19th Stem Cell Club Meeting

Neural Specification

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

Date: January 17th, 2007 (Wednesday)
Time: 5:15 pm
Venue: Creation, Matrix building, level 4

Host: Paul Robson, ***GIS***

Time	Title	Speaker
5:15-5:55	Transcriptional control of midbrain dopaminergic neuron development.	Siew-Lan Ang ***NIMR, London, UK***
5:55-6:35	Characterization of the neurogenic programme activated by proneural transcription factors in neural stem cells.	François Guillemot ***NIMR, London, UK***
6:35 –	Networking Session	

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Transcriptional Control of Midbrain Dopaminergic Neuron Development

Siew-Lan Ang

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The transcriptional control of dopaminergic differentiation in the midbrain is intensively studied because of the role of midbrain dopaminergic (mDA) neurons in diverse neurological disorders. In recent years, several transcription factors including Otx2, Lmx1a, Engrailed1, Engrailed2, Msx1, Nurr1 and Pitx3 have been shown to regulate either specification or differentiation of mDA neurons. In contrast, the winged helix transcription factors Foxa1 and Foxa2 are required for both these processes. Using loss and gain of function studies in mice, our data show that Foxa1 and Foxa2 cooperate to regulate distinct molecular targets during specification and differentiation of mDA neurons. Interestingly, genetic evidence indicates that these functions require different gene dosage of *Foxa1* and *Foxa2*. Altogether, our data indicate that Foxa1 and Foxa2 regulate multiple phases of mDA differentiation in a dosage dependent manner. In this talk, I will also summarise recent progress in our understanding of the genetic program regulating mDA neuron differentiation.

References

Vernay, B., Koch, M., Vaccarino, F., Briscoe, J., Simeone, A., Kageyama, R. and Ang, S.-L. (2005). Otx2 regulates subtype specification and neurogenesis in the midbrain. J. Neurosci. 25, 4856-4867.

Kele, J., Simplicio, N., Ferri, A. L., Mira, H., Guillemot, F., Arenas, E., and Ang, S.-L. (2006). Neurogenin 2 is required for the development of ventral midbrain dopaminergic neurons. Development 133, 495-505.

Ang, S.-L. (2006). Transcriptional control of midbrain dopaminergic neuron development. Development 133, 3499-3506.

Characterization of The Neurogenic Programme Activated by Proneural Transcription Factors in Neural Stem Cells

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The generation of new neurons from neural stem cells is a complex process involving the tight coordination of multiple cellular activities, including cell cycle exit, initiation of neuronal differentiation and cell migration. Proneural genes have been associated with the regulation of neurogenesis in a number of experimental models. In the mouse embryonic forebrain, mutant analysis has established that these genes regulate multiple steps in neurogenesis, including the specification of the subtype identity of neurons, the initiation of their differentiation and their migration. Proneural genes therefore play an important role in integrating different cellular events into a coherent developmental programme of neurogenesis. The mechanisms underlying the diverse functions of proneural genes, which encode bHLH transcription factors, remain unknown. Using a combination of microarray analyses, promoter studies and bioinformatics, we have begun to progress in the identification of the regulatory pathways activated by proneural proteins during neurogenesis.