

**NUS Graduate School for Integrative Sciences and Engineering
Research Project Write-up**

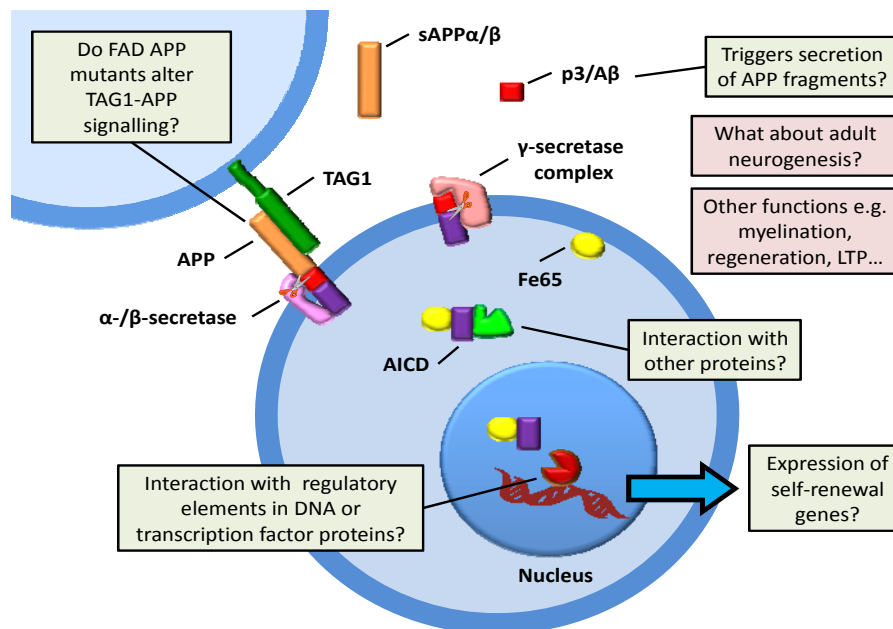
Title of Project : Amyloid precursor protein (APP) signaling in physiology and Alzheimer's disease (AD)

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Short Description

Proteolytic cleavage of amyloid precursor protein (APP) to produce the amyloid beta peptide (A β) contributes to the pathophysiology of Alzheimer's disease (AD). Some familial AD (FAD) cases are associated with mutations of APP that lead to increased A β deposition. A β is produced when APP is cleaved first by β -secretase and subsequently by γ -secretase. However, this cleavage process also releases an extracellular soluble APP (sAPP) fragment and an APP intracellular domain (AICD), which play a role in cellular signaling. We have recently found that a novel ligand of APP, TAG1, can trigger proteolytic cleavage of APP, leading to AICD-dependent regulation of neurogenesis (Ma et al., 2008; see Mattson and van Praag, 2008, for commentary). This novel signaling pathway opens new doors for investigation of the normal physiological and pathophysiological regulation and functions of APP. Some of the questions to be addressed are summarized in the diagram below.



Ma, QH, T Futagawa, WL Yang, XD Jiang, L Zeng, D Takeda, RX Xu, D Bagnard, M Schachner, AJ Furley, D Karagogeos, K Watanabe, **G S Dawe*** and Z Xiao* "A TAG1-APP signalling pathway through Fe65 negatively modulates neurogenesis". *NATURE CELL BIOLOGY*, 10, no. 3 (March 2008): 283-294. (*Corresponding authors)

Mattson, MP, van Praag, H "TAGING APP constrains neurogenesis". *NATURE CELL BIOLOGY*, 10, no. 3 (March 2008): 249-50.