

Kimiko Shimizu, Ph.D.
清水 貴美子

Title: Professor

Address: 3190 Gofuku, Toyama 930-8555, JAPAN

University of Toyama

Organization for International Education and Exchange

Email: kshimizu@ctg.u-toyama.ac.jp

<https://researchmap.jp/kimikoshimizu>

<https://orcid.org/0000-0003-4943-2552>



Additional post

- Project Researcher in The University of Tokyo (Center for Disease Biology and integrative Medicine)

Email: shimizuk@g.ecc.u-tokyo.ac.jp

- Visiting lecturer in Toho University (Medical school)

Research Keyword

circadian rhythm, SCOP, Ras-MAPK, learning & memory, anxiety, neurosteroids, spine, biochemistry, molecular biology, behavior, mouse, monkey

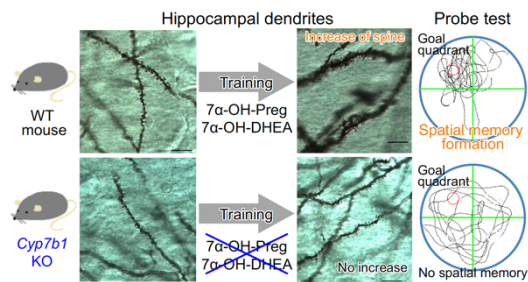
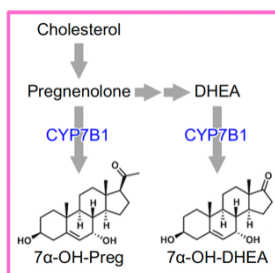
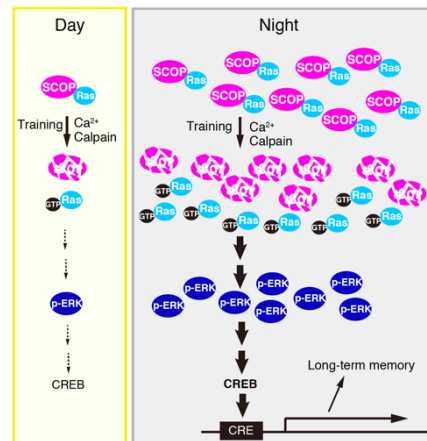


Research Overview

I investigate circadian changes in memory and emotion and their molecular mechanisms in mice. Using behavioral, biochemical, molecular biological, and genetic methods, I systematically elucidate memory and emotion's molecular and physiological functions through multi-level experiments from molecular to behavioral analysis.

Circadian clocks control long-term recognition memory formation in a circadian manner. Disruption of the central clock (hypothalamic suprachiasmatic nucleus) or the hippocampal clock (loss of clock molecules in the hippocampus) lose circadian change in long-term memory. Circadian variation in the amount of SCOP in the hippocampal lipid rafts regulates the K-Ras-ERK/MAPK-CREB pathway. It produces diurnal rhythm in long-term memory performance (Nat. Commun. 7, 12926, 2016). Anxiety-like behavior in mice also has a circadian rhythm. It is controlled by the circadian clock and SCOP in the amygdala (Sci. Rep. 6, 33500, 2016).

Novel neurosteroids, 7 α -hydroxypregnenolone and 7 α -hydroxydehydroepiandrosterone, are synthesized in the mouse brain after spatial learning. These steroids contribute to remote memory via remodeling dendritic spines in hippocampal neurons (iScience 23, 101559, 2020).



Selected Publications

- Shimizu K.*, Inoue S., Oishi T., Takada M., Fukada Y., and Imai H. Diurnal variation in declarative memory and the involvement of SCOP in cognitive functions in nonhuman primates. *Molecular Brain* 16: 31 (2023) DOI: 10.1186/s13041-023-01022-0
- Takeuchi S., Shimizu K., Fukada Y., and Emoto K. The circadian clock in the piriform cortex intrinsically tunes daily changes of odor-evoked neural activity. *Commun. Biol.*, 6: 332 (2023) DOI: 10.1038/s42003-023-04691-8
- Maehata K., Shimizu K.*, Ikeno T., Wang Q., Sakurai A., Wei Z., Pan Y., Takao T., Fukada Y.* Hippocampal 7 α -hydroxylated neurosteroids are raised by training and bolster remote spatial memory with increase of the spine densities. *iScience* 23, 101559 (2020) DOI:10.1016/j.isci.2020.101559
- Wang Q., Shimizu K., Maehata K., Pan Y., Sakurai K., Hikida T., Fukada Y., and Takao T.* Lithium ion adduction enables UPLC-MS/MS-based analysis of multi-class 3-hydroxyl group-containing keto-steroids. *Journal of Lipid Research* 61, 570-579 (2020) DOI: 10.1194/jlr.D119000588
- Shimizu, K.*, Fukada, Y. Stereotaxic surgery for suprachiasmatic nucleus lesions in mice. *Bio-protocol* 7: 2346 (2017) DOI:10.21769/bioprotoc.2346
- Shimizu, K*, Kobayashi, Y., Nakatsuji, E., Yamazaki, M., Shimba, S., Fukada, Y.* SCOP/PHLPP1 β mediates circadian regulation of long-term recognition memory. *Nature communications* 7: 12926 (2016) DOI:10.1038/ncomms12926
- Nakano, J., Shimizu, K.*, Shimba, S., Fukada, Y.* SCOP/PHLPP1 β in the basolateral amygdala regulates circadian expression of mouse anxiety-like behavior. *Scientific Reports* 6: 33500 (2016) DOI:10.1038/srep33500
- Shimizu, K., Mackenzie, S. M., and Storm, D.R. SCOP/PHLPP and its functional role in the brain. *Molecular Biosystems* 6: 38-43 (2010) DOI:10.1039/B911410F
- Shimizu, K., Phan, T., Mansuy, I.M. and Storm, D.R.* Proteolytic Degradation of SCOP in the Hippocampus Contributes to Activation of MAP Kinase and Memory. *Cell* 128: 1219-1229 (2007) DOI:10.1016/j.cell.2006.12.047
- Cheng, H-Y. M., Papp, J. W., Varlamova, O., Dziema, H., Russell, B., Curfman, J.P., Nakazawa, T., Shimizu, K., Okamura, H., Impey, S., and Obrietan, K.* microRNA Modulation of Circadian-Clock Period and Entrainment. *Neuron* 54: 813-829 (2007) DOI:10.1016/j.neuron.2007.05.017
- Shimizu, K., Okada, M., Nagai, K. and Fukada, Y.* Suprachiasmatic nucleus circadian oscillatory protein, a novel binding partner of K-Ras in the membrane rafts, negatively regulates MAPK pathway. *J. Biol. Chem.* 278: 14920-14925 (2003) DOI:10.1074/jbc.M213214200
- Takano, A., Shimizu, K., Kani, S., Buijs, R.M., Okada, M. and Nagai, K.* Cloning and characterization of rat casein kinase I ϵ . *FEBS letters* 477: 106-112 (2000) DOI:10.1016/S0014-5793(00)01755-5
- Shimizu, K.*, Okada, M., Takano, A. and Nagai, K. SCOP, a novel gene product expressed in a circadian manner in rat suprachiasmatic nucleus. *FEBS letters* 458: 363-369 (1999) DOI:10.1016/S0014-5793(99)01190-4
- Shimizu, K., Nagai, N. and Nakagawa, H.* An immunotoxin, anti-VIP antibody-ricin A chain conjugate, eliminates neurons in the hypothalamic suprachiasmatic nucleus selectively and abolishes the circadian rhythm of water intake. *Brain Res. Bull.* 41: 369-378 (1996)
- Shimizu, K., Hibino, H., Komenami, N., Nagai, N., Nagai, K. and Nakagawa, H.* Permissive effect of VIP on the hyperglycemic response induced by 2-deoxy-D-glucose. *Neurosci. Lett.* 175: 157-160 (1994)