CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

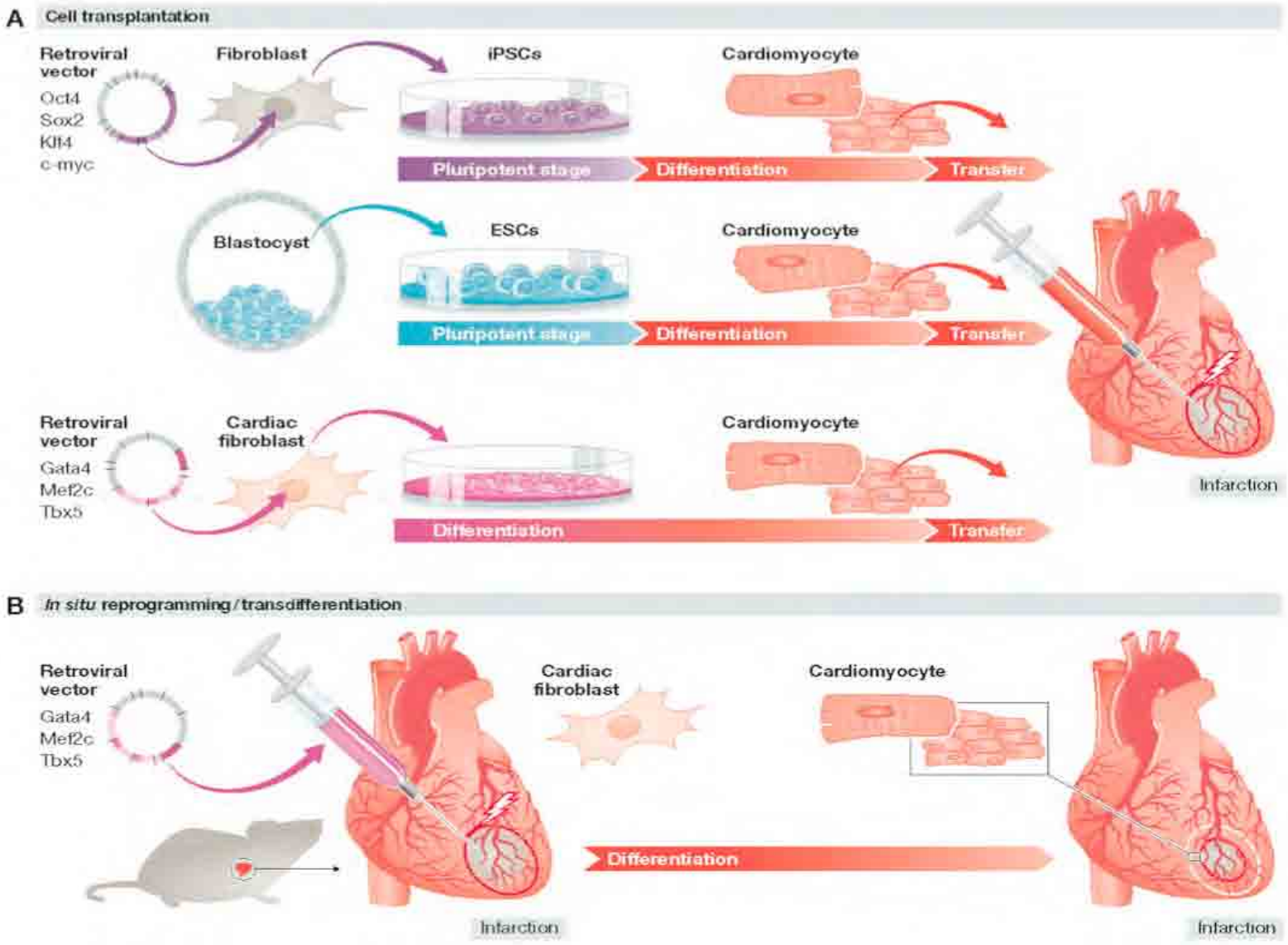
President's Report

Alan O. Trounson

ICOC Meeting – May 2012

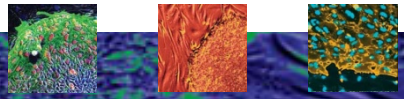
San Francisco, CA

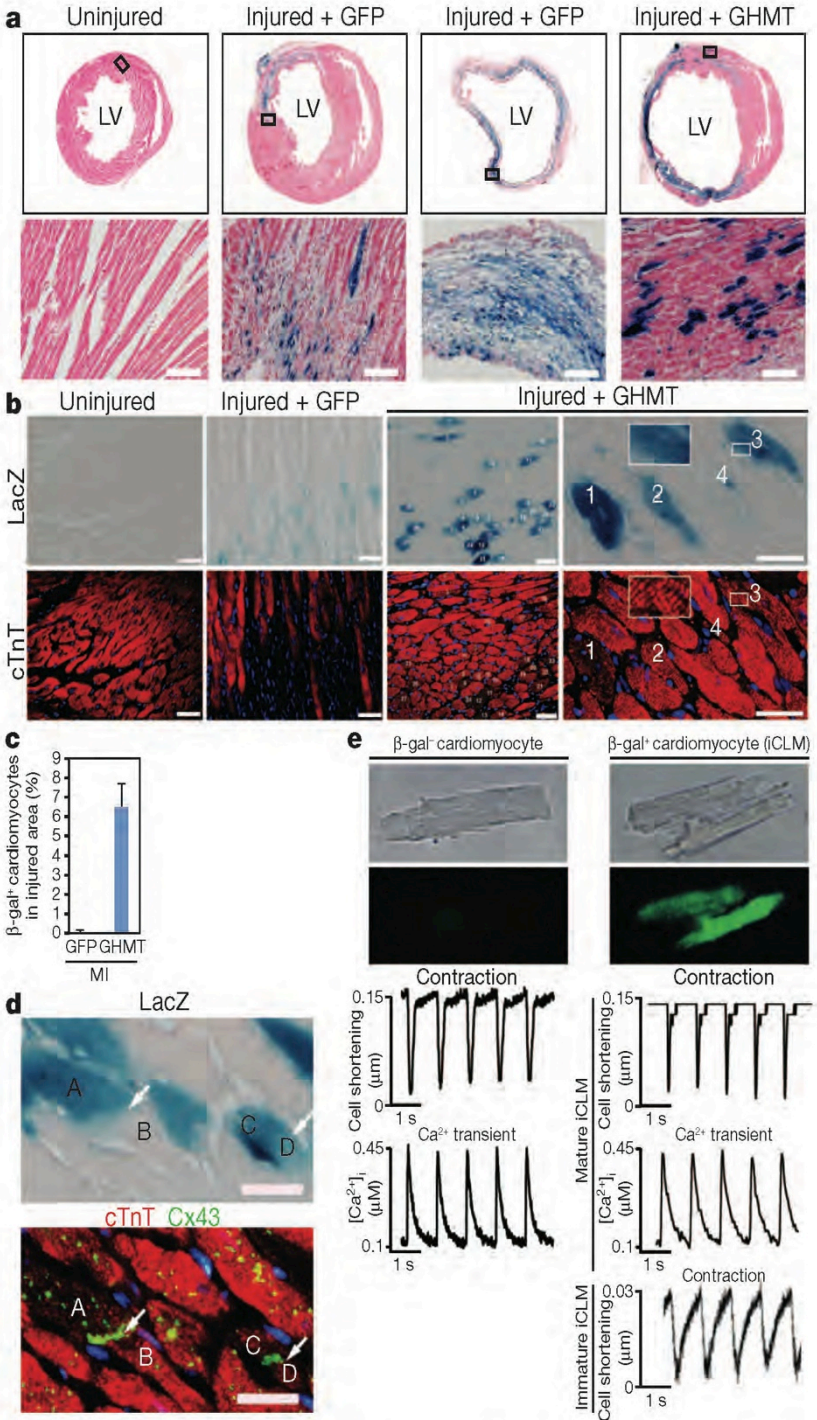
Qian etal. In vivo Reprogramming of Cardiac Fibroblasts into Induced Cardiomyocytes.
Deepak Srivastava's lab Gladstone Inst. *Nature* March 2012



Heart repair by reprogramming non-myocytes with cardiac transcription factors. Song etal., Eric Olson's Lab Uni Texas SouthWestern Med Cent. *Nature* May 13 2012

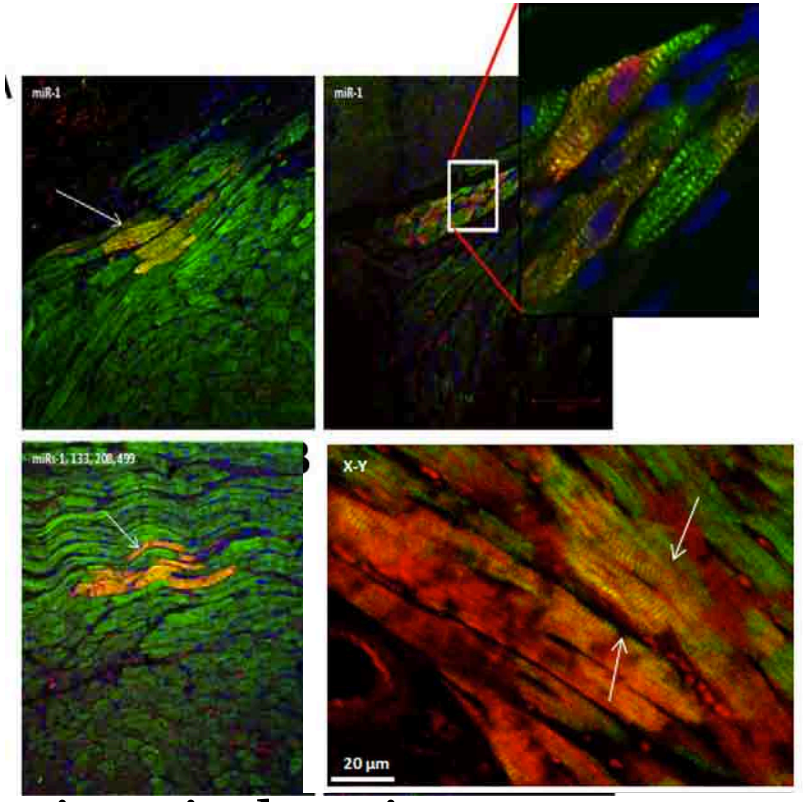
- They showed four transcription factors; GATA4, HAND2, MEF2C and TBX5 cooperate to reprogram cardiac fibroblasts (~9%) into beating heart muscle cells in vitro
- Retroviral - forced expression of these transcription factors in dividing non-cardiomyocytes in mice reprograms some of these cells into functional myocytes, improving cardiac function and adverse ventricular remodeling after MI
- INDEPENDENT CONFIRMATION




a
Uninjured
Injured + GFP
Injured + GFP
Injured + GHMT
LV
LV
LV
LV
b
Uninjured
Injured + GFP
Injured + GHMT
LacZ
cTnT
1
2
3
4
1
2
3
4
c
β-gal+ cardiomyocytes in injured area (%)
0
1
2
3
4
5
6
7
8
9
GFP
GHMT
MI
d
LacZ
A
B
C
D
cTnT Cx43
A
B
C
D
e
β-gal- cardiomyocyte
β-gal+ cardiomyocyte (iCLM)
Contraction
Contraction
Cell shortening (μm)
0.15
0
1 s
Ca2+ transient
[Ca2+]i (μM)
0.45
0.1
1 s
Mature iCLM
Cell shortening (μm)
0.15
0
1 s
Ca2+ transient
[Ca2+]i (μM)
0.45
0.1
1 s
Contraction
Immature iCLM
Cell shortening (μm)
0.03
0
1 s

MicroRNA-Mediated In Vitro and In Vivo Direct Reprogramming of Cardiac Fibroblasts to Cardiomyocytes

Jayawardena etal. Duke Cardiac Res Cent. *Circulation Research* published online April 26, 2012



- A combination of miRNAs 1, 133, 208, and 499 capable of inducing direct cellular reprogramming of fibroblasts to cardiomyocyte-like cells in vitro.
- miRNA-mediated reprogramming was enhanced 10-fold on JAK inhibitor I treatment.
- Administration of lentiviral miRNAs into ischemic mouse myocardium resulted in evidence of direct conversion of cardiac fibroblasts to cardiomyocytes in situ.

Derivation and cardiomyocyte differentiation of induced pluripotent stem cells from heart failure patients. Zwi-Dantsis etal., Lipor Gepstein's lab Haifa, Israel. *Eur Heart J* May 22, 2012

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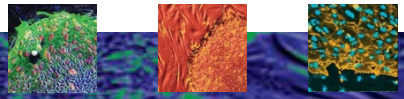
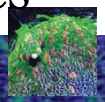
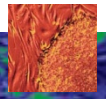
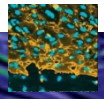
- iPSC reprogrammed cells from skin samples of patients with advanced heart failure – differentiated into functional cardiomyocytes
- They showed synchronized electrical activity between the human cardiomyocytes and neonatal rat heart myocytes in co-culture
- When transplanted into rat hearts, they engrafted, survived and structurally integrated with rat cardiomyocytes



Decade-Long Safety and Function of Retroviral-Modified Chimeric Antigen Receptor T Cells. Scholler etal. Uni Penn. Cellgene, UCSF, UCLA, Walter Reed Nat Mil Med Center. Sci Transl. Med. 2 May 2012

- There has been success of adoptive T cell gene transfer for cancer and HIV
- However, a key concern with the potential use of retroviral vectors has been whether expansion of cells harboring vectors integrated near genes involved in growth control will inevitably result in clonal proliferation
- Three large clinical trials to evaluate gammaretroviral vector engineered T cells for HIV
- Found donor T cells in 98% samples tested after 11 years at frequencies above T cell levels after most vaccine approaches
- Transgene retained expression and function
- No evidence of vector-induced immortalization
- Donor T cells had stable levels of engraftment – decay half life was >16 years
- These results will guide a wide variety of human studies

Decade-Long Safety and Function of Retroviral-Modified Chimeric Antigen Receptor T Cells. Scholler etal *Science Trans. Med* 2 May 2012

A

Annual	1	2	3	4	5	6	7	8	9	10	11	Total
Detected	*20*	*25*	*33*	*31*	*28*	*25*	*24*	*13*	*8*	*4*	*1*	212
Tested	*20*	*25*	*35*	*33*	*29*	*26*	*24*	*15*	*9*	*4*	*1*	221

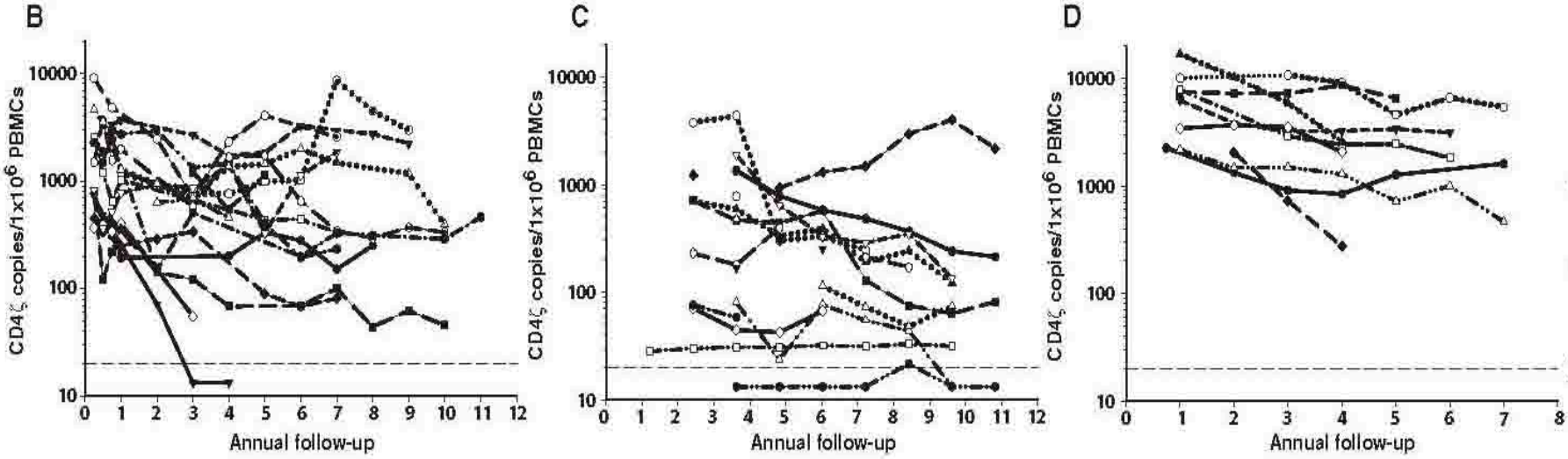


Fig. 1. Persistence of CD4ζ-modified CAR T cells over 11 years after infusion. (**A**) Total samples tested at annual visits and the corresponding number of samples with detectable CD4ζ. (**B** to **D**) Persistence of CAR T cells for the 43 individual patients in the (B) Mitsuyasu (*8*), (C) Deeks (*9*), and (D) Aronson (clinicaltrials.gov NCT01013415) trials at annual visits beginning at 1 year after infusion. The limit of detection (LOD) for the assay is plotted as a dotted reference line.

New Hires

- Bill Gimbel, IT Director, CIRM Contractor & Scholastic Inc., 5/16/12 hire date

Upcoming RFAs

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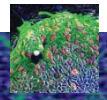
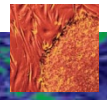
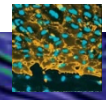
- **Early Translational III**
  - ICOC Funding Decision – this meeting
- **Basic Biology IV**
  - GWG Review of Applications – June
- **iPSC Initiative**
  - Posting of RFAs – June
- **Genomics Initiative**
  - Posting of RFA - July

Upcoming RFAs (cont'd)

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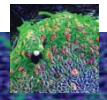
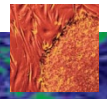
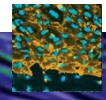
- **Disease Team Therapy Development**
  - ICOC Funding Decision – July
- **New Faculty Physician Scientist Translational Research Award**
  - GWG Review of Applications – October
- **Strategic Partnership I Awards**
  - GWG Review of Applications – September (tentative)

Collaborative Funding Program

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Current Composition = **21** participants

Disease Foundation Outreach:

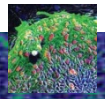
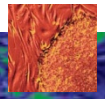
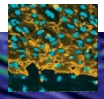
- Muscular Dystrophy Association has signed an MOU
- 3rd Foundation to join (NYSCF; JDRF)
- Additional Foundation outreach underway

Basic Biology IV RFA:

- India, France, China and Germany participating as potential co-funders
- 1st involvement for India and France

4th Annual Funders Meeting:

To be held during ISSCR

Creation of Scientific Resource Web Portal

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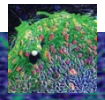
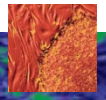
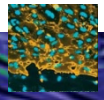
- Goals:
  - Facilitate access and information exchange among scientists in California and CFP jurisdictions
  - Enhance ability of California stem cell researchers to locate resources worldwide

- Partner: “Science Exchange”

Creation of CFP Web Portal

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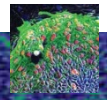
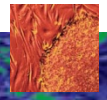
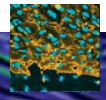
- Mechanism
  - Add portal to existing Science Exchange platform
  - CIRM and CFPs will populate site with relevant, non-confidential info
  - Zero Cost Agreement
- Timing
  - “Beta project” underway with Germany
  - Full operation target by year end

Creation of CFP Web Portal

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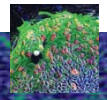
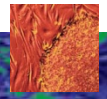
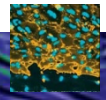
Possible Uses

- CA researchers can locate qualified partner researchers eligible for CFP funding in specific RFAs
- CFP researchers can identify California researchers with desired skill sets/expertise

Performance Audit

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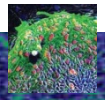
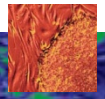
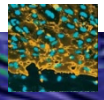
- Found to be in full compliance
- Gave recommendations for improved performance
- Staff plan for following up:
  - Analyze each recommendation
  - Take appropriate action
  - Track outcomes
  - Present full plan at next ICOC meeting

CIRM – China/MOST Workshop on Stem Cell Research

- Focused on networking and exploring collaborative opportunities between stem cell scientists in China and California
- To be held June 10-11, 2012 in Shanghai, China
- Attendance by 10-12 California scientists and 15-20 Chinese scientists including leading stem cell researchers from throughout China
- Scientific focus on neurodegenerative diseases, spinal cord injury and repair, and basic stem cell biology

Brazil/Argentina/California CFP Workshop

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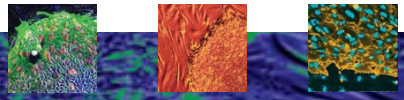
- São Paolo, Brazil, October 1-2, 2012
- Confirmed attendees:
  - 11 from California (City of Hope, Keck Graduate Institute, Salk Institute, Stanford, UCD, UCI, UCSB, UCSD, UCSF, USC)
  - 4 from Argentina
  - 19 from Brazil
- Topics:
  - Stem cell approaches to neurodegeneration, cardiovascular, eye and liver diseases



Industry Engagement

- BIO, June 19: CIRM will co-host with ARM and HSCI a workshop during the BIO conference
  - Focus will be on regenerative therapies in the clinic

- Stem Cell Meeting on the Mesa, Oct 30-31: Planning underway for the second industry partnering conference as part of Stem Cell Meeting on the Mesa

- Strategic Partnership RFA Posted/Webinar
  - Deadline for letters of intent was May 16th
  - CIRM, led by Ellen Feigal, held a webinar regarding the RFA; in addition to outlining the requirements, provided guidance on how to prepare a strong RFA

- Outreach to VCs and Pharma continues

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Finance Report

May 24, 2012

Financial Highlights
As of April 30, 2012

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

- YTD (to April '12) OpEx: $11.0mm
  - Prior period (to Apr '11): $10.1mm
- Grant disbursements YTD: $193.5mm
  - Prior period: $171.6mm
- Available bond cash: $92.8mm
  - Decrease of $65.0mm from 1/31/12

Note: Numbers are preliminary and unaudited

Operating Expense Detail

Dollars in 000s	Jul 2011-Apr 2012	Jul 2010-Apr 2011	Variance	Variance
Employee Expenses	$ 7,545	$ 6,608	$ 937	14%
Contracting	1,537	1,418	119	8%
Grant Reviews	303	441	(138)	-31%
Travel	292	227	65	29%
IT	591	886	(295)	-33%
ICOC	102	102	-	0%
Scientific Meetings	317	179	138	77%
Office & General Exp	302	266	36	14%
Total	$ 10,989	$ 10,127	$ 862	9%

Major drivers of OpEx variance vs. prior period:

- Employees: Increase from 46 to 54 FTEs and merit adjustments
- Contracting: $350K for IOM
- Scientific Meetings: WSC Summit for $111K
- Meetings: Grantee meeting was $175K (every 18 months); costs of GWG held in April 2012 not yet reflected in actual expenditures

Notes: Numbers are preliminary and unaudited. Only "Employee Exp." accurately reflects costs in the period; posting of all other expense categories lags significantly.

Forecast to Year-End

Dollars in millions	FY11/12 Budget	FY11/12 Forecast	Variance	Variance	Notes
Employee Expenses	$ 10.3	$ 9.3	$ (1.1)	-10%	Several open positions during year
Contracting	3.3	3.0	(0.3)	-10%	
Grant Reviews	1.2	0.8	(0.4)	-33%	Savings on GWG meetings
Travel	0.5	0.5	0.0	0%	
IT	1.3	1.6	0.3	21%	Not comparable to FY12/13 line item
ICOC	0.3	0.2	(0.2)	-50%	
Scientific Meetings	0.8	0.6	(0.3)	-34%	Savings on CDAP and workshops
Office & General Exp	0.7	0.6	(0.1)	-12%	
Total	$ 18.5	$ 16.5	$ (2.0)	-11%	

Forecast is based on actual expenses through 4/30/12; FY11/12 budget; and projections through FYE. This forecast is intended for assessment of ongoing expense rate and therefore includes FY10/11 encumbrances for FY11/12 services and expenses paid from donated funds.