JAMES RENNIE BEQUEST

REPORT ON EXPEDITION/PROJECT/CONFERENCE

Expedition/Project/Conference Title: Keystone Symposium: From Stem Cells to Therapy.....

Travel Dates: March 29th – April 3rd 2003. .....

Location: Steamboat Springs, Colorado, USA .....

Group Member(s): Yasmin Babaie.....

Aims: To learn about the breadth of research being carried out in the field of stem cell research.
To present a poster of my work to date and get feedback on it.

OUTCOME (not less than 300 words):-

Travel Grant Report

Each year, the Keystone Symposia conferencing organization holds a conference based on the biology and applications of stem cell research. The fast development of this area of research has meant that increasingly, scientists can look to the future and the potential therapeutic uses of stem cells.

In previous Keystone stem cell conferences, the emphasis has been more on the use of embryonic stem cells for regenerative medicine. An increase in research hinting that adult stem cell populations may be more plastic than previously thought, together with the restrictions now in place on human embryonic stem cell research in a number of countries, meant that this year there was an increased focus on the isolation, expansion and manipulation of adult stem cells.

Around 650 people attended the conference. There were nearly 50 speakers and 300 posters presented over the 5 days. Finding people you wanted to speak to was very difficult despite the compulsory display of name tags! The structure of the conference was based around its location at the ski resort of Steamboat Springs. After a morning session, we were free until 5pm every day to hit the slopes! For a ski novice like myself, the conditions could not have been better! There had been fresh snow the day we arrived and we had good sun almost every day which made my first voyage down the slopes much more enjoyable…although it did feel quite weird skiing in a T shirt with the sun blazing all day!

This left most of the delegates sunburnt, physically exhausted but mentally buzzing for the evening sessions. These were followed with 3-hour poster sessions late into the evening. Even with all that time, I felt I barely had a chance to see all the posters I was interested in, which was a testament to the quality of the work on display.

Robert Langer was first to speak at the conference. He is Professor of Chemical and Biomedical Engineering at MIT and won the Draper Prize (the Nobel prize equivalent of the engineering world) for bioengineering of drug delivery systems in 2002. This is a great achievement if you consider

that in 2001 the winners were the inventors of the Internet! He highlighted the huge demand for tissue transplants and the need for structural organization of cells before transplantation. His research is based on the development of biodegradable polymer scaffolds that would provide a dynamic surface for cell growth and differentiation.

Next to speak were Martin Pera and James Thomson. Martin Pera gave a very interesting presentation on the gene expression profile of human embryonic stem (ES) cells. Particular points of interest included the varying expression of key genes for the maintenance of ES pluripotency e.g. Oct3/4 across a phenotypically uniform cell colony. James Thomson, who hit the headlines as the first person to isolate human ES cells, spoke about genetically manipulating human ES cells via homologous recombination – another world first.

Continuing the human ES theme was Melissa Carpenter, formerly of the Geron Corporation, who spoke about the variability between different human ES cell lines with respect to gene expression, cell dynamics and genomic stability. Ronald Goldstein followed with promising results from the transplantation and successful integration and differentiation of human ES cells into the chick embryo.

There was a definite focus on haematopoiesis and haematopoietic progenitor cells this year. Of particular interest to me was the talk given by Kyunghee Choi on her research to identify and isolate the haemangioblast: the putative bipotential precursor of all haematopoietic and vascular tissues. Her team has an *in vitro* culture assay for a cell believed to be the haemangioblast. She reported further characterisation of this cell and suggested a pathway for differentiation of the haemangioblast and its behaviour under different stimuli. The expression pattern of the SCL/tal 1 gene during development was discussed by her and several others as an important gene for haemangioblast identity and progenitor commitment.

The focus of the conference shifted gradually from ES cells and ES derived progenitors to adult stem cells, their surprising plasticity and how to manipulate them.

The Side Population cell identified on the basis of its ability to efflux Hoechst stain was a popular research area both in the talks and posters presented. SP cells were being isolated from a variety of tissues and their plasticity was being investigated.

Stem cell niches in mammalian epidermis, the germline and the intestinal epithelium were all discussed as were the growth factors involved and other stimuli that activated the niche and the signaling pathways that were involved in self-renewal. The Wnt signaling pathway in particular, was implicated.

Steve Goldstein discussed the important but often overlooked area of mechanical stimulation of cells. This is a phenomenon which is common *in vivo* but that is rarely recreated *in vitro*. It was clear that fluid shear, the effects of pressure and direct strain in the form of surface traction can be crucial for the stimulation of biochemical signaling cascades.

The topics for discussion then progressed to actual attempts at tissue engineering and its challenges.

The immunological properties of human ES cells were discussed by Micha Drukker, as were the ways in which these properties could be manipulated to enable more successful transplantation of human ES cells. There were also several more technical talks on scalable protocols for the controlled differentiation of ES cells.

The final session of the conference brought us all back to what our ultimate goal is: regenerative medicine. Gregory Korbutt discussed the derivation of pancreatic islet cells from various sources for the treatment of diabetes. Curt Freed ended the conference with a talk on the potential for cell-based therapies for human neurodegenerative disorders with a focus on Parkinson's disease. He included in his talk, before and after videos of patients who had received cell-based treatments for Parkinson's disease that was no longer responsive to drug treatment – the improvements were astonishing and very encouraging.

There were so many impressive posters that I cannot mention all the interesting ones! However the highlights for me included all the new differentiation work being carried out with human ES cells. A number of groups presented data on the successful generation of cardiomyocytes (with regular beating rhythms!), an array of haematopoietic cell types from the lymphoid and myeloid lineages as well as neuronal cells and pancreatic islet cells. There were several posters on the characterisation of different human ES cell lines and adult stem cell populations using affymetrix chips, as well as work on showing the plasticity of adult stem cell populations

There were some posters on the role of physical forces on the growth of cells in culture. If stem cell technology is going to be scaled up, physical stimulation may be an easier and less expensive route to stimulating pathways for differentiation as opposed to the addition of numerous expensive growth factors. Involving physical forces on cells may mimic the *in vivo* setting of these cells as well, affording scientists a better chance of differentiating cells that have responded to similar signals to what they would have been subject to in the body, thus making them more suitable for transplantation and engraftment.

My awareness of the range of research being carried out in the field of stem cell biology and transplantation is much greater after having attended this conference. It also provided me with a great opportunity to speak to some of the most eminent scientists in my field of research. It gave me a chance to discuss my own work and get some invaluable technical advice and constructive criticism on what I am trying to achieve. My only warning to future attendees of this conference is: prepare to be in awe of the quality and quantity of work that is out there. It can be somewhat overwhelming! My attendance at the conference would not have been possible without the support of the James Rennie Bequest that I would like to thank for its generosity.