세미나 초록

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발표 주제	The modulation of γ-secretase in Alzheimer's disease
발표 내용	Alzheimer's disease (AD) is caused by synaptic and neuronal loss in the brain. One of the characteristic hallmarks of AD is senile plaques containing amyloid β-peptide (Aβ). Aβ is produced from amyloid precursor protein (APP) by sequential proteolytic cleavages by β-secretase and γ-secretase, and the polymerization of Aβ into amyloid plaques is thought to be a key pathogenic event in AD. Since γ-secretase mediates the final cleavage that liberates Aβ, γ-secretase has been widely studied as a potential drug target for the treatment of AD. γ-Secretase is a transmembrane protein complex containing presenilin, nicastrin, Aph-1, and Pen-2, which are sufficient for γ-secretase activity. γ-Secretase cleaves more than 140 substrates, including APP and Notch. Previously, γ-secretase inhibitors (GSIs) were shown to cause side effects in clinical trials due to the inhibition of Notch signaling. Therefore, more specific regulation or modulation of γ-secretase is needed. In recent years, γ-secretase modulators (GSMs) have been developed. To modulate γ-secretase and to understand its complex biology, finding the binding sites of GSIs and GSMs on γ-secretase as well as identifying transiently binding γ-secretase modulatory proteins have been of great interest.