

Call for Joint Research Project Proposals FY 2023

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) Purification of supra molecular complexes and analyses of their constituents by mass spectrometry
 - (v) Multi-dimensional fluorescence imaging analysis with a multi-point scanning microscope
 - (vi) Elucidation of the pathology of mental/neurological diseases by analyzing neural activity dynamics
- (3) Planned collaborative project (Center for Animal Resources and Collaborative Study)
Themes:
 - (i) Production of advanced animal models
 - (ii) Analysis of behavior, metabolism, and physiological functions of mice and rats

*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
(Research term: April 2023 to March 2024 for all themes listed above)

2. 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.

3. 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.

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 you will have to declare that you have your supervisor's approval when making an online application.

4. Deadline for proposals

17:00 Friday, December 2, 2022

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.

5. 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.

6. Date of decision regarding proposal acceptance

Around March 2023.

7. Joint Researchers

If a joint research project is successfully accepted, the representative and joint researchers will carry out the accepted project as Collaborative Researchers. (NINS-Regulations No. 16 of 2004).

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

Travel expenses will be borne by NIPS when visiting the institute as a Collaborative Researcher (Article 4 of the same Regulations). For more details, please refer to item 8. Travel Expenses.

National Institute for Physiological Sciences Visiting Researcher Handling Rules (Japanese only): <https://www.nips.ac.jp/profile/9-16seikisoku16.pdf>

8. Travel expenses

Travel expenses will be reimbursed pursuant to the NINS Regulations for Travel Expenses within the budget.

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

*In such cases, the undergraduate student is required to carry out the procedures prescribed in the NINS Guidelines for Undergraduate Students (or the Equivalent) Who Participate in Collaborative Projects at NINS Okazaki Three Institutions.

*Graduate and undergraduate students are required to have Personal Accident Insurance for Students Pursuing Education and Research (including Liability Insurance Coupled with PAS) provided by the Japan Educational Exchanges and Services, or insurance that is equivalent or more comprehensive.

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

9. Research expenses

Research expenses will be borne by NIPS as allowed by its budget. (Expenses must not be used outside of NIPS.)

10. 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.

11. Gene recombination experiments

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

12. 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 NINS Animal Experimentation Committee.

13. 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 new proposed project uses the Magnetic Resonance Apparatus (3-T, 7-T) for humans, the approval of the Ethics Committee for Human Research of National Institutes of Natural Sciences will be required after the safety review by the NIPS Interactive Cooperative Project Promotion Committee.

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

14. 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.

15. 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.

16. Submission of research report

After the research project is finished, the principal investigator must submit a research report to the Director-General within 30 days of the completion date.

The report will be included and published in the NIPS Catalogue.

17. 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. When you use the Animal Resource Center, please also be sure to clearly **indicate it in the Acknowledgment**.

Example (for NIPS): "This study was supported by the Joint Research Program (XX NIPS YYY) of the National Institute for Physiological Sciences."

Example (for Animal Resource Center): "This study was supported by the Joint Research Program (XX NIPS YYY) of the Center for Animal Resources and Collaborative Study of NINS."

* Please replace "XX NIPS YYY" with the project number, which will be provided when the project is adopted.

18. 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/site/rule/1127.html>

19. Accommodations

We have accommodations for use by researchers who participate in joint research.

20. Promotion of gender equality

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

21. 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.

22. 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

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 for the purpose of conducting the project.

For more details on (1) through (3), please refer to the NIPS website:
https://www.nips.ac.jp/collabo/child_rearing_support.html.

23. Contact for inquiries and report submission

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

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<<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/profile/access/>).

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.

II. Planned collaborative projects (NIPS)

1) Outline:

Planned collaborative projects are conducted on research themes designated by NIPS and are listed below. Accepted projects will be conducted at NIPS facilities.

(Themes)

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

Using the most advanced electron microscopy techniques such as those involving the phase-contrast method, we perform single-particle analysis of proteins and functional and morphological 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.

(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).

(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.

(iv) Purification of supra-molecular complexes and analyses of their constituents by mass spectrometry

To understand the functions of proteins in living organisms, it is essential to precisely identify the constituents of supra-molecular complexes. We thus purify protein complexes from tissues and cells with an emphasis on their specificity, and then identify constituents of the complexes with mass spectrometry.

Target antigens for autoantibodies in autoimmune diseases are also identified.

(v) 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.

(vi) 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.

- 2) Contact person: Before submitting any proposal, please consult with one of the NIPS members listed below according to your interest.
 - (i) Project Prof. MURATA (Division of Structural Biology), Prof. FURUSE (Division of Cell Structure), and Adjunct Prof. OHNO (Division of Ultrastructural Research)
 - (ii) Assoc. Prof. NARUSHIMA (Division of Homeostatic Development) or Assoc. Prof. MURAKOSHI (Section of Multiphoton Neuroimaging)
 - (iii) Assoc. Prof. Kobayashi (Section of Viral Vector Development) for preparation and provision of viral vectors
Prof. ISODA (Division of Behavioral Development) for gene transfer into primates
 - (iv) Prof. FUKATA (Division of Membrane Physiology)
 - (v) Prof. NEMOTO (Division of Biophotonics)
 - (vi) Prof. KITAJO (Division of Neural Dynamics)
- 3) Others: No project can be conducted for over 5 years on the same research theme.

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 advanced 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) Assoc. Prof. HIRABAYASHI, Masumi, Section of Mammalian Transgenesis, Center for Genetic Analysis of Behavior, Animal Resource Center

(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, metabolism, and physiological functions of mice and rats

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

(Person in charge) Assis. Prof. CHIKEN, Section of Multilayer Physiology, Center for Genetic Analysis of Behavior, Department of Model Animal Phenotype Analysis, Animal Resource Center Multi-level Physiological Function Analysis Room

(B) Energy intake and expenditure in free-moving animals

(Person in charge) Prof. MINOKOSHI, Division of Endocrinology and Metabolism

- (C) Body temperature, heart rate, and blood pressure in free-moving animals
(Person in charge) Prof. TOMINAGA, Division of Cell Signaling
 - (D) Non-invasive 4-dimensional cardiac function and capillary blood flow imaging using anesthetized mice
(Person in charge) Prof. NISHIDA, Division of Cardiocirculatory Signaling
 - (E) Mouse temperature preference assays with a thermal gradient ring
(Person in charge) Prof. TOMINAGA, Division of Cell Signaling
 - (F) Multicellular activity measurement and manipulation in vivo
(Person in charge) Prof. WAKE, Division of Multicellular Circuit Dynamics
 - (G) Functional analysis of neuroimmune interactions in mouse models of diseases
(Person in charge) Prof. MURAKAMI, Division of Molecular Neuroimmunology
- (Note) Until FY 2021, the above (B) to (D) were conducted at NIPS under a joint research theme titled "Analysis of metabolic physiology for mice and rats."
- 2) Person in charge
Before submitting any proposal, please meet in advance with one of the members listed above, as appropriate based on your interest.
 - 3) Overview of equipment used for analyzing metabolic physiology in mice and rats
Please refer to Annex 1.
 - 4) Other:
No project can be conducted for over 5 years on the same research theme.
Specific-pathogen free animals will be used for planned collaborative projects conducted at the Animal Resource Center facilities. If you would like to know further information concerning SPF animals, please contact NIPS person in charge.

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
In principle, the meeting must be carried out in the Okazaki area of NINS.
However, considering the COVID-19 pandemic, an online or hybrid meeting may be recommended. For more information, please refer to the "Research Guidelines Aimed at Preventing the COVID-19 Outbreaks Within the National Institute for Natural Sciences (NIBB, NIPS, IMS, and EXCELLS)" (<https://www.nips.ac.jp/release/pdf/kijyun200409.pdf>).
Please note that you can hold a meeting in the Okazaki Conference Center of NINS. 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, applications for a NIPS research meeting and a NIPS international workshop outside the NINS Okazaki area are possible. 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

In principle, the meeting must be carried out in the Okazaki area of NINS.

However, considering the COVID-19 pandemic, an online or hybrid meeting may be recommended. For more information, please refer to the "Research Guidelines Aimed at Preventing the COVID-19 Outbreaks Within the National Institute for Natural Sciences (NIBB, NIPS, IMS, and EXCELLS)" (<https://www.nips.ac.jp/release/pdf/kijyun200409.pdf>).

Please note that you can hold a meeting in the Okazaki Conference Center of NINS. For details on applying for its use, please contact the Joint Research Section of the International Research Cooperation Division (TEL: +81-564-55-7138).

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)

2) Overview of the MRI scanner installed at NIPS

Please refer to Annex 2.

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)

Assoc. Prof. FUKUNAGA (Division of Cerebral Integration)

4) Other

When making a proposal, please select a theme that will enable the project to be completed within three years.

List of host researchers

(NIPS)

(April 1, 2023)

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 Membrane Physiology	FUKATA, Masaki	FUKATA, Yuko	<0564>59-5873
	Division of Structural Biology	(Concurrent/ Project) MURATA, Kazuyoshi		<0564>55-7872
	Division of Neural Development & Regeneration (Adjunct Division)	(Adjunct) SAWAMOTO, Kazunobu		
Department of Homeostatic Regulation	Division of Cell Structure	FURUSE, Mikio	IZUMI, Yasushi	<0564>59-5277 <0564>59-5279
	Division of Cell Signaling (Concurrent division)	TOMINAGA, Makoto	SOKABE, Takaaki (Project) KASHIO, Makiko (Project) MARUYAMA, Kenta	<0564>59-5286 <0564>59-5287 <0564>59-5296
	Division of Cardiocirculatory Signaling (Concurrent division)	NISHIDA, Motohiro	(Project) NISHIMURA, Akiyuki	<0564>59-5560
	Division of Endocrinology and Metabolism	MINOKOSHI, Yasuhiko		<0564>55-7742
	Division of Molecular Neuroimmunology	(Concurrent) MURAKAMI, Masaaki	(Project) HASEBE, Rie	<0564>55-7729
	Division of Ultrastructural Research (Adjunct Division)	(Adjunct) OHNO, Nobuhiko		<0564>59-5279
	Division of Multicellular Circuit Dynamics	(Concurrent) WAKE, Hiroaki		<0564>55-7724
Department of Fundamental Neuroscience	Division of Homeostatic Development		NARUSHIMA, Madoka	<0564>55-7854
	Division of Visual Information Processing	YOSHIMURA, Yumiko		<0564>55-7731
	Division of Biophotonics (Concurrent division)	NEMOTO, Tomomi	ENOKI, Ryosuke	<0564>59-5255 <0564>59-5258

Department	Division	Professor	Associate Professor	TEL
Department of System Neuroscience	Division of Behavioral Development	ISODA, Masaki	(Project) TOMATSU, Saeka (Project) GO, Yasuhiro	<0564>55-7761 <0564>55-7764 <0564>55-7824
	Division of Neural Dynamics	KITAJO, Keiichi		<0564>55-7751
	Division of Sensory and Cognitive Brain Mapping	TAKEMURA, Hiromasa		<0564>55-7861
	Division of Cerebral Integration		FUKUNAGA, Masaki	<0564>55-7844
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	(Adjunct) INUI, Koji	FUKUNAGA, Masaki	<0564>55-7845 <0564>55-7842
	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 Mammalian Transgenesis		HIRABAYASHI, Masumi	<0564>59-5265
	Section of Multilayer Physiology	(Concurrent) NISHIJIMA, Kazutoshi		<0564>55-7781

(Center for Animal Resources and Collaborative Study)

(April 1, 2023)

	Professor	Associate Professor	Assistant Professor	TEL
	(Center Director) MINOKOSHI, Yasuhiko NISHIJIMA, Kazutoshi (Concurrent) TOMINAGA, Makoto (Concurrent) NISHIDA, Motohiro (Concurrent) MURAKAMI, Masaaki (Concurrent) WAKE, Hiroaki	(Concurrent) HIRABAYASHI, Masumi	(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 Membrane Physiology (Prof. FUKATA, Masaki and Assoc. Prof. FUKATA, Yuko) uses a unique biochemical method to identify synaptic protein complexes in brain tissue, and then uses the complexes in conjunction with a hippocampal neural cell primary culture system, genetically modified mice, etc., to clarify the mechanism that controls synaptic transmission efficiency. In addition, focusing on palmitoylation, the Division identifies specific palmitoylating enzymes and analyzes the localization and kinetics of synaptic proteins mediated by these enzymes.

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 200-kV 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 Cell Signaling (Thermal Biology Group, ExCELLS) (Prof. TOMINAGA, Makoto, Assoc. Prof. SOKABE, Takaaki, Project Assoc. Prof. KASHIO, Makiko and Project Assoc. Prof. MARUYAMA, Kenta) aims to clarify the molecular mechanisms of thermosensitivity and

pain sensitivity centering on TRP channels, which serve as biomolecular sensors necessary for cells survival. In addition to analyses using electrophysiological, molecular cell biological, and biochemical techniques, the Division conducts studies at an individual level using genetically modified animals. Such studies include behavioral analysis of temperature, taste, and mechanical stimulus reception using *Drosophila*, and analysis of effects of pesticides and repellents. In addition, the Division analyzes the evolution of temperature-sensitive TRP channels because it is considered that organisms evolutionarily adapted to changes in environmental temperature by dynamically changing their temperature sensitivities.

The Division of Cardiocirculatory Signaling (Cardiocirculatory Dynamism Research Group of the ExCELLS) (Prof. NISHIDA, Motohiro and Project Assoc. 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 Endocrinology and Metabolism (Prof. MINOKOSHI, Yasuhiko) studies the control mechanisms, mainly involving the hypothalamus, that underlie the regulation of whole-body energy metabolism. Specifically, the Division aims to elucidate the mechanism of eating and food preference and the means by which taste sensitivity is controlled by the hypothalamus, as well as the mechanism whereby metabolic homeostasis is maintained by the autonomic nervous system at the molecular, tissue, and individual levels. The Division also studies the relationship between disordered homeostasis and obesity, diabetes, and lifestyle-related diseases.

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 non-immune 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 Ca^{2+} 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 and Project Assoc. Prof. GO, Yasuhiro) 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 brain waves 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.

The Division of Cerebral Integration (Assoc. Prof. FUKUNAGA, Masaki) advances experimental studies on higher cerebral cortex activities related to cognition, memory, emotion, judgment, intention, behavior, and social ability using neuroimaging techniques. The Division aims to understand higher brain function dynamically and globally by utilizing non-invasive brain function imaging techniques to assess local circulatory changes and alterations in energy metabolism associated with cranial nerve activity.

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 (Adjunct Prof. INUI, Koji and Assoc. Prof. FUKUNAGA, Masaki) supports collaborative studies on brain function measurement in humans and monkeys using high-field magnetic resonance imaging (3T and 7T) devices equipped at NIPS. The Section promotes research on functional-anatomical mapping of the primate brain. The Section also promotes the elucidation of human brain functions by supporting the analysis of data obtained through the joint use of the whole-brain magnetoencephalography (MEG), which was conducted until FY2021.

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 joint research projects.

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 Mammalian Transgenesis (Assoc. Prof. HIRABAYASHI, Masumi) develops more efficient techniques to produce genetically modified animals and performs reproduction engineering research such as gamete preservation of genetically modified animals,

microinsemination, and establishment of rat embryonic stem cells and induced pluripotent stem cells. Its aim is to achieve further technological advances in developmental engineering techniques.

The Section of Multilayer Physiology, (Prof. NISHIJIMA, Kazutoshi) is equipped with apparatuses for chronological and automatic measurement of physiological functions and metabolic parameters of mice and rats. Using these apparatuses, the Section 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.

(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 1

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

【Major items to be analyzed and/or measured】

- 1) Energy intake and expenditure in free-moving animals
- 2) Body temperature, heart rate, and blood pressure in free-moving animals
- 3) Non-invasive 4-dimensional cardiac function and capillary blood flow imaging using anesthetized mice
- 4) Mouse temperature preference assays using a thermal gradient ring
- 5) Evaluation of behaviors related to emotions, leaning, and memories
- 6) Multicellular activity measurement and manipulation in vivo
- 7) Functional analysis of neuroimmune interactions in mouse models of diseases

【Equipment】

- Device for simultaneously measuring energy metabolism and activity of small animals using mass spectrometry (Arco System, Shinfactory, for mice)
- Brain wave-measuring apparatus (Nihon Kohden, AB611J)
- Electromyograph (Nihon Kohden, AB611J)
- Telemetry automatic measurement system for chronic experiments (Harvard Bioscience, mouse, rat, etc.)
- Olympus FV100, 4D ultrasound imaging device VEVO3100 (Primetech Corporation, for mice)
- Isolated heart perfusion system (Primetech Corporation, for mice and rats)
- Thermal Gradient Ring (Ugo Basile, for mice)
- 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)
- Rotarod 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)
- Nikon A1MP+ holographic microscope (Nikon & Division of Multicellular Circuit Dynamics, for mice and rats)
- X-ray irradiation device (MediXtec, for mice and cells)

ANNEX 2

Overview of magnetic resonance imaging (MRI) scanners

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

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 shimming, automatic shimming 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 shimming, automatic shimming 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