Midwest Stem Cell Therapy Center

Annual Report

Legislative Update

Senate Public Health and Welfare Committee
Senate Ways and Means Committee

April 30, 2015

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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

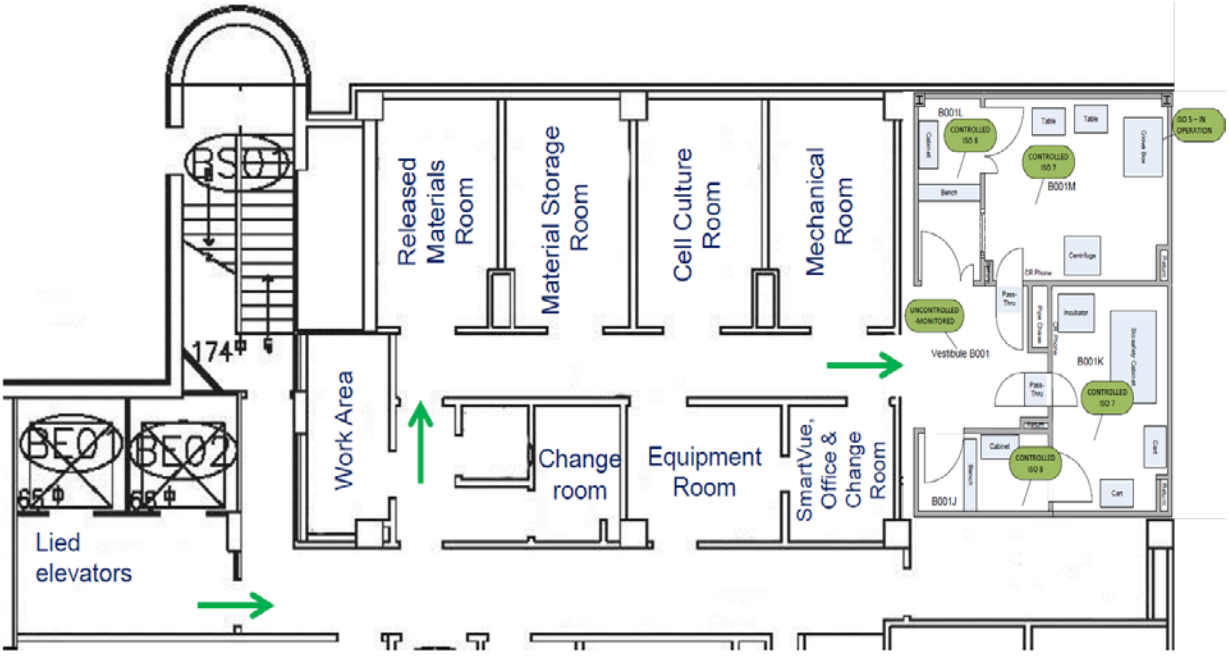
A. ADVISORY BOARD

- 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 6 meetings of the Board thus far, with the next meeting scheduled for June 5, 2015.

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: Recruited
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) 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). The concepts underlying all of these guidelines are directed at the ultimate goal of safeguarding the health of the patient. GMP 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 facility is a necessary aspect of processing and manufacturing clinical grade cellular products.

MSCTC's FDA registered GMP facility (FEI# 3011110836):

- Adheres to GMP 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 and the Wharton's Jelly fraction of human umbilical cord
- 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 inaugural conference was held Nov 23, 2013
            - 18 speakers and panelists and approximately 150 attendees
            - Extremely positive feedback
        - The third annual conference is scheduled for September 18 and 19, 2015
    - 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:**
    - Two 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
- **Plans:**
    - The Third Midwest Conference on Cell Therapy and Regenerative Medicine (Sep 18-19, 2015) will be held at the Kansas City Convention Center
    - Update MSCTC website with clinical trial information from www.Clinicaltrials.gov
    - 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**
    - Completed clinical trial manufacturing of multiple batches of bone marrow stem cells for evaluation in critical limb ischemia patients
    - 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 completed in 12/2013, participant long-term follow-up until 12/2014
    - Agreement in place as a clinical site for the conduct of the Capricor sponsored ALLSTAR clinical study
        - Intracoronary injection of cardiac stem cells in patients with heart attacks
    - Initiated umbilical cord stem cell project with the Kansas University Cancer Center
        - Successfully isolating and expanding adult stem cells from human umbilical cord
        - Project likely to lead to the first adult stem cell IND from the MSCTC
    - Preliminary discussions completed and SBIR submitted for gene therapy to treat aplastic anemia. This is a collaboration with Stowers and a private California company

- **Plans:**
  - Continue to identify and collaborate with internal research laboratories who are identifying possible disease specific adult stem cell applications
  - 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
  - **Exciting future trials include**:
    - Chimeric antigen modification of immune cells for patients with melanoma and other solid tumors
    - 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 has 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 Facilities registration updated
    - Expanded GMP facilities registration beyond bone marrow cells to also include umbilical cord as a stem cell source
    - Expanded GMP facilities registration to include induced Pluripotent Stem Cells as potential products
  - Completed external GMP audit
    - Observations addressed
  - FDA contact made regarding pre-clinical and clinical requirements
    - Investigational New Drug Application (IND) template developed for adult stem cells
  - Developed specific IND plan for umbilical cord adult stem cells evaluation in the treatment of GvHD
    - initiated Pre-IND communication with the FDA for GvHD project
- **Plans**:
  - Meet with FDA District Office to discuss facility and future efforts
    - FDA District Office representatives agreed to meet just prior to first IND submission
  - Complete GvHD related Pre IND meeting with the FDA
  - Complete preclinical studies, agreed to with the FDA, and submit IND

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.
  - 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 recruit additional scientists and clinicians from other specialties
    - Postdoctoral fellows and Research Associates

- **<u>Accomplishments</u>**
  - Initiated 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
  - Preliminary discussions underway to evaluate stem cell applications in the treatment of Inclusion Body Myositis (IBM)
    - Collaboration with Drs. Mazen Dimachkie, and Richard Barohn, neurologists and clinician scientists

- **<u>Plans</u>**:
  - Complete proof of principle studies in ALS
  - Conduct initiate evaluation of umbilical cord MSCs for potential impact on heart repair following a heart attack
  - Based on preliminary discussions, initiate proof of principle study to evaluation adult stem cell applications in the treatment of IBM.

- Finalize decisions on ALS and IBM and, as appropriate, initiate discussions with the FDA related to the appropriate R&D path to IND(s) for each of these orphan diseases

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 will be 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.

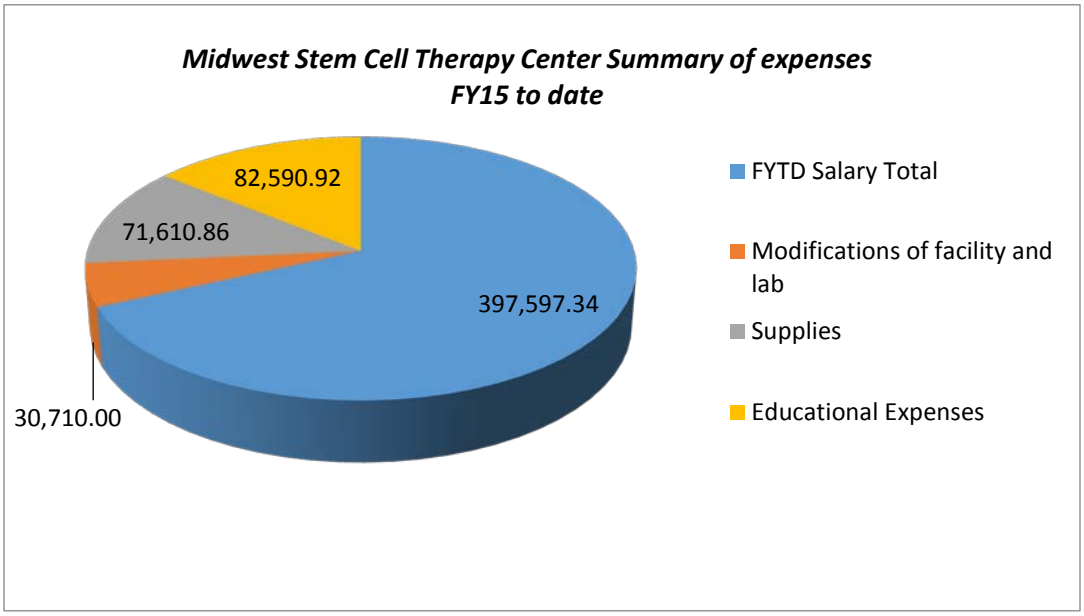
- **Accomplishments:**
  - Initiated the Communications and Marketing effort on April 1, 2015
    - Developed plan to Market the Midwest Stem Cell Therapy Center to capitalize on third party adult stem cell manufacturing
    - 54 small to mid-size companies have been identified as potential clients for GMP stem cell manufacturing
      - Original client contact plan delayed to allow establishment of Communications and Marketing effort with experienced staff member
- **Plans:**
  - Implement potential clients contact effort in July, 2015
    - Follow up with phone conversation in August if no response received
    - For potential clients who attend the 2015 Midwest Conference on Cell Therapy and Regenerative Medicine, set meeting to speak to them directly
  - Update MSCTC website
  - Advertise at Kansas universities and other locations in the Midwest regarding stem cell collaborations and GMP manufacturing

I. EXPENSE REPORT

FY15 – Total amount received: $754,500

TABLE 1: *Actual Expenses through 3/31/2015*

		% total
Salary Total	*397,597.34*	*51%*
Modifications of facilities	*710.00*	*0%*
Supplies	*71,610.86*	*9%*
Educational Expenses	*82,590.92*	*11%*
Total Expenses to date (less Educational income)	*552,509.12*	*73%*



1. Salary – this figure comprises the salary and fringe of the Director, GMP Facility Manager, Scientist, Executive Assistant, Financial Assistant, Quality Assurance Supervisor, Quality Control Supervisor, Research Associate Production, Communications Specialist, and Regulatory Assistant.

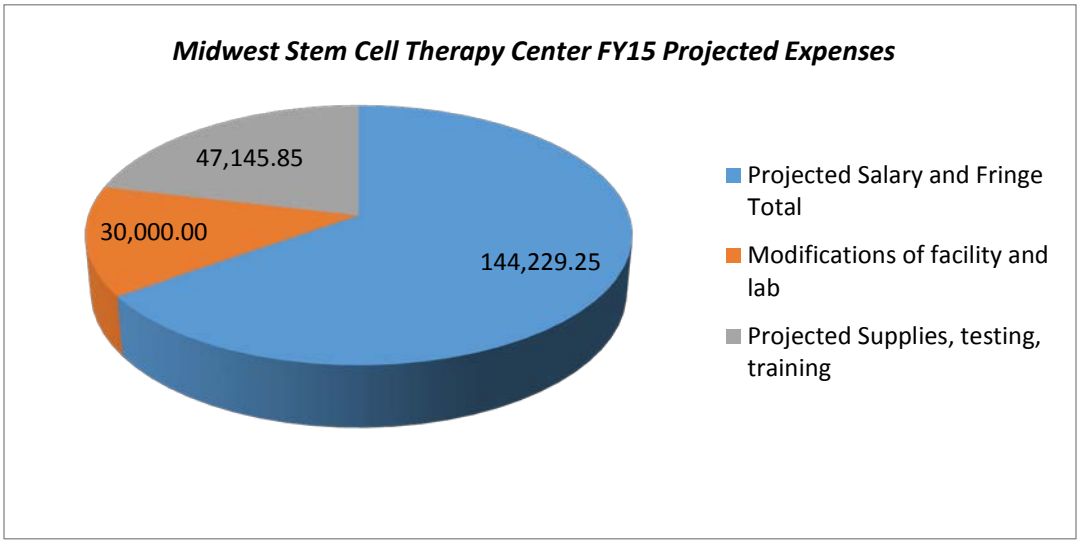
2. Modifications of facilities – although our state of the art clean room facility meets FDA standards and requirements, we will be contracting with AES to modify the clean room and the projected expense will be $30,000 (see in Table 2.)

3. Supplies – the biggest portion of our supply expenses is spent on insurance. Of the $71,610.86, $10,953.30 was for validation and calibration; $13,500 was paid to a 3rd party group for a mock audit to ensure we are in FDA compliance; and $31,500 was paid to carry insurance for the production of our clinical study supplies. The remaining was supplies to maintain clean room standards, gowning supplies for both guests to enter the suite and the production staff in the clean room, and other various operating expenses.

4. Educational Expenses – we held our second conference, Midwest Conference on Cell Therapy and Regenerative Medicine, on September 18th and 20th 2014. It was organized with collaboration from the KUMC Division of Continuing Education. There were 187 attendees present from all over the country. The conference generated $23,097 in registration, vendor fees, and industry contributions.

TABLE 2: *Projected Expenses for remaining FY15*

		% total
Projected Salary and Fringe Total	*144,145.85*	*19%*
Projected Supplies	*47,145.85*	*4%*
Modifications of facilities	*30,000.00*	*4%*
Projected Expenses	*221,291.70*	*29%*

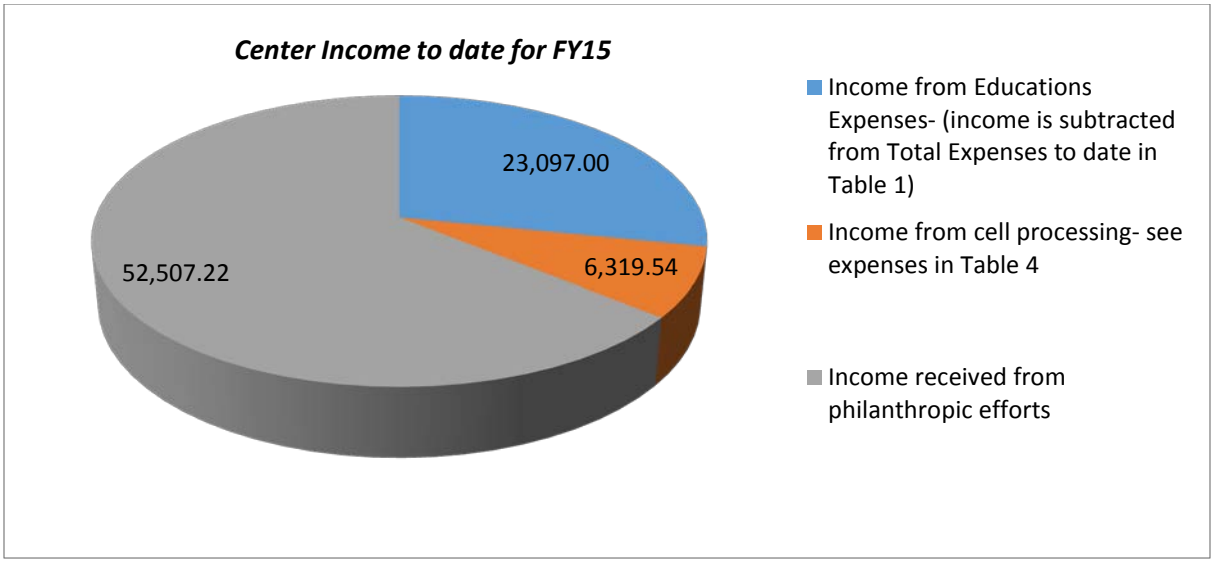


1. Projected Salary – comprises the salary and fringe for the remainder of FY15.
2. Projected Supplies – will need to have additional equipment validated and certified and will continue to maintain a clean room standard with cleaning and gowning supplies and other various operating expenses.
3. Modifications of facilities – we will need to modify our GMP Clean Room suite to accommodate growth and new equipment for future studies.

J. INCOME REPORT

TABLE 3: *Center Income to date for FY15:* ***Total $81,923***

Income from Educations Expenses- (income is subtracted from Total Expenses to date in Table 1*)*	*23,097.00*
Income from cell processing- see expenses in Table 4	*6,319.54*
Income received from philanthropic efforts	*52,507.22*



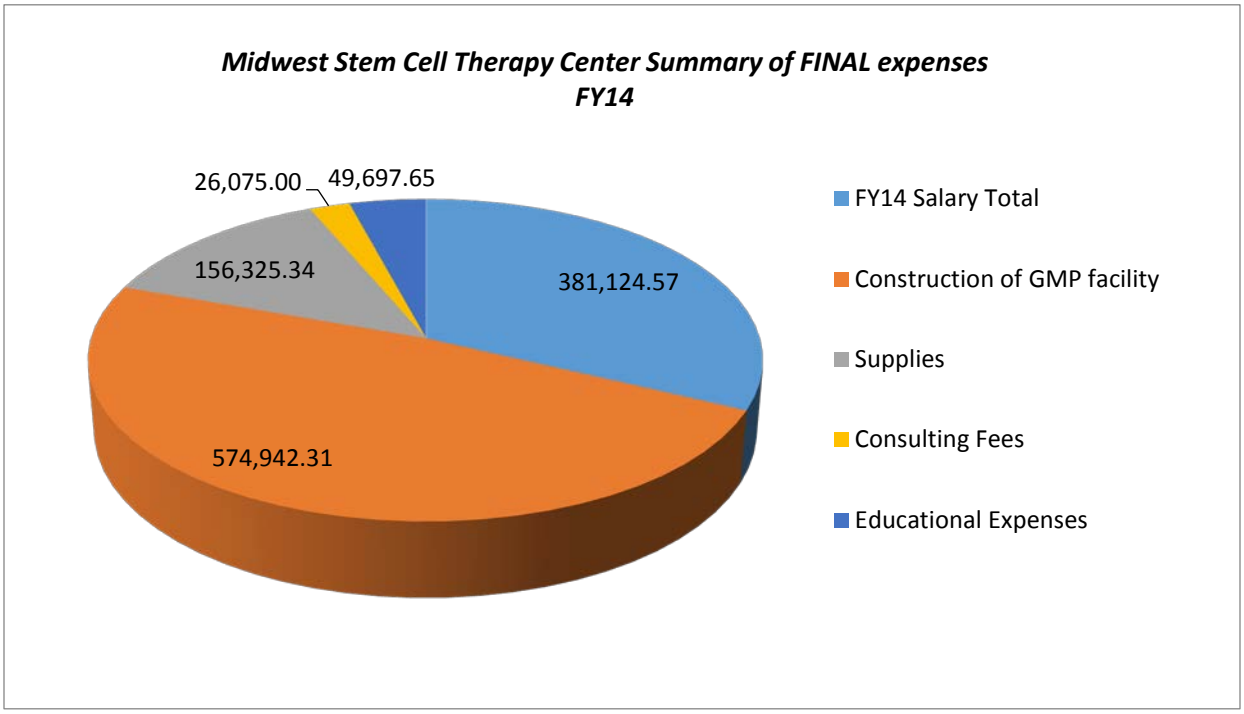
1. Income from educational activities – as in Table 1, we generated a small income for the conference. The attendees paid a registration fee and we had 4 vendors who paid to exhibit for the duration of the conference. We were able to apply this income to the entire balance due for the conference- making the total expense for the conference $59,493.92 and off-setting the financial burden to a limited extent.
2. Income from cell processing – we currently have one sponsor study underway in MSCTC. Like for all future studies, our intention is to conduct clinical trials with a sponsor, which will generate income for the Center.
3. Income from philanthropy: The MSCTC received donations from a number of individuals during the 'ice bucket challenge' in 2014.

Table 4: *FY15 Income for clinical studies*	*6,319.54*	Percentage of total income
Expenses for Study Income		
Testing supplies for study specific (particle count plates)	1,349.00	*21%*
Cleaning supplies for study specific production	1,457.26	*23%*
Total Study related expenses	*2,806.26*	*44%*

1. Study expenses – we are able to charge the study sponsor for specific supplies needed for their study and the expense is paid from the income received
2. The insurance for the production was paid by the MSCTC.
3. Training supplies – for new studies and staff, training is conducted with materials supplied by the sponsor or, utilizing umbilical cord MSCs obtained from consenting donors at no cost.
4. Testing supplies – the study SOP will dictate if any additional particle testing be performed, and if so, testing supplies are charged against the income.

TABLE 5: *Fiscal Year 2014 Final Expenses*

FY14 Salary Total	*381,124.57*	*32%*
Construction of GMP facility	*574,942.31*	*48%*
Supplies	*156,325.34*	*13%*
Consulting Fees	*26,075.00*	*2%*
Educational Expenses	*49,697.65*	*4%*
Total Expenses for FY14	*1,188,164.87*	



K. 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:

- 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
- Reaching self-sustainability with a multipronged approach: cell manufacturing, marketing, and licensing.
- Acquiring state-of-the-art instrumentation for cell processing, outcome assessment, in vivo imaging, stem cell sorting (FACS), 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.