Happy New Year to all of our colleagues at UC Davis who work on or are interested in Stem Cells!

We have prepared a short January 2010 newsletter to update you on progress for the new Institute for Regenerative Cures building, to inform you about Stem Cell Program-related Cores/ Infrastructure that has been developed, and to let you know about upcoming grants from the California Institute for Regenerative Medicine (CIRM).

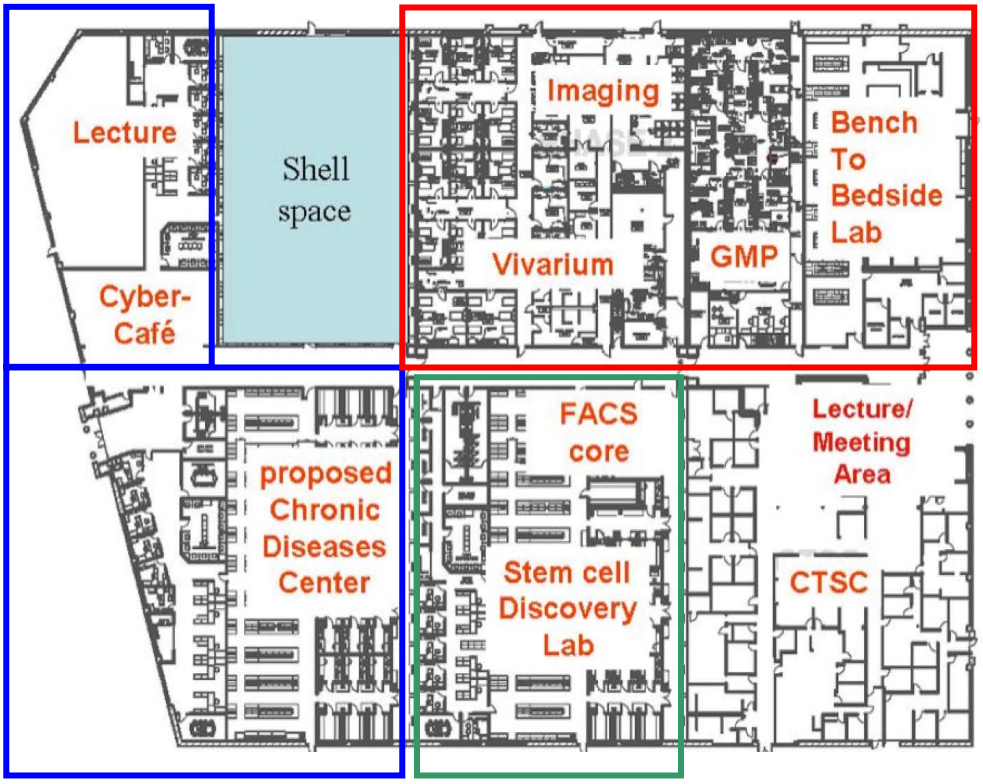
Groundbreaking for the new Institute for Regenerative Cures was in Sept 2008 and it was a cavern – a big empty warehouse surrounding the CTSC at Stockton and Broadway. Dean Pomeroy had the vision to make it into our hub for Regenerative Medicine. Thank you to Alice Tarantal, Gerhard Bauer, and Mark Romney and his crew for working so diligently with me for almost a year to prepare the major facilities grant, for which we were awarded $20,082,400.00 from CIRM for bricks, mortar, and equipment. The contractors, Turner construction, Mark Romney, John Gambone, Gerhard Bauer (GMP Director) and the whole team have done an amazing job of bringing the blueprints to life. Move-in will occur in phases over the next several months.

The newly constructed UC Davis Good Manufacturing Practice (GMP) facility in the IRC is the largest academic GMP facility north of Los Angeles. It is a 6 manufacturing room, Class 10,000, state of the art, multi-use clean room facility and has an associated product scale up and testing lab. It has some very unique features, such as a GMP grade FACS sorter, the ability of switchable room pressurization to achieve negative room pressurization for gene therapy vector manufacturing, and also a hot cell for clinical grade PET reagent manufacturing (Bottom right- purchased through an equipment grant obtained by Julie Sutcliffe). The facility has been approved by the FDA in a Type C meeting with the agency. It is opening currently. Below is a link to the GMP facility video that CIRM produced about this facility one month ago.
http://www.youtube.com/user/CIRMTV#p/a/u/0/Pg2mH5cOB9s

The GMP facility has been designed to perform any type of manufacturing of cellular therapies, but due to its versatility, can be adapted to manufacturing of other products. For any product manufactured that will be used as a therapeutic, the GMP facility staff will help with establishment of Standard Operating Procedures (SOPs), Quality Control and Quality Assurance, storage and release of the product.

If you have interest in using the facility, we invite you to come in small to large groups to visit during the month of January, while we can walk through prior to the official scrub down. We have hourly rates for use of the facility and product manufacturing established, thanks to Stem Cell Program Manager Geralyn Annett, working closely with our UCD Rates Committee. If you have an interest in using the facility to develop a gene therapy, cellular therapy, or other product for use in the clinic, or know of outside companies or collaborators who might want to contract, please feel free to come see this facility before the first week in February, when the official scrubdown will begin prior to use in generating clinical products.

Please contact GMP Director Gerhard Bauer for rates and availability:
Gerhard.bauer@ucdmc.ucdavis.edu



Institute for Regenerative Cures. The renovation of the 109,000 ft^2 Facility is underway, with the first phase (red box) nearly complete. The state-of-the-art facility provides a GMP Facility for Cell and Gene Therapies and other therapeutics. The vivarium is for pre-clinical testing of human cells and other therapeutics in mice. The CTSC is adjacent, facilitating translation to the clinic.

Proposed: C06 grant submitted (Berglund PI)

CIRM-funded/currently under renovation

CIRM-funded: near completion

Right – shared bench to bedside lab, IRC. Induced pluripotent stem cell derivation will be performed in the Stem Cell Core, in the “Bench to bedside” lab equipped with 6 tissue culture rooms and shared bench space for training postdocs, students and techs participating in the stem cell program, to facilitate maintenance of stem cells derived from consented patient samples.

Stem Cell Program Core Facilities and Resources - *The Stem Cell Program provides multiple cores and services summarized below, including a retroviral and lentiviral vector core, a Flow sorting and FACS analysis core, an immune deficient mouse core, and provides scale-up services for development of novel therapeutics in the GMP facility.*

Flow-Assisted Cell Sorting (FACS) Facility– FACS for the Stem Cell Program is run through the Cancer Center Optical Biology Program by Carol Oxford, Technical Director, and Bridget McLaughlin. Ms. Oxford, a well-respected expert in her field, has overseen the Optical Biology Shared Resource at UC Davis for the past decade. Ms. McLaughlin, also an expert in the field, operates the cell sorter for the stem cell program, assists with experimental design, maintains all instruments and is in charge of scheduling their use and reporting usage for billing. The **Cytopeia InFlux** is a high-speed cell sorter with six lasers and 16 parameter measurement capability, and was purchased for the Stem Cell Program. This instrument can detect 14 simultaneous fluorescent parameters. Up to 4 populations can be sorted simultaneously. A biohazard containment system is in place. To use the facility in its current home in the Oak Park Building, or in the IRC in future months, please book via the Opticore website:

http://ccresources.ucdmc.ucdavis.edu/csr/optical.csr?pg=opticalservicesrates

Stem Cell Program's Vector Facility– A centralized service for the development and production of viral vectors necessary for gene transfer in research experiments and pre-clinical studies. Expert technical staff will consult with investigators to plan and develop vectors to fit individual project requirements, design and construct novel vectors and generate purified recombinant moloney murine retrovirus and lentivirus. Quality control testing will include vector titering and replication-competent retrovirus (RCR) and Lentivirus (RCL) assays. The core has been generating iPSC from patient samples for some of the groups working in the Stem Cell Program and now, with the advent of non-integrating vectors and protein-only development of these cell lines, will assist faculty with the development, isolation and purification of vectors and recombinant technology to generate the new cell lines. To use services please contact Vector Core Director Karen Pepper at:

Karen.pepper@ucdmc.ucdavis.edu

Karyotyping - in development: The karyotyping service is currently run by a UCD volunteer, Catherine Nacey, on an ad-hoc basis, in collaboration with Sutter hospital. This allows us to monitor the stability of human ES and Induced pluripotent stem cell lines. With future equipment purchase we may be able to provide this as an affordable service for UCD investigators.

Specific Pathogen Free Barrier Facility (SPF) Vivarium - The current vivarium space for the stem cell programis quite crowded in the basement of the Research III building but the new IRC vivarium will allow expansion and increased availability of services. The new facility consists of approximately 10,500 sf^2 of shower-in, disease-free housing for experimental animals comprised of fourteen holding/ procedure rooms. These rooms are separated into four suites of three rooms and one suite of two rooms. The following resources will be situated within the animal facility:
A tissue culture room for cell isolation, the animal irradiator for transplantation procedures, and separate imaging and behavioral testing rooms.

Immune deficient mouse core for teratoma testing to validate pluripotentiality - Dr. Nolta has established the Immune Deficient Mouse Core at Sacramento campus. Animal care is provided by the Center for Laboratory Animal Science. The core performs procedures on NOD/SCID, NOD/SCID/B2M null, and NOD/SCID/ IL2Rg (gamma chain)-/- mice for faculty investigators on a fee-for service basis. Induced pluripotent stem cell lines generated for investigators will be tested there for pluripotentiality (teratoma formation), a hallmark of the induction process. For rates and availability please contact Core Director Jeannine McGee: Jeannine.mcgee@ucdmc.ucdavis.edu

California Institute for Regenerative Medicine: **http://cirm.ca.gov/UpcomingRFAs**

Upcoming RFA Schedule

The following is a provisional schedule for the release of upcoming RFAs. This schedule will be updated periodically to provide California researchers with advance notice of upcoming funding opportunities. More details about individual RFAs will be available following concept approval by CIRM's governing board, the Independent Citizens Oversight Committee, typically 1-3 months before RFA release.

RFA #	Title	Date for RFA Release (Provisional)	Funding Partner(s)
10-01	Early Translation II read the approved concept	mid-February 2010	TBD
10-02	Tool, Technologies for Bottlenecks	March/April, 2010	TBD
10-03	Basic Biology III	August, 2010	TBD
10-04	Disease Team II	Late Fall, 2010	TBD

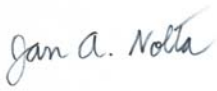
The translational round RFA will be posted in Feb. 2010. It is for work that needs more benchwork before proposing a stem cell-based therapy, such as optimizing conditions, defining sorting methods, selecting between two potential candidate cell types or differentiation protocols, etc. These should again be for 3 to 6 million. The approved RFA concept is attached on the next page.

The next round of disease team grants will be for cell products or their derivatives where everything has been optimized at the bench already and the product is in IND-enabling scale-up and animal/toxicity studies prior to clinical trials. Again these grants are expected to be for up to $20 mil, and some of this can be allocated to phase 1 trial costs (a change from the 2009 round).

Important information in the current fiscal crisis is that the CIRM funds are currently secure since grant allocations come from the sale of privately-placed 30-year bonds rather than the General State Budget. Prior to 2010, CIRM's bonds were forward capitalized and the agency paid its own interest, so during its first five years CIRM had no cost impact on the state's general fund. For more detail please see: http://cirm.ca.gov/PressRelease_011510

If you have questions about these grants or are interested in applying for one or contributing to a larger team, please contact me via email and we will set up a time to discuss.

Thanks to all of our program affiliates, and please come visit us in the new year!!



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RFA 10-01 CONCEPT
CIRM EARLY TRANSLATIONAL II RESEARCH AWARDS

PLEASE READ THE RFA WHEN IT IS RELEASED FOR FINAL AND FULL INFORMATION

Purpose and Objectives

The purpose of the CIRM Early Translational II Research Awards is to fund studies to move promising basic research in stem cell science toward the clinic. To this end, these awards will support two categories of research projects:

1) Development Candidate Awards (DC Awards) will support research that results in a novel stem cell-derived development candidate that meets an unmet medical need. By the end of the award period, these projects must have completed all necessary activities to result in a development candidate ready to start Investigational New Drug (IND)-enabling preclinical development

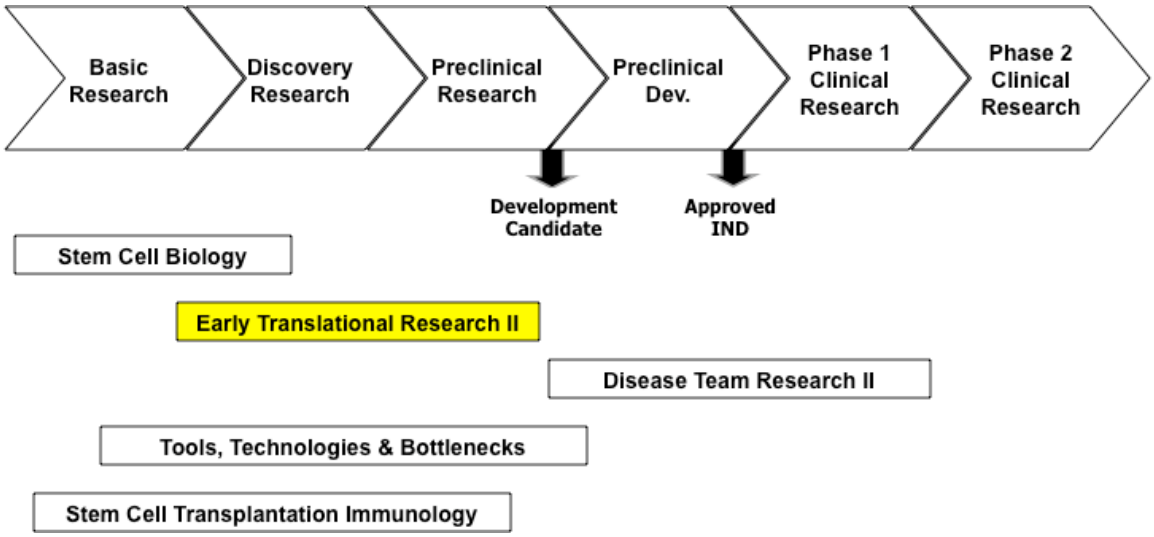
2) Development Candidate Feasibility Awards (DCF Awards) will support research directed towards the goal of obtaining a novel stem-cell-derived development candidate. Unlike the above Development Candidate Awards, by the end of the award period, applicants for these awards do not need to have completed all the necessary activities required to start preclinical development necessary for a regulatory filing. Rather, these awards are intended to allow investigators to conduct research to *identify or determine feasibility* of a given potential development candidate. For example, applicants for these awards may wish to identify a lead candidate, reproducibly establish disease-modifying activity or screen multiple candidates against a single, defined disease target.

For both types of awards, to be responsive to this RFA, applicants must have already identified a single disease target for therapeutic (diagnostic) intervention and have a scientifically justifiable hypothesis for the proposed development candidate.

In addition, CIRM will prioritize proposals:
- Resulting in a novel cell therapy development candidate derived from pluripotent cells (DC Award);
- Leading to a novel cell therapy development candidate derived from pluripotent cells (DCF Award);
- Based on human pluripotent stem cells (e.g. human pluripotent stem cells used for drug or diagnostic discovery).
- Ineligible for or unlikely to receive timely or sufficient federal funding

Research that is outside of the scope of these awards includes:
- Target discovery.
- IND-enabling preclinical development activities (e.g. GMP production, GLP toxicology and tumorigenicity studies).
- Clinical studies. Analysis of human subject samples, if directly related to the proposed research, can be funded.

Diagram of Stage Specificity of Current and Upcoming RFAs



CIRM Award Information

CIRM proposes to fund:

- Development Candidate Awards with justifiable total requested funds for each award over three years of up to $6.0 million for a total of up to $60 million
- Development Candidate Feasibility Awards with justifiable total requested funds for each award over three years of up to $2 million for a total of up to $20 million
- Total program cost of up to $80 million.

For-profit applicant organizations will be permitted to apply for either grants or loans. Non-profit applicant organizations will be funded through grants

Loan Information

Loans will be administered over a six- or ten-year term to be determined by the loan applicant. Loans will be recourse or non-recourse. The interest on six-year loans will be prime plus 300 basis points; the interest on ten-year loans will be prime plus 500 basis points. The prime rate will be that on the date the ICOC authorizes funding of the loan.

CIRM Institutional Eligibility

- All CIRM supported research must be conducted in the state of California
- Open to all academic, non-profit and for-profit institutions in the state of California
- For this RFA, CIRM will use its pre-application process; therefore no limits will be applied on the number of pre-applications an eligible institution can submit.

CIRM Investigator Eligibility

As a multidisciplinary team often most effectively conducts translational research, this award will be open to:

- A Principal Investigator (PI) and, in the case of Development Candidate Awards, up to 1 Co-Principal Investigator (Co-PI) with Ph.D., M.D or equivalent degrees who are

authorized by the applicant and Co-PI institutions to conduct the proposed research in California.
- PIs and Co-PIs must commit 20% and 15% effort respectively towards programs supported under this RFA.

CIRM encourages collaborative endeavors between non-profit and for-profit institutions.

Collaborative Funding Partner Participation

CIRM has established a program with several other government agencies that fund stem cell and regenerative medicine research. Through this Collaborative Funding Partner program, California-based PIs can collaborate with a Funding Partner PI from a Funding Partner applicant institution eligible for funding from one of CIRM's collaborative funding partners to bring important additional resources to proposed projects. If a collaborative funding proposal is approved CIRM will fund all project work done within the State of California and its Funding Partner will fund all project work within its jurisdiction.

Provisional Time Table:

• Release of RFA 10-01	mid Feb	2010
• Pre-Applications due	Mar 18	2010
• Applications due	July	2010
• Grants Working Group Review of Applications	Sept	2010
• ICOC Approval	Oct	2010