

**Read Research Program
October 2009**

I. INTRODUCTION

Major research areas

Bench-to-bedside translation/development of cellular therapies

Major BSRI collaborations

Rosa Sanchez-Rosen, MD

Major non-BSRI collaborations

Jeff Bluestone, PhD (UCSF)

Michael Matthay, MD (UCSF)

David McKenna, MD (University of Minnesota)

Susan Fisher, PhD (UCSF)

Yerem Yeghiazharians, MD (UCSF)

Harold Bernstein, MD (UCSF)

Jeff Lotz, PhD (UCSF)

Mitch Berger, MD (UCSF)

Staff

Yelena Dayter

II. PROGRAM SUMMARY/ PROGRESS REPORT/PLANS

Background

The field of clinical cellular therapies has grown dramatically since its beginnings in traditional bone marrow transplantation in the 1960s. Scientific advances in the 1980s and 1990s, notably in molecular biology, genetics, and immunology, spurred interest and development of a broad range of novel cell-based therapies, including immunotherapies and gene therapies. More recently, advances in stem cell biology have led to rapidly increasing understanding of adult and embryonic stem cells, and translational opportunities for treatment of cancer, diabetes, cardiovascular disease, neurological disease, autoimmune disease, and numerous other ailments. The most striking recent advance-- the discovery that adult somatic cells can be reprogrammed or induced to become pluripotent—has raised the possibility that a broad range of diseases may be amenable to cellular and regenerative therapies using autologous cells.

The role of transfusion medicine specialists in the bench-to-bedside translation of cellular therapies is based largely on practical expertise in cell collection, donor testing for infectious diseases, and ex vivo manipulation of cells using standardized, clinically feasible methods, and quality system practices in an FDA-regulated environment. Regardless of where the expertise lies, the greatest barrier to clinical cell therapy is the exorbitant cost of developing novel products for clinical trials. NHLBI's Production Assistance in Cellular Therapies (PACT) program, the California Institute of Regenerative Medicine (CIRM), and others have developed funding initiatives to address this issue. These funding agencies have also recognized the need for true multidisciplinary teams to maximize the likelihood of getting these new therapies developed and into clinical trial.

Program Goals

My overall goal for this program is to develop and expand Blood Systems' role and expertise in the rapidly evolving field of cell and tissue therapies. To accomplish this goal, it has been necessary to build infrastructure, expertise, and collaborations. The specific goals originally listed in 2007 were:

- **Support basic, translational, and product development research** in cell & tissue therapies
- **Establish a cell sourcing program** to serve academic and biotechnology customers with research cell and plasma products and to promote BSRI's research and development activities
- **Develop improved methods for ex vivo cell manipulation** that can be used in the clinical manufacture of cell and tissue therapy products
- **Collaborate with academic-based investigators and biotechnology companies** to develop novel cell & tissue therapy products and assays that can be tested in clinical trials
- **Collaborate with clinical hematopoietic transplant (BMT) programs** to develop, collect, process, test, and store conventional cell therapy products from bone marrow and apheresis sources
- **Establish a public cord blood bank** to serve patients who need stem cell transplants from unrelated donors and to support research and development on cord blood as a source of hematopoietic and immune cells
- **Promote education and training** in cell & tissue therapies for scientific, medical, technical, and donor/patient care staff

SAN FRANCISCO ACTIVITIES

Cell Sourcing Program

Rationale: Ready access to peripheral blood mononuclear cells (and other human cells) is critical to provide "raw material" to investigators for development of novel cell therapies, and for other research at BSRI and beyond. BSRI's most immediate need was to support a high-profile, well-funded UCSF development project on T regulatory cells, so establishing this program was my highest priority when I arrived in November 2006. I aimed to set up the program in a manner that would make the program self-supporting, by selling products to external customers.

Status: The program has been established in San Francisco, after the following products have been developed, with specifications available to customers:

1. Mononuclear cells from Trima plateletpheresis residuals
2. Apheresis mononuclear cells from normal research subjects
3. Purified lymphocytes and monocytes from automated elutriation of apheresis MNCs

The primary paying customer for these research products is Genentech, where they are used for a wide variety of discovery research projects in immunology and oncology.

BSRI investigators and UCSF collaborators also have access to these products. Specific BSRI activities supported with these products include:

Norris lab: MNCs cryopreserved for (1) use as irradiated feeder cells for CD4 clones in Elispot assay to test HIV peptide specificity, (2) optimization of T cell assays (antibody titration, Treg and Th17 panels for flow cytometry, IFN gamma and IL-17 Elispot, and proliferation) to support characterization of T cell responses to WNV in blood donors, (3) microchimerism project, (4) pathogen reduction project, and (5) training of summer students.

Simmons lab: (1) Monocytes (and macrophages differentiated from them) used to demonstrate the cellular tropism of Chikungunya virus. (2) Elutriated platelets used to show that HCV binds to platelets, and to study mechanism of that binding; studies suggest that this binding may be important for dissemination of HCV.

Read lab: Manufacturing process development for T regulatory cells.

Specific Collaborative Projects

A. T Regulatory Cells for Treatment of Type 1 Diabetes Mellitus

PI: Jeffrey Bluestone, PhD

Rationale: It is well-established in animal models that abnormalities of T regulatory cells play a critical role in the pathogenesis of autoimmune disease and graft-versus-host disease. In addition, there are numerous studies suggesting that Treg deficits may be an underlying cause of human autoimmune disease. The Bluestone lab at UCSF has developed methods for expanding Tregs that maintain suppressor cell activity while minimizing effector cell function. Bluestone and his collaborators in the **JDRF-supported Collaborative Center for Cell Therapy** have proposed to translate Treg therapy into patients with Type 1 diabetes mellitus (T1DM), an autoimmune disease. The goal is to re-establish immune tolerance in these patients. Bluestone and others have demonstrated in NOD mice that adoptive transfer of Tregs can slow disease progression and in some cases reverse new onset disease. The proposed clinical trial will use autologous, peripheral blood, flow-sorted, culture-expanded polyclonal T regulatory cells in adult patients with new-onset T1DM.

Status and Plans: In collaboration with Bluestone & staff, I worked from early 2007 through March 2009 on development of a clinical-scale process to generate autologous Tregs for this phase I clinical trial in T1DM. This project consumed much more time than one would expect from a 5% effort. Specifically, I:

- provided input on both product manufacturing and clinical trial design on conference calls and in meetings
- prepared or edited relevant sections of the pre-IND packet for submission to FDA,
- interacted with UCSF apheresis staff regarding appropriate methods for collection of MNCs from normal donors and patients
- trained (or arranged for training at NIH) staff from both the Bluestone research lab and the UCSF GMP facility on product development
- participated in meetings with UCSF microbiology to establish and validate appropriate sterility testing methods for human cellular products from the UCSF GMP facility
- established a collaboration with Gambro (now Caridian) for studies of the closed automated system (Elutra) for enrichment of lymphocytes, and performed elutriation of normal donor MNCs to isolate lymphocytes for flow sorting
- performed product development studies - evaluation of Haemonetics MNC collections, evaluation of Biosafe Sepax closed system ficoll-hypaque density gradient procedures
- provided cryopreservation SOPs and advice to Bluestone lab staff, and facilitated manufacture of a clinical-grade pentastarch (an ancillary product) by a commercial manufacturer for testing in cryopreservation of Tregs by UCSF
- provided Trima MNCs and elutriated lymphocytes for Treg flow sorting experiments at UCSF

My overall efforts with this group were aimed to design, evaluate, and validate an appropriate scaled-up, clinical manufacturing process for autologous Tregs. The UCSF team has concluded that it is not possible to replicate their research process for isolating and expanding Tregs in a clinical-grade process. They have also concluded that these cells cannot be cryopreserved. They are therefore planning to move their research manufacturing process, performed by one research tech and uses whole blood, ficoll-hypaque in tubes, and flow sorting, into the GMP facility. Although the target date for starting the clinical trial was October 2008, the clinical trial has not yet started.

B. Allogeneic Mesenchymal Stem Cells for the Treatment of Acute Respiratory Failure from Acute Lung Injury

PI: Michael Matthay, MD

Rationale: Acute Lung Injury (ALI) is a major cause of acute respiratory failure in critically ill patients in the United States, occurring in 200,000 patients in the U.S. annually, with high mortality (40%),

accounting for approximately 75,000 deaths per year. Randomized clinical trials based in part at UCSF and supported by the National Heart, Lung, & Blood Institute have demonstrated the benefit of specific ventilator and supportive strategies in treating ALI. However, there has been no progress in identifying specific pharmacologic therapies that reduce lung injury and mortality. Evidence from Matthay's studies in mice demonstrated that treatment with allogeneic mesenchymal stem cells (MSCs) reduces ALI, pulmonary edema and mortality in an endotoxin model of ALI. The Matthay laboratory has also tested the therapeutic value of allogeneic human MSC obtained from an NIH repository (Dr. Darwin Prockop, Tulane University) in a novel *ex vivo* perfused human lung preparation. These studies demonstrate that intrapulmonary administration of allogeneic human MSCs after the establishment of endotoxin-induced lung injury reduces pulmonary edema and neutrophil-dependent inflammatory lung injury. Therefore, cell-based therapy with allogeneic MSCs is a promising new approach for treatment of human ALI. This bench-to-bedside project aims to develop allogeneic bone marrow-derived MSCs for a phase 1 clinical trial in ALI.

Status and Plans: Application to CIRM for a disease team planning grant was favorably reviewed but not funded. I collaborated on submission of a **grant application to NHLBI's PACT program, which was approved** to engage the **University of Minnesota's cell therapy facility (including collaborator, David McKenna, MD)** to manufacture well-characterized, clinical-grade human MSCs for preclinical studies that would lead to an IND application, and eventual clinical trial using the same MSC product. To date, preclinical studies performed with the clinical-grade MSCs have replicated the previous results demonstrating reduction of pulmonary edema and neutrophil-dependent inflammatory lung injury in the *ex vivo* perfused lung model. Further, we have demonstrated that intravenous administration is equivalent to intratracheal administration in the *ex vivo* perfused lung model.

It is noteworthy that the safety profile of allogeneic MSCs has been favorable across diverse disease applications, in many academic and industry-sponsored clinical trials. I have recently initiated discussions with FDA/CBER's Office of Cell, Tissue, and Gene Therapy to discuss what further preclinical studies, if any, would be required for the IND application. Funding for the proposed clinical trial is still in question. Matthay's recent application to NIH/NHLBI, "Cell-Based Therapy for Acute Lung Injury", was favorably reviewed, scored in the 9th percentile, but was not funded.

C. Optimization of Human Embryonic Stem Cell Derivation Techniques and Production/Distribution of GMP-Grade Lines

PI: Susan Fisher, PhD

Rationale: New human embryonic stem cell (hESC) lines are needed for basic & translational research, and for clinical product development. These lines should be well-characterized and manufactured by methods that ensure their quality and reproducibility. The objective of this project is to generate new hESC lines either from intact human embryos, or from individual blastomeres from cleavage-stage embryos. *(Note that the banked tissue and cell lines are considered source materials for manufacture of the cell therapy product. While the cell therapy product is subject to cGMP and IND regulations, the source material is not the product—therefore it is subject to qualification activities similar to those used for ancillary reagents used in product manufacture. FDA/CBER has guidances relevant to cell line production when the intent is use in product manufacture.)*

Status/Plans: This **CIRM grant was funded for 3 years beginning Fall 2008**. Work is progressing in the Fisher lab on optimization of culture technology, including use of serum-free media. Optimized methods will be transferred to the UCSF GMP facility in Fall 2010, at which time I will be involved in the project.

D. Cell Therapy for Cardiovascular Disease - UCSF

Cardiology investigators have embraced the promise of cell-based therapies for treatment of cardiovascular disease (mostly acute myocardial infarction (MI) and chronic heart failure), using cell sources ranging from bone marrow and peripheral blood mononuclear cells, to more highly selected CD34+ cell populations, to skeletal myoblasts and more recently pluripotent stem cell-derived cardiomyocytes. UCSF cardiologists and stem cell investigators are interested in this area. I have specifically worked with:

Yerem Yeghiazharians, MD: Although initial plans were for a trial of genetically modified endothelial cells for treatment of acute MI, a subsequent proposal was to initiate a clinical trial of intracoronary injections of bone marrow-derived mononuclear cells. However, the high cost of product development has led this group to opt for participation as a clinical site in the industry-sponsored **Osiris Phase 2 clinical trial of allogeneic MSCs after acute MI**. This study is now open to enrollment at UCSF.

Harold Bernstein, MD: In fall 2008, I provided substantial input on the IND development process to this investigative team for a grant application to **CIRM's Early Translational Research Award**, entitled **"Overcoming Bottlenecks to Cardiac Regeneration Therapy"**, which proposed development of a large animal model for an hESC-derived cardiomyocyte therapy for heart failure. **The grant was not funded.**

E. CIRM Disease Teams

CIRM's ultimate vision is to move stem cell therapies into real treatments for patients in California. CIRM program staff clearly defined review criteria in Disease Team RFA that distinguished them from conventional research grants. The Disease Team competition was preceded by planning grants of 6 months duration. In addition to a clear scientific rationale for development, each application had to demonstrate that they had established a functional multidisciplinary team, similar to those used in the drug development industry, and present a well-defined development plan to achieve IND submission in 4 years.

CIRM RFA 07-04: CIRM Disease Team Planning Awards

From Jan – June 2009, I participated in planning activities (meetings, conference calls) for CIRM Disease Team grants with the following teams who received planning grants:

- Diabetes - Bluestone (UCSF) and Baetge (Novocell, Inc, San Diego)
 - Participated in early conference calls
 - Decision to have Novocell, Inc PI take lead based on their development of combination product (embryonic stem cell-derived islets, encapsulated in biomaterial)
 - Planning resulted in submission of pre-app, which passed CIRM triage, and submission of **full grant, "Cell Therapy for Diabetes"-- Recommended for funding**
- Sickle Cell Disease - Walters (Oakland Children's/CHORI) and Kohn (LA Children's/UCLA)
 - Participated in planning conference. Oakland Children's/CHORI decided not to submit a grant on their own.
 - Resulted in submission of pre-app, which passed CIRM triage, and submission of **full grant, "Stem Cell Gene Therapy for Sickle Cell Disease" from UCLA (PI Kohn) – Recommended for funding**
- Heart Failure - Srivastava (UCSF/Gladstone Institutes) and Roberts (Stanford)
 - Participated in one planning meeting at Stanford
 - Planning resulted in Gladstone-Stanford collaborative team for Embryonic Stem Cell-Derived Cardiomyocytes for Treatment of Chronic Heart Failure.
 - **Pre-app did not pass CIRM triage process**

CIRM RFA 0901: CIRM Disease Team Research Awards

From June-July 2009, I participated in grant preparation activities with several teams that decided to submit pre-applications for these 4-year, \$20 million disease team awards. My participation ranged from telephone advice about the IND process (in the case of Epilepsy) to extensive interactions and grant-writing (in the case of Glioblastoma). The results of this competitive process will be announced at the October 27/28 CIRM ICOC meeting.

- Epilepsy - Kriegstein (UCSF)
 - Proposed use of neural stem cells for surgical implantation during temporal lobe ablative surgery for intractable epilepsy
 - This group did not receive a planning grant, but decided to submit a pre-application. **Pre-app did not pass CIRM pre-app triage process**

- Arthritis/Cartilage Repair – Lotz (UCSF)
 - Proposed development of complex combination product, consisting of autologous MSCs + juvenile allogeneic chondrocytes co-cultured, embedded in biomaterial, then implanted with scaffold material, for repair of knee cartilage defects.
 - This group had a planning grant, and submitted a pre-application, which passed CIRM triage process to submit a full application
 - PI contacted me, through UCSF CTSI, in late stages of grant preparation to review their application, and to be included on Leadership team as representative from UCSF CTSI for human subjects and regulatory issues
 - **Full grant submission, “Stem Cells for Treating Pre-Arthritic Focal Cartilage Defects”, reviewed by CIRM, Not recommended for funding**

- Glioblastoma – Berger (UCSF neurosurgery), Snyder (Burnham Institute), Cavaneer (UCSD), Verma (Salk Institute), and Liao (UCLA neurosurgery).
 - Proposed development of neural stem cells genetically modified to express anti-tumor agent, for treatment of recurrent glioblastoma multiforme, based on observation of neural stem cell homing to brain tumors-- stem cells used to deliver “payload” directly to tumor sites
 - Planning grant was held by Snyder (Burnham) and Cavaneer (UCSD)
 - Pre-application passed CIRM triage process. Snyder (Burnham) engaged UCSF neurosurgery because of pre-clinical animal models and clinical trials experience in glioblastoma
 - I was contacted by UCSF Neurosurgery, late in the grant-writing process, to participate on conference calls, and review and prepare a product/IND development plan, which was a critical part of the grant submission
 - **Full grant submission, “Stem Cell-Mediated Oncocidal Gene Therapy of Glioblastoma” reviewed by CIRM, Recommended for funding**

F. Conference: Stem Cell Translation: Best Practices and Regulatory Considerations **Program Director: Elizabeth Read, MD**

Rationale: Many stem cell investigators and teams are unfamiliar with FDA requirements and regulatory process for IND submission, the differences between basic science and development activities, and the complexity of interactions among the parties engaged in these activities. This conference was encouraged by Marie Csete, MD/PhD, CIRM's CSO, to be held ahead of the CIRM Disease Team grant submissions. The goals of the conference were to provide (1) education on clinical product development and regulatory aspects of the bench-to-bedside translation of stem cell therapies, and (2) a public forum for parties from academia, industry, and the US Food and Drug Administration (FDA) to have productive dialogue on approaches and best practices to optimize success in moving stem cell products into clinical trials.

Status & Plans

The conference was supported by a **CIRM Conference Grant** of \$30,000. I wrote the conference grant, and organized/chaired the conference. The organizing committee consisted of myself, Shelly Heimfeld, PhD (Fred Hutchinson Cancer Center), Darin Weber, PhD (Biologics Consulting Group), Marie Csete, MD PhD (CIRM), and David Scadden, MD (Harvard; representative from ISSCR's Translation Committee). This was an all-day event held on May 2, 2009 in San Diego, CA, immediately prior to the annual meeting of the International Society for Cellular Therapy (ISCT). The conference was primarily sponsored by CIRM and ISCT, with co-sponsorships by Blood Systems Research Institute, UCSF's Clinical & Translational Science Institute (CTSI), and the International Society for Stem Cell Research (ISSCR). We primarily used a case study format using real cell therapy products in development. The conference was exceptionally well-received, and we have been encouraged by attendees to continue running this conference on an annual basis.

ARIZONA ACTIVITIES

Public Cord Blood Bank in Arizona

In February 2008, I wrote a contract application in response to an RFP published by the Arizona Biomedical Research Commission, entitled "Arizona Non-Embryonic Stem Cell Repository", to obtain \$5 million over 5 years to establish a public cord blood bank in Arizona. The application was never formally reviewed by AZ, and therefore was not funded, due to state budgetary issues.

During May-August 2008, I explored options for public cord blood banking using a model of remote collections (e.g., in California and/or Arizona) in partnership with an existing public cord blood bank (e.g., M.D. Anderson, other). This model is currently favored by NMDP and HRSA as a more cost-effective approach to public banking. I had extensive discussions with NMDP, HRSA, MD Anderson, the Joanne Pang Foundation (which has funds for public collections in Northern CA), and BSI Medical. In August 2008, I proposed this model to BSI as an option to consider. In August 2009, a proposal using this model was submitted by BSI Medical Affairs during the project prioritization process.

Cell Sourcing Program

Dr. Leon Su, Medical Director of the blood center at UBS-Arizona, is interested in establishing cell sourcing activities in Arizona. In September 2009, I began to educate and train him and his staff on basic procedures and have provided guidance to them on interactions with potential customers, including IRB/human subjects issues. Dr. Su is evaluating potential customers in Arizona, and I joined him in a meeting with investigators at the Arizona Biodesign Institute (infectious disease and immunology) in early October 2009. While UBS-Arizona is setting up, we have begun to support one AZ Biodesign Institute investigator with research products from San Francisco.

Cancer Immunotherapy at Mayo/Scottsdale

Peter Cohen, MD, a cancer immunotherapy expert at Mayo/Scottsdale with NIH R01 funding, works on dendritic cell immunotherapy for solid tumors. In September 2008, he proposed a collaborative bench-to-bedside project that would involve BSL's Stem Cell Lab, and potentially UBS-Arizona's apheresis service, to collect and process peripheral blood monocytes for autologous dendritic cells for cancer immunotherapy. From September-November 2008, I worked with Dr. Cohen to define a project plan and presented it to BSL's Stem Cell Lab, which further defined the project requirements. The Stem Cell Lab has not yet begun work on this project.

Clinical Stem Cell Laboratory

At Dr. Tomasulo's request, I carried out an analysis of the Stem Cell Lab's workload, capabilities, expertise, resources, and prospects for supporting future R&D activities, and submitted my assessment in July 2009. The Lab, for many years under the direction of Blood Systems Laboratories, was transferred to BSI Medical Affairs in August 2009. Concurrently, Dr. Frank Nizzi was appointed as the Lab's Medical Director as part of his promotion to Vice President, Clinical Services, BSI.

III. GRANTS, CONTRACTS, AND AWARDS

Current

CIRM New Cell Lines Awards. PI: S. Fisher (UCSF), "Optimization of Human Embryonic Stem Cell Derivation Techniques and Production/Distribution of GMP-Grade Lines"

EJR to be funded at 5% effort for year 3, starting September 2010

This project aims to derive new embryonic stem cell lines using GMP, for use in research, development, and future clinical trials.

CIRM Conference Grants. PD: EJ Read (BSRI), "Translation of Stem Cell Therapies: Best Practices and Regulatory Considerations"

May-October 2009

This grant funded an educational conference held on May 2, 2009.

Pending

CIRM Disease Team Awards. PI: M. Berger (UCSF), "Stem Cell Mediated Oncocidal Gene Therapy of Glioblastoma"

12/01/09-11/30/13

This grant will fund development by a multidisciplinary disease team of a novel gene-modified neural stem cell product for a clinical trial in glioblastoma multiforma.

CIRM Disease Team Awards. PI: J. Lotz (UCSF), "Stem Cells for Treating Pre-Arthritic Focal Cartilage Defects"

12/01/09-11/30/13

This grant will fund development by a multidisciplinary disease team of a novel complex stem cell-based product, combined with biomaterials, for treatment of knee cartilage defects.

Participated in proposal (not included in budget)

CIRM Disease Team Planning Award (Bluestone)

"A CIRM Disease Team for the Treatment and Cure of Diabetes"

Recommended for funding

CIRM Disease Team Planning Award (Srivastava)

"Pluripotent Stem Cell-Based Therapy for Heart Disease"

Recommended for funding

Completed

Juvenile Diabetes Research Foundation 2005-1168 (Bluestone)

Project 1: "Expansion of Tregs for Treatment of Autoimmune Disease"

8/1/07 – 7/31/09

This project was focused on development of an autologous T regulatory cell product to be used under IND in a clinical trial of cell therapy for type 1 diabetes mellitus.

Unsuccessful Applications

NIH/NHLBI Challenge Grants, PI: M. Matthay (UCSF), "Cell-Based Therapy for Acute Lung Injury"
Submitted June 2009

This project aimed to perform translational and developmental studies leading to initiation of a phase 1 clinical trial of MSCs in acute lung injury.

CIRM Early Translational Awards, PI: H Bernstein (UCSF), "Overcoming Bottlenecks to Cardiac Regeneration Therapy"

Submitted November 2008

This project aimed to develop a large animal (non-human primate) model to evaluate efficacy and safety of an embryonic stem cell-derived cardiomyocyte product for therapy of acute myocardial infarction.

CIRM Disease Team Planning Awards, PI: M Matthay (UCSF), "Allogeneic Mesenchymal Stem Cells for the Treatment of Acute Lung Injury"

Submitted December 2007

This application was for planning activities of a multidisciplinary disease team to develop an allogeneic MSC product for treatment of acute lung injury.

Arizona Biomedical Research Commission, PI: EJ Read, "Arizona Non-Embryonic Stem Cell Repository (ANeSCR)"

Submitted February 2007

This project aimed to establish a public cord blood bank in Arizona that would also support research activities.

IV. OTHER SIGNIFICANT ACTIVITIES

Education and Training

Since February 2009, I have served as mentor to Rosa Sanchez, MD, a pediatric hematologist-oncologist and transfusion medicine specialist who received a NHLBI-sponsored 5-year career development (K07) award in pediatric transfusion medicine (PTM), beginning Fall 2007. Dr. Sanchez-Rosen has been working primarily with UCSF's Medical Education department on development of a PTM curriculum, and on a clinical research study of microchimerism in neonatal ICU patients who have been transfused (with Mike Busch). NHLBI's PTM program officer, who also serves as program officer for the PACT program, has invited us to work with her on organizing a **State-of-the-Science conference on Pediatric Cellular Therapies**. Dr. Sanchez-Rosen will take the lead on this, and I will serve as her advisor.

Additional teaching activities include lectures on cell therapies to BCP/UCSF Transfusion Medicine fellows.

University Service Activities

UCSF Committee on Human Research (CHR)

Since March 2009, I have served as BSRI's representative to this institutional review board. In addition to presenting BSRI's protocol applications, I review other UCSF applications.

UCSF Gamete, Embryo, and Stem Cell Research Oversight Committee (GESCR)

Since May/June 2009, I have served as an ad hoc reviewer for clinical trial applications requiring GESCR review.

UCSF Clinical & Translational Science Institute (CTSI)

Since mid-2008, I have interacted extensively with the CTSI's Regulatory Knowledge & Support Program, to

- provide advice on IND submissions through the RKS consult service
- give seminars to the UCSF community on "Regulatory Considerations for Stem Cell Translation" in March & April, 2009

These activities have led me to several of the cell therapy collaborations described above.

I have recently been invited by Clay Johnston, CTSI's Director, to serve as a member of the new CTSI-RKS Advisory Board, which will meet 6 times/year over the next year to provide strategic advice to CTSI on regulatory issues impacting clinical & translational research at UCSF.

Voluntary Professional Activities

Advisory Council on Blood Stem Cell Transplantation (ACBSCT)

I am completing a 2 year term on this HHS Advisory Council (January 2008 – December 2009). In addition to providing general advice to HRSA/HHS on a variety of issues related to unrelated donor programs and access to hematopoietic transplantation, I was appointed Chair of the Cord Blood Bank Accreditation Committee to lead the process of recommending to HHS the recognition of one or more accreditation organizations for HRSA-supported public cord blood banks.

United States Pharmacopeia (USP)

I am serving a 5-year term (2005-2010) on the Cell, Tissue, and Gene Therapy Expert Panel for USP's Biologics & Biotechnology initiatives. In addition to general review and advice on our panel's initiatives, I am serving as Chairperson of a subgroup writing a USP chapter on Flow Cytometry for characterization of cellular products.

International Society for Cellular Therapy (ISCT)

In 2007 and 2008, I served as the Chair of the ISCT-sponsored Somatic Cell Therapy Symposium in Bethesda, MD.

American Association of Blood Banks (AABB)

Until 2009, I served as a member of AABB's Cellular Therapies Committee. I have recently been elected to the new AABB Cell Therapy Section Coordinating Committee.

America's Blood Centers (ABC)

Over the past 2 years, I have served as ABC's liaison to the Cell Therapy Circular of Information (CT-COI) Committee, and as ABC's liaison to the FDA Cell Therapy Liaison Committee.

V. ABSTRACTS, PUBLICATIONS, AND PRESENTATIONS

Publications (November 2006 – October 2009)

Kurlander RJ, Tawab A, Fan Y, Carter CS, **Read EJ**. A functional comparison of mature human dendritic cells prepared in fluorinated ethylene-propylene bags or polystyrene flasks. Transfusion 2006;46:1494-504.

Read EJ. Chance favors the prepared mind: A tribute to Charles S Carter Jr (1954-2006). Cytotherapy 2006;8:191-3.

Khuu HM, Patel N, Carter CS, Murray PR, **Read EJ**. Sterility testing of cell therapy products: Parallel comparison of automated methods with a CFR-compliant method. Transfusion 2006;46:2071-2082.

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Sloand EM, **Read EJ**, Scheinberg P, Tang Y, More K, Leitman SF, Maciejewski J, Young NS. Mobilization, collection, and immunomagnetic selection of peripheral blood CD34 cells in recovered aplastic anemia patients. Transfusion 2007;47:1250-3

Mielke S, Nunes R, Rezvani K, Fellowes VS, Venne A, Solomon SR, Fan Y, Gostick E, Proce DA, Scotto C, **Read EJ**, Barrett AJ. A clinical scale selective allodepletion approach for treatment of HLA-mismatched and matched donor-recipient pairs using expanded T lymphocytes as antigen-presenting cells and a TH9402-based photodepletion technique. Blood 2008;111:4392-402.

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Shin JW, Jin P, Fan Y, Slezak S, David-Ocampo V, Khuu HM, **Read EJ**, Wang E, Marincola FM, Stroncek DF. Evaluation of gene expression profiles of immature dendritic cells prepared from peripheral blood mononuclear cells. Transfusion 2008;48:647-57.

de Silva R, Raval AN, Hadi M, Gildea KM, Bonafacino AC, Yu ZX, Yau YY, Leitman SF, Bacharach SL, Donahue RE, **Read EJ**, Lederman RJ. Intracoronary infusion of autologous mononuclear cells from bone marrow or granulocyte-colony stimulating factor –mobilized apheresis product may not improve remodeling, contractile function, perfusion, or infarct size in a swine model of large myocardial infarction. Eur Heart J 2008;48:647-57.

Arbab AS, Janic B, Knight RA, Anderson SA, Pawelcywk E, Rad A, **Read EJ**, Pandit SD, Frank JA. Detection of migration of locally implanted AC133+ stem cells by cellular magnetic resonance imaging with histological findings. FASEB J. 2008;22:3234-46.

Mackall CL, Rhee EH, Carter CS, **Read EJ**, Khuu HM, Leitman SF, Bernstein D, Tess M, Long LM, Grindler D, Merino M, Kopp W, Berzofsky, Helman LJ. A pilot study of consolidative immunotherapy in patients with high risk pediatric sarcomas. Clinical Cancer Research 2008;14:4850-8.

Gee A, Sumstad D, Stanson J, Watson P, Proctor J, Kadidlo D, Koch E, Sprague J, Wood D, Styers D, McKenna D, Gallelli J, Griffin D, **Read EJ**, Parish B, and Lindblad R. A multi-center comparison study between the Endosafe® PTS™ rapid release testing system and conventional test methods for detecting endotoxin in cell therapy products. Cytotherapy, 2008;10:427-35.

Tawab A, Fan Y, **Read EJ**, Kurlander RJ. Effect of ex vivo culture duration on phenotype and cytokine production by mature dendritic cells derived from peripheral blood monocytes. Transfusion 2009; 49:536-47.

Read EJ, Khuu HM. Use of a facility master file to facilitate regulatory submissions for cell therapy products. In Gee AP (ed): Cell Therapy: cGMP Facilities and Manufacturing. Springer, 2009.

Presentations (November 2006 - October 2009)

“Cord Blood from Matched Unrelated Donors: Receipt, Thaw, and Infusion”

Invited workshop presentation for “Setting the Stage for Successful Cord Blood Unit Receipt, Thaw, and Infusion” at NMDP Council Meeting, Minneapolis, MN, November 11, 2006.

“Management of Cell Therapy Products with Positive Microbial Cultures”

Invited workshop co-chair presentation at Pharma Conference “FDA and the Changing Paradigm for HCT/P Regulation”, San Antonio, TX, January 24, 2007.

“Proposal for Public Cord Blood Banking in Arizona”

Presentation to the Arizona State Senate Health Committee, Phoenix, AZ, February 1, 2007.

“Development of Dendritic Cell Cancer Vaccines for Early Phase Clinical Trials in an Academic Facility”

Invited panel presentation at NCI/FDA Workshop “Bringing Therapeutic Cancer Vaccines and Immunotherapies through Development to Licensure”, Bethesda, MD, February 8, 2007.

“Comments of the International Society (ISCT) for Cellular Therapy to FDA Cellular, Tissue, and Gene Therapies Advisory Committee on Cord Blood Draft Guidance”

Presentation during public comments session at FDA Advisory Committee meeting, Gaithersburg, MD, March 30, 2007.

“Bench to Bedside Translation of Cell & Tissue Therapies”

Presentation at Blood Systems/UBS Medical Directors’ Annual Meeting, San Francisco, CA, May 11-12, 2007.

“Introduction to Cell & Tissue Therapies”

Lecture for UCSF Biomedical Sciences graduate school Stem Cell course, San Francisco, CA, May 22, 2007.

“Unlicensed Cord Blood Products: What should we do?” Invited presentation at FDA Cell Therapy Liaison Meeting, Bethesda, MD, June 7, 2007.

“Stability Testing of Cell Therapy Products”

AABB Audioconference on Storage and Stability Programs for Cell Therapy Products, June 27, 2007

“Bench to Bedside Translation of Cell & Tissue Therapies”

ABC Annual Meeting, Vancouver, BC, Canada, August 4, 2007.

“Bench to Bedside Translation of Cell & Tissue Therapies”

IABS meeting, Sao Paulo, Brazil, September 19, 2007 (delivered by audioconference).

Meeting Co-Chair, and Chair for session on Product Sterility Testing

Somatic Cell Therapy Symposium, Bethesda, MD, September 26-28, 2007

“Management of Cell Therapy Products from Ineligible Donors”

AABB Audioconference on HCT/P Donor Dilemmas, October 3, 2007

“CGMPs, CGTPs, and Regulations for Cell & Tissue Therapies”

Blood Systems Audioconference, October 10, 2007.

Workshop Chair, "Application of New Technologies to Cell and Tissue Processing"
AABB Annual Meeting, Anaheim, CA, October 20, 2007.

"Donor Eligibility Issues for Cell Therapy Products"

Invited workshop co-chair presentation at Pharma Conference "FDA and the Changing Paradigm for HCT/P Regulation", San Antonio, TX, January 9, 2008.

"Cellular Therapy: Bench to Bedside"

Invited presentation at Annual Meeting of the California Blood Bank Society, San Diego, CA, April 24, 2008.

"Cord Blood Bank Accreditation"

Work Group Chair Presentation to DHHS Advisory Council on Blood Stem Transplantation, Rockville, MD, April 28, 2008.

"Demystifying FDA's Requirements: How to Review and Implement Cell Therapy Regulations and Guidance Documents" Webinar presentation for International Society of Cellular Therapy, September 10, 2008.

"Cord Blood Bank Accreditation Work Group Update"

Presentation to DHHS Advisory Council on Blood Stem Cell Transplantation, Bethesda, MD, December 15, 2008.

"Standards and Regulations for Cellular Therapy Products"

Invited presentation at meeting of CIRM Medical & Ethical Standards Work Group, Los Angeles, CA, February 17, 2009.

"Regulations for Stem Cell Therapy Product Development"

Seminars for UCSF Clinical & Translational Science Institute (CTSI)'s Regulatory Knowledge & Support Program, San Francisco, CA, March 25, April 1, and April 6, 2009.

Conference Chair, "Stem Cell Translation: Best Practices and Regulatory Considerations," Sponsored by CIRM and ISCT, San Diego, CA, May 2, 2009.

"IND Planning and Preparation for Stem Cell Therapies"

Presentation at "Stem Cell Translation: Best Practices and Regulatory Considerations", San Diego, CA, May 2, 2009.

"Case Study on Donor Testing"

Invited panel presentation at Global Regulatory Perspectives Workshop, ISCT Annual Meeting, San Diego, CA, May 3, 2009.

"Academic Perspective on Clinical Development of Novel Cell Therapies"

Invited panel presentation at workshop, "Nuts and Bolts of Operational Planning and Implementation of Mesenchymal Stem Cell Clinical Trials", ISCT Annual Meeting, San Diego, CA, May 4, 2009.