20th Stem Cell Club Meeting

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

Date: February 14th, 2007 (Wednesday)
Time: 5:30 pm
Venue: Exploration, Matrix building, level 4

Host: Justine Burley, ***NUS***

Time	Title	Speaker
5:30-6:00	**Asymmetric divisions and the control of self-renewal vs. differentiation.**	William Chia ***Temasek Lifesciences Laboratory***
6:00-6:30	**The immune phenotype of hESC.**	Suzanne Kadereit ***Stem Cell Bank***
6:30 –	Networking Session	

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Asymmetric Divisions and the Control of Self-Renewal vs Differentiation

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Asymmetric cell division is a fundamental mechanism for generating cellular diversity during development. Much of our understanding of this process have been derived from the study of *Drosophila* embryonic neural progenitors, neuroblasts, which undergo a series of stem-cell-like asymmetric divisions; each division producing a larger apical daughter which retains a neuroblast identity and a smaller basal daughter, called ganglion mother cell (GMC), which can divide only once to generate two neurons. The distinct identities of the two daughters is mediated through the preferential segregation of the cell fate determinants Prospero (a transcription regulator), Numb (a molecule which controls receptor signalling) and Brat (a tumour suppressor) to just one (the GMC) daughter. The characteristic features of the neuroblast asymmetric division - basal localisation of the cell fate determinants, apical/basal orientation of the mitotic spindle, as well as the generation of an asymmetric mitotic spindle leading to the production of daughters of unequal size - appear all to be controlled by a complex of proteins which are themselves asymmetrically localised to the apical cortex of neuroblasts. These include the Drosophila homologues of the evolutionarily conserved protein cassettes Par3-Par6-aPKC and components of heterotrimeric G protein signalling (G i-Pins-Loco) as well as the non-conserved molecule Inscuteable which possibly links these protein cassettes together. Recent studies have shown that brain tissues derived from animals mutant for various components of the asymmetric division machinery when transplanted into normal adult hosts can undergo uncontrolled proliferation, invade other tissues and kill the host. In my talk I will present new data and discuss two issues:

1. How asymmetric division controls the proliferative potential of the daughter cells derived from neural progenitors. I will present data suggesting that one genetic hierarchy responsible (at least in part) for this control comprises of Aurora A, Numb and Notch. Another mode of control involves Polo kinase acting through Numb and Notch. In the context of our system, Polo, AurA and Numb appear to display properties that are reminiscent of tumour suppressors.
2. The apparent overlap in the regulation of cell cycle progression and asymmetry.

The immune phenotype of hESC

Suzanne Kadereit
Singapore Stem Cell Consortium, Stem Cell Bank

Despite great interest in human embryonic stem cells (hESC) for regenerative medicine, to date, only a few groups have investigated the immune properties of human embryonic stem cells. Reduced immune reaction in the presence of hESC reported by others, suggested that hESC are immunologically privileged. We therefore investigated the mechanisms underlying the reduced responses of human lymphocytes to hESC and showed that the presence of hESC could reduce T-cell proliferation against allogeneic and xenogeneic antigens, as well as against the stronger plate-bound anti-CD3 and anti-CD28 antibody stimulation. Decreased proliferation was not due to an increase in apoptosis, nor to an increase in $FoxP3^{+}$ regulatory T cells. Rather, the presence of hESC during stimulation resulted in an increase in surface CTLA-4 expressing T cell proportions. Concomitantly, there was an increase in IL-10 secretion by T cells in the presence of hESC. Both CTLA-4 and IL-10 are crucial negative regulators of T-cell immunity and our results suggest that the T-cell proliferation-modulating effect of hESC is mediated at least in part through upregulation of these two molecules. Interestingly, this effect appears to be mediated by membrane-bound molecules on hESC, rather than by soluble molecules secreted by hESC, as only fixed hESC were used.