Stem Cell Differentiation Monitor

Updated: December 11, 2007

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Problem Statement:

Embryonic stem cells (ESCs) have the capacity to differentiate into every cell type in the body, and therefore can theoretically be used to generate cells and tissues to cure a variety of diseases. Our client in the Odorico Lab (Department of Surgery) has derived foregut-committed cell lines from ESCs (which correspond to progenitor cells of the gut region that develops primarily into pancreas) and would like to differentiate these ESCs into insulin-producing pancreatic beta-like cells. These cells could replace or supplement transplanted donor beta cells. The mechanisms required to differentiate ESCs into these pancreatic cells is currently unknown, and this device would aid in researching such mechanisms. Our client would like to test a large number of growth factors for their ability to affect conversion of these precursor cells to mature insulin-secreting cells. In addition, a recapitulation of the 3-dimentional embryonic environment to prompt cells to adopt a pancreatic cell fate, perhaps using a Matrigel substrate, is desirable. A small scale cell culture using microfluidics to set up growth factor gradients is one approach that could be successful.

Client Requirements:

- A high-throughput way to culture Endodermal SCs (foregut-committed cells) with growth factor gradients.
- Need to be able to perform antibody staining on the cells following culture to determine whether they differentiated appropriately.
- Create a three dimensional embryonic growth environment.

Design Requirements:

1. Physical and Operational Characteristics

a) *Performance Requirement:* Must be more efficient than current methods for testing the effects of growth factors. Each unit should be capable of holding at least 100 cells (1000 -5000 would be better). Must be compatible for imaging (i.e. thin enough that it can fit in microscope fixture, glass thin enough to be viewed through). Must be able to withstand immunofluorescence. Capable of setting up tests for a variety of growth factors and gradients of those GFs.

b) *Safety:* No potentially harmful materials.

c) *Accuracy and Reliability:* The gradient formed should range from 10ng/mL to 150ng/mL of a given growth factor. Due to the lengths of the experiments, sink and source replenishing will need to take place.

Minimal disturbing of the gradient is a must to obtain accurate results. Also to ensure accuracy of the system cell nutrients and waste need to be taken into account in the design. Cells need to be fed once a day and cell waste (e.g. lactic acid) needs to be expelled from the system. Also the entire system must be sterile.

d) *Life in Service:* For the duration of the study, which is currently unknown (likely 7-28 days).
e) *Operating Environment:* Should be able to withstand 37^0 Celsius environment, tissue culture conditions, and imaging.
f) *Ergonomics*: Should be relatively easy to use and clean (but probably it will be disposable, so cleaning it is not essential).
g) *Size and Shape:* Must be small enough to fit in the imaging devices as well as the incubator.
h) *Weight:* Not a big concern, due to the small size, however should be under 1 lb
i) *Materials:* Must allow cell adhesion. Must be sterile. Imaging of cells while they are growing using an inverted phase microscope is also important.
j) *Aesthetics, Appearance, and Finish:* Not important, except for imaging purposes, as stated above.

2. Product Characteristics:

a) *Quantity:* One device is required at this time, but more would be desirable in the future.
b) *Budget:* $500.

3. Miscellaneous:

a) *Standards and Specifications:* No specific standards will be required for project.
b) *Customer:* Since cell signaling is vital to the development of cells and shear force is an unwanted byproduct, a no flow system of establishing a gradient would be ideal. Also multiple growth factor gradients may be wanted by the customer
c) *Patient-related concerns:* Cells must live in a sterile environment and get adequate nutrients. Also cell waste must be expelled from the system
d) *Competition*: None