Stem Cell Club

Stem Cells and Cellular Therapies

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

Date: 15th December 2005, Thursday
Time: 5.45-8.00pm
Venue:Breakthrough theatrette, Matrix, Biopolis

Time	Title	Speaker
5.45-6.15	*Scale up Strategies to bring Embryonic Stem cells into therapeutic and pharmacological applications*	Robert Zweigerdt (ES Cell International)
6.15-6.45	*Cell-based Treatment of Diabetes Mellitus: Of Mice and Pigs*	Kon Oi Lian, (NCC)
6.45-8.00	*Cheese and Wine*	

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Scale up Strategies to bring Embryonic Stem cells into therapeutic and pharmacological applications

Alan Coleman and **Robert Zweigerdt**, ES Cell International, Singapore.

Embryonic Stem (ES) cells constitute a promising source for the generation of differentiated cell types (neural lineages, beta cells and bona fide cardiomyocytes) for development of tissue replacement therapies, cell type specific drug discovery screens, and drug toxicological assays.

It is well established that Embryoid Body (EB) formation is a successful strategy to induce differentiation of ES cells in vitro. With special attention to cardiomyocyte induction we and others recently demonstrated efficient ES cell differentiation in long term "floating EB" suspension cultures. (Zandstra et al. Tissue Eng 2003; Zweigerdt et al. Cytotherapy 2003).

To more readily generate a large scale approach we have developed a system that allows EB formation in a fully controlled, stirred 2 litre bioreactor following inoculation with mouse ES cells (Schroeder et al., Biotechnol Bioeng 2005). By optimizing stirrer speed, high density suspension cultures containing $12.5x10^6$ cells/mL were obtained. To establish the utility of this protocol to generate therapeutic numbers of differentiated cells, ES cells expressing a transgene comprised of a cardiomyocyte-restricted promoter driving expression of an antibiotic resistance gene were utilized. Antibiotic treatment of differentiating ES cells resulted in the generation of essentially pure cardiomyocyte cultures, with a total yield of $1.28x10^9$ cells/2 litres.

The potential utility of this protocol, issues relevant for its transfer to human ES cells, as well as alternative strategies will be discussed.

Cell-based Treatment of Diabetes Mellitus: Of Mice and Pigs

Kon Oi Lian, National Cancer Centre, Singapore.

Development of cell-based treatment of diabetes mellitus is motivated by the high morbidity that this chronic disease continues to exact in end-organ damage e.g. blindness from retinopathy, renal failure from diabetic nephropathy, other macro- and microvascular injury and neuropathy. Current efforts are focused mainly on allogeneic islet transplantation, directing the differentiation of stem cells into islets and transdifferentiation of somatic cells into β cells.

We have adopted a different approach by selecting the adult hepatocyte as a potential cellular vehicle for quasi-physiological regulated insulin replacement. I will outline the rationale of our work and present data of partial correction of murine diabetes with syngeneic hepatocytes that led us to adapt this approach to implantation of autologous human insulin-secreting hepatocytes in diabetic pigs. Our current treatment protocol combines surgery, cell isolation, transfection with a non-viral vector and re-implantation in a procedure that is completed within a single 5-hour session. Data from an ongoing study of 12 diabetic Yorkshire pigs indicate partial but significant metabolic correction for at least 10 months as assessed by several indices i.e. fasting glycemia and triglyceridemia, fasting serum human C-peptide, serum fructosamine, acute blood glucose and C-peptide responses to intravenous glucose tolerance testing, and body weight gain. Preliminary observations suggest that implantation of insulin-secreting autologous hepatocytes may also protect diabetic pigs against target organ damage compared to untreated diabetic pigs.