STEM CELL SOCIETY
SINGAPORE

STEM CELL CLUB

Tuesday, 01 February 2011
Breakthrough Theatrette, Matrix Building Level 4, 30 Biopolis Street, Singapore 138671

PROGRAMME

4.30 – 5.30pm

Prof Noel Buckley
Professor of Molecular Neurobiology & Head of Neuroscience Dept, Institute of Psychiatry, King's College London

"Neural stemness: What is it and why does it matter?"

5.30pm onwards

Network Social
Provided by Stem Cell Society Singapore

Network Social is for Members of Stem Cell Society Singapore ONLY.
For non-members who wish to attend, please sign up for membership at www.stemcell.org.sg/join_membership.php.

Hosted By

Dr Ng Huck Hui
Senior Group Leader, Genome Institute of Singapore

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"Neural stemness: What is it and why does it matter?"

ABSTRACT

The cardinal cells of the nervous system, neurons, astrocytes and oligodendrocytes are all ultimately derived from neural stem cells (NSCs). The earliest NSCs are the neuroepithelial cells lining the embryonic neural tube, which later transform into radial glia. Most radial glia subsequently undergo terminal differentiation into neurons or glia. However, a small population persist into adulthood where they occupy discrete neurogenic niches in the subventricular zone of the lateral wall of the lateral ventricle and the subgranular zone of the dentate gyrus. Analysing the interplay of signals, transcription and epigenetic pathways that define and regulate 'neural stemness' is essential to understanding the molecular basis of cell diversity within the nervous system. Equally, this understanding is key to successful deployment of NSCs in regenerative medicine strategies to combat neurological and neurodegenerative pathologies and trauma. This consensus view of neurogenic and non-neurogenic astrocytes is challenged by studies demonstrating that both immature parenchymal astrocytes and reactive astrocytes in the adult brain also have neurogenic potential. Recruitment of this latent neurogenic capacity could provide a novel potential therapeutic strategy for replacement of function lost in injury or disease, since, unlike neurogenic astrocytes, parenchymal reactive astrocytes are invariably present at the site of injury or degeneration.

Here, I will present an overview of our attempts to unravel the regulatory processes that underlie 'neural stemness'. These attempts cover a 'bottom up' one-gene approach, focussing on the role of a single transcription factor, REST; and a global 'top-down' approach aimed at identifying potential regulatory pathways by transcriptional profiling of neurogenic and non-neurogenic astrocytes.

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SPEAKER
Prof Noel Buckley

BIOGRAPHY

Noel Buckley is Professor of Molecular Neurobiology and Head of the Department of Neuroscience and Deputy Director of the MRC Centre for Neurodegeneration Research at the Institute of Psychiatry, King's College London. My research centres on transcriptional and epigenetic programmes that underwrite the development and maintenance of the nervous system. One transcription factor that has provided the focus for much of these studies is REST, a multifunction transcription factor that silences many genes in both neural and non-neural cells. In collaboration with Larry Stanton at GIS, we have identified several thousand target genes in embryonic stem cells and neural stem cells and their differentiated progeny. Together with Elena Cattaneo at the University of Milan we have also identified many REST protein coding and ncRNAs target genes that are dysregulated in Huntington's Disease, some of which may contribute to neuronal dysfunction and neuronal degeneration. Using this knowledge we are currently attempting to rescue aberrant gene expression using both *in vitro* and *in vivo* models of HD. As part of a consortium funded by a Wellcome Trust / MRC collaborative award, we are looking at genome-wide targets of novel transcription factors discovered in GWAS studies of motor neuron disease. Recently we have begun to use similar approaches to identify transcriptional and epigenetic pathways that underwrite neural stemness and neural differentiation by isolating specific interneuron lineages both *in vitro* and *in vivo*. Linked to this effort is collaboration with Jonathon Mill on a NIH Epigenomics Roadmap Initiative looking at epigenetic changes in the Alzheimer's brain.

Underpinning all of these efforts is a belief that understanding cell phenotype and cell state requires extensive knowledge of the transcriptome and epigenome. To date, most such studies have relied heavily on cell lines to deliver sufficient quantities of homogeneous material. Over the next few years, we will see the application of improved technologies that will allow us to dissect regulatory pathways in vivo based on isolation and analyses of small numbers of homogeneous cell populations derived from key developmental stages. Further, it is becoming increasingly clear that many of the regulatory pathways that are operative during development are the same as those that are dysfunctional in both neurodegenerative and neurodevelopmental disorders. It is this latter perspective that provides a clear translational link between studies of regulatory neural mechanisms and understanding disease aetiology.