

*39th Stem Cell Club meeting
jointly organised with the Neuroscience Club on*

Adult Neurogenesis

*(Organised by the Stem Cells Research Singapore Website Committee
<http://www.stemcell.edu.sg>)*

Date: September, 11th, 2008 (**Thursday**)

Time: 5:30 pm

Venue: Aspiration, Level 2M, Matrix

Hosts: Sohail Ahmed and Colin Blakemore

Time Title

Speaker

**5:30-6:00 Neuroregeneration of the adult
mammalian brain**

***Eyleen Goh**
Duke-NUS Graduate
Medical School,
Singapore*

**6:00-6:30 Alzheimer's signals constrain
neurogenesis**

***Zhi-cheng Xiao**
IMCB and SGH,
Singapore*

**6:30 - Wine and Cheese
(at Invitrogen facilities, 4th floor Chromos)**

Neuroregeneration of the Adult Mammalian Brain

Eyleen Goh, Duke-NUS Graduate Medical School, Singapore

Adult neurogenesis occurs throughout life in discrete regions of the adult mammalian brain. New neurons exist in the adult brains of many different species, and are continuously generated and integrated into the existing circuitry. But little is known about the molecular mechanisms regulating the development and integration of adult-born neurons including differentiation, growth, migration, path-finding and synapse formation. We used mouse genetics in combination with short-hairpin RNA technology and retroviral technique to study the molecular mechanisms of these newborn neurons. An understanding of the developmental processes of these newly generated neurons is not only important for deciphering the mystery in the adult brain, but also paving the way for cell-replacement therapy. Stem cells transplanted into the adult brain can then be effectively accustomed for different brain disorders. Neuroregeneration of the adult brain with exogenous or resident progenitor cells will also be discussed.

Ge S, Goh EL, Sailor KA, Kitabatake Y, Ming GL, Song H. GABA regulates synaptic integration of newly generated neurons in the adult brain. *Nature*. (2006) 439: 589-93.

Goh EL, Ma D, Ming GL, Song H. Adult neural stem cells and repair of the adult central nervous system. *J Hematother Stem Cell Res*. (2003) 12: 671-9.

Alzheimer's signals constrain neurogenesis

Zhi-cheng Xiao, Institute of Molecular and Cell Biology and Neurobiology Laboratory, Dept. of Clinical Research, Singapore General Hospital, Singapore 169608. (Tel: 65 6326 6195; Fax: 65 6321 3606)

Both Notch and the amyloid precursor protein (APP) are type I transmembrane proteins mediating cell fate selection. Their core signaling mechanisms involve Regulated Intramembrane Proteolysis (RIP) through γ -secretase-dependent cleavage. The release of amyloid precursor protein (APP) intracellular domain (AICD) may be triggered by extracellular cues through γ -secretase-dependent cleavage. AICD binds to Fe65, which may play a role in AICD-dependent signaling. However, the functional ligand was not characterized. We have identified TAG1 as a functional ligand of APP. Through extracellular interaction with APP, TAG1 both increases AICD release and triggers Fe65-dependent activity in a γ -secretase-dependent manner. TAG1, APP and Fe65 co-localize in the neural stem cell niche of the fetal ventricular zone. Neural precursor cells from TAG1^{-/-}, APP^{-/-} and TAG1^{-/-}&APP^{-/-} mice show aberrantly enhanced neurogenesis, significantly reversed in TAG1^{-/-} mice by TAG1 or AICD but not AICD mutated at the Fe65 binding site. Notably, TAG1 reduces normal neurogenesis in Fe65^{+/+} mice. Abnormally enhanced neurogenesis also occurs in Fe65^{-/-} mice but cannot be reversed by TAG1. These results describe a TAG1-APP signaling pathway that negatively modulates neurogenesis through Fe65.

1. Q.H. Ma, W.L. Yang, T. Futagawa, X.D. Jiang, Y. Takeda, R.X. Xu, D. Bagnard, M. Schachner, A.J. Furley, D. Karagogeos, K. Watanabe, G.S. Dawe, and Z.C. Xiao (2007) TAG-1 acts as a functional ligand for APP to trigger AICD transcriptional activation and negatively modulate neurogenesis. *Nature Cell Biology* (cover story) 10 (3), 283-294.
2. L. Lu, X. Chen, C.W. Zhang, W.L. Yang, Y.J. Wu, L. Sun, L.M. Bai, X.S. Gu, S. Ahmed, G.S. Dawe, and Z.C. Xiao (2007) Morphological and Functional Characterization of Predifferentiation of Oligodendrocyte-Like Cells from Human Bone Marrow Stromal Cells through Activation of F3/Notch Signaling in Mouse Retina. *Stem Cells* 26 (2), 580-590.
3. X.Y. Cui, Q.D. Hu, M. Tekaya, Y. Shimoda, B.T. Ang, D.Y. Nie, L. Sun, W.P. Hu, M. Karsak, T. Duka, Y. Takeda, L.Y. Ou, G.S. Dawe, F.G. Yu, S. Ahmed, L.H. Jin, M. Schachner, K. Watanabe, Y. Arsenijevic, and Z.C. Xiao (2004). NB-3/Notch1 pathway via Deltex1 promotes neural progenitor cell differentiation into oligodendrocytes. *J. Biol. Chem.* 279, 25858-25865.
4. Q.D. Hu, B.T. Ang, M. Karsak, W.P. Hu, X.Y. Cui, T. Duka, Y. Takeda, W. Chia, S. Natesan, Y.K. Ng, E.A. Ling, T. Maciag, D. Small, R. Trifonova, R. Kopan, H. Okano, M. Nakafuku, S. Chiba, H. Hirai, J.C. Aster, M. Schachner, C.J. Pallen, K. Watanabe, and Z.C. Xiao (2003). F3/Contactin acts as a functional ligand for Notch during oligodendrocyte maturation. *Cell* (cover story) 115, 163-175.