

Neuroscience of Sleep

Principal Investigator Masashi Yanagisawa

E-mail.address yanagisawa.masa.fu@u.tsukuba.ac.jp

URL: <https://wpi-iiis.tsukuba.ac.jp/>

<http://sleepymouse.tsukuba.ac.jp/>



Other Faculty Members

Professor Hiromasa Funato: funato.hiromasa.km@u.tsukuba.ac.jp

Assistant Professor Takeshi Kanda: kanda.takeshi.fu@u.tsukuba.ac.jp

Assistant Professor Chika Miyoshi: miyoshi.chika.ft@u.tsukuba.ac.jp

Assistant Professor Tomoyuki Fujiyama: fujiyama.tomoyuki.gf@u.tsukuba.ac.jp

Major Scientific Interests of the Group

- 1) Exploring genes regulating sleep/wake
- 2) Real-time visualization and manipulation of neuronal mechanisms controlling sleep/wake
- 3) Finding new drugs for sleep disorders

Projects for Regular Students in Doctoral or Master's Programs

- 1) Large-scale, forward genetic screening of genes for sleep/wake regulation in mutagenized mice
- 2) Screening for orexin receptor agonists
- 3) Analysis of sleep and wakefulness in genetically modified mice
- 4) In vivo real-time imaging of neuronal activities in freely behaving mice

Study Programs for Short Stay Students (one week – one trimester)

- 1) EEG/EMG electrode implantation and recording in mice
- 2) Patch clamp recording in cells and brain slices
- 3) Imaging of nerve cell activities in brain slices

Selected Publications

- 1) Funato H., Miyoshi C., Fujiyama T., Kanda T., Sato M., Wang Z., Ma J., Nakane S., Tomita J., Ikkyu A., Kakizaki M., Hotta N., Kanno S., Komiya H., Asano F., Honda T., Kim J.S., Harano K., Muramoto H., Yonezawa T., Mizuno S., Miyazaki S., Connor L., Kumar V., Miura I., Suzuki T., Watanabe A., Abe M., Sugiyama F., Takahashi S., Sakimura K., Hayashi Y., Liu Q., Kume K., Wakana S., Takahashi J.S., Yanagisawa M. Forward genetic analysis of sleep in randomly mutagenized mice. *Nature* 539: 378-383, 2016
- 2) Ogawa, Y., Irukayama-Tomobe, Y., Murakoshi, N., Kiyama, M., Ishikawa, Y., Hosokawa, N., Tominaga, H., Uchida, S., Kimura, S., Kanuka, M., Morita, M., Hamada, M., Takahashi, S., Hayashi, Y., Yanagisawa, M. Peripherally administered orexin improves survival of mice with endotoxin shock. *eLife* DOI: 10.7554/eLife.21055, 2016
- 3) Irukayama-Tomobe, Y., Ogawa, Y., Tominaga, H., Ishikawa, Y., Hosokawa, N., Ambai, S., Kawabe, Y., Uchida, S., Nakajima, R., Saitoh, T., Kanda, T., Vogt, K., Sakurai, T., Nagase, H., Yanagisawa, M. A non-peptide orexin type-2 receptor agonist ameliorates narcolepsy-cataplexy symptoms in mouse models. *Proc. Natl. Acad. Sci. USA* 114: 5731-5736, 2017
- 4) Kaushik, M.K., Aritake, K., Imanishi, A., Kanbayashi, T., Ichikawa, T., Shimizu, T., Urade, Y., Yanagisawa, M. Continuous intrathecal orexin delivery inhibits cataplexy in a murine model of narcolepsy. *Proc. Natl. Acad. Sci. USA* 115:6046-6051, 2018
- 5) Wang, Z., Ma, J., Miyoshi, C., Li, Y., Sato, M., Ogawa, Y., Lou, T., Ma, C., Gao, X., Lee, C., Yang, X., Zhou, S., Hotta-Hirashima, N., Klewe-Nebenius, D., Ikkyu A., Kakizaki, M., Kanno, S., Cao, L., Peng, J., Yu, Y., Funato, H., Yanagisawa, M., Liu, Q. Quantitative phosphoproteomic analysis of the molecular substrates of sleep need. *Nature* 558: 435-439, 2018
- 6) Honda, T., Fujiyama, T., Miyoshi, C., Ikkyu, A., Hotta, N., Kanno, S., Mizuno, S., Sugiyama, F., Takahashi, S.,

- Funato, H., Yanagisawa, M. A single phosphorylation site of SIK3 regulates daily sleep amounts and sleep need in mice. *Proc. Natl. Acad. Sci. USA* 115: 10458-10463, 2018
- 7) Miyoshi, C., Kim, S.J., Ezaki, T., Ikkyu, A., Kanno, M., Kakizaki, M., Yamada, M., Wakana, S., Yanagisawa, M., Funato, H. Methodology and theoretical basis of forward genetic screening for sleep/wakefulness in mice. *Proc Natl Acad Sci. USA* 116: 16062-16067, 2019
 - 8) Miyazaki, T., Kanda, T., Tsujino, N., Ishii, R., Nakatsuka, D., Kizuka, M., Kasagi, Y., Hino, H., Yanagisawa, M. Dynamics of Cortical Local Connectivity during Sleep-Wake States and the Homeostatic Process. *Cereb Cortex* 30: 3977-3990, 2020
 - 9) Park, M., Miyoshi, C., Fujiyama, T., Kakizaki, M., Ikkyu, A., Honda, T., Choi, J., Asano, F., Mizuno, S., Takahashi, S., Yanagisawa, M., Funato, H. Loss of the Conserved PKA Sites of SIK1 and SIK2 Increases Sleep Need. *Scientific Reports* 10: 8676, 2020
 - 10) Hirose, Y., Kitazono, T., Sezaki, M., Abe, M., Sakimura, K., Funato, H., Handa, H., Vogt, K., Yanagisawa, M. Hypnotic effect of thalidomide is independent of teratogenic ubiquitin/proteasome pathway. *Proc. Natl. Acad. Sci. USA* 117: 23106-23112, 2020
 - 11) Ogawa, Y., Miyoshi, C., Obana, N., Yajima, K., Hotta, N., Ikkyu, A., Kanno, S., Soga, T., Fukuda, S., Yanagisawa, M. Gut microbiota depletion by chronic antibiotic treatment alters the sleep/wake architecture and sleep EEG power spectra in mice. *Scientific Reports* 10: 19554, 2020