22nd Stem Cell Club Meeting

Mesenchymal stem cells and cord lining cells

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

Date: April, 18th 2007 (Wednesday)
Time: 5:30 pm
Venue: Matrix, Aspiration Theatrette, Level 2M

Host: Lim Sai Kiang, GIS

Time	Title	Speakers
5:30-6:10	*Maintenance of adult stem cell self-renewal with heparan sulfate*	**Torben Helledie** *IMCB*
6:10-6:50	*Umbilical cord lining cells as potential therapeutic bioimplants for metabolic disorders*	**Kon Oi Lian** *NCC*
6:50-	**Wine and Cheese (at Invitrogen facilities, 4th floor, Chromos)**	

Maintenance of adult stem cell self-renewal with heparan sulfate

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Therapies that seek to utilize adult human mesenchymal stem cells (hMSCs) are hampered by insufficient numbers of these rare cells. However, the long-term *ex vivo* expansion of these cells that is necessary to attain therapeutic numbers directly correlates with a loss of multipotentiality due to a change in the microenvironment. Heparan sulfate (HS), a key component of the stem cell microenvironment, is known to protect growth factors from degradation and is necessary for the formation of specific activating receptor complexes. Here we show that a specific HS (HS-2), purified for its ability to potentiate the effects of fibroblast growth factor-2 (FGF-2), can, when added, significantly increase the expansion of hMSCs in an uncommitted state. Upon exposure to HS-2, hMSCs are stimulated to enter the cell cycle, resulting in an 8-fold increase in cell number and resultant colony forming units (CFU-Fibroblastic) after three weeks in culture without a loss of multipotentiality. Cell surface marker and gene expression profiling were then used to monitor the effect of HS-2 on long-term cultures of hMSCs, with the resulting stem cell signature showing that HS-2 protects against a temporal loss of stemness. Thus HS offers a novel means for potentiating the self-renewal of stem cells that is independent of exogenous applications of growth and adhesive factors that can otherwise compromise stem cell fate.

Umbilical cord lining cells as potential therapeutic bioimplants for metabolic disorders

Jaichandran Sivalingam, Sze Sing Lee, Wai Har Ng, Siew Hong Leong, Shruti Krishnan, Toan Thang Phan* and **Oi Lian Kon**
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Cell-based therapy of metabolic disorders that is safe, efficacious, durable, simple and physiological remains a future prospect. We are investigating transfected human umbilical cord-lining cells as potential candidates having several of the aforementioned properties for treatment of two model disorders, viz. haemophilia A and diabetes mellitus. Our efforts currently focus on defining genomic integration sites, evaluating genomic and genetic sequelae of site-specific integration in umbilical cord-lining cells, and exploring conditions that favour engraftment *in vivo*. In this presentation, I will summarise our findings to date on locations of integration sites, and comparisons of the genomes and transcriptomes of wild type and stably transfected mesenchymal and epithelioid cord-lining cells. Employing ligation-mediated PCR and DNA sequencing, classical and spectral karyotyping, high-resolution copy number analysis and global transcriptional profiling, our data suggest that site-specific integration is likely to have superior biosafety compared to transduction with retroviral vectors. Preliminary data show the capacity of stably transfected cord-lining cells to secrete factor VIII and insulin efficiently. Comparative transcriptional profiling has identified a subset of genes expressed in umbilical cord-lining cells that are glucose-stimulated and whose promoters may thus endow these cells with the ability to physiologically regulate the expression of an insulin transgene, and thus function *in vivo* as surrogate β cells.