

## List of host researchers

(2021/4/1)

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 Membrane Physiology	FUKATA, Masaki	FUKATA, Yuko	<0564>59-5873
	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 Cell Signaling (Concurrent division)	TOMINAGA, Makoto	SOKABE, Takaaki	<0564>59-5286 <0564>59-5287
	Division of Cardiocirculatory Signaling (Concurrent division)	NISHIDA, Motohiro		<0564>59-5560
	Division of Endocrinology and Metabolism	MINOKOSHI, Yasuhiko	NAKAJIMA Ken-ichiro	<0564>55-7742
	Division of Ultrastructural Research (Adjunct Division)	(Adjunct Prof. ) OHNO, Nobuhiko		
Department of Fundamental Neuroscience	Division of Cerebral Circuitry		KUBOTA, Yoshiyuki	<0564>59-5282
	Division of Homeostatic Development		NARUSHIMA, Madoka (Project) AGETSUMA, Masakazu	<0564>55-7851 <0564>55-7854
	Division of Visual Information Processing	YOSHIMURA, Yumiko		<0564>55-7731
	Division of Biophotonics	NEMOTO, Tomomi	ENOKI, Ryosuke	<0564>59-5255 <0564>59-5258
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 System Neurophysiology	NAMBU, Atsushi		<0564>55-7771
	Division of Neural Dynamics	KITAJO, Keichi		<0564>55-7751
	Division of Cerebral Integration	SADATO, Norihiro	FUKUNAGA, Masaki	<0564>55-7841 <0564>55-7844
Supportive Center for Brain Research	Section of Brain Structure Information		MURATA, Kazuyoshi	<0564>55-7872 <0564>59-5290
	Section of Multiphoton Neuroimaging		MURAKOSHI, Hideji	<0564>55-7857
	Section of Electron Microscopy	(Concurrent) FURUSE, Mikio	(Concurrent) MURATA, Kazuyoshi (Concurrent) KUBOTA, Yoshiyuki	<0564>59-5277
	Section of Brain Function Information	(Concurrent) SADATO, Norihiro (Adjunct Prof) INUI, Koji	CHIKAZOE, Junichi	<0564>55-7845
Center for Genetic Analysis of Behavior	Section of Viral Vector Development	(Concurrent) NAMBU, Atsushi	KOBAYASHI, Kenta	<0564>55-7827
	Section of Mammalian Transgenesis		HIRABAYASHI, Masumi	<0564>59-5265
	Section of Metabolic Physiology	(Concurrent) MINOKOSHI, Yasuhiko		<0564>55-7741

## Department of Molecular and Cellular Physiology

The Division of Biophysics and Neurobiology (Prof. KUBO, Yoshihiro) uses an *in vivo* expression system to study dynamic structure–function relationships, with a focus on the mechanisms of ion channels, receptors, and G proteins, which are key elements of the nervous system. The Division also uses genetically modified mice in order to clarify the functional significance of each element in the cranial nervous system.

The Division of Membrane Physiology (Prof. FUKATA Masaki) 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 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) 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, Exploratory Research Center on Life and Living Systems (ExCELLS)) (Prof. TOMINAGA, Makoto and Assoc. Prof. SOKABE, Takaaki) 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 mice. Behavioral analysis of temperature, taste, and mechanical stimulus reception using *Drosophila*, and analysis of effects of pesticides and repellents are also performed. 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) 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 and Assoc. Prof. NAKAJIMA Ken-ichiro) 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 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**

The Division of Cerebral Circuitry (Assoc. Prof. KUBOTA, Yoshiyuki) aims to elucidate the structural basis of cortical microcircuits as well as the principles of their involvement in learning. This is done by combining in vivo brain observation / virus tracing using a two-photon microscope with synaptic connection analysis using 3-dimensional reconstruction of electron microscopic serial sections.

The Division of Homeostatic Development (Assoc. Prof. NARUSHIMA, Madoka and Project Assoc. Prof. AGETSUMA, Masakazu) 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  $\text{Ca}^{2+}$  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) 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 System Neurophysiology (Prof. NAMBU, Atsushi) strives to clarify the brain mechanisms underlying voluntary movements, and to understand the pathophysiology of movement disorders due to malfunctions of these mechanisms. To this end, the Division records nerve activity in the basal ganglia, cerebellum, and cerebrum in primates, rodents, and other disease model animals, and manipulates this activity with neuropharmacological, photochemical, chemogenetic, and other techniques.

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 Cerebral Integration (Prof. SADATO, Norihiro) 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 Brain Structure Information (Assoc. Prof. MURATA, Kazuyoshi) aims to elucidate the complex biological functions of the brain based on its structure. A 200-kV cryo-electron microscope is used for structural analysis of biomolecular samples. Some samples may be analyzed with an energy filter, a phase plate, a sample stage with larger tilt, etc., in combination with the cryo-electron microscope.

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, Assoc. Prof. MURATA, Kazuyoshi, and Assoc. Prof. KUBOTA, Yoshiyuki) has introduced a new microtome-integrated scanning electron microscope for conducting connectomics studies. With this device, the Section automatically captures several hundred to a thousand sequential electron microscope images a day and reconstructs them into 3D models.

The Section of Brain Function Information (Prof. SADATO, Norihiro, Assoc. Prof. CHIKAZOE, Junichi, and Adjunct Prof. INUI, Koji) supports collaborative studies on brain function measurement in humans and monkeys using high-field magnetic resonance imaging (3T and 7T) and magnetoencephalography (MEG) devices equipped at NIPS. The Section also promotes research on functional–anatomical mapping of the primate brain. A 7-T magnetic resonance imaging device for evaluating humans was installed in 2014. It was confirmed that the device can be operated in a stable manner so it will be generally available for collaborative research projects. In addition, the Section promotes collaborative projects specializing in basic brain science that evaluate humans using whole-head magnetoencephalography.

### **Center for Genetic Analysis of Behavior**

The Section of Viral Vector Development (Prof. NAMBU, Atsushi 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) produces and provides genetically modified animals (transgenic and gene-targeted rats and mice), making full use of molecular biology and developmental engineering techniques. To make further advances at the technological level, the Section also 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.

The Section of Metabolic Physiology (Prof. MINOKOSHI, Yasuhiko) is equipped with and conducts joint research using apparatuses for chronological and automatic measurement of physiological functions and metabolic parameters of mice and rats. The apparatuses can measure the following: 1) single-unit recordings from motor related brain regions in an awake state; 2) energy intake and expenditure in free-moving animals; 3) body temperature, heart rate, and blood pressure in free-moving animals; 4) non-invasive echographic imaging of tissue structure-function relationships (liver, kidney, and blood vessels), 4-dimensional changes in cardiac functions, and capillary blood flow (brain and umbilical cord) in anesthetized mice; and 5) mouse temperature preference assays with a thermal gradient ring.

## ANNEX 1

### 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.)

#### 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:  $^1\text{H}$
- 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:  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{17}\text{O}$ ,  $^{19}\text{F}$ ,  $^{23}\text{Na}$ ,  $^{31}\text{P}$

- 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 ( $^1\text{H}$ ), circular polarized transmit/receive head coil ( $^1\text{H}$ ,  $^{23}\text{Na}$ ,  $^{31}\text{P}$ ), transmit/receive surface coil ( $^{13}\text{C}$ ,  $^{17}\text{O}$ ,  $^{19}\text{F}$ ), 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



## ANNEX 2

### Overview of the whole-head type magnetoencephalography (MEG) device installed at NIPS

Overview of the Vectorview whole-head type MEG device installed at NIPS (2002, Neuromag)

#### 1. Sensor

- (1) Number of channels: 306 channels
- (2) Induction coil: flat-bottomed gradiometer, 204 channels  
magnetometer, 102 channels
- (3) System noise: 5 fTesla  $\sqrt{\text{Hz}}$  or less
- (4) Sensor arrangement: 102 sensor units evenly distributed over 1220 cm<sup>2</sup>  
Each sensor unit incorporates two orthogonal gradiometers and magnetometers
- (5) Measurement position: sitting position or supine position

#### 2. Shielded room

- (1) Inner dimension: width 3 m x depth 4 m x height 2.4 m
- (2) Outer dimension: width 3.6 m x depth 4.6 m x height 3 m
- (3) Shielding ratio 0.1 Hz, 42 dB or more  
1.0 Hz, 60 dB or more  
10 Hz, 80 dB or more

#### 3. Active shielding system

An active shielding system is adopted to reduce the influence of the environmental magnetic field at low-frequency bands. The change in the environmental magnetic field at 1 Hz or less is decreased.

#### 4. Analysis control device (UNIX Workstation HP/UX J6700)

- (1) Control device Connected to sensor system via Ethernet  
Analogue inputs: MEG: 306 channels  
EEG input: 128 channels  
A/D conversion: 24-bit/Save 32-bit  
Sampling (up to 8 kHz)
- (2) Key processing functions Signal source estimation: Single/multi-dipole estimation  
(Sphere model/Real shape model)  
MCE  
Signal processing: Digital filter, FFT, etc.
- (3) Data storage device 5-inch magneto-optical disk 9.1 GB/disk