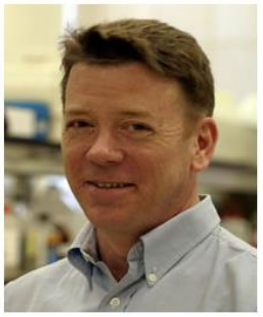
第334回 大阪大学神経科学懇話会

日時：平成27年11月26日（木）17:30 – 18:30

場所：医学部 講義棟　2階　第2講義室



演者：Dr. Paul Fraser

Professor, Department of Medical Biophysics,
Professor, Tanz Centre for Research in Neurodegenerative Disease,
Jeno Diener Chair in Neurodegenerative Disease, University of Toronto, Canada

演題：
SUMOylation Pathways in Synaptic Development and Neurodegeneration

要旨：

Small ubiquitin-like modifier-1 (SUMO1) plays a number of roles in cellular events and recent evidence has given momentum for its contributions to neuronal development and neurological disorders. We have generated a SUMO1 transgenic mouse model with overexpression in neurons in an effort to identify in vivo conjugation targets and the functional consequences of their SUMOylation. A high-expressing line was examined which displayed elevated levels of mono-SUMO1 and increased high molecular weight conjugates in all brain regions. Immunoprecipitation of SUMOylated proteins from total brain extract and proteomic analysis revealed a number of candidate proteins from a variety of functional classes, including a number of synaptic and cytoskeletal proteins. SUMO1 modification of synaptotagmin-1 was found to be elevated as compared to non-transgenic mice. This observation was associated with an age-dependent reduction in basal synaptic transmission and impaired presynaptic function as shown by altered paired pulse facilitation, as well as a decrease in spine density. The changes in neuronal function and morphology were also associated with a specific impairment in learning and memory while other behavioral features remained unchanged. These findings and others will be discussed which point to a significant contribution of SUMO1 modification on neuronal function which has implications for mechanisms involved in mental retardation and neurodegeneration.

主要論文

SUMOylation Is an Inhibitory Constraint that Regulates the Prion-like Aggregation and Activity of CPEB3. Cell Rep. 2015 Jun 23;11(11):1694-702.

SUMO1 Affects Synaptic Function, Spine Density and Memory. Sci Rep. 2015 May 29;5:10730.

ALS/FTD Mutation-Induced Phase Transition of FUS Liquid Droplets and Reversible Hydrogels into Irreversible Hydrogels Impairs RNP Granule Function. Neuron. 2015 Oct 28. pii: S0896-6273(15)00924-1

Impaired Cholinergic Excitation of Prefrontal Attention Circuitry in the TgCRND8 Model of Alzheimer's Disease. J Neurosci. 2015 Sep 16;35(37):12779-91.

Appoptosin-Mediated Caspase Cleavage of Tau Contributes to Progressive Supranuclear Palsy Pathogenesis. Neuron. 2015 Sep 2;87(5):963-75.

1α,25-Dihydroxyvitamin D3 reduces cerebral amyloid-β accumulation and improves cognition in mouse models of Alzheimer's disease. J Neurosci. 2014 May 21;34(21):7091-101.

連絡先： 大阪大学連合小児発達学研究科　分子生物遺伝学領域　　松﨑 伸介（内線3313/3848）