Midwest Stem Cell Therapy Center

Annual Report

Legislative Update

Senate Public Health and Welfare Committee
Senate Ways and Means Committee

March 7, 2017

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

I. OVERVIEW

Over the past decade, adult stem cell transplantation has emerged as an effective therapeutic option for organ repair. Emerging evidence from numerous scientific reports, both from animal models and human studies, supports the notion that adult stem cells are able to heal damaged tissues and restore function. These adult stem cells from bone marrow, umbilical cord blood, and other sources have the potential to cure diseases for which no effective treatment is available at this time. Indeed, growing scientific evidence supports 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 broad and multi-faceted approach has been developed as outlined below.

III. COMPONENTS AND PROGRESS REPORT

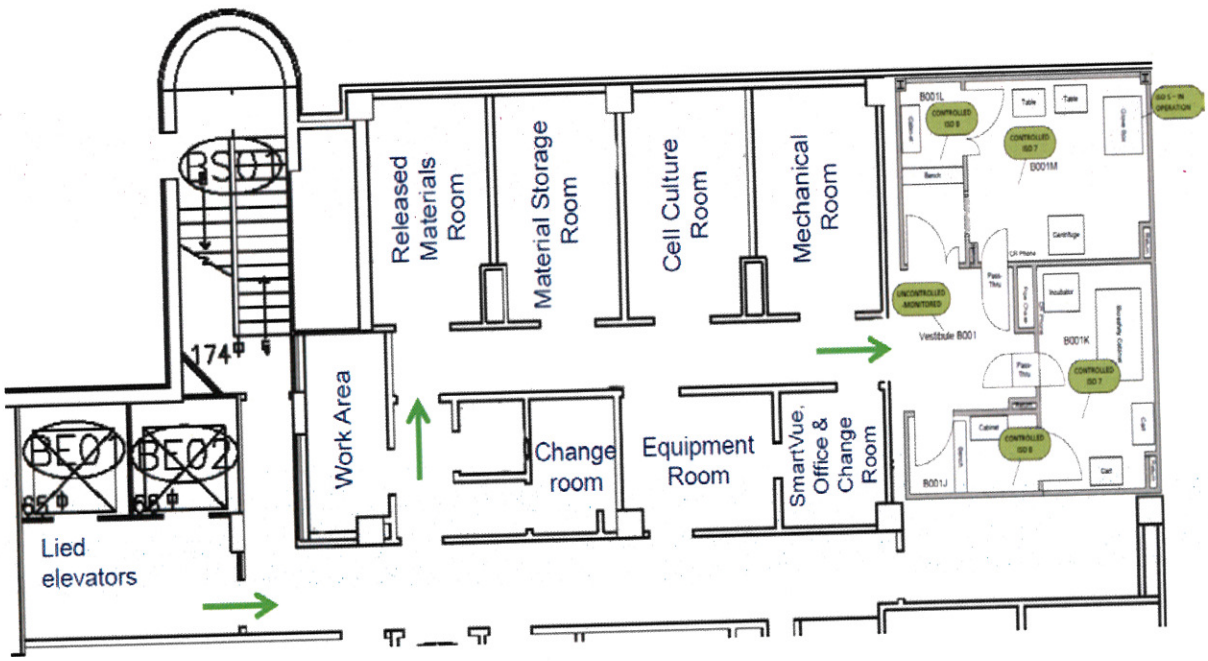
A. ADVISORY BOARD

- 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 Quarterly and, as necessary, to assure continued MSCTC progress
  - The next meeting is scheduled on March 9, 2017.

B. SCIENTIFIC AND ADMINISTRATIVE PERSONNEL

1. Center Director: Recruited
2. GMP Manager: Open
3. GMP consultant: Recruited
4. Financial assistant (part-time): Recruited
5. Research Associate, Production: Recruited
6. Quality Control Supervisor (part-time): Recruited
7. Quality Assurance Supervisor: Recruited
8. Research Scientist (25% effort): Recruited

C. FACILITY FOR CLINICAL GRADE CELL PROCESSING/MANUFACTURING



The MSCTC currently occupies approximately 8200 ft^2 of space, including office (1260 sqft), laboratories (5100 sqft) and GMP manufacturing (1000 sqft) 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 an FDA registered facility and 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 and the supporting infrastructure 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

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
- Train students and postdoctoral fellows in stem cell research and related techniques

- Seminars and Local School Outreach, 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 introduction to adult stem cells and their applications

- **Accomplishments:**
  - Four successful conferences on adult stem cell therapy
    The 4th Annual Midwest Conference on Cell Therapy and Regenerative Medicine was held on September 16-17, 2016
    - 35 speakers and panelists and approximately 140 attendees
    - Monsignor Tomasz Trafny, Head of Science and Faith department in the Pontifical Council for Culture at The Vatican, gave a Keynote Address
  - 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
  - A total of five students have thus far gained first-hand, meaningful scientific experience in adult stem cell research and therapy. They include 3 Medical Students (KU School of Medicine), one undergraduate student from the Ohio State University, and one high school student from New York, NY.
  - 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 on a global basis
    - Defined searches in the most sought after areas of stem cell therapy available
- **Plans:**
  - The 5thMidwest Conference on Cell Therapy and Regenerative Medicine (Sep 15-16, 2017) will be held at the Sheraton Overland Park hotel in Kansas
  - Continued training of students and fellows on various aspects of adult stem cell therapy and research. One KU School of Medicine student will train in stem cell research in MSCTC this summer. One student is expected to return from New York for additional experience.
  - Post regular unbiased commentaries on articles published on stem cell therapy in scientific journals as well as lay media

- Update the MSCTC Facebook webpage with trending scientific information regarding adult stem cell therapy

E. Clinical Trials and Therapy

- **Accomplishments**
  - Completed follow-up phase of PreSERVE AMI trial that tested autologous bone marrow CD34+ 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) (heart attack)
    - Multicenter clinical trial sponsored by Amorcyte (Neostem)
    - Enrollment and long-term follow-up completed. Study closed.
  - Enrollment was open for the ALLSTAR clinical study (sponsored by Capricor, Inc.)
    - Intracoronary injection of cardiac stem cells in patients with heart attacks
  - Patient recruitment underway for the conduct of ACTIsSIMA clinical trial (sponsored by San Bio)
    - Study of modified adult 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
    - Developed and standardized isolation and expansion process as well as characterization methods 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
    - IND to be submitted soon. This will be the first adult stem cell IND from the MSCTC and KUMC
  - Collaborative agreement and budget being negotiated 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
  - A 20-year agreement has been executed with a California company to recover and bank adult stem cells
    - Revenue starting to be realized
  - Agreement with a second company to recover and bank adult stem cells is being evaluated

- **Plans:**
  - Engage the KUMC Organizational Improvement Office (OIO) in **strategic planning** for the center. While the planning effort is comprehensive and will relate to all aspects of the center's operation, special focus will be on supporting our clinical trials and therapeutic efforts. The OIO team has developed a planning process based on best practices from a variety of Baldrige Award-winning organizations. The Baldrige Award program is a federal program through the National Institute of Standards and Technology in the Department of Commerce.
  - Continue to identify and collaborate with internal research laboratories who are identifying possible disease specific adult stem cell applications
  - Foster collaborations with external Midwest Universities, Centers and Institutions to bring opportunities identified at these institutions to fruition
  - 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 initiatives will 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 continues to maintain translational and regulatory efforts focused on the requirements for R&D that occur during discovery, proof of concept and pre-clinical evaluation and culminates in the submission of a New Drug Application (NDA) to the FDA requesting marketing approval.

- **Accomplishments**
  - GMP/GTP Facilities registration for the following:
    - 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
  - Developing Wharton's Jelly MSC-specific IND for the treatment of GvHD
    - Completed all preclinical studies required for the IND application. The IND application itself is being finalized.
- **Plans:**
  - File the IND requesting approval to initiate human clinical trials for GVHD

G. Basic Research Program

- **Core group of stem cell researchers**
  - Basic scientists/Translational researchers
    - Buddhadeb Dawn, M.D.
    - Neil Dunavin, M.D.
    - Hartmut Jaeschke, 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.
    - Ben Woolbright, Ph.D.
    - Yu-Ting Xuan, Ph.D.
    - Tom Yankee, 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
- **<u>Accomplishments</u>**
  - 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 (Drs. Nishimune, Barohn)
    - Studies in progress with regard to trophic factor production influenced by MSC
  - Liver failure
    - Collaboration with Drs. Hartmut Jaeschke and Ben Woolbright
    - Completed 3 successful animal studies for the treatment of acetaminophen damaged liver
    - Next steps being defined
  - Cardiovascular
    - Collaboration with investigators within KU Cardiovascular Research Institute
    - Studies in MI Mouse models

- Repair of spinal cord
  - MSCTC demonstrated the generation of two types of neurons from Wharton's Jelly MSCs
  - Next steps being planned
- Stroke and Traumatic Brain Injury
  - MSCTC demonstrated the generation of two types of neurons from WJMSCs
  - Initial studies awaiting funding
- Cartilage Repair
  - MSCTC studies have proven the potential of WJMSCs to differentiate into chondrocytes
  - Nest steps, including funding, being discussed
- Cord Blood Stem Cells
  - Additional proof of concept studies needed before getting into IND enabling pre-clinical development

- **Plans**:
  - Complete proof of principle studies in mouse models of ALS
  - Determine options for the development of adult stem cells in the treatment of acetaminophen-induced liver injury leading to human clinical trials
  - Examine the potential of adult stem cell therapy for other liver diseases
  - Evaluate the potential of umbilical cord MSCs for heart repair following a heart attack
  - Explore adult stem cell therapy for Traumatic Brain Injury when funding is available
  - Define next steps for the evaluation of cartilage repair

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 and the first half of FY17 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. Additionally, we will continue to work closely with KU Endowment to connect with donors interested in supporting the MSCTC and continuing to build the MSCTC brand.

- **Accomplishments:**
  - Marketed the Midwest Stem Cell Therapy Center to potential third parties seeking adult stem cell manufacturing. Secured one contract. Others at various stages of negotiation.

- Developed a relationship with Monsignor Tomasz Trafny, the Head of Science and Faith Department in the Pontifical Council for Culture at The Vatican and Executive Director of STOQ Project at The Vatican.
  - Msgr. Trafny visited the MSCTC in 2016 and gave a Keynote Address at the 4th Annual Midwest Conference on Cell Therapy and Regenerative Medicine
- Established communications with the Archdiocese of Kansas City. Msgr. Trafny visited the Archdiocese for a 2-hour meeting on September 15, 2016 that resulted in excellent exchange of ideas and information on topics relevant for adult stem cell therapy and science.

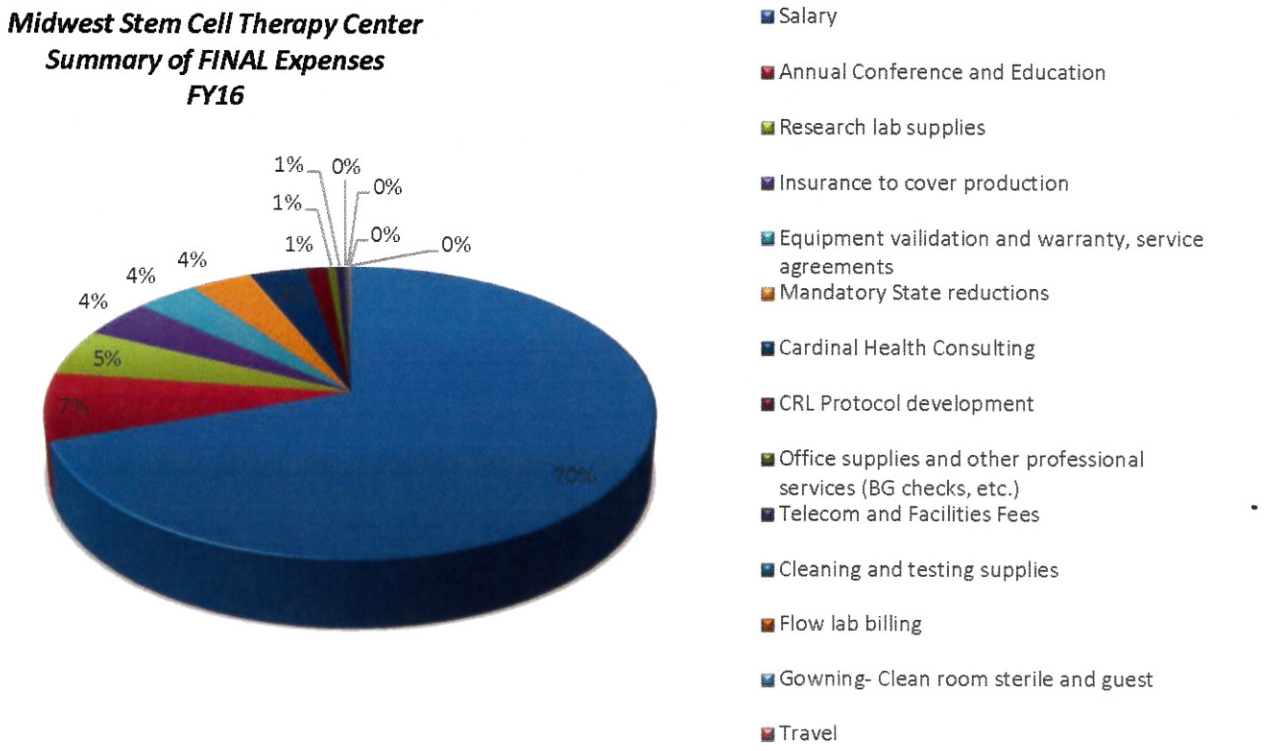
- **Plans:**
  - Continue outreach efforts with potential clients seeking adult stem cell manufacturing locations
  - Continue periodic updates of the MSCTC website
  - Advertise at Kansas universities and other locations in the Midwest regarding stem cell collaborations and GMP manufacturing
  - Develop plans to engage officials from The Vatican as well as the KC Archdiocese

I. Expense and Income Report

State appropriations

FY16 – Total amount received: $754,500

Expenses		% of FY total
Salary	$525,117.65	69.60%
Annual Conference and Education	$56,300.00	7.46%
Research lab supplies	$38,251.00	5.07%
Insurance to cover production	$31,800.00	4.21%
Equipment validation and warranty, service agreements	$28,449.49	3.77%
Mandatory State reductions	$27,879.00	3.70%
Cardinal Health Consulting	$25,873.07	3.43%
CRL Protocol development	$10,000.00	1.33%
Office supplies and other professional services (BG checks, etc.)	$3,875.17	0.51%
Telecom and Facilities Fees	$3,632.82	0.48%
Cleaning and testing supplies	$1,524.24	0.20%
Flow lab billing	$1,101.57	0.15%
Gowning- Clean room sterile and guest	$576.99	0.08%
Travel	$119.00	0.02%
FY16 Final Expenses Total	$754,500.00	



FY17 Year to Date Sources and Spends

Total amount received: $754,500

Table 1

Actual Expenses through 1/31/17		*% of FY Total*
Salary	*265,641.77*	*35.21%*
Annual Conference and Education	*66,872.35*	*8.86%*
Research lab supplies	*41,734.40*	*5.53%*
Mandatory State reductions	*29,033.00*	*3.85%*
Insurance to cover production	*21,200.00*	*2.81%*
Equipment validation and warranty, service agreements	*16,899.92*	*2.24%*
Lab Equipment	*12,069.78*	*1.60%*
Cardinal Health Consulting	*10,578.70*	*1.40%*
Telecom and Facilities Fees	*2,153.75*	*0.29%*
Karyotyping	*1,134.00*	*0.15%*
Gowning- Clean room sterile and guest	*1,037.22*	*0.14%*
Office supplies and other professional services (BG checks, etc.)	*969.13*	*0.13%*
Cleaning and testing supplies	*669.20*	*0.09%*
Travel	*330.83*	*0.04%*
Flow lab billing	*265.88*	*0.04%*
Total Fiscal Year expenses through 1/31/17	***470,589.93***	***62.4%***

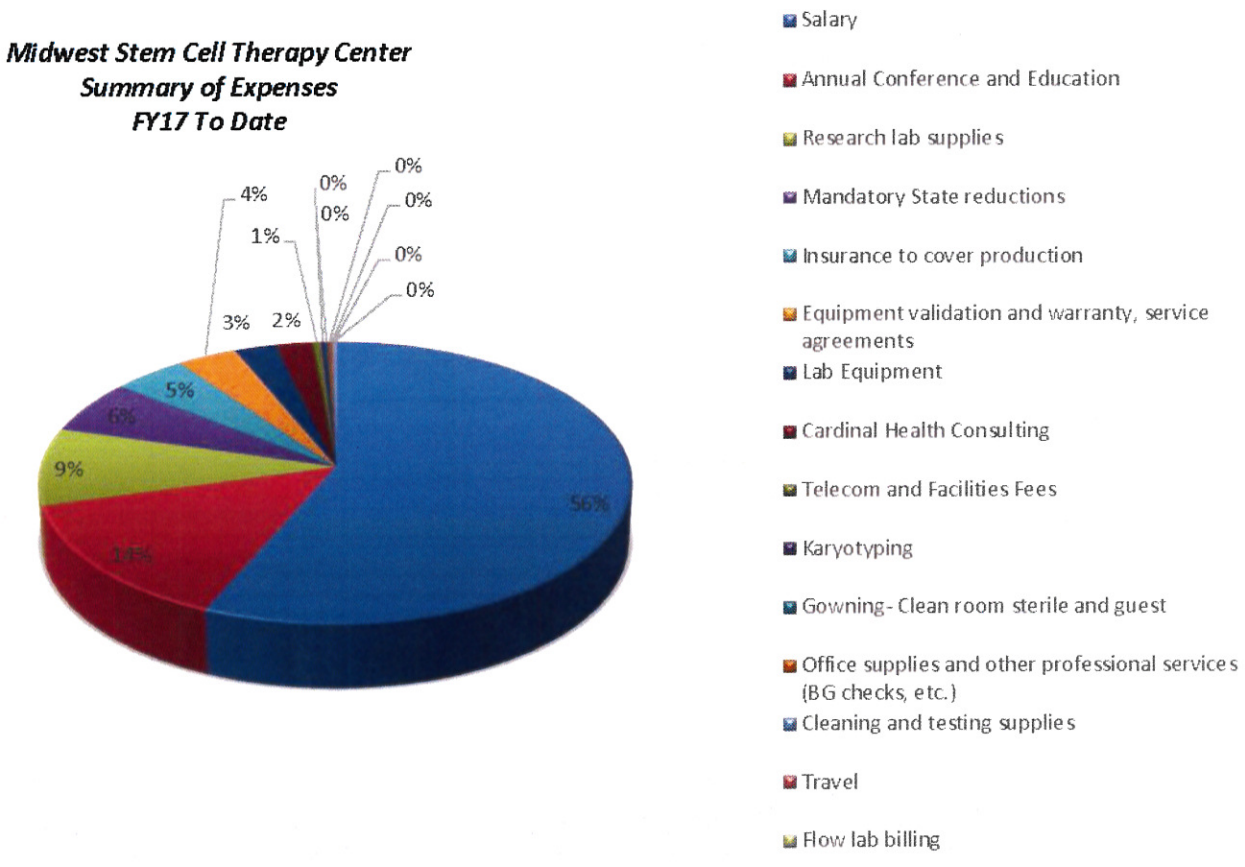
Table 2

Projected Expenses for the remaining FY17		*% of FY Total*
Projected Salary and Fringe Total	*172,064.61*	*22.81%*
Projected Supplies	*48,076.46*	*6.37%*
Projected Cardinal Health Consulting	*30,507.75*	*4.04%*
Projected Consulting Fees	*30,000.00*	*3.98%*
Projected Equipment validation and calibration	*1,780.00*	*0.24%*
Projected Telecom	*1,481.25*	*0.20%*
Projected Expenses for remaining FY17	***283,910.07***	***37.6%***

Table 3

Center Income to date for FY17 (through 1/31/17)

GMP Manufacturing income	*4,609.01*
Educational related income	*2,000.00*
Clinical Trial income	*947.37*
Total Center Income to date for FY17	***7,556.38***



J. VISION FOR THE FUTURE

Through support from the State of Kansas, establishing a solid donor base, third party adult stem cell manufacturing, and external grants, **establish the Midwest Stem Cell Therapy Center as the place to go to obtain adult stem cell therapy**. To this end, MSCTC staff and Advisory Board members along with KUMC Office of Organizational Development are developing a long-range strategic plan that will incorporate the following elements:

- Achieve self-sustainability with a multipronged approach that will include developing and licensing novel adult stem cells for therapy, third-party manufacturing of adult stem cell products, processing and banking adult stem cells and marketing
- Advancing cutting-edge adult stem cell therapy in the Midwest through increasing number of human clinical trials
- Develop a 'Service Line' model for enhanced delivery of regenerative medicine locally
- 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 devices for cell administration
- 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.

Midwest Stem Cell Therapy Center

Status Update
March 7, 2017

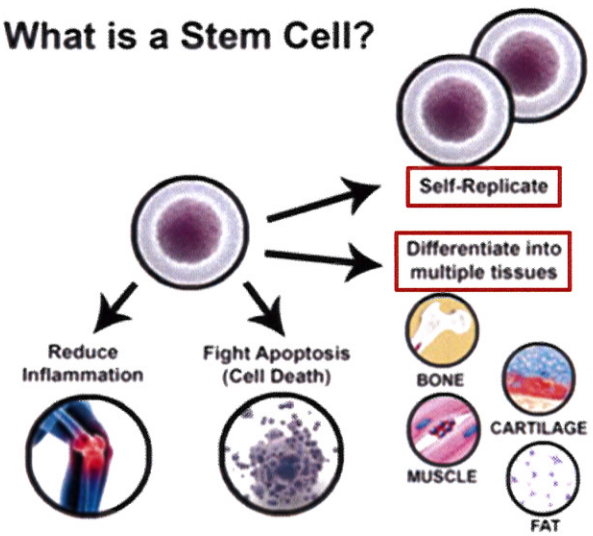
Buddhadeb Dawn, MD, FACC, FAHA, FACP
Director, Midwest Stem Cell Therapy Center

Professor of Medicine and Molecular and Integrative Physiology
Maureen and Marvin Dunn Professor of Cardiovascular Diseases
Director, Division of Cardiovascular Diseases
Director, Cardiovascular Research Institute
University of Kansas Medical Center

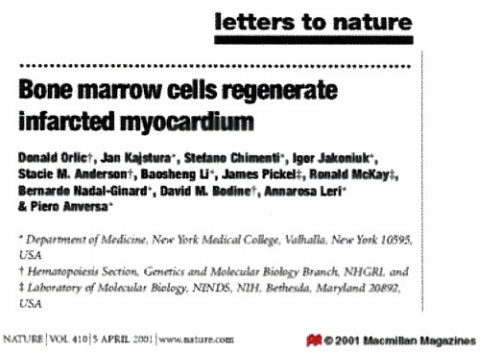
KU MIDWEST STEM CELL THERAPY CENTER
The University of Kansas

THE UNIVERSITY OF KANSAS HOSPITAL

What is a Stem Cell?



Heart Repair with Adult Bone Marrow Cells



letters to nature

Bone marrow cells regenerate infarcted myocardium

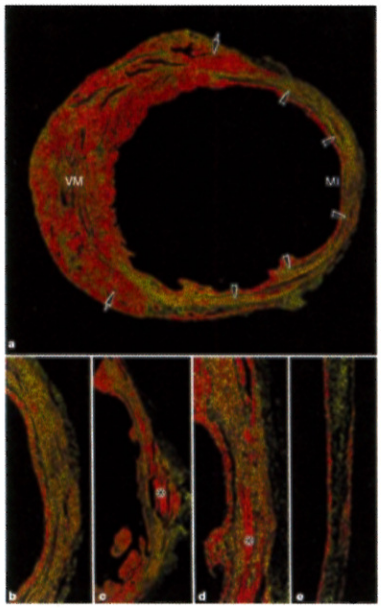
Donald Orlic†, Jan Kajstura*, Stefano Chimenti*, Igor Jakoniuk*, Stacie M. Anderson†, Baosheng Li*, James Pickel‡, Ronald McKay‡, Bernardo Nadal-Ginard*, David M. Bodine†, Annarosa Leri* & Piero Anversa*

** Department of Medicine, New York Medical College, Valhalla, New York 10595, USA*
† Hematopoiesis Section, Genetics and Molecular Biology Branch, NHGRI, and ‡ Laboratory of Molecular Biology, NINDS, NIH, Bethesda, Maryland 20892, USA

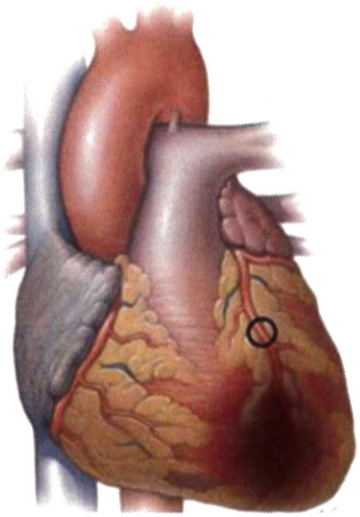
NATURE | VOL 410 | 5 APRIL 2001 | www.nature.com

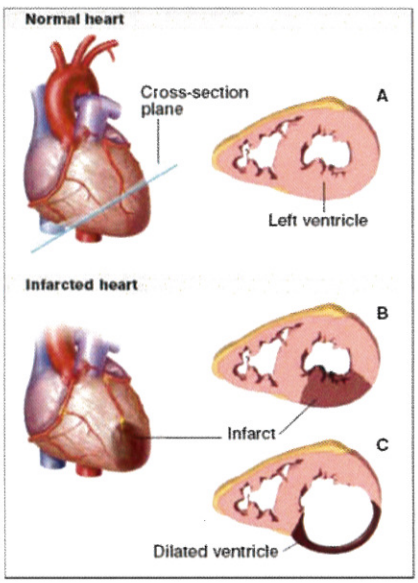
Nature. 2001 Apr 5;410(6829):701-5.

Lin-/c-kit+ BMCs



Infarcted Heart – Target for Adult Stem Cell Therapy



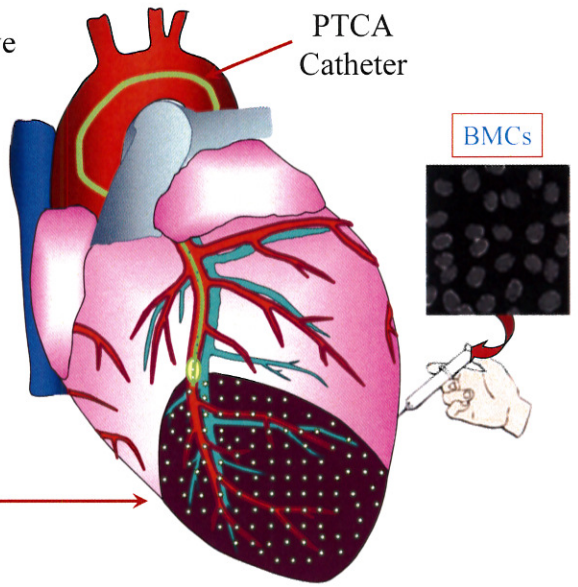


Thygesen *et al.* J Am Coll Cardiol 2012;60:1581-98.

Source: http://www.health-pic.com/complications-of-myocardial-infarction/

Injection of BMCs for Heart Repair in Humans

More than 60 studies have been completed and published



Clinical Track

Afzal et al. *Circulation Research* 2015;117:558-575

Adult Bone Marrow Cell Therapy for Ischemic Heart Disease

Evidence and Insights From Randomized Controlled Trials

Muhammad R. Afzal, Anweshan Samanta, Zubair I. Shah, Vinodh Jeevanantham, Ahmed Abdel-Latif, Ewa K. Zuba-Surma, Buddhadeb Dawn

From the Division of Cardiovascular Diseases, Cardiovascular Research Institute, and the Midwest Stem Cell Therapy Center, University of Kansas Medical Center, Kansas City (M.R.A., A.S., Z.I.S., B.D.); Heart and Vascular Specialists of Oklahoma, Oklahoma City (V.J.); Division of Cardiology, University of Kentucky, Lexington (A.A.-L.); and Department of Cell Biology, Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Krakow, Poland (E.K.Z.-S).

- 48 RCTs were included in this meta-analysis
- A total of 2,602 patients
  (1,468 BMC-treated and 1,134 control patients)

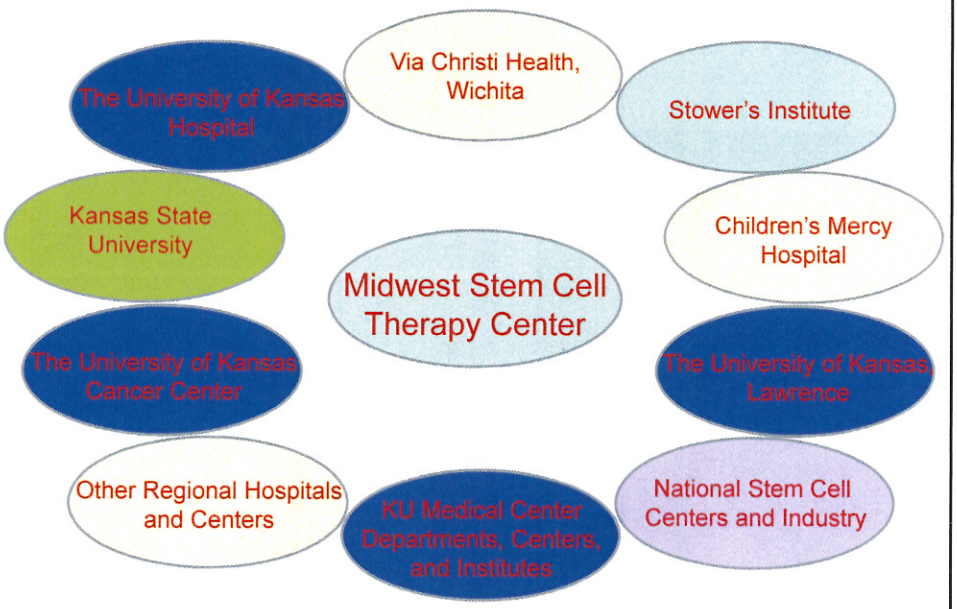
Compared with controls, in BMC-treated patients:

- LVEF improved by 2.92%
- LV end-systolic volume decreased by 6.37 ml
- LV infarct scar size reduced by 2.25%
- LV end-diastolic volume decreased by 2.26 ml (P=0.06)

NHLBI Centers for Stem Cell Therapy

Senate Bill 199

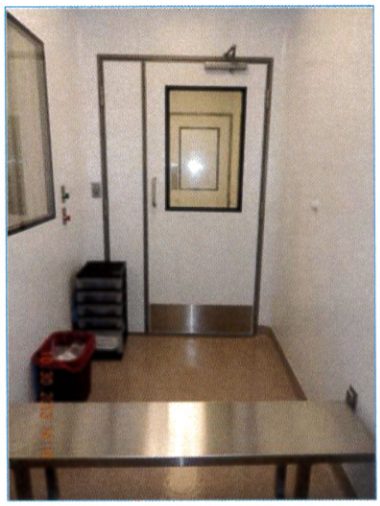
Stem Cell Hub

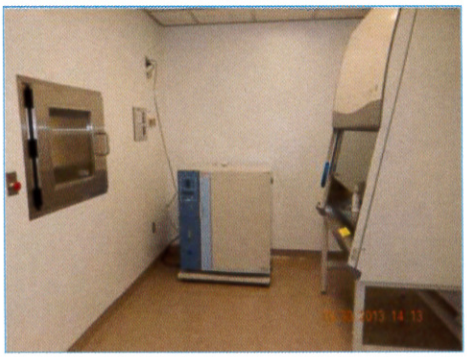


Objectives of the Center - I

- 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

Good Manufacturing Practice Facility



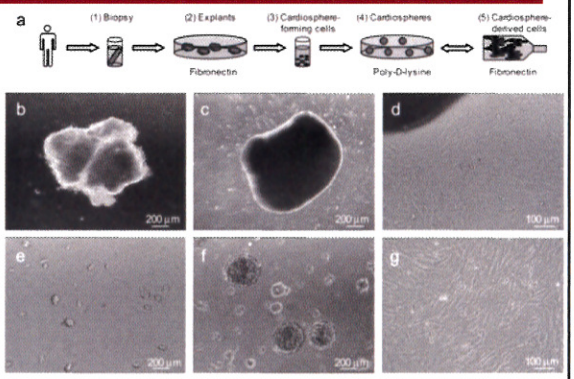


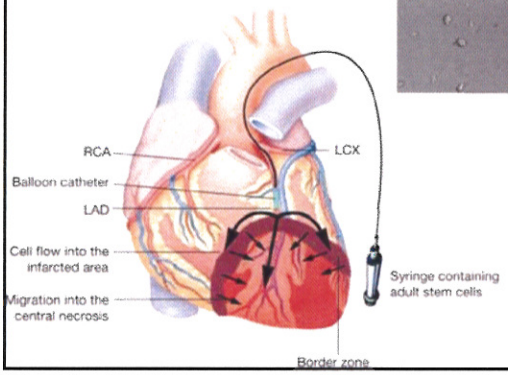
Focus Areas for Adult Stem Cell Therapy

- Stroke and Neurodegenerative diseases
- Cancer and immunotherapy
- Cardiac and vascular
- Musculoskeletal, trauma, skin, burn, wounds, autoimmune diseases

Clinical Trials for Heart

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





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

Clinical Trial for Stroke

ACTIsSIMA

- Modified adult bone marrow stem cells (SB623) for patients with motor deficiency following an ischemic stroke
- US Biotech company sponsoring trial
- Open to enrollment

Clinical Trial for Cancer

- Graft vs. Host Disease
  - Wharton's Jelly mesenchymal stem cells to be injected intravenously to combat GvHD
  - Methods to expand cells under GMP conditions have been developed
  - Preclinical studies near completion
  - IND to be submitted to the FDA soon

Preclinical Projects

Amyotrophic Lateral Sclerosis (Lou Gehrig's Disease)

- KU Dept of Neurology collaboration
- Initial Proof of Concept studies ongoing

Liver repair

- KU Department of Pharmacology and Toxicology collaboration
- Pre-PreIND items being developed

Additional KUMC Collaborations

- Heart scar repair
  - KUMC, Cardiovascular Research Institute
- Spinal cord repair
  - KUMC, Dept. of Molecular and Integrative Physiology
- Stroke and traumatic brain injury
  - KUMC, Dept. of Rehabilitation Medicine
- Cartilage Repair
  - KUMC, Dept. of Orthopedic Surgery

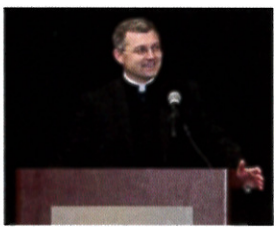
Objectives of the Center - II

- 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

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

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
- Income received from GMP manufacturing and externally funded projects
- Clinical Trials

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
- Brand recognition
- Abundance of collaborators
- Continued funding from the State of Kansas

Business Initiatives

Sponsored R&D and Fee-for-Service

- Dental pulp MSC company
  - Isolation, recovery of dental pulp MSCs and long-term banking
  - Contract for business over the next 20 years executed
- Gene therapy company
  - Gene Therapy for Aplastic Anemia
  - Contract in development
- Company operating clinics
  - Adipose MSC treatment for Osteoarthritis/Cartilage Repair
  - Project discussions to resume this week
- Cord blood and tissue storage company
  - Fee for service for developing methods, processing blood and tissue, and long-term storage
  - Project scope and budget discussion underway

Clinical Trials

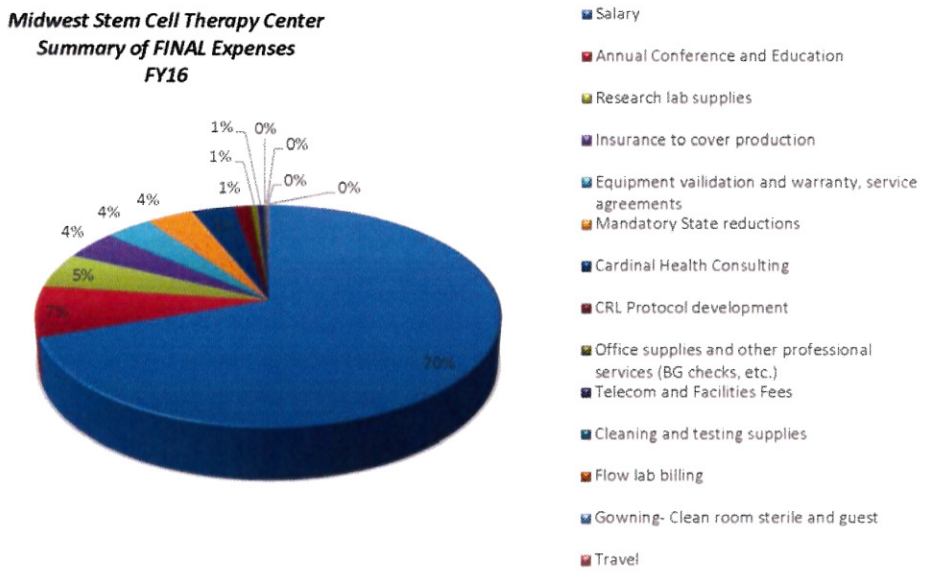
FY16 Expense Report

State appropriations

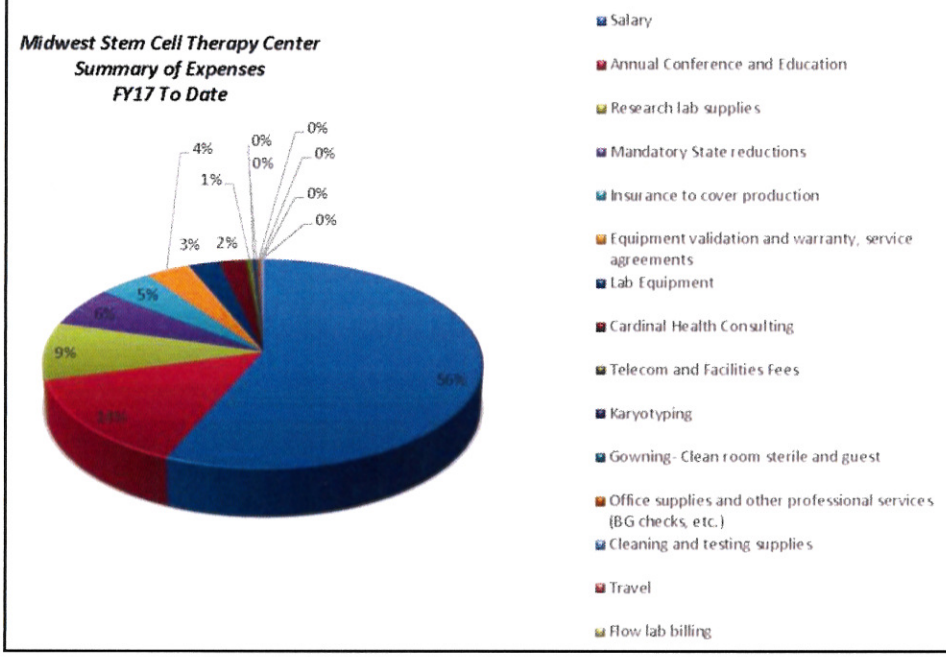
FY16 – Total amount received: $754,500

Expenses		% of FY total
Salary	$525,117.65	69.60%
Annual Conference and Education	$56,300.00	7.46%
Research lab supplies	$38,251.00	5.07%
Insurance to cover production	$31,800.00	4.21%
Equipment validation and warranty, service agreements	$28,449.49	3.77%
Mandatory State reductions	$27,879.00	3.70%
Cardinal Health Consulting	$25,873.07	3.43%
CRL Protocol development	$10,000.00	1.33%
Office supplies and other professional services (BG checks, etc.)	$3,875.17	0.51%
Telecom and Facilities Fees	$3,632.82	0.48%
Cleaning and testing supplies	$1,524.24	0.20%
Flow lab billing	$1,101.57	0.15%
Gowning- Clean room sterile and guest	$576.99	0.08%
Travel	$119.00	0.02%
FY16 Final Expenses Total	$754,500.00	

FY16 Expense report



FY17 Sources and Spends (Year to Date)



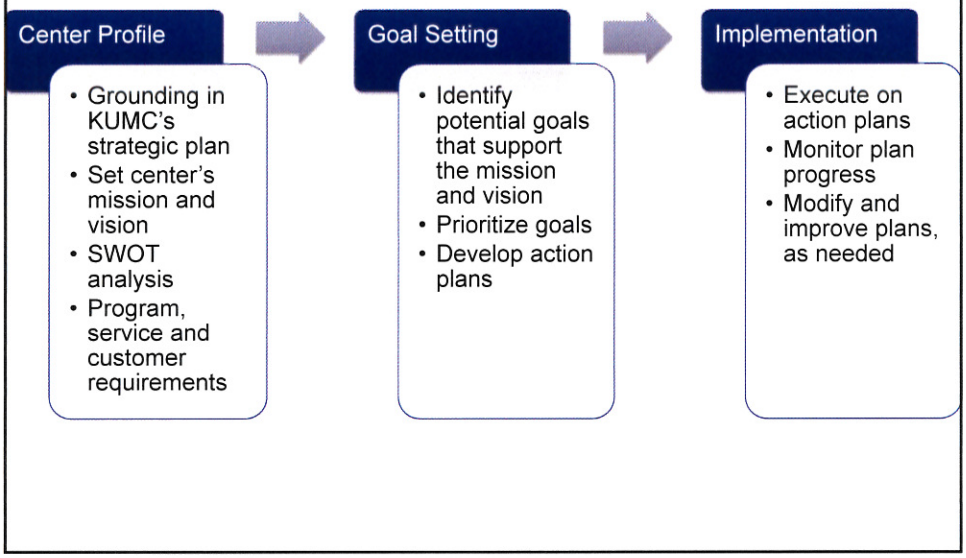
Midwest Stem Cell Therapy Center: Accomplishments

- Brought industry-sponsored adult stem cell therapy trials to Kansas and the Midwest
- Built a GMP, started the production of clinical grade adult stem cells
- Close to initiating home-grown stem cell therapy trial for cancer patients
- Initiated business and fee-for-service collaborations, generating revenue
- Collaborating widely both within and outside of KU with regional institutions as well as businesses
- Trained students and researchers
- Conducted 4 very successful adult stem cell conferences
- Created a database for adult stem cell information on the web
- Established MSCTC presence on the web
- Addressing patient concerns and comments on a regular basis, providing information about adult stem cells
- Performing cutting-edge basic science research with iPSC and other cells

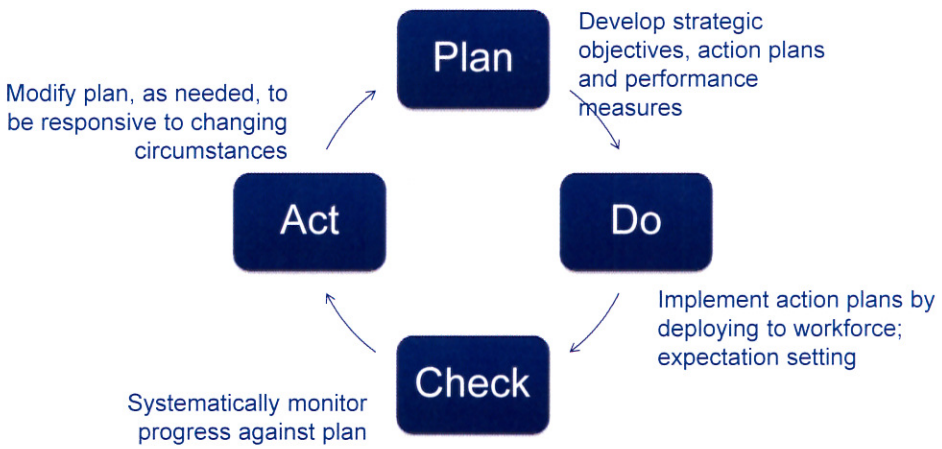
MSCTC Vision for Growth

- Advance cutting-edge adult stem cell therapy
  - Multi-center adult stem cell trials
  - Deliver therapy locally in Kansas in the form of trials through clinics
  - Promote local basic/clinical investigators
- Produce patient-specific adult stem cells locally and generate new business
  - Expand the physical capacity/facility
- Advance basic stem cell research
  - Innovation

Strategic Plan Development



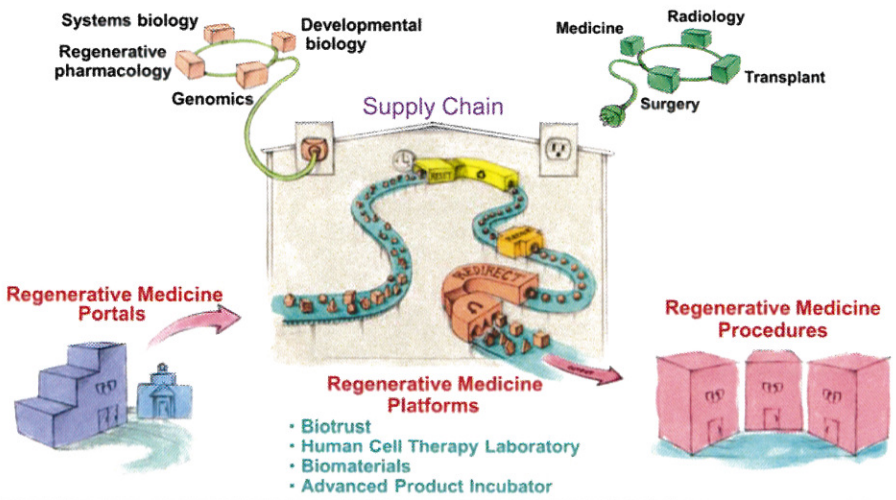
Strategic Plan Deployment



MSCTC 2.0

Terzic et al. *Stem Cells Translational Medicine* 2015;4:1-7

Regenerative Medicine Service Line



Conclusions

- Adult stem cell therapy can potentially cure diseases that are major health problems
- The importance of a local adult stem cell center delivering adult stem cell therapy to Kansans cannot be overemphasized
- MSCTC has been successful within its means
- A strategic planning will take this highly functional center to the next level to deliver adult stem cell therapies and potentially benefit many more patients in a large territory

THANK YOU

CHARLOTTE
LOZIER
INSTITUTE

Kansas' Unique Midwest Stem Cell Therapy Center

Written Testimony of David A. Prentice, Ph.D.
Vice President and Research Director, Charlotte Lozier Institute
Adjunct Professor of Molecular Genetics, John Paul II Institute, Catholic University of America
Founding Member, Do No Harm: The Coalition of Americans for Research Ethics

Senate Ways and Means Committee and Senate Public Health and Welfare Committee
House Appropriations Committee and House Health and Human Services Committee
State of Kansas
March 7, 2016

The Distinguished Chairs and Honored Members of the Committees.

I am a cell and developmental biologist, currently working for the Charlotte Lozier Institute in Washington, D.C. as Vice President and Research Director; I also serve as an adjunct professor at a Washington, D.C. university, and as an Advisory Board Member for the Midwest Stem Cell Therapy Center, the unique comprehensive stem cell center in Kansas. Previously I spent 10 years as Senior Fellow for Life Sciences at another policy think tank in Washington, D.C., and prior to that almost 20 years as Professor of Life Sciences at Indiana State University, and Adjunct Professor of Medical and Molecular Genetics, Indiana University School of Medicine. Before that I was a faculty member in the Department of Obstetrics, Gynecology and Reproductive Sciences, University of Texas Medical School at Houston. My post-doctoral work was done at Los Alamos National Laboratory. I have done federally-funded laboratory research, lectured, and advised on these subjects extensively in the U.S. and internationally. I've taught embryology, developmental biology, molecular biology and biochemistry for over 35 years to medical and nursing students, as well as undergraduate and graduate students. I am proud to be a native Kansan, born in La Crosse, Kansas, raised near Parker, Kansas, with my degrees (B.S. and Ph.D.) from the University of Kansas.

Thank you for the opportunity to testify on the progress of the Midwest Stem Cell Therapy Center, the unique Kansas stem cell initiative. I was honored to assist with development of the Kansas adult stem cell center, and testified in 2013 in support of the bill, SB199, that made the Center a reality. Thank you for your support of this unique and successful idea that puts patients first. Currently I serve as a member of the Center's Advisory Board.

We're aware that many new legislators have joined the ranks of these committees. Some may be unaware of the Center and its work, and others may want to be refreshed on the how and why the Center came into existence. Dr. Dawn will address the "How" as well as the recent work of the Center, and our goals moving forward. I would like to go over the "Why" of the Center's inception and its focus on patients and therapies.

Stem cell treatments using adult stem cells from bone marrow, umbilical cord blood, and other tissue sources have been, and continue to be, a cutting-edge medical technology. Kansas, by virtue of its investment in the Midwest Stem Cell Therapy Center, has taken a leading role in bringing patient-focused, non-controversial stem cell therapies to patients. The Kansas stem cell center is focused on patients, providing therapies using non-controversial, non-embryonic stem cells. The MSCTC also works to fulfill its mission through dissemination of information, with a comprehensive view of all aspects of providing adult stem cell therapies to patients. In short, the mission of the MSCTC it to improve health and quality of life through innovative

treatment, education and research in adult stem cell therapy. In the less than four years in which the Center has been in existence, it has made significant progress in fulfilling this mission for Kansans.

A stem cell has two chief defining characteristics: 1) it continues to grow and divide, maintaining a pool of cells for future use, and 2) given the correct signal, a stem cell will differentiate or specialize into any number of specific mature cell types. The flexibility of stem cells potentially to form many different types of tissues has led doctors to envision use of stem cells for "Regenerative Medicine"—injecting stem cells, e.g., from bone marrow, into damaged tissues so that the stem cells can "regenerate" healthy tissue.

Adult stem cells are the gold standard of stem cells when it comes to treating patients. Adult stem cells are "tissue" stem cells, taken from virtually any body tissue. Bone marrow and peripheral blood are still the most common source to obtain adult stem cells, but they can also be derived from muscle, brain, heart, skin, and even liposuctioned fat. In addition, the same or similar type of stem cell can be harvested from umbilical cord blood as well as from the solid part of the umbilical cord (termed Wharton's jelly). Adult stem cells can be harvested without harming the stem cell donor; in roughly half of cases, the patient is the source of her own stem cell transplant. And adult stem cells are being used today to treat thousands of patients each year, for dozens of different conditions.

These are facts that many Kansans, the public and physicians alike, do not know. The lack of knowledge affects health as well as life. At this point there are few sources for patients or physicians to learn about adult and cord blood stem cell transplants. One that is often used is the website clinicaltrials.gov, run by the FDA and NIH.

Over the past few years the explosion in numbers of patients treated and in numbers of adult stem cell clinical trials has blossomed. In 2012 there were a little over 2500 adult stem cell clinical trials listed in the database. Currently here are over **3,600 ongoing or completed clinical trials using adult stem cells** listed,[1] with over 70,000 people around the globe receiving adult stem cell transplants each year. There have now been **well over one million adult stem cell transplants** total.[2] The applications of adult and cord blood stem cells in clinical therapy are growing rapidly, and much of the growth in this area is taking place in the United States;[3] Kansas continues to position itself as one of the leaders in these therapies. Although the MSCTC has been in existence for less than four years, in a very real sense many other states and stem cell programs are rushing to catch up with the Kansas center.

There are an estimated 53 stem cell centers of one type or another nationwide. Most of these"stem cell centers" in the United States focus on basic research, with little or no patient contact or clinical component. By the same token, most "stem cell treatment centers" or bone marrow transplant centers emphasize only specific clinical treatments but do not educate the public or physicians. None of the identified stem cell centers provide a comprehensive program of treatment, education, research, and training as does the MSCTC. This is also true in terms of patient focus. For example, California has the largest state-funded stem cell program in the country, and started its program with a focus on embryonic stem cells; yet it is

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[1] Search term: http://www.clinicaltrials.gov/ct2/results?term=adult+stem+cell+transplants&type=Intr accessed March 5, 2017.

[2] Gratwohl A *et al.*, One million haemopoietic stem-cell transplants: a retrospective observational study, *Lancet Haematology* 2, e91, March 2015

[3] Niederwieser D *et al.*, Hematopoietic stem cell transplantation activity worldwide in 2012 and a SWOT analysis of the Worldwide Network for Blood and Marrow Transplantation Group including the global survey, *Bone Marrow Transplantation* 51, 778-785, June 2016; doi:10.1038/bmt.2016.18

turning to adult stem cells for a chance at success with patients.[4] Likewise the state of Maryland has switched its emphasis on research grants to adult stem cells.[5]

There has also been a surge of interest at the federal level. The General Accounting Office documents that seven different federal agencies invested a total of $2.89 billion in regenerative medicine from 2012-2014.[6] The agencies are focusing on numerous areas of investigation but a number of them overlap with existing priorities of the MSCTC, including stroke, traumatic brain injuries, limb repair. And again, in comparing various other state and collaborative initiatives, even though the Kansas adult stem cell center has been in existence less than four years, it already surpasses many other longer-standing initiatives, and the others are working to catch up with the Kansas MSCTC. The MSCTC has also already developed strong relationships with the FDA and templates for approval of IND's, the documents needed for legal FDA approval to proceed with patient trials and treatments. The federal government just a few months ago passed the 21st Century Cures initiative, which will open even more avenues for the Kansas adult stem cell center to make further adult stem cell clinical trials and treatments accessible to Kansans.

The MSCTC is in the process of developing numerous new and innovative therapies using adult stem cells, including regenerative therapies for brain, heart, spinal cord, liver, joints, and also graft-versus-host disease, which can be a serious complication for some bone marrow adult stem cell transplants. Some of the specific projects are already underway, some others in pre-clinical research phase, and others in planning stages.

A substantial amount of previous work with adult stem cells has been the successful application of the cells for treatment and recovery from **various cancers**. The KU Cancer Center itself performed over 300 marrow and blood stem cell transplants for cancer treatments in 2015. While a number of these therapies have moved into standard medical practice, as seen by the numbers treated at the KU Cancer Center, one of the leaders in this field, there is still much work to be done to increase the efficacy of stem cell transplants for cancer and to treat even more cancer types.

Beyond cancer, adult stem cells are also showing therapeutic promise for other diseases and conditions where there has previously been no available treatment option. The published scientific literature now documents therapeutic success in trials of adult stem cells for patients with dozens of other conditions. I'd like to use the rest of my presentation to mention several of the promising results using adult stem cells for patients. Some of these are already under development at the MSCTC, while others represent additional possible targets for the Center in the future.

One example that is moving rapidly into the clinic is use of adipose (fat)-derived adult stem cells for joints and cartilage replacement. Pers *et al.* showed decrease of pain and increase of function using the patient's own adult stem cells to treat osteoarthritis.[7] A Swiss group has also shown effectiveness of adult stem cells to repair cartilage injuries.[8] There have not been enough validated, controlled studies using adult stem cells

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[4] Gene Tarne, The Ethical Stems of Good Science, Charlotte Lozier Institute, https://lozierinstitute.org/the-ethical-stems-of-good-science/, October 1, 2012

[5] Gene Tarne and Andrew Mullins, Maryland Joins the Trend for Ethical Stem Cell Research, Charlotte Lozier Institute, https://lozierinstitute.org/maryland-joins-the-trend-for-ethical-stem-cell-research/, October 1, 2013

[6] U.S. Government Accountability Office. Regenerative Medicine. Federal Investment, Information Sharing, and Challenges in an Evolving Field. GAO-15-1553, June 2015.

[7] Pers Y-M *et al.*, Adipose Mesenchymal Stromal Cell-Based Therapy for Severe Osteoarthritis of the Knee: A Phase I Dose-Escalation Trial, *Stem Cells Translational Medicine* 5, 847–856, July 2016, doi: 10.5966/sctm.2015-0245

[8] Mumme M *et al.*, Nasal chondrocyte-based engineered autologous cartilage tissue for repair of articular cartilage defects: an observational first-in-human trial, *Lancet* 388, 1985–1994, October 22, 2016, doi: 10.1016/S0140-6736(16)31658-0

to treat cartilage and joint problems, and this opens an area for the MSCTC to do such approved studies, an area where the Center has already proven its expertise and value.

Another area of progress, which we've mentioned before in presentations, is use of adult stem cells for skin repair, especially after burns. While it sounds a bit like science fiction, there is now a "skin gun" being tested to spray adult stem cells onto burns and other wounds, that can quickly provide a sterile seal for the skin and induce skin regrowth more rapidly than usually seen with grafts. The use of adult stem cells in this application is being expanded and has already shown great potential for burn and wound healing.[9]

One area of intense study both at the MSCTC as well as in other research centers is neurological conditions, including autoimmune diseases. There continues to be progress in treating relapsing-remitting multiple sclerosis with adult stem cells, and the most recent papers show long-term remission of at least 5 years for half of the patients.[10] The disease myasthenia gravis has also shown positive response when patients are treated with their own adult stem cells.[11]

One area of active work is the use of adult stem cells from the solid part of the umbilical cord to manage **graft-versus-host disease**, a significant problem sometimes seen with transplants for cancer.[12] A groundbreaking study by MSCTC faculty has advanced a promising therapy using adult stem cells to treat this condition, and an approved clinical trial is about to begin.

Repair of heart damage is an ongoing area of research and trials at the MSCTC, including current clinical trials,[13] as well as basic investigations into new potential cardiac repair technologies.[14] Dr. Dawn is one of the world leaders in this area, and several members of the MSCTC faculty are renowned in the use of adult stem cells.

The MSCTC and associated medical center faculty are also developing collaborative studies in cell therapies using chimeric antigen receptors-T cell (CAR-T). These cell-based therapeutic techniques are designed to assist a patient's immune system in attacking and resisting cancer.[15] A version of this system was used recently to treat a young girl in the U.K. who had leukemia.[16] Immune cells underwent genetic engineering to make them resistant to chemotherapy and so that they would not cause a GVHD reaction. The girl could then be treated with high-dose chemotherapy yet maintain her "borrowed" immune system. Once the

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[9] Esteban-Vives R *et al.*, Second-degree burns with six etiologies treated with autologous noncultured cell-spray grafting, *Burns* 42, e99-e106, 2016, doi: 10.1016/j.burns.2016.02.020; AND Esteban-Vives R *et al.*, Calculations for reproducible autologous skin cell-spray grafting, *Burns* 42, 1756-1765, 2016, doi: 10.1016/j.burns.2016.06.013

[10] Muraro PA *et al.*, Long-term Outcomes After Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis, *JAMA Neurology* published online February 20, 2017, doi: :10.1001/jamaneurol.2016.5867

[11] Bryant A *et al.*, Myasthenia Gravis Treated With Autologous Hematopoietic Stem Cell Transplantation, *JAMA Neurology* 73, 652-658, 2016, doi:10.1001/jamaneurol.2016.0113

[12] McGuirk JP *et al.*, Wharton's Jelly-Derived Mesenchymal Stromal Cells as a Promising Cellular Therapeutic Strategy for the Management of Graft-versus-Host Disease, *Pharmaceuticals* 8, 196-220, 2015, doi: 10.3390/ph8020196

[13] Afzal MR *et al.*, Adult Bone Marrow Cell Therapy for Ischemic Heart Disease. Evidence and Insights From Randomized Controlled Trials, *Circulation Research* 117, 558, 2015

[14] Rajasingh S et al., Generation of Functional Cardiomyocytes from Efficiently Generated Human iPSCs and a Novel Method of Measuring Contractility, PLoS ONE 10(8):e0134093, 2015. doi:10.1371/journal.pone.0134093

[15] Qasim W *et al.*, Molecular remission of infant B-ALL after infusion of universal TALEN gene-edited CAR T cells, *Science Translational Medicine* 9, eaaj2013, 25 January 2017, doi: 10.1126/scitranslmed.aaj2013

[16] Jennifer Couzin-Frankel, Baby's leukemia recedes after novel cell therapy, Science 350, 731, November 15, 2015

leukemia was eradicated, she received an adult stem cell transplant to generate her own new immune and blood system.

Treatment for peripheral artery disease is also being actively pursued. Rather than amputation, a patient's limb can have circulation restored using adult stem cells..[17]

Sickle cell anemia, a serious, genetically acquired condition, has also been successfully treated using donor adult stem cell transplant. The medical literature now even notes that, "Hematopoietic stem cell transplantation (HSCT) is the only curative therapy for sickle cell disease."[18] The techniques have been refined now so that they are not only successful at alleviating symptoms with children, but also adults with sickle cell anemia.[19]

As already discussed, neurological conditions are one area of active study for MSCTC. A research report last year found that stroke patients treated with adult stem cells, even years after the stroke event, showed significant improvement in function.[20] A local clinical trial using adult stem cells for stroke patients has been initiated through the Center.

Kansas' Midwest Stem Cell Therapy Center is unique, comprehensive, and focused on the patients first. It encompasses clinical treatments, basic and translational research, education and training, a valuable resource for cell processing, and a center for stem cell information including development of a one-of-a-kind clinical database. It is well on the way to becoming a national focal point for adult stem cell therapies, trials, and collaborations, as well as for education and training.

Kansas is at the forefront in adult stem cell therapies and information for physicians and patients around the world.

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[17] See, *e.g.,* Burt RK *et al.*, Autologous peripheral blood CD133þ cell implantation for limb salvage in patients with critical limb ischemia, *Bone Marrow Transplantation* 45, 111-116, 2010, published online 18 May 2009; Amann B *et al.*, Autologous Bone Marrow Cell Transplantation Increases Leg Perfusion and Reduces Amputations in Patients With Advanced Critical Limb Ischemia Due to Peripheral Artery Disease, *Cell Transplantation* 18, 371-380, 2009

[18] Bernaudin F *et al.*, Long-term results of related myeloablative stem cell transplantation to cure sickle cell disease, *Blood* 110, 2749-2756, 2007

[19] Hsieh MM *et al.*, Nonmyeloablative HLA-Matched Sibling Allogeneic Hematopoietic Stem Cell Transplantation for Severe Sickle Cell Phenotype, *JAMA*. 312, 48-56, 2014, doi:10.1001/jama.2014.7192

[20] Steinberg GK *et al.*, Clinical Outcomes of Transplanted Modified Bone Marrow–Derived Mesenchymal Stem Cells in Stroke: A Phase 1/2a Study, *Stroke* 47, 1817-1824, July 2016, doi: 10.1161/STROKEAHA.116.012995

David A. Prentice, Ph.D.
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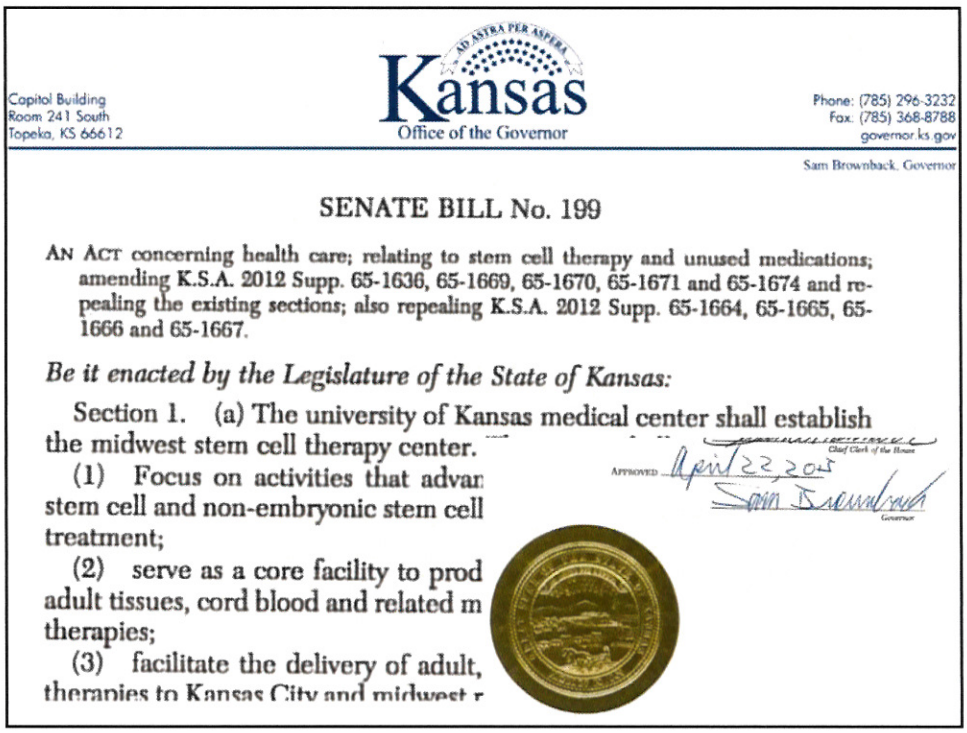
Washington, D.C.

CHARLOTTE LOZIER INSTITUTE



Capitol Building
Room 241 South
Topeka, KS 66612

Kansas
Office of the Governor

Phone: (785) 296-3232
Fax: (785) 368-8788
governor.ks.gov

Sam Brownback, Governor

SENATE BILL No. 199

AN ACT concerning health care; relating to stem cell therapy and unused medications; amending K.S.A. 2012 Supp. 65-1636, 65-1669, 65-1670, 65-1671 and 65-1674 and repealing the existing sections; also repealing K.S.A. 2012 Supp. 65-1664, 65-1665, 65-1666 and 65-1667.

Be it enacted by the Legislature of the State of Kansas:

Section 1. (a) The university of Kansas medical center shall establish the midwest stem cell therapy center.

(1) Focus on activities that advar stem cell and non-embryonic stem cell treatment;

(2) serve as a core facility to prod adult tissues, cord blood and related m therapies;

(3) facilitate the delivery of adult, therapies to Kansas City and midwest r

Chief Clerk of the House

APPROVED April 22, 2013

Sam Brownback
Governor

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

Improve health and quality of life through innovative treatment, education and research in adult stem cell therapy

Adult Stem Cells: The Best Kept Secret In Medicine

David Prentice
5:24 PM 08/22/2016

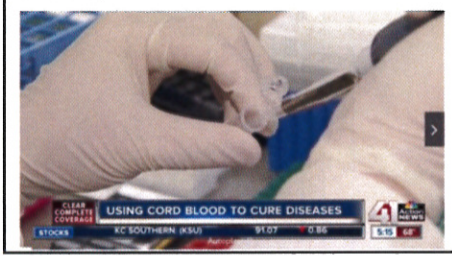
THE DAILY CALLER

Stem cell therapies and their lifesaving results are arguably the best kept medical secret. Stem cells are currently being used in several thousand FDA-approved clinical trials, are treating tens of thousands of patients every year, and cumulatively over 1.5 million people have been treated to date. Yet these numbers, and the lifesaving results from stem cells for dozens of conditions, are unknown to most. Why the information blackout? Perhaps for lack of an adjective.

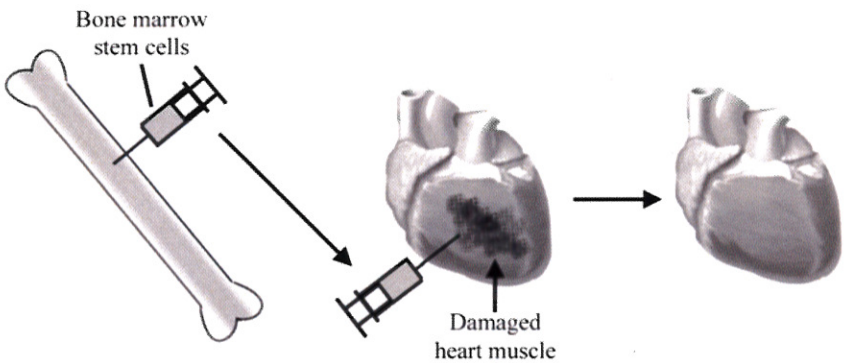
You see, those heartening numbers are all due to *adult* stem cells. Long ignored by the media and disparaged even by many in the scientific community, adult stem cells – those not dependent on the destruction of embryos – are the true gold standard for stem cells, especially when it comes to treating patients.

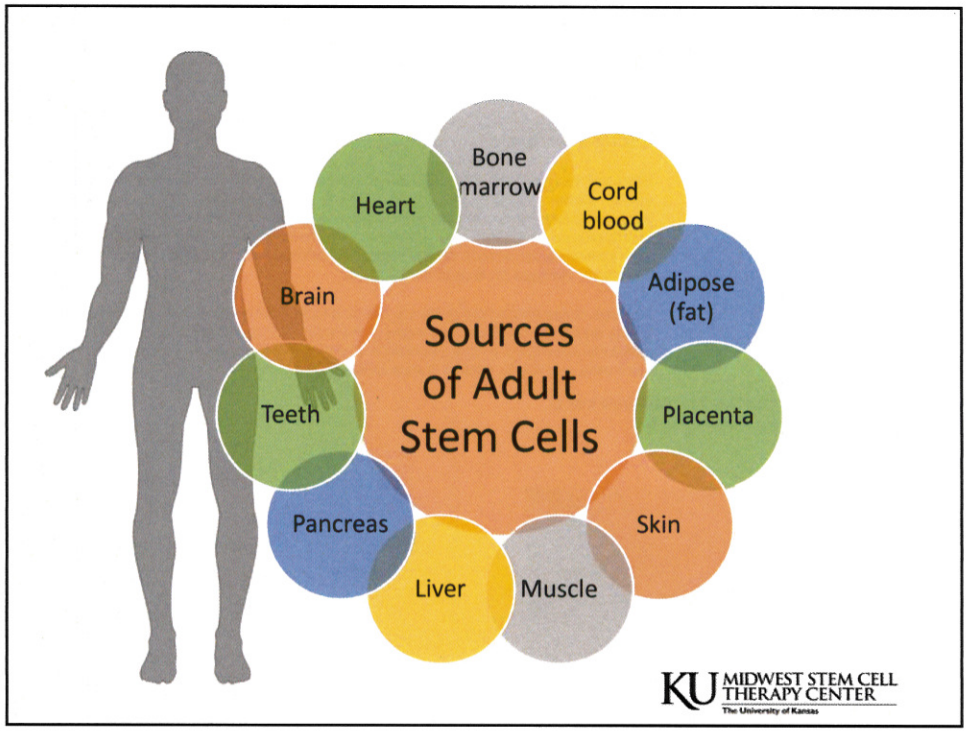
University of Kansas doctor praises cord blood stem cells for saving lives

BY: Josh Helmuth
POSTED: 5:28 PM, Sep 16, 2016
UPDATED: 7:43 PM, Sep 16, 2016



Regenerative Medicine with Stem Cells



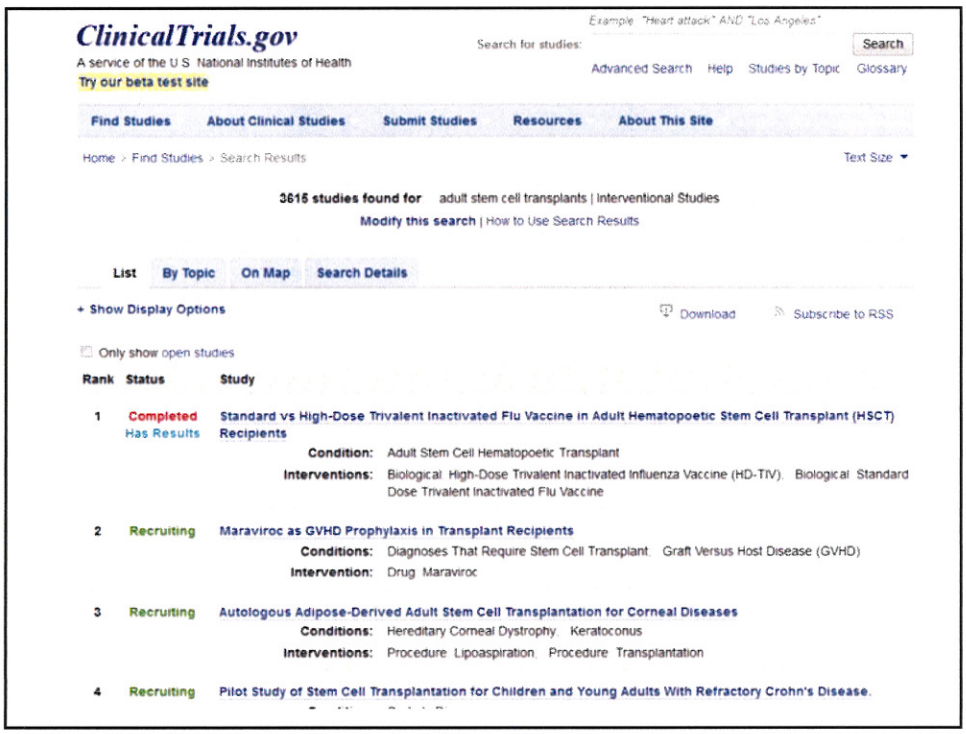


Application of adult and cord blood stem cells in clinical trials and therapies rapidly blooming.
Now over 70,000 people a year receive adult stem cell transplants.

2012- **over 2,500 clinical trials** using adult stem cells listed in NIH/FDA-approved clinical trials database*
March 17, 2013- **over 2,600**
September 17, 2014- **over 2,900**
April 29, 2015- **3,099**
February 6, 2016- **3,326**

*accessed:
http://www.clinicaltrials.gov/ct2/results?term=adult+stem+cell+transplants&type=Intr

KU MIDWEST STEM CELL THERAPY CENTER
The University of Kansas



ClinicalTrials.gov

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

Try our beta test site

Example: "Heart attack" AND "Los Angeles"

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Rank	Status	Study
1	Completed Has Results	Standard vs High-Dose Trivalent Inactivated Flu Vaccine in Adult Hematopoetic Stem Cell Transplant (HSCT) Recipients **Condition:** Adult Stem Cell Hematopoetic Transplant **Interventions:** Biological: High-Dose Trivalent Inactivated Influenza Vaccine (HD-TIV); Biological: Standard Dose Trivalent Inactivated Flu Vaccine
2	Recruiting	Maraviroc as GVHD Prophylaxis in Transplant Recipients **Conditions:** Diagnoses That Require Stem Cell Transplant; Graft Versus Host Disease (GVHD) **Intervention:** Drug: Maraviroc
3	Recruiting	Autologous Adipose-Derived Adult Stem Cell Transplantation for Corneal Diseases **Conditions:** Hereditary Corneal Dystrophy; Keratoconus **Interventions:** Procedure: Lipoaspiration; Procedure: Transplantation
4	Recruiting	Pilot Study of Stem Cell Transplantation for Children and Young Adults With Refractory Crohn's Disease.

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

Alois Gratwohl, Marcelo C Pasquini, Mahmoud Aljurf, Yoshiko Atsuta, Helen Baldomero, Lydia Foeken, Michael Gratwohl, Luis Fernando Bouzas, Dennis Confer, Karl Frauendorfer, Eliane Gluckman, Hildegard Greinix, Mary Horowitz, Minako Iida, Jeff Lipton, Alejandro Madrigal, Mohamad Mohty, Luc Noel, Nicolas Novitzky, José Nunez, Machteld Oudshoorn, Jakob Passweg, Jon van Rood, Jeff Szer, Karl Blume†, Frederic R Appelbaum, Yoshihisa Kodera, Dietger Niederwieser, for the Worldwide Network for Blood and Marrow Transplantation (WBMT)

Summary

Background The transplantation of cells, tissues, and organs has been recognised by WHO as an important medical task for its member states; however, information about how to best organise transplantation is scarce. We aimed to document the activity worldwide from the beginning of transplantation and search for region adapted indications and associations between transplant rates and macroeconomics.

Methods Between Jan 1, 2006, and Dec 31, 2014, the Worldwide Network for Blood and Marrow Transplantation collected data for the evolution of haemopoietic stem-cell transplantation (HSCT) activity and volunteer donors in the 194 WHO member states.

Findings 953 651 HSCTs (553 350 [58%] autologous and 400 301 [42%] allogeneic) were reported by 1516 transplant centres from 75 countries. No transplants were done in countries with fewer than 300 000 inhabitants, a surface area less than 700 km², and a gross national income per person of US$1260 or lower. Use of HSCT increased from the first transplant in 1957 to almost 10 000 by 1985. We recorded a cumulative total of about 100 000 transplants by 1995, and an estimated 1 million by December, 2012. Unrelated donor registries contributed 22·3 million typed volunteer donors and 645 646 cord blood products by 2012. Numbers of allogeneic HSCTs increased in the past 35 years with no signs of saturation (R^2=0·989). Transplant rates were higher in countries with more resources, more transplant teams, and an unrelated donor infrastructure.

Interpretation Our findings show achievements and high unmet needs and give guidance for decisions; to grant access for patients, to provide a donor infrastructure, and to limit overuse by defining risk and region adapted indications for HSCT as an efficient and cost-effective approach for life-threatening, potentially curable diseases.

Lancet Haematol 2015; 2: e91–100

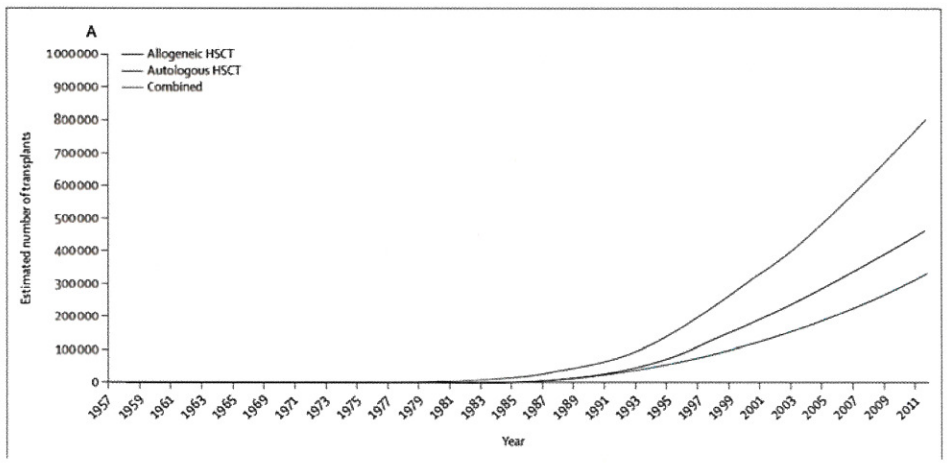
Published Online February 27, 2015 http://dx.doi.org/10.1016/S2352-3026(15)00028-9

See Comment page e83

See Online for podcast interview with Dietger Niederwieser

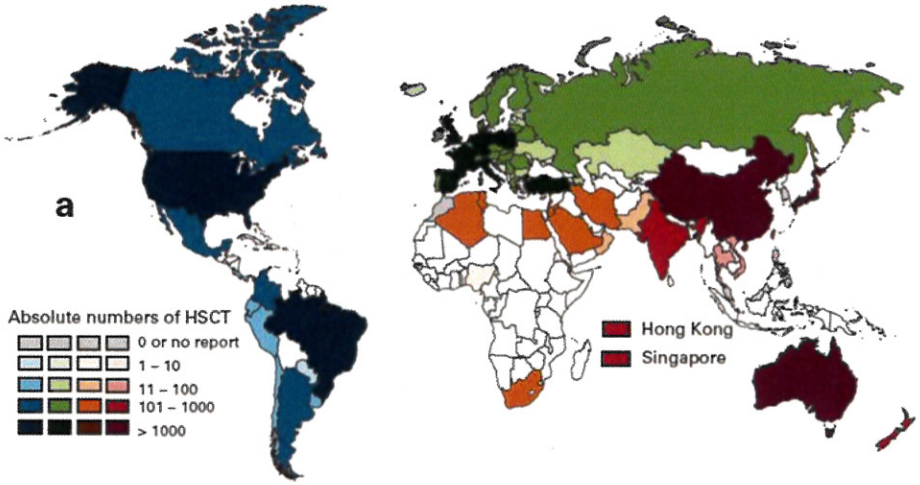
Worldwide Network for Blood and Marrow Transplantation (WBMT) Transplant Activity Survey Office, University Hospital, Basel, Switzerland (Prof A Gratwohl MD, H Baldomero BMS, Prof J Passweg MD); **The Center for International Blood and Marrow Transplant Research (CIBMTR), Medical College of Wisconsin, Milwaukee, USA** (M C Pasquini MD, Prof M Horowitz MD); **The Eastern Mediterranean Blood and Marrow Transplantation**

Cumulative HSCT, 1957-2012

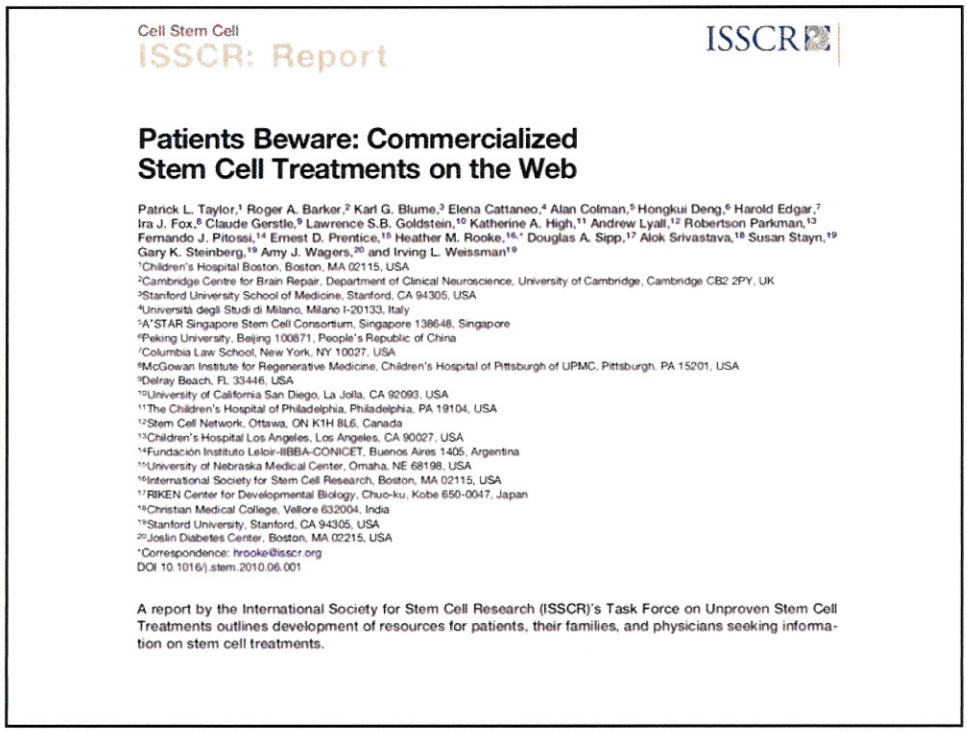


Gratwohl A *et al.*, One million haemopoietic stem-cell transplants: a retrospective observational study, *Lancet Haematology* 2, e91, March 2015

Absolute number of HSCT in participating countries, 2012



Niederwieser D *et al.*, Hematopoietic stem cell transplantation activity worldwide in 2012 and a SWOT analysis of the Worldwide Network for Blood and Marrow Transplantation Group including the global survey, *Bone Marrow Transplantation* 51, 778-785, June 2016; doi:10.1038/bmt.2016.18



Cell Stem Cell
ISSCR: Report

ISSCR

Patients Beware: Commercialized Stem Cell Treatments on the Web

Patrick L. Taylor,[1] Roger A. Barker,[2] Karl G. Blume,[3] Elena Cattaneo,[4] Alan Colman,[5] Hongkui Deng,[6] Harold Edgar,[7] Ira J. Fox,[8] Claude Gerstle,[9] Lawrence S.B. Goldstein,[10] Katherine A. High,[11] Andrew Lyall,[12] Robertson Parkman,[13] Fernando J. Pitossi,[14] Ernest D. Prentice,[15] Heather M. Rooke,[16,*] Douglas A. Sipp,[17] Alok Srivastava,[18] Susan Stayn,[19] Gary K. Steinberg,[19] Amy J. Wagers,[20] and Irving L. Weissman[19]
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[3]Stanford University School of Medicine, Stanford, CA 94305, USA
[4]Università degli Studi di Milano, Milano I-20133, Italy
[5]A*STAR Singapore Stem Cell Consortium, Singapore 138648, Singapore
[6]Peking University, Beijing 100871, People's Republic of China
[7]Columbia Law School, New York, NY 10027, USA
[8]McGowan Institute for Regenerative Medicine, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA 15201, USA
[9]Delray Beach, FL 33446, USA
[10]University of California San Diego, La Jolla, CA 92093, USA
[11]The Children's Hospital of Philadelphia, Philadelphia, PA 19104, USA
[12]Stem Cell Network, Ottawa, ON K1H 8L6, Canada
[13]Children's Hospital Los Angeles, Los Angeles, CA 90027, USA
[14]Fundación Instituto Leloir-IIBBA-CONICET, Buenos Aires 1405, Argentina
[15]University of Nebraska Medical Center, Omaha, NE 68198, USA
[16]International Society for Stem Cell Research, Boston, MA 02115, USA
[17]RIKEN Center for Developmental Biology, Chuo-ku, Kobe 650-0047, Japan
[18]Christian Medical College, Vellore 632004, India
[19]Stanford University, Stanford, CA 94305, USA
[20]Joslin Diabetes Center, Boston, MA 02215, USA
*Correspondence: hrooke@isscr.org
DOI 10.1016/j.stem.2010.06.001

A report by the International Society for Stem Cell Research (ISSCR)'s Task Force on Unproven Stem Cell Treatments outlines development of resources for patients, their families, and physicians seeking information on stem cell treatments.

Approximately 53 programs nationwide doing research in the stem cell field.

Most "stem cell centers" focus on basic research with little or no clinical component.

Most "stem cell treatment centers" emphasize certain clinical treatments but do not educate the public or physicians.

None of the identified stem cell centers provide a comprehensive program of treatment, research, training and education as does the MSCTC

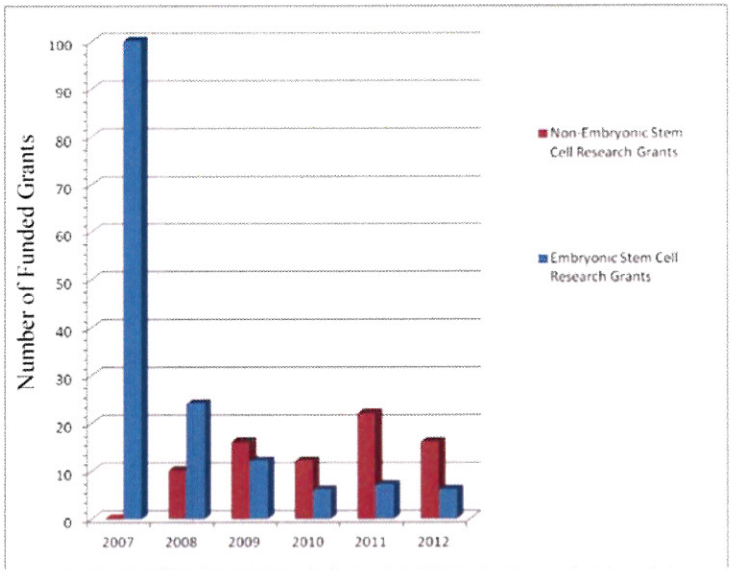
Examples:

- Oklahoma Center for Adult Stem Cell Research (OCASCR)
- Regenerative Medicine Program at the University of Nebraska Medical Center
- Center for Regenerative Medicine and Cell Based Therapies at Ohio State University
- National Center for Regenerative Medicine at Case Western Reserve University
- Tulane Center for Stem Cell Research and Regenerative Medicine
- McGowan Institute for Regenerative Medicine at the University of Pittsburgh Medical Center
- University of Minnesota Stem Cell Institute

Other U.S. State and Collaborative Initiatives

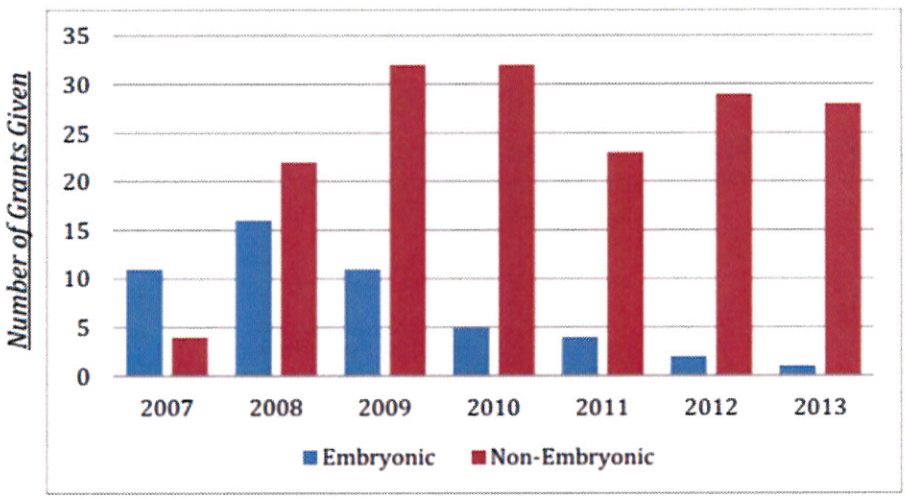
State	Funding Started	Funding Amount	Annual Funding (Average)	Funding to date	Outcomes to date
California	2004	$3B	$172.7M	$1.9B	>>100 grants, 10 clinical studies (FY'15)
Connecticut	2005	Annual Appropriation	$9.8M	$78.6M (2013)	≈ 100 funded research grants
Maryland	2006	Annual Appropriation	$14.4M	$120M (2005-2015) $9.4M in FY'16	349 research grants
New Jersey	2006	$250M	$27.8M	$250M	All for buildings
New York	2007	Annual Appropriation	$37.5M	$300M	> 50 research grants
Minnesota	2013	$50M	$4.3M	≈ $8.7M	None reported
GE Healthcare FedDev Ontario	2016	$28.1M	TBD	$0M	None
Kansas	**2013**	**10.7M**	**$0.9M**	**$2.7M**	**15 research collaborations**

California Funding More Adult Stem Cell Research



From: Gene Tarne, "The Ethical Stems of Good Science", Charlotte Lozier Institute, 2012

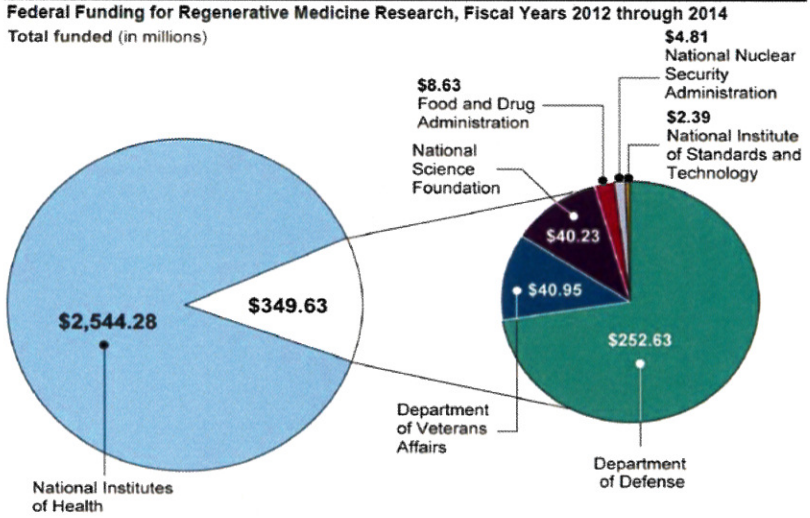
Maryland Funding More Adult Stem Cell Research



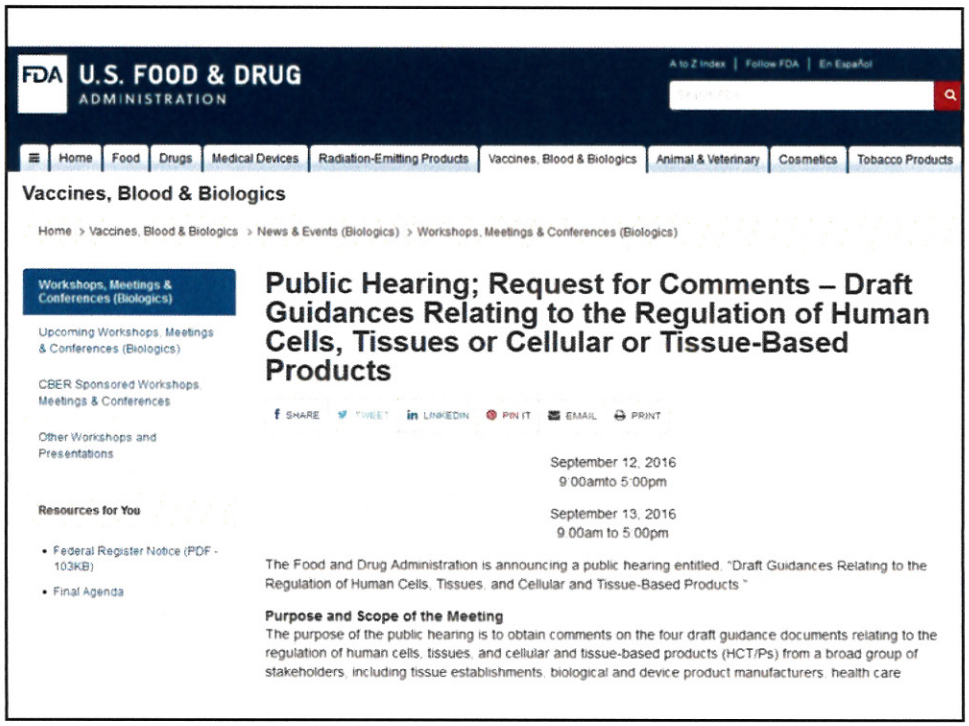
From: Gene Tarne and Andrew Mullins, "Maryland Joins the Trend for Ethical Stem Cell Research", Charlotte Lozier Institute, October 2013

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



Source: GAO analysis of agency funding on regenerative medicine research. | GAO-15-553



Congress votes on sweeping biomedical bill

NIH would get $4.8 billion for key research initiatives

By **Jocelyn Kaiser, Jeffrey Mervis,** *and* **Kelly Servick**

Congress this week was poised to begin voting on a sweeping biomedical innovation bill that includes nearly $5 billion in dedicated funding for a trio of major research initiatives at the National Institutes of Health (NIH). The bill also includes measures to speed the approval of new drugs and medical devices by the Food and Drug Administration (FDA), and it would create a mechanism for catalyzing efforts to streamline federal regulations that universities and academic researchers regard as burdensome.

The bill's FDA provisions aim to accelerate the agency's review of some new drugs and medical devices. In certain cases, FDA would allow companies to run smaller clinical trials or rely on evidence collected outside of trials to support approval. In an apparent bid to boost stem cell and other experimental therapies, the current draft also directs FDA to give special attention to treatments designated as "regenerative advanced therapy." If a treatment meets the criteria—for example, if it is based on stem cells or other tissues and addresses an unmet medical need—regulators can offer a company faster review, or more flexibility in setting trial endpoints.

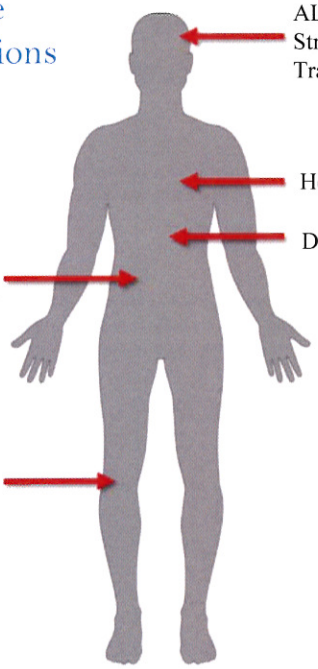
Science Home News Journals Topics Careers

Under 21st Century Cures legislation, stem cell advocates expect regulatory shortcuts

By Kelly Servick | Dec. 12, 2016, 2:45 PM

WEST PALM BEACH, FLORIDA—As the 21st Century Cures Act **cleared the U.S. Senate** last week, many attendees of the annual World Stem Cell Summit (WSCS) here took a victory lap. The meeting assembled some of the lawyers, analysts, and activists who have long pushed for reform of how the U.S. Food and Drug Administration (FDA) handles regenerative medicine. And the **behemoth biomedical bill** predicted to get a presidential signature this week could allow some stem cell products a faster and more flexible premarket approval process.

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.

KU MIDWEST STEM CELL THERAPY CENTER
The University of Kansas

STEM CELLS TRANSLATIONAL MEDICINE

HUMAN CLINICAL ARTICLE

Adipose Mesenchymal Stromal Cell-Based Therapy for Severe Osteoarthritis of the Knee: A Phase I Dose-Escalation Trial

YVES-MARIE PERS,[a,b] LARS RACKWITZ,[c] ROSANNA FERREIRA,[a] OLIVER PULLIG,[d] CHRISTOPHE DELFOUR,[e] FRANK BARRY,[f] LUC SENSEBE,[g] LOUIS CASTEILLA,[h,i] SANDRINE FLEURY,[g,h,i] PHILIPPE BOURIN,[g,i] DANIÈLE NOËL,[b] FRANÇOIS CANOVAS,[k] CATHERINE CYTEVAL,[l] GINA LISIGNOLI,[m] JOACHIM SCHRAUTH,[n] DANIEL HADDAD,[n] SOPHIE DOMERGUE,[o] ULRICH NOETH,[c] CHRISTIAN JORGENSEN,[a,b] ON BEHALF OF THE ADIPOA CONSORTIUM

[a]Clinical Immunology and Osteoarticular Diseases Therapeutic Unit, Lapeyronie University Hospital, Montpellier, France; [b]INSERM, U1183, Saint-Eloi Hospital, Montpellier, France; [c]Department of Orthopaedic Surgery, König-Ludwig-Haus, University of Würzburg, Würzburg, Germany; [d]Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB, Translational Center "Regenerative Therapies for Oncology and Musculoskeletal Diseases," Würzburg, Germany; [e]Department for Cell and Tissue Pathobiology of Tumor, Hospital Saint Eloi, Montpellier, France;

STEM CELLS TRANSLATIONAL MEDICINE 2016;5:847–856

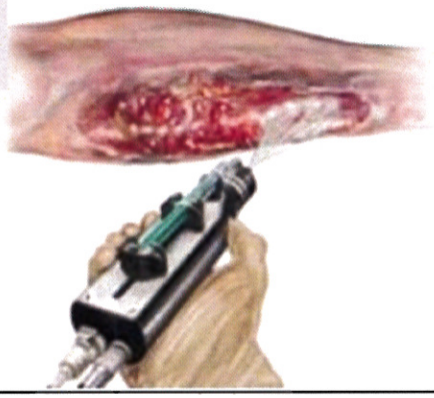
Nasal chondrocyte-based engineered autologous cartilage tissue for repair of articular cartilage defects: an observational first-in-human trial

Marcus Mumme, Andrea Barbero*, Sylvie Miot, Anke Wixmerten, Sandra Feliciano, Francine Wolf, Adelaide M Asnaghi, Daniel Baumhoer, Oliver Bieri, Martin Kretzschmar, Geert Pagenstert, Martin Haug, Dirk J Schaefer, Ivan Martin, Marcel Jakob*

Lancet 2016; 388: 1985-94 October 22, 2016

Interpretation Hyaline-like cartilage tissues, engineered from autologous nasal chondrocytes, can be used clinically for repair of articular cartilage defects in the knee. Future studies are warranted to assess efficacy in large controlled trials and to investigate an extension of indications to early degenerative states or to other joints.

Skin Gun – Spray-On Adult Stem Cells



Second-degree burns with six etiologies treated with autologous noncultured cell-spray grafting

Roger Esteban-Vives [a], *Myung S. Choi* [b], *Matthew T. Young* [a], *Patrick Over* [a], *Jenny Ziembicki* [c], *Alain Corcos* [c], *Jörg C. Gerlach* [a,*]

[a] *Department of Surgery and Bioengineering, McGowan Institute for Regenerative Medicine, University of Pittsburgh, Pittsburgh, PA, USA*
[b] *School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA*
[c] *The University of Pittsburgh Medical Center, UPMC Mercy Hospital Trauma Services and Burn Center, Pittsburgh, PA, U*

studies on this technology, suitable indications will be interesting. We present case information on severe second-degree injuries after gas, chemical, electrical, gasoline, hot water, and tar scalding burns showing one patient per indication. The treatment results with autologous non-cultured cells, support rapid, uncomplicated re-epithelialization with aesthetically and functionally satisfying outcomes. Hospital stays averaged 7.6 ± 1.6 days.

BURNS 37 (2011) 955–974

Calculations for reproducible autologous skin cell-spray grafting

Roger Esteban-Vives [a], *Matthew T. Young* [a], *Toby Zhu* [b], *Justin Beiriger* [c], *Chris Pekor* [a], *Jenny Ziembicki* [d], *Alain Corcos* [d], *Peter Rubin* [e], *Jörg C. Gerlach* [a,*]

[a] *Bioreactor Group, McGowan Institute for Regenerative Medicine, University of Pittsburgh, Pittsburgh, PA, USA*
[b] *The Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA, USA*
[c] *The Department of Bioengineering, Case Western Reserve University, Cleveland, OH, USA*
[d] *University of Pittsburgh Medical Center, UPMC Mercy Trauma and Burn Center, Pittsburgh, PA, USA*
[e] *The Plastic Surgery Department, University of Pittsburgh, Pittsburgh, PA, USA*

BURNS 40 (2014) 1756–1765

Long-term Outcomes After Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis

Paolo A. Muraro, MD; Marcelo Pasquini, MD; Harold L. Atkins, MD; James D. Bowen, MD; Dominique Farge, MD; Athanasios Fassas, MD; Mark S. Freedman, MD; George E. Georges, MD; Francesca Gualandi, MD; Nelson Hamerschlak, MD; Eva Havrdova, MD; Vassilios K. Kimiskidis, MD; Tomas Kozak, MD; Giovanni L. Mancardi, MD; Luca Massacesi, MD; Daniela A. Moraes, MD; Richard A. Nash, MD; Steven Pavletic, MD; Jian Ouyang, MD; Montserrat Rovira, MD; Albert Saiz, MD; Belinda Simoes, MD; Marek Trněný, MD; Lin Zhu, MD; Manuela Badoglio, MSc; Xiaobo Zhong, MS; Maria Pia Sormani, PhD; Riccardo Saccardi, MD; for the Multiple Sclerosis–Autologous Hematopoietic Stem Cell Transplantation (MS-AHSCT) Long-term Outcomes Study Group

IMPORTANCE Autologous hematopoietic stem cell transplantation (AHSCT) may be effective in aggressive forms of multiple sclerosis (MS) that fail to respond to standard therapies.

OBJECTIVE To evaluate the long-term outcomes in patients who underwent AHSCT for the treatment of MS in a large multicenter cohort.

CONCLUSIONS AND RELEVANCE In this observational study of patients with MS treated with AHSCT, almost half of them remained free from neurological progression for 5 years after transplant. Younger age, relapsing form of MS, fewer prior immunotherapies, and lower baseline EDSS score were factors associated with better outcomes. The results support the rationale for further randomized clinical trials of AHSCT for the treatment of MS.

JAMA Neurol. doi:10.1001/jamaneurol.2016.5867
Published online February 20, 2017.

Editorial
Author Audio Interview
Supplemental content

Myasthenia Gravis Treated With Autologous Hematopoietic Stem Cell Transplantation

Adam Bryant, MD; Harold Atkins, MD, FRCPC; C. Elizabeth Pringle, MD; David Allan, MD, MSc; Grizel Anstee, MD; Isabelle Bence-Bruckler, MD, FRCPC; Linda Hamelin, MScN; Michael Hodgins, MD; Harry Hopkins, RPh, FCSHP; Lothar Huebsch, MD, FRCPC; Sheryl McDiarmid, MBA; Mitchell Sabloff, MD, FRCPC; Dawn Sheppard, MD, MSc, FRCPC; Jason Tay, MD, MSc, FRCPC; Christopher Bredeson, MD, MSc, FRCPC

IMPORTANCE Some patients with myasthenia gravis (MG) do not respond to conventional treatment and have severe or life-threatening symptoms. Alternate and emerging therapies have not yet proved consistently or durably effective. Autologous hematopoietic stem cell transplant (HSCT) has been effective in treating other severe autoimmune neurologic conditions and may have similar application in MG.

OBJECTIVE To report 7 cases of severe MG treated with autologous HSCT in which consistent, durable, symptom-free, and treatment-free remission was achieved.

CONCLUSIONS AND RELEVANCE Autologous HSCT results in long-term symptom- and treatment-free remission in patients with severe MG. The application of autologous HSCT for this and other autoimmune neurologic conditions warrants prospective study.

JAMA Neurol. 2016;73(6):652-658. doi:10.1001/jamaneurol.2016.0113

Editorial page 624
Supplemental content at jamaneurology.com
CME Quiz at jamanetworkcme.com and CME Questions page 768

Pharmaceuticals **2015**, *8*, 196-220; doi:10.3390/ph8020196

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Review

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,†]

[1] Blood and Marrow Transplant Program, The University of Kansas Medical Center, 2330 Shawnee Mission Pkwy., Suite 210 Mailstop 5003, Westwood, KS 66205, USA

[2] Department of Anatomy and Physiology, Kansas State University, 1600 Denison Ave., Coles Hall 228, Manhattan, KS 66506-5802, USA; E-Mails: robs32@vet.k-state.edu (J.R.S.); mjzuniga@k-state.edu (M.Z.); weiss@vet.k-state.edu (M.L.W.)

[†] These authors contributed equally to this work.

[*] Author to whom correspondence should be addressed; E-Mail: jmcguirk@kumc.edu (J.P.M.); Tel.: +913-588-6029; Fax: +913-588-3996.

Academic Editor: Shin Mineishi

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

Clinical Track

Adult Bone Marrow Cell Therapy for Ischemic Heart Disease

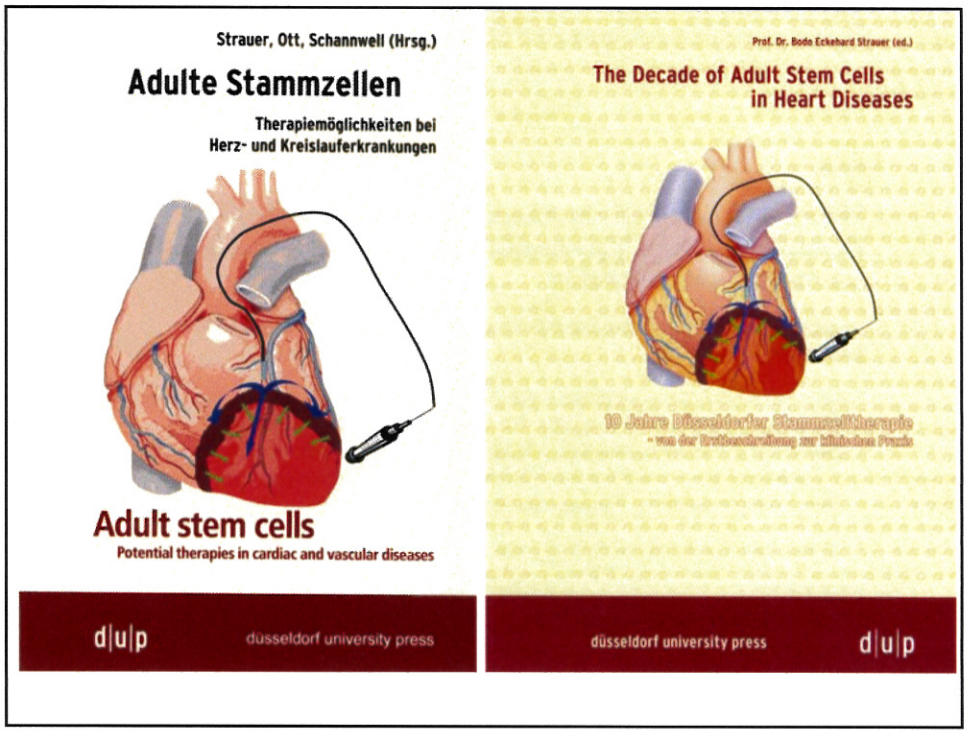
Evidence and Insights From Randomized Controlled Trials

Muhammad R. Afzal, Anweshan Samanta, Zubair I. Shah, Vinodh Jeevanantham, Ahmed Abdel-Latif, Ewa K. Zuba-Surma, Buddhadeb Dawn

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**


Strauer, Ott, Schannwell (Hrsg.)
Adulte Stammzellen
Therapiemöglichkeiten bei
Herz- und Kreislauferkrankungen
Adult stem cells
Potential therapies in cardiac and vascular diseases
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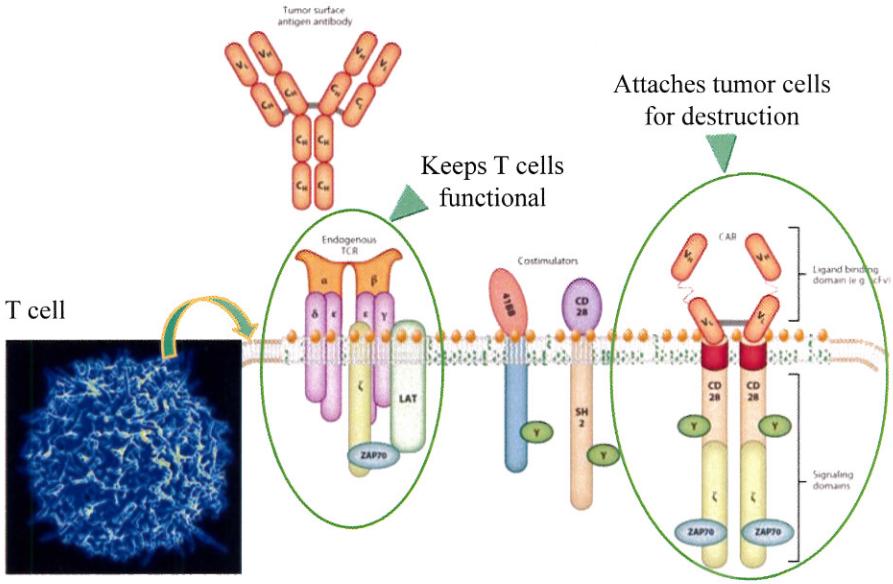
düsseldorf university press
Prof. Dr. Bodo Eckehard Strauer (ed.)
The Decade of Adult Stem Cells
in Heart Diseases
düsseldorf university press
d|u|p


What if you could do this after a heart attack?
ATLANTA – Emory University physicians are revolutionizing heart care by using a patient's own stem cells to restore damaged heart muscle after a heart attack. It's one of hundreds of treatments developed at Emory, where doctors don't just practice medicine, they advance it. For more information, visit www.emoryheart.org.

CAR-T Cell Therapy - Cancers



Source: ninds.nih.gov

Barrett DM, et al. *Annu Rev Med* 2014;65:333-47.

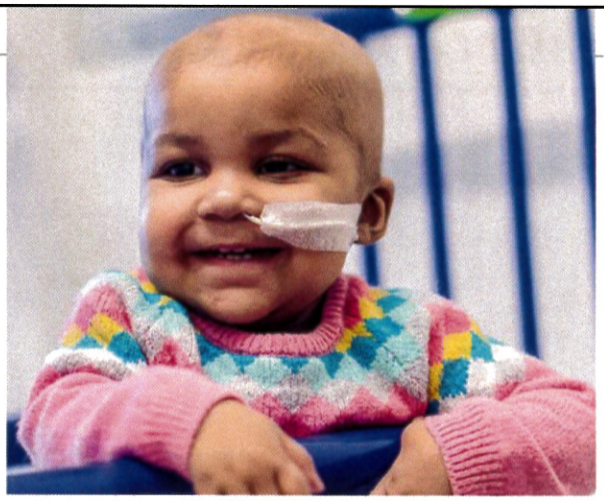
Molecular remission of infant B-ALL after infusion of universal TALEN gene-edited CAR T cells

Waseem Qasim,[1,2]* Hong Zhan,[1] Sujith Samarasinghe,[2] Stuart Adams,[2] Persis Amrolia,[1,2] Sian Stafford,[1] Katie Butler,[1] Christine Rivat,[1] Gary Wright,[2] Kathy Somana,[2] Sara Ghorashian,[1] Danielle Pinner,[2] Gul Ahsan,[2] Kimberly Gilmour,[2] Giovanna Lucchini,[2] Sarah Inglott,[2] William Mifsud,[2] Robert Chiesa,[2] Karl S. Peggs,[3] Lucas Chan,[4] Farzin Farzeneh,[4] Adrian J. Thrasher,[1] Ajay Vora,[5] Martin Pule,[3] Paul Veys[1]

Autologous T cells engineered to express chimeric antigen receptor against the B cell antigen CD19 (CAR19) are achieving marked leukemic remissions in early-phase trials but can be difficult to manufacture, especially in infants or heavily treated patients. We generated universal CAR19 (UCART19) T cells by lentiviral transduction of non–human leukocyte antigen–matched donor cells and simultaneous transcription activator-like effector nuclease (TALEN)–mediated gene editing of T cell receptor α chain and CD52 gene loci. Two infants with relapsed refractory CD19$^+$ B cell acute lymphoblastic leukemia received lymphodepleting chemotherapy and anti-CD52 serotherapy, followed by a single-dose infusion of UCART19 cells. Molecular remissions were achieved within 28 days in both infants, and UCART19 cells persisted until conditioning ahead of successful allogeneic stem cell transplantation. This bridge-to-transplantation strategy demonstrates the therapeutic potential of gene-editing technology.

Qasim *et al., Sci. Transl. Med.* **9**, eaaj2013 (2017) 25 January 2017

CAR-T cells
and
Genetically-modified
stem cell applications



CANCER IMMUNOTHERAPY

Baby's leukemia recedes after novel cell therapy

Gene editing used to create "off-the-shelf" T cells

By Jennifer Couzin-Frankel SCIENCE 13 NOVEMBER 2015 • VOL 350 ISSUE 6262 731

Bone Marrow Transplantation (2010) 45, 111–116

www.nature.com/bmt

ORIGINAL ARTICLE

Autologous peripheral blood CD133+ cell implantation for limb salvage in patients with critical limb ischemia

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We report the safety and feasibility of autologous CD133+ cell implantation into the lower extremity muscles of patients with critical limb ischemia, whose only other option was limb amputation. Nine patients participated in the study: seven patients suffering from arteriosclerosis obliterans, one with thromboangiitis ob-

Introduction

Initial presentation of peripheral arterial disease (PAD) is intermittent claudication with pain in the calf, thigh or buttock that is elicited by exertion and relieved with a few minutes of rest. Over time, the disease progresses to critical

Helen Thomas, 80, was treated for peripheral artery disease with her own adult stem cells. The transplant saved her leg from amputation.

Long-term results of related myeloablative stem-cell transplantation to cure sickle cell disease

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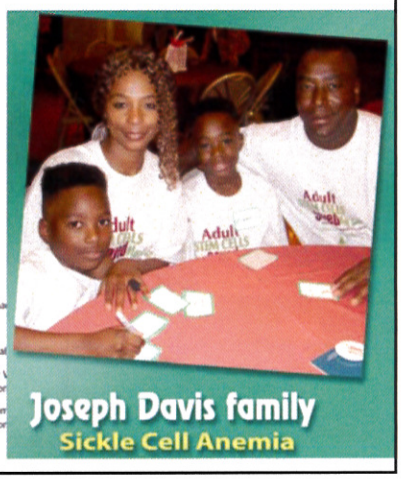
"Hematopoietic stem cell transplantation (HSCT) is the only curative therapy for sickle cell disease."



Original Investigation

Nonmyeloablative HLA-Matched Sibling Allogeneic Hematopoietic Stem Cell Transplantation for Severe Sickle Cell Phenotype

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IMPORTANCE Myeloablative allogeneic hematopoietic stem cell transplantation (HSCT) is curative for children with severe sickle cell disease, but toxicity may be prohibitive for adults. Nonmyeloablative transplantation has been attempted with degrees of preparative regimen intensity, but graft rejection and graft-vs-host disease remain significant.

OBJECTIVE To determine the efficacy, safety, and outcome on end-organ function with this low-intensity regimen for sickle cell phenotype with or without thalassemia.

Editorial
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Stanford researchers 'stunned' by stem cell experiment that helped stroke patient walk

By Ariana Eunjung Cha

The Washington Post

Clinical Outcomes of Transplanted Modified Bone Marrow–Derived Mesenchymal Stem Cells in Stroke: A Phase 1/2a Study

Gary K. Steinberg, MD, PhD; Douglas Kondziolka, MD; Lawrence R. Wechsler, MD; L. Dade Lunsford, MD; Maria L. Coburn, BA; Julia B. Billigen, RN, BS; Anthony S. Kim, MD, MAS; Jeremiah N. Johnson, MD; Damien Bates, MD, PhD; Bill King, MS; Casey Case, PhD; Michael McGrogan, PhD; Ernest W. Yankee, PhD; Neil E. Schwartz, MD, PhD

Background and Purpose—Preclinical data suggest that cell-based therapies have the potential to improve stroke outcomes.

Methods—Eighteen patients with stable, chronic stroke were enrolled in a 2-year, open-label, single-arm study to evaluate the safety and clinical outcomes of surgical transplantation of modified bone marrow–derived mesenchymal stem cells (SB623).

Results—All patients in the safety population (N=18) experienced at least 1 treatment-emergent adverse event. Six patients experienced 6 serious treatment-emergent adverse events; 2 were probably or definitely related to surgical procedure; none were related to cell treatment. All serious treatment-emergent adverse events resolved without sequelae. There were no dose-limiting toxicities or deaths. Sixteen patients completed 12 months of follow-up at the time of this analysis. Significant improvement from baseline (mean) was reported for: (1) European Stroke Scale: mean increase 6.88 (95% confidence interval, 3.5–10.3; $P<0.001$), (2) National Institutes of Health Stroke Scale: mean decrease 2.00 (95% confidence interval, −2.7 to −1.3; $P<0.001$), (3) Fugl-Meyer total score: mean increase 19.20 (95% confidence interval, 11.4–27.0; $P<0.001$), and (4) Fugl-Meyer motor function total score: mean increase 11.40 (95% confidence interval, 4.6–18.2; $P<0.001$). No changes were observed in modified Rankin Scale. The area of magnetic resonance T2 fluid-attenuated inversion recovery signal change in the ipsilateral cortex 1 week after implantation significantly correlated with clinical improvement at 12 months ($P<0.001$ for European Stroke Scale).

Conclusions—In this interim report, SB623 cells were safe and associated with improvement in clinical outcome end points at 12 months.

Clinical Trial Registration—URL: https://www.clinicaltrials.gov. Unique identifier: NCT01287936.

(*Stroke*. 2016;47:00-00. DOI: 10.1161/STROKEAHA.116.012995.)

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