Interdisciplinary Stem Cell Institute
University of Miami
Cell Processing Facility (CPF)

Aisha Khan, M.Sc, M.B.A
Executive Director of Laboratory Operations
Interdisciplinary Stem Cell Institute
The Miller School of Medicine, University of Miami

03/14/2017
Introduction

- Serves as a manufacturing resource for the various clinical programs
- Facilitates translational research
- Provides regulatory and scale-up expertise to bridge the gap between basic and clinical research applications
- Provides services throughout the IND application development process, from the proof-of-principle and pre-clinical testing to clinical trial phase.
Facility Credentials

Equipped to do Phase I, II and III clinical trials

Equipped to manufacture licensed cellular products for new therapies and tissue-engineered end-products.

Services regional and national research efforts in reparative/regenerative medicine

Serves as a national resource for translational research in the area of cellular therapy

FACT Site

FDA registered

FACT accredited

TRANSLATIONAL CELL PROCESSING
Biomedical Research Building, 9th floor
(12,931.28 sq. ft., 85 rooms). Red square indicates location of the cell processing Facility
Floor Plan of the CPF 9TH floor BRB building

Legend
950 – General Area of Development Lab
951-Tissue Culture Room
952-Tissue Culture Room

Cleanroom Facility
937 – Gowning in of the Cleanroom
939 – Clean Storage Room
945-General Area
942- Cryogenic Freezer Room
944-Gowning out of the Cleanroom
946 – Tissue Culture Room
947 – Tissue Culture Room
948 – Tissue Culture Room
949 – Tissue Culture Room

Ancillary Areas
938 –Clean Storage Room
941 – Cryogenic Freezer storage Room
Products

- MSCs – Human
- MSCs – Rat
- MSCs – Porcine
- MSCs – Canine
- c-Kit+ Cardiac Progenitor Stem Cells – Human
- c-Kit+ Cardiac Progenitor Stem Cells – Porcine
- c-Kit+ Cardiac Progenitor Stem Cells – Rat
- c-Kit+ Kidney Progenitor Stem Cells – Porcine
- Human Dendritic Cells
- Human Tumor Lysate
- Human Schwann Cells
- Rat, Porcine, & Primate Schwann Cells
- gene-modified CD34+ hematopoietic cells

- Cord Tissue Derived MSCs
- Cord Blood Derived MSCs
- Placental MSCs
- Exosomes
- Human and Porcine iPSC
- Human T-Cell
- Human T-regulatory Cells
- Human NK Cells
- Amniotic Fluid Stem Cells
- Human Dental Pulp Stem Cells
Clinical Products

Products being used for clinical trials:
- MSCs
- Bone Marrow Mononuclear Cells
- Schwann Cells
- Dendritic Cells
- Tumor Lysate
- Cord Tissue Derived MSC
- CD34+ Cells
Mesenchymal Stem Cell Manufacturing

- GLP Manufacturing
- GMP Manufacturing
- Enabled 15 phase I/II INDs
Manufacturing Steps of Schwann Cells

- GLP Manufacturing
- GMP Manufacturing
- Enabled 3 phase I/II INDs
Dendritic Cell Vaccine for Malignant Glioma and Glioblastoma, sarcoma and brain tumor

- GMP Manufacturing
- Enabled 3 phase I/II INDs
MULTICENTER CLINICAL TRIALS
Cardiovascular Cell Therapy Research Network (CCTRN)
Endomyocardial Biopsy
Autologous

Endomyocardial Biopsy

Digestion

Magnetic Selection

Expansion

C-Kit Cardiac Stem Cells (CSCs)

• GLP Manufacturing
• GMP Manufacturing
• 1 phase I/II INDs at ISCI
• Manufactures for 7 center for phase II trial

Safe
Potent
Characterized
Full Dose

Clinical Applications

C-Kit CSCs

cGMP Compliant Manufacturing
Examples of iPSC studies at ISCI

<table>
<thead>
<tr>
<th>Basic Research (Human and mouse iPSCs)</th>
<th>Preclinical Research (Human and swine iPSCs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Modeling molecular and cellular mechanisms of myocardial lineage development</td>
<td>• Development of clinical-grade, autologous and allogeneic iPSC-derived cardiomyoblasts for cell-based therapy in response to heart damage</td>
</tr>
</tbody>
</table>
Clinical-grade manufacturing of iPSC-derived CPCs expressing the novel receptor

Human and porcine iPSC MCBs from cGMP-grade MSCs

Establishment of xeno-free cGMP compliant monolayer differentiation protocols

Scale-up differentiation and purification of CPCs

Quantum System (Terumo)

Porcine model of MI

Product Release Tests

<table>
<thead>
<tr>
<th>Assay Release</th>
<th>Identity &amp; Purity</th>
<th>SSEA-4 &gt;70%, Tra-1-60 &gt;70%, Tra-1-81 &gt;70%, Oct3-4 &gt;70%; Purity: CD34 &lt;5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pluripotency Markers</td>
<td>Safety</td>
<td>46, XX or 46, XY</td>
</tr>
<tr>
<td>Karyotype Analysis</td>
<td>Safety</td>
<td>Negative</td>
</tr>
<tr>
<td>Mycoplasma Testing</td>
<td>Safety</td>
<td>Negative</td>
</tr>
<tr>
<td>Sterility Testing</td>
<td>Safety</td>
<td>No trace of episomal plasmid DNA detected</td>
</tr>
<tr>
<td>Endotoxin Testing</td>
<td>Safety</td>
<td>Standard QC release (&lt;0.5 EU/ml)</td>
</tr>
<tr>
<td>Vector Clearence</td>
<td>Safety</td>
<td>STR Profile of starting population and iPSC line are identical</td>
</tr>
<tr>
<td>STR Genotyping</td>
<td>Purity &amp; Identity</td>
<td>% viability &gt;50; minimum cell number/vial</td>
</tr>
<tr>
<td>Cell Count &amp; Viability</td>
<td>Safety</td>
<td>Standard MCB Release Panel</td>
</tr>
</tbody>
</table>

Safety, identity, purity, viability

Assay qualification & Validation

Xeno-free, Virus-free Feeder-free, Transgene Free product

SOP and quality control documents

Assay Qualification

Xeno-free, Virus-free Feeder-free, Transgene Free MCB

SOP and quality control documents

Safety, identity, purity, viability
Development Capabilities
Lab Capabilities

IncuCyte® applications for cell monitoring & workflows

Cells are monitored non-invasively, within the incubator and images are automatically analyzed so investigator can always see what happened when and where.
Quantum® Cell Expansion System

Automated cell culture platform that can help simplify the open, labor-intensive manual tasks associated with flask-based culture.

QiIAcube

This instrument allows for high-throughput extraction of DNA and RNA.

MoFlow Cell Sorter

High-speed sorter, compatible with array of laser options. High viability, yield and purity with an analysis rate of 100,000 events per second and sort rates of up-to 70,000 events per second are standard.
Thank you