CAMD セミナー

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A152T human tau variant, genetically linked to Alzheimer's disease, induces behavioral, synaptic, and neuropathological changes without the formation of matured tau aggregates

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The microtubule-associated protein tau (MAPT) accumulates in the brains of patients with neurodegenerative disorders collectively known as tauopathies, including Alzheimer's disease (AD) and frontotemporal dementia-spectrum (FTD-s) disorders. However, disease-linked mutations in the gene that encodes tau in humans, *MAPT*, cause FTD-s, but not AD. Recently, a new *MAPT* variant encoding an A152T substitution was reported to augment the risk for both FTD-s and AD (Coppola et al, 2012; Kara et al, 2012; Lee et al, 2013). Therefore, A152T substitution is genetically linked not only to FTD-s, but also to AD. Investigating the *in vivo* effects of this variant could shed light on the role of tau in these distinct conditions and help identify pathogenic convergence points that may be amenable to therapeutic intervention. Dr. Maeda and his colleagues therefore generated transgenic mice with neuronal expression of A152T-variant hTau (hTau-A152T). To distinguish the effects of the variant from those of hTau overexpression *per se*, they generated transgenic mice expressing wildtype hTau (hTau-WT) at comparable levels. In this lecture, Dr. Maeda will present comparisons of these new models by biochemical, histopathological, electrophysiological, and behavioral analyses.