

第47回最先端脳科学セミナー

Towards Organism-level Systems Biology by Next-generation Genetics and Whole-organ Cell Profiling.

演者:

上田 泰己 教授

東京大学大学院 医学系研究科 システムズ薬理学教室
理化学研究所 生命機能科学研究センター 合成生物学研究室 チームリーダー

日時:

2019. 2月22日 Fri. 17:00~18:30

場所:

薬学部研究棟 II 7階 セミナー室 8

要旨

The system-level identification and analysis of molecular and cellular networks in mammals can be accelerated by 'next-generation' genetics, defined as genetics that does not require crossing of multiple generations of animals to achieve the desired genetic makeup. We recently established a highly efficient procedure for producing knock-out (KO) mice by 'Triple-CRISPR' method that targets a single gene by triple gRNAs in the CRISPR/Cas9 system achieves almost perfect KO efficiency (96%-100%). We also established a highly efficient procedure for producing knock-in (KI) mice within a single generation, by 'ES-mouse' method, where we treat ES cells using three inhibitors to keep their potency and then inject such ES cells into 8-cell-stage embryos. These procedures dramatically shorten the time required to produce KO or KI mice from about a couple of year down to ~3 months. The produced KO and KI mice can be also systematically profiled at a single-cell resolution by whole-organ cell profiling realized by a tissue-clearing method 'CUBIC' and the advanced light-sheet microscopy. In this talk, I will describe the establishment and application of these technologies to analyze three states (NREM Sleep, REM sleep and awake) of mammalian brains and discuss the current challenges and future opportunities in next-generation mammalian genetics and whole-organ cell profiling toward organism-level systems biology.

- References**
1. Susaki et al. Cell, 157(3): 726-39, (2014).
 2. Tainaka et al. Cell, 159(6):911-24(2014).
 3. Susaki et al. Nature Protocols, 10(11):1709-27(2015).
 4. Sunagawa et al, Cell Reports, 14(3):662-77 (2016).
 5. Susaki and Ueda. Cell Chemical Biology, 23(1):137-57(2016).
 6. Tatsuki et al. Neuron, 90(1) : 70-85 (2016).
 7. Tainaka et al. Annual Review of Cell and Developmental Biology, 32, 713-741 (2016).
 8. Ode et al, Molecular Cell, 65, 176-190 (2017).
 9. Kubota et al, Cell Rep. 20, 236-250 (2017).
 10. Nojima et al, Scientific Reports. 9269 (2017).
 11. Shinohara et al, Molecular Cell. 67, 783-798 (2017).
 12. Ukai et al, Nat. Protoc. 12, 2513-2530 (2017).
 13. Murakami et al, Nat. Neuroscience, 21, 625-637 (2018).
 14. Niwa et al, Cell report, 24, 2231-2247 (2018).
 15. Tainaka et al, Cell report, 24, 2196-2210 (2018).

※ 本セミナーは、大学院医学薬学教育部「脳科学特論」の一環です。履修者は、レポートの提出が必要です。また、大学院の単位認定の対象となります。

主催：医・生化学 井ノ口 馨

第47回セミナー世話人：医・生化学 Seung-Min Um 内線 7227