ii) Analysis of behavior and physiological functions of mice and rats

We measure behaviors and physiological of mice and rats, including disease models.

This year we focus on mouse analyses. The items analyzed and the persons in charge are listed below:

(Analyzed items, persons in charge)

(A) Evaluation of behaviors related to emotions, learning, and memories, and analyses of neural and muscular activities

Open field, light/dark transition test, elevated plus-maze, forced swimming, rotarod test, passive avoidance, fear conditioning, and Morris water maze tests, Barnes circular maze test, recordings of neural (single unit, local field potential, etc.) and muscular activities under awake states

(Person in charge), Assistant Prof. CHIKEN (Section for physiological analysis of animal models, Animal Resource Center, Section of Multilayer Physiology, Center for Genetic Analysis of Behavior)

(B) Non-invasive 4D ultrasound imaging of cardiac function and capillary blood flow in mice and cardiac function measurement using isolated perfused hearts

(Person in charge) Prof. NISHIDA (Division of Cardiocirculatory Signaling)

(C) Functional analysis of neuroimmune interactions in mouse models of diseases

(Person in charge) Prof. MURAKAMI (Section of Multiphoton Neuroimaging)

(D) Multicellular activity measurement and manipulation in vivo

We measure activities of brain cell groups under awake conditions, mainly using bioimaging techniques. Furthermore, by manipulating such cell groups with holographic microscopy, the causal relationships between such cell group activities and the subject's behaviors can be demonstrated.

(Person in charge) Prof. WAKE (Division of Multicellular Circuit Dynamics)

(E) Physiological measurements and analysis in vivo

We measure electrical activities of brain nerve cells, mainly via electrophysiological analysis, and correlate the measurement results with bioelectrical signals from tests such as electrocardiograms and electromyograms.

(Person in charge) Prof. WAKE (Division of Multicellular Circuit Dynamics)

(iii) Behavioral and neural activity analysis of macaque monkeys

Using macaque monkeys as model animals, we will mainly evaluate social behavior and measure and analyze social-related neural activity.

(Person in charge) Prof. ISODA (Division of Behavioral Development)

ii) Person in charge

Before submitting any proposal, please meet in advance with one of the members listed above, as appropriate based on your interest.

iii) Overview of equipment used for analyzing metabolic physiology in mice and rats

Please refer to Annex 2.

iv) Other: No project can be conducted for over 5 years on the same research theme. When making an application for ongoing projects, please indicate the updates from the previous year's proposal in your application.

IV. NIPS Research Meeting

1) Purpose and Overview

The NIPS research meeting is a relatively small group meeting (about 100 people or fewer) for debating the creation of new academic fields and developing new technologies. At least one NIPS professors or associate professors must participate in each meeting. Travel expenses of participants will be partly borne by NIPS.

2) Duration

The duration of each research meeting cannot be longer than 3 days.

3) Venue

As a general rule, in-person and hybrid (both in-person and virtual) meetings must be carried out at a facility located within the Okazaki area of NINS. Virtual-only meetings may be accepted.

Please note that you can hold a meeting in the Okazaki Conference Center (OCC) of NINS (<http://www.orion.ac.jp/occ/>). For details on reservation procedures, please contact the Joint Research Section of the International Research Cooperation Division (r7133@orion.ac.jp).

In addition, to contribute to the research communities surrounding NIPS and to Japanese universities, we plan to annually adopt one proposal (or more if possible) for both a NIPS research meeting and a NIPS international workshop outside the NINS Okazaki area. Preferably the venue will be a university or other related institute. As a general rule, the research meeting cannot be held in conjunction with any other event, such as an academic conference or the like. Travel expenses for these research meetings will be handled in accordance with the rules for those held in the Okazaki area.

4) Others

If any research meeting is to be held on the same theme for more than 3 years, its significance must be reviewed. If you desire to continue the meetings for over 3 years, we expect a new development to be included in the proposal.

Please pay special consideration to gender equality when selecting participants in the proposed project.

We welcome meetings that allow participants to join online.

V. NIPS International Workshop

1) Purpose and Overview

To promote the internationalization and development of NIPS, we hold a NIPS International Workshop that invites several scientists from around the world. The Workshop is held in English. You can submit the same content as both a NIPS Research Meeting proposal and a NIPS International Workshop proposal. If both of the proposals are approved, the project will be held as an International Workshop. We plan to adopt one to three proposals for the International Workshop every year.

At least one or more NIPS professors or associate professors must participate in each workshop. The expected number of participants in a Workshop is 50 to 100. The International Workshops are relatively small events compared to the NIPS International Symposium, which is held once or twice every year.

2) Duration

The duration of an International Workshop cannot be longer than 3 days.

3) Venue

As a general rule, in-person and hybrid (both in-person and virtual) meetings must be carried out at a facility located within in the Okazaki area of NINS. Virtual-only meeting may be accepted.

Please note that you can hold a meeting in the Okazaki Conference Center (OCC) of NINS

(<http://www.orion.ac.jp/occ/>). For details on applying for its use, please contact the Joint Research Section of the International Research Cooperation Division (r7133@orion.ac.jp).

In addition, to contribute to the research communities surrounding NIPS and to Japanese universities, we plan to annually adopt one proposal (or more if possible) for both a NIPS research meeting and a NIPS international workshop outside the NINS Okazaki area.

VI. Cooperative studies by functional imaging

1. Magnetic resonance imaging (MRI) scanner

1) Research themes

For collaborative studies using our MRI scanner, we have defined the following two research themes. Under these themes, researchers inside and outside NIPS aim to comprehensively elucidate biological functions from the molecular level to the individual level.

- i) Non-destructive, 3-dimensional observation of the inside of living organisms
- ii) Continuous observation of morphological and energy states associated with biological activities (including brain activation tests)

Please note that our 7-T magnetic resonance device will be used for technical examination and development related to imaging and image processing for a while.

2) Overview of the MRI scanner installed at NIPS

Please refer to Annex 3.

- #### 3) Before submitting any proposal, please consult with one of the NIPS members listed below based on your interest.

Prof. ISODA (Division of Behavioral Development)

Prof. KITAJO (Division of Neural Dynamics)

Prof. TAKEMURA (Division of Sensory and Cognitive Brain Mapping)

Project. Prof. FUKUNAGA (Section of Brain Function Information)

4) Other

When making a proposal, please select a theme that will enable the project to be completed within three years. If you are making an application for ongoing projects, please indicate the updates from the previous year's proposal in your application.

Annex 1

List of host researchers

(NIPS)

(2024/4/1)

Department	Division	Professor	Associate Professor	TEL
Department of Molecular and Cellular Physiology	Division of Biophysics and Neurobiology	KUBO, Yoshihiro	TATEYAMA, Michihiro	<0564>55-7831 <0564>55-7832
	Division of Structural Biology	(Concurrent/ Project) MURATA, Kazuyoshi		<0564>55-7893
	Division of Neural Development & Regeneration (Adjunct Division)	(Adjunct Prof.) SAWAMOTO, Kazunobu		
Department of Homeostatic Regulation	Division of Cell Structure	FURUSE, Mikio	IZUMI, Yasushi	<0564>59-5277 <0564>59-5279
	Division of Cardiocirculatory Signaling (Concurrent division)	(Concurrent) NISHIDA, Motohiro	(Project) NISHIMURA, Akiyuki	<0564>59-5560
	Division of Molecular Neuroimmunology	(Concurrent) MURAKAMI, Masaaki	(Project) HASEBE, Rie	<0564>55-7729
	Division of Ultrastructural Research (Adjunct Division)	(Adjunct Prof.) OHNO, Nobuhiko		<0564>59-5279
Department of Fundamental Neuroscience	Division of Multicellular Circuit Dynamics	(Concurrent) WAKE, Hiroaki		<0564>55-7724
	Division of Homeostatic Development		NARUSHIMA, Madoka	<0564>55-7854
	Division of Visual Information Processing	YOSHIMURA, Yumiko		<0564>55-7731
	Division of Biophotonics (Adjunct Division)	NEMOTO, Tomomi	ENOKI, Ryosuke	<0564>59-5255 <0564>59-5258
Department of System Neuroscience	Division of Behavioral Development	ISODA, Masaki	(Project) TOMATSU, Saeka	<0564>55-7761 <0564>55-7764
	Division of Neural Dynamics	KITAJO, Keiichi		<0564>55-7751
	Division of Sensory and Cognitive Brain Mapping	TAKEMURA, Hiromasa		<0564>55-7861

Department	Division	Professor	Associate Professor	TEL
Supportive Center for Brain Research	Section of Multiphoton Neuroimaging		MURAKOSHI, Hideji	<0564>55-7857
	Section of Electron Microscopy	(Concurrent) FURUSE, Mikio	KUBOTA, Yoshiyuki	<0564>59-5277 <0564>59-5282
	Section of Brain Function Information	(Project) FUKUNAGA, Masaki		<0564>55-7842
		(Adjunct Prof.) INUI, Koji		
	Section of Cellular Electrophysiology	(Concurrent) YOSHIMURA, Yumiko		<0564>55-7731
Center for Genetic Analysis of Behavior	Section of Viral Vector Development	(Concurrent) ISODA, Masaki	KOBAYASHI, Kenta	<0564>55-7827
	Section of Multilayer Physiology	(Concurrent) NISHIJIMA, Kazutoshi		<0564>55-7781
	Research Enhancement Strategy Office/Section of Advanced Research Support		(Project) MARUYAMA, Megumi	<0564>55-7803

(Center for Animal Resources and Collaborative Study)

(2024/4/1)

	Division	Professor	Associate Professor	TEL
	(Center Director) NISHIJIMA, Kazutoshi (Concurrent) NISHIDA, Motohiro (Concurrent) MURAKAMI, Masaaki (Concurrent) WAKE, Hiroaki (Concurrent) ISODA, Masaki		(Concurrent) CHIKEN, Satomi	<0564>55-7742

(NIPS)

Department of Molecular and Cellular Physiology

The Division of Biophysics and Neurobiology (Prof. KUBO, Yoshihiro and Assoc. Prof. TATEYAMA, Michihiro) aims to clarify the mechanisms of ion channels, receptors, and G proteins, which are key elements of the nervous system. The Division approaches structure-function relationships and structural dynamics of the elements through biophysical analyses with the electrophysiological and optical techniques in in vitro expression systems.)

The Division of Structural Biology (Material-Life Boundary Research Group, Exploratory Research Center on Life and Living Systems (ExCELLS)) (Project Prof. MURATA, Kazuyoshi) strives to elucidate the functions of biomolecular complexes from a structural perspective. The Division uses a cryo-electron microscope to perform structural analyses of biomolecular complexes. In addition, electron tomography and serial block-face scanning electron microscopy (SBF-SEM) is used for morphological and structural analyses of intracellular biomolecular complexes.

The Division of Neural Development & Regeneration (Adjunct Division, Adjunct Prof. SAWAMOTO, Kazunobu) studies the mechanism whereby neurons and glial cells are generated during brain development and regeneration after brain injury. The Division also tries to stimulate these regeneration processes.

Department of Homeostatic Regulation

The Division of Cell Structure (Prof. FURUSE, Mikio and Assoc. Prof. IZUMI, Yasushi) focuses on the molecular basis of cell-cell junctions involved in epithelial barrier function and passive transfer via paracellular pathways. In addition to basic analysis using cultured epithelial cells, the Division is proceeding with individual-level analysis using genetically modified mice and *Drosophila* in conjunction with techniques in the fields of cell biology and physiology.

The Division of Cardiocirculatory Signaling (Cardiocirculatory Dynamism Research Group of the ExCELLS) (Prof. NISHIDA, Motohiro and Project Prof. NISHIMURA, Akiyuki) aims to clarify the mechanism that controls the cardiovascular adaptation or maladaptation to hemodynamic load. Specifically, it strives to elucidate the molecular mechanism of cardiovascular homeostasis from the viewpoint of signal transduction by using a wide range of techniques, including creation of model mice for human cardiovascular disease, measurement of cardiovascular functions using isolated organs, signal transduction analysis using primary cultured cardiomyocytes, and in situ imaging of post-translational protein modification based on chemical principles.

The Division of Molecular Neuroimmunology (Prof. MURAKAMI, Masaaki and Project Assoc.Prof. HASEBE, Rie) has been analyzing tissue-specific autoimmune diseases and found two novel concepts. One is the gateway reflex, which is a novel mechanism of neuroimmune interactions, and the other is the IL-6 amplifier, which is a fundamental mechanism of inflammation in nonimmune cells including tissue-specific cells. The IL-6 amplifier is activated by the simultaneous activation of STAT3 and NF- κ B followed by the excessive activation of NF- κ B. As for the gateway reflex, six types have been reported so far. Environmental and artificial stimulations, including gravity, electrical stimulation, pain, stress, light, and inflammation in joints, activate specific neural

pathways, which induce activation of the IL-6 amplifier at specific blood vessels of target organs, particularly those with blood barriers, such as the central nervous system. Activation of the IL-6 amplifier accumulates autoreactive CD4⁺ T cells in the blood around the specific blood vessels, resulting in the development of tissue-specific inflammatory diseases. The lab is investigating details about the neural pathways for the six as well as searching for new gateway reflexes.)

The Division of Ultrastructural Research (Adjunct Division) (Adjunct Prof. OHNO, Nobuhiko) aims to clarify the molecular backgrounds of structural and functional changes in the nervous system in myelin diseases. To this end, the Division uses imaging techniques such as 3-dimensional microstructure analysis involving microtome-integrated serial block-face scanning electron microscopy (SBF-SEM). In addition, by combining such imaging techniques with cultured models and genetically modified animals, the Division is elucidating the mechanisms of dynamic changes in organelles (e.g., mitochondria) in the nervous system and developing technologies to control these changes.

Department of Fundamental Neuroscience

In the Division of Multicellular Circuit Dynamics (Prof. WAKE, Hiroaki), we mainly use two-photon microscopy to visualize the structure and function of neurons and glial cells in the mouse brain under awake conditions and extract their activities in physiological and pathological conditions. Furthermore, we are using holographic microscopy to manipulate neurons and glial cells activity with high spatiotemporal resolution based on this activity information.)

The Division of Homeostatic Development (Assoc. Prof. NARUSHIMA, Madoka) focuses on the remodeling of neuronal circuits during the developmental and injury recovery periods. In particular, they are involved in the following: 1) electrophysiological analysis of synaptic transmission and receptor functions; (2) analysis of plastic changes in the functions of the inhibitory neurotransmitters GABA and glycine, especially from the viewpoint of the intracellular regulation mechanism for chloride ion concentration; and (3) use of in vivo multiphoton laser microscopy to determine the morphological and behavioral changes in neuronal circuits during the developmental period and in various disease states, and the contribution of glial cells to these changes.

The Division of Visual Information Processing (Prof. YOSHIMURA, Yumiko) characterizes the neural circuits of the visual cortex and elucidates the mechanisms underlying the experience-dependent development of the cortex. To this end, cortical slices and anesthetized and conscious mice are analyzed with the combined use of local laser light stimulation and electrophysiological and Ca²⁺ imaging techniques.

The Division of Biophotonics (Biophotonics Research Group of the ExCELLS) (Prof. NEMOTO, Tomomi and Assoc. Prof. ENOKI, Ryosuke) advances the development and application of cutting-edge imaging devices, including in vivo two-photon microscopes, multi-beam scanning-type two-photon microscopes, and two-photon super-resolution microscopes. The Division also conducts research in the field of chronobiology, for instance utilizing imaging techniques to examine the neuroscientific basis of circadian rhythms.

Department of System Neuroscience

The Division of Behavioral Development (Prof. ISODA, Masaki, Project Assoc. Prof. TOMATSU, Saeka) aims to clarify the neural basis of social cognitive functions via studies of system neuroscience using primates. To this end, the Division conducts integrated analyses combining behavioral, electrophysiological, and neuropharmacological techniques, and also utilizes neuroanatomical methods and selectively manipulates neural circuits using viral vectors.

The Division of Neural Dynamics (Prof. KITAJO, Keiichi) aims to unveil the functional roles of diverse neural dynamics in brain information processing. In particular, experiments involving the non-invasive measurement of human electroencephalogram and brain stimulation are used in conjunction with data analysis (nonlinear dynamics, network analysis, statistical machine learning methods, etc.) to model the information-processing mechanisms of the human brain and thereby clarify pathological conditions and individual characteristics.

The Division of Sensory and Cognitive Brain Mapping (Prof. TAKEMURA, Hiromasa) aims to investigate structure-function relationship in the human brain primarily based on neuroimaging methods. Specifically, the Division combines structural neuroimaging (diffusion and quantitative MRI) and functional neuroimaging (functional MRI) to investigate brain structure and function, in order to perform comparisons between human and animal brains as well as evaluate consequence of disorders)

Supportive Center for Brain Research

The Section of Multiphoton Neuroimaging (Assoc. Prof. MURAKOSHI, Hideji) explores cell functions by imaging cell morphology, signal transduction, and molecular interactions using unique two-photon microscopy techniques and two-photon fluorescence resonance energy transfer (FRET) microscopy. In addition to state-of-the-art optical technology, the Section develops novel fluorescent proteins and photoresponsive protein molecules. By combining these technologies with the patch clamp method, the Section aims to elucidate the functions of nerve cells and cultured cells.

The Section of Electron Microscopy (Prof. FURUSE, Mikio and Assoc. Prof. KUBOTA, Yoshiyuki) has introduced a microtome-integrated scanning electron microscope (SBF-SEM) for conducting connectomics analyses. With this device, the Section automatically captures several hundred to a thousand sequential electron microscope images a day and reconstructs them into 3D models. In addition, local neural networks in the cerebral cortex are analyzed using wide-area electron microscope image datasets and correlative light-electron microscopy, the latter of which seamlessly combines *in vivo* imaging by a two-photon microscope and an automated tape-collecting ultramicrotome (ATUM)-SEM.

The Section of Brain Function Information (Project Prof. FUKUNAGA, Masaki and Adjunct Prof. INUI, Koji) supports neuroimaging studies in humans and monkeys using high-field (3T and 7T) MRI, and promotes research on brain functional and structural analysis. Research areas in this section include basic research using MRI, technical development, and mathematical analysis of large multicenter clinical neuroimaging studies. The Section also supports the analysis of data obtained by collaborative projects involving magnetoencephalography (MEG) measurements conducted through academic year 2021, with the goal of advancing the evaluation of

human brain functions.

The Section of Cellular Electrophysiology (Prof. YOSHIMURA, Yumiko) explores the structures and dynamic control of neural circuits and the action and control mechanisms of synaptic transmission by applying an electrophysiological method (patch clamp technique) to different brain areas (e.g., cerebral cortex, basal ganglia and cerebellum), mainly using sample slices. The Section also aims to elucidate the developmental mechanisms of brain and nervous system diseases and to develop novel treatment methods by performing pathological analyses of mice with gene mutations related to these diseases. In this Section, Assist. Professors OTSUKA, Takeshi and SATAKE, Shin'Ichiro will mainly promote the joint research project.

Center for Genetic Analysis of Behavior

The Section of Viral Vector Development (Prof. ISODA, Masaki and Assoc. Prof. KOBAYASHI, Kenta) develops high-quality and high-performance virus vectors that can be applied to: i) analysis of the neural basis of higher brain functions using model animals such as primates and rodents, and ii) pathological analysis of mental and neurological diseases. In addition, it serves as a central hub for providing viral vectors in response to requests from other laboratories. Through such efforts, the Section actively promotes joint research.

The Section of Multilayer Physiology, (Prof. NISHIJIMA, Kazutoshi) promotes collaborative research for the evaluation of behaviors related to emotions, learning and memories, and for the recordings and analysis of neural (single-unit, local field potential, etc.) and muscular activities in an awake state.

Research Enhancement Strategy Office and Section of Advanced Research Support

The Research Enhancement Strategy Office and the Section of Advanced Research Support (Project Assoc. Prof. MARUYAMA, Megumi) promotes efforts to establish a new NIPS research strategy based on surveys of domestic and international research trends, and provides administrative support services as a hub for local and international research communities. The Office and Section are also engaged in interdisciplinary joint research on deepening the relationship between science and society. This research includes the field of neuroethics, which deals with the ethical and social issues that accompany the development of neuroscience research.

Center for Animal Resources and Collaborative Study

The Center for Animal Resources and Collaborative Study develops experimental animals (including mice, rats, rabbits, and monkeys) based on their characteristics (e.g., genetic recombination) and analyzes their phenotypes (physiological functions such as behavior, electrical activity, metabolism, etc.) from the perspectives of veterinary medicine and laboratory animal sciences. In addition, the Center develops strain preservation techniques and husbandry practices that are suitable for different animal species to improve the quality of animal experiments and animal welfare.

Annex 2

Overview of equipment used for analyzing physiology in mice and rats

【Major items to be analyzed and/or measured】

- (A) Evaluation of behaviors related to emotions, learning, and memories, and analyses of neural and muscular activities
- (B) Non-invasive 4D cardiac function and capillary blood flow ultrasound imaging in mice
- (C) Functional analysis of neuroimmune interactions in mouse models of diseases
- (D) Multicellular activity measurement and manipulation *in vivo*
- (E) Physiological measurements and analysis *in vivo*

【Equipment】

- Brain wave-measuring apparatus (Nihon Kohden, AB611J)
- Electromyograph (Nihon Kohden, AB611J)
- Telemetry automatic measurement system for chronic experiments (Harvard Bioscience, mouse, rat, etc.)
- 4D ultrasound imaging device VEVO3100 (Primetech Corporation, for mice)
- Isolated heart perfusion system (Primetech Corporation, for mice and rats)
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- Open field test analyzer (Section of Instrument Design Room of NIPS and other, for mice)
- Light/dark transition test device (O'HARA, for mice)
- Barnes circular maze test device (O'HARA, for mice)
- Elevated plus-maze test analyzer (Section of Instrument Design Room of NIPS and other, for mice)
- Forced swimming test analyzer (Section of Instrument Design Room of NIPS and other, for mice)
- Rota-rod test analyzer (Ugo Basile, for mice RotaRod NG, 47650)
- Passive avoidance test analyzer (O'HARA, for mice)
- Fear conditioning test analyzer (O'HARA and other, for mice)
- Morris water maze pool (O'HARA and other, for mice)
- Intellicage: group-housed automated high-throughput behavioral and cognitive screening system (TSE-systems, for mice)
- Nikon A1MP+holographic microscope (Nikon & Division of Multicellular Circuit Dynamics, for mice and rats)
- The head-mounted miniature microscope (INSCOPIX)
- X-ray irradiation device (MediXtec, for mice and cells)
- silicon CMOS digital neural probe (Neuropixels)

Annex 3

Overview of magnetic resonance imaging (MRI) scanners installed at NIPS

Performance and features of the MRI scanner installed at the NIPS Supportive Center for Brain Research (two 3-T Verio scanners, 2009, Siemens Co.; one 7-T scanner, 2014, Siemens Co., Ltd.)

3-T Verio

1. Superconducting magnet

- 1) Magnetic field strength: 3 Tesla, magnet inner diameter 70 cm
- 2) Magnetic field uniformity: 0.03 ppm or less (spherical range with a diameter of 20 cm, volume residual mean squared method)
- 3) Shimming: Active + passive shimmming, automatic shimmming for each subject
- 4) Liquid helium evaporation: 0.01 L/year or less

2. Imaging functions

- 1) Nuclei: ^1H
- 2) Pulse sequence: echo planar imaging, turbo spin echo imaging, etc.
- 3) Slice direction: axial, sagittal, coronal, oblique
- 4) Min. slice thickness: 1 mm (2-dimensional imaging), 0.3 mm (3-dimensional imaging)
- 5) Gradient magnetic field: 45 mTesla/m, rise time 0.225 ms
- 6) Probe: 32-channel head coil, circular polarized body coil, etc.
- 7) Data processing device: Automatically saves obtained images in DICOM format via Windows network
- 8) Other functions: T1, T2, T2*, proton density-weighted images, MR angiography, diffusion-weighted image, image statistical processing software, communication mediation relay system for simultaneously measuring neural activity during interaction between two individuals

7-T MRI

1. Superconducting magnet

- 1) Magnetic field strength: 7 Tesla, magnet inner diameter 60 cm
- 2) Magnetic field uniformity : 1 ppm or less (spherical range with a diameter of 25 cm, volume residual mean squared method)
- 3) Shimming: Active + passive shimmming, automatic shimmming for each subject
- 4) Liquid helium evaporation: 0.01 L/year or less

2. Imaging functions

- 1) Nuclei: ^1H , ^{13}C , ^{17}O , ^{19}F , ^{23}Na , ^{31}P
- 2) Pulse sequence: echo planar imaging, turbo spin echo imaging etc.
- 3) Slice dimensions: axial, sagittal, coronal, oblique
- 4) Min. slice thickness: 0.5 mm (2-dimensional imaging), 0.05 mm (3-dimensional imaging)
- 5) Gradient magnetic field: 70 mTesla/m, rise time 0.350 ms
- 6) Probe: 32-channel receive-only head coil (^1H), circular polarized transmit/receive head coil (^1H , ^{23}Na , ^{31}P), transmit/receive surface coil (^{13}C , ^{17}O , ^{19}F), etc.
- 7) Data processing device: Automatically saves obtained images in DICOM format via Windows network
- 8) Other functions: T1, T2, T2*, proton density-weighted images, MR angiography, diffusion-weighted image, image statistical processing software