Research Center for Medical Sciences
Division of Neuroscience

Fusao Kato, *Professor and Director*

General Summary

Historical overview

The Laboratory of Neurophysiology, created as the second division of the Department of Neuroscience in 2001, was the predecessor of the present Department of Neuroscience. Fusao Kato was appointed as the Director of the Laboratory and remained so after its renewal as the Department of Neuroscience in 2014. Since the beginning, this division has been the core of research and education in non-clinical neuroscience at Jikei University. The number of the people who have belonged to this Department, including the staffs and students, counts more than 120 and, notably, 21 PhD students wrote their thesis based on the research done in this division and have been doctorated in these 20 years.

Missions

We have the following three missions. 1) Education of neuroscience, neurophysiology in particular, to the undergraduate medical school students. 2) Education and training of PhD students in graduate school to help them advance their research and make an independent researcher in the medical field. 3) Advancing the state-of-art top-class neuroscience research, which would allow collaborations with the researchers in clinical areas to address unsolved issues in the clinics. These issues include, for example, chronic pain, neuronal plasticity and chronic diseases caused by stress. As many functions in the peripheral organs are monitored, regulated and integrated by the brain, approaches from neuroscience are necessary to solve a wide range of remaining problems associated with diseases in the whole body.

Scientific goals

A particular example of this unsolved clinical problem is pain. In particular, more than 15% of the population in advanced countries suffer from chronic pain, defined as pain lasting or recurring for more than three months. Without doubt, pain is a biologically necessary function that detects aversive situations in the body and urges reactions to improve the situation. At the same time, however, pain is highly distressing and disturbs the daily life and thoughts of patients. This situation is more difficult in patients with chronic primary pain, which is pain without an identifiable cause in the site where one feels pain. Lines of evidence including those from our Department indicate that the pain-associated neuronal plasticity the pain network in the brain is one of the mechanisms underlying such chronic pain, which is the central subjects of the Department of Neuroscience. To identify the mechanisms underlying the plastic changes, we use approaches at the molecular, cellular, synaptic, and network levels. These approaches include the patch-clamp analysis of synaptic transmission, the high-frame rate Ca^{2+} imaging, and behavioral anal-

yses combined with most updated "optogenetic" and "chemogenetics" approaches. These latter approaches enable to artificially control the activity of specific neuron ensemble, which we connect brain activity imaging with the high-magnetic field (9.4 T) small-animal MRI.

Social engagement
In addition to these missions, we also participate in a wide range of social activities, including board members of scientific societies, the member of the Science Council of Japan and committee members of the International Association for the Study of Pain.

Research Activities

In the 2019 fiscal year, we have examined the following subjects.
1. Identification of the role of the central amygdala in widespread hypersensitivity through selective activation and inhibition of GABAergic neurons using VGAT-cre rats and chemogenetics
2. Analysis of the activation patterns of the lateral parabrachial nucleus and the basolateral/central amygdalae using c-Fos immunohistochemistry in a newly developed, formalin-induced model of latent inflammatory pain
3. Analysis of the role of inflammatory factors in the plastic changes of the central pain network during the shift from acute pain to chronic pain
4. Development of methods of selective gene expression in the trigeminal ganglion using adeno-associated viruses
5. Evaluation of spontaneous/voluntary behaviours in animals with collagen-induced rheumatoid arthritis using a wheel-running paradigm and temperature-dependent choice
6. Visualization of neuronal activation and dopamine receptor expression in the brain reward system in response to acute itch using multiple single RNA imaging
7. Fast intracellular Ca imaging for comparing the neuroglial responses to exogenous oxytocin in the central amygdala of female mice from before pregnancy to before and after delivery
8. Behavioral analysis of the relationships of the social rank order of individual mice to glucose tolerance and insulin release regulation

Publications

Oto Y, Takahashi Y, Kurosaka D, Kato F. Alterations of voluntary behavior in the course of disease progress and pharmacotherapy in mice with collagen-induced arthritis. *Arthritis Res Ther.* 2019 Dec 12; **21**(1): 284. doi: 10.1186/s13075-019-2071-z. PMID: 31831067; PMCID: PMC6909634.
Arimura D, Shinohara K, Takahashi Y, Sugimura YK, Sugimoto M, Tsurugizawa T, Marumo K, Kato F. Primary Role of the Amygdala in Spontaneous Inflammatory Pain-Associated Activation of Pain Networks - A Chemogenetic Manganese-Enhanced MRI Approach. *Front Neural Circuits.* 2019 Oct 1; **13**: 58. doi: 10.3389/fncir.2019.00058. PMID: 31632244; PMCID: PMC6779784.