東京大学グローバル COE 特別セミナー

理学系研究科 生物化学専攻セミナー

演者： Professor **Z. Josh Huang**, Ph.D.
Cold Spring Harbor Laboratory, New York, U.S.A.

演題：Towards a Genetic Dissection of GABAergic Circuits in Cerebral Cortex: Chandeliers light up the path

日時：平成 23 年 7 月 19 日（火）13：00〜14：00

場所：東京大学理学部 3 号館 3 階 327 号室

In the mammalian neocoertex, the delicate balance and functional dynamics of neural circuits are achieved through a rich repertoire of inhibitory control mechanisms. A key obstacle to understanding cortical inhibitory circuitry is unraveling the diversity of GABAergic interneurons. This diversity poses general questions in circuit analysis: how are diverse cell types generated and assembled into stereotyped local circuits, and how do they differentially contribute to circuit operations that underlie cortical functions ranging from perception to cognition? Using genetic engineering and the Cre/LoxP strategy in mice, we have generated and characterized ~20 Cre knockin driver lines that reliably target major classes and lineages of GABAergic neurons. More distinct populations are captured by intersectional strategy and by engaging lineage and birth timing mechanisms. Genetic targeting allows reliable identification, monitoring, and manipulation of GABAergic neurons, thereby enabling systematic and comprehensive analysis from cell fate specification, migration, connectivity, to their function in networks and behavior.

In particular, we have genetically captured chandelier cells (CHCs), the most distinctive class of cortical interneurons. CHCs exclusively innervate pyramidal cells at the axon initial segment, the site of action potential generation. CHCs may thus exert decisive control over pyramidal cell firing, thereby dynamically configure neural ensembles. Because of their exceptional stereotypy and specificity, genetic access to CHCs establishes a powerful experimental paradigm for studying their “life history”, from origin to their integration into cortical circuits. Conserved from mouse to man, CHCs have been implicated in several brain disorders including schizophrenia and epilepsy. A comprehensive analysis of CHCs not only will provide a key entry point to understanding the assembly and function of cortical circuitry but also will shed light into the pathogenic mechanisms of neuropsychiatric disorders. Current progress will be presented.

References

Fu, Y. and Huang, Z.J. (2010) *Proc. Nat. Acad. Sci. U.S.A.* **52**, 22699-22704.
DiCristo, G. et al. (2007) *Nature Neurosci.* **10**, 1569-1577.
Chattopadhayaya, B.et al. (2007) *Neuron* **54**, 889-903.

世話人：坂野　仁（内線 24396）