

# Exhibit 2-1



# Exhibit 2-2

January 3, 2011

Protocol Number: 101-01

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Study Title: Tissue Procurement for Non-therapeutic Research

Sponsor: StemExpress, LLC.

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## Standard Operating Procedure

### 1. Purpose

This SOP covers Tissue Procurement for Non-therapeutic Research.

This protocol describes the set up, equipment and procedures for procuring cadaverous tissue to use in non-therapeutic research.

### 2. Scope

This applies to all procurements for non-therapeutic research.

### 3. Prerequisites

The day before surgery:  
Check WebOffice for researcher requests;  
Determine your location for the next day;  
Call the clinic to verify how many surgeries are scheduled.

### 4. Responsibilities

It is the procurement technician's responsibility to bring the general and medical supplies listed in this SOP to each clinic. The clinic staff will identify donors. It is the procurement technician's responsibility to retrieve the tissue and package it appropriately for the given researcher. It is also the procurement technician's responsibility to update WebOffice so everyone is aware what tissue has been obtained and for whom.

### 5. Equipment

General supplies:  
Current blank RPR (Researcher Procurement Record)  
logs Pre-printed FedEx forms

General supplies:

Current blank RPR (Researcher Procurement Record) logs  
Pre-printed FedEx forms

Medical supplies:

Scrubs  
RPMI  
Hepes Solution with antibiotic added  
Petri dishes  
Shipping boxes  
Personal instruments to procure  
Conical tubes  
Mini urine specimen cups  
Cold packs

**6. Procedure**

On the day of surgery, the following steps are taken to procure tissue from POC: Arrive at the clinic and change into scrubs.

Inform the consenting staff of which gestations to consent. Place chucks down.

Set up the light box, instruments, RPMI, Hepes, petri dishes and tubes or cups. Set up enough blood draw bags for the day.

Get out the sequential numbering labels.

Print a copy of the day's Procurement Schedule.

Follow along with the chart flow so you know what gestations to expect.

If required, initiate blood draw from clinic staff. We do NOT want a patient label on the blood tube. Give the clinic staff the blood bags and correct blood tubes for the given researcher. If these are blood samples to accompany the tissue sample, number them in order as soon as complete. See the SOP "Maternal Blood Samples for Infectious Disease Testing" for specific guidance on those blood samples.

Once a consenting donor has undergone surgery, procure the specimen(s) on the petri dish and light box.

With minimal manipulation after isolating the specimen(s), move the petri dish to the packaging room and carefully transfer the specimen(s) to the appropriate container (conical tube or mini urine specimen cup). Add the researchers media of choice and seal with parafilm.

Keep track of time, gestation, fetal foot size or sono report and date.

Package the specimens and blood tubing for shipment once all specimens have a number. Be sure to place them on ice or cold packs.

Note the specimen numbers on the

RPR log. For delivery:

If the specimen is local courier, be sure to call the courier once you know you have obtained an appropriate specimen.

If the specimen is going by FedEx, be sure to know the local cut-off times for your closest FedEx office. Each FedEx location is listed under "contacts" in WebOffice. Always know which FedEx you will be dropping off at and consider traffic. Log on to [www.fedex.com](http://www.fedex.com) with your assigned log on and password. Print shipping label and affix to box.

All instruments must be sterilized once you are done for the day.

Clean the area(s) thoroughly and discard all unused POC in the appropriate receptacle. Gather your supplies to leave and change out of your scrubs.

# Exhibit 2-3

7-17-15

(1) 18 mm = 15.2 weeks in Trizol @ 3:30

- from leg & forearms

(2) - 30 mm = 19.6 weeks

forearm

BL in Trizol + TPer 5:05

\*NB - clint now uses diroxin only on 20wk

9-10-15  
24 mm = 17.4 wks.

sim. intestine project  
Day 1

9-11-15

(1) 20 mm = 16 weeks

(2) 12 mm = 13 weeks

divided into 3 parts:

1) duodenum =



no stomach, but definitely a wide me  
inserted stretched over scissors blade

2) cecum & appendix

stretched over forceps

3) general intestine; no mesenterium present, took from smaller  
diameter end + 4 cm  
stretched over forceps

10-2-15

(1) 26 mm = 18 wks

10-21-15

(1) 9 mm = 12 wks

9 cm long segment - know it's small in testine because it was attached  
to the stomach. Divided into 4 pieces

(2) 19 mm = 15.4 wks

14.5 cm long small intestine segment

1-15-10

(2) 26mm - 18 weeks

Skin from upper arm (looks degraded)

Retina → [redacted]

MZ

[redacted]

1-15-10

(3) 23mm - 17 weeks

SKIN from lower leg

2 MZ

[redacted]

of appendix

→ [redacted]

(4) 44mm = 21.5 weeks Treated with digoxin

Heart mushy; GI discolored + liver; skin loose

Eyes discolored red Retinas → [redacted] for coverslips 1/2 Epo 1/2 10 Epo

(5) 30mm = 19.6 weeks (DIG)

♀ 4-10

(1) 33mm = 20.7 weeks Digoxin - observations

- Cord blood
  - Lung
  - heart
  - skin
  - brain
  - Lung
  - skin
- } Trizol
- } formalin

- heart - entire organ mushy
- Kidneys - discolored dark red; lack of form
- GI discolored
- Lungs - mushy, + discolored w/ blood

6 coverslips - Brain - DMEM complete



██████████

Thanks for the update, that is fantastic data! We will try to get later gestation lung for you, sometimes we can get up to 20-22 weeks, but it is unusual these days to get non-digoxin exposed samples beyond 18 weeks (i.e., no living tissues). We can get cord blood, which I am sure you can as well. What about MSCs from tracheal aspirates of ELBW infants? I know the yield would be low, but perhaps the first 48 hours of tracheal secretions could be collected. We will continue to look for later gestational age samples for you.

>>> ██████████ 8/1/2012 1:17 PM >>>

Dear Prof. ██████████ dear ██████████

Thank you very much for the lung samples you have sent me so far. I just want to give you a quick update on what I have done by now and what I am up to:

I managed to isolate the mesenchym from those tissues and showed that at 15.6 wk of age (the latest lung) all of the cells are what we call "Mesenchymal Stem Cell" by now. I have included FACS-data, showing the positivity for the standard MSC-markers CD105 (PerCP-Cy 5.5), CD90 (FITC) and CD73 (APC) as well as for the newly proposed CD146 (PE as drop-in in CD105/CD73/CD90 cocktail). The population is negative for CD34, CD45, CD14, CD19 and HLA-DR (as "negative Cocktail", all PE), fulfilling the actual criteria to state them MSC's. Interestingly, no GD2 (Disialoganglioside 2, PE as drop-in in CD105/CD73/CD90 cocktail) can be found on those cells: This marker has been described on MSC's from the bone marrow, non-expression on our cells supports the hypothesis of a huge MSC family with a large variety of differentially expressed markers. It is obvious that the term "MSC" represents are a huge family of cells, each with different properties, abilities, living in different niches of the body.

It has been described (Hershenson et.al.: *Pediatrics*, 2010 and *Am J Physiol Lung Cell Mol Physiol*, 2012) that resident lung MSC's (e.g. the ones I've isolated) play a major roll in the development of BPD, e.g. that there is a coincidence of MSC's in the tracheal aspirate and the risk to develop BPD later on. The (premature?) differentiation of MSC's into Myofibroblasts might be one of the major processes here. However, it still remains unclear how the Mesenchym with its stem cells and all the other resident lung cells interact in the normal and disrupted development, leading to either healthy or BPD-lung.

We want to address this point using

- a) isolated MSC's from fetal lungs, showing their functional properties and abilities in Hyperoxia and Normoxia
- b) a human fetal lung explant culture in Hyperoxia and Normoxia.

We also want to see if MSC's from the human umbilical cord have beneficial effects on cell survival, growth and development in those settings.

For all the experiments, it might be best to have "older" tissue >15 week of age, for the lung explant culture the oldest lung available is best. Prof. ██████████ told me, that you are working on the effects of Digoxin (right?) in extreme premature babies - is there a chance to get one of those lungs? I'm very excited about this collaboration and happy with the way it works right now! If you have any questions, please feel free to contact me via eMail or lab-phone.

Once again, thank you very much for the opportunity to work with those tissues!

Regards from Edmonton,

██████████

Ps: I also managed to isolate SP-C positive cells form the same sample, but have to fine-tune the separation process to increase the yield. I'll keep you posted.

Attachments:

Flow Cytometry Data for human fetal lung derived MSC's  
Immunocytochemistry revealing a MSC - Myofibroblast subpopulation