Module 11: Stem Cells
Assignment
Total Point Value = 30

Due by midnight on Day 7 of Module 11
This should be submitted to Blackboard as a pdf.

1. Please identify which stem cell type or type***s*** (embryonic, somatic, or iPS) fit each of the following descriptions. Some have 1 answer, some have more than 1 answer.

a. Derivation requires informed consent	ESC, iPS
b. Has forced expression of several transcription factors	iPS
c. Includes mesenchymal stem cells	Somatic
d. Totipotent	ESC, iPS
e. Low efficiency in creation	iPS
f. Limited quantities in the body	Somatic
g. Used in the Advanced Cell Technology clinical trial	ESC
h. Self renews and differentiates	ESC, iPS, somatic

2. Understanding the three models of stem cell proliferation please discuss which model a tissue engineer would hope is correct and why?
The models for stem cell proliferation covered in this module were clonal succession, deterministic and stochastic-based proliferation. The reasons that these models were developed were to aid researchers in the understanding of stem cell pool behavior so that they could maximize use and manipulation of these cells therapeutically. As an engineer the first thing you want to maximize is resource. This means you would want a population that is *reliably* going to self-renew to maintain the pool. You also want a resource that can differentiate into the needed therapeutic phenotype. Depending on the application one could argue that any of the models are ideal. If for example homing of stem cells is shown to be inefficient then you may not want a clonal succession model which requires a new stem cell clone be called from its dormant niche each time an older clone burns out. Clonal succession does however provide an efficient means of producing a lot of a single cell type (think of a proliferation-tree here and how many differentiated cells you can get in 3-4 divisions vs a deterministic model), which is advantageous for an acute injury. Deterministic and stochastic models can reproduce stem cells at the site of injury. Stochastic models are the least reliable and therefore the least desirable for predicting and manipulating cell behaviors but they give the engineer the ability to adapt proliferation (by changing the probabilities depending on environmental or time-based variables).

3. As we saw this week in lecture, there are a limited number of clinical trials using embryonic stem cells. One company, Geron, which pioneered clinical use of hESCs, stopped their trial. Please explain why Geron halted their clinical trial utilizing hESC-derived oligodendrocytes to treat spinal cord injuries? And second, explain why they stopped pursuits of stem cell research entirely? Does this surprise you?
Geron stopped their clinical trial because they want to focus their efforts on cancer therapeutics not because of negative results from the trial. Further, they are no longer pursuing ANY stem cell-based therapies. They announced that this was a business decision and that the cost-benefit analysis showed that they money they would need to move forward with stem cell-based therapies wasn't as lucrative as other avenues. Other potential reasons for the decision include the advent of iPS cells, and regulatory hurdles associated with hESCs. Along with the announcement Geron had to return a $6.5million loan to the California Institute of Medicine.

4. The following review article discusses how chromatic regulation and structure is involved in stem cell creation (iPSCs), pluripotency and differentation. At the beginning of this semester we started a discussion on epigenetics - how chromatin compaction can regulate protein expression. In reading this article you'll

continue that discussion. After reading please provide a critical review of no more than 400 words. This review should include the following points:

- how histone acetylation and methylation regulate gene expression
- the differences in chromatin structure between stem and differentiated cells
- the model of nuclear compartmentalization

Article: Serrano, L., Vazquez, B.D., and Tischfield, J. *Chromatin Structure, pluripotency and differentiation.* Experimental Biology and Medicine. 238: 259-270. 2013. **(see attached pdf)**

References

Question 2:
http://news.sciencemag.org/2011/11/geron-bails-out-stem-cells

Assignment Rubric

Question	Component	Total Point Value
1	A	1.5
	B	1.5
	C	1.5
	D	1.5
	E	1.5
	F	1.5
	G	1.5
	H	1.5
2		5
3		5
4		8

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