Things to Review

• Approximately 1/3 multiple choice, 2/3 short answer
• ~5 main topics (lecture + paper discussion)
• 2 Homeworks
• 5 paper presentations
• In-class exercises/discussions (e.g. questions I posed during lecture period)

Topics Areas of Particular Emphasis:
• Role of stem cell niches in stem/progenitor expansion & differentiation
• Types of microenvironmental signals, methods for systematically testing signals
• Approaches for optimizing stem cell protocols
• Methods for testing effects of mechanical forces on stem cells
• Mechanisms of mechanical sensing in stem cells
• Examples of microfabrication and high-throughput technologies
• Challenges related to scale-up, and commonly used strategies
• Overall design of transplantation and drug screening approaches
1. You are performing research to identify how microenvironmental signals influence the proliferation and differentiation of cardiac progenitor cells that you have isolated from rat hearts. In one approach, you are analyzing the cardiac progenitor cells in perfusion culture within a microfluidic device.

When you compare microfluidic perfusion culture to static culture in tissue culture plates, you observe significant differences in the amount of progenitor proliferation (perfusion > static). However, the cell culture medium and surface substrate are the same in both conditions.

- (a) Describe 2 differences between these culture platforms that could possibly lead to the observed differences in proliferation.
Sample Questions

- (b) Describe an experimental approach that you could perform to determine which of the differences in microenvironmental signals above is most critical for the observed effect.
2. Time-lapse imaging analysis has been applied towards the culture of human ES cells. These experiments allow for the tracking of individual cells and their fates (e.g. cell death, cell division). Normal ES cells exhibit substantial cell death during the initial phases of culture (panel A below). Interestingly, after numerous passages ES cells become ‘adapted’, with a larger fraction of cells surviving and forming colonies (panel B).
Sample Questions

(a) Despite the improved survival and proliferation demonstrated by adapted cells, there may be a problem with utilizing this culture adaptation for the expansion of cells for therapeutic applications. What is this potential problem?
Sample Questions

(b) Treatment of the ES cells with a retrovirus expressing the transcription factor Nanog causes the normal ES cells to behave similar to adapted cells, without the need for extensive culture adaptation time.
Is there any potential problem with using this treatment for therapeutic applications? Why or why not?