CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

President's Report

Alan O. Trounson

ICOC Meeting – September 2012

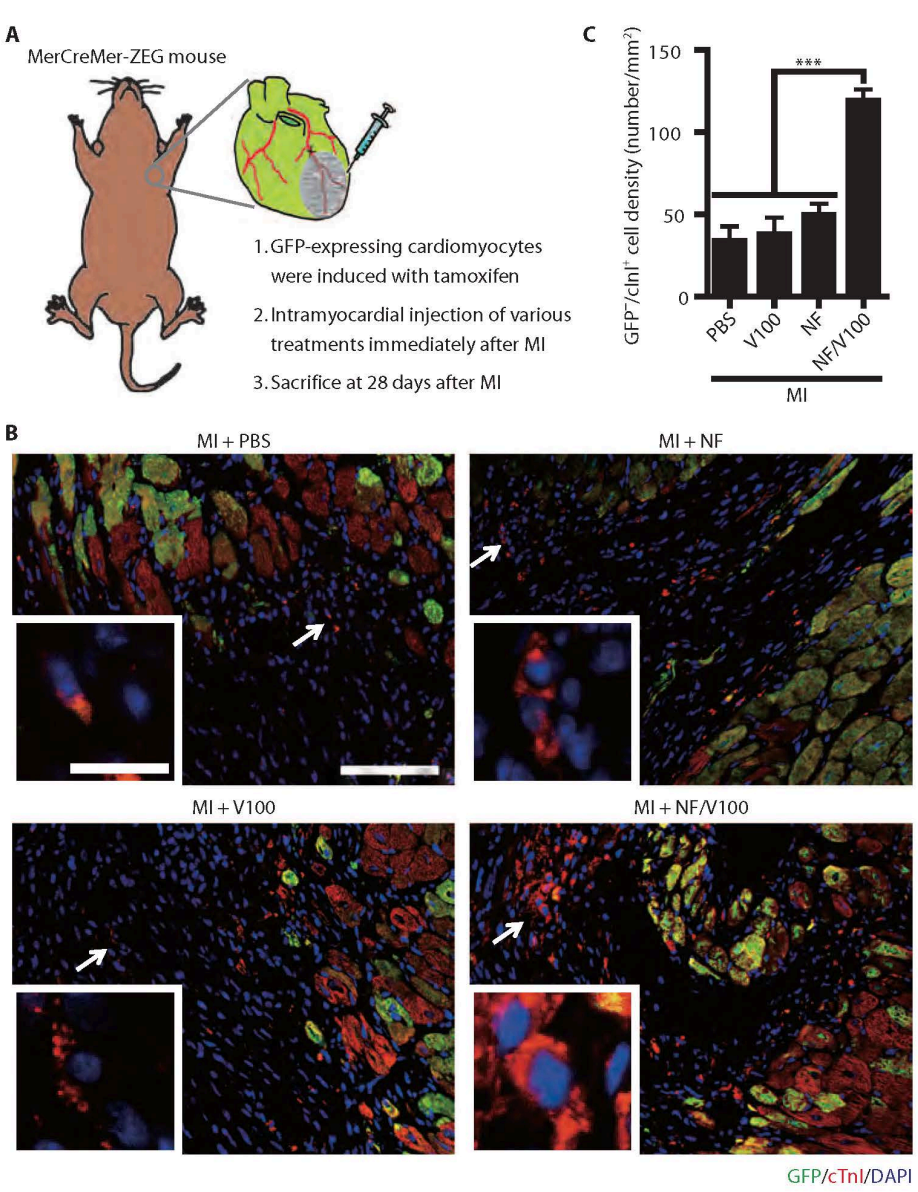
San Francisco, CA

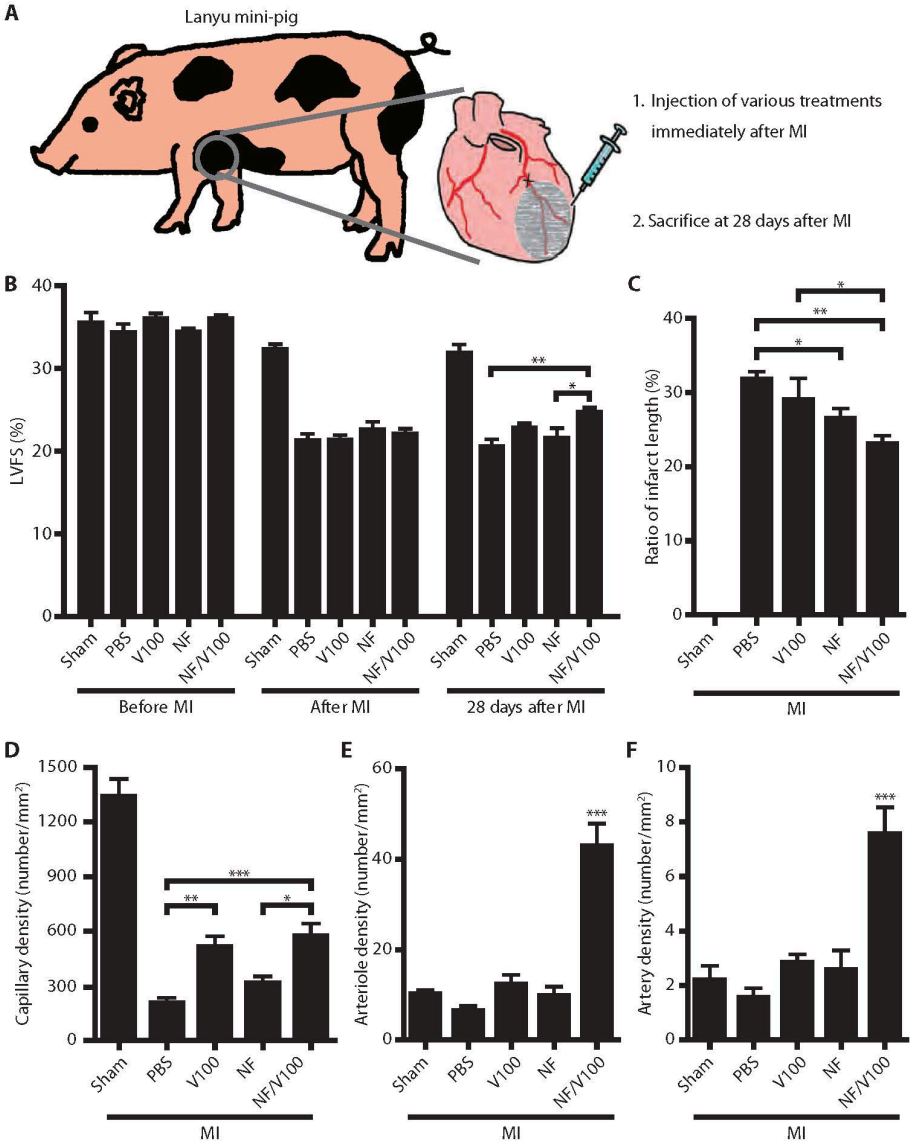
Arteriogenesis and Cardiac Repair.

Yi-Dong Lin et al. Institute of Biomedical Sciences, Academia Sinica, Taipei.

Sci Transl Med 8 August 2012, 4(146) 4, 146ra109 (2012)

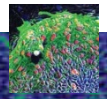
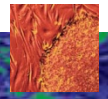
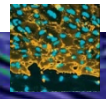
- Studied the use of self- assembling nanofibres (NFs)together with VEGF for angiogenesis and cardiac repair in two animal models of myocardial infarction (MI)
- When injected into heart immediately after MI and 28 days in rats – showed that NFs + VEGF significantly improved improved cardiac function and prevented tissue remodeling, collagen deposition and scar formation – reducing infarct size.
- Studies in pigs given NFs + VEGF immediately after MI confirmed the rat data.
- NFs + VEGF promoted arteriogenesis – recruiting myofibrils and cardiomyocytes to damaged muscle.
- Encouraging approach using a nanobiotechnology and growth factor


A
MerCreMer-ZEG mouse
1. GFP-expressing cardiomyocytes were induced with tamoxifen
2. Intramyocardial injection of various treatments immediately after MI
3. Sacrifice at 28 days after MI
C
GFP⁻/cInI⁺ cell density (number/mm²)
150
100
50
0
***
PBS
V100
NF
NF/V100
MI
B
MI + PBS
MI + NF
MI + V100
MI + NF/V100
GFP/cTnI/DAPI


A
Lanyu mini-pig
1. Injection of various treatments immediately after MI
2. Sacrifice at 28 days after MI
B
LVFS (%)
40
30
20
10
0
**
*
Sham
PBS
V100
NF
NF/V100
Before MI
After MI
28 days after MI
C
Ratio of infarct length (%)
40
30
20
10
0
*
**
*
Sham
PBS
V100
NF
NF/V100
MI
D
Capillary density (number/mm²)
1500
1200
900
600
300
0
***
**
*
Sham
PBS
V100
NF
NF/V100
MI
E
Arteriole density (number/mm²)
60
40
20
0
***
Sham
PBS
V100
NF
NF/V100
MI
F
Artery density (number/mm²)
10
8
6
4
2
0
***
Sham
PBS
V100
NF
NF/V100
MI

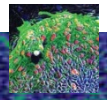
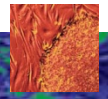
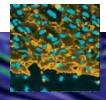
Small Molecule-Mediated TGF-b Type II Receptor Degradation Promotes Cardiomyogenesis in Embryonic Stem Cells. Willems etal. Mark Mercola's lab, Sanford Burnham Instit. *Cell Stem Cell* Aug 3, 2012; 11:242

- A mouse ES cell assay for expression of the Myh6-GFP cardiac marker was used for high throughput screening of small molecule library to identify a molecule that is an inducer of type II TGF-b receptor (TGFBR2) degradation-1 (ITD-1).
- Effectively cleans the receptor from the cell surface – selectively inhibiting Ca signaling.
- ITD-1 selectively enhanced the differentiation of uncommitted mesoderm progenitors to cardiomyocytes
- ITD-1 optimally differentiated human ES cells - doubling yields to ~60% cardiomyocytes.
- Could be used to maximize yield of cardiomyocytes from hESCs

Human ES-cell-derived cardiomyocytes electrically couple and suppress arrhythmias in injured hearts. Shiba etal. Instit Stem Cell Biol Regen Med, U Wash. *Nature* Aug 5, 2012

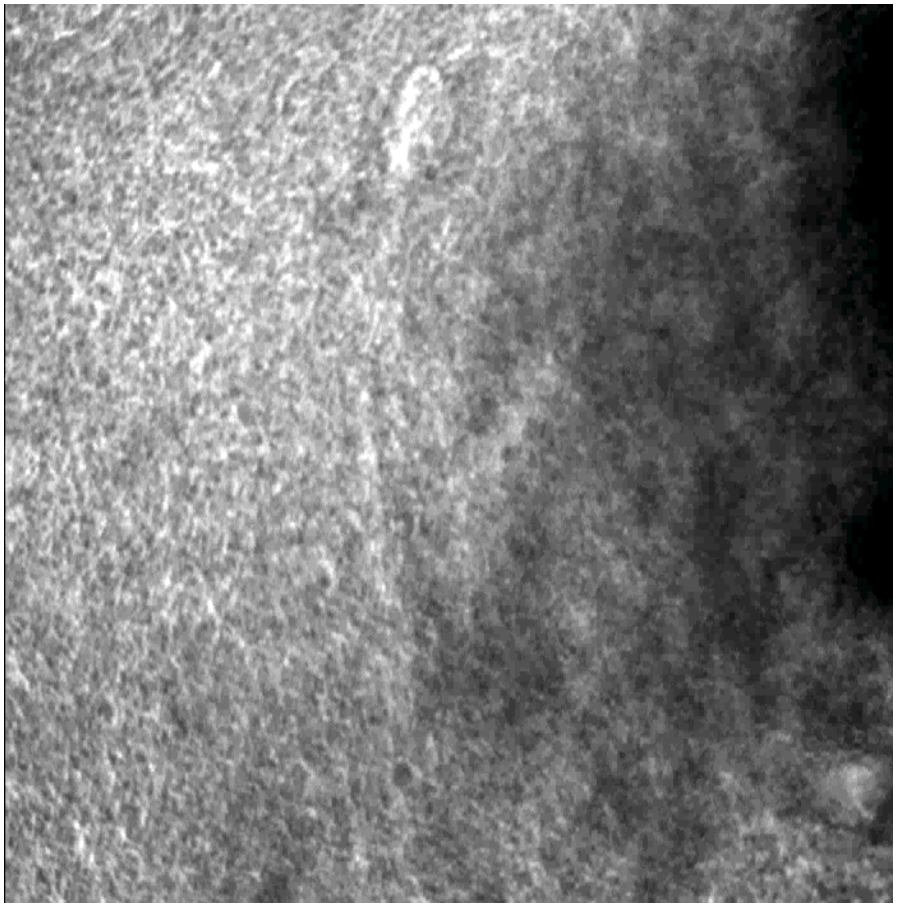
- Used a guinea-pig model (200-250bpm) for grafting hESC derived cardiomyocytes (spontaneously beat at 50-150bpm and can paced to 240 bpm) 10days after cardiac cryo injury-MI.
- Demonstrated hESC-CMs protection against arrhythmias and beat synchronously with GP host cardiomyoctes.
- Improved heart muscle function and significantly reduced spontaneous and induced tachycardia.
- Showed 1:1 host-graft calcium release coupling in uninjured hearts and heterogeniety in injured hearts.
- This supports the further exploration for use of hESC derived CMs in mechanical and electrical heart regeneration in the human.

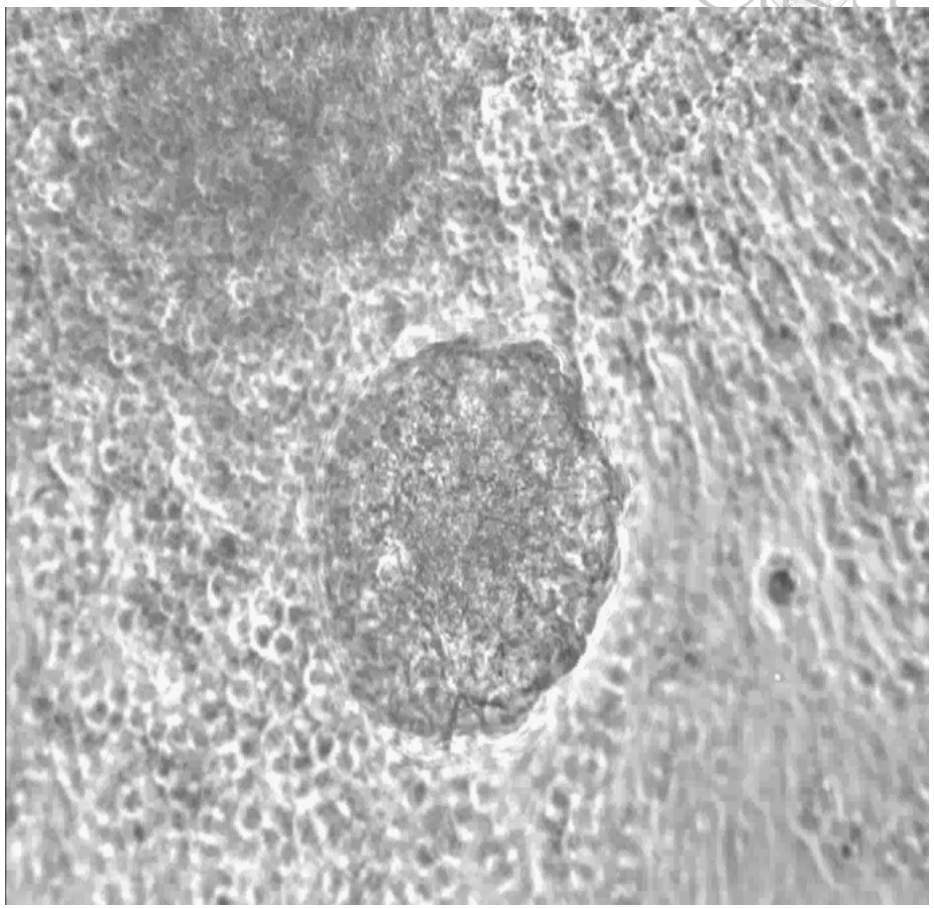




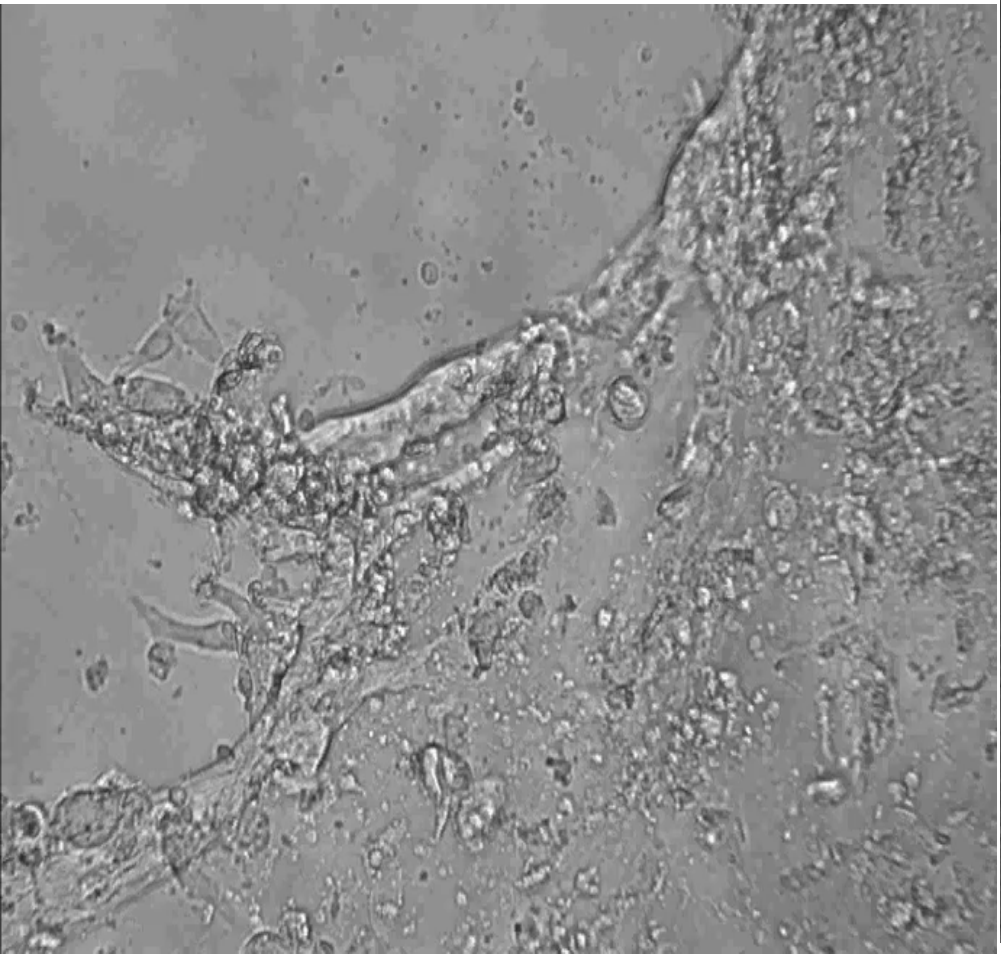
Comparison of Cardiomyogenic Potential among Human ESC and iPSC Lines. Sepac etal. John Lough lab Med Coll. Wisconsin

Cell Transplantation Aug 2012

- Studied 2 ESC and 2 iPSC lines differentiation into rhythmically contracting cardiomyocytes within 3 weeks using Activin-A and Bmp4.
- All cell lines expressed the cardiomyocyte lineage markers MESP1, ISL1 and NKX2.5.
- ESCs had widespread sarcomere striations, were multilayered and showed rhythmical contraction – for up to 1 year in culture.
- iPSCs had poor terminal differentiation – with few sarcomere striations, were not multilayered and had sporadic contractility.
- See videos: http://www.mcw.edu/cellbiology/johnloughphd.htm.

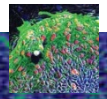
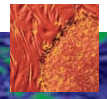
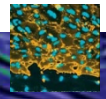






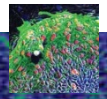
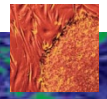
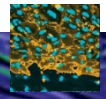
RFA Program

- **Disease Team Therapy Development**
  - ICOC Funding Decision (cont'd) – this meeting
- **Research Leadership**
  - ICOC Funding Decision (cont'd) – this meeting
- **Basic Biology IV**
  - ICOC Funding Decision – this meeting
- **Genomics Initiative**
  - RFA Posted – August
  - Webinar – September 11

RFA Program (cont'd)

- **Early Translational IV**
  - RFA Posting – September
- **Strategic Partnership I Awards**
  - GWG Review of Applications – September
- **New Faculty Physician Scientist Translational Research Award**
  - GWG Review of Applications – October
- **iPSC Initiative**
  - GWG review of Applications - December

Meetings and Workshops

- Held since July ICOC
  - Creativity Awards Annual Poster Day, August 13 Stanford Univ
- Upcoming
  - CIRM webinar on Immune Response in Stem Cell-based Therapy, leading experts from FDA, industry, academia September 27, 2012
  - CIRM's Collaborative funding partner workshop, Brazil October 1-2, 2012 Sao Paolo
  - CIRM/FDA roundtable on Best Practices in Clinical Design for First In Human Stem Cell-based Therapy October 16, 2012 Rockville, MD
  - CIRM's Alpha Clinic, Nov 14-15, 2012 Palo Alto
  - CIRM Grantee Meeting, March 6-8, 2013
  - CIRM/NIH Parkinson's Disease Meeting, March 21-22, 2013

Creativity Awards- Summer 2012 Poster Day

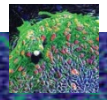
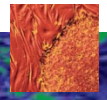
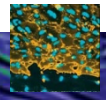
- All day event held at Stanford Stem Cell Building on August 13th
- 65 scientific posters presented by high school interns from 9 funded California Institutions
- 150 attendees including student interns, Program Directors, PIs, mentors and CIRM staff
- KGO-TV science reporter interviewed CIRM SO Mani Vessal at CIRM and two selected students from CHORI and UCSF. The story will air in the next week

Stem Cell Alpha Clinics Workshop

November 14 and 15, Stanford

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

- Goal: to define what clinical capacity is needed to accelerate development of safe, effective, and accessible cell therapies
- Participants will include a range of stakeholders:
  - Investigators from academia and industry
  - Clinical trial specialists
  - Cell manufacturers
  - Patient advocates
  - Representatives from funding agencies, insurers, health care providers, pharmaceutical industry, and investors

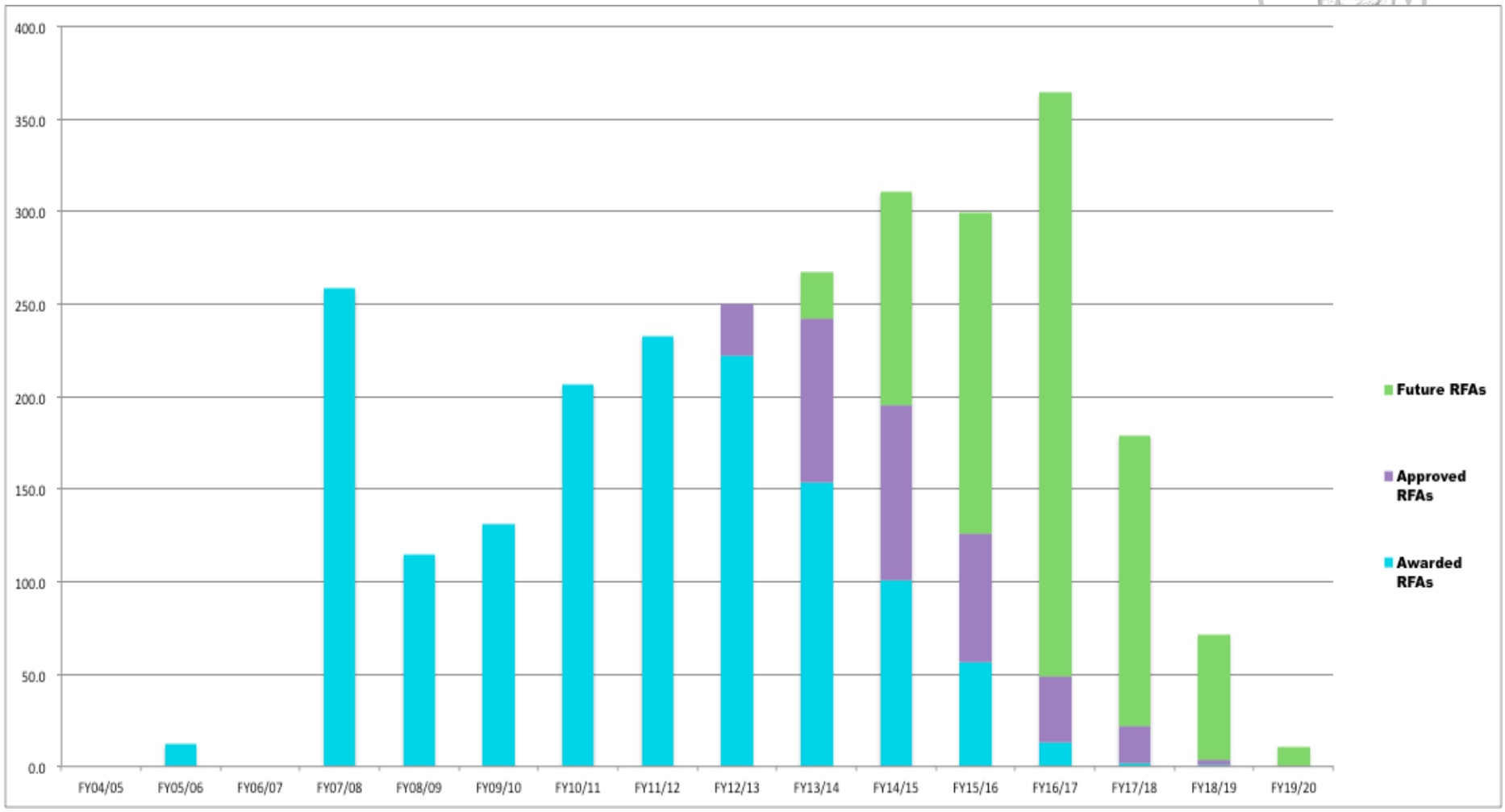
Business Development

- Strategic Partnership Funding RFA 1
  - Will be reviewed September 12-14
  - Strong interest shown by industry
  - Long term forecast contemplates replenishment and a number of rounds
  - This RFA is a cornerstone of CIRM's industry engagement initiatives

Commercialization Update

- Tracking of spin-outs arising in whole or in part from CIRM Funding
  - 8 companies identified
  - Information continues to be assembled
  - Companies
    - Regenerative Patch Technologies – Disease Team 1 award
    - Oceanside Biotechnology LLC – New Faculty 1
    - Didmi, Inc – T&T 1
    - Tolerogen, Inc – Seed Grant
    - CytoRay, Inc – T&T 1
    - ChemRegen – Seed Grant
    - jCyte, Inc * - ET2
    - Neurona, Inc* – Comprehensive Grant

AWARDS FORECAST



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The state stem cell agency

Finance Report

September 6, 2012

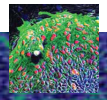
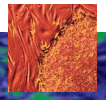
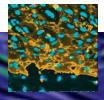
Financial Highlights for 11/12 FY

As of June 30, 2012

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

- Final Year-end OpEx 11/12 FY: $15.4mm
  - Prior FY OpEx 10/11 FY: $14.1mm

- Grant disbursements 11/12 FY: $232.1mm
  - Prior period 10/11 FY: $201.4mm

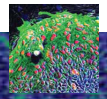
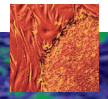
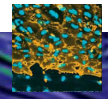




2011/12 Final Expenditures

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Dollars in millions	FY11/12 Budget	FY11/12 Final	Variance	Variance
Employee Expenses	$10.3	$9.3	$1.1	11%
Contracting	$3.3	$2.5	0.9	26%
Grant Reviews	$1.2	$0.6	0.6	49%
Travel	$0.5	$0.4	0.1	26%
IT	$1.3	$1.5	(0.2)	-16%
ICOC	$0.3	$0.1	0.2	56%
Scientific Meetings	$0.8	$0.6	0.2	27%
Office & General Exp	$0.7	$0.4	0.2	36%
Total	$18.5	$15.4	$3.1	17%

Final expenses through 6/31/12, including accruals and expenses paid from donated funds. The final expenses include 10/11 encumbrances for 11/12 services to provide for assessment of ongoing expense rate.

Operating Expense Detail

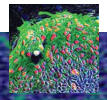
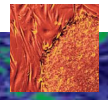
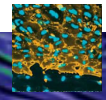
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Dollars in 000	Jul 2011-Jun 2012	Jul 2010 - Jun 2011
Employee Expenses	9,250	8,043
Contracting	2,470	2,760
Grant Reviews	603	612
Travel	367	405
IT	1,546	1,350
ICOC	140	199
Scientific Meetings	613	284
Office & General Exp	423	406
Total	15,413	14,059

Major drivers of OpEx variance vs. prior period:

- Employees: Increase from 46 to 54 FTEs and merit adjustments
- Scientific Meetings: WSC - $111K; Grantee Meeting - $253K

Note: 10/11 expenses have been adjusted by encumbrances for 11/12 services to provide for assessment of ongoing expense rate.

2012/13 Fiscal Year

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

- 2011/12 Annual Financial Audit
- Available bond cash as of July 31, 2012 $104.6mm
  - Increase of $53.7mm from 6/30/12
    - Bond Proceeds & Commercial Paper
- 2012/13 financial status to be presented at next ICOC meeting