CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

The state stem cell agency

President's Report

Alan O. Trounson

ICOC Meeting – January 2011

Agenda Item # 7

Bob Edwards IVF Pioneer– Nobel Prize for Physiology 2010 – friend and colleague

Harris Poll: Sept. 28-30 showed overwhelming public support for hESC research

- Included 2,113 adults aged 18 and over
- Americans overwhelmingly support embryonic stem cell research, and that backing stretches across a broad range of demographic groups, including Republicans, Catholics and born-again Christians, according to a new *Harris Interactive/HealthDay* poll.
- Almost three-quarters (72 percent) of the adults surveyed believe that scientists should be allowed to use embryonic stem cells left over from in vitro fertilization procedures to search for potential treatments or ways to prevent diseases such as Parkinson's disease, Alzheimer's, diabetes and other conditions.
- Only 12 percent oppose using stem cells for biomedical research, numbers that mirror those from a similar poll conducted in 2005.
- "There is now overwhelming public support for using embryonic stem cells in biomedical research," said Humphrey Taylor, chairman of the Harris Poll. "Even among Catholics and born-again Christians, relatively few people believe that stem cell research should be forbidden because it is unethical or immoral."

An Important Milestone in Stem Cell Research

GERON INITIATES CLINICAL TRIAL OF HUMAN EMBRYONIC STEM CELL-BASED THERAPY IN PATIENTS WITH SPINAL CORD INJURY

First Patient Treated at Shepherd Center in Atlanta

MENLO PARK, Calif., October 11, 2010 – Geron Corporation (Nasdaq: GERN) today announced the enrollment of the first patient in the company's clinical trial of human embryonic stem cell (hESC)-derived oligodendrocyte progenitor cells, GRNOPC1. The primary objective of this Phase I study is to assess the safety and tolerability of GRNOPC1 in patients with "complete" American Spinal Injury Association (ASIA) Impairment Scale grade A thoracic spinal cord injuries. Participants in the study must be newly injured and receive GRNOPC1 within 14 days of the injury.

geron

www.geron.com

Stanford joins first embryonic-stem-cell therapy clinical trial

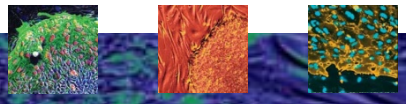
The first clinical trial of cells derived from human embryonic stem cells began in October 2010 in a paralyzed patient at the Shepherd Center in Atlanta. Today, Stanford University School of Medicine and Santa Clara Valley Medical Center became the third site to participate in the trial, which will enroll up to 10 patients with spinal cord injuries at up to seven institutions nationwide.

Stem Cells Used to Fight Woman's Brain Tumor – CBS Evening News: Nov 11, 2010

- **Ben Tracy Speaks Exclusively to the 1st Patient to Have Stem Cells Injected Into Her Brain to Fight a Tumor**
- Jenn Vonckx has been leaning on her family a lot lately. Just three weeks ago doctors in her hometown of Seattle, Wash., told her there was nothing more they could do to treat the tumor in her brain. They gave her two months to live.

  "It's a short time when they tell you that - wow - you wouldn't even believe how short it feels," says Vonckx.

  She didn't know that near Los Angeles, Dr. Karen Aboody has been working on a revolutionary new cancer treatment for the very worst brain tumors called glioblastomas, the same kind Vonckx has.

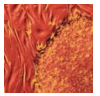
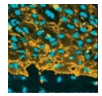


Highly Efficient Reprogramming to Pluripotency and Directed Differentiation of Human Cells with Synthetic Modified mRNA

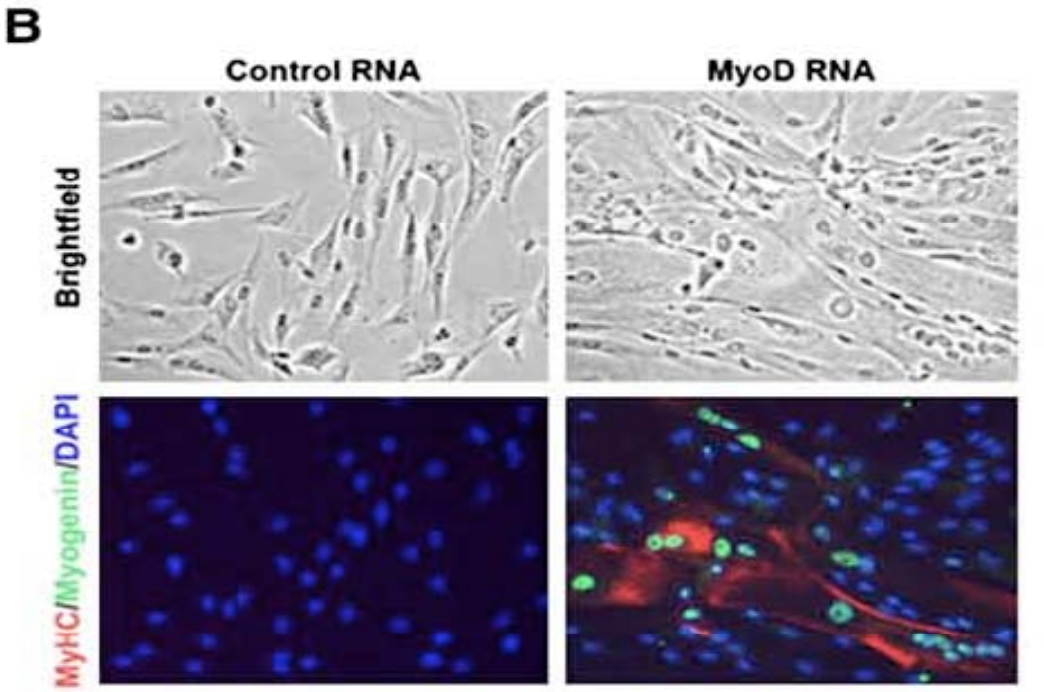
Warren et al., Derrick Rossi's Lab, Harvard Medical School

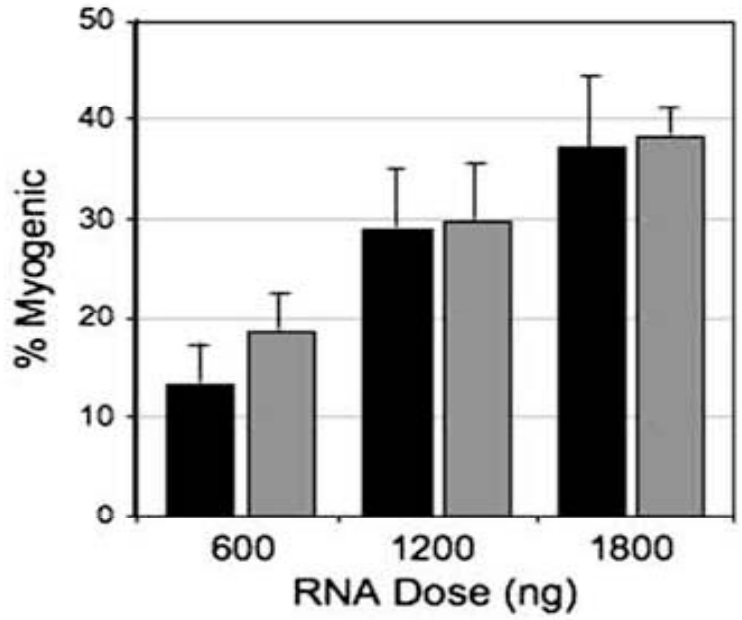
Cell Stem Cell 7:1-13 Nov 5th 2010

- They describe a simple non-integrating transfection method for reprogramming adult cells to iPSCs using synthetic mRNA encoding *KLF4*, *c-MYC*, *OCT4*, *SOX2* and *LIN28*, modified to overcome innate antiviral responses for 17 days in culture
- Greater efficiency than other methods (4.4% in low oxygen culture)
- Hierarchical clustering of transcriptional profiles showed that clones of RiPSCs were closer to ESCs than virally derived iPSCs – more closely recapitulate the molecular signature of ESCs
- The same technology can efficiently direct differentiation of these RiPSCs into myogenic cells – synthetic MYOD for 3 days
- This will enable large scale industrial manufacturing of RiPSCs and their derivatives for scientific and clinical use

Production of Patient Specific Myoblasts



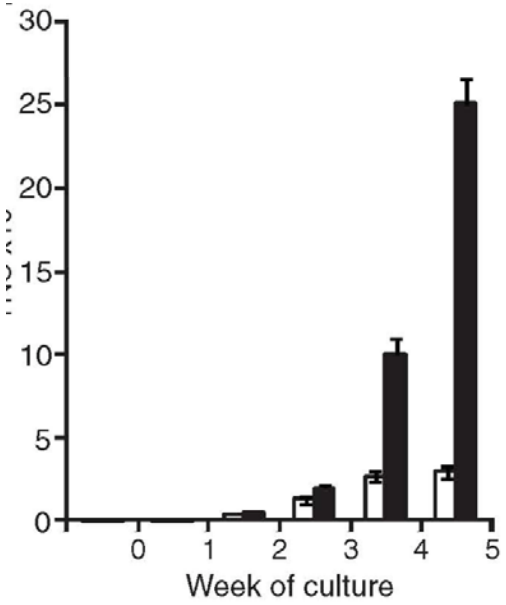


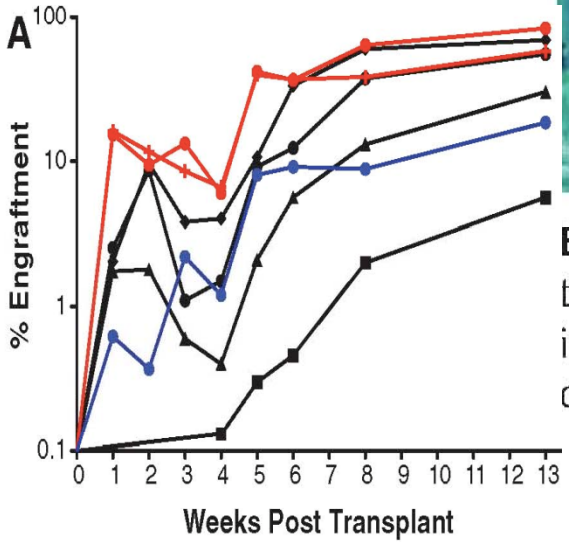
Aryl Hydrocarbon Receptor Antagonists Promote the Expansion of Human Hematopoietic Stem Cells

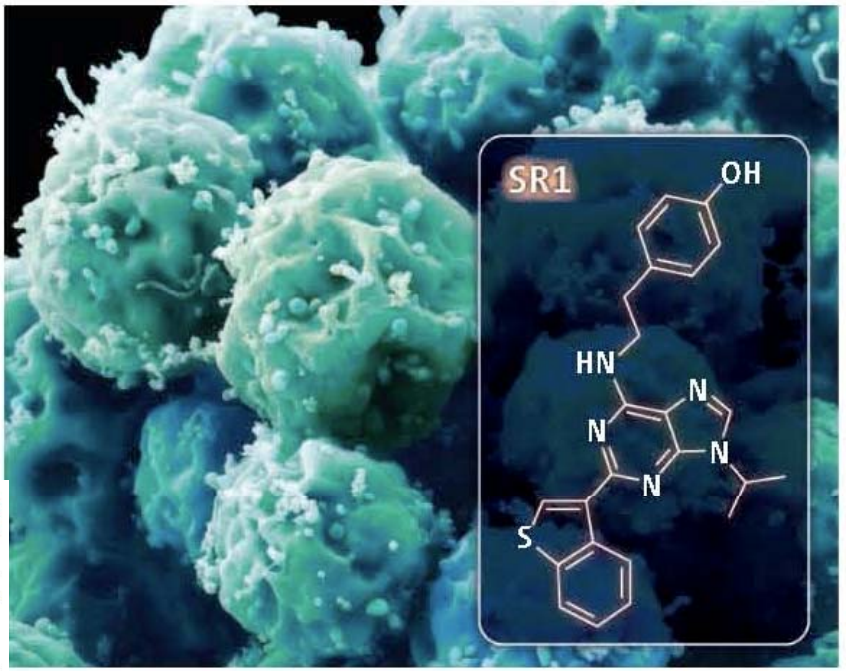
Boitano et al., Pete Schultz's group at Scripps and Novartis Research Foundation, *Science* 329 Sept 10 2010

- Expansion of $CD34^+$ cells x50
- x17 increase in cells with the ability to engraft immunodeficient mice

Culture in SR1 over 5 weeks maximized the number of $CD34^+$ cells







Expansion enhancer. The compound SR1 promotes the self-renewal of human hematopoietic stem cells in culture. SR1 is an antagonist of the aryl hydrocarbon receptor. Sauvageau & Humphries Science

Black – 1000, 3000, 10000 unculturedCD34 cells
Blue – 10000 cultured control conditions
Red – 300, 10000 SR1 cultured CD34 cells

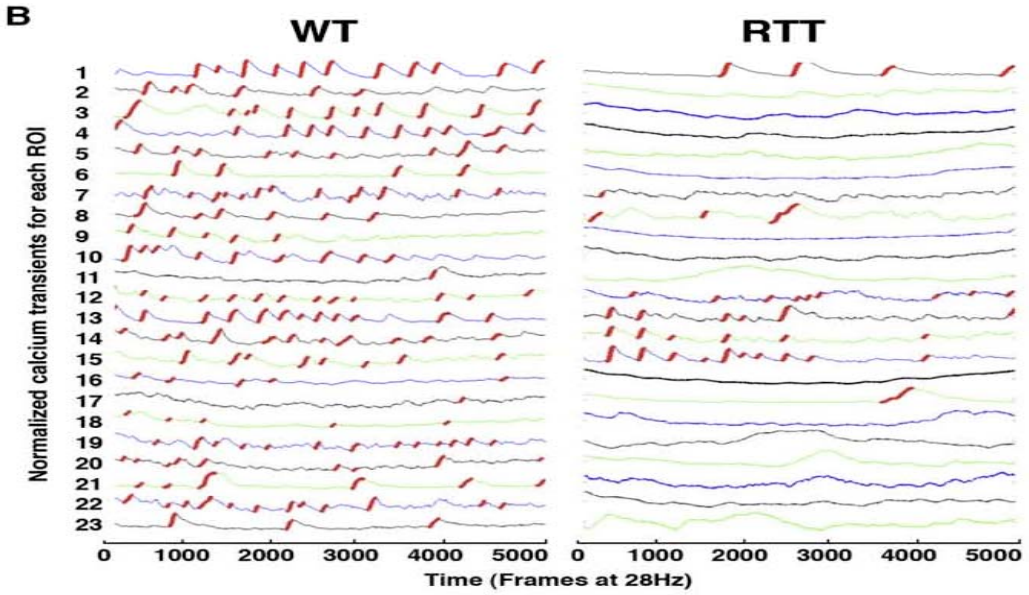
* CIRM Funded (Training)

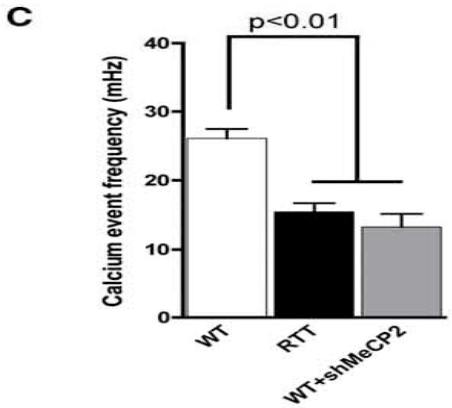
Robo4 Cooperates with Cxcr4 to Specify Hematopoietic Stem Cell Localization to Bone Marrow Niches. Stephanie Smith-Berdan et al., E. Camilla Forsberg's Lab, UC Santa Cruz.
***Cell Stem Cell*, 2011; 8 (1): 72-83**

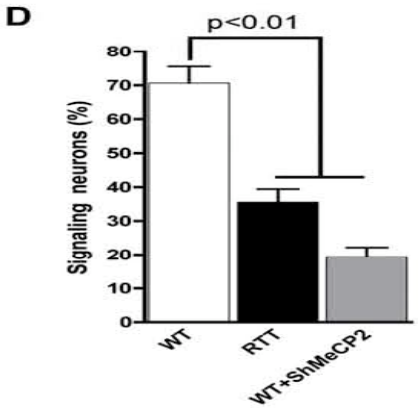
- Found the rare molecule Robo4 only in HSC and endothelium of blood vessels
- Required together with Cxcr4 for anchoring HSCs in bone marrow niche
- Robo4 is now a target for molecules that will interfere with HSC anchoring to enable a rich supply of HSCs to be released into blood for harvest of HSCs for clinical use

*CIRM Funded (New Faculty 1 & Training)

"A model for neural development and treatment of Rett Syndrome using human induced pluripotent stem cells" Marchetto etal., Rusty Gage and Alysson Muotri labs, UC SD and Salk Instit. Cell Nov 12th 2010







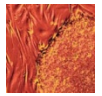
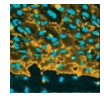
Prepared iPSCs from Rett Synd patients. Formulated a culture system that generated neurones. These has fewer synapses, reduced spine density, smaller soma size, Altered Ca signaling and electro – physiological defects compared to controls.

Showed that drugs could attenuate these defects when used prior to presentation of the the phenotype – early in the developmental window. Valuable Disease in a Dish Model for autism spectrum disease.

*CIRM funded (New Cell Lines & Comprehensive)

President's Priorities

- External 2010 Review – Draft Revised Operational report in preparation
- Met with CA stem cell science leaders UC SD for information exchange
- Clinical RFA – Four final applications to be reviewed in Feb
- Disease Teams – Projects are all underway and satisfactory beginning
- President's Evaluation – restructure proposed to Chair
- California Stem Cell Research Leadership Awards – continuing discussions
- Alliance for Regenerative Medicine – National industry consortium - preparing white papers and workshops on key regulatory issues
- Consortium for Regenerative Medicine (CIRM initiated) – Roundtable with FDA on animal models
- Collaborating Partners – MOU with India signed, NIH Clinical Institute – draft agreement exchanged, visit to China scheduled for March
- Genomics and Stem Cell Centers of Excellence in California – information gathering
- Workshop Reports: SCNT report posted, iPSC Bank report in preparation
- CIRM Translational Model likely to be adopted by new NIH Translational Center (NY Times Sun Jan 23rd)

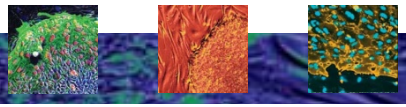




VP R&D

- We posted the RFP for the Search Firm in July of 2009 and Levin and Company was chosen in August of 2009.

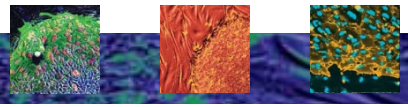
  *106 candidates were reviewed and considered.
  *17 candidates were interviewed

- Appointment made January 2011



VP R&D: Ellen Feigal MD

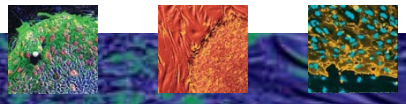
- Med School – UC Davis
- Residency Internal medicine – UC Davis & Stanford
- Fellow UCSF – cell regulation in AIDS-assoc. lymphoma
- UC SD – PI on RO1 – therapeutic approaches to A-a lymph.
- 1992 NCI – Cancer Therapy Evaluation Program
  - AIDS malignancy clinical trials consortium
  - Deputy Director Div Cancer Treatment & Diagnosis
- 2004 VP Clinical Science of new Translational Genomics Res Institute (non-profit) – clinical partnerships across Arizona
- 2006 Directed medical devices and imaging programs of Critical Path Institute (non-profit) – orphan diseases



VP R&D: Ellen Feigal MD

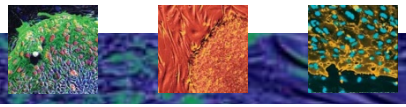
- 2006 - UCSF Adjunct professor – Director American Course on drug Development and Regulatory Sciences
- 2007 - CMO Insys Therapeutics Inc – supportive care oncology and neurological diseases. Developed, designed and oversaw Phase I and Phase III trials
- 2008 – Amgen Exec. Med Director Global Development.

  Clinical development of therapeutics in hematology/oncology. Evaluating investigational agents, interface with patient advocacy organizations, clinical guidance docs for therapeutic/steering committees and cross functional teams



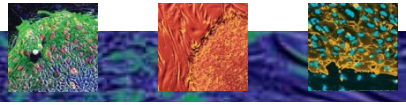
VP R&D: Ellen Feigal MD

- "Highly organized and focused and action oriented. Her style is to generate team effort and inspire... I would say her grandest quality is her capacity for effective leadership, thought, and an inspirational style that motivates both individuals and groups. "
- "She is a brilliant clinical scientist who knows drug development very well. She is very creative, very dedicated, very focused, and very hard working. Every effort or project that she undertakes is done in time. She is someone I would rank as a superstar."



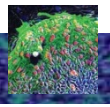
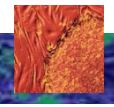
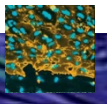
Workshop: CIRM-iPSC Banking Workshop - Nov 17-18, 2010

- Attended by 60 clinicians, researchers and cell banking professionals from the academic institutions and industry from US and abroad
- Discussed issues and considerations related to the development of the iPS bank from patients with broad haplotype from variety of diseases that could be used by California investigators for basic and applied research in regenerative medicine, drug discovery and toxicology
- Overall there was consensus among the workshop attendees that availability of bank of well characterized cell lines from number of diseases with patient clinical history and genotype will provide a valuable resource to stimulate basic and clinical research
- A summary of the workshop in the form of report will be written and recommendations from the workshop will be considered in deciding if a RFA or RFP is needed to fund these efforts



Personnel

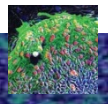
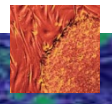
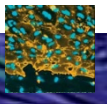
Doug Kearney
Grants Management Specialist
(U.C. San Francisco)

CIRM's Economic Impact Study

ICOC

January 2011

Economic Impact Study

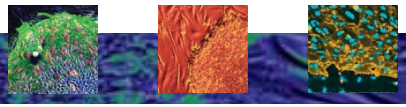
Goal –

Measure the economic activity created in California from CIRM's research investments

This interim study (2006-2014) is based on:

- Awards Committed (July 2010) - $1.05 Billion
- Matching Funds - CIRM's Major Facilities:
  - $562 Million – construction and equipment
  - $322 Million – recruitment and related capital costs

Conducted by Dr José Alberro, Director, BRG



Economic Impact Study

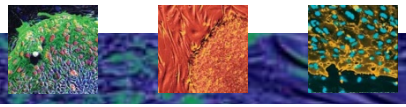
Outcome Measurements -

<u>One-time economic impacts</u> – short term

- <u>Direct</u> – jobs supported directly by CIRM funds along with related tax revenues
- <u>Indirect</u> – jobs and related tax revenues resulting from CIRM funds used to purchase supplies and equipment
- <u>Induced</u> – jobs and related tax revenues resulting from non-research related expenditures (overall expansion of economic activity)

<u>On-going economic impacts</u> – long lasting

- Long term benefits from supporting and stimulating “cluster” activity in the biotech industry
- Savings to the healthcare system (the topic of another report)



Economic Impact Study

Method –

Study uses **IMPLAN** (**IM**pact analysis for **PLAN**ning) -

Developed in mid-1980s; used by

- More that 100 State agencies (4 in California)
- More than 250 Colleges and Universities

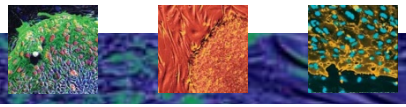
Computes employment multipliers for many types of investments:

Investment Type	**Employment Multiplier**
Training	1.55
Research	2.44
Facilities	2.19
Equipment	4.34
Average	**2.28**

Economic Impact Study

Jobs Created -

	Amount (x million)	**FTEs** (Job Years) (1 FTE = 1 job year = 2080 hours)
Grants & Loans	$1,051	13,586
Match/Leverage	$884	11,068
TOTAL	**$1,935**	**24,654**



Economic Impact Study

Tax Revenues to California -

TAX	AMOUNT (x million)
Sales	$49.1
Property	$39.1
Personal Income	$56.1
Corporate Income	$6.7
Other*	$50.6
TOTAL	**$201.6**

* Includes fines, fees, motor vehicle tax and state employment taxes

Economic Impact Study

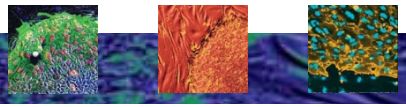
Results are conservative –

They do not include:

- Activity generated by research awards made between now and 2014
- Activity generated by the biotech sector (too early to measure)

Similar studies in other states have yielded higher estimates. However most:

- Include savings to the health care system
- Include growth in industry (biotech)
- Do not describe their methods



CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

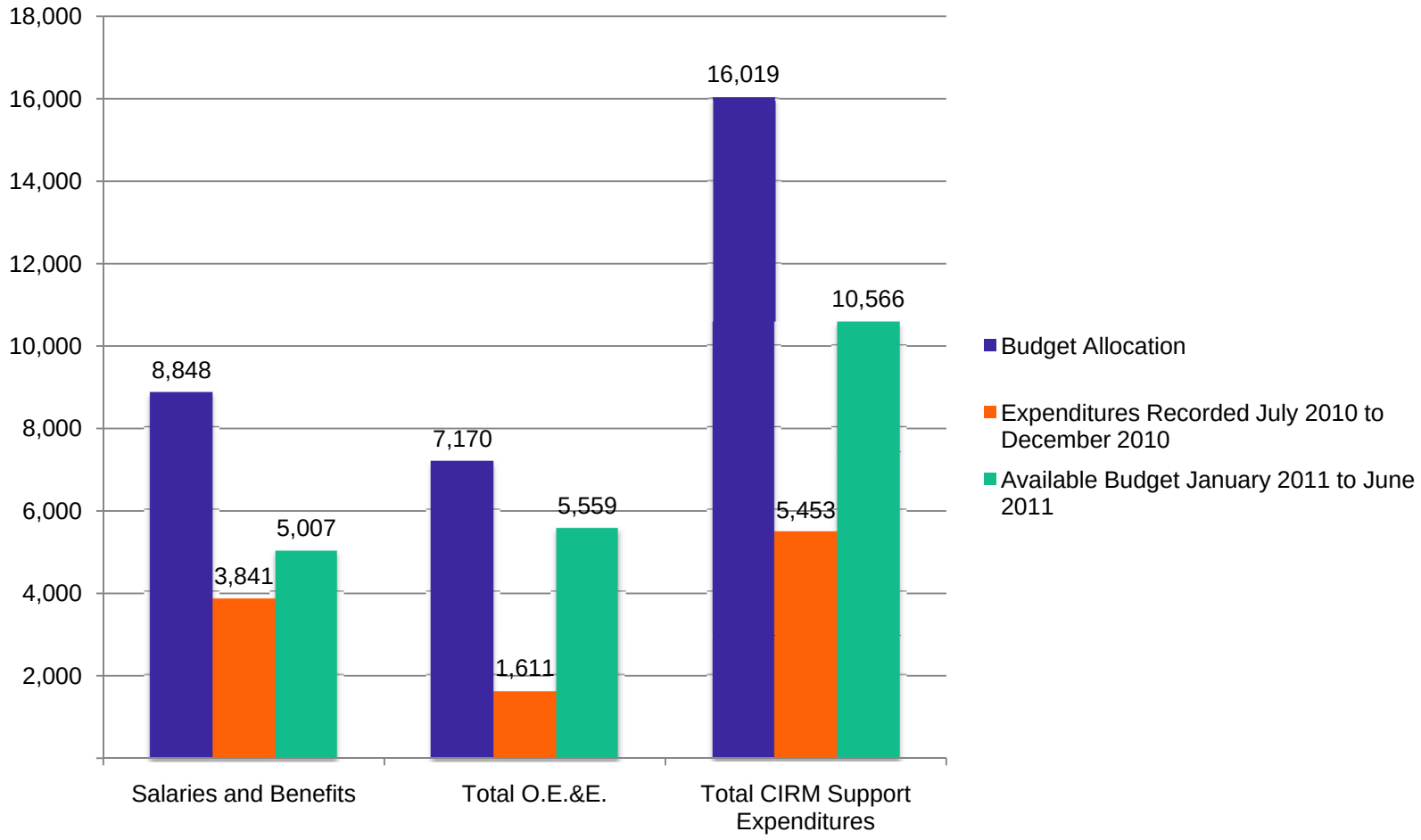
The state stem cell agency

2010-11 Budget Allocation and Expenditure Report Posted Through December 31, 2010

January 2011- ICOC Meeting

Chila Silva-Martin
Financial Services Officer

Fiscal Year 2010-11
Expenditures Posted Through December 2010



OPERATING BUDGET
Budgeted/Posted
July 1, 2010 to Dec 31, 2010