**Assignment 11: Stem Cells**

**Cell and Tissue Engineering**

**Problems**

1. Please identify which stem cell type or types (embryonic, somatic, or iPS) fit each of the following descriptions. Some have 1 answer, some have more than 1 answer.
   1. Derivation requires informed consent

embryonic

b. Has forced expression of several transcription factors

iPs

c. Includes mesenchymal stem cells  
 somatic

d. Totipotent

sembryonic

e. Low efficiency in creation

iPS

f. Limited quantities in the body

somatic

g. Used in the Advanced Cell Technology clinical trial

embryonic

h. Self renews and differentiates

embryonic, somatic, iPS

1. Understanding the three models of stem cell proliferation please discuss which model a tissue engineer would hope is correct and why?

**Clonal succession model**: in this model, stem cells are in a dormant state waiting and once triggered any of these stem cells could differentiate and proliferate into a large population of mature cells. These stem cells are available for the lifetime of the organism. The mature clone eventually burns out and a new stem-cell take over for cell production.

**Deterministic model**: this model assumes that the stem cells can self-renew and differentiate into a mature cell or 1 stem-cell daughter with a given probability p (mature cell: p and stem-cell:1-p).

**Stochastic model**: the behavior of the outcome of differentiation is random in nature; i.e., a stem cell can generate 0,1 or 2 stem cells as daughter cells; and ca be regulated like the deterministic model by tissue environment and be influenced by telomer length.

A tissue engineer, would like to rely on the deterministic model, which, compared to the clonal succession or stochastic models, under deterministic conditions, can either differentiates into a mature specialized cell; for example, for tissue repair, or a stem cell to replace itself.

1. 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. Begin by reading the article from ScienceMag about Geron. 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?

After a year, Geron decided to stop a trial to treat 8 patients with spinal cord injury, by injecting them with hESC-derived oligodendrocytes stem cells. At that time, it has already spent $170 million with $25 million as a loan from the California Institute for Regenerative Medicine, a government funded institution (Lukovic et al.). It is reasonable to assume that the cost would have at least doubled as such study to be approved by the FDA, requires a continuous monitoring of the patients for injury improvements, adverse events, or comorbidities issues for many years. Also, around the same period (slide 23 11CD), until today, there has been 4 x times less NIH funding for human embryonic research compared to non-embryonic and iPSC research. Maybe around the same time, NIH guidelines were likely being communicated. In addition, Geron funded Dr Thomson research in 1998. In 2011, 3 years after, Geron did not have yet any FDA approved stem cell therapy. Geron executive committee, probably then realized that the investment needed to continue the trial but also their stem cell research; was too steep, and could have jeopardize; maybe other more promising research. With this context; it seems expected that Geron; as a public company under the pressure of investors, took the only decision they could have made and step to pursue stem cell research altogether.

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

<https://www-science-org.proxy1.library.jhu.edu/content/article/geron-bails-out-stem-cells>

Lukovic, Dunja, et al. “Perspectives and Future Directions of Human Pluripotent Stem Cell-Based Therapies: Lessons from Geron’s Clinical Trial for Spinal Cord Injury.” *Stem Cells and Development*, vol. 23, no. 1, Jan. 2014, pp. 1–4. *DOI.org (Crossref)*, https://doi.org/10.1089/scd.2013.0266.

