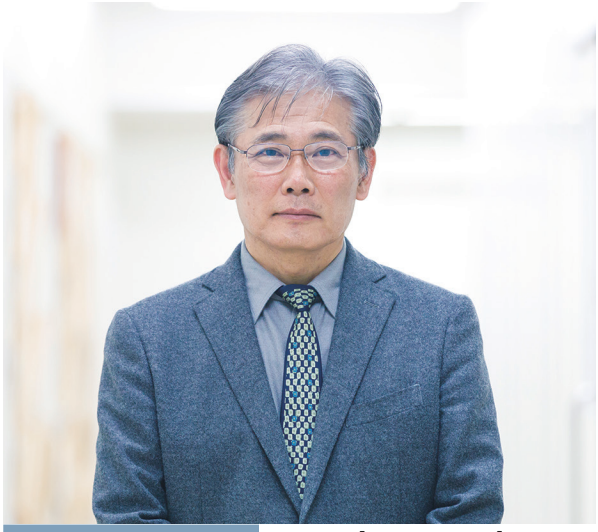
# Homeostatic Mechanism Research Unit

## Overview

Many organisms have the ability of homeostasis to maintain body temperature, blood pressure, osmotic pressure of body fluids, blood sugar level, and other parameters of their internal environment within a certain range, despite variations in the external environment. This ability, gained through evolution, is crucial to maintaining life. Homeostasis is made possible by the delicate communication of the brain and nervous system with organs, or that of organs with each other. For example, when an organism becomes dehydrated, sodium concentration within the body fluids rises, creating an appetite for fluid and decreasing the amount of urine. However, the mechanisms that trigger these maintenance functions are not fully understood. Our research interests focus on the homeostatic mechanisms especially for the three areas: body fluid homeostasis, blood pressure, and obesity.




**Research Unit Leader** **Masaharu Noda**

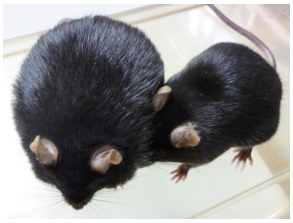
**Profile**

2019 Specially Appointed Professor, Research Unit Leader, Homeostatic Mechanism Research Unit, Institute of Innovative Research, Tokyo Institute of Technology
1991 Professor, Division of Molecular Neurobiology, National Institute for Basic Biology (NIBB); Professor, Basic Biology, the Graduate University for Advanced Studies (Sokendai)
1989 Visiting Scholar, Max Planck Institute for Developmental Biology
1985 Assistant Professor, Kyoto University Faculty of Medicine (Molecular Genetics)
1984 Assistant, Kyoto University Faculty of Medicine (Medical Chemistry)
1983 Researcher, Grant-in-Aid for Encouragement of Scientists, Japan Society for the Promotion of Science (JSPS)
1983 Doctor of Medical Science, Graduate School of Medicine, Kyoto University
1979 Master of Engineering, Graduate School of Engineering, Kyoto University

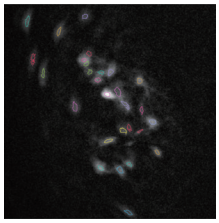

## Research goals

- In *body fluid homeostasis*, we discovered that the brain has a system that monitors the fluctuation of sodium concentration in body fluids and that there are neurons that drive intakes of fluids or salts. Our goal is to understand the control mechanisms underlying these nervous systems.
- *Blood pressure* is greatly affected by factors such as salt, stress, and obesity. We have identified the brain mechanisms underlying salt-induced elevations in blood pressure. This unit seeks to uncover the mechanisms responsible for blood pressure elevations caused by stress and obesity. Additionally, we will aim to reveal the mechanisms by which combinations of multiple factors cause even higher elevations in blood pressure.
- In *obesity*, as it progresses, fat accumulates not only in fat cells, but also in the liver and other organs. Since accumulation of ectopic fat causes various diseases, we also intend to elucidate the mechanisms that control fat accumulation.

## Understanding the central mechanisms of homeostasis and leading to drug discovery

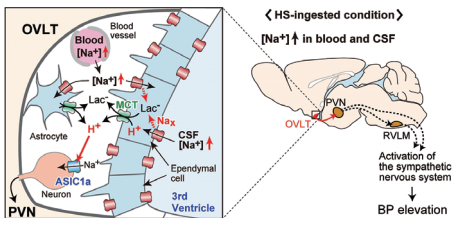


- Control of blood pressure by salt, stress, and obesity
- Control of water/salt-intake behaviors according to body fluid conditions
- Control of obesity and ectopic lipid accumulation



**Analysis of neural activity by *in vivo* calcium imaging**

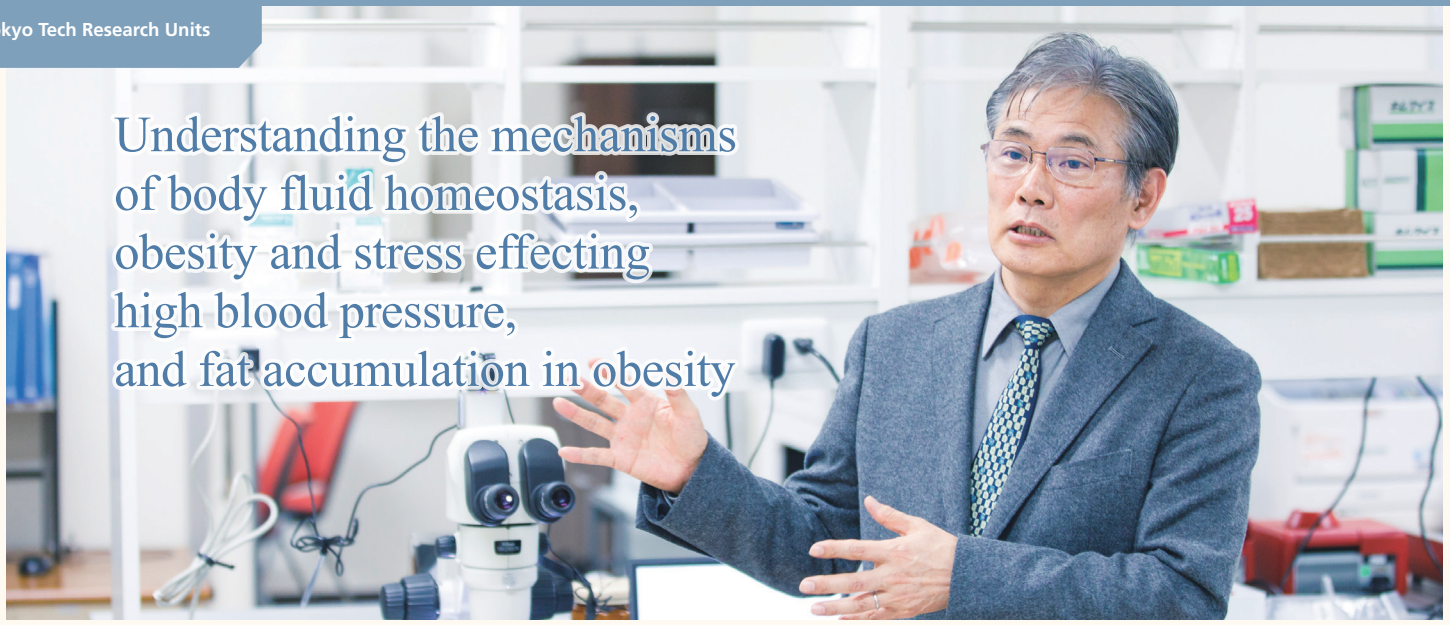
- Genetic manipulation
- Optogenetics
- Real-time imaging




**Central mechanisms responsible for salt-induced hypertension**

Elucidation of brain mechanisms

→ **Development of breakthrough drugs**



# Understanding the mechanisms of body fluid homeostasis, obesity and stress effecting high blood pressure, and fat accumulation in obesity

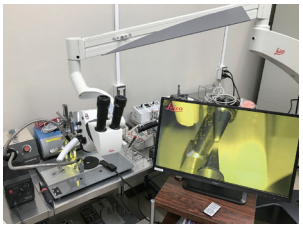
## Q What are the strengths of this research unit?

Our laboratory has developed multiple techniques in molecular biology and neurophysiology to investigate the functions and physiological roles of neurotransmitters and ion channels. Recently, we identified the sensor in the brain that monitors sodium concentration in body fluids. We showed that it plays a central role in water and salt intake behavior and the onset of hypertension. In our research on metabolism, we have already identified enzymes that are responsible for controlling insulin and leptin receptor activity. Currently, we are using optogenetics to artificially control a specific neural activity, as well as imaging technique to monitor the activity of individual neurons in real time. This allows us to analyze, directly and in detail, the roles of specific neural circuits and their control mechanisms.

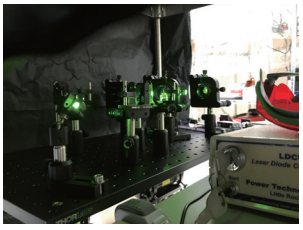
## Q What is the path to achieving the unit's goals?

In the first three years, using the latest techniques such as optogenetics and calcium imaging to manipulate and examine the activity of specific neural pathways in real time, we will elucidate the neural circuits and neural mechanisms that regulate blood pressure and water/salt appetite. We will also uncover the mechanisms regulating fat accumulation by using genetically modified mice. Then, in the following two years, we will look in depth at the mechanisms for information integration when blood pressure is regulated by multiple factors. In addition, we will work to develop ways to suppress the accumulation of ectopic fat.

### Equipments for real-time measurement



Mouse brain operation equipment



Laser equipment for irradiating brain nuclei

## Q How will this research unit's achievements impact future society?

Various drugs are being developed for treating hypertension by acting on the peripheral nervous system, blood vessels, and the kidney. However, it is difficult to completely control blood pressure, and doctors always tell their patients to reduce their salt intake. This is because the role of the central nervous system in blood pressure control is not well understood. Similarly, with obesity, which is closely related to blood pressure, we do not know how fat is distributed to fat tissue and organs, such as the liver. If we could prevent hypertension and the accumulation of ectopic fat, it would greatly reduce the prevalence of metabolic syndrome, a cause of strokes and heart ailments. I believe that our unit's work to understand these mechanisms will lead to the development of new drugs and radically change medical treatments.

Contact us

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