



President's Report

Alan O. Trounson

ICOC Meeting – December 2011

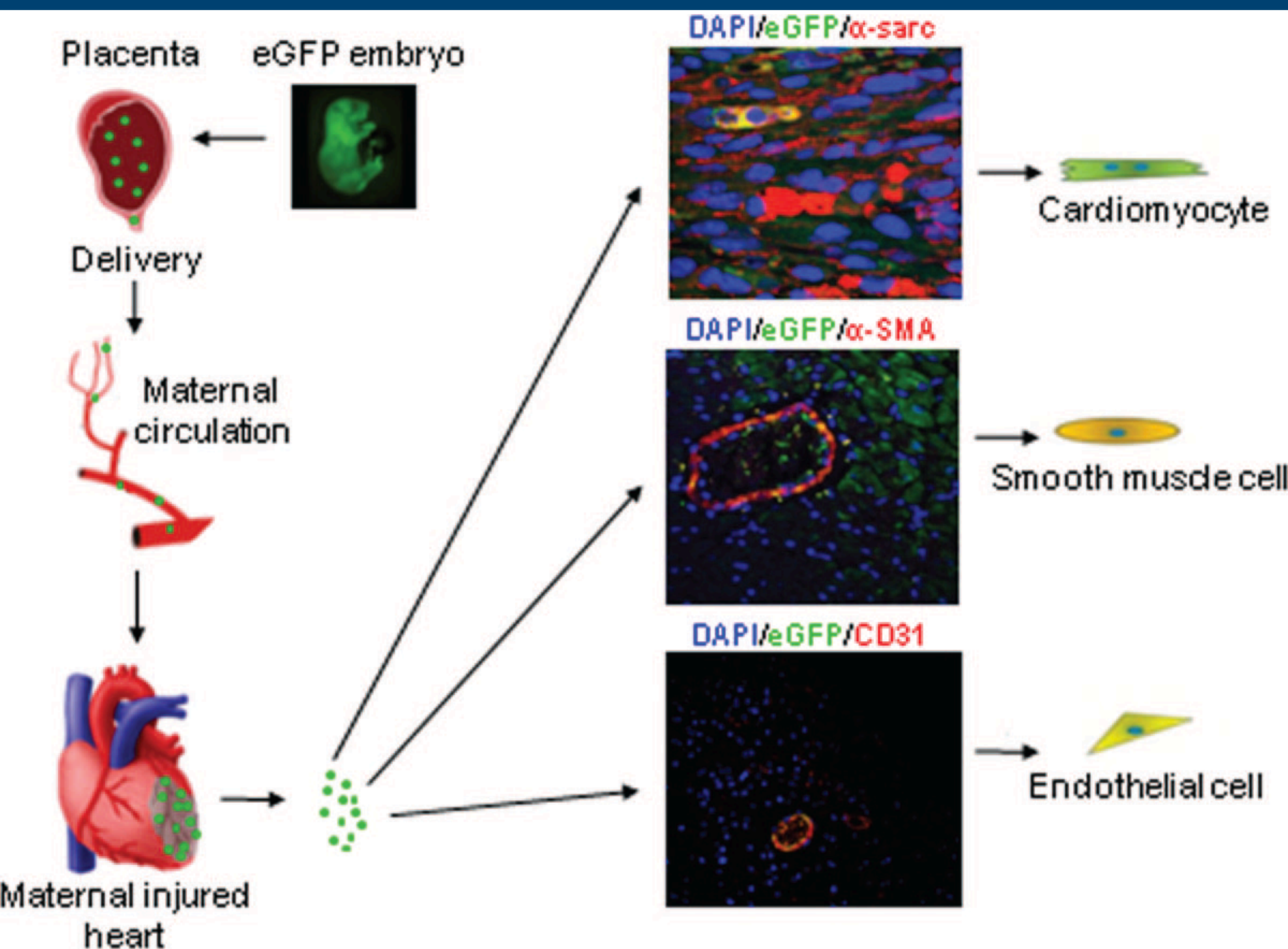
Los Angeles, CA

Fetal Cells Traffic to Injured Maternal Myocardium and Undergo Cardiac Differentiation. Kara et al. Mt Sinai School Med NY. Circulation Res. Dec 9 2011



- Fetal cells enter the maternal circulation and persist for decades.
- In mice, GFP labelled fetal cells home to injured maternal hearts (induced myocardial infarction – day 12 gestation) and differentiated into endothelial cells, smooth muscle cells, and cardiomyocytes (1 or 2 weeks after induction of MI).
- There were 120x more GFP cells in maternal heart than controls and 20x more than sham operated mice at 1 week (less at 2 weeks but 12x and 8x, respectively).
- GFP cardiomyocytes beat in sync with neighboring maternal cardiomyocytes.
- Fetus is protecting the mothers heart (note 50% of women recover from heart failure spontaneously peripartum – highest of any known group with cardiomyopathy)
- 40% express Cdx2 – associated with trophoblast stem cells considered to be solely of placental origin.

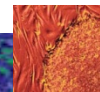




Using iPSC-derived neurones to uncover cellular phenotypes associated with Timothy syndrome. Pasca et al., Dept Neurobiology Stanford. Nature Med. Nov 27 2011

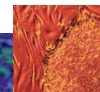


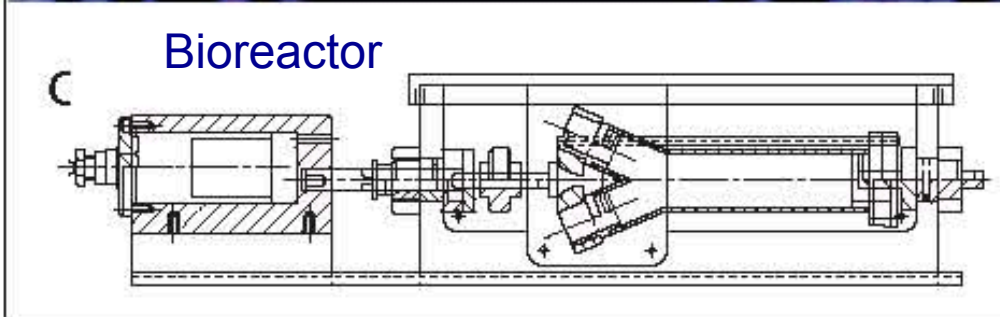
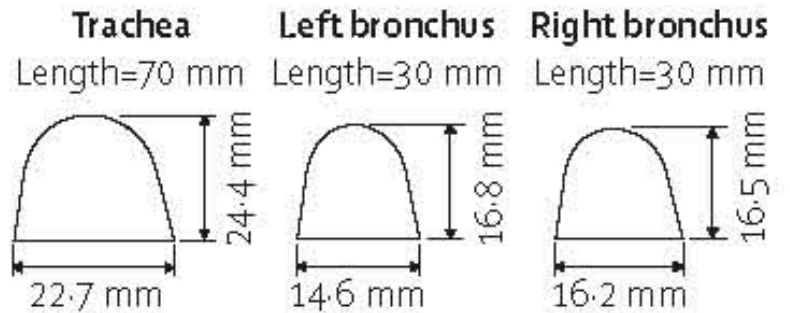
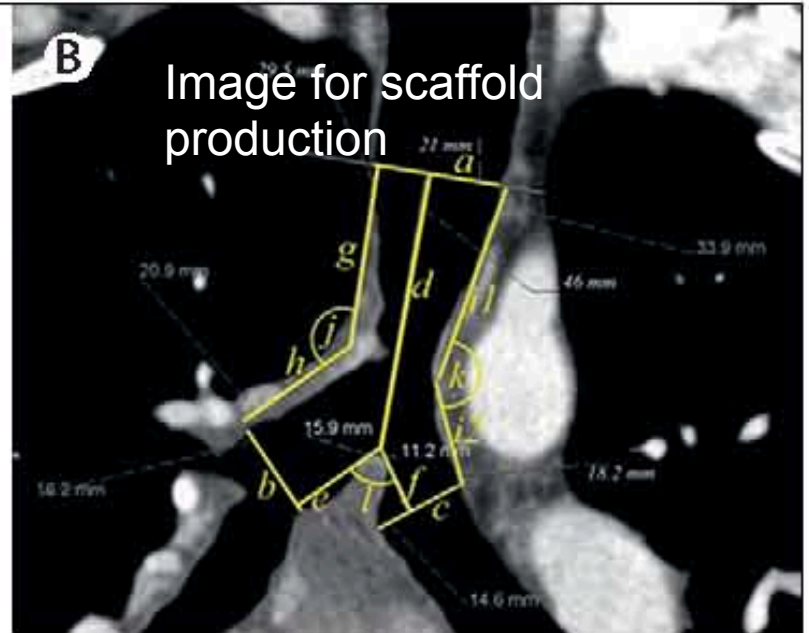
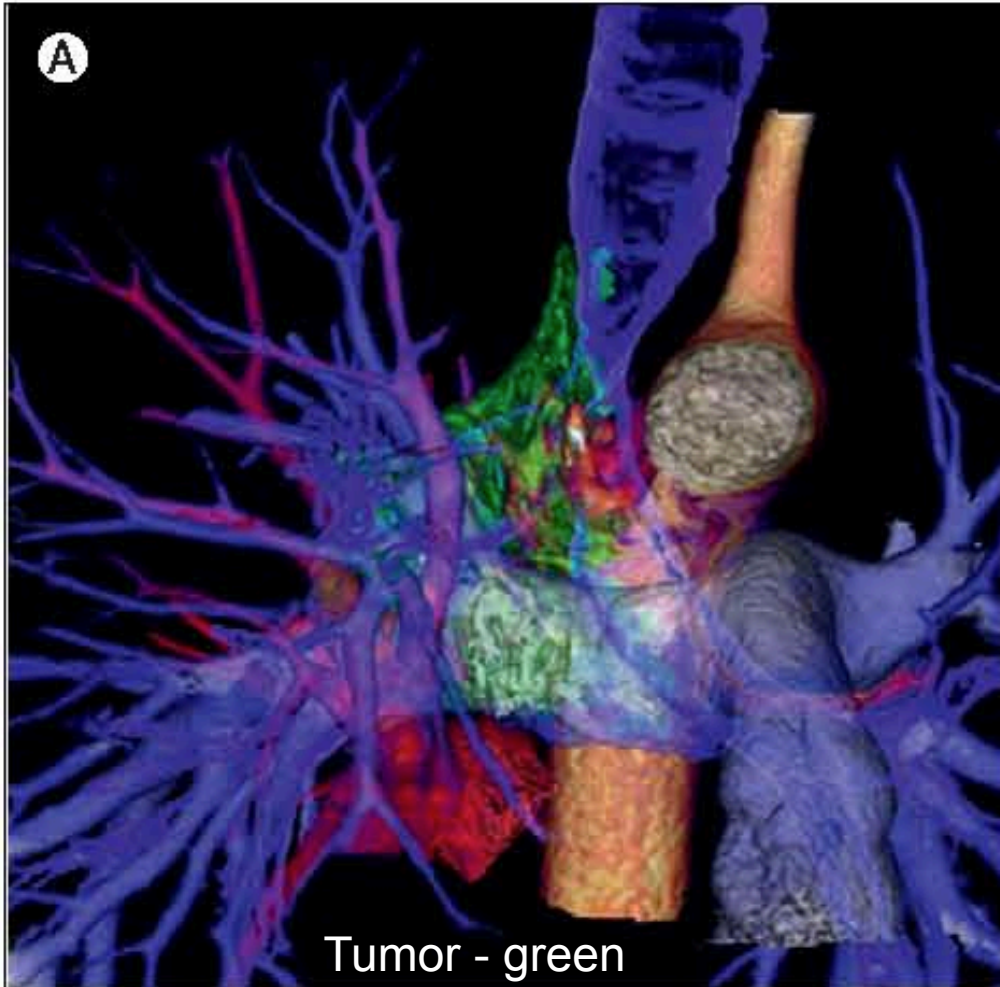
- Defects in voltage-gated calcium channels are related to autism, bipolar disorder, and schizophrenia. Timothy syndrome is caused by a point mutation in an alternatively spliced exon of the L-type channel $Ca_v1.2$ (inactivates the channel) – 60% have autism
- iPSCs have the Ca channel defect – they show differentiation defects in Ca signaling, decreased gene expression in lower cortical layers and callosal projection neurons, and abnormal expression of tyrosine hydroxylase, and increased production of norepinephrine and dopamine.
- The phenotype can be reversed by treatment with roscovitine – a cyclin-dependent kinase inhibitor and atypical L-type-channel blocker.
- Shows $Ca_v1.2$ regulates differentiation of cortical neurons and causes autism in Timothy syndrome.



Tracheobronchial transplantation with stem cell seeded bioartificial nanocomposite: a proof of concept study. Jungebleuth et al., Paolo Macchiarini's lab Karolinska Institute. Sweden

- Tracheal cancer patient involving trachea and main bronchi – requires complete resection of tumor and airways.
- Developed a POSS-PCU (nanocomposite polymer – polyhedral oligomerisilsesqui-oxane covalently bonded to poly-carbonate urea, processed by an extrusion-phase-inversion method. To exactly fit the anatomical replacement of excised trachea.
- Seeded in bioreactor with autologous bone marrow mononucleocytes for 36 hrs.
- Postoperative GCSF and epoetin beta.
- Functional 5 months after grafting – extracellular matrix coating, CD105 – stromal MSCs, patent anastomoses, lined with vascularized neomucosa and partly covered with healthy epithelium, upregulation of epoetin receptors, antiapoptotic genes, miR-34. miR-449 biomarkers.





Dopamine neurons derived from human ES cells efficiently engraft in animal models of Parkinson's Disease. Kriks et al.,m Lorenz Studer's Lab Sloan Kettering NY. *Nature* Nov 6 2011

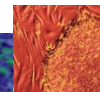


- Dopamine (DA) neurons can be derived from human ES and iPS cells and despite promise in vitro – they have performed poorly in vivo.
- The team has produced DA neurons using a novel floor-plate-strategy. Involves 11 days exposure to sonic hedgehog and canonical WNT signaling giving DA engraftable neurons after 25 days
- Showed efficient integration engraftment of these cells in rodent models (mouse and rat) and monkey model of Parkinson's Disease
- They survived with full functional competence as DA midbrain neurons – without any overgrowth.
- These data are encouraging for the use of pluripotent stem cells for complete specification of the DA neurons that are needed for restoration of health in Parkinson's Disease.



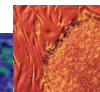
Geron Trial

- On Nov. 14th, Geron announced discontinuance of its spinal cord trial and its hESC research program
 - A number of employees have or will be let go by year end, and some will stay until the first half of 2012
- The reason is strictly financial – with limited funds available it has decided to focus on its oncology programs currently in clinical trials
- Geron has committed to following the patients who have already been enrolled and to collect data and update FDA and the medical community on progress
- All funding provided by CIRM for the clinical trial has been returned by Geron
- Geron has reported that it is seeking a partner to enable continued development of its stem cell programs
- CIRM has communicated its willingness to transfer the loan to a new entity, pending proper diligence review and all in accordance with CIRM procedures



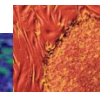
Non-Patentability of hESC Inventions IN EU

- Brustle v. Greenpeace (EU Court of Justice)
- Cell Stem Cell Article (Dec 2, 9:499-500,2011):
 - Expect significant but varied impact in EU; this will not mark the end of hESC work in Europe
 - Basic Science: Minimal impact predicted
 - Translational Science: Impact expected but participants will respond in accord with their individual interests
 - Clinical Trials: Expect trials will still occur in EU



Upcoming RFAs

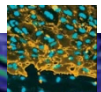
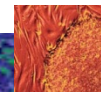
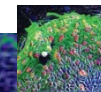
- **Creativity Awards**
 - GWG review of Applications – February 2012
- **Early Translational III**
 - GWG Review of Applications – March 2012
- **Disease Team Therapy Development**
 - Part 2 Research Award GWG review of Applications – April 2012
- **Basic Biology IV**
 - GWG Review of Applications – June 2012
- **iPSC Initiative**
 - Concept Proposal – October 2012
- **Genomics Initiative**
 - Concept Proposal – January 2012



CIRM engaged in Public-Private Partnership with NINDS on Neurodegenerative Disease Modeling/Drug Discovery



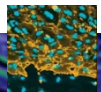
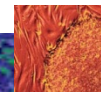
- 2011 NINDS proposed a public private partnership e.g., gov't agency, patient advocate foundations, and biopharmaceutical industry in iPSC research resource
 - iPSC research resource in neurodegenerative diseases, targeted to disease modeling/drug discovery
 - Competition among currently funded consortia in Huntington's Disease, Parkinson's Disease and Amyotrophic Lateral Sclerosis
 - Review criteria - Significance, Investigators, Innovation, Approach, Environment; Productivity, Milestones, Resource Sharing Plans



CIRM is funding California Component



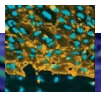
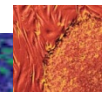
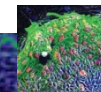
- CIRM to provide funding to meritoriously reviewed California applicants
 - CIRM component \$150k/yr x 2 yrs; NINDS/partners \$4.5M/yr 2011; 2012 commitment pending appropriation
 - Applications received June 2011; reviewed August 2011
 - California PI Thompson, UC Irvine, with focus on Huntington's Disease



Benefit of partnership for CIRRM

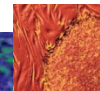


- Opportunity to play a leadership role in national effort
- Leverages existing resources and expertise
- Provides valuable insights on disease modeling and drug discovery efforts
- Enables access of iPSC lines and data from national resource on neurodegenerative diseases
- Opportunities for more in-depth interactions with industry, translational scientists, and patient advocacy engagement
 - focus on increasing knowledge of strategic therapeutic areas
 - catalyzing development of more accurate and predictive screens for drug discovery and development



CFP Update

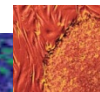
- NIH
 - Potential DTTD Research Award Collaboration considered
 - Parkinson's Disease Roundtable discussion
 - Standardization Efforts
 - Study Subject Consents
 - Material Transfer Agreements
- ET III RFA: China, Germany, Japan
- BB IV RFA: China, Germany, France, India



Initiation of NIH collaborations



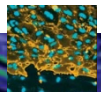
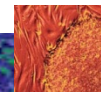
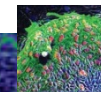
- In October CIRM added the National Institutes of Health to its network of collaborative funding partners. Since that time, CIRM and NIH have been exploring various areas in which they can jointly support stem cell research. Our preliminary discussion suggest that Parkinson's disease may be one area where the strengths, resources and interests of NIH and CIRM can effectively join forces.
- To help us further analyze this possibility, CIRM is hosting a roundtable discussion on Friday December 16th at CIRM headquarters in San Francisco.
- This event is the first of several that will provide an opportunity for CIRM funded Parkinson's researchers to share information with NIH representatives and help us brainstorm about the most effective path for NIH and CIRM to jointly pursue in support of Parkinson's research.



CIRM and NIH Roundtable Discussion on Parkinson's Disease Research



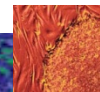
- December 16, 2011 CIRM will host an interactive roundtable discussion with NIH and CIRM funded investigators on Parkinson's Disease with the intent of identifying areas in which CIRM and NIH can most effectively support PD research
 - Builds upon recent collaborative agreement signed between CIRM and NIH to work together on translational program areas of mutual interest
 - NIH work includes clinical trials, screening, cell lines, novel cell culture for DA neuron generation, GMP manufacture and development of assays



Stem Cell Meeting on the Mesa, and Investor and Partnering Forum Nov 30-Dec 1, 2011



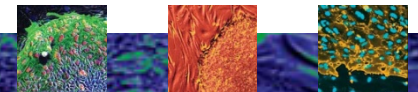
- 6th Annual Scientific Symposium, and 1st Annual Investor and Partnering Forum in San Diego, brought together the scientific research and business development communities with the goal of advancing the latest in stem cell science and research into tangible cures for debilitating diseases and injuries;
- Celebrated opening of Sanford Consortium for Regenerative Medicine on November 29th -
 - Collaboratory will enable scientists from UC San Diego, Salk Institute for Biological Sciences, Sanford-Burnham Medical Research Institute, La Jolla Institute for Allergy and Immunology and Scripps Research Institute to hasten pace of progress for development of diagnostics, treatments and potential cures



Stem Cell Meeting on the Mesa, and Investor and Partnering Forum Nov 30-Dec 1, 2011



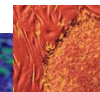
- CIRM was one of five primary organizers of the event (Connect, Salk Institute, Sanford Consortium, Alliance for Regenerative Medicine, and CIRM)
 - Leading CIRM's coordination was Elona Baum, General Counsel and VP of Business Development; Opening by ICOC Chair Jon Thomas; ICOC Vice-Chair, Duane Roth, played a pivotal role in organizing the Forum; ICOC member Bert Lubin, panel member on Public and Private Pathways for Reimbursement; Pat Olson, Exec Dir of Scientific Activities, chaired Disease Teams panel; Elona Baum chaired Building Regulatory Pathway for Regenerative Medicine and participant on Access to Finance – Industry Wide Issues panels, and Ellen Feigal, SVP Research and Development chaired Confronting the Translational Challenge – Collaborative Models to Advance Early-Stage RM Programs panel
- Over 650 registered for Scientific Symposia, and 250 participated in Investor and Partnering Forum. More than 35 corporate presentations and six panels focused on business of RM
 - Featured speakers included Greg Lucier, Chair and CEO, Life Technologies; Matthias Steger, Global Head Research and Technology Partnering, Roche; Sir Ian Wilmut, Director, MRC Centre for Regenerative Medicine, Univ of Edinburgh and Rudolf Jaenisch, Founding Member, Whitehead Institute and Prof Massachusetts Institute of Technology



Upcoming Workshops/Meetings

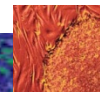


- Tissue Engineering Workshop: *Engineering Strategies, Opportunities, and Challenges for Tissue Repair and Regeneration*
 - Goal: To address the opportunities for stem cell use in tissue engineering
 - January 12-13, San Francisco
 - Closed meeting: Cold Spring Harbor Rules to enable discussion of unpublished data
- Roundtable on Parkinson's Disease
 - Goal: To address collaboration opportunities with the NIH in Parkinson's Disease
 - December 16, CIRM



New Appointments

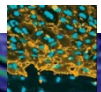
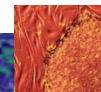
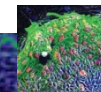
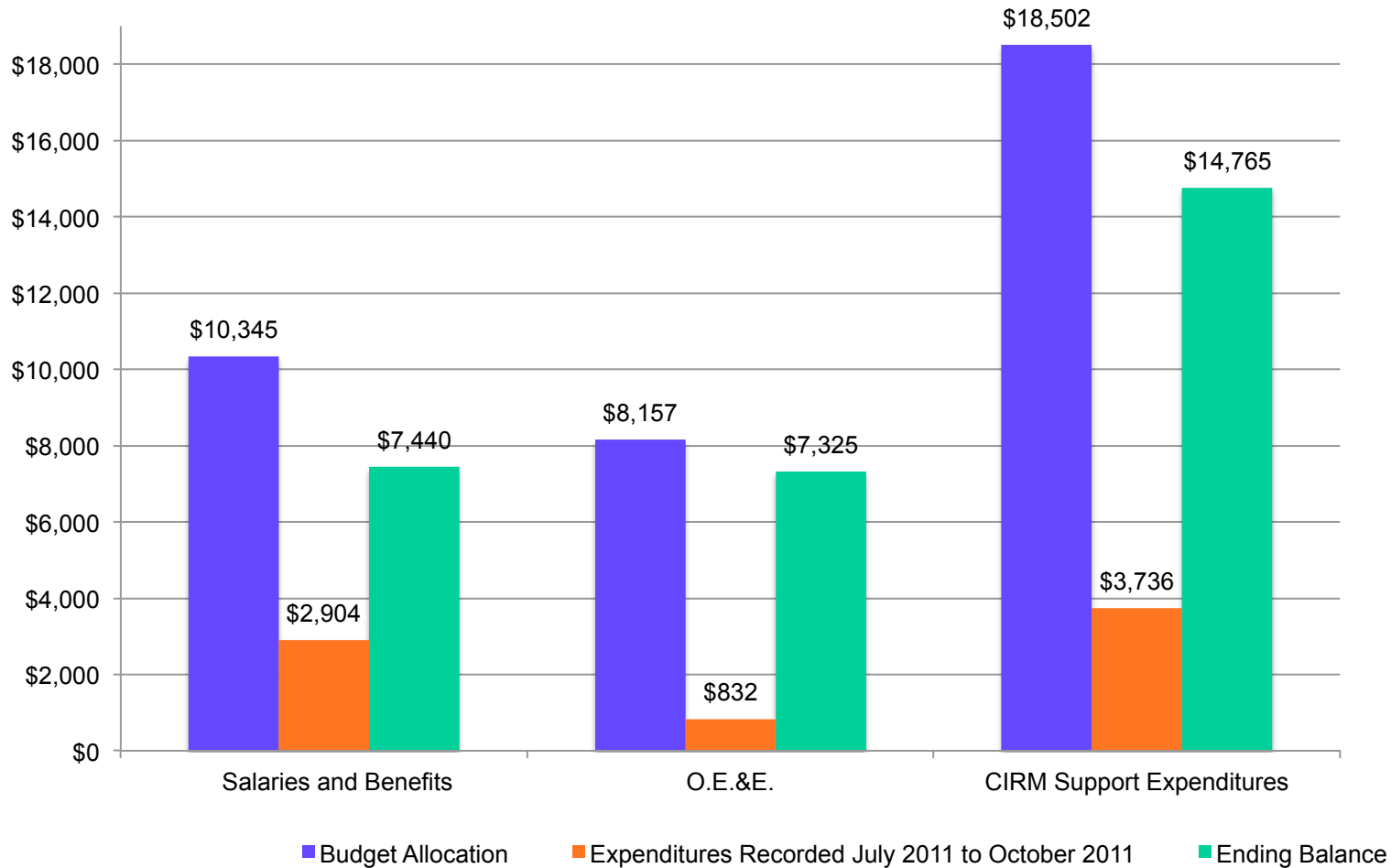
- **Matthew Plunkett, CFO, November 28, 2011**



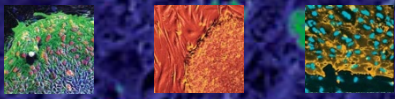
Fiscal Year 2011-12

Expenditures Recorded Through October 2011

(OE&E expenditures do not include Lags)







2011-12 Budget Allocation and Expenditure Report

**Recorded Through October 31, 2011
December 8, 2011 ICOC Board Meeting**