# Midwest Stem Cell Therapy Center

## *Annual Report*

Legislative Update

Senate Public Health and Welfare Committee
Senate Ways and Means Committee

February 8, 2016

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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

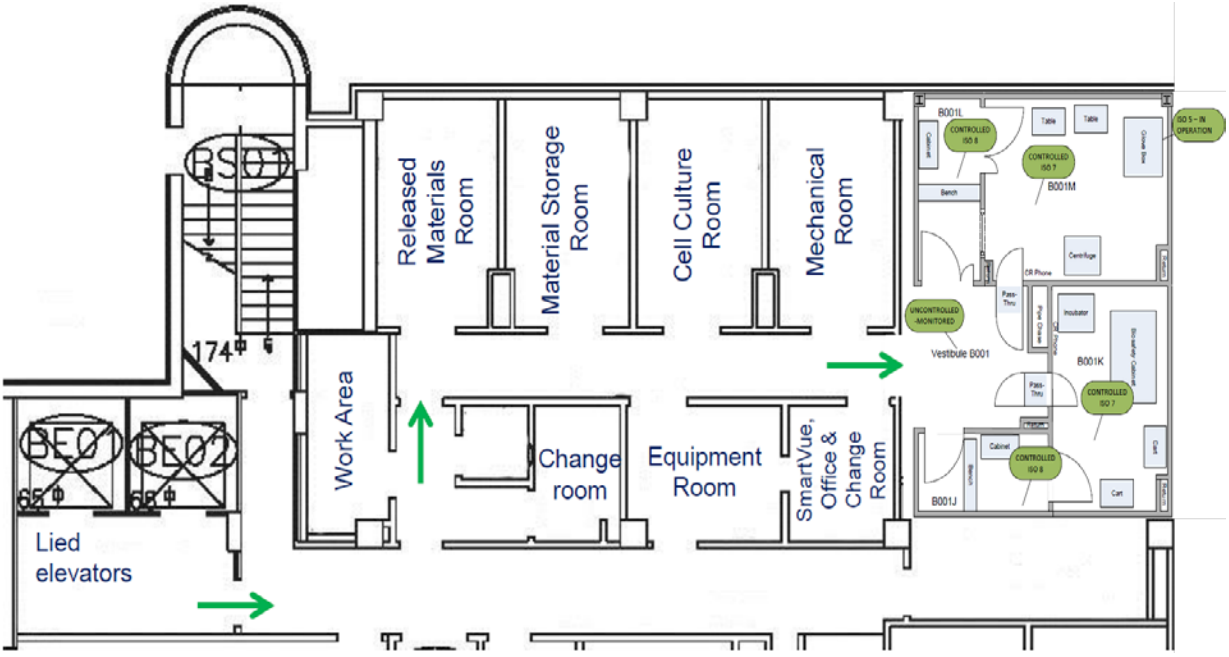
### A. ADVISORY BOARD

- 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

- **<u>Plans</u>:**
  - 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

- **<u>Accomplishments</u>**
  - 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

- **<u>Plans</u>**:
  - 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

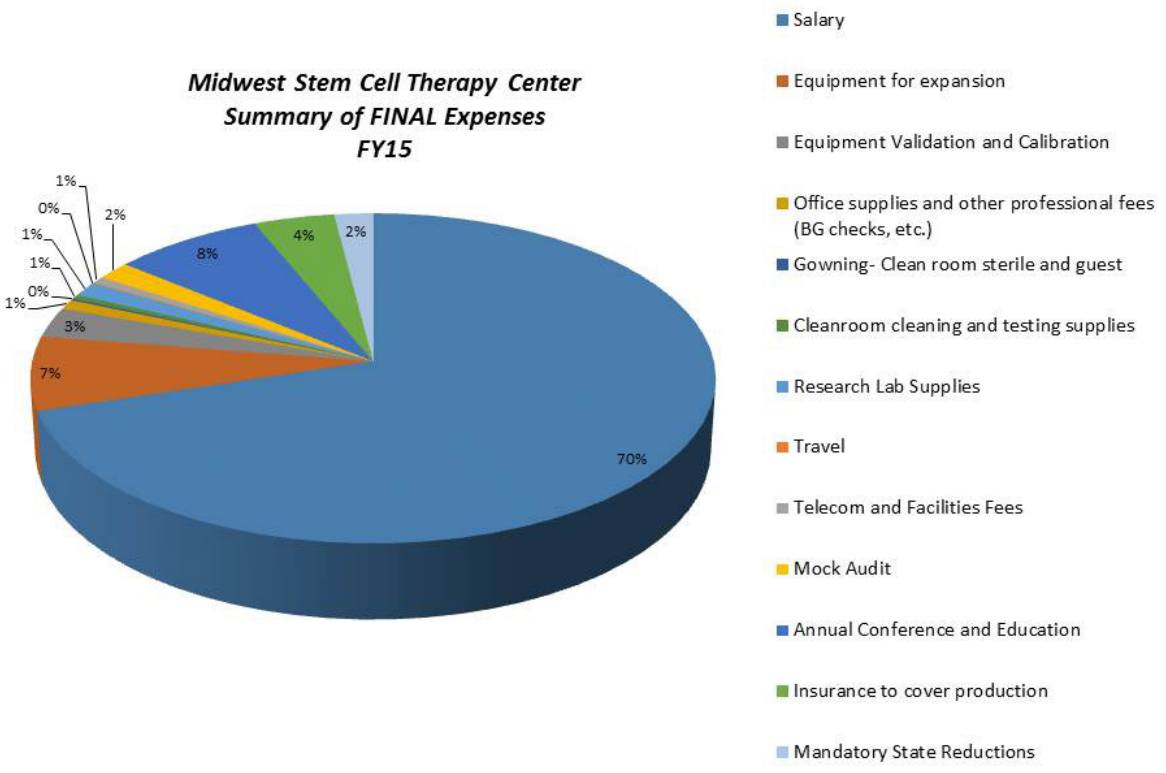
- **Plans:**
  - Continue outreach efforts with potential clients seeking adult stem cell manufacturing locations
  - Continue periodic updates of the MSCTC website
  - Advertise at Kansas universities and other locations in the Midwest regarding stem cell collaborations and GMP manufacturing

## 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 |
| Legisltative 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.**