# 東北大学脳科学 GCOE セミナーのお知らせ

日時　2009 年 6 月 4 日（木）15:00〜16:30

会場　星陵キャンパス・1 号館 2 階　大会議室

演者　Daisuke Sakai, Ph.D.
Stowers Institute for Medical Research, Kansas

演題　Novel function for the Treacher Collins syndrome gene *Tcof1* in the mitosis of neural progenitors as well as the pathogenesis of microcephaly

Treacher Collins syndrome (TCS) is a congenital birth defect characterized by severe craniofacial defects. The disorder is caused by mutations in *TCOF1* which encodes protein known as Treacle that localizes to nucleolus and functions in ribosome biogenesis. In heterozygous *Tcof1* mice which model the severe form of TCS, ribosome biogenesis is impaired resulting in p53 checkpoint activation and dependent apoptosis in neural crest progenitors. In this study, we demonstrate that microcephaly is a phenotypic feature observed in our TCS mouse model as it is in many TCS patients. Furthermore, we have uncovered that endogenous Treacle is localized to the centrosome and kinetochore in mitotic cells. Knock-down of *Tcof1* causes abnormal chromosome alignment and delayed mitotic exit in HeLa cells. Consequently we observed abnormally scattered mitotic progenitor cells in ventricular zone, randomization of mitotic spindle orientation and reduced numbers of neuronal progenitor cells and neurons in the telencephalon of *Tcof1* mutant. These results suggest that the function of Treacle is important for proper mitotic cell division of progenitor cells and cell fate determination of daughter cells, thus providing a direct link between mitotic defects and microcephaly. Furthermore, we revealed that Treacle directly bound and co-localized with PLK1, an important regulator of mitotic progression. Taken together our results show that the novel complex formed by Treacle and PLK1 is essential for brain development through control of mitotic spindle orientation and progression of mitosis.

**References**:

Sakai D and Trainor PA., *Int J Biochem Cell Biol.*, 41(6): 1229-1232, 2009.
Jones NC *et al.*, *Nat Med.*, 14(2): 125-133, 2008.

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日時　2009 年 6 月 4 日（木）16:30〜18:00

会場　星陵キャンパス・1 号館 2 階　大会議室

演者　Tadashi Nomura, Ph.D.
Department of Cell and Molecular Biology, Karolinska Institute, Stockholm, Sweden

演題　Heterogeneity and plasticity of neurogenic niche cells in the adult subventricular zone

Neurogenesis continues at restricted regions in the adult mammalian brain. The subventricular zone (SVZ) of the lateral ventricle is one of the largest neurogenic zone in the adult forebrain, where multi-potential neural stem cells are maintained in the specialized cellular and molecular microenvironment, called niche. Here I will talk about two topics related on heterogeneity and plasticity of the SVZ niche cells. First, I will introduce a fate mapping study of SVZ neural stem/progenitor cells. Taking advantage of inducible *Cre-loxP* system, we identified distinct population of SVZ neural stem/progenitor cells, which contribute to different types of olfactory bulb interneurons. Next, I will introduce our recent data on plasticity of SVZ niche cells. Ependymal cells are ciliated epithelial cells that demarcate the SVZ from the lateral ventricle. We clarified that EphB2 tyrosine kinase receptor plays an essential role for the maintenance of ependymal cell identity. Interestingly, disruption of EphB-ephrin-B signaling induced mutual fate conversion between ependymal cells and SVZ astrocytes. Thus, SVZ niche components have high plasticity and remodeling capacity to respond local environmental changes. In this talk I will discuss molecular mechanisms conferring flexibility of SVZ niche cells, which are essential to maintain homeostasis in the adult neurogenic zone.

**Selected references**:

Carlén M *et al.*, *Nature Neurosci*., 12(3): 259-267, 2009.
Barnabé-Heider F *et al.*, *Nature Methods,* 5(2): 189-196, 2008.
Holmberg J *et al.*, *Genes Dev*., 19(4): 462-471, 2005.

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