

Progress Report 11: April 11 –April 17

Title: Device to monitor/control differentiation of stem cells to pancreas (Spring 2008)
Client: Victoria Browning Ph.D.
Advisor: Naomi Chesler Ph.D.
Team Members: Dhaval Desai (Team Leader)
Tim Pearce (BSAC)
Jon Baran (BWIG)
Tess Rollmann (Communications)

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-dimensional 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.

Restatement of Team's Goals

- Figure out gradient formation; contact Vinay if necessary.
- Perhaps carry out some cell seeding work on the side.

Summary of Team Accomplishments

- On Tuesday, we started out by using the device with two channels (one for the agarose and one for the cells). We had some agarose that someone had made earlier. We added the agarose to the agarose entry port. But the agarose entered the "cell channel". Then, to prevent the agarose from entering the "cell channel", we took some PDMS, "sealed" one of the cell ports, and then added the agarose. The agarose only entered the agarose channel. But, the agarose didn't solidfy quickly enough. We tried matrigel instead of agarose but we pretty much saw the same thing as above.
- On Wednesday, Dhaval made some agarose solution (1.5% agarose in TBE buffer). This solution freezes at approximately 35 degrees so we thought that we could use this to fill our agarose channel. But what we found that the agarose solidifies before it even enters the channel. So, instead of filling the whole channel, we just put a small drop of agarose on the access port of the source. We filled the source with dextran solution. A gradient was formed at about 6 hours. The pictures of the gradient are shown in the attached file.
- On Thursday, we tried to repeat the gradient we observed on Wednesday. The experiments are currently running and so the results will be discussed next time.

Statement of Team's Goals

- Validate gradient formation and gradient concentration (using MATLAB) with repeated experiments.
- Combine cell culture and gradient formation.
- Begin working on the final poster and paper.

Project Schedule

September 7	Form team, select project, contact client, email team roles to advisor
September 14	Background and research on project, create problem statement, begin PDS
September 21	Brainstorming, begin developing designs
September 28	Brainstorming
October 5	Finalize three alternative designs
October 12	Work on mid-semester presentation (oral and power point)
October 19	Mid-semester presentations
October 25	Submit design notebooks for advisor review
October 26	Design on final design
November 2	Work on design
November 9	Work on design
November 16	Work on design
November 23	Thanksgiving break

November 30	Work on poster presentation
December 7	Final poster presentation, put poster presentation on team web site by 10:00am
December 12	Hand in written report and notebook to advisor
December 14	Final meeting with advisors
January 25	Assign team roles, create timeline
February 1	Cell viability tests, growth factor diffusivity coefficient calculations, modify device
February 8	Cell viability tests, growth factor diffusivity coefficient calculations, modify device
February 15	Cell viability tests, growth factor diffusivity coefficient calculations, modify device
February 22	Cell viability tests, growth factor diffusivity coefficient calculations, modify device
February 29	Test design, work on midsemester presentations
March 7	Midsemester presentations
March 14	Test design
March 21	Spring Break
March 28	Test design
April 4	Distinguished Entrepreneurship Lecture in Tong
April 11	Test design
April 18	Test design, work on poster
April 25	Test design, work on poster and final paper
May 2	Final Poster Presentations
May 7	Hand in paper and design notebooks, update website, final client meeting.
May 9	Final Meeting with Advisor

Project Difficulties

- Setting up a maintainable gradient on such a small scale could be very challenging, and all of the possible methods are considerably complicated and will require significant research
- Getting the Matrigel into the channel using passive pumping is difficult, but doable.
- We were not able to produce a gradient in our microchannel using small pore sized membranes. An alternate design idea might be needed.

Activities

- **Dhaval (Team Leader, Communications)**
 - Team meetings – 6 hrs
 - Progress Report – 0.5 hr
 - Total: 6.5 hrs
- **Tim (BSAC)**
 - Advisor meeting – 0.5 hour
 - Team meetings – 5 hrs
 - Total: 5.5 hrs
- **Jon (BWIG)**
 - Advisor meeting – 0.5 hrs
 - Team meetings – 3 hrs
- **Tess**
 - Total: 3.5 hrs
 - Advisor meeting – 0.5 hour
 - Team meetings – 4 hrs
 - Total: 4.5 hrs
- **Total Team Hours for this Week: 20 hrs**
- **Running Total for Each Member (hrs):**
 - Dhaval – 50.5
 - Tim – 55.5
 - Jon – 49.5
 - Tess – 51

Project Timeline (next page)

Task	Jan	February					March				April			May	
	25	1	8	15	22	29	7	14	21	28	4	11	18	25	2
Preliminary Steps															
Assign team roles	■								■						
Meetings															
Meeting with client	■	■		■		■			■	■	■	■	■	■	
Friday team meetings	■		■	■	■	■	■	■	■	■	■	■	■	■	
Meetings outside of class	■								■	■	■	■	■	■	
Design															
Cell viability testing			■	■	■	■	■	■	■						
Growth factor diffusivity coefficient testing									■	■	■	■	■	■	
Deliverables															
Progress Reports	▨	▨													
Project Design Specification	■	■													
Mid-semester presentation					■	■	■	■							
Final presentation												■	■	■	
Final paper												■	■	■	
Other duties															
BSAC meetings			▨		▨		▨		■	▨		▨			
Updating website			▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨
Contacting client/suppliers	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨

Key:	▨ Tess	▨ Dhaval	▨ Tim	▨ Jon	■ All
	■ Holiday(s)				

Only individual tasks are indicated with special gradients

Expenses

All other material donated from Browning, Berthier, Williams, Beebe.