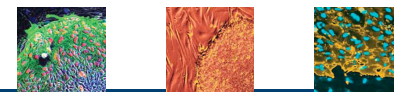


# President's Report

**Alan Trounson**

**September 25, 2008**

**Agenda Item No. 6**



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# New Developments in Stem Cells (1)

## Immunosuppressive therapy mitigates immunological rejection of human embryonic stem cell in mice

Swijnenburg RJ, Schrepfer S, Govaert JA, Cao F, Ransohoff K, Sheikh AY, Haddad M, Connolly AJ, Davis MM, Robbins RC, Wu JC.

Proc Natl Acad Sci U S A. 2008 Sep 2;105(35):12991-6. [Medicine Stanford U](#)

Survival of hESC after transplant is significantly limited mice with a normal immune system. Repeated transplantation resulted in accelerated hESC death, suggesting an adaptive immune response.

Immunosuppression was shown to significantly extend graft survival.

These data demonstrate that strategies for immune tolerance are needed for clinical application of ESC therapies.



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## New Developments in Stem Cells (2)

### Non-insulin producing pancreatic cells reprogrammed to insulin producing beta cells in live mice

**Qiao Zhou, Juliana Brown, Andrew Kanarek, Jayaraj Rajagopal & Douglas A. Melton** Nature Aug 27, 2008: Harvard Stem Cell Institute

Nine individual adenoviruses expressing 9 different transcription factors were pooled and injected into the pancreas of immune compromised mice to determine if they would induce exocrine cells to form new insulin producing cells. If three of these transcription factors are expressed in the infected cells they reprogrammed pancreatic exocrine cells in adult mice into cells that closely resemble insulin producing beta cells. In diabetic mice this cocktail of transcription factors returned the mice towards a normoglycaemic state.

This a gene therapy that has implications for stem cell therapies and is potentially an important new step towards the treatment of diabetes.



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## New Developments in Stem Cells (3)

### Transplanted human embryonic stem cell-derived neural precursors protected animal model of multiple sclerosis

Aharonowiz M, Einstein O, Fainstein N, Lassmann H, Reubinoff B, Ben-Hur T. PLoS ONE. 2008 Sep 5;3(9):e3145. Hadassa Uni, Israel

Transplanted hESC-derived neural progenitor cells significantly reduced the clinical signs of experimental autoimmune encephalomyelitis (EAE) in a mouse model of MS. Transplanted neural progenitors migrated to the host white matter, but differentiation to mature oligodendrocytes and remyelination were negligible. However, CNS inflammation and tissue injury showed an attenuation of the inflammatory process in transplanted animals, which was related to the reduction of both axonal damage and demyelination – an improvement in the autoimmune component of MS.

Hence the therapeutic effect of hESC transplantation was not related to graft or host remyelination but was mediated by an immunosuppressive neuroprotective mechanism. Similar observations have been made using mesenchymal stem cells (Bernard), suggesting such control studies should be conducted.



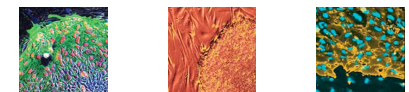
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# New Developments in Stem Cells (4)

## Assessment of drug induced fetal toxicity using human embryonic stem cells

Mehta A, Konala VB, Khanna A, Majumdar AS. Cell Biol Int. 2008 Aug 20  
Regenerative Medicine Group, Navi Mumbai-400 701, India.

They tested various grades of embryotoxic compounds using an assay based on real time gene expression analysis to check the alterations in germ layer (endoderm, mesoderm and ectoderm) marker expression upon drug treatment. The results showed that assays involving 12 genes in differentiating hES cells could serve as a reliable, sensitive and robust method to assess the embryotoxic potential of compounds. 9-10 genes were altered by embryotoxic compounds, 5-7 were dysregulated by weak embryotoxic compounds and 1-2 by non-toxic compounds.



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# New Developments in Stem Cells (5)

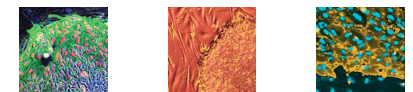
## Gene expression profiles can define classes of human stem cell lines

Müller FJ, Laurent LC, Kostka D, Ulitsky I, Williams R, Lu C, Park IH, Rao MS, Shamir R, Schwartz PH, Schmidt NO, Loring JF.

Nature. 2008 Aug 24. Scripps Research Institute

A database of global gene expression profiles was created and analyzed (called the 'stem cell matrix') that enables the classification of cultured human stem cells in the context of a wide variety of pluripotent, multipotent and differentiated cell types. A clustering method was used to categorize a collection of approximately 150 cell samples. It showed pluripotent stem cell lines group together, whereas other cell types, including brain-derived neural stem cell lines, are very diverse. Bioinformatic analysis uncovered a protein-protein network (PluriNet) that is shared by all pluripotent cells (embryonic stem cells, embryonal carcinomas and induced pluripotent cells).

These data are useful in characterizing pluripotent cells and deviations from true ESC form.



# Personnel

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**John Robson**

**Vice President, Operations**

(McGill University)

**Amy Cheung**

**Senior Administrative Assistant**

(formerly with Australian Trade Commission)



# President's Priorities

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- Stem Cell Awareness Day
- CIRM Grantees Conference
- Cancer Workshop
- GWG Tools and Technologies Review
- IP Workshops
- Revision of Strategic Plan
- International Connections
- Staff Issues – General Counsel
- Completing Major Facilities Contracts
- Translation and Disease Team Discussions





# President's Priorities

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## Update on International & National Linkages

- **Completed MOU's**



# Collaborative Funding: Intellectual Property Issues (1/2)



- Scientific teams must negotiate re: IP rights and responsibilities **but:**
  - Californians must remain fully bound by CIRM IP Regulations
  - Non-Californians should adhere to Access Plans and CalRx Pricing when acting in California
  - March-In Rights should be secure
  - CIRM and Co-funder will review IP Agreements pre-funding



# Collaborative Funding: Intellectual Property Issues (2/2)



- Detailed IP requirements may vary depending on Co-Funder
  - CIRM takes no position on revenue sharing for non-Californians
  - CIRM will receive adequate reporting (project and budget)



# Workshops Completed



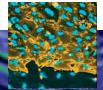
- **Toxicology – report available on CIRM website**
- **Cancer Stem Cell Workshop**
- **IP Regs & Grant Writing Public Sessions**



# CIRM Workshop – Cancer Stem Cells



- Purpose: Input on:
  - CIRM's involvement in CSC research
  - Cooperative program between CA and Canada
- Participants: Pre-eminent California cancer researchers
- Consensus on following:
  - Expansion of CIRM support for CSC, through existing and targeted programs
  - Encourage and facilitate research collaborations that enhance knowledge and clinical progress (compatible with CIRM policies)
  - A CIRM/Canada collaboration should be vigorously pursued



# Upcoming Workshops



- **Cell Production Facilities – Nov 3, 2008**
- **Immunology – Feb 2009**
- **UK MRC-Cal-CIRM – 2009**



# CIRM Grantee Meeting



- Over 400 registrants from throughout California including international speakers and guests and ICOC Board Members
- Kick-Off Event at the new Jewish Museum attracted over 250 guests
- Science Writers Workshop attended by over 30 journalists from all major wires, local press and scientific press
- Exciting networking opportunities among CIRM faculty, scholars, and trainees
- Collaborations established among scientists
- 130 posters and 30 presentations of primary, unpublished data (abstracts available)



# Grant Reviews

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- **COMPLETED GRANT REVIEWS**
  - Tools & Technologies (Double Review)
  
- **UPCOMING GRANT REVIEWS**
  - Training Grants II (CIRM Scholars)
  - Bridges to Stem Cell Research





# RFA

- **Early Translational Research I**
  - RFA Released – August 2008
  - GWG Review – February 2009
  - ICOC Approval – May 2009



# Upcoming RFAs

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- **Disease Team Research Awards**
  - RFA to be released – February 2009
  - GWG Review – Summer 2009
  - ICOC Approval – Late Summer/Fall 2009

