グローバルＣＯＥセミナー

演者： Karen Zito, PhD

Center for Neuroscience, University of California Davis

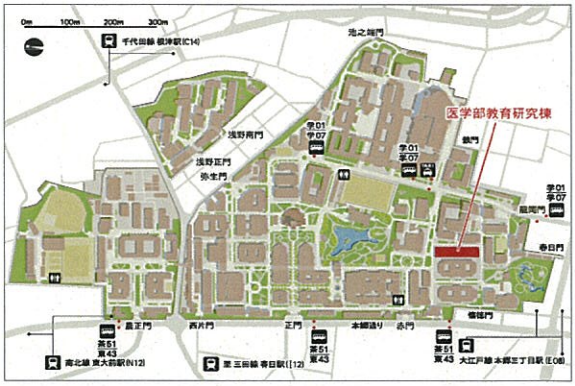
演題： Activity-dependent regulation of dendritic spine growth and stabilization

要旨：

Growth and stabilization of new dendritic spines is thought to play an important role in experience-dependent circuit plasticity in the mammalian brain. To gain insight into the mechanisms that lead to new spine growth, we examined the role of the proteasome in regulating outgrowth of new spines. Using pharmacological manipulations and two-photon time-lapse imaging of GFP-transfected hippocampal pyramidal neurons, we found that acute inhibition of the proteasome blocked activity-induced new spine growth. Remarkably, a single point mutation of serine 120 to alanine of the Rpt6 proteasomal subunit in individual neurons was sufficient to block activity-induced new spine growth. Signaling through NMDA receptors and CaMKII, but not PKA, is required to facilitate activity- and proteasome-dependent spine outgrowth. Our data support a model in which neural activity facilitates new spine growth via an NMDA receptor- and CaMKII- dependent increase in local proteasomal degradation. To investigate the mechanisms by which spines were stabilized following new spine outgrowth, we examined whether long-term potentiation (LTP), a key cellular mechanism thought to underlie learning, plays a role in selective stabilization of new spines. Using two-photon glutamate uncaging, we stimulated individual new spines with patterns that induced LTP and then monitored spine survival rates using time-lapse imaging. We found that an LTP-inducing stimulus increased the long-term survivorship of individual new spines, demonstrating for the first time a direct link between LTP and new spine stabilization. Our work provides new insights into the activity-dependent mechanisms that promote new spine growth and stabilization as circuits are modified during experience-dependent plasticity.

日時：平成24年2月14日(火)11：00～12：00

場所：東京大学医学部教育研究棟13階　第8セミナー室



皆様のご来聴を心よりお待ちしております。

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