第４８回 プロテオーム医療創薬研究会

【実施日】　2013 年９月 20 日(金)　14:00～15:00

【会　場】　横浜市立大学　福浦キャンパス
臨床研究棟　１階修士講義室

【来場者】　約 18 名

【内　容】

演題：「The effects of amyloid-beta on glutamatergic synapses」

講師：Helmut W. Kessels　Ph.D.
（Netherlands Institute for Neuroscience Department head）

発表要旨：The early stages of Alzheimer's disease pathogenesis are thought to occur at the synapse, since synapse deficits are the best correlate of memory dysfunction. Considerable evidence suggests that Aβ, a secreted proteolytic derivative of amyloid precursor protein (APP), is important for the early synaptic failure that is seen in Alzheimer's disease pathogenesis. However, the molecular target or signaling pathways through which Aβ conducts this synaptic failure remains unclear. We found that elevated Aβ requires ion-flux independent function of NMDA-receptors to produce synaptic depression. Furthermore, Aβ leads to selective loss of synaptic NR2B-responses effecting a switch in NMDA-receptor subunit composition from NR2B to NR2A, a process normally observed during development. Our results suggest that conformational changes of the NMDA-receptor NR2 subunit, and not ion flow through its channel, are required for Aβ to produce synaptic depression and a switch in NMDA receptor composition. This novel Aβ-induced signaling mediated by alterations in NR2B conformation may be targets for therapeutic intervention of Alzheimer's disease.