8th Stem Cell Summit

- 8th Stem Cell Research and Regenerative Medicine
- Stem Cell Commercialization and Partnering

**KEYNOTE SPEAKERS:**

- Glen Prestwich, Presidential Professor, Director Therapeutic Biomaterials Center, Special Presidential Assistant for Faculty Entrepreneurism, Department of Medicinal Chemistry, University of Utah
- Devyn M. Smith, Chief Operating Officer, Neusentis Research Unit, Pfizer Worldwide R&D
- Leanna Caron, Vice President & General Manager, Cell Therapy & Regenerative Medicine, Genzyme
- Douglas W. Losordo, Vice President, Medical Director of New Therapies, Baxter

**FEATURED SPEAKERS:**

- Brock Reeve, Executive Director, Stem Cell & Cancer Research Institute, Harvard Stem Cell Institute
- Tina Palomäki, SWP and CPWP, EMA & Finnish Medicines Agency
- Gregory Bonfiglio, Managing Partner, Proteus Venture Partners
- Sridaran Natesan, Vice-President, External Innovation, Sanofi-Aventis

... and more.

Don't miss this opportunity to network with colleagues in academia and industry to discuss and share the latest developments in the stem cell research. Hear from top executives and representatives from Sanofi-Aventis, Athersys, Pfizer, Advanced Cell Therapeutics, Novartis, ViaCyte, Baxter, Cytori Therapeutics, Life Technologies, Fate Therapeutics, BioTime, Genzyme, Osiris, Pluristem, Harvard Stem Cell Institute, ReNeuron, SanBio, and many more!

Visit www.gtcbio.com for more details!
Day 1 - Thursday, April 19, 2012

7:00  Registration & Continental Breakfast
7:55  Welcome & Opening Remarks

**KEYNOTE PRESENTATION**

8:00  Clinical Biomaterials for Regenerative Medicine: From Bench to Business

Glen Prestwich, Presidential Professor, Director, Therapeutic Biomaterials Center, Special Presidential Assistant for Faculty, Entrepreneurism Department of Medicinal Chemistry, University of Utah

Faculty entrepreneurism is a scholarly activity. First, I will describe how we have implemented policies at the University of Utah that encourage faculty and student entrepreneurial activities through the Entrepreneurial Faculty Scholars and the Young Entrepreneurial Student Scholars programs. Then, I will describe a case study for commercialization of a university technology in the area of regenerative medicine.

Clinical biomaterials for regenerative medicine. Injectable and biocompatible vehicles for delivery, retention, growth, and differentiation of progenitor cells are needed for cell therapy. We created a synthetic extracellular matrix (sECM) from hyaluronic acid (HA) that affords highly reproducible, manufacturable, approvable, and affordable biomaterials. The in situ crosslinkable sECM hydrogels can be customized for use with progenitor and mature cell populations obtained in many tissues, including skin, fat, liver, heart, brain, muscle, bone, and cartilage. In addition, sECMs have been developed for rapid expansion and recovery of cells in 3-D, and for the bioprinting of engineered tissue constructs. The technology is being commercialized in three fields of use: human medical devices, cell therapy and research tools for 3-D cell culture, and veterinary wound care and adhesion prevention.

**Funding Opportunities  (Joint Session)**

Moderator: Casey Case, Vice President, Research, SanBio

8:45  Seed Funding Start-Ups in Emerging Technologies: Perspectives on Cell Therapeutics

Alain Vertes, Ph.D., MBA, Sloan Fellow, London Business School

9:10  State Funding Opportunities for Stem Cell Research & Commercialization

Susan Windham-Bannister, Ph.D., Associate Professor, Anatomy and Cell Biology, Massachusetts Life Sciences Center

This presentation will discuss state funding opportunities through the Massachusetts Life Sciences Center for stem cell-related research and commercialization. Through a series of research matching grant programs and financing opportunities the Life Sciences Center has resources available to support stem cell research, and to invest in company formation and growth for research that has the potential for commercialization.

**FEATURED PRESENTATION**

9:35  A New Model For The Commercialization of Regenerative Medicine Technologies

Gregory A. Bonfiglio, Managing Partner, Proteus Venture Partners

10:00  Morning Break

**Regulatory Guidance & Updates (Joint Session)**

**FEATURED PRESENTATION**

10:30  Regulatory Requirements for Stem Cell-based Medicinal Products in the EU

Tiina Palomäki, Ph.D., SWP and CPWP, EMA, and Finnish Medicines Agency

Stem cells hold the promise as a source of cells for therapeutic applications in various conditions, including metabolic, degenerative and inflammatory diseases, for the repair and regeneration of damaged or lost tissues and also in the treatment of cancer. The two principal characteristics that define stem cells, i.e. capacity to self-renew and differentiate make stem cells attractive and promising source for cellular replacement therapies. However, the same characteristics can be seen as the primary cause of additional risks of tumourigenicity as well as of unintended differentiation at ectopic locations. Safe therapeutic application of stem cells necessitates understanding the possible risks. Stem cells represent a spectrum of different cell-based products with varying amount of scientific data and clinical experience. Similarly, perceived risks associated with different types of stem cells are not the same.

In the EU, the regulatory framework for development of stem cell-based medicinal products is laid down in the legislation and in the guidelines. Existing EU guidance on cell based medicinal products lays down general outlines that are applicable to all cell based-medicinal products including stem cells. In addition, stem cell-associated additional safety concerns are covered in the recent Reflection paper on stem cell based medicinal products which highlights the potential and theoretical safety concerns based on the current scientific understanding, as well as the technical and methodological challenges related to non-clinical and clinical development of stem cell based products.
Factors such as minimum manipulation and the Notified Body if performed in the same surgical procedure. The risks associated with the stem cell therapy include toxicity data relevant to the cell source and the route of delivery. The BLA process is exclusive for biological products that exceed the definition of minimum manipulation. The cell source and the associated handling of safety testing based on the risks associated with their use of human RPE cells derived from human embryonic stem cells for treating various ophthalmic diseases. Considering that therapies involving human embryonic stem cell derived products are few and the FDA and other regulatory bodies have limited experience, challenges exist for both the sponsors of such programs as well as the regulatory bodies responsible for their review.

The case study presented will address some of the lessons learned during the IND and CTA preparation and preparation for clinical trials for ACT’s use of human RPE cells derived from human embryonic stem cells for treating various ophthalmic diseases.

In developing regulatory packages for cellular therapy trials there are a number of considerations to take into account which include the regulatory perspectives that are incorporated at the earliest stages into efficacy and pre-clinical toxicology studies, manufacturing approaches, and analytical testing methods, all with the goal of conducting clinical evaluations.

European Union (EU): The regulatory framework in Europe for Device-based Cell Therapies consists of a variety of directives and regulations to include Directive 2001/83/EEC, Directive 2004/23/EEC, Directive 93/42/EEC, Directive 2003/63/EEC, and Regulation 1394/2007. Device-based Autologous Cell Therapies are regulated solely by the Notified Body if performed in the same surgical procedure. Factors such as minimum manipulation and the same essential function should be considered in determining the regulatory pathway. The European Medicines Authority (EMA) is a centralized pan-European regulatory authority that approves Advanced Therapy Medicinal Products (ATMP) such as gene therapy, somatic cell therapy, and tissue engineered products. Qualified device-based cell therapies are typically approved by a Notified Body in three to six months. EMA products require clinical trials and a lengthy regulatory process that spans multiple years.

Benefits of Presentation:
- Participants will understand the regulatory framework for device-based cell therapies in the US and EU.
- Participants will be able to identify the appropriate level of safety testing based on the risks associated with their cell therapy.
- Participants will be able to navigate a device-based pathway with the lowest regulatory burden.

**11:45  Device-Based Regulatory Framework for Cell Therapies**

*Kenneth Kleinhenz, Vice President, Regulatory Affairs and Quality Assurance, Cytori Therapeutics*

United States Food and Drug Administration (FDA): Device-based Cell Therapies are regulated under 21 CFR (Code of Federal Regulations) by FDA through a variety of means to include 510k process, PMA (PreMarket Application) process, and the BLA (Biological License Application) process. The 510k and PMA processes are designed for devices while the BLA process is exclusive for biological products that exceed the definition of minimum manipulation. The cell source and the associated handling/manipulations determine the complexity of the required safety profile. Device-based Cell Therapies that undergo the PMA or BLA process require extensive safety and toxicity data relevant to the cell source and the route of delivery. The risks associated with the stem cell therapy dictate the safety and toxicity profile.

European Union (EU): The regulatory framework in Europe for Device-based Cell Therapies is delineated in various European Directives and Regulations. For instance, Directive 2001/83/EEC, Directive 2004/23/EEC, Directive 93/42/EEC, Directive 2003/63/EEC, and Regulation 1394/2007. Device-based Autologous Cell Therapies are regulated solely by the Notified Body if performed in the same surgical procedure. Factors such as minimum manipulation and the same essential function should be considered in determining the regulatory pathway. The European Medicines Authority (EMA) is a centralized pan-European regulatory authority that approves Advanced Therapy Medicinal Products (ATMP) such as gene therapy, somatic cell therapy, and tissue engineered products. Qualified device-based cell therapies are typically approved by a Notified Body in three to six months. EMA products require clinical trials and a lengthy regulatory process that spans multiple years.

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shown that engineered human mesenchymal stem cells and neural stem cells expressing novel secretable anti-angiogenic and pro-apoptotic proteins have anti-tumor effects in culture. Using our recently established malignant, invasive and resection models of human glioma that mimic clinical settings and bi-modal optical imaging, we show that secreted therapeutic proteins are continuously delivered by SC, target both the primary and the invasive tumor deposits and have profound anti-tumor effects. These studies demonstrate the strength of employing engineered stem cells and real time imaging of multiple events in preclinical-therapeutic tumor models and form the basis for developing novel cell based therapies for cancer.

2:20 Development of an Encapsulated Stem Cell-Based Therapy for Diabetes

Olivia Kelly, Ph.D., Director, Cell Biology, ViaCyte

ViaCyte is a preclinical company developing a stem cell-based therapy for insulin-dependent diabetes. The therapy is a combination product comprised of pancreatic progenitor cells, pro-islet, encapsulated within a retrievable delivery ENCAPTRA device. After implantation, encapsulated pro-islet differentiates into glucose-responsive, insulin-secreting cells. The renewable starting material for pro-islet manufacturing is human embryonic stem cells that are directed to differentiate to pancreatic cell product using scalable processes. The bio-stable ENCAPTRA device is designed to fully contain cells and to protect cells from immune attack. The goal is to develop a product that will achieve insulin independence, reduce diabetes-related complications, and eliminate the need for continuous immunosuppressant drugs.

2:45 Improving Fertility in Women through Egg Stem Cell-based Clinical Platforms

Jonathan Tilly, Ph.D., Director, Vincent Center for Reproductive Biology, Massachusetts General Hospital; Professor, Obstetrics, Gynecology & Reproductive Biology, Harvard Medical School, Harvard University

Fertility plummets in most women in their late 30s and early 40s, even with the use of in-vitro fertilization (IVF), due to a declining egg cell reserve and reduced egg quality. The latter reflects diminished cellular energy in eggs with age, which increases the incidence of genetic errors in embryos, implantation failure (miscarriage) and certain birth defects (for example, Down syndrome). Building on prior mouse work published in Nature in 2004 (428:145-150), this year we reported the isolation of precursor (stem) cells that generate new eggs in the ovaries of reproductive age women (Nature Medicine 2012 18: 413-421). These cells, which are intellectually protected as a novel composition of matter (U.S. Patent 7,955,846) licensed exclusively to OvaScience, Inc. (www.ovascience.com), open unprecedented options to consider for improving natural and assisted reproduction.

- We have devised a strategy for harvesting mitochondria, which are cellular energy-producing powerhouses, from a patient’s egg stem cells, and then introducing these mitochondria into that same patient’s eggs during IVF. This technology, termed AUGMENT (autologous germline mitochondrial energy transfer), is expected to reinvigorate failing eggs for improved IVF success rates.

- We have developed screening platforms to identify biological and chemical entities that increase the rate at which egg stem cells generate new eggs, which may permit development of therapies for increasing egg cell numbers in vivo.

- We are testing methods to generate functional human eggs from egg stem cells outside the body, which may provide an unlimited source of eggs for use in IVF procedures.

3:15 Afternoon Break

Advances in Regenerative Engineering and Tissue Engineering

Moderator: Robert Deans, Executive Vice President, Regenerative Medicine, Athersys

3:45 Human Decidua-derived Mesenchymal Stem Cells Tropism Towards Mammary Tumors in Vitro and in Vivo: Potential Future Application as Therapeutic Delivery Vehicles

Ana Flores, Ph.D., Principal Investigator, Regenerative Medicine Group, Instituto de Investigación Hospital 12 de Octubre

Estrogen is an essential hormone during the normal growth and development of breast tissue. However, it is associated with an increased risk for breast cancer in women. Treatments for breast cancer have been based in blocking the estrogen receptor (ER) in ER-positive patients. However, some patients do not respond to the hormonal treatment. Mesenchymal stem cells have affinity to tumor sites where they home affecting their biology and growth. Mesenchymal stem cells could be use as cellular vehicles of therapeutic agents to graft into the tumor reducing the side effects and the doses to be administered to the patients. Previously, we have isolated mesenchymal cells from the decidua of the human placenta and named as decidua-derived mesenchymal stem cells (DMSCs). These cells showed high proliferation and differentiation capacity into cells from the three embryonic layers. Besides, DMSCs are adult stem cells without ethical concerns, have low risk of viral infection and low or non-immune response, exhibit genomic stability under extended culture periods suggesting that DMSCs can be a safe product for future clinical applications.

This presentation will discuss:
- The “in vitro” and “in vivo” migration capacity of DMSCs in a rat model of chemically induced mammary tumors.
- The potential use of DMSCs as delivery vehicles of anti-tumor drugs in the treatment of mammary cancers.
- The safety and engraftment capability of transplanted DMSCs.
- To our knowledge, this is the first report demonstrating placenta-derived mesenchymal stem cells capacity as cellular vehicles for breast anti-cancer therapies.

4:10 Phototunable Biomaterials for Studies on Stem Cells and Motor Neuron Biology

Mirza Peljto, Ph.D., Anseth Research Group, University of Colorado, Department of Chemical and Biological Engineering, Howard Hughes Medical Institute

Recent advances in hydrogel chemistries offer an opportunity for culturing of mammalian embryonic stem (ES) cells and ES cell derived neurons using three-dimensional (3D) platforms that more closely mimic the in vivo milieu. Our group is focused on developing hydrogel biomaterials that rely on exploitation of cell-cell, cell-extracellular matrix, and cell-signaling interactions in to maintain mouse ES cells in a pluripotent state, direct their differentiation into highly pure and distinct subtypes of spinal cord motor neurons, and to manipulate ES motor axon outgrowth. Using a thiol-ene chemistry to create PEG based gels, we demonstrate that E-cadherin and laminin support the pluripotent ES cell state in contrast to fibronectin, which drives ES cell differentiation under identical feeder-free culture conditions. In addition, we are currently developing methods that will allow us to establish 3D gradients of chemical cues for efficient patterning and specification of well-described motor neuron subtypes from ES cells. Moreover, we have developed a hydrogel system enabling us to encapsulate individual ES motor neurons and to promote their long-term survival. ES motor neurons encapsulated in these 3D matrices obtain in vivo like morphologies and extend axons away from their cell bodies. Axonal extension can be further guided by local and sustained release of axon guidance cues. In sum, this talk will highlight advances in: combinations of biomaterials and stem cell biology, culture and maintenance of ES cells in 3D, directed motor axon guidance in 3D, and potential insights into both basic sciences and regenerative medicine.

4:35 Maintenance of Endothelial Cells in a Suspended Angiogenic State to Expand Stem and Progenitor Cells via Angiocrine Factors

Daniel J. Nolan, Angiocrine Bioscience; Senior Scientist, Cornell University

Endothelial cells (ECs) are now appreciated for being far more than inert conduits for blood flow. We are now unraveling their functions as platforms for in vivo and in vitro stem cell expansion. The adenoviral protein E4, open reading frame 1, is capable of stabilizing the ECs in vitro to release them from dependence on serum and extravagant levels of exogenous cytokines. The endothelial monolayers then become bioreactors for various organ specific stem cells in both mouse and human systems. This feat is achieved by the various growth factors released by endothelial cells, angiocrine factors, which are indispensable for tissue repair. Importantly, these stabilized ECs are able to confer their serum independence to the co-cultured stem and progenitor cells. In this context, human umbilical vein endothelial cells infected with the E4 protein are used to amplify hematopoietic stem cells from both adult mouse and human umbilical cord blood in a serum and cytokine free environment. Both expansions result in bona fide stem and progenitor cell expansions capable of serial reconstitutions in animal models. Among all organs, the endothelial cells are diversified drastically in structure and angiocrine profiles creating organ specific niches for the maintenance and recovery from damage for each tissue. This has lead to the development of the first set of organ specific endothelial cells from mouse which are independent of oncogene-mediated immortalization and serum-dependent growth.

Benefits:
- Presentation of unpublished data describing the enhanced angiogenic protocols now possible
- First presentation of non-immortalized serum independent mouse endothelial cells
- Review of most up to date data concerning organ specific vascular niches in stem cell growth

5:00 Cell Therapies in The Lung

Mauricio Rojas, M.D., Assistant Professor, University of Pittsburgh

Over the past few years, stem cells has emerged as a possible important therapy on lung disorders. Consistent with this idea, infusion of a specific stem cell populations termed bone marrow derived mesenchymal stem cells (MSCs) appear to be important in the regulation of acute inflammatory process. We are presenting examples of the use of MSC in acute and chronic diseases in the lung. We demonstrated that MSC administration prevented endotoxin induced Acute Lung Injury (ALI), suppressing the endotoxin induced pro-inflammatory cytokines. To demonstrate the clinical relevance of these results, we are presenting data that will show the preclinical data of the use human B-MSCs in animal models of acute lung injury, pulmonary fibrosis and lung transplantation. In addition some novel data will be presented to relate changes associated with aging and impairment of the biological activity of B-MSC

Benefits:
- Present different animal models of lung injury
- We will review the last advances on the use of stem cells in lung injury
- Evaluate the possible use of MSCs in pulmonary fibrosis and acute lung injury
- Discuss the future of cell therapies in the lung
- Aging and stem cells

5:25 Networking Reception and Poster Session
As the population ages and the acute mortality from cardiovascular disease decreases, a large population of patients is emerging who have symptomatic chronic ischemic vascular disease, many of whom remain severely symptomatic despite exhausting conventional medical therapy and mechanical revascularization. Mounting evidence suggests that microvascular insufficiency plays a significant role in the pathophysiology of ischemia. At the present time, there are no therapies that directly address the needs of this patient population.

Pre-clinical and early clinical data indicate that a variety of growth factors and stem/progenitor cells may be employed therapeutically for repair and replenishment of the microcirculation of ischemic tissue. Early phase clinical trials using autologous CD34+ cells have been completed providing data of feasibility, safety and bioactivity. Pivotal trials are under way to determine if the intramyocardial delivery of CD34+ cells can alleviate symptoms and improve exercise tolerance in this patient population which currently has no therapeutic options.

Accordingly, the goal of ischemic tissue repair appears feasible and is being developed using a variety of biologics in human clinical trials. The evolution of the strategy of ischemic tissue repair will require an ongoing dialogue between clinicians, scientists, regulators and industry to take full advantage of advances in our understanding of the biology of these processes and their appropriate application to patients to fill a large and growing unmet medical need.

Adherent stem cells exert significant benefit in acute ischemic injury via trophic pathways modulating inflammation, angiogenesis, cytoprotective pathways, and importantly modulation of the systemic immune response. Athersys has developed an adherent adult stem cell platform, MultiStem, with demonstrated potency in treatment of ischemic injury. As opposed to single modality drug approaches, stem cell therapy provides benefit in a multimodal context, stimulating parallel repair pathways in dynamic response to the microenvironment. MultiStem is advantageous by an extensive ex vivo expansion capacity allowing manufacturing through a master cell bank and providing uniform single donor clinical product for all patients on study. Clinical development status of Phase II studies in Stroke will be presented, with underlying PK/PD pre-clinical studies supporting clinical design. Additional CNS development programs are active in spinal cord repair, multiple sclerosis, and traumatic brain injury. Pre-clinical data describing mechanistic pathways and therapeutic hypotheses will be presented.
Benefits:
- Building a PK/PD profile for adherent stem cell therapy
- Leveraging mechanistic understanding in clinical design
- How modulating the systemic immune system can impact acute CNS injury
- Rationale for why cell therapy may succeed in stroke where drugs fail

9:35 [Oral Presentation from Exemplary Submitted Abstracts]

To be considered for an oral presentation, please submit an abstract here.

10:05 Morning Break

10:45 Clinical Development of Universal Myeloid Progenitors for the Treatment of Chemotherapy and Radiation Induced Neutropenia

Rakumar Mandalam, Ph.D., President & Chief Executive Officer, Cellerant Therapeutics

Cellerant Therapeutics is developing a novel universal cellular therapy for the treatment of chemotherapy and radiation induced neutropenia. Based on the potential of adult hematopoietic stem cells to differentiate into all myeloid and lymphoid cell types, a process to generate large and reproducible quantities of common myeloid progenitors (CLT-008) has been developed. These cells have the ability to differentiate into functional neutrophils and platelets in vivo. Pre-clinical in vivo studies have demonstrated that the myeloid progenitors prevent fungal and bacterial infection, provide protection from lethal radiation, and enable engraftment of low dose of stem cells. Furthermore, these cells do not persist long-term and their function is not MHC-restricted. CLT-008 is currently being evaluated in two Phase 1 clinical trials: (a) patients undergoing cord blood transplants for the treatment of hematological malignancies and (b) patients receiving intensive chemotherapy for high risk leukemia or myelodysplasia. The clinical development path for neutropenia and acute radiation syndrome applications will be discussed in this talk.

11:10 Challenges for Clinical Translation of Stem Cells and Tissue Engineering

Shay Soker, Ph.D., Professor, Regenerative Medicine, Wake Forest Institute for Regenerative Medicine

Regenerative medicine and tissue engineering have recently showed the potential for "bench-to-bedside" clinical translation. Tissue engineering uses cells, seeded onto biomaterials (scaffolds), to create tissue constructs that can be transplanted to replace damaged of missing tissues and organs. Researchers developed cutting-edge technologies to engineer tissue constructs, namely skin, bladders, vessels and upper airways that were used to treat patients. Alternatively, cells, in combination with growth factors, are delivered to a damaged tissue for repair. Stem cells represent an ideal source of cells for cell therapy and for ex-vivo bioengineered tissues. We explored new sources of stem and progenitor cells for clinical use that can be retrieved without complications to the patient, and expanded in vitro to large numbers, without changing their properties and differentiation capabilities. The stem/progenitor cells were successfully seeded biomaterials and the resulting constructs tested in preclinical models. However, in these studies the tissues were implanted without the reconstruction of the vascular supply, and the nutrients and oxygen were supplied by diffusion. A new technology, intact organ decellularization that produces “natural tissue” scaffolds (made of tissue extracellular matrix-ECM), was recently applied to engineer hearts, livers lungs, kidneys, pancreata and small intestine. The utilization of autologous stem/progenitor cells may limit the response of the immune system to a ‘non harmful’ inflammatory reaction to the transplanted animal-derived ECM. In this presentation we will discuss the advantages of stem/progenitors cells from different sources and their potential for clinical use alone, or in combination with biomaterial scaffolds.

11:35 The PISCES Clinical Trial in Stroke Disability – Recent Data and Future Directions

John Sinden, Ph.D., Chief Scientific Officer, ReNeuron

The PISCES clinical trial in 12 moderate to severely disabled stroke patients is the UK’s first fully regulated commercially sponsored stem cell clinical trial. It is the first clinical trial in stroke patients with neural stem cells worldwide. The first clinical data from a reasonable number of patients is now emerging, and some data trends will be updated in my talk.

We are currently preparing full clinical development plans and designing first Phase II efficacy trials for stroke, as well as for other indications. Our experiences are guiding these plans and my talk will also cover our thinking on clinical development strategies for our stem cell products in stroke, as well as limb ischemia and retinitis pigmentosa.

Benefits:
- Learn about ReNeuron's most recent progress
- ReNeuron's stem cell assets are being rapidly progressed into trials – see our strategy

12:00 Lunch provided by GTC

Bringing Research to Drug Discovery

Moderator: Philip Gregory, Chief Scientific Officer, Sangamo BioSciences

1:00 A Human iPSC Model of Cardiac Arrhythmia for Drug Development

Masayuki Yazawa, Ph.D., Neurobiology, Stanford University School of Medicine
More than a million American people suffer from cardiac arrhythmias. However, little is known about the pathophysiological process that leads to these diseases. An important limitation has been the difficulty of studying arrhythmias and finding drugs in human cardiomyocytes (CMs). To address this concern, I have developed methods for using human induced pluripotent stem cells to generate CMs from individuals with Timothy syndrome (TS), a genetic disorder characterized by QT prolongation and ventricular tachycardia. Imaging and electrophysiological studies revealed deficits in contraction, electrical signaling and calcium handling in TS ventricular CMs. To rescue the phenotypes, I tested a variety of drugs including ion channel blockers and beta-blocker and found that the roscovitine could rescue the phenotypes in TS CMs. The technology that I developed using human model of arrhythmias provides a useful new platform not only for studying disease mechanisms but also for developing new drugs to treat cardiac arrhythmias.

1:25 Stem Cell-based Research in a Pharmaceutical Company: Turning an Innovative Technology into a Transformative Approach to Drug Design

Arnaud Lacoste, Ph.D., Project Team Leader, Novartis

Academic research and literature have revealed that stem cell-based approaches have the potential to revolutionize the practice of medicine. Several biotech companies are already developing stem cell-based projects for cell replacement therapies, disease modeling or toxicology studies. These first initiatives will undoubtedly open novel avenues for the design of future therapeutics. But to truly revolutionize the practice of medicine, stem cell-based technologies must be embraced by pharmaceutical companies, which in most cases, are the only institutions with the specific experience and considerable resources required to develop medicines that meet regulatory agency standards and patients needs. Because many stem cell-related concepts are radically different from those of traditional R&D, integrating them into today’s Pharma culture raises a number of challenges in terms of research, recruitment, training, in-licensing and knowledge management.

We will describe how, in our experience, developing stem cell-based projects inside a pharmaceutical company has begun to reveal what scientific challenges must be solved for high-throughput production of stem cell-based models, what QC and product validation standards are required from service providers or biotech companies and what changes in the Pharma culture will be necessary to make stem cell-based technologies transformative in modern medicine.

1:50 Mesenchymal Stromal Progenitors: Novel Biologics In Oncology?

Massimo Dominici, M.D., Assistant Professor, Medical Oncology; Head Laboratory of Cell Biology and Advanced Cancer Therapy. Dpt. Oncology, Hematology & Respiratory Diseases, University-Hospital of Modena (Italy); Treasurer, International Society for Cellular Therapy

Mesenchymal stromal/stem cell (MSC) might be acting by different means to regenerate tissues: on one side by differentiation and on the other by secreting molecules to rescue tissues. The extent of these two different contributions to organ repair is still under investigation, but certainly growing evidence suggests that in some selected cases (heart, kidney) stromal function may be driving the benefit. This concept suggests that MSC might be valuable sources of a novel class of biological, considered as "cytopharmaceutical" products. In addition, thanks to established gene engineering approaches is possible to induce or enhance biological production useful in several fields of medicine and in particular for cancer. Gene therapy (GT) constitutes a promising approach to eliminate cancer cells possibly sparing normal tissues. Cytotoxic genes can be transferred directly into tumor cells causing their death or, alternatively, one can use genetically modified healthy cells as vehicles to deliver cytotoxic compounds capable to induce tumor apoptosis. Between these possible cellular vectors, we focused on MSC. These cells can be easily obtained from marrow and adipose tissue (AT). MSC can extensively ex vivo expanded, genetically modified and re-infused in vivo without relevant side effects. Based on our understanding of differentiation capacity of MSC after in vivo infusion and on recently published data, this paper has the goal to present the impact of genetically modified MSC as a platform of drug delivery and drug discovery for cancer. Beside several aspects of tumor and MSC interactions shall be clarified, different anti-tumor molecules could be produced by MSC and we will present approaches where modified MSC can encode for biologic showing several advantages in comparison with more traditional delivery manners.

2:15 Zinc Finger Nuclease – Edited Stem Cells: New Possibilities for Research and Therapy

Philip Gregory, Chief Scientific Officer, Sangamo BioSciences

The ability to engineer the precise genetic modifications of human stem cells would both accelerate research and extend the range of their potential therapeutic application. This possibility is now being realized via the use of zinc finger nucleases (ZFNs). ZFNs are customizable, sequence-specific endonucleases that can be designed to introduce a discrete cleavage event at any user-chosen location within the stem cell genome. By adjusting conditions under which the cleavage event is subsequently repaired, one may efficiently and precisely disrupt or edit the targeted locus, or integrate a larger, gene-sized DNA fragment. This technology – which is portable to any eukaryote – has been used for diverse applications, including therapeutic gene modification in primary cells, trait stacking of producer cell lines for improved manufacture of biologics, and gene targeting in previously refractory
species such as nematodes, rabbits, zebrafish and rats. This talk will describe recent applications of this technology in human stem cells. Examples include gene tagging in embryonic stem cells, gene targeting in induced pluripotent stem cells, and gene addition at safe harbors in a variety of stem cell types. Preclinical proof-of-concept studies towards the development of autologous, CCR5-disrupted CD34 stem cells as a treatment for HIV will also be presented.

2:40  Gene-modified Mesenchymal Stromal Cells for Chronic Stroke: Translation to the Clinic

Casey Case, Vice President, Research, SanBio

SB623 is an adult stem cell product derived from mesenchymal stem cells (MSCs) by transient transfection with Notch-1. It has proven effective in a variety of neurodegenerative diseases. SB623 is not cell replacement therapy. It works by mechanisms including trophic support, production of beneficial extracellular matrix and immunomodulation. A clinical trial has been initiated in patients with stable stroke deficits. This talk will focus on the mechanism of action and the translation of this product from bench to clinic.

3:05  Modulation of Neural Stem Cells in Alzheimer's Disease

Orly Lazarov, Ph.D., Associate Professor, Anatomy and Cell Biology, University of Illinois at Chicago

It is now abundantly clear that neural stem cells exist in the adult mammalian brain throughout life. They reside in the subgranular layer of the dentate gyrus and in the subventricular zone. Neural stem cells have the capability to self-renew, proliferate and differentiate into neurons and glia. The existence of neurogenesis permits a high level of brain plasticity and provides a source of new neurons and glia. Thus, modulation of neurogenesis has a high therapeutic value, once the molecular signaling regulating these processes is unraveled. This might be particularly critical during aging, as a dramatic decline in extent of neurogenesis takes place in the brains of mid-life and aging mammals. This decline may underlie, at least in part, reduced memory function in aging, and may promote higher susceptibility to aging-linked memory disorders, such as Alzheimer’s disease. Interestingly, we show that neurogenesis is impaired early in life in Alzheimer’s mouse models, and that major players in Alzheimer’s disease regulate neural progenitor cell proliferation and differentiation. This suggests a molecular link between neurogenesis and Alzheimer’s disease and implies that impairments in neurogenesis may contribute to or exacerbate the disease. In summary, modulation of neurogenesis would provide a way to compensate for a decline in brain plasticity and function in aging and in Alzheimer’s disease.

Benefits:
- Understanding the therapeutic potential of neurogenesis in the adult brain
- Understanding the significance of age-linked decline in neurogenesis
- Understanding the role of neurogenesis in Alzheimer’s disease
- Gaining an insight into the molecular cross talk between neurogenesis and Alzheimer’s disease

3:00  Conference Concludes
Day 1 - Thursday, April 19, 2012

7:00  Registration & Continental Breakfast

7:55  Welcome & Opening Remarks

**KEYNOTE PRESENTATION**

8:00  Clinical Biomaterials for Regenerative Medicine: From Bench to Business

**Glen Prestwich**, Presidential Professor, Director, Therapeutic Biomaterials Center, Special Presidential Assistant for Faculty, Entrepreneurism Department of Medicinal Chemistry, **University of Utah**

Faculty entrepreneurship is a scholarly activity. First, I will describe how we have implemented policies at the University of Utah that encourage faculty and student entrepreneurial activities through the Entrepreneurial Faculty Scholars and the Young Entrepreneurial Students Scholars programs. Then, I will describe a case study for commercialization of a university technology in the area of regenerative medicine.

Clinical biomaterials for regenerative medicine. Injectable and biocompatible vehicles for delivery, retention, growth, and differentiation of progenitor cells are needed for cell therapy. We created a synthetic extracellular matrix (sECM) from hyaluronic acid (HA) that affords highly reproducible, manufacturable, approachable, and affordable biomaterials. The in situ crosslinkable sECM hydrogels can be customized for use with progenitor and mature cell populations obtained many tissues, including skin, fat, liver, heart, brain, muscle, bone, and cartilage. In addition, sECMs have been developed for rapid expansion and recovery of cells in 3-D, and for the bioprinting of engineered tissue constructs. The technology is being commercialized in three fields of use: human medical devices, cell therapy and research tools for 3-D cell culture, and veterinary wound care and adhesion prevention.

**Funding Opportunities   (Joint Session)**

*Moderator: Casey Case, Vice President, Research, SanBio*

8:45  Seed Funding Start-Ups in Emerging Technologies: Perspectives on Cell Therapeutics

**Alain Vertes**, Ph.D., MBA, Sloan Fellow, **London Business School**

9:10  State Funding Opportunities for Stem Cell Research & Commercialization

**Susan Windham-Bannister**, Ph.D., Associate Professor, Anatomy and Cell Biology, **Massachusetts Life Sciences Center**

This presentation will discuss state funding opportunities through the Massachusetts Life Sciences Center for stem cell-related research and commercialization. Through a series of research matching grant programs and financing opportunities the Life Sciences Center has resources available to support stem cell research, and to invest in company formation and growth for research that has the potential for commercialization.

**FEATURED PRESENTATION**

9:35  A New Model For The Commercialization of Regenerative Medicine Technologies

**Gregory A. Bonfiglio**, Managing Partner, Proteus Venture Partners

10:00  Morning Break

**Regulatory Guidance & Updates (Joint Session)**

**FEATURED PRESENTATION**

10:30  Regulatory Requirements for Stem Cell-based Medicinal Products in the EU

**Tiina Palomäki**, Ph.D., SWP and CPWP, EMA, and Finnish Medicines Agency

Stem cells hold the promise as a source of cells for therapeutic applications in various conditions, including metabolic, degenerative and inflammatory diseases, for the repair and regeneration of damaged or lost tissues and also in the treatment of cancer. The two principal characteristics that define stem cells, i.e. capacity to self-renew and differentiate make stem cells attractive and promising source for cellular replacement therapies. However, the same characteristics can be seen as the primary cause of additional risks of tumourigenicity as well as of unintended differentiation at ectopic locations. Safe therapeutic application of stem cells necessitates understanding the possible risks. Stem cells represent a spectrum of different cell-based products with varying amount of scientific data and clinical experience. Similarly, perceived risks associated with different types of stem cells are not the same.

In the EU, the regulatory framework for development of stem cell-based medicinal products is laid down in the legislation and in the guidelines. Existing EU guidance on cell based medicinal products lays down general outlines that are applicable to all cell based-medicinal products including stem cells. In addition, stem cell-associated additional safety concerns are covered in the recent Reflection paper on stem cell based medicinal products which highlights the potential and theoretical safety concerns based on the current scientific understanding, as well as the technical and methodological challenges related to non-clinical and clinical development of stem cell based products.
10:55 Ophthalmic Disease Treatment with Embryonic Stem Cell Derived hRPE

Edmund Mickunas, Vice President, Regulatory Affairs, Advanced Cell Technology

In developing regulatory packages for cellular therapy trials there are a number of considerations to take into account which include the regulatory perspectives that are incorporated at the earliest stages into efficacy and preclinical toxicity studies, manufacturing approaches, and analytical testing methods, all with the goal of conducting clinical evaluations.

Considering that therapies involving human embryonic stem cell derived products are few and the FDA and other regulatory bodies have limited experience, challenges exist for both the sponsors of such programs as well as the regulatory bodies responsible for their review.

The case study presented will address some of the lessons learned during the IND and CTA preparation and preparation for clinical trials for ACT’s use of human RPE cells derived from human embryonic stem cells for treating various ophthalmic diseases.

11:20 Learning’s from a Positive CBER Panel Meeting for an Allogeneic Cell Therapy

Patrick Bilbo, Vice President, Regulatory Affairs & Government Relations, Organogenesis

11:45 Device-Based Regulatory Framework for Cell Therapies

Kenneth Kleinhenz, Vice President, Regulatory Affairs and Quality Assurance, Cytori Therapeutics

United States Food and Drug Administration (FDA): Device-based Cell Therapies are regulated under 21 CFR (Code of Federal Regulations) by FDA through a variety of means to include 510k process, PMA (PreMarket Application) process, and the BLA (Biological License Application) process. The 510k and PMA processes are designed for devices while the BLA process is exclusive for biological products that exceed the definition of minimum manipulation. The cell source and the associated handling/manipulations determine the complexity of the required safety profile. Device-based Cell Therapies that undergo the PMA or BLA process require extensive safety and toxicity data relevant to the cell source and the route of delivery. The risks associated with the stem cell therapy dictate the safety and toxicity profile.

European Union (EU): The regulatory framework in Europe for Device-based Cell Therapies consists of a variety of directives and regulations to include Directive 2001/83/EC, Directive 2004/23/EC, Directive 93/42/EC, Directive 2003/63/EC, and Regulation 1394/2007. Device-based Autologous Cell Therapies are regulated solely by the Notified Body if performed in the same surgical procedure. Factors such as minimum manipulation and same essential function should be considered in determining the regulatory pathway. The European Medicines Authority (EMEA) is a centralized pan-European regulatory authority that approves Advanced Therapy Medicinal Products (ATMP) such as gene therapy, somatic cell therapy, and tissue engineered products. Qualified device-based cell therapies are typically approved by a Notified Body in three to six months. EMEA products require clinical trials and a lengthy regulatory process that spans multiple years.

Benefits of Presentation:
- Participants will understand the regulatory framework for device-based cell therapies in the US and EU.
- Participants will be able to identify the appropriate level of safety testing based on the risks associated with their cell therapy.
- Participants will be able to navigate a device-based pathway with the lowest regulatory burden.

12:10 Lunch on Your Own

Novel Technologies in Stem Cell Research

Moderator: David Ruff, Principal Scientist, Life Technologies Corporation

1:30 Automated Production of CD34+ Cell Grafts for Post Infarct Myocardial Regeneration

Philippe Henon, M.D., Chief Operating Officer & Chairman, CellProthera

The therapeutical use of (PB) CD34+ cells for heart repair would represent a disruptive approach in the treatment of acute myocardial infarct (AMI). Starting December 2002, we have conducted a Phase-I clinical study to determine safety, feasibility and therapeutical effects of direct intracardiac reinjection of autologous CD34+ cells collected into the PB by leukapheresis after G-CSF mobilization in patients suffering from very bad prognosis AMI. The whole clinical procedure was feasible and safe. All patients, except one, are alive and well with a present average follow up of 72 months, including 3 patients who avoided a heart transplant initially scheduled. All these patients showed a progressive and significant improvement of all cardiac function parameters. Sustained LVEF improvement was correlated with PetScan demonstration of myocardium structure and vascularization regeneration, with a dramatic New York Heart Association (NYHA) grade improvement. In parallel, we demonstrated in G-CSF-mobilized CD34+ cells the presence of subpopulations featuring morphology, gene expression, and immunocytochemistry characteristics of both immature and mature endothelial and cardiomyocyte progenitor cells.

To simplify this therapeutical process and to propose it to as many AMI patients as possible, we are presently developing an automatic device and disposable kits allowing standardized GMP production of large amounts of autologous CD34+ cells, starting from a single total blood sample withdrawn from patients within the few days
following AMI occurrence. This automatic device would be further displayed in agreed cell therapy centres to produce after a 9-day cell processing, autologous cell grafts containing at least 50 x 106 CD34+ cells, ready to be directly reinjected into patients’ AMI lesion through an intra-ventricular catheter.

We expect this innovative approach to become in the very near future the “gold standard” treatment of severe AMI, avoiding the occurrence of a further chronic heart failure which is associated with a high rate of morbidity / mortality and high health costs. It could even be considered as an actual alternative to heart transplant in many cases.

1:55 Stem Cells Driven Paradigm Shift for Drug Discovery and Development

Petter Björquist, Ph.D., Senior Principal Scientist, Department Head, Collectics Stem Cells

Human pluripotent stem cells (hPSC) have the ability to proliferate indefinitely and to differentiate into virtually any cell type. These features can be harnessed to generate large quantities of partially differentiated progenitors or terminally differentiated specialised cells. Recent technical advancements have now made it possible to culture hPSC under standardised, defined and feeder free conditions which allows for cost efficient large scale cell production. This is a requirement for future developments of in vitro and in vivo applications based on these cells. Such applications can include in vitro toxicity testing, compound screening, or cell therapy. This presentation will illustrate new achievements using hPSC, from basic biology and generation and banking of multiple new cell lines, to commercialisation of products. Differentiation of hPSC towards hepatocytes and cardiomyocytes will be highlighted together with examples of current and future opportunities to use these cells for the assessment of adverse side effects of drugs. It is anticipated that the implementation of human stem cell based assays in the drug discovery process will lead to lower attrition rates and the development of safer new drugs. Finally, some novel advancements and future visions in the area of regenerative medicine will presented.

Benefits:
- How can stem cells improve the drug discovery process?
- Targeted medicine using stem cells
- Are we able to select the genetic background of our preclinical models?
- Genetic diversity from banks of human induced pluripotent stem cells
- Cells as drugs; is there a business model?

2:45 Advantages of Manufacturing Cells in a Three Dimensional Manner

William Prather, R.Ph., M.D., Senior Vice President, Corporate Development, Pluristem

The norm for the cell therapy industry is to manufacture cells in a two-dimensional flat surface such as a multi-flask or petri dish. However, Pluristem expands their placental-derived mesenchymal-like stromal cells (MSCs) in a proprietary three-dimensional process where cells are seeded onto polyester wafers that are placed in a bioreactor. This 3D expansion methodology allows Pluristem important advantages to the manufacture of their cells. These include the extreme economic efficiencies and added quality control by expanding cells in a 2D versus 3D manner but also the ability to manipulate and control the physical environment in which these cells are grown three dimensionally that, in turn, changes the shape, transcriptome and secretome of the cell. Pluristem, therefore, has the ability to manufacture specific PLacental-eXpanded (PLX) cell products for specific indications.

3:15 Afternoon Break

3:45 Human Embryonic Stem and Induced Pluripotent Stem Cells: Biotechnology Entering a New Era of Complexity

Michael D. West, Chief Executive Officer, BioTime

Human embryonic stem (hES) and induced pluripotent stem (iPS) cells have the potential to differentiate into all human somatic cell types. This pluripotency combined with the immortality of the cells while propagated in the undifferentiated state, enables novel methods to generate all human cell types even those with targeted genetic modifications. Nevertheless, the usefulness of this platform for the manufacture of human cell-based therapies is...
challenged by a lack of technologies that reproducibly yield identified, purified, and scalable sources of the many hundreds of cell types in the human body. A large-scale combinatorial cloning protocol will be described that has yielded over 200 purified and scalable monoclonal human embryonic progenitor cell types. These lines display a wide array of markers of primitive endodermal, mesodermal, ectodermal, and neural crest types with diverse site-specific homeobox gene expression. A fate space screening protocol utilizing approximately 100 of these EP lines has demonstrated the novel multipotency of human embryonic progenitor cell lines. Seven EP lines show a robust induction of chondrogenic gene expression during differentiation. Other lines show properties consistent with myogenic, blood brain barrier, perivascular, and other somatic cell lineages. In summary, the diversity, scalability, and relative stability of clonal hES-derived embryonic progenitor cell types offers a novel avenue for the mapping of the human embryome, the discovery of novel differentiation conditions for hES-derived cells, and when derived from cGMP hES or iPS master cell banks, may offer a novel manufacturing protocol increasing the purity of clinical-grade cell-based therapies.

Benefits:
• Novel methods of manufacturing purified products from hES and iPS cells
• A comparison of the properties of embryonic progenitors and adult stem cells
• The mapping of the human embryome

Partnerships & Acquisitions

Moderator: Petter Björquist, Ph.D., Senior Principal Scientist, Department Head, Cellectis Stem Cells

KEYNOTE PRESENTATION

4:10 The Dating Game: Finding the Right Partner
Devyn M. Smith, Ph.D., Chief Operating Officer, Neusentis Research Unit, Pfizer Worldwide R&D

The Regenerative Medicine industry continues to expand as development assets continue to advance in the pipeline, while commercial products also continue to grow. Over the last five years there have been a series of partnerships and acquisitions in the Regen Med space. These have been a mix of licensing of clinical assets and early research collaborations with academia and biotechs. Recently, we have seen activity involving commercialized Regen Med products including an acquisition of Advanced BioHealing by Shire. In addition, we have seen some negative readouts and news around the Regen Med space. What is the impact of the negative newsflow? What are the drivers for the more recent deals? What can biotechs do to position themselves attractively to potential partners? What does the future hold for the industry, particularly as it relates to partnerships/acquisitions from large companies? We will discuss these topics in this session.

8:00 KEYNOTE PRESENTATION
Leanna Caron, R.Ph., MBA, Vice President & General Manager, Cell Therapy & Regenerative Medicine, Genzyme

Partnerships & Acquisitions (continued)

Moderator: Petter Björquist, Ph.D., Senior Principal Scientist, Department Head, Cellectis Stem Cells

8:45 Trends in Cell Therapy Partnerships
Frederic Chereau, President & Chief Executive Officer, Pervasis Therapeutics

9:10 Cost-efficient Technology Development in Consortia
Frank-Roman Lauter, Head Business Development, Berlin-Brandenburg Center for Regenerative Therapies

9:35 [Oral Presentation from Exemplary Submitted Abstracts]
To be considered for an oral presentation, please submit an abstract here.

10:15 Morning Break

10:45 Panel Discussion
Panel Discussion: Partnerships & Acquisitions
Moderator: Alain Vertes, Ph.D., MBA, Sloan Fellow, London Business School

Panelists:
William Prather, R.Ph., M.D., Senior Vice President, Corporate Development, Pluristem
Devyn M. Smith, Ph.D., Chief Operating Officer, Neusentis and Pharmatherapeutics Clinical Research, Pfizer
Petter Björquist, Ph.D., Senior Principal Scientist, Department Head, Cellectis Stem Cells
Commercialization of stem cells and regenerative medicines is a long road, often dependent on external funding and long term partnerships. In order to achieve funding and bring the product to market, a solid business plan is vital. An ideal cell therapy product business model is one that fits well with the company’s overall strategic plan, and has integrated all of the relevant biological and technical aspects of the product throughout its lifecycle. Considering all of the technology’s components can help determine the appropriate manufacturing approach to take, and help to determine if the technology can be a good fit within a company’s portfolio.

Conventional wisdom has it that if the technology is autologous, then there will be a primary emphasis on a service model, while allogeneic products’ model is akin to a pharma/long term storage model. However, only taking “allo vs auto” into account is not sufficient for building an appropriate business model for a cell therapy. Further, “allogeneic” merely means that the donor and recipient are different people, it does not automatically mean a mass batch, pharmaceutical-like production model will apply. This session will look at the components of a cell therapy business plan and the key factors in commercialization, and beneficially, will use product examples to illustrate main points.

1:25 Advances in the Clinical and Key Lessons Learned

Daniel Shoemaker, PhD., Chief Technology Officer, Fate Therapeutics
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