



The state stem cell agency

President's Report

Alan O. Trounson

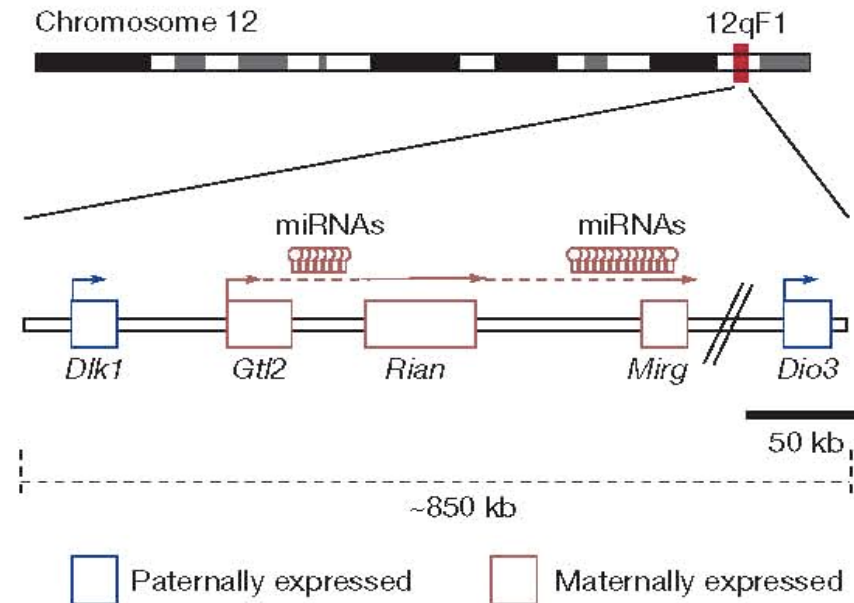
ICOC Meeting – June 2010

Agenda Item #5

Only difference between mESCs and miPSCs at imprinted gene cluster Dlk-Dio3 (ESC=SCNT≠iPSC)

Stattfeld et al., *Nature* 2010 Hochedlinger Lab

- Aberrant silencing of the Dlk1-Dio3 gene cluster in mouse iPSCs Ch12
- These iPSCs poor chimeric development and failure to form entirely iPSC mice
- In iPSCs with normal expression of Dlk-Dio3 formed high grade chimeras and viable all iPSC mice
- The expression state of this single imprinted gene cluster appears to determine the difference between full developmental potential mESCs and miPSCs .



Migration of engrafted neural stem cells is mediated by CXCL12 signaling through CXCR4 in MS model

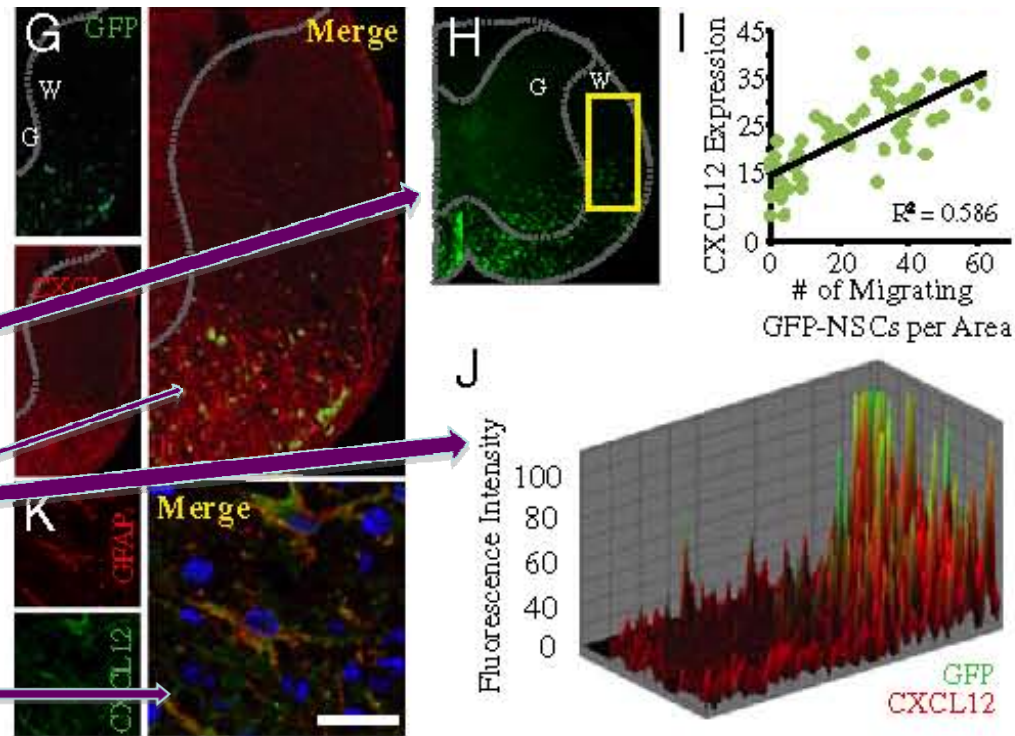
Carbajal et al., *PNAS* May 7 2010, Tom Lane's lab UCI

- MS is a demyelinating disease foci of inflammation and progressive myelin loss in CNS – loss of message transmission down axons
- Viral-induced immune-mediated demethylation in mice
- CXCL12 is an inflammatory chemokine – recruited by CXCR4 receptor
- Surgical engraftment of GFP+ neural stem cells – results in migration, proliferation and differentiation to OPCs – remyelination
- Anti-CXCL12 impaired migration and proliferation
- CXCR4 antagonist likewise

Association of CXCL12 expression and GFP

NSCs migrate to areas rich for CXCL12 (red)

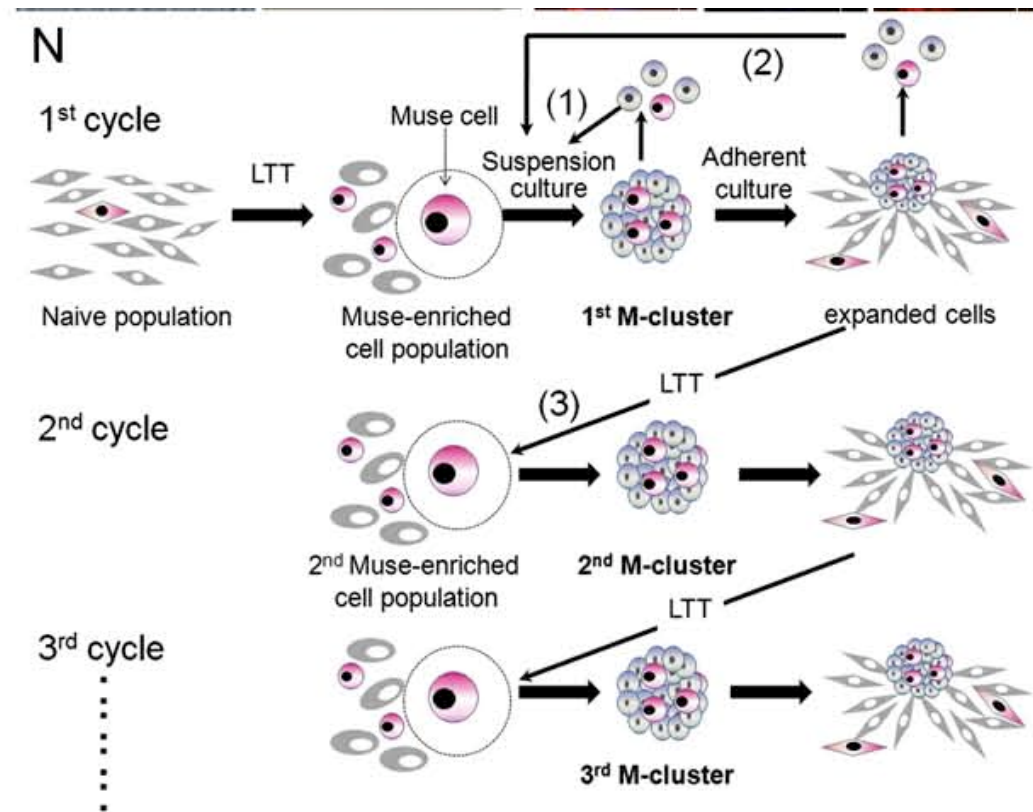
Astrocytes produce CXCL12



Unique multipotential stem cells in human MSC populations

Kuroda et al., Tohoku and Kyoto University *PNAS* March 29 2010

- Can isolate single cells from cultured skin fibroblasts, BM stromal cells or BM aspirates by long-term trypsinization (LTT)
- Self renew and express genes of the ectoderm, endoderm and mesoderm in vitro and in vivo
- Integrate into damaged skin, muscle, or liver
- Their proliferation is not very high and do not form teratomas
- Are these rare cells really pluripotent?

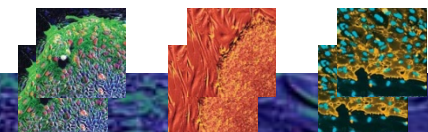


Reprogramming T Cells to Natural Killer -like Cells upon Bc11b Deletion

Li et al., Wellcome Trust Sanger Istit Cambridge *SciencExpress* 10 June 2010



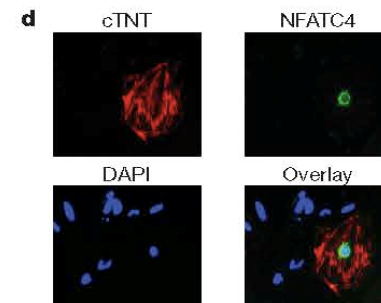
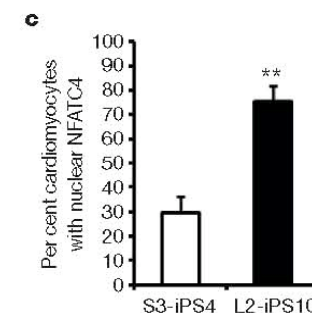
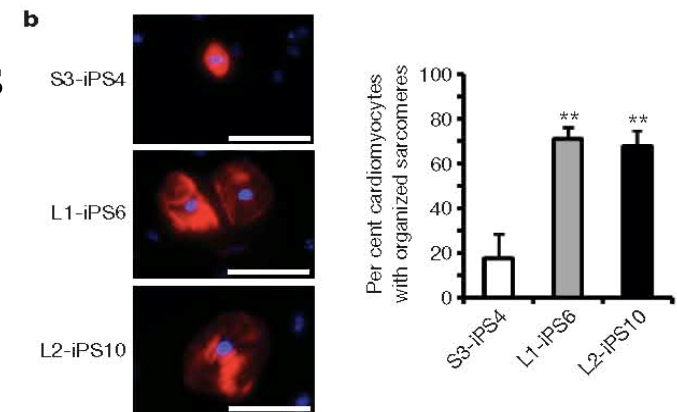
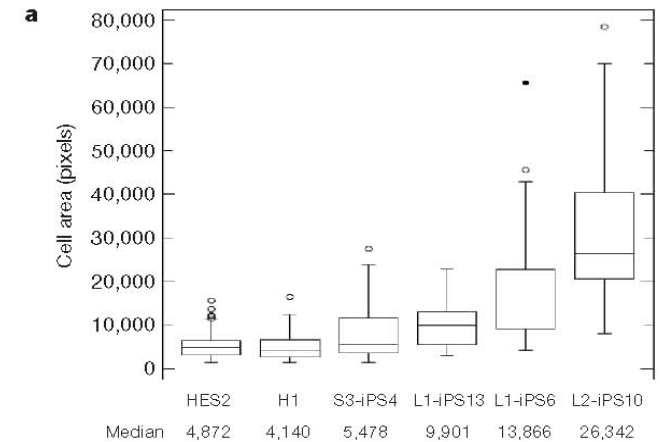
- T cells (thymus) critical for adaptive immunity
- NK lymphocytes – innate immune system – tumor surveillance, defense against microbes and viruses
- Transcription factor Bc11b expressed in all T cells
- Deleting Bc11b turns off T cell gene expression and induced NK cell phenotype capable of preventing tumor metastasis in vivo
- An example of reprogramming cell type by manipulation of transcription factors – potential therapeutic model



“Disease in a dish” iPSCs as models of Leopard Syndrome

Carvajal-Vergara et al., Ihor Lemischka’s Lab
Mt Sinai School Med. NY, *Nature* June 2010

- LS is an autosomal-dominant disorder – relatively prevalent RAS-mitogen-activated protein kinase signaling diseases
- Major phenotype is hypertrophic cardiomyopathy
- iPSCs from LS produce larger cardiomyocytes higher degree of sarcomeric organization and preferential localization of NFATC4 in the nucleus compared with unaffected sibling controls
- Provides the opportunity to determine the molecular and signaling pathways that cause the phenotype. Also enables the design of high throughput screening for new drugs to treat LS



President's Priorities

- VP R&D Search
- California Stem Cell Leadership – CIRM Procedures/Developments
- Financial Forecasting and CIRM Mission
- ISSCR/CIRM Regulatory Workshop
- SCNT Workshop
- Regulatory Harmonization Workshop
- Alliance for Regenerative Medicine
- CIRM 2010 Review
- Communications and Collaborative Funding Agreements/Contracts
- CIRM Scientific Creativity Internships
- Standards Working Group

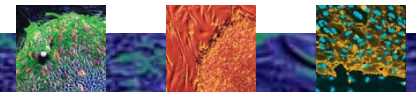


Personnel

**Mani Vessal, PhD, Science Officer
(Stanford University)**

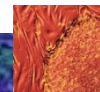
**Arie Abo, PhD, Science Officer
(Nuvelo Inc.)**

**Jenny Lam, Grants Management
Specialist
(Kaiser Research Foundation Institute)**



Upcoming RFAs

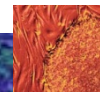
- **Early Translational II**
 - Post RFA – Feb 2010
 - Receipt of pre-apps – March 18th (112)
 - Full Grant applications – June 30th
 - Review – Sept 2010
 - ICOC – Oct 2010
- **Tools, Technologies & Bottlenecks**
 - Post RFA – April 2010
 - Receipt of pre-apps – May 19, 2010 (226)
 - Full Grant applications – Aug 26, 2010
 - Review – November 2010
 - ICOC – January 2011
- **Clinical**
 - Posting RFA – late July 2010
 - Review – January 2011
 - ICOC – March 2011



Upcoming RFAs

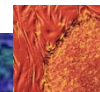
Research Leadership Awards

Application Deadline	GWG Review	ICOC Review
February 18, 2010	March 2010	April 2010
June 17, 2010	July 2010	August 2010
September 30, 2010	November 2010	December 2010
December 2, 2010	January 2011	February 2011



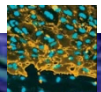
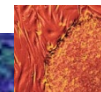
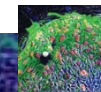
CIRM grantee Joanna Wysocka wins Outstanding Young Investigator Award

- Assistant Professor of developmental biology at Stanford University School of Medicine
- SEED and New Faculty Awards grantee to study how cells determine their eventual fate in a developing embryo



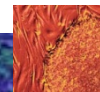
ISSCR 2010: Breaking Science: Direct Reprogramming

- Identified 3 factors that convert murine fibroblasts into functional neurons in vitro (up to 20% efficiency); not yet successful with human (M. Wernig).
- Reprogramming murine fibroblasts to motor neurons (5-6 factors) not functionally characterized yet; looking feasible with human
- Reprogrammed adult mouse and human astrocytes to neurons in vitro with 2 factors, 60% efficiency (M. Goetz)
- Reprogrammed murine cardiac fibroblasts to functional cardiomyocytes in vitro with 3 factors (17% efficiency).
Direct reprogramming – did not go through progenitor.
(D. Srivastava)



Online Journal

- **GOALS FOR TRANSLATIONAL JOURNAL**
 - Fill a gap in the exchange of ideas
 - current stem cell journals prefer basic science
 - current translational journals too broad
 - Need to publish negative data quickly
 - hard to get this published at all
 - quick notice avoids wasted replication
 - Establish the translational pathway, standards and SOPs for stem cell therapies – embraced by researchers, biotech companies, FDA, ISSCR and preclinical interests
 - Consolidate cell-based translational work
 - create a synergistic community within academia, biotech industry and regulatory bodies
 - Academic researchers would publish translational research and if “high impact factor number,” journal would be compatible for academic advancement
 - Provide venue for Case studies from CIRM
 - modeled on MGH case studies in NEJM
 - Seek proposals from the science publishing industry, e.g., Stem Cells, Nature, PLOS



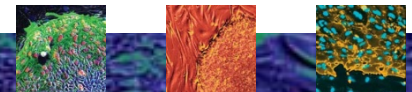
Online Journal

BUSINESS MODEL FOR JOURNAL

- Online, open access publishing journal with rapid turn-around for authors
- Accelerate publishers' entry into field
 - short term subsidy to cover start-up costs
 - phase out subsidy in 2 to 3 years
- Publisher to provide business plan
 - page charges, ad revenue to cover costs
- Independent management, editors, editorial board and reviewers
- The publication's first issue date should be within six months of the commencement of this contract

BUDGET

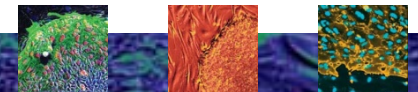
- 3 year budget requiring a subsidy not to exceed \$200,000 in the first year and suggesting the ability to become self-sustaining after three years



Upcoming Workshops



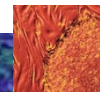
- MRC UK/CIRM - SCNT/Parthenogenesis, San Francisco - June 13-14th
- ISSCR/CIRM/ISCT – Clinical Trials Regulatory Harmonization, San Francisco - June 15th
- The Netherlands/CIRM Science Collaboration – June 16th
- 2nd Annual International Funders Workshop – June 17, 2010
- ISSCR Annual Meeting, San Francisco - June 16-19th
- New York/CIRM Science Collaboration – Q3
- iPSC Banking – Q3/4



Bridges Program 2010 Trainee Meeting



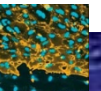
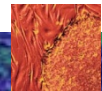
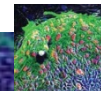
- **July 8-9, 2010 in San Francisco**
- **Annual meeting for Bridges Trainees, Program Directors, and Trainee Mentors**
- **Features poster presentations by trainees, guest speakers, networking and educational sessions**



Matters of Significance

- **CIRM Program for Disease applications**
Dr. Pat Olson

- **Forecasting CIRM expenditures to match its mission**
Dr. John Robson





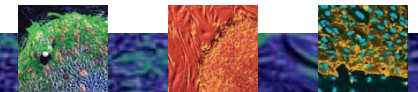
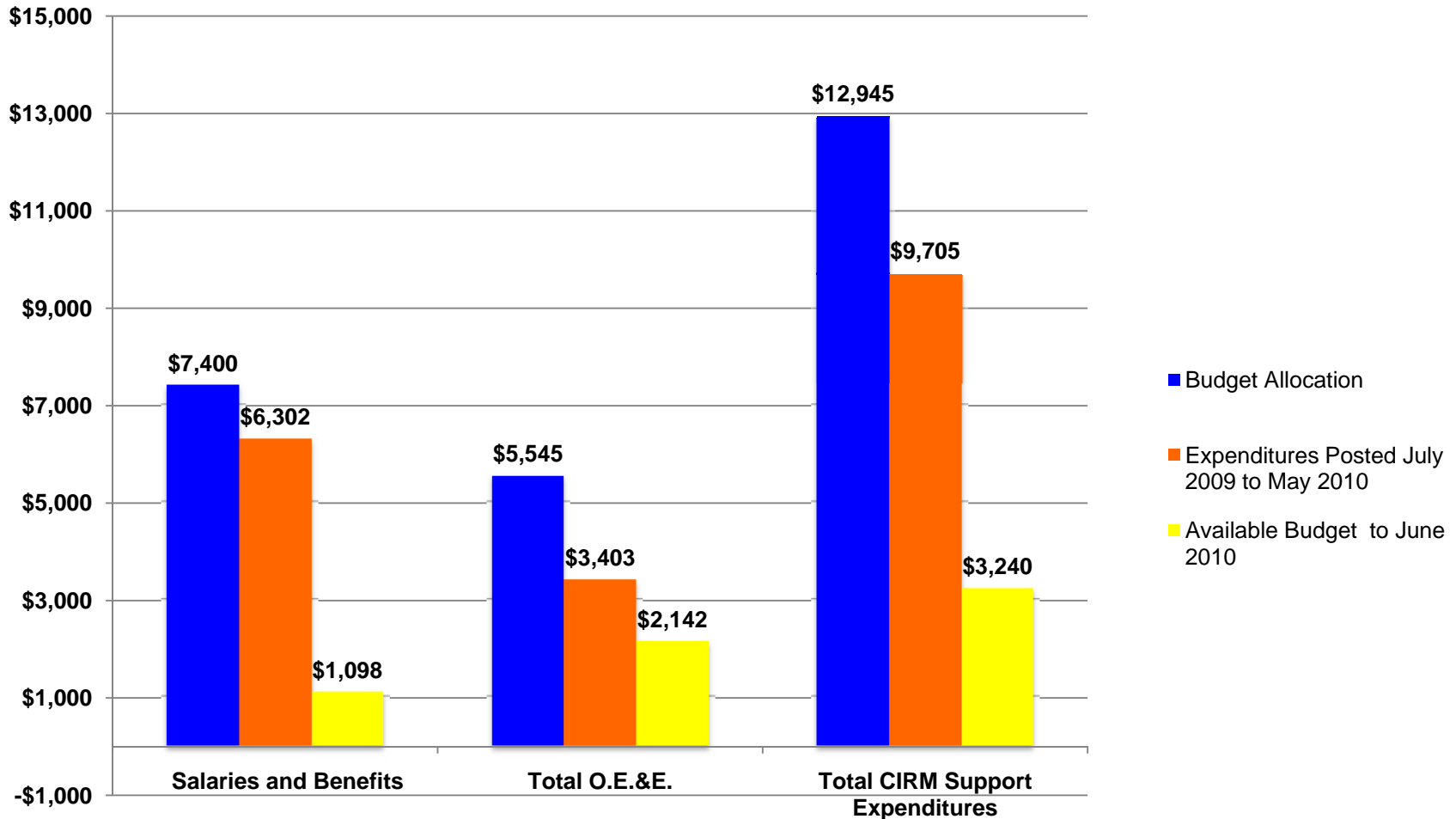
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2009-10 Budget Allocation and Expenditure Report

Posted Through May 31, 2010

June 22-23, 2010 ICOC Board Meeting

Fiscal Year 2009-10 Expenditures Posted Through May 2010



Fiscal Year 2009-10

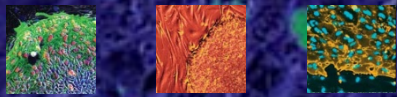


Percentage
of Budget
Allocation
Posted

Fiscal Year 2009-10

Description	Budget Allocation	Expenditures Posted 7/1/09-3/31/10	Available Budget Allocation 4/1/10-6/30/10	Percentage of Budget Allocation Posted
<u>Personnel Services</u>				
Salaries and Benefits	7,400	6,302	1,098	85%
<u>Operating Expenses and Equipment</u>				
Interagency Agreements	208	141	67	
External Contracts	2,088	1,269	819	
ICOC, Science, Work Group Meetings	1,329	770	559	
Other Travel	497	225	272	
Furniture and Equipment (Non-IT)	50	66	-16	
Information Technology	818	610	208	
Other O.E.&E.	556	321	235	
Total Operating Exp and Equip	5,545	3,403	2,142	61%
Total CIRRM Support Expenditures	12,945	9,705	3,240	75%





The state stem cell agency

CIRM Financial Projections ICOC – June 2010

**John Robson, PhD
VP Operations**

CIRM Funding Financial Projections to 12/31/11



Includes:

All programs approved by the ICOC

Programs with ICOC concept approval:

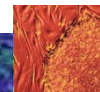
Immunology - \$30 million

Research Leadership Awards - \$44 million

Early Translation 2 – \$80 million

Tools and Technology - \$40 million

Clinical Development- \$50 million



CIRM Funding Financial Projections to 12/31/11

