Center for Regenerative Medicine and Cell Based Therapies

Arts & Sciences, Dentistry, Engineering, Medicine, Nursing, Pharmacy, Veterinary Medicine + Business

Improving People's Lives through innovations in personalized health care
4/3/12 Battelle Visit

- Carol Sabourin, Senior Research Leader/Chief Scientist, Center for Life Sciences Research, Health and Life Sciences Global Business
- Herbert Bresler, Chief Scientist, Health and Life Sciences Global Business
- CRMCBT to partner with Battelle
Moss Appointed Surgeon-in-Chief at Nationwide Children's Hospital

Released: 2/3/2011 6:00 AM EST
Source: Nationwide Children's Hospital
EXECUTIVE SUMMARY

Regenerative medicine is the next evolution of medical treatments. Derived from the fields of tissue engineering, tissue science, biology, biochemistry, physics, chemistry, applied engineering and other fields, regenerative medicine is the first truly interdisciplinary field that utilizes and brings together nearly every field in science. This new field holds the realistic promise of regenerating damaged tissues and organs \textit{in vivo} (in the living body) through reparative techniques that stimulate previously irreparable organs into healing themselves. Regenerative medicine also empowers scientists to grow tissues and organs \textit{in vitro} (in the laboratory) and safely implant them when the body is unable to be prompted into healing itself.
Regenerative Medicine and Cell-Based Therapies

“While there is activity in this field at Ohio State, it is currently fragmented across multiple programs, departments and even colleges with no one unifying approach. A branded Center for Regenerative Medicine and Cell-Based Therapies could create a forum for faculty and students to identify opportunities to participate in this field of study, where before the opportunities were not available. The Center for Regenerative Medicine and Cell-Based Therapies can “de-fragment” this activity by creating awareness of a central place supporting these activities”
PubMed
2011-2012 (Ohio State):

Wound – 117
Stem Cell – 75
Tissue Engg – 30
Progenitor Cell – 22
CRM-CBT announced and website launched by Dr. Gabbe on March 23rd, 2012
5th annual T2C conference

DAY 1: Friday March 23, 2012

7:00 AM REGISTRATION & BREAKFAST

7:45 AM Welcome & Opening Remarks
Steven Gabea, MD
The Ohio State University Medical Center
E. Christopher Black, MD
The Ohio State University Medical Center
Peter Mohler, PhD
Director of Davis Heart and Lung Research Institute

8:00 AM Reconstructing the Process of Wound Healing: Insights
Growth Across Organisms
Paul Martin, PhD
University of Bristol, United Kingdom

8:45 AM Cell Biology of Wounds
Jeffrey Davidson, PhD
Vanderbilt University School of Medicine

9:15 AM Wound Inflammation
Sasha Lazovich, MD
New Jersey Medical School
University of Medicine & Dentistry of New Jersey

SAVE THE DATE
6th T2C
March 14-16, 2013
The Ohio Union
Rao Named First Director of New Center For Regenerative Medicine

Dr. Mahendra S. Rao was recently appointed director of the new NIH Intramural Center for Regenerative Medicine. The NIH-ICRM is an initiative to create a world-class center of excellence in stem cell technology on campus, including induced pluripotent stem cells (iPSC), which can have applications in many systems and organs of the body. This is an initiative of the NIH Common Fund and will be administered by NIAMS.

“Dr. Rao’s varied experience makes him perfectly qualified to bring large groups together in order to move stem cell technologies through clinical trials and beyond to the clinic,” said NIH director Dr. Francis Collins, announcing the appointment.

A major goal for the center is to build on existing NIH investments in stem cell research to advance translational studies and ultimately cell-based therapies in the Clinical Center. The center will also serve as a resource for the scientific community, providing stem cells, as well as the supporting protocols and standard operating procedures used to derive, culture and differentiate them into various cell types.

In addition to the NIH-ICRM director position, Rao will hold a joint research appointment in NIAMS and NINDS.

NIAMS scientific director Dr. John O’Shea noted, “Dr. Rao is an ideal choice to lead the NIH-ICRM at this pivotal time for stem cell research. His unique background will serve him and the center well as we move forward to fulfill the great promise of stem cell technology.”

Rao is internationally renowned for his research involving human embryonic stem cells and other somatic stem cells. He has worked in the stem cell field for more than 20 years, with stints in academia, government and regulatory affairs and industry. He received his M.D. from Bombay University in India and his Ph.D. in developmental neurobiology from California Institute of Technology.

Following postdoctoral training at Case Western Reserve University, he established his research laboratory in neural development at the University of Utah. He next joined the National Institute on Aging as chief of the neurosciences section, where he studied neural progenitor cells and continued to explore his longstanding interest in their clinical potential.

Most recently, he spent 6 years as vice president of regenerative medicine at Life Technologies, Carlsbad, Calif. He also co-founded Q Therapeutics, a neural stem cell company based in Salt Lake City.
3/30/12 Visit to ABIA and the NPIC
News: FDA turns to Akron partnership to help bring safer medical devices to patients

FDA turns to Akron partnership to help bring safer medical devices to patients
12/19/2011

From joint replacement implants and cancer drug delivery systems to pacemakers and stents used in blood vessels, many medical devices aimed at healing the body have one thing in common: polymers. Now, as the number of patients needing such devices to get them back on the road to recovery grows, so does the need for biomedical implants to be safe, effective and compatible with the body’s own tissue.

That’s why the Food and Drug Administration is turning to Akron — specifically, the Austen BioInnovation Institute in Akron (ABAI), a partnership of The University of Akron, Northeast Ohio Medical University (NEOMED), Summa Health System, Akron Children’s Hospital, the Akron General Health System and The John S. and James L. Knight Foundation — to help determine the safety and reliability of medical devices made with biomaterials.

At an event in January at UA’s National Polymer Innovation Center, Dr. Matthew Becker (far left), associate professor of polymer science at UA, led a tour of the facility. Here, U.S. Assistant Secretary of Commerce for Economic Development John Fernandez, UA President Dr. Luis M. Proenza and Austen BioInnovation Institute in Akron President and CEO Dr. Frank L. Douglas view a state-of-the-art research instrumentation lab in the facility’s large high-bay area.
4/25/12 Matthew Becker Visit to CRMCBT

- Chandan Sen
- Richard Hart
- Keith Gooch
- Derek Hansford
- Samir Ghadiali
- Nicanor I. Moldovan

Matt Becker lecture: "Accelerating the Clinical Translation of Biomaterials Using Combinatorial Methods"

Collaboration areas available with Polymer materials and CRMCBT
Hello Dr. Sen,
I am Bill Marras from the College of Engineering. We are working on the development of a Spine Research Institute in the College and I would like to chat with you about a potential cross hire between your group and the Engineering for someone specializing on pro-inflammatory cytokine responses. Would you have a few moments to talk some time?
Thanks in advance,
Bill Marras

--
William S. Marras, Ph.D.
Honda Chair Professor
Director, Biodynamics Laboratory
Director, COHAM
Executive Director, Institute for Ergonomics
Department of Integrated Systems Engineering
The Ohio State University
1971 Neil Avenue, Rm 210
Columbus, Ohio 43210

phone: 614.292.6670
fax: 614.292.7852

http://biodynamics.osu.edu
James Partnership

PELOTONIA
AUGUST 10–12, 2012

ONE GOAL

2012 RAISED TO DATE: $1,054,823
RIDERS: 2689 DAYS UNTIL RIDE: 105

TOP 10 FUNDRAISERS
1. Team Huntington  $123,503.61
2. Team Buckeye  $120,812.28
3. Limited Brands Peloton  $73,741.52
4. Team Excel  $36,132.88
5. Turner Construction Pelot...  $20,820.00
6. Team Dexey  $25,901.00
7. Continental Office Enviros...  $23,000.34
8. Porter Wright  $20,900.00
9. JPMorgan Chase  $17,143.10
10. Stefanie's Team of Hope  $14,965.00

TOP 10 PELOTONS

Wexner Medical Center
Synergizing strengths and leveraging resources to catalyze scientific innovation...

Turning the scientific discoveries of today into the disease prevention strategies, health diagnostics and health treatments of tomorrow.

MY RESEARCH RECORD
DHLRI Partnership

Why our research is important:
Read Connor's story

Register for the Connor Senn Symposium May 8th, 2012

Join us for the Connor Senn Memorial Game
OSU vs The Columbus Crew

Research + Clinical Trials

DHLRI Research
DHLRI is currently comprised of over 200 members with approximately $20M in annual funding.

DHLRI News & Events
11th Annual Connor Senn Memorial Game
Connor Senn Symposium Non-Medical Attendee Registration
Words of Wellness - "Saving Women’s Hearts"
Study - Pregnancy Increases Fatal Heart Attack Risk

News + Events

Ways to Support

Donate Now
Click on the hand to link to online giving.

Advocacy
Actively support initiatives around cardiovascular and pulmonary diseases.

Volunteer
Volunteer your time, talents and skills.
Introduction to the IGERT Program

The Integrative Graduate Education and Research Traineeship (IGERT) program, initiated in 1997 and now comprising approximately 125 award sites, continues into its sixth annual competition. The IGERT program has been developed to meet the challenges of educating U.S. Ph.D. scientists, engineers, and educators with the interdisciplinary backgrounds, deep knowledge in chosen disciplines, and technical, professional, and personal skills to become in their own careers the leaders and creative agents for change. The program is intended to catalyze a cultural change in graduate education, for students, faculty, and institutions, by establishing innovative new models for graduate education and training in a fertile environment for collaborative research that transcends traditional disciplinary boundaries. It is also intended to facilitate greater diversity in student participation and preparation, and to contribute to the development of a diverse, globally-engaged science and engineering workforce.

IGERT is an NSF-wide endeavor involving the Directorates for Biological Sciences (BIO), Computer and Information Science and Engineering (CISE), Education and Human Resources (EHR), Engineering (ENG), Geosciences (GEO), Mathematical and Physical Sciences (MPS), Social, Behavioral, and Economic Sciences (SBE), the Office of Polar Programs (OPP), and the Office of International Science and Engineering (INT).
Stem Cell Core – Phase I
Tissue Engineering Core – Phase II
COM Stem Cell

Are you interested in extramural funding related to stem/progenitor/marrow-derived/cancer stem cells?

<table>
<thead>
<tr>
<th>Answer Options</th>
<th>Response Percent</th>
<th>Response Count</th>
</tr>
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<tbody>
<tr>
<td>Yes</td>
<td>78.7%</td>
<td>48</td>
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<tr>
<td>No</td>
<td>21.3%</td>
<td>13</td>
</tr>
</tbody>
</table>

answered question 61
skipped question 1

Are you interested in extramural funding related to stem/progenitor/marrow-derived/cancer stem cells?
Stem Cell Core Advisory Group

Doug Kniss (Chair),
Alicia Bertone (Co-chair)
Lynn O’Donnell
Hiranmoy Das
Mahmood Khan
Nic Moldovan
Derek Hansford
Carmen Cantemir
Sashwati Roy
Glioma Cancer Stem Cell
Administrative Space – 7th Floor BRT
Stem Cell Core Space – Basement BRT
Recruits......Done

Brent D. Toto, MHA
Administrative Director, CRMCBT
Recruits......Done

José Javier Otero, MD, PhD
Assistant Professor of Pathology, The Ohio State University

General Mission
The mission of the experimental neuropathology laboratory is to seek fundamental understanding of the mechanisms of diseases affecting the central and peripheral nervous systems. My particular focus is in the understanding of developmental and neoplastic disorders of the CNS.
Recruits......In Progress

Prof. Jianjie Ma
Doctors re-grow human heart

BY SARAH SWONG
CONTRIBUTING REPORTER
Tuesday, April 3, 2012

A Yale doctor's innovative stem cell procedure may change the field of regenerative medicine.
Do you have anyone else being recruited in this space?
First Synthetic Nanofiber Transplant in the World
*contact us about custom scaffolds for your application
Ohio State Comprehensive Wound Center Announced as Flagship Partner of Heal Logic

Jeff Nelson, President, announced the strategic relationship on April 19th.

Heal Logic is the new name of merged National Healing Corporation and Diversified Clinical Services. The partnership will be a catalyst to further elevate research opportunities and improving patient outcomes at the Wexner Medical Center and nationally in the field of wound care.
CRMCBT Annual Retreat August 17-18, 2012
Thank you
CRMCBT Funding Tracks - Discussion

- Program Project
- Program RFA
- Industry Partnership
- Publications and Productivity Track (Conference Travel Awards or Core Fee)
- Inter-College Partnership

- CCTS
- Pelotonia Cancer
- Cardiovascular DHLRI
- Akron FMC Track
- IP Track
College of Arts and Sciences (ASC)

Peter March
Divisional Dean of Natural and Mathematical Sciences
College of Arts and Sciences
Merger of Five Legacy Colleges (2010)

- College of Arts
- College of Biological Sciences
- College of Humanities
- College of Mathematical and Physical Sciences
- College of Social and Behavioral Sciences

College of Arts and Sciences
Statistical Abstract (2010-2011)

- 1,176 full-time tenured/tenure track faculty

- 846 full-time staff

- 2,536 graduate students (1,038 Master’s students and 1,498 PhD students)

- 29,306 undergraduate student majors
Program/Degree Statistics

Undergraduate Students
- 100 majors and 103 minors
- 8 undergraduate degrees offered
- 5,305 undergraduate degrees awarded
- 455 associate degrees award (regional campuses)

Graduate Students
- 47 Doctoral programs and 40 Masters programs
- 8 graduate degrees offered
Research Activity (FY 2011)

- $78,736,147 in external grants and contracts.
- $60,564,762 grants and contract expenditures.
- 20+ Centers/Institutes, including:
  - Advanced Computing Center for Arts and Design
  - Center for Applied Plant Sciences
  - Center for Emergent Materials
  - Center for Ethics and Human Values
  - Center for Human Resources Research
  - Center for RNA Biology
  - Mathematical Biosciences Institute
Battelle Contacts for CRMCBT

Expertise:

- Medical Device Development
  - Concept Through Clinical Prototype
  - Detailed Problem Solving

- Cell-Based Therapy Manufacturing Systems
  - System Design, Development and Testing (Biological and Engineering)

- GLP and non-GLP Studies
  - Wound Healing Models
  - Infectious Disease Models
  - Toxicity, Safety & Efficacy

Primary Contacts:

- Herb Bresler, PhD breslerh@battelle.org
- Carol Sabourin, PhD sabourinc@battelle.org
- Nancy Bordelon bordelonn@battelle.org
From Bench to Bedside

Jed Johnson, PhD

www.nanofibersolutions.com
First Nanofiber Trachea Implant in Man
Future Steps

1. Support Environment
   - From idea through clinicals to FDA approval
   - In vitro expertise, animal models, human patients
   - Open to OSU and outside technologies

2. Build value internally prior to entering market

3. Build/Retain high-tech jobs with long-term economic impact and significant patient impact

A Destination for Life-Impacting Technologies
Center for Regenerative Medicine and Cell Based Therapies Operations Update 4/27/2012

Vincent J. Pompili, MD, FACC
Professor of Internal Medicine
Director of Interventional Cardiovascular Medicine and Cardiac Catheterization Laboratories
Director Cardiovascular Cell-Based Therapies
The Ohio State University
Cell populations $133^+ \text{ vs. } 34^+$ selection using CliniMacs or Isolex systems

133+/34-/31- 133+/34+/31- 133-/34+/31- 133-/34-/31+

Further Differentiation

133+/34+/31-

Hemangioblasts Hematopoietic Stem Cells Endothelial Cells

133+ selection

34+ selection

31+ are MHC +

Cell Differentiation Pathway

Wexner Medical Center
UCB CD133⁺ Cells and Vascular Flow

SEACOAST 18 Month Follow up

Clinical Outcomes
- Improvement in Ischemia
- Improvement in EF
- Seattle Angina Questionnaire

Change in Area of Reference Ischemia with Tc99 Sestamibi Perfusion

At six month follow-up the mean Ejection Fraction for the cohort was 56.44 (increase of +0.94 p = NS) with 6 of the 9 patients treated having an improvement in their EF scores.
CD133+ Cell Expansion
Aminated Nanofiber Matrix

Hai-Quan Mao et al; Biomaterials. 2006 Dec;27(36):6043-51
Cell Adhesion on Nanex Fibers vs. Aminated Film
MACS Sorted CD133 Surface Phenotype of Primary and Expanded Cells

<table>
<thead>
<tr>
<th></th>
<th>Primary</th>
<th>Expanded</th>
</tr>
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<tbody>
<tr>
<td>CD133</td>
<td>91.77</td>
<td>24.2</td>
</tr>
<tr>
<td>CD34</td>
<td>93.56</td>
<td>93.1</td>
</tr>
<tr>
<td>CXCR4</td>
<td>8.66</td>
<td>96.8</td>
</tr>
</tbody>
</table>

Percent Surface Expression
Stemness

Nanex 133+ Cell

Endothelial Cells

Vascular Smooth Muscle Cells

Erythrocytes
Nanofiber Expansion and Genetic modification of CD133+ cells increases neovascularization.
Magellan System Marrow Concentrator

- Portable-OR compatible
- Rapid tissue fractionation
- Small tissue volumes
- Bedside processing
- Reduced risk of contamination
- Consistent, reproducible forecasted results
  - Independent of hematocrit
  - Independent of operator
Magellan-Processing Marrow

Operation of system

60cc of marrow prior to procedure

Centrifugal spin setting: 15 minutes.
Volume settings: touch pad.

Optical sensor transfers blood in, platelet gel out, via closed system.

MNC tensile strength determined by calcium thrombin additive.

Figure 2. Preparation of APG

These photos were taken with a strobe to show the Magellan® disposable in motion during separation.
### Arteriocyte Partnership

<table>
<thead>
<tr>
<th>Year</th>
<th>Milestone</th>
</tr>
</thead>
<tbody>
<tr>
<td>2004</td>
<td>Arteriocyte Inc. founded; establishes key research collaborations and recruits Donald Brown as first employee</td>
</tr>
<tr>
<td>2005-2006</td>
<td>Executed first FDA safety study for coronary infusion of marrow derived stem cells in chronic ischemic patients, funded by NIH</td>
</tr>
<tr>
<td>2007</td>
<td>Formed Arteriocyte Medical Systems and acquired the Magellan™ Platelet Rich Plasma business from Medtronic</td>
</tr>
<tr>
<td>2008</td>
<td>First Military Contract for Advanced Theater Blood Pharming Technology Development</td>
</tr>
<tr>
<td>2008-09</td>
<td>Built an integrated sales operation across 15 states</td>
</tr>
<tr>
<td></td>
<td>First OUS shipments to six countries</td>
</tr>
<tr>
<td>2009</td>
<td>Transferred Magellan™ manufacturing into the United States</td>
</tr>
<tr>
<td></td>
<td>Launched MAR01&lt;sup&gt;®&lt;/sup&gt; into the U.S.</td>
</tr>
<tr>
<td></td>
<td>First Military Contract for Compartment Research</td>
</tr>
<tr>
<td></td>
<td>Received $5 Million state of Ohio grant for Magellan™</td>
</tr>
<tr>
<td>2010</td>
<td>Consolidated worldwide distribution for entire Magellan™ franchise, including cardiac surgery channel</td>
</tr>
<tr>
<td></td>
<td>Built out Cleveland Research and Development Center</td>
</tr>
<tr>
<td></td>
<td>First NCI and NIAD grants on NANEX&lt;sup&gt;®&lt;/sup&gt;</td>
</tr>
<tr>
<td>2011</td>
<td>FDA IDE for Magellan™ MAR01&lt;sup&gt;®&lt;/sup&gt; for Critical Limb ischemia</td>
</tr>
<tr>
<td></td>
<td>CRADA with Military’s ISR on Magellan™ and NANEX&lt;sup&gt;®&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>First Military Contracts for Burn Remediation and Post Surgical infection prevention For Combat Wounded Soldiers</td>
</tr>
<tr>
<td></td>
<td>Magellan added to Federal Supply Schedule</td>
</tr>
<tr>
<td></td>
<td>Received $1 Million State of Ohio Award for NANEX&lt;sup&gt;®&lt;/sup&gt;</td>
</tr>
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<td></td>
<td>Struck Partnership with Allosource on MAR0Match &amp; MAR0Fuse</td>
</tr>
<tr>
<td></td>
<td>MAR01&lt;sup&gt;®&lt;/sup&gt; revenue exceeds $3 Million (2nd full year on market)</td>
</tr>
</tbody>
</table>

**FUNDING TO DATE:**
$24 million non-dilutive grant funding from NIH, DARPA, State of Ohio and other public sponsors

**OWNERSHIP**
Medical Systems Unit (Arteriocyte Medical Systems, Inc.)
- DW Healthcare Partners
- Arteriocyte Inc.
- Senior Management
- Key Advisors
- Employees

Cellular Therapies Unit (Arteriocyte Inc.)
- Senior Management
- Case Western Reserve University
- Employees
Medical Devices
The Company’s Medical Systems unit will launch two forms of Demineralized Bone Matrix in early 2012 (MAR0Match® and MAR0Fuse®). When both are combined with MAR01 at bedside, the resulting living cell embedded graft material provides the orthopedic surgeon with the handling and irrigation resistant characteristics of dbm gels, and the living cell wicking characteristics of dbm powders.

The Medical Systems Unit has also licensed two class 1 medical devices for tissue aspiration including certain strategic investment and distribution rights to Control Medical’s ASPIRE sterile disposable handheld tissue aspirator. The company holds exclusive distribution rights for surgical aspiration of bone marrow and plans to launch the ASPIRE device in FY2012.

Cellular Products
MAR01 for Amputation Prevention, Myocardial Injection, Compartment Syndrome, Burns

The Magellan technology is an FDA 510(k) approved device and sterile disposable system for the laboratory and bedside manufacture of Platelet Rich Plasma as deemed necessary by the clinician. Arteriocyte is currently developing Magellan’s MAR01® technology toward Class III indications in 4 clinical targets, all with current funding provided by the Department of Defense and the State of Ohio.

NANEX®
NANEX® technology is a nanofiber based electro-spun PES (polyethylene sulphone) that mimics the three-dimensional structure of innate bone marrow. The NANEX® fibers are treated through a proprietary process that results in up to 40 nano-moles/cm² concentration of a peptide bond (CONH) in a positive charged scaffold-which attracts CD34+ and CD133+ stem cells. The resulting three-dimensional structure mimics the bone marrow environment, allowing a rapid growth of stem cells while maintaining their undifferentiated state.

Arteriocyte is also developing the NANEX® expansion technology to launch research based stem cell lines for drug toxicity for the Pharma industry, and human clinical stem cell culturing for transplant center use, including a current NIH (National Heart Lung Blood Institute) funded study for the company’s “first in man” use of NANEX® expanding allo-cord stem cells for Critical Limb Ischemia.
Interdisciplinary Program Building

- OSU Partnership with Arteriocyte Inc
  - Pre-clinical core lab studies for CLI, Bone marrow transplant engraftment, Acute MI, compartment syndrome
  - Multispecialty clinical trial activity
  - Orthopedic Surgery (Compartment Syndrome/ TKA antibiotic co-delivery
  - Vascular Surgery-CLI phase I and II clinical trials
  - Cardiology-Acute MI trial
Leveraging Unique Strengths

- Successful CV animal core facility for pre-IND animal studies for clinical trials in CLI, BMT, and acute MI
- Successful partnership in 5 awarded phase I and phase II SBIR/STTR grants in past 5 years
- Collaborative partnership with Industry and clinical investigators
Thank You
Center for Regenerative Medicine and Cell Based Therapy: Operations Committee - April 27, 2012

Lynn O’Donnell, PhD
Director, Cell Therapy Laboratory
The Ohio State University James Cancer Hospital and Solove Research Institute
Cell Therapy Laboratory: Regenerative Medicine Clinical Trials Activity

**Completed Studies**
- **Osiris** Protocol 403 (Pompilli) – Prochymal® (allogeneic, cultured BM MSCs) for IV infusion following AMI – Phase II, multicenter, randomized, double-blind, placebo-controlled study

**In Process Studies**
- **Arteriocyte** Protocol ART 10-001 (Go) – Magellan® System (to prepare autologous bone marrow concentrate) for intramuscular injection to treat CLI – Phase I, non-randomized, feasibility study
- **Amorcyte** Protocol 002 (Pompilli) – AMR-001 (autologous CD34+ cells from BM) for Intra-coronary Infusion following AMI (STEMI) – Phase II, prospective, randomized, double-blind, placebo-controlled study

**Pending Studies**
- **Allocure** Protocol AC 6071103 (Firstenberg) – AC607 (allogeneic, cultured BM MSCs) for renal arterial infusion in patients with Acute Kidney Injury following Cardiac Surgery – Phase II multicenter, randomized, double-blind, placebo-controlled study
- **Biomet** BB-IDE 13996 (PI @ Riverside) – MarrowStim® PAD Kit (to prepare autologous bone marrow concentrate) for intramuscular injection to treat CLI with severe Peripheral Arterial Disease (PAD) – Phase I/II, multicenter, randomized, double-blind, placebo-controlled study
- **NIH/NHLBI** (CTSN & CCTRN) / **Mesoblast** LVAD Cell Therapy Trial (Sai-Sudhakar) – Revascor™ (allogeneic cultured BM MPC/MSCs) for direct myocardial injection in LVAD recipients – Phase II, prospective, multi-center, double-blind, randomized, single dose cohort, sham procedure controlled trial
<table>
<thead>
<tr>
<th>PI or Sponsor</th>
<th>Project Description</th>
<th>Barriers to Success</th>
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</thead>
<tbody>
<tr>
<td>Arteriocyte / Pompilli</td>
<td>Umbilical cord blood expansion on Nanex™ nanofibers for CLI, other</td>
<td>Poor expansion with cryopreserved, HLA-matched allogeneic CBUs; insufficient staff availability to trouble-shoot</td>
</tr>
<tr>
<td>(NIH SBIR funded)</td>
<td></td>
<td>-----------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Wesolowski / Das</td>
<td>Expansion of autologous gamma delta T cells from peripheral blood by culture with bisphosphonates for immunotherapy of breast cancer</td>
<td>Returned for more pre-clinical studies (not ready for translational development)</td>
</tr>
<tr>
<td>Vasu / Yu</td>
<td>Allogeneic NK cell enrichment, activation and expansion with IL2 for post-BMT immunotherapy of hematologic malignancies</td>
<td>Very early stages, currently unfunded (Division / department support), other barriers unknown</td>
</tr>
<tr>
<td>Devine / Baiocchi</td>
<td>Allogeneic gamma interferon-secreting cell enrichment for treatment of CMV or EBV post-BMT</td>
<td>Insufficient staff availability, flow expertise and availability</td>
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</table>
Cell-Based Therapies: Operations = Logistics = How

- Definitions of Logistics:
  - “the detailed coordination of a complex operation involving many people, facilities, or supplies” (New Oxford American Dictionary)
  - “the detailed organization and implementation of a complex operation” (Oxford Dictionary online)
  - commonly seen as a branch of engineering that creates "people systems" rather than "machine systems“ (Wikipedia)

- Questions for Discussion – How to move the CRMCBT forward
  - Where are the existing barriers for OSU investigators? Should we poll Center members or other PIs?
  - What gaps can be filled quickly? What roles & services can be filled by the lab? Assay development? Translational development? Preclinical cells sourcing? Study implementation (industry sponsors) – budgets, contracts, etc?
  - Begin hiring and equipping lab now?
Opportunities at the College of Nursing

Jodi McDaniel, PhD
Assistant Professor
The Ohio State University College of Nursing
Vision

- The Ohio State University College of Nursing is the world’s preeminent college known for accomplishing what is considered impossible through its transformational leadership and innovation in nursing and health, evidence-based practice and unsurpassed wellness.

Bernadette Mazurek Melnyk, PhD, RN, CPNP/PMHNP, FNAP, FAAN
Associate Vice President for Health Promotion
University Chief Wellness Officer
Dean, College of Nursing
Interdisciplinary Program Building

Faculty research

- Health-risk assessment/health-risk reduction
  - smoking cessation, cancer screening in vulnerable and ethnically diverse populations, epidemiology of antibiotic resistant infections, adolescent obesity, mental health

- Women’s and infant health
  - prevention and early treatment of sexually transmitted infections, premature birth in high risk, underserved populations

- Symptom biology and management
  - cancer cachexia, wound healing, complications of pregnancy, growth of premature infants

- Decision-making processes
Interdisciplinary Collaboration

The CON faculty actively engage in research with faculty in other colleges in addition to other universities and clinical facilities to solve common health problems.

- College of Medicine
- College of Public Health
- College of Education & Human Ecology
- College of Dentistry
- Nationwide Children’s Hospital
- Arthur G. James Cancer Hospital
- Richard J. Solove Research Institute
- Chalmers P. Wylie VA Ambulatory Care Center
Developing Health Care Solutions

Entrepreneurial Leader

Dr. Melnyk

- Center for Transdisciplinary Evidence-based Practice (CTEP)
- Research Intensive Workshop (summer 2012)
- Nurse Athlete Program – Partnering with Human Performance Institute
Regenerative Medicine and Cell-based Therapies
Comparative, Veterinary and Applied Programs

Alicia L. Bertone, DVM, PhD, Diplomate ACVS
Trueman Family Endowed Chair

Veterinary Medicine; leaders in approved regenerative biologic products and clinical application

OSUCVM Clinical Trial – Dfb-BMP2
VETERINARY MEDICINE – A Leader in Regenerative Medicine

1. **Strong Medical and Basic Scientists at Universities**
2. **Receptive Market**
3. **Limited FDA Regulatory Control**
4. **Preclinical Models for Human Diseases**
5. **Veterinary Clinical Medicine [Application and Therapeutics]**

VETERINARY MEDICINE – Leaders In:
1. **Comparative Medicine and Research**
2. **Preclinical Research for Devices and Products**
3. **Clinical Commercialization of New Technologies**
4. **Intellectual Property Capture**
5. **One Medicine Crosses Disciplines of Cancer, Orthopedics, Transplantation, Neurology; Dominant Areas of First Users**
Cell-based Molecular Therapy Preclinical Data for Human; Comparative Science; Veterinary Patient Application and Market

Large animal, immunocompetent, autologous harvest

Dermal fibroblasts or BMDMSC

Collagenase digestion

Ad-BMP2

In Vitro Gene Transfer

We can accomplish bone regeneration in clinical animal patients

- Infected bone or failed arthrodesis
- Cell serves as Vector for molecular therapy
- Dermofibroblasts or Stem Cells
- Blood clot created with thrombin
- Inject cells into blood clot or PRP

**Clinicians**
Adin Lab: Islet transplantation research

Tolerogenic Vaccine

Innate Immunity

Islet Encapsulation

Clinical Dog Transplant

Decrease Hypoxic Stress

Bili 20uM/kg

Wexner Medical Center
Figure 1. Above: Inverted microscope views and scatter patterns of canine myeloid cell populations. Bone marrow stem cells were differentiated into dendritic cells (a) or macrophages (c) and compared against a canine macrophage cell line b). These cells were evaluated phenotypically demonstrating that the canine cell line most closely resembled CD11c+ canine DCs.
The functional ability of canine myeloid cells can be altered upon exposure to environmental factors. In this study, soluble tumor factors were able to produce canine myeloid cells with altered phagocytic abilities. Myeloid cells exposed to soluble tumor factors had decreased phagocytosis as shown by a decreased percentage of cells containing phagocytosed beads and decreased relative mean fluorescence intensity (indirectly indicating the number of phagocytized beads). The upper panel shows a histogram of the cell population while lower show corresponding images on an inverted fluorescent microscope.
Tissue-Engineered Trachea
Nanofiber Solutions, Inc.

3-D scaffold constructs

Scaffold with cells

OSU collaborators
Drs. Matthew Allen and Christopher Adin
VETERINARY MEDICINE – Animal Stem Cell Core

Our CVM has been a CHAMPION of the Regenerative Medicine Initiative

New Renovation of VMAB 325D – GLP laboratory for stem cell culture and characterization of animal stem cells
Cryopreservation of animal stem cells in collaboration with the CCC biorepository for animal cells. (CTSA, Dr London)
Veterinary Medicine – Collaborations and Future

- Preclinical Studies and Animal Models
- BioRepository and BioSpecimen cryopreservation for stem cell animal models
  - Feline stem cells for renal disease
  - Islet cell differentiation from feline stem cells
  - Chondrogenesis from equine fetal stem cells
NSF CNAPBD Research Structure
Center for Affordable Nanoengineering of Polymeric Biomedical Devices
Director: L. James Lee
Gene and Oligonucleotide Therapy

Use of nucleic acids for the treatment of diseases

Genes

Oligonucleotides
(MicroRNA, SiRNA, antisense ODN…)

Cell

Nucleus

Cytosol

mRNA

Protein

Engineered Cells

- Therapeutic protein production
- Gene therapy
- Cancer treatment
- Somatic cellular differentiation
- Induced pluripotent stem cells

- High transfection efficiency
- Dosage control
- Minimum cell damage
Transfection Pathways: Endocytosis, Fusion, Injection

Chemical/Biological Methods
- Endocytosis
- Fusion
- Injection

Physical Methods
- Gene Gun
- Microinjection
- Electroporation

Transfection Pathways:
- HIV Virus
- Clathrin Independent
- Caveolae
- Macropinocytosis
- Nucleus
- Early endosome
- Late endosome
- Endosome
- Nanochannel
- Microchannel
Nanochannel Electroporation (NEP) for Gene Transfection

Guan and Lee, PNAS, 2005
Guan, Yu, Lee, Advanced Materials, 2007
Guan, Boukany, Chiou, Hemminger, Zha, Cavanaugh, Lee, Advanced Materials, 2010
High Throughput NEP

- Cell loading previously carried out on a single cell basis via optical tweezers (laborious and slow)
- New NEP designs include a preloading reservoir filled with a known number of cells
- Cells move into the microchannels (in close contact with the nanochannels) via rotation allowing loading of hundreds of cells

Cell loading

OSKM expression (24 h after NEP)
NEP Transfected Cells after 2 and 3 Weeks of Culture Showing Endogenous Oct4 Expression
Cells Removed from Chip after 2 and 3 Weeks and Cultured on Matrigel Showing More Pluripotent State
Biodegradable Cell Based Drug Delivery Devices

Dopamine Release in vitro / in vivo

Comparison of dopamine release profiles *in vitro*

Comparison of serum dopamine concentrations in mice
*Statistically significant increase in serum dopamine concentration compared to PBS control device (p < 0.005).

Collaboration with William Carson (MD, OSU Comprehensive Cancer Center)
Transplantation of Pancreas Islet

Collaboration with Adin Christopher, MD
(Department of Veterinary Clinical Sciences, OSU)
Transplantation of Pancreas Islet Microcapsules

Collaboration with Adin Christopher, MD (Department of Veterinary Clinical Sciences, OSU)
Encapsulated Thermogenic Cells Reduce Obesity

Magnetic resonance imaging

Histological imaging of visceral fat

Collaboration with Dr. Ouliana Ziouzenkova (Department of Human Nutrition)
Construction of 3D Multiple Cell-Scaffold Complex

ES cells in Scaffold #1

CO₂ fusing in buffer

NIH 3T3 cells in Scaffold #2

3D cell-scaffold complex

Yang, Xie, Kang, Kniss and Lee
Journal of American Chemical Society
(2006)
Islet-like Structures for Diabetes Research and Treatment

- Insulin injections → standard treatment for type-I diabetes; however, partial and/or chronic hyper/hypoglycemic states are common → detrimental long term side effects
- Transplantation of allogeneic islets can restore euglycemia to diabetic patients → widespread use has been significantly hampered by donor tissue scarcity
- Micro/nanofabricated platform used to control human precursor cell clustering and differentiation towards an insulin-expressing phenotype
- Fully biodegradable platform → go beyond in vitro applications and in the future be adapted as an implantable cell cluster carrier to assist anti-diabetic cell-based therapies

Hansford (BME) Lannutti Lee