グローバルＣＯＥ特別セミナー

演者： Dr. Chen Zhang, PhD

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演題： Presenilins are essential for regulating neurotransmitter release

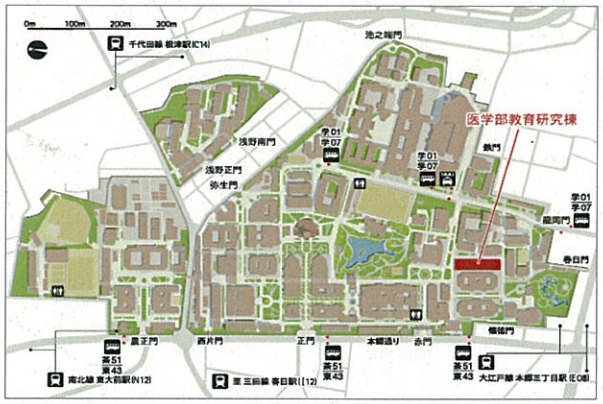
要旨：

Mutations in the presenilin genes are the major cause of familial Alzheimer's disease (AD). Loss of presenilin activity and/or accumulation of amyloid-β peptides have been proposed to mediate the pathogenesis of AD by impairing synaptic function. However, the precise site and nature of synaptic dysfunction caused by loss of presenilins remain unknown. Here we employ a genetic approach to inactivate presenilins conditionally in either presynaptic (CA3) or postsynaptic (CA1) neurons of the hippocampal Schaeffer-collateral pathway. We found that long-term potentiation (LTP) induced by theta burst stimulation is decreased after presynaptic but not postsynaptic deletion of presenilins. Moreover, presynaptic but not postsynaptic inactivation of presenilins impairs short-term plasticity and synaptic facilitation. Strikingly, depletion of endoplasmic reticulum calcium-stores by thapsigargin or inhibition of calcium-release from these stores by ryanodine receptor inhibitors mimics and occludes the effects of presynaptic presenilin inactivation. Collectively, these results reveal a selective role for presenilins in the activity-dependent regulation of neurotransmitter release and LTP induction via modulation of intracellular calcium-release in presynaptic terminals, and further suggest that presynaptic dysfunction might be an early pathogenic event leading to dementia and neurodegeneration in AD.

Keyword(s): Alzheimer's disease, Presenilins, Transmitter release, Calcium stores

日時：平成23年12月7日(水)15：00～16：00

場所：東京大学医学部教育研究棟2階　第1・第2セミナー室



神経生理学教室の Dr Tiago Branco と連続で開催します。
皆様のご参加を心よりお待ちしております。

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