세미나 초록

발표주제	The Impact of Circadian Protein on Lipid-droplet Regulation in Microglia and Tauopathy
발표내용	In general, Alzheimer's disease (AD) patient loses their biological rhythm and have disrupted circadian system as well as at the molecular levels. Among the clock-related genes, REV-ERBα (*Nr1d1*) is considered as a circadian repressor that has been implicated in the regulation of lipid metabolism and expressed in microglia time-dependently. However, it remains unknown whether microglial REV-ERBα contributes to lipid regulation and further affects AD pathology. Here, we show that REV-ERBα knockout causes lipid-droplet (LD) accumulation with induction of Plin2, a marker of LD, in microglia and exacerbates tauopathy in a sex-dependent manner. Cultured REV-ERBα deficient microglia is sensitively responded to tau-mediated inflammation by tau-brain extract (TBE) treatment and less internalized tau aggregate with lipid expression. *In vivo*, microglial REV-ERBα depleted tau-expressing mice resulted in much more accumulation of phosphorylated-tau (pTau) with gliosis than control on both genetic P301S tau mutant and tau P301L viral injecting mice model, especially in male when female shows less expression of pTau in the hippocampus. These data highlight an importance of regulating lipid content by controlling microglial REV-ERBα activity on tauopathy and shed light on the mechanism underlying the increased risk of AD depending on gender.