

# **Midwest Stem Cell Therapy Center**

## ***2022 Annual Report***

Legislative Update

Senate Ways and Means Committee / Senate Public Health and Welfare Committee  
House Appropriations Committee / House Health and Human Services Committee

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### **I OVERVIEW**

Adult stem cell transplantation has been shown as an effective therapeutic option for organ repair in certain situations and in the case of bone marrow stem cells, able to cure disease. Evidence from numerous scientific reports, both from animal models and human studies, continues to support the notion that adult stem cells may heal damaged tissues and restore function. Scientific evidence supports the potential efficacy of adult stem cell therapy for diverse pathological conditions, such as acute graft versus host disease, stroke, spinal cord injury, and many others.

Until the passage of KS Senate bill No. 199, there was no comprehensive center or program in Kansas or the surrounding region for the investigation and development of adult stem cells for treating various human health conditions. This bill enabled the establishment of the Midwest Stem Cell Therapy Center (MSCTC) in July 2013, at the University of Kansas Medical Center and implementation of a coordinated effort for the identification and development of potential application for non-embryonic stem cells.

### **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 was developed and implemented, as outlined below.

### III. COMPONENTS AND PROGRESS REPORT

#### A. ADVISORY BOARD

- An Advisory Board representing various stakeholders was assembled with periodic reappointment or replacement of individual members at intervals specified in the bill.
  - Information related to individual members is available at [www.kumc.edu/msctc](http://www.kumc.edu/msctc).
- The Board meets Quarterly and, as necessary, to assure continued MSCTC progress
  - The next meeting is scheduled for 7<sup>th</sup> March 2022.
  - Current Board members include
 

David Prentice, PhD	Senator Mike Thompson
Weijing Sun, M.D.	Bassam Mattar, MD
Frank Blecha, PhD	Matthias Salathe, M.D.
Ms. Ruth Colyer	Representative Dan Hawkins
Greg Lakin, DO	Mr. Jeff Wright
Jenny Robinson, PhD	Scott Weir, Pharm.D., PhD
James Sherley, M.D., PhD	

#### B. SCIENTIFIC AND ADMINISTRATIVE PERSONNEL

1. Center Director: Recruited
2. GMP Manager: Recruited
3. Research Associate, Production: Recruited
4. Research Associate, Production): Recruited
5. Quality Control Supervisor (0.5FTE): Recruited
6. Quality Assurance Supervisor (0.5FTE): Recruited
7. Administrative Assistant (0.5 FTE): Recruited

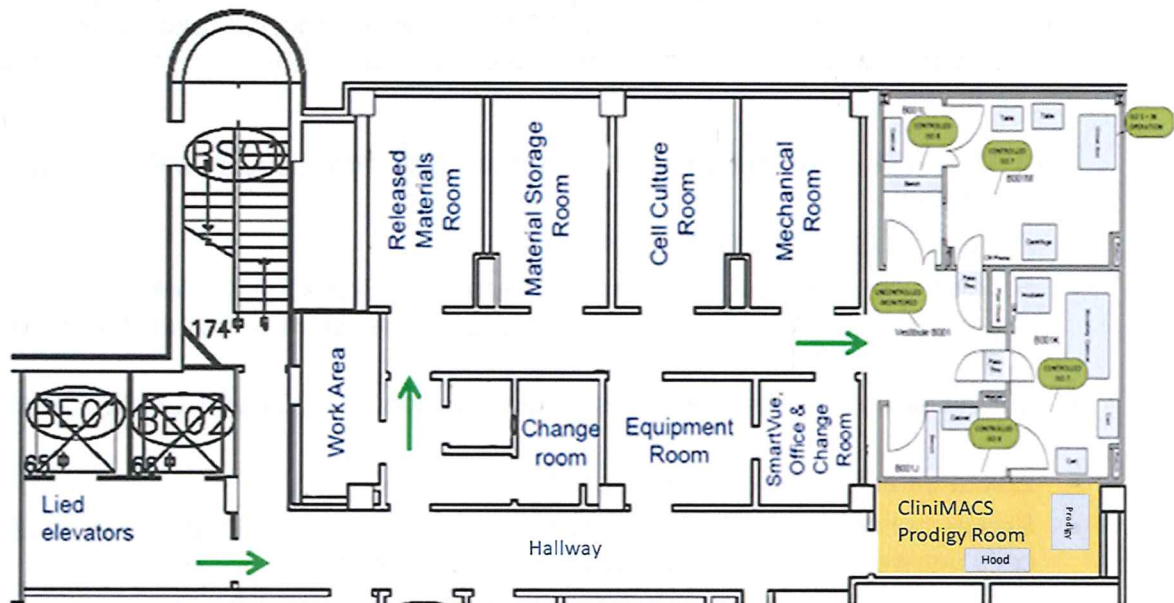
#### C. Scientific Advisory Committee

1. A 7-member Scientific Advisory Committee was formed in Sept 2018. Members are from KUMC and represent Neurology, Orthopedics, Diseases of the aged, Oncology, Pharmacology and Toxicology, and Legal, with the purpose to identify

and foster the development of adult stem cell applications in the treatment of various human health conditions and guide the MSCTC in this mission.

2. The Scientific Advisory Committee meets every 4 months and, as necessary, to assure continued progress on agreed upon projects. The next meeting is scheduled on in Feb 2022.

#### D. FACILITY FOR CLINICAL GRADE CELL PROCESSING/MANUFACTURING



The MSCTC within KU Medical Center currently occupies approximately 4270 ft<sup>2</sup> of space (including office [943 ft<sup>2</sup>], laboratories [1815 ft<sup>2</sup>] and GMP manufacturing [1508 ft<sup>2</sup>] areas). The space is utilized for R&D related to cell isolation and expansion, process development, analytical methods development, quality control testing and clinical grade adult stem cell manufacturing. The manufacturing area is an FDA registered facility and is designed and operates to meet FDA compliance and environmental quality requirements as defined in the Good Manufacturing Practice (GMP) and Good Tissue Practices (GTP) guidelines. In 2021 another room was added next to the GMP space which houses the CliniMacs bioreactor (highlighted in yellow in above diagram) that will be used for CAR T manufacture and cell separation and growth.

'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 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.

The GMP/GTP facilities were established in 2013 and they need upgrading and renovation which will be undertaken in 2022. These changes will also meet the FACT accreditation standards. Approximately 50,000\$ funds will be used for this purpose in the fiscal year

**MSCTC's FDA registered Good Manufacturing Practices (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)
- Educates and trains all relevant personnel
- Serves current MSCTC efforts well with capacity for up to 4 batches of adult stem cells per week if staffed and equipped to address volume
- The lab space is being expanded to accommodate the CAR cell manufacturing

**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 the Wharton's Jelly fraction of human umbilical cord, dental pulp stem cells and cells provided by industry sponsors – these include bone marrow stem cells.
  - Developing cell culture and cell expansion processes as well as characterization methodology suitable for specific therapeutic purposes
  - Expansion and banking of adult stem cells for future use by donors
  - Manufacturing of expanded/activated gamma delta T cell subsets for immunotherapeutic implications
  - GMP capabilities to support processing of stem cell therapy for various sponsor initiated clinical trials

## E. 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 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 conversation with those enquiring about stem cells
  - Professional and public forums like town hall or similar meetings

- **Accomplishments:**

- Seven successful conferences on adult stem cell therapy with the 7<sup>th</sup> Annual Midwest Conference on Cell Therapy and Regenerative Medicine held on September 19th, 2020. Due to the pandemic the conference was virtual.
  - There were 24 speakers and panelists and approximately 162 attendees at the virtual event. Continuing medical education units were given to eligible attendees.
- In lieu of a 2019 Midwest Conference on Cell Therapy and Regenerative Medicine, members of the MSCTC in collaboration with medical departments at the University of Kansas Medical Center presented at various locations to update the Medical Centers and the public regarding advances in adult stem cell research and therapy. In 2020 and 2021 due to the pandemic live meetings were not held but virtual meetings were done instead at the following events
  - KUMC-Salina
  - KU Medical Center, Kansas City- Research and Discovery Rounds
  - KUMC- Hays Medical Center (04/2021)
  - MSCTC Webinar in collaboration with Sartorius (10/2021)
- 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 website is also linked to ClinicalTrials.gov, the NIH/FDA database for global clinical trials which provides immediate access to the most current clinical trial information on a global basis via defined searches in the most sought-after areas of stem cell therapy available
- A total of eight students have thus far gained first-hand, meaningful scientific experience in adult stem cell research and therapy. They include 4 Medical Students (KU School of Medicine), one undergraduate student from the Ohio

State University, and three-high school students from Kansas City, KS and New York, NY

- **Plans:**
  - Continuation of updates to the MSCTC Facebook webpage with trending scientific information regarding adult stem cell therapy
  - Continuation of “town hall’ virtual meetings to disseminate information related to stem cell therapies in Kansas. Will look forward to hosting live events in 2022!
  - Present our research at National and International meetings related to adult stem cell research and therapy.
  - Planning is being finalized for the 8<sup>th</sup> Midwest Conference on Cell Therapies and Regenerative Medicine for Sept 16<sup>th</sup>, 2022. Due to the ongoing pandemic, this conference will again be virtual.

## F. CLINICAL TRIALS AND THERAPY

- **Accomplishments – In 2021, due to circumstances related to the pandemic, commencement of new trials and enrollment on current trials was slower than anticipated.**
  - In collaboration with the University of Kansas Cancer Center, MSCTC completed a Phase I human clinical trial utilizing adult stem cells isolated from human umbilical cord, for the treatment of Graft vs Host Disease. This safety trial represents the first adult stem cell product candidate (MSCTC-0010) developed within the Midwest Stem Cell Therapy Center. The trial was a 10-patient safety study and was completed in Sept 2019.
  - Abstract of the Phase I GvHD study was presented as a poster at the virtual International Society Cell and Gene Therapy (ISCT) meeting held on 05/28-05/29/20. This clinical study was published in Stem cell Review and Reports in Aug 2020. doi: 10.1007/s12015-020-10015-8.
  - This study has now expanded to Phase Ib study for 10 additional patients with increased dose of the MSCTC-0010. Two patients were enrolled and infused on this Phase Ib clinical protocol in 09/2021.
  - In collaboration with In8Bio and the University of Kansas Cancer Center, initiated a First-in-human Phase I trial of ex vivo expanded and activated  $\gamma\delta$  T Cells (EAGD) following haploidentical BMT and post-BMT cyclophosphamide. The study enrolled 6 patients.
  - Project with Plus Therapeutics using adipose derived stem cells-In collaboration with Dr. Dimachkie (KU- Neurology), MSCTC, and KU research institute submitted proposals to the FDA for using adipose derived stem cells as a therapy for inclusion body myositis (IBM). FDA approved the IBM protocol, and a 6 patient study is initiated by Fall 2021 and awaiting patient recruitment.
  - MSCTC is a contract manufacturer for MSCTC-0010 product for a Phase I bradykinesia study by IMAC Regen. IMAC Regen has an approved IND to initiate the

clinical trial (15 patient study) using MSCTC-0010 cell therapy product. The study has opened and enrolled 7 patients.

- MSCTC is an investigational product storage, handling, and dispensing site for MASTERS-2 clinical trial (sponsored by Athersys, Inc.). Two patients have been enrolled in this study
  - Administration of allogeneic adult bone marrow stem cells for treatment of acute ischemic stroke and enhanced recovery
- MSCTC is an investigational product storage, handling, and dispensing site for ADMIRE-CDII clinical trial (sponsored by TiGenix, Inc.). Seven patients have been enrolled in this study
  - Administration of allogeneic adult adipose derived stem cells for treatment of perianal fistula in patients with Crohn's disease
- Acute Myeloid leukemia vaccine study: this study is in collaboration with Beth Israel Hospital and has been IRB approved at KUMC. MSCTC will manufacture the hybridoma vaccine in the GMP space.
- Continuing to collaborate with a California company to recover and bank adult dental pulp stem cells under a 20-year contract
  - Revenue continues to be realized
- **Plans:**
  - Grant funding has been submitted in collaboration with the University of Kansas Cancer Center, for a Phase II study for the demonstration of efficacy of MSCTC-0010 in acute graft versus host disease.
  - Collaboration with Dr. Nirali Shah from the NIH for the manufacture of Chimeric Antigen Receptor -T cells in the GMP lab for the treatment of lymphoma.
  - Continue to identify and collaborate with internal research laboratories who are identifying possible disease specific adult stem cell applications – orthopedics, hepatology, neurology and pulmonary medicine.
  - Foster collaborations with external 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
  - Establish cryopreserved batches of Wharton's Jelly mesenchymal stem cells by 3D manufacture process developed at the MSCTC. This will involve the purchase of 2 bioreactors. These cells will be used for the Phase II acute graft versus host disease clinical trial
  - Obtain funding for a trial of MSCTC-0010 in Covid and viral related pulmonary complications in patients needing care in the intensive care unit.

## G. 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
    - adipose tissue
    - Peripheral blood mononuclear cells
- Developed and gained approval for Wharton's Jelly MSC-specific IND for the treatment of GvHD
- In collaboration with KU Neurology and Plus Therapeutics, MSCTC assisted and gained approval for IDE from the FDA to test the safety of adipose derived stem cells for Inclusion body myositis
- In 2021 the GMP lab underwent an exhaustive overview of its operations, including review of standard operating procedures, quality audits and compliance. This was undertaken by Cardinal Health as well as consultation with the Federation for the Accreditation of Cellular therapy (FACT). Recommendations from these reviews are being implemented with the goal of the GMP lab to be FACT accredited in the future.

- **Plans:**

- Continue evaluation of additional applications for MSCTC-0010 that can capitalize on the work already completed and further potential uses for these MSCs
- Continue quality improvements as specified by FACT guidelines with the goal of FACT accreditation

## H. RESEARCH PROGRAM

- **Laboratory stem cell researchers**

- Basic scientists/Translational researchers
  - Hartmut Jaeschke, Ph.D. (KUMC Hepatology)
  - Randolph Nudo, Ph.D. (KUMC Neurology – Stroke and TBI)
  - Jinxi Wang, M.D., Ph.D. (KUMC Orthopedics)



- Linheng Li, PhD (Stowers' Institute -Stem cell expansion)
  - Andy Godwin, PhD (KUMC, Pathology)
  - David Akhavan, M.D., Ph.D. (KUMC Radiation Oncology)
  - Haitham Abdel-Hakim, MD (KUMC BMT)
  - Mathias Salathe, MD (KUMC pulmonary and critical care)
  - Raju Vamsi, PhD, University of Alabama
  - James Sherley, PhD, (Asymtrix -Proliferation kinetics of WJ MSC)
- **Clinician stem cell researchers at KUMC**
    - Joseph McGuirk, DO (BMT)
    - Sunil Abhyankar, M.D. (BMT)
    - Sabreena Slavin, M.D. (Neurology)
    - Florence Hosseini Aslinia, M.D. (Gastroenterology)
    - Mazen Dimachkie, M.D. (Neurology)
- **Accomplishments**
    - Liver failure
      - Collaboration with KUMC Pharmacology, Toxicology & Therapeutics (Dr. Jaeschke)
      - Further research being conducted to better define mechanism
      - Pilot grant has been awarded by KUMC research funding
      - Midwest Biomedical Accelerator Consortium (MBArc) grant (\$200,000) was awarded for this project in Sept 2020
    - Stroke and Traumatic Brain Injury
      - Collaboration with KUMC Institute for Neurological Discovery (Dr. Nudo)
      - Pilot grant has been awarded by KUMC research funding
    - ALS Research
 

Application for an STTR grant was submitted Jan 5, 2022, for the use of selective WJ MSC in an ALS mouse model.
    - Bronchitis Research
 

Collaboration with Dr. Vamsi at the University of Alabama on a ferret model of lung inflammation. Plan for R-21 grant submission
    - Cartilage Repair
      - Collaboration with KUMC Orthopedics (Dr. Wang) and Pilot grant has been awarded by KUMC research funding
      - Collaboration with Dr. Wang with funding from Elixell for arthritis project
    - WJC Exosome Research
      - Collaboration with KUMC BMT (Drs. Andy Godwin and Abdelhakim)
  - **Plans:**
    - Complete proof of principle studies in mouse models of ALS and initiate pre-

- IND effort
- Complete proof of principle studies in mouse models of live hepatotoxicity and initiate pre-IND effort
- Explore adult stem cell therapy for Traumatic Brain Injury
- Explore adult stem cell therapy for cartilage repair
- Explore exosomes secreted by Wharton's jelly MSC in their role in GvHD
- Explore cell-based immunotherapy (CAR T / NK therapy) for hem and solid tumors
- Continue collaborations with external institutions – Georgia Tech and University of Alabama in lung inflammation research

## **I. COMMUNICATION AND MARKETING**

Communication and Marketing efforts within the MSCTC continue to focus on building a brand and increasing awareness of the Center. Focus during FY22 has been to establish awareness of the capabilities of the MSCTC with companies conducting basic research and clinical trials to drive third party manufacturing. Long-term, this function continues to be 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 with KU Endowment and KUMC Senior Leadership 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.
- Hosting “town hall” meetings various locations in Kansas to increase public awareness of Stem Cell Therapies

- **Plans:**

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

## J. GRANTS

While the annual support from the Kansas Legislature has allowed the Center to progress in the identification of various leads for the use of adult stem cells therapy in human disease, expansion into preclinical development and clinical studies have required significant additional funding. In 2021, the staff within MSCTC along with collaborators in other departments within KUMC, have submitted NIH and FDA grants, and are actively pursuing donations from external philanthropists, to help fund the expansion of the GvHD clinical study and obtain support for ALS preclinical and clinical studies.

- **Accomplishments:**

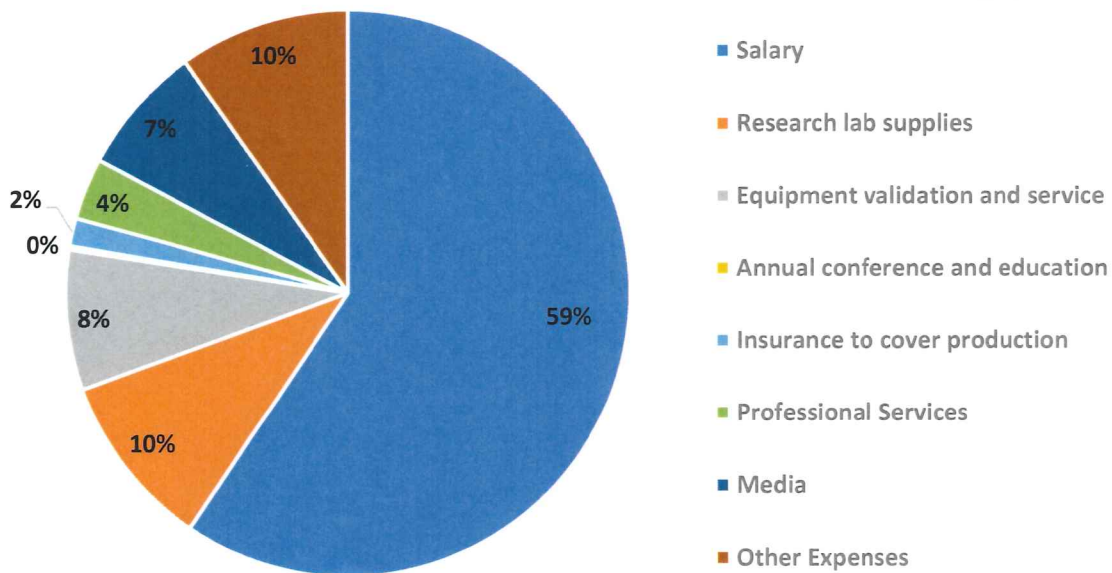
- Submitted FDA sponsored grant RFA-FD-21-001: Clinical Studies of Orphan Products Addressing Unmet Needs of Rare diseases (R01) Clinical trials required in October 6, 2021 The MSCTC, along with the University of Kansas Medical Center submitted the grant requesting for funding to further investigate the safety and efficacy of the repeated high dose administration of WJMSC in the treatment of High Risk and Steroid Resistant GvHD following bone marrow transplant. If funded, the project award period is for 3 years with \$500,000 total costs per year.
- Submitted a NIH SBIR/STTR phase I and phase II grant proposal for Engineered WJMSC for the Treatment of ALS on Jan 5, 2022, for 3 million dollars

## K. EXPENSE AND INCOME REPORT

State appropriations: FY22

Total amount received: \$751,363.00

<b>Expenses</b>		<b>% of FY total</b>
<b>Salary</b>	<b>\$446,795</b>	<b>59.5%</b>
<b>Research lab supplies</b>	<b>\$75,302</b>	<b>10.0%</b>
<b>Equipment validation and service</b>	<b>\$60,279</b>	<b>8.0%</b>
<b>Annual conference and education</b>	<b>\$1,500</b>	<b>0.2%</b>
<b>Insurance to cover production</b>	<b>\$11,979</b>	<b>1.6%</b>
<b>Professional Services</b>	<b>\$26,514</b>	<b>3.5%</b>
<b>Media</b>	<b>\$55,519</b>	<b>7.4%</b>
<b>Other Expenses</b>	<b>\$73,474</b>	<b>9.8%</b>
Office supplies and other	\$3,848	0.5%
Telecom and facilities fees	\$65,354	8.7%
Travel	\$4,272	0.6%
<b>FY22 Final Expenses Total</b>	<b>\$751,363</b>	<b>100.0%</b>



FY22 Year to Date Sources and Spends

Total amount received: \$751,363

**Table 1**

<b>Actual Expenses through 12/31/21</b>		<b>% of FY total</b>
Salary	\$211,815	28.2%
Research lab supplies	\$52,352	7.0%
Equipment validation and service	\$31,369	4.2%
Annual conference and education	\$1,500	0.2%
Insurance to cover production	\$11,979	1.6%
Professional Services	\$16,197	2.2%
Media	\$16,604	2.2%
Office supplies and other	\$2,048	0.3%
Telecom and facilities fees	\$10,674	1.4%
Travel	\$1,872	0.2%
<b>Total Fiscal Year expenses through 12/31/2021</b>	<b>\$356,411</b>	<b>47.4%</b>

**Table 2**

<b>Projected Expenses for remaining FY22</b>		<b>% of FY total</b>
Projected Salary	\$234,980	31.3%
Projected Research lab supplies	\$22,950	3.1%
Projected Equipment validation and service	\$28,910	3.8%
Projected Annual conference and education	\$0	0.0%
Projected Insurance to cover production	\$0	0.0%
Projected Professional Services	\$10,317	1.4%
Projected Media	\$38,915	5.2%
Projected Office supplies and other	\$1,800	0.2%
Projected Telecom and facilities fees	\$54,680	7.3%
Projected Travel	\$2,400	0.3%
<b>Projected Expenses for remaining FY22</b>	<b>\$394,952</b>	<b>52.6%</b>

**Table 3**

**Center Income to date for FY22 (through 12/31/21)**

Clinical Trial support	\$414
Cellular Therapeutics endowment	\$0
Manufacturing, Sales, & Education income	\$51,178
<b>Total Center Income to date for FY21</b>	<b>\$51,592</b>

