Midwest Stem Cell Therapy Center

Annual Report

Legislative Update

House Appropriations Committee

February 8, 2016

Presented by Buddhadeb Dawn, M.D.
Director, Midwest Stem Cell Therapy Center

I. OVERVIEW

Therapy with adult stem cells from bone marrow, umbilical cord blood, and other sources has the potential to cure diseases for which no effective treatment is available at this time. In addition to bone marrow transplantation as an integral part of cancer therapy, growing scientific evidence tends to support the efficacy of adult stem cell therapy for diverse pathological conditions, including heart attacks, stroke, spinal cord injury, and many others. However, there was no comprehensive center or program in Kansas or in the surrounding region until a senate bill (No. 199) was passed by the Kansas Legislature to enable the establishment of Midwest Stem Cell Therapy Center (MSCTC) in July 2013.

II. GOALS

The goals of MSCTC are broad:

- Focus on activities that advance adult, cord blood and related stem cell and non-embryonic stem cell research and therapies for patient treatment;
- Serve as a core facility to produce clinical grade stem cells from adult tissues, cord blood and related materials for use in clinical trials and therapies;
- Facilitate the delivery of adult, cord blood and related stem cell therapies to Kansas City and Midwest region hospitals where appropriate;
- Partner and collaborate with the blood and marrow transplant center of Kansas to foster a regional network of physicians trained in adult, cord blood and related stem cell therapy applications;
- Create and maintain a database resource for physicians and patients that provides a comprehensive global list of available stem cell clinical trials and therapies;
- Initiate clinical trials with adult, cord blood and related stem cells;
- Create education modules to train and educate physicians and research scientists about peer-reviewed adult, cord blood and related stem cell therapy applications for patients;
- Distribute information to Kansas physicians about methods for successful treatments with adult, cord blood and related stem cells through basic and clinical research;
- Inform the public on available adult, cord blood and related stem cell therapeutic options.

To assure that each of the goals is accomplished and that the Midwest Stem Cell Therapy Center reaches the expectations of the Kansas Legislature, a multi-pronged approach has been developed as outlined below.

III. COMPONENTS AND PROGRESS REPORT

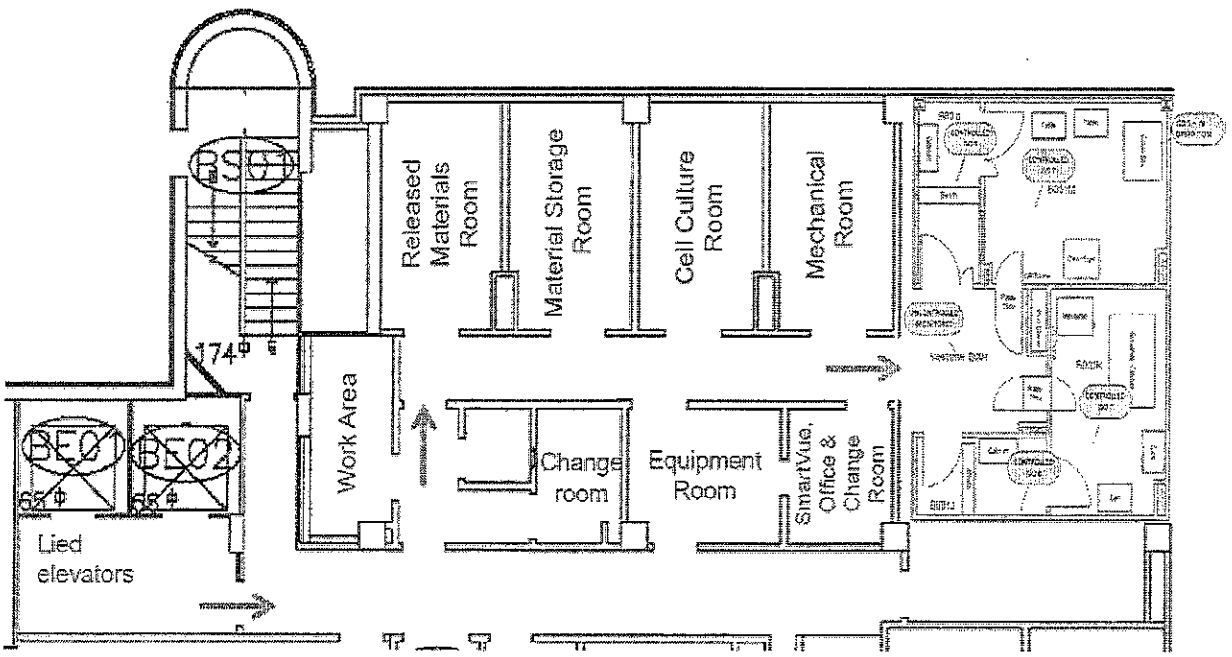
A. ADVISORY BOARD

- A 15-member Advisory Board representing various stake-holders has been assembled
  - Information related to individual members is available at www.kumc.edu/msctc.
- The Board meets 4 times per year and, as necessary, to assure continued MSCTC progress
  - There have been 9 meetings of the Board thus far, with the next meeting scheduled for March 10, 2016.

B. SCIENTIFIC AND ADMINISTRATIVE PERSONNEL

1. Center Director: Recruited
2. GMP Manager: Recruited
3. Financial assistant (part-time): Recruited
4. Research Associate, Production: Recruited
5. Quality Control Supervisor (part-time): Recruited
6. Quality Assurance Supervisor: Recruited
7. Regulatory Personnel: Open
8. Communications and Marketing: Recruited
9. Biostatistician (20% effort, to increase as necessary)
   - Support available as necessary through the Biostatistics Department at KUMC

C. FACILITY FOR CLINICAL GRADE CELL PROCESSING/MANUFACTURING



The MSCTC currently occupies approximately 8200 ft^2 of space, including office (1260 sq ft), laboratories (5100 sq ft) and GMP manufacturing (1000 sq ft) areas. The space is utilized for R&D related to cell isolation and expansion, process development, analytical methods development and clinical grade manufacturing. The manufacturing area is designed and operates to meet FDA compliance and environmental quality requirements as outlined in the Good Manufacturing Practice (GMP) and Good Tissue Practices (GTP) guidelines.

'Good Manufacturing Practice' guidelines define the quality standards for the production and testing of medicinal products, medical devices, and other pharmaceutical products as required by the Food and Drug Administration (FDA). In addition to GMP requirements, the 'Good Tissue Practice' guidelines define the requirements that govern the methods used in, and the facilities and controls used for, the manufacture of Human Cell Therapy and Gene Therapy Products in a way that prevents the introduction, transmission, or spread of communicable diseases by these products. The concepts underlying all of these guidelines are directed at the ultimate goal of safeguarding the health of the patient. GMP/GTP guidelines cover quality and safety standards in all aspects of the manufacturing process, including the infrastructure, buildings, equipment, personnel training, ingredients, the manufacturing process, and quality control process. Having a fully functional GMP/GTP facility is a necessary aspect of processing and manufacturing clinical grade cellular products.

MSCTC's FDA registered GMP facility (FEI# 3011110834):

- Adheres to GMP and GTP regulations
- Follows appropriate Standard Operating Procedures relevant for the characterization and manufacturing processes required to assure the availability of consistent adult stem cells
- Maintains the highest standards of Quality Control (QC) and Quality Assurance (QA)
- Educations and trains all relevant personnel
- Serves current MSCTC efforts well with capacity for up to 6 batches of adult stem cells per week if staffed and equipped to address volume

Location: Lower level of Lied building within the KUMC campus

Services being offered:

- Processing adult stem cells for the purpose of therapeutic transplantation in patients
  - Source of adult stem cells include bone marrow, the Wharton's Jelly fraction of human umbilical cord and cells provided by industry sponsors
- Developing cell culture and cell expansion processes as well as characterization methodology suitable for specific therapeutic purposes and to meet targeted milestones and regulatory requirements

D. Training and Education Initiatives

- **Components**
  - Midwest Conference on Cell Therapy and Regenerative Medicine

- Disseminating knowledge related to the use of adult stem cells in human clinical trials
- Educating scientists on the latest research techniques and development requirements
- Informing the public about the latest adult stem cell treatment options
- The 3rd Annual conference was held on September 18-19, 2015
  - 30 speakers and panelists and approximately 150 attendees
  - Extremely positive feedback
- The fourth annual conference is scheduled for September 16 and 17, 2016

- Grand rounds and seminars
  - Inform the public, scientists, and clinicians about available and developing adult stem cell treatments – through web portals and global resources: database of available treatments and clinical trials, publication of stem cell "consumer reports" and 1:1 conversations with those enquiring about stem cells
  - Professional and public forums similar to town hall or similar meetings
  - Elementary and secondary school science and health lesson plans

- **Accomplishments:**
  - Three very successful conferences on adult stem cell therapy
  - The MSCTC website provides extensive and disease-specific information on adult stem cell therapy, both preclinical and human studies.
    - Numerous original and review articles are freely accessible to the public
  - The MSCTC is now tied into ClinicalTrials.gov, NIH/FDA database for global clinical trials
    - Provides immediate access to the most current clinical trial information
    - Defined searches in the most sought after areas of stem cell therapy available
- **Plans:**
  - The Fourth Midwest Conference on Cell Therapy and Regenerative Medicine (Sep 16-17, 2016) will be held at the Sheraton Overland Park hotel in Kansas
  - Training students and fellows various aspects of adult stem cell therapy and research
  - Post regular unbiased commentaries on articles published on stem cell therapy in scientific journals as well as lay media

E. Clinical Trials and Therapy

- **Accomplishments**
  - Completing follow-up phase of PreSERVE AMI which evaluates autologous bone marrow cell therapy in patients with reduced cardiac function following ST-Elevation Myocardial Infarction (STEMI)
    - Randomized, double-blind, placebo-controlled Phase 2 trial in patients with reduced cardiac function after ST-Elevation Myocardial Infarction (STEMI)
    - Multicenter clinical trial sponsored by Amorcyte (now Neostem)
    - Enrollment and long-term follow-up completed in 12/2015

- Patient recruiting underway for the conduct of the Capricor sponsored ALLSTAR clinical study
  - Intracoronary injection of cardiac stem cells in patients with heart attacks
- Final steps being completed to allow initiation of Patient recruitment for the conduct of the SanBio sponsored ACTIsSIMA clinical study
  - Study of Modified bone marrow stem cells (SB623) in Patients with chronic motor deficit resulting from ischemic stroke
- Initiated umbilical cord stem cell project with the Kansas University Cancer Center
  - Standardized isolation and expansion process as well as characterization methods in place for adult stem cells from human umbilical cord
  - Completed a successful pre-IND meeting with the FDA
    - Reached agreement on information to be generated and presented prior to the initiation of human clinical trials by the KU Cancer Center
  - Project likely to lead to the first adult stem cell IND from the MSCTC
- EXCELLENT (CD34+ cell therapy in heart failure patients)
  - CELLPROTHERA (France) and Biocardia collaboration
  - Possible long-term manufacturing of their stem cells for supply in US if site approved
  - Next contact mid to late summer following Phase II initiation in Europe
- Collaborative agreement being drafted for a company sponsored study for gene therapy to treat aplastic anemia.
  - This is a collaboration with Stowers Institute for Medical Research and a private California company
- NIH Grant being submitted today for study of gene therapy to treat Severe Compromise Immune Deficiency
  - This is a collaboration with the KUCC, a private company in California and Stowers Institute for Medical Research
- Agreement being finalized establishing a long-term contract with a California company to recover and bank adult stem cells

- **Plans**:
  - Continue to identify and collaborate with internal research laboratories who are identifying possible disease specific adult stem cell applications
  - Foster collaborations with Kansas State University and Wichita State University to assure opportunities identified at these institutions
  - Continue to identify and establish external opportunities to utilize the MSCTC core skills in the evaluation of adult stem cell applications to improve human health
  - **Future trials include**:
    - Establish cryopreserved batches of bone marrow, Wharton's Jelly and adipose tissue MSCs as well as induced-pluripotent stem cells for evaluation in multiple diseases

- Expansion and transplantation of hematopoietic adult stem cells

F. Regulatory

The MSCTC established an in-house regulatory effort during mid-1st qtr. 2015. This effort is focused on the regulatory requirements for R&D that occurs during discovery and proof of concept and culminates in the submission of a New Drug Application (NDA) to the FDA requesting marketing approval.

- **Accomplishments**
  - GMP/GTP Facilities registration updated
    - Expanded GMP/GTP facilities registration for various stem cell sources including
      - bone marrow
      - umbilical cord
      - umbilical cord blood
      - adipose tissue
      - induced Pluripotent Stem Cells
      - Gene-editing activities within the facilities
  - Initiated Whartons' Jelly MSC specific IND plan for the treatment of GvHD
    - Successful Pre-IND meeting held with the FDA
- **Plans**:
  - Per agreement with the FDA District Office, meet with them prior to filing the GVHD IND to discuss facility and future efforts
  - Complete GvHD pre-clinical activities and file the IND requesting approval to initiate human clinical trials

G. Basic Research Program

- **Core group of stem cell researchers**
  - Basic scientists/Translational researchers)
    - Omar Aljitawi, M.D.
    - Buddhadeb Dawn, M.D.
    - Michael Detamore, Ph.D.
    - Rajasingh Johnson, Ph.D.
    - Joseph McGuirk, M.D.
    - Hiroshi Nishimune, Ph.D.
    - Doug Myers, M.D.
    - Deryl Troyer, Ph.D.
    - Mark Weiss, Ph.D.
    - Yu-Ting Xuan, Ph.D.
    - Tom Yankee, Ph.D.
    - Hartmut Jaeschke, Ph.D.
    - Ben Woolbright, Ph.D.

- Clinician researchers
  - Kamal Gupta, M.D.
  - Clay Quint, M.D.
  - Sunil Abhyankar, M.D.
  - Sid Ganguly, M.D.
  - Richard Barohn, M.D.
  - Mazen Dimachkie, M.D.
  - Mark Wiley, M.D.
  - Randall Genton, M.D.
  - Ashwini Mehta, M.D.
  - Matt Earnest, M.D.
  - Peter Tadros, M.D.
  - Louis Wetzel, M.D.
- Need to continue to recruit additional scientists and clinicians from other specialties .
  - Postdoctoral fellows and Research Associates

- **Accomplishments**
  - Continue to pursue proof of principle studies for treatment of Amyotrophic Lateral Sclerosis (ALS/Lou Gehrig's Disease) with adult stem cells in collaboration with KUMC Neurology Department researchers
    - Animal study awaiting data relative to trophic factor secretion
  - Liver failure
    - Completed 3 successful animal studies for the treatment of acetaminophen damaged liver
  - Collaboration with Hartmut Jaeschke and Ben WoolbrightCardiovascular
    - Guangming Cheng, CVRI
  - Study in MI Mouse model to being plannedSpinal cord repair
    - Animal study awaiting demonstration of neuron generation for WJMSCs
  - Stroke and Traumatic Brain Injury
    - Initial studies awaiting funding
  - Cartilage Repair
    - WJMSCs shown to differentiate into chondrocytes
    - Follow-up discussion to initiate project
  - Cord Blood Stem Cells
    - Monthly progress meetings with KUCC representatives (Drs. McGuirk, Aljitawi and Abhyankar) and Stowers Institute representatives (Drs. Linheng Li and John Perry) continue to discuss expansion
    - Additional proof of concept studies needed before getting into IND enabling pre-clinical development

- **Plans**:
  - Complete proof of principle studies in ALS
  - Determine options for the development of adult stem cells in the treatment of

acetaminophen damaged liver toward clinical trials

- Explore treatment of other liver related disease with adult stem cells
- Conduct initiate evaluation of umbilical cord MSCs for potential impact on heart repair following a heart attack
- Follow up on Traumatic Brain Injury study when funding is available
- Follow up on cartilage repair to determine next best steps

H. COMMUNICATION AND MARKETING

Communication and Marketing efforts within the MSCTC are focused on building a brand and increasing awareness of the Center. Focus during FY16 has been to secure donations through individual donors, groups and disease specific societies, and establishing awareness of the capabilities of the MSCTC with companies conducting basic research and clinical trials to drive third party manufacturing. Long-term, this function is expected to help drive awareness and growth of the MSCTC nationally and internationally through the identification of communication channels that take advantage of current technology, continuously disseminating information related to the status, achievement of objectives and competitive advantage of the MSCTC, working closely with KU Endowment to connect with donors interested in supporting the MSCTC and continuing to build the MSCTC brand.

- **Accomplishments:**
  - Participated in the initial KUEA crowdfunding effort
    - Reached 25% of our target donation goal
  - Continue to Market the Midwest Stem Cell Therapy Center to potential third parties seeking adult stem cell manufacturing
  - Established communications with the Archdiocese of Kansas City
  - Established communications with the Vatican Science and Faith Department at the Pontifical Council for Culture

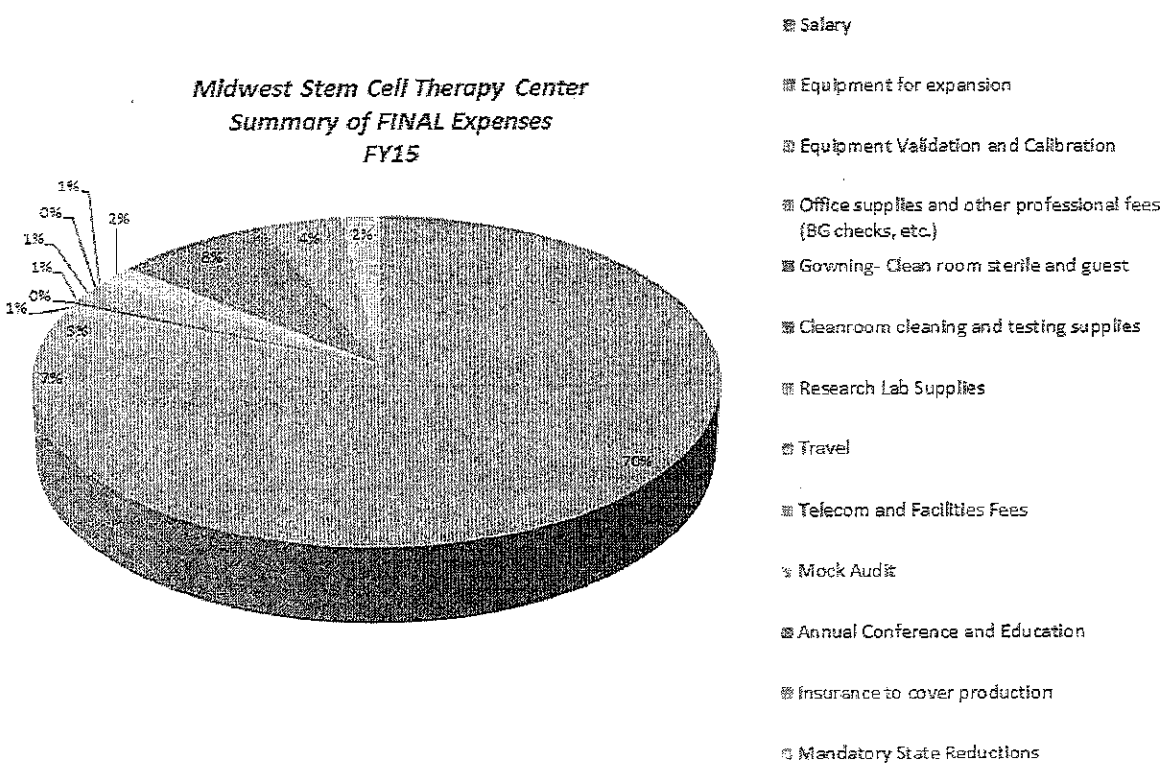
- **Plans:**
  - Continue outreach efforts with potential clients seeking adult stem cell manufacturing locations
  - Continue periodic updates of the MSCTC website
  - Advertise at Kansas universities and other locations in the Midwest regarding stem cell collaborations and GMP manufacturing

I. EXPENSE AND INCOME REPORT

State appropriations

- Received $754,500 in July 2014

Total State FY15 Midwest Stem Cell Therapy Center Allocation	$ 754,500.00	
Expenses		
Salary	$ 529,648.95	70.2%
Equipment for expansion	$ 54,702.12	7.3%
Equipment Costs	$ 22,282.75	3.0%
Office Supplies and other professional fees (BG checks, etc.)	$ 7,037.20	0.9%
Gowning- Clean room sterile and guest	$ 1,413.90	0.2%
Cleaning and testing supplies	$ 3,290.21	0.4%
Research Lab Supplies	$ 10,483.07	1.4%
Travel	$ 708.01	0.1%
Telecom and facilities fees	$ 4,900.03	0.6%
Mock Audit	$ 13,500.00	1.8%
Annual Conference	$ 59,493.92	7.9%
Advisory Board meeting expenses (quarterly meetings)	$ 44.28	0.0%
Insurance to cover production	$ 31,800.00	4.2%
Mandatory State reductions	$ 15,168.00	2.0%
	$ 754,472.44	



FY15 Sources and Spends

FY15 Other Revenue

- GMP Manufacturing Income and Philanthropic contributions

FY15 Other Revenue	
GMP Manufacturing (Lifecells)	6,319.54
KU Cancer Center transfer for project collaboration	77,323.00
Philanthropic transfer for cell expansion equipment	147,795.00
Subtotal of revenue	231,437.54

FY15 Other Expenses		
Capital Equipment	$	80,672.84
Equipment (validation, service agreements, room validation)	$	1,294.30
Schendel	$	568.55
Propharma QA/QC (split cost with STC)	$	1,400.00
Gowing- clean room sterile and guest	$	252.74
Office supplies for GMP suites and other professional fees	$	156.50
Cleaning and Testing supplies	$	2,422.47
Research Lab supplies	$	18,026.95
GMP Facility modification	$	1,778.00
Cell Expansion equipment	$	103,588.83
*Subtotal of expenses**	$	210,161.18

FY15 Percent of Expenses to Income 91%

FY15 Sources and Spends

EVC Advisory Board and Official Hospitality via KUEA

- Received one time allocation of discretionary funds of $15,000 in August 2014 to cover all Advisory Board and Official Hospitality related expenses (e.g. conference) as that language is currently not in the legislative bill for the State appropriation funds

FY15 KUEA-EVC MSCTC Advisory Board and Official Hospitality		
One time allocation from EVC	$	15,000.00

FY15 KUEA-EVC MSCTC Board and Hospitality Expenses		
Annual Conference hospitality	$	890.00
Visitor hospitality expenses	$	165.85
Advisory Board expenses	$	2,526.23
Legislative update meeting	$	3,209.92
Professional and office fees not allowed on state funds	$	162.36
*Subtotal of expenses**	$	6,954.36

FY15 Percent of Expenses to Income 46%

FY15 Sources and Spends

FY15 Other Revenue – KUEA Donations

- ALS "Ice Bucket Challenge" donations

FY15 KUEA ALS Ice Bucket Challenge donations	$ 48,647.90

FY15 KUEA ALS related Expenses	
Credit card fees	$ 1,151.74
Nishimune support	$ 2,531.17
Transfer to Neurology for ALS stem cell research	$ 46,112.08
Subtotal of expenses	$ 49,794.99

FY15 Percent of Expenses to Income	102%

- General gift donations made to the MSCTC

FY15 KUEA MSCTC General Donations	$ 2,480.00

$90 of total contributions were named in honor or Marjorie Prentice

FY15 Sources and Spends

FY15 Summary – Percent Expenses to Income from all sources

FY15 All Income	
State Appropriation	$ 754,500.00
GMP Manufacturing	$ 6,319.54
KU Cancer Center transfer for project collaboration	$ 77,323.00
Philanthropic transfer for cell expansion equipment	$ 147,795.00
EVC Advisory board and official hospitality one time allocation	$ 15,000.00
ALS Ice Bucket Donations	$ 48,647.90
MSCTC General Donations	$ 2,480.00
Total of all FY15 Income	$ 1,052,065.44

FY15 All Expenses	
State Approriation	$ 754,472.44
GMP Manufacturing related income and cell expansion and equip.	$ 210,161.18
Advisory Board and official hospitality	$ 6,954.36
ALS Ice Bucket - Neuro support	$ 48,643.25
KUEA online credit card processing fees	$ 1,151.74
Total of all FY15 expenses	$ 1,021,382.97

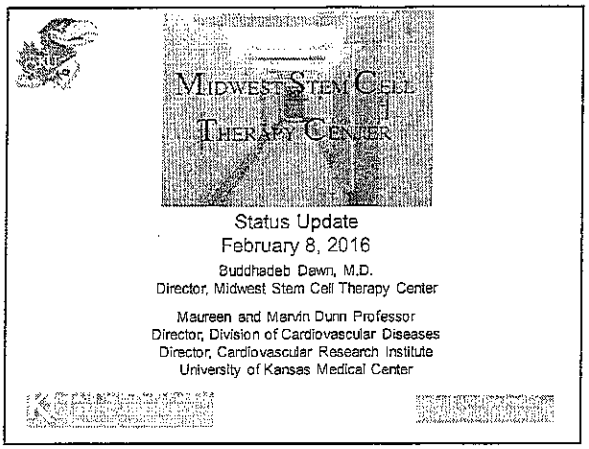
FY15 Percent of Expenses to income	97%

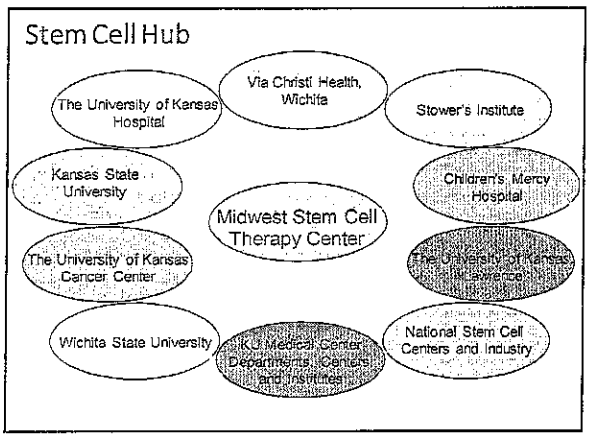
J. VISION FOR THE FUTURE

Through near-term support from the State of Kansas, establishing a solid donor base, third party adult stem cell manufacturing and grants from disease specific societies, NIH, NCI, etc., establish the Midwest Stem Cell Therapy Center as the place to go to obtain adult stem cell therapy. This will be accomplished by:

- Reaching self-sustainability with a multipronged approach: cell manufacturing, marketing, and licensing.
- Advance cutting-edge adult stem cell therapy in the Midwest through increasing number of trials
- Increasing the clinical trial/research workforce and build appropriate infrastructure
- Acquiring state-of-the-art instrumentation for cell processing, outcome assessment, in vivo imaging, stem cell sorting, and appropriate administration systems
- Recruiting excellent scientists and clinicians engaged in basic and translational stem cell research
- Performing cutting-edge bench-to-bedside adult stem cell translational trials in humans by collaborating with the FDA

Kansas can be the leader in providing adult stem cell treatments and information to physicians and patients around the world.

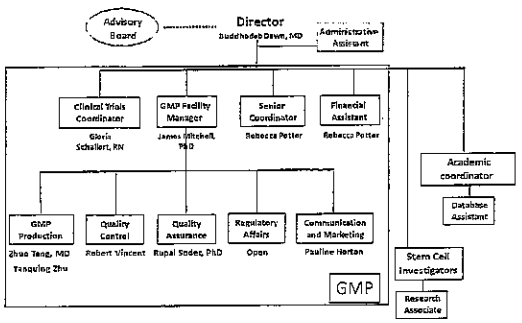




Objectives of the Center - I

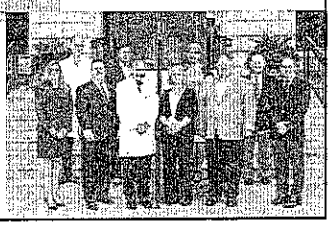
- To *advance* adult, cord blood and related stem cell research and therapies for *patient treatment*
- To serve as a *core facility* to produce clinical grade stem cells
- To initiate *clinical trials* with adult, cord blood, and related stem cells

MSCTC Organizational Chart

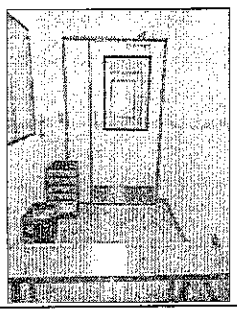


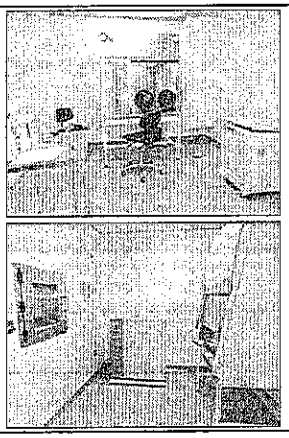
MSCTC Staff

MSCTC Advisory Board



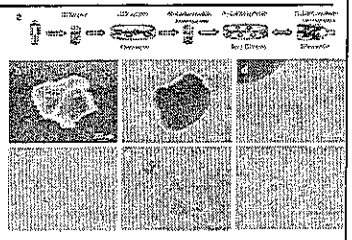
Good Manufacturing Practice Facility

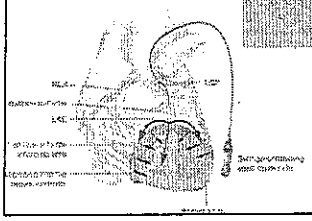




Current Clinical Trials

ALLSTAR: Heart-derived stem cells for patients with heart attack



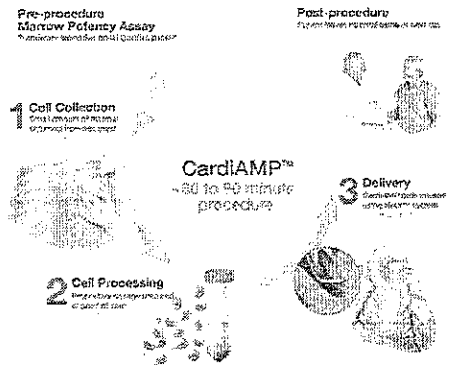


PreSERVE AMI Bone marrow-derived CD34+ cells for patients with heart attack

Future Clinical Trials of Heart Repair

- CardiAMP
  - Selected autologous bone marrow mononuclear cells delivered intramyocardially to repair cardiac tissue in patients with heart failure
  - Initial evaluation of clinical study requirements underway by KU
  - CDA has been signed

CardiAMP



Future Clinical Trials of Heart Repair

- EXCELLENT
  - Multicenter Phase III study of cardiac repair in patients with heart attack and reduced heart function
  - Peripheral blood CD34+ stem cells will be expanded in a proprietary StemXpand automated cell processing system and injected using a helical needle
  - Collaboration with CellProthera
  - Possible long-term stem cell manufacturing for supply in US if site approved
  - Site visit tentatively mid to late summer

Future Clinical Trials for Stroke

ACTIsSIMA

- Modified adult bone marrow stem cells (SB623) for patients with motor deficiency following an ischemic stroke
- US Biotech company sponsoring trial
- Study to start in near future

ACTIsSIMA

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

A Study of Modified Stem Cells in Stable Ischemic Stroke

This study is ongoing, but not accepting participants.

ClinicalTrials.gov Identifier: NCT01287507

Sponsor: SanBio, Inc

Information provided by (Responsible Party): SanBio, Inc.

First received: January 27, 2011
Last updated: November 10, 2015
Last verified: November 2015

History of Changes

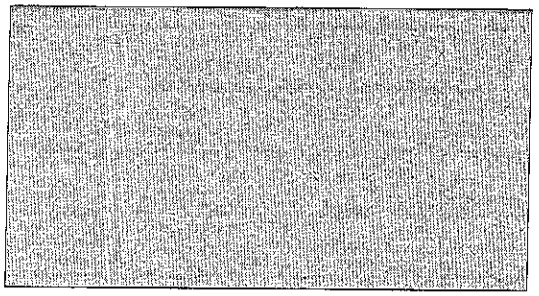
Full Text View | Tabular View | No Study Results Posted | Disclaimer | How to Read a Study Record

Purpose

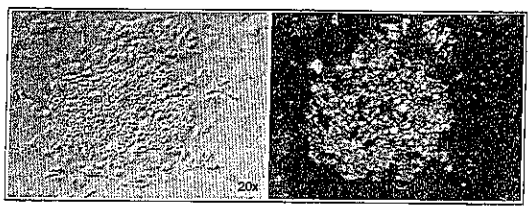
The primary purpose of the clinical study is to determine the safety of a modified stem cell SB623 when administered to chronic, stable hemiparetic stroke patients. A second purpose is to determine whether SB623 might improve stroke symptoms. Chronic, stable ischemic stroke patients must be between 6 and 60 months after their stroke, and with only one prior stroke, both and with no further improvement from physical therapy.

Condition	Intervention	Phase
Chronic Ischemic Stroke	Biological: SB623	Phase 1 Phase 2

Umbilical Cord-derived Mesenchymal Stem Cells (UC-MSCs)



Human iPS Cells



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Areas of Research Focus

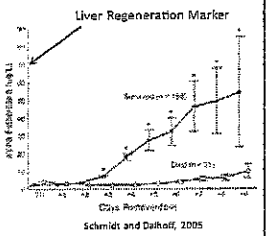
- Cancer and Immunotherapy
- Stroke and Neurodegenerative Disease
- Cardiac and Vascular Disease
- Musculoskeletal Disease and Trauma

Current Pre-Clinical Projects

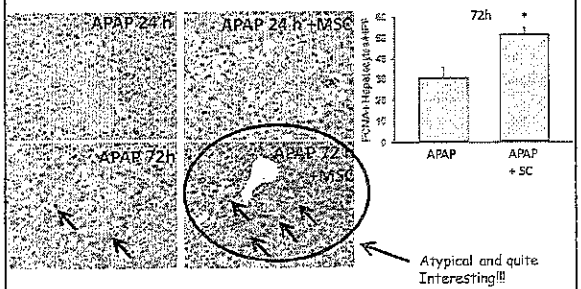
- Graft vs. Host Disease (GvHD)
  - Collaboration with University of Kansas Cancer Center
  - FDA teleconference was held on 2/5 - approved for preclinical work
  - IND to be written and submitted for FDA approval to conduct a Phase I human clinical study

Liver Regeneration Predicts Survival in Patients with Acetaminophen Overdose

- Liver has native potential for regeneration
- However, after an acute liver injury, some patients will progress to an advanced state called Acute Liver Failure
- Mesenchymal stem cells may be able to stimulate regeneration in these patients, providing an entirely novel therapeutic option



Enhanced Liver Regeneration in MSC Post-treated Mice 72h after Acetaminophen Dose



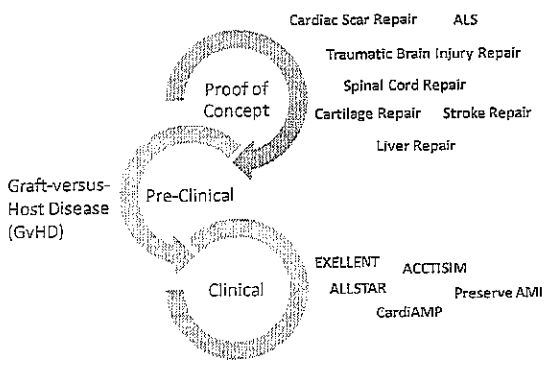
Additional KUMC Collaborations

- Amyotrophic Lateral Sclerosis (Lou Gehrig's disease)
  - KUMC, Dept. of Neurology, Dept. of Anatomy and Cell Biology
  - WJMSCs shown to produce cytokines believed to be important in nerve repair
- MI Scar Repair
  - KUMC, Cardiovascular Research Institute
  - Animal studies to begin 1st Qtr 2016
- Cartilage Repair
  - KUMC, Dept. of Orthopedic Surgery
  - WJMSCs being evaluated to determine their ability to differentiate into chondrocytes, the cells that generate and maintain cartilage matrices

Additional Internal Collaborations

- Spinal Cord Repair
  - KUMC, Dept. of Molecular and Integrative Physiology/Dept. of Pathology and Laboratory Medicine
  - WJMSCs being evaluated for the capacity to differentiate into neurons
- Stroke and Traumatic Brain Injury Repair
  - KUMC, Dept. of Rehabilitation Medicine
  - WJMSCs being evaluated for the capacity to differentiate into neurons

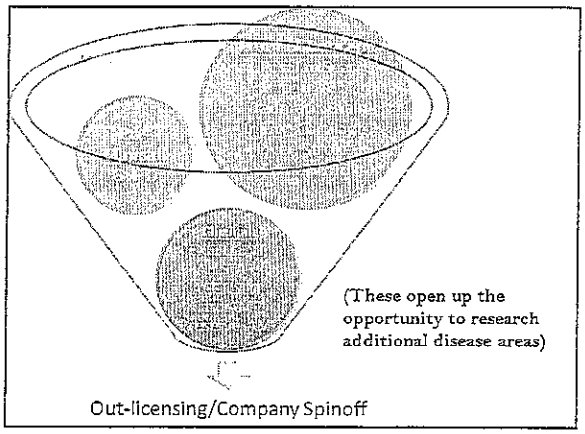
Project Pipeline



FDA Clinical Trial Process

Investigational New Drug Application (IND)
Researcher files an IND with the FDA to begin testing the treatment in people.

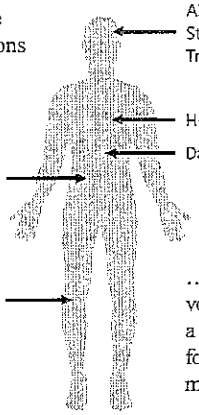
New Drug Application (NDA) Submitted to the FDA and contains all data gathered to date about the drug. An NDA may exceed 100,000 pages.



(These open up the opportunity to research additional disease areas)

Out-licensing/Company Spinoff

Just a few of the diseases/conditions the Center is currently researching…



ALS
Stroke
Traumatic brain injury

Heart failure

Damaged spinal cord

Liver disease

Damaged cartilage

…As well as Graft-versus-Host Disease, a complication following bone marrow transplant.

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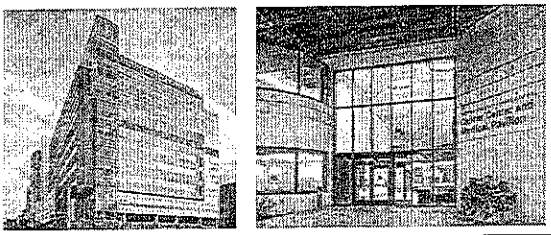
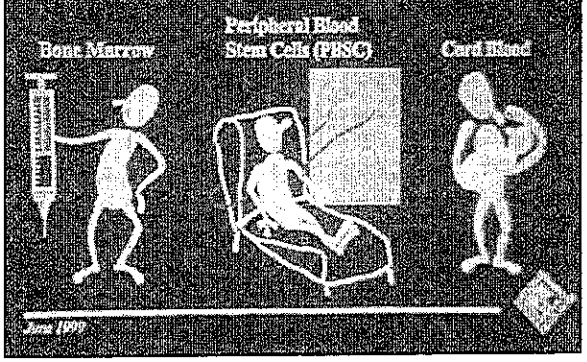
Advances in Stem Cell Transplantation and Cellular Therapeutics

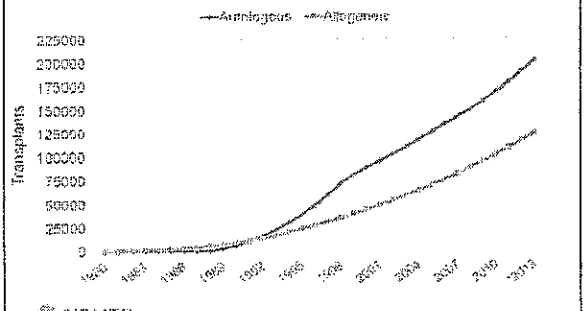
Dr. Joseph McGuirk
Medical Director, Blood and Marrow Transplantation
Division Director, Hematologic Malignancies & Cellular Therapeutics



Sources of Stem Cells



Cumulative Plot of Transplant Recipients in the US by Transplant Type



CIBMTR

*2013 Data are complete

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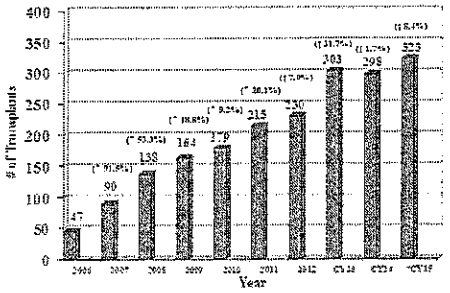
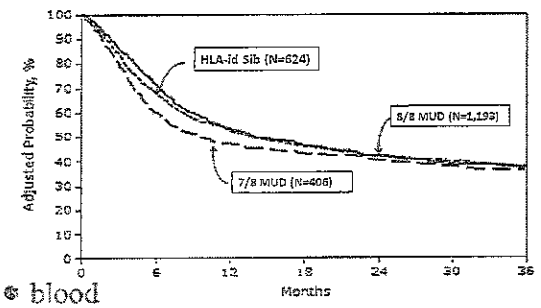
Blood & Marrow Transplant – Annual Volume (CY)



28

Adjusted probability of overall survival in 2223 adult AML patients by donor type



blood

Wael Saber et al. Blood. 2012;119:3908-3916

©2012 by American Society of Hematology

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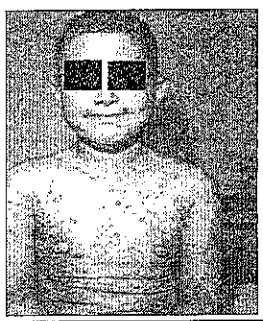
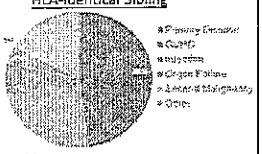
Causes of Mortality related to Allogeneic BMT

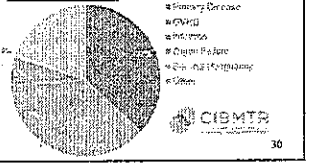
(2011-2012)



HLA-identical Sibling



Unrelated Donor



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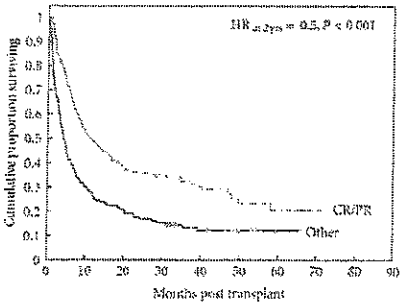
Overall Survival in Steroid-responsive and refractory aGVHD



J Westin et al. *Adv Hematol.* 2011;2011:601953.

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THE UNIVERSITY OF KANSAS CANCER CENTER NCICC

MSCs for GVHD – Summary

- 20 studies used MSCs for GVHD grade 2-4
- MSCs have a positive effect (varies between studies)
- Conditioning varied from myeloablative, nonmyeloablative, RIC, DLI, etc.
  - No apparent difference in response
- MSCs from HLA identical, haploidentical and unrelated, unmatched have been used
  - No apparent differences in response
- MSCs from fresh or frozen/thawed

Source: Mark Wall

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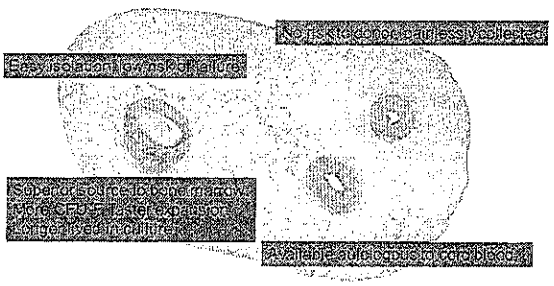
Wharton's Jelly Cells – the MSCs of the Umbilical Cord



Umbilical cord is not biohazardous waste.
It is a mine!

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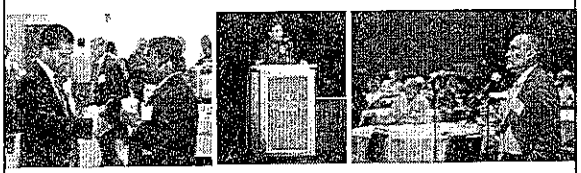
Objectives of the Center - II

- Informing the public on available adult, cord blood, and related stem cell therapeutic options
- Creating and maintaining a database of available stem cell clinical trials and therapies
- Foster a regional network of physicians trained in adult stem cell therapy applications

Dissemination of Information

- Website (www.kumc.edu/msctc)
- Compilation of an extensive resource for adult stem cell information
- Providing answers via emails/meetings
- Conferences

Midwest Conference on Cell Therapy and Regenerative Medicine

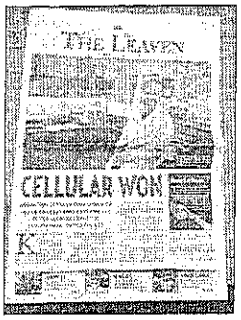


September 16-17, 2016
Sheraton Overland Park, KS

Objectives

- Continue to be a reliable and trustworthy source for practitioners who want up-to-date information on adult stem cell therapy
- Continue to build awareness of Center

Establishing Relationships

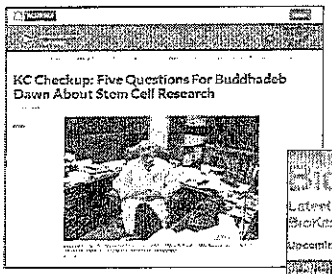


Archdiocese of Kansas City

Vatican

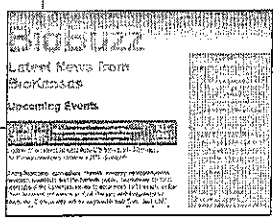
Monsgr. Tomasz Trafny
Head of Science and Faith Department
at the Pontifical Council for Culture

Establishing Relationships



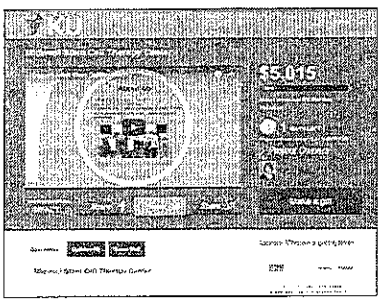
KC check-up

BioKansas

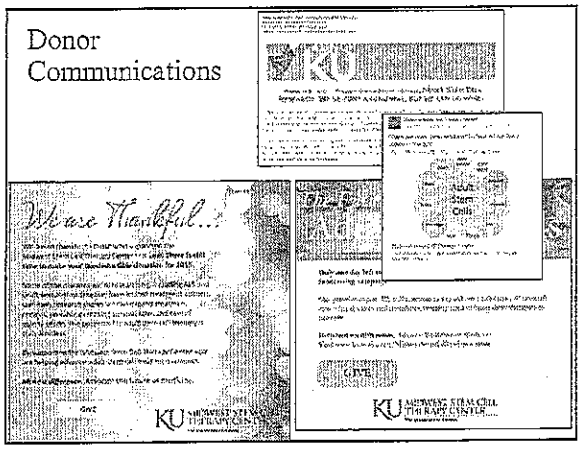


Establishing Relationships

- KU Communications departments
- KU Endowment
  - Pilot for new crowdfunding initiative



Donor Communications



MSCTC Fiscal Overview

The MSCTC is currently funded by:

- State of Kansas annual appropriation
- Donor giving routed through KU Endowment
- EVC discretionary KUEA fund for Advisory Board and other official hospitality expenses
  - "Official hospitality" needs to be added to the State budget bill
- Income received from GMP manufacturing and externally funded projects
- Clinical Trials

Prepared by R. Potter

Major Support from KU Medical Center and the Kansas Legislature

- Funds toward initial GMP construction, personnel salary and benefits
- Space and other key infrastructure support
- Administrative support, RI
- Brand recognition
- Abundance of collaborators
- Continued funding from the State of Kansas

Business Initiatives

Sponsored R&D

- Nueterra
  - Adipose MSC treatment for Osteoarthritis Cartilage Repair
  - Project proposal being drafted by Nueterra for review
- Stemodontics
  - Isolation, recovery of dental pulp MSCs and long-term banking
  - Contract for business over the next 10 years in final stages
- Applied Stemcell
  - Gene Therapy for Aplastic Anemia
  - Contract in development
- Cell Prothera
  - Expanding bone marrow CD34+ cells using proprietary StemXpand Automated system
- KUCC and Stowers
  - Cord Blood Stem Cell Expansion for transplant
  - Cord Blood IRB approved, work to start in 2016

Business Initiatives

Clinical Trials

- Capricor
  - ALLSTAR – MI Scar repair
- Sanbio
  - ACTIsSIMA – Stroke repair

Sale of Stem Cells

- Developed process
- Documents being developed

Grant Initiatives

- Gene Therapy for Aplastic Anemia patients
  - Applied StemCell submitted an SBIR grant
    - Included KUCC, Stowers and MSCTC
    - Opportunity to resubmit following company funded proof of concept
- Gene Therapy for Severe Cellular Immunodeficiency patients
  - Includes KUCC and Stowers
  - Applying for an NIH U01 grant due February 8, 2016

Philanthropic Initiatives

- Crowdfunding
- Working with KU Communications departments to increase awareness
- Midwest Stem Cell Therapy Center Website

FY15 Expense Report

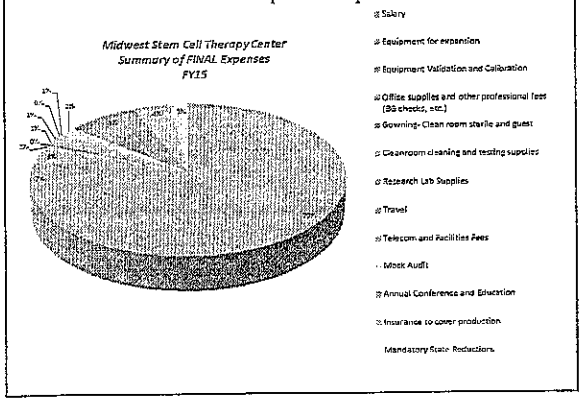
State appropriations

- Received $754,500 in July 2014

Total State FY15 Midwest Stem Cell Therapy Center Allocation	$ 766,500.00	
Expenses		
Salary	$ 519,646.93	70.2%
Equipment for expansion	$ 54,709.12	7.4%
Equipment Costs	$ 22,282.75	3.0%
Office Supplies and other professional fees (BS checks, etc.)	$ 2,037.20	0.3%
Gowning- Clean room sterile and guest	$ 1,413.90	0.2%
Cleaning and testing supplies	$ 3,200.21	0.4%
Research Lab Supplies	$ 10,483.07	1.4%
Travel	$ 708.01	0.1%
Telecom and facilities fees	$ 4,500.03	0.6%
Mock Audit	$ 13,500.00	1.8%
Annual Conference	$ 50,498.92	7.2%
Advisory Board meeting expenses (quarterly meetings)	$ 44.28	0.0%
Insurance to cover production	$ 31,800.00	4.2%
Mandatory State reductions	$ 15,338.00	2.0%
	$ 754,472.46	

We not receive $26 invoice from HP before FY15 cutoff. Total sent back to state: $27.54

FY15 Expense report



FY15 Sources and Spends

FY15 Other Revenue

- GMP Manufacturing Income and Philanthropic contributions

FY15 Other Revenue		
GMP Manufacturing (Tiltworks)		6,318.54
KU Cancer Center transfer	for project collaboration	77,503.00
Philanthropic transfer	for cell expansion equipment	147,795.00
	Subtotal of revenue	231,437.54

FY15 Other Expenses		
Capital Equipment	$	80,677.84
Equipment [validation, service agreements, room validation]	$	1,294.30
Schendel	$	508.55
Prepharme QA/QC built cost with STC)	$	1,400.00
Sewing- clean room sterile and guest	$	252.76
Office supplies for GMP suites and other professional fees	$	156.50
Cleaning and Testing supplies	$	2,422.42
Research Lab supplies	$	18,026.05
GMP Facility modification	$	1,795.00
Cell Expansion equipment	$	103,555.83
*Subtotal of expenses**	$	210,161.13

FY15 Percent of Expenses to Income 91%

FY15 Sources and Spends

EVC Advisory Board and Official Hospitality via KUEA

- Received one time allocation of discretionary funds of $15,000 in August 2014 to cover all Advisory Board and Official Hospitality related expenses (e.g. conference) as that language is currently not in the legislative bill for the State appropriation funds

FY15 KUEA-EVC MSCTC Advisory Board and Official Hospitality		
One time allocation from EVC	$	15,000.00

FY15 KUEA-EVC MSCTC Board and Hospitality Expenses		
Annual Conference hospitality	$	590.00
Visitor hospitality expenses	$	165.85
Advisory Board expenses	$	2,526.28
Legislative update meeting	$	3,203.92
Professional and office fees not allowed on state funds	$	162.36
*Subtotal of expenses**	$	6,994.30

FY15 Percent of Expenses to Income 46%

FY15 Sources and Spends

FY15 Other Revenue – KUEA Donations

- ALS "Ice Bucket Challenge" donations

FY15 KUEA ALS Ice Bucket Challenge donations		
	$	48,607.90

FY15 KUEA ALS related Expenses		
Credit card fees	$	1,191.74
Nishimune support	$	2,531.17
Transfer to Neurology for ALS stem cell research	$	46,112.08
Subtotal of expenses	$	49,794.99

FY15 Percent of Expenses to Income 102%

- General gift donations made to the MSCTC

FY15 KUEA MSCTC General Donations		
	$	2,430.00

$30 of total contributions were named in honor or Marjorie Prentice

The funds were spent in FY16, most general donations occurred late FY

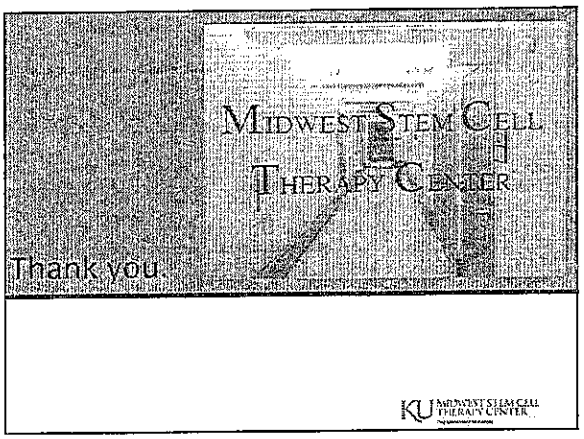
FY15 Sources and Spends

FY15 Summary – Percent Expenses to Income from all sources

FY15 All Income	
State Appropriation	$ 754,500.00
GMP Manufacturing	$ 6,319.54
KU Cancer Center transfer for equipment for project collaboration	$ 77,823.00
Philanthropic transfer from Hale Foundation for cell expansion equip.	$ 147,795.60
MC Advisory board and official hospitality one time allocation	$ 15,000.00
ALS Ice Bucket Donations	$ 48,647.80
MSCTC General Donations	$ 2,430.00
Total of all FY15 income	$ 1,052,015.44

FY15 All Expenses	
State Appropriation	$ 754,472.44
GMP Manufacturing related income and cell expansion and equip.	$ 210,161.38
Advisory Board and official hospitality	$ 6,954.88
ALS Ice Bucket - Neuro support	$ 48,643.25
KUEA online credit card processing fees	$ 3,151.74
Total of all FY15 expenses	$ 1,023,383.97

FY15 Percent of Expenses to Income 97%



Midwest Stem Cell Therapy Center

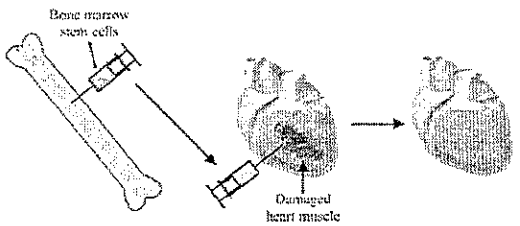
David A. Prentice, Ph.D.
Charlotte Lozier Institute
Washington, D.C.

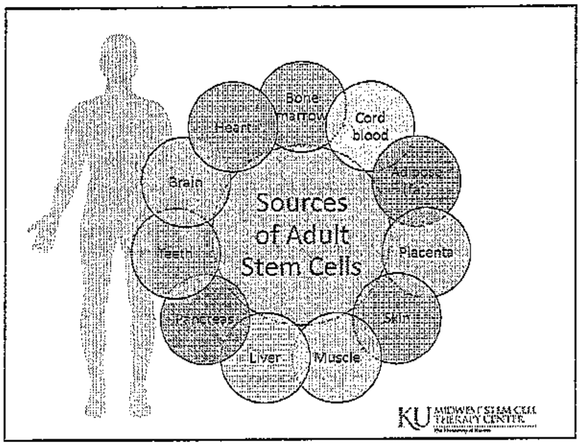
CHARLOTTE LOZIER INSTITUTE

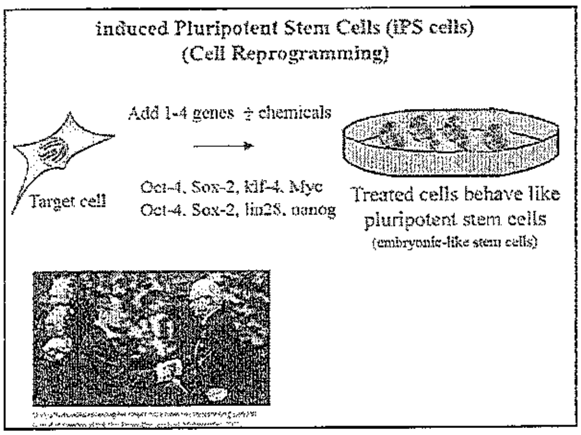
Midwest Stem Cell Therapy Center
Kansas' Unique Stem Cell Center

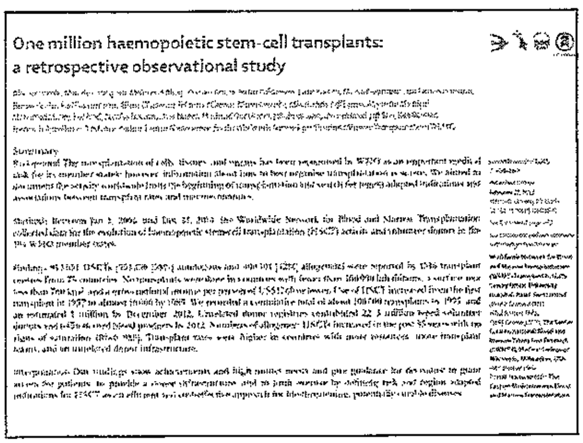
- Focus on therapy
- Exclusively non-embryonic
  No embryonic stem cells. No fetal tissue.
- Focus on dissemination of knowledge
- Comprehensive

Regenerative Medicine with Stem Cells

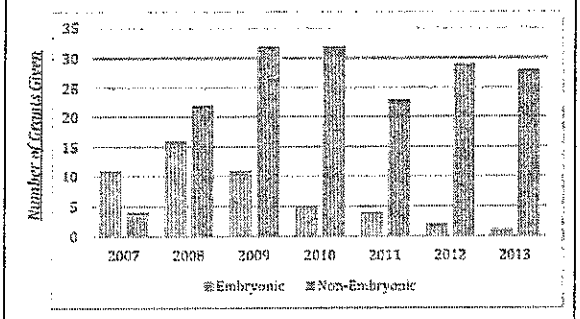



Sources
of Adult
Stem Cells
Bone marrow
Cord blood
Adipose
Placenta
Skin
Muscle
Liver
Pancreas
Teeth
Brain
Heart
KU MIDWEST STEM CELL THERAPY CENTER


induced Pluripotent Stem Cells (iPS cells)
(Cell Reprogramming)
Add 1-4 genes ± chemicals
Target cell
Oct-4, Sox-2, klf-4, Myc
Oct-4, Sox-2, lin28, nanog
Treated cells behave like
pluripotent stem cells
(embryonic-like stem cells)


One million haemopoietic stem-cell transplants:
a retrospective observational study

Maryland Funding More Adult Stem Cell Research



From: Gene Tarne and Andrew Mullins, "Maryland Joins the Trend for Ethical Stem Cell Research", Charlotte Lozier Institute, October 2013

Seven federal agencies invested—that is, conducted or funded—approximately $2.89 billion in regenerative medicine research in fiscal years 2012 through 2014. Most (88 percent) was invested by the National Institutes of Health. Agencies funded research related to their missions, including basic research to enhance general scientific knowledge, clinical research to move scientific discoveries into practical applications, and research to develop regulatory science.

Federal Funding for Regenerative Medicine Research, Fiscal Years 2012 through 2014
Total (dollars in millions)

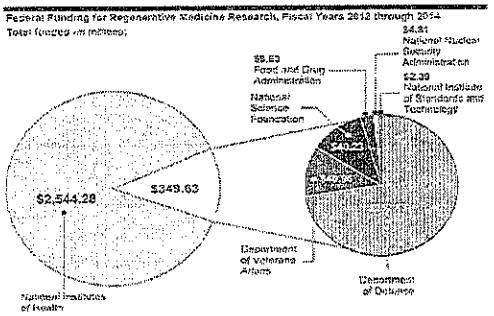


Table 1: Federal Agencies That Conducted or Funded Regenerative Medicine Research, Fiscal Years 2012 through 2014

Federal agency	Agency mission	Regenerative medicine research conducted includes
Department of Defense	Provide the military forces needed to deter war and to protect the security of the country	Research and applications for active-duty personnel including limb repair, traumatic brain injury, and battlefield injuries
Department of Veterans Affairs	Provide veterans and eligible beneficiaries with the health and services	Research and applications for the veteran population including limb repair, traumatic brain injury, and care for returning veterans, as well as for chronic conditions and other conditions for an aging veteran population
Food and Drug Administration within the Department of Health and Human Services	Protect the public health by ensuring the safety, efficacy, and security of human drugs, biological products, medical devices, food supply, cosmetics, and products that emit radiation	Safety and effectiveness research related to regulation of regenerative medicine products and standards development
National Institute of Standards and Technology within the Department of Commerce	Promote innovation and industrial competitiveness by advancing measurement science, standards, and technology	Measurements science and development of consensus documentary standards and standard reference materials to facilitate commercialization of regenerative medicine products[a]
National Institutes of Health within the Department of Health and Human Services	Seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability	Biomedical applications and basic, clinical, and translational research, including stem cells and tissue engineering
National Nuclear Security Administration within the Department of Energy	Enhance national security through the military application of nuclear science, responsible for issues of nuclear defense nonproliferation, and naval reactors	Research and development, including basic research and experiments designed to determine the ability of new scientific tools, technical concepts, or devices
National Science Foundation	Promote and advance fundamental scientific progress	Basic research with a focus on expanding current scientific knowledge

Other US State and Collaborative Initiatives

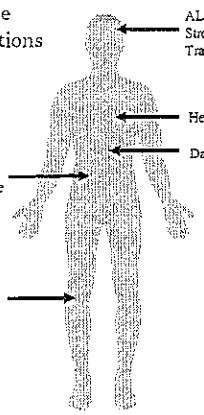
	2004	$3B	$172.7M	$1.9B	>>100 grants, 10 clinical studies (FY'15)
	2005	Annual Appropriation	$9.8M	$78.6M [2018]	≈ 100 funded research grants
	2006	Annual Appropriation	$14.4M	$120M (2005-2015) $9.4M in FY'16	849 research grants
	2006	$250M	$27.8M	$250M	All for buildings
	2007	Annual Appropriation	$37.5M	$300M	≈ 50 research grants
	2013	$50M	$4.3M	≈ $8.7M	None reported
	2016	$28.1M	TBD	$0M	None
Kansas	2013	10.7M	$0.9M	$2.7M	15 research collaborations

MSCTC Areas of Focus

Adult Stem Cell Therapy

- Stroke and Neurodegenerative Diseases
- Cancer and Immunotherapy
- Cardiovascular Disease
- Musculoskeletal, Trauma, Skin, Burns, Wounds, Autoimmune

Just a few of the diseases/conditions the Center is currently researching…



…As well as Graft-versus-Host Disease, a complication following bone marrow transplant.

KU Midwest Stem Cell Therapy Center

Pharmaceuticals 2015, *8*, 196-220

Wharton's Jelly-Derived Mesenchymal Stromal Cells as a Promising Cellular Therapeutic Strategy for the Management of Graft-versus-Host Disease

Joseph P. McGuirk [1,*], J. Robert Smith [2], Clint L. Divine [1], Micheal Zuniga [2] and Mark L. Weiss [2,*]

Received: 10 December 2014 / Accepted: 8 April 2015 / Published: 16 April 2015

Abstract: Allogeneic hematopoietic cell transplantation (allo-HCT), a treatment option in hematologic malignancies and bone marrow failure syndromes, is frequently complicated by Graft-versus-host disease (GVHD). The primary treatment for GVHD involves immune suppression by glucocorticoids. However, patients are often refractory to the steroid therapy, and this results in a poor prognosis. Therefore alternative therapies are needed to treat GVHD. Here, we review data supporting the clinical investigation of a novel cellular therapy using Wharton's jelly (WJ)-derived mesenchymal stromal cells (MSCs) as a potentially safe and effective therapeutic strategy in the management of GVHD. Adult-derived sources of

Adult Bone Marrow Cell Therapy for Ischemic Heart Disease

Evidence and Insights From Randomized Controlled Trials

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Rationale: Notwithstanding the uncertainties about the outcomes of bone marrow cell (BMC) therapy for heart repair, further insights are critically needed to improve this promising approach.
Objective: To delineate the true effect of BMC therapy for cardiac repair and gain insights for future trials through systematic review and meta-analysis of data from eligible randomized controlled trials.

Circulation Research August 28, 2015

RESEARCH ARTICLE

Generation of Functional Cardiomyocytes from Efficiently Generated Human iPSCs and a Novel Method of Measuring Contractility

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Abstract

Human induced pluripotent stem cells (iPSCs) derived cardiomyocytes (iCMCs) would provide an unlimited cell source for regenerative medicine and drug discoveries. The objective of our study is to generate functional cardiomyocytes from human iPSCs and to develop a novel method of measuring contractility of CMCs. In a series of experiments, adult human skin fibroblasts (HSF) and human umbilical vein endothelial cells (HUVECs) were treated with a combination of pluripotent gene DNA and mRNA under specific conditions. The iPSC

Concise Review: Review and Perspective of Cell Dosage and Routes of Administration From Preclinical and Clinical Studies of Stem Cell Therapy for Heart Disease

Samuel Golpanian,[a,b] Ivonne H. Scholman,[a,c] Ray F. Ebert,[a] Alan W. Heldman,[a,c] Darry L. DiFede,[a] Phillip C. Yang,[a] Joseph C. Wu,[a] Roberto Bolli,[a] Emerson C. Perin,[a] Lea Moye,[a] Robert D. Simari,[a] Ariel Wolf,[a] Joshua M. Hare,[a,c] for the Cardiovascular Cell Therapy Research Network

Key Words. Stem cell • Cardiovascular disease • Cell dosage • Route of administration

Abstract

An important stage in the development of any new therapeutic agent is establishment of the optimal dosage and route of administration. This can be particularly challenging when the treatment is a biologic agent that might exert its therapeutic effects via complex or poorly understood mechanisms. Multiple preclinical and clinical studies have shown paradoxical results, with inconsistent findings regarding the relationship between the cell dose and clinical benefit. Such phenomena can, at least in part, be attributed to variations in cell dosing or concentration and the route of administration (ROA). Although clinical trials of cell-based therapy for cardiovascular disease began more than a decade ago, specification of the optimal dosage and ROA has not been established. The present review summarizes what has been learned regarding the optimal cell dosage and ROA from preclinical and clinical studies of stem cell therapy for heart disease and offers a perspective on future directions. STEM Cells Translational Medicine 2016;5:186–195

Association of Nonmyeloablative Hematopoietic Stem Cell Transplantation With Neurological Disability in Patients With Relapsing-Remitting Multiple Sclerosis

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IMPORTANCE No current therapy for relapsing-remitting multiple sclerosis (MS) reverses significant neurological disability.

OBJECTIVE To determine the association of nonmyeloablative hematopoietic stem cell transplantation with neurological disability and other clinical outcomes in patients with MS.

JAMA. 2019;321(20):1968-1979. doi:10.1001/jama.2019.4799

Umbilical Cord Mesenchymal Stromal Cell With Autologous Bone Marrow Cell Transplantation in Established Type 1 Diabetes: A Pilot Randomized Controlled Open-Label Clinical Study to Assess Safety and Impact on Insulin Secretion

Diabetes Care 34(11):2348–2354, 2011 DOI: 10.2337/dc11-0116

Jingmin Qu,[1] Zhuqing Wu,[2] Yuanyuan Tong,[1,3] Lianming Chen,[1] Lu Chen,[3] Shanshan Huang,[1] Wenbin Wu,[1] Fenglin Liu,[1] Zhongyang Wu,[2] Alberto Pugnale,[4,5] Antonella Pellegrini,[2,4,5] Camillo Ricordi,[2,4,5,6] and Xiaobing Fan[1,3]

OBJECTIVE

To determine the safety and effects on insulin secretion of umbilical cord (UC) mesenchymal stromal cells (MSCs) plus autologous bone marrow mononuclear cell (aBM-MNC) stem cell transplantation (SCT) without immunotherapy in established type 1 diabetes (T1D).

Intraportal Infusion of Bone Marrow Mononuclear or CD133+ Cells in Patients With Decompensated Cirrhosis: A Double-Blind Randomized Controlled Trial

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Key Words. Cirrhosis • Hematopoietic stem cell • Regenerative medicine • Cell-based therapy

Abstract

The present study assessed the effects of intraportal infusions of autologous bone marrow-derived mononuclear cells (MNCs) and/or CD133+ cells on liver function in patients with decompensated cirrhosis. We randomly assigned 27 eligible patients to a placebo, MNCs, and/or CD133+ cells. Cell infusions were performed at baseline and month 3. We considered the absolute changes in the Model for End-Stage Liver Disease (MELD) scores at months 3 and 6 after infusion as the primary outcome. The participants and those who assessed the outcomes were unaware of the treatment intervention assignments. After 6 months, 9 patients were excluded because of liver transplantation (n = 3), hepatocellular carcinoma (n = 1), loss to follow-up (n = 3), and death (n = 2). The final analysis included 4 patients from the CD133+ group, 8 from the MNC group, and 6 from the placebo group. No improvement was seen in the MELD score at month 6 using either CD133+ cells or MNC infusions compared ... toward a higher mean absolute

Stem Cells Translational Medicine 2016;5:87–94

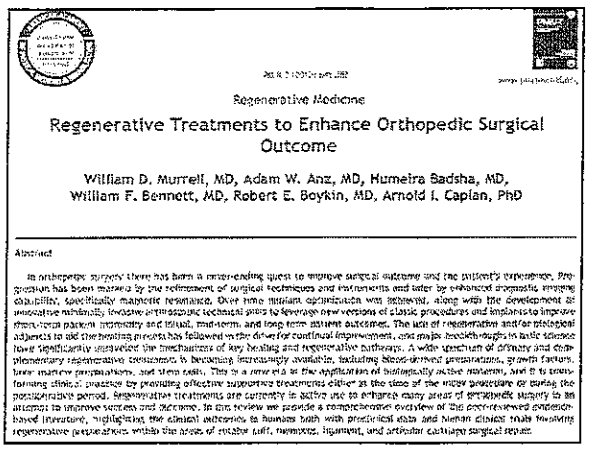
Engineering pulmonary vasculature in decellularized rat and human lungs

[illegible]

Bioengineered lungs produced from patient-derived cells may one day provide an alternative to donor lungs for transplantation therapy. Here we report the regeneration of functional pulmonary vasculature by repopulating the vascular compartment of decellularized rat and human lung scaffolds with human cells, including endothelial and perivascular cells derived from induced pluripotent stem cells. We describe improved methods for delivering cells into the lung scaffold and for maturing ...

Small airway-on-a-chip enables analysis of human lung inflammation and drug responses *in vitro*

[illegible]



Regenerative Medicine

Regenerative Treatments to Enhance Orthopedic Surgical Outcome

William D. Murrell, MD, Adam W. Anz, MD, Humeira Badsha, MD, William F. Bennett, MD, Robert E. Boykin, MD, Arnold I. Caplan, PhD

Abstract

In orthopedic surgery there has been a never-ending quest to improve surgical outcome and the patient's experience. Progression has been marked by the refinement of surgical techniques and instruments and later by enhanced diagnostic imaging capability, specifically magnetic resonance. Over time implant optimization was achieved, along with the development of innovative minimally invasive arthroscopic technical skills to leverage new versions of classic procedures and implants to improve short-term patient morbidity and initial, mid-term, and long-term patient outcomes. The use of regenerative and/or biological adjuncts to aid the healing process has followed in the drive for continual improvement, and major breakthroughs in basic science have significantly unraveled the mechanisms of key healing and regenerative pathways. A wide spectrum of primary and multipotentiary regenerative constructs is becoming increasingly available, including blood-derived preparations, growth factors, bone marrow preparations, and stem cells. This is a new era in the application of biologically active materials, and it is transforming clinical practice by providing effective supportive treatments either at the time of the index procedure or during the postoperative period. Regenerative treatments are currently in active use to enhance many areas of orthopedic surgery in an attempt to improve success and outcome. In this review we provide a comprehensive overview of the peer-reviewed evidence-based literature, highlighting the clinical outcomes in human both with preclinical data and human clinical trials involving regenerative perspectives within the areas of rotator cuff, meniscus, ligament, and articular cartilage surgical repair.

Bioengineered vocal fold mucosa for voice restoration

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Patients with voice impairment caused by advanced vocal fold (VF) fibrosis or tissue loss have few treatment options. A transplantable, bioengineered VF mucosa would address the individual and societal costs of voice-related communication loss. Such a tissue must be biomechanically capable of aerodynamic-to-acoustic energy transfer and high-frequency vibration and physiologically capable of maintaining a barrier against the airway lumen. We isolated primary human VF fibroblasts and epithelial cells and cocultured them under organotypic conditions. The resulting engineered mucosae showed morphologic features of native tissue, proteome-level evidence of mucosal morphogenesis and emerging extracellular matrix complexity, and rudimentary barrier function in vitro. When grafted into canine larynges ex vivo, the mucosae generated vibratory behavior and acoustic output that were indistinguishable from those of native VF tissue. When grafted into humanized mice in vivo, the mucosae survived and were well tolerated by the human adaptive immune system. This tissue engineering approach has the potential to restore voice function in patients with otherwise untreatable VF mucosal disease.

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Human CD34$^+$ CD133$^+$ Hematopoietic Stem Cells Cultured with Growth Factors Including Angptl5 Efficiently Engraft Adult NOD-SCID Il2rγ$^{-/-}$ (NSG) Mice

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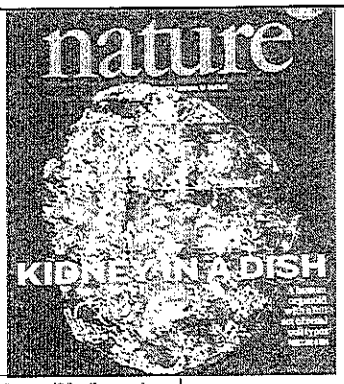
Abstract

Increasing demand for human hematopoietic stem cells (HSCs) in clinical and research applications necessitates expansion of HSCs in vitro. Before these cells can be used they must be carefully evaluated to assess their stem cell activity. Here, we expanded cord blood CD34$^+$ CD133$^+$ cells in a defined medium containing angiopoietin-like 5 and insulin-like growth factor binding protein 2 and assessed the cells for stem cell activity in NOD-SCID Il2rγ$^{-/-}$ (NSG) mice by multi-lineage engraftment, long term reconstitution, limiting dilution, and serial reconstitution. The phenotype of engrafted cells was characterized by flow cytometry during the course of expansion and following engraftment in mice. We show that the SCID repopulating activity resides in the CD34$^+$ CD133$^+$ fraction of expanded cells and that CD34$^+$ CD143$^+$ cell number correlates with SCID repopulating activity before and after culture. The expanded cells mediate long-term hematopoiesis and serial reconstitution in NSG mice. Furthermore, they efficiently reconstitute not only neonate but also adult NSG recipients, generating human blood cell populations similar to those reported in mice reconstituted with uncultured human HSCs. These findings support an expansion of long-term HSCs in our culture and show that expression of CD34 and CD133 serves as a marker for HSC activity in human cord blood cell cultures. The ability to expand human HSCs in vitro should facilitate clinical use of HSCs and large-scale construction of humanized mice from the same donor for research applications.

Citation: Drake AC, Khoury M, Leskov I, Iliopoulos BP, Fragoso M, et al. (2011) Human CD34+ CD133+ Hematopoietic Stem Cells Cultured with Growth Factors Including Angptl5 Efficiently Engraft Adult NOD-SCID Il2rγ-/- (NSG) Mice. PLoS ONE 6(12): e28966. doi:10.1371/journal.pone.0028966



Kidney organoids from human iPS cells contain multiple lineages and model human nephrogenesis

Adoptive cell transfer as personalized immunotherapy for human cancer

Steven A. Rosenberg* and Nicholas P. Restifo*

Adoptive cell therapy (ACT) is a highly personalized cancer therapy that involves administration to the cancer-bearing host of immune cells with direct anticancer activity. ACT using naturally occurring tumor-reactive lymphocytes has mediated durable, complete regressions in patients with melanoma, probably by targeting somatic mutations exclusive to each cancer. These results have expanded the reach of ACT to the treatment of common epithelial cancers. In addition, the ability to genetically engineer lymphocytes to express conventional T cell receptors or chimeric antigen receptors has further extended the successful application of ACT for cancer treatment.

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CAR-T cells
and
Genetically-modified
stem cell applications

CANCER IMMUNOTHERAPY

Baby's leukemia recedes after novel cell therapy

Genetically engineered immune cells eliminate cancer in two children

Adult Stem Cells Save Lives, Improve Health

Midwest Stem Cell Therapy Center

- Unique, comprehensive center
- Focus- patients, education, research, training
- Source of clinical-grade stem cells.
- Global resource for patients and physicians

Kansas a leader in adult stem cell therapies and information for physicians and patients around the world