BIOENG 116 Spring 2013 Name:_____
Midterm SID:_____

Please write your name and SID on each page of the exam. Write LEGIBLY and clearly. Only exams written in PEN will be considered for regrades.

Part 1. (30 points) Multiple Choice: Clearly write the letter of your choice in the space provided. (3-pts each)

1) For cell transplantation, allogeneic cells

A. are immune acceptable
B. can be made available of-the-shelf
C. may have problems of pathogen transmission
D. can be immune rejected
E. A, B and C
F. B and C
G. B, C and D

G

2) Which of the following isn't a component of the cell ECM?

A. Collagen type I
B. Fibronectin
C. Hyaluronic acid
D. Matrix metalloproteinase

D

3) Which of the following can be classified as cell-cell signaling in the microenvironment? Write the letters for all that apply.

A. Endocrine signaling
B. Notch signaling
C. Neuronal signaling
D. Paracrine signaling

B, C, D

4) The cell-cell adhesion may involve (write the letters for all that apply):

A. integrins
B. cadherins
C. intermediate filament attachment to cadherins
D. junctions that allow ion transport

B,C,D or
A,B,C,D

5) Which of the following isn't a part of the angiogenic process?

A. Endothelial cell activation
B. Increased production of angiostatin
C. Formation of holes in the ECM
D. Mitosis

B

6) Adult stem cells are

A. Totipotent
B. Unipotent
C. Pluripotent
D. Multipotent

D

7) Which of the following Yamanaka factors is an oncogene?

A. c-myc
B. Oct-4
C. Sox2
D. Klf4 (sometimes people also treat Klf4 as an oncogene, but we didn't talk about it in the class; so either A or A/D can get full credit)

A or A,D

8) Apoptosis is involved in the following processes (write the letters for all that apply):

A. Maintenance of adult tissue
B. Suppressing tumor growth
C. Embryo development
D. Telomerase activation

A, B, C

9) Which of the following isn't one of the steps of cell migration?

A. Recycling
B. Release
C. Ejection
D. Extension
E. A and C

C

10) Chemotaxis can be quantified using

A. Boyden chamber
B. Micropatterning of flow chamber
C. TUNEL assay
D. BrdU
E. A and B
F. B and C
G. C and D

E

Part 2. (20 points) True or False: Write "True" if the statement is true or "False" if the statement is false. If "False", provide a *brief* sentence on why it is false. (2-pts each)

1) For a 3D scaffold, the larger the pore size, the faster the cells could migrate into it.

False. There is an optimum pore size, typically around a similar length scale as the size of the cells, above which migration decreases.

2) A signaling molecule can bind to different types of receptors and induce totally different signaling in cells.

True.

3) Diffusion limit slows down cell migration on the surface of the scaffolds.

False. Diffusion limit of molecules are several magnitudes smaller, therefore it is not a limiting factor in cell migration in 2D (on the surface).

4) Fully differentiated neurons are able to replicate and repair injuries.

False. Fully differentiated neurons can't proliferate.

5) Progenitor cells can form teratomas when injected into immunodeficient mice.

False. Embryonic stem cells or iPS cells (pluripotent) form teratomas. Progenitor cells are typically unipotent.

6) FACS can be used to sort iPS cells from hematopoietic stem cells.

True. There are some markers specific to hematopoietic stem cells.

7) Cells undergo more mechanical stress in MACS than FACS.

False. The shear stress in FACS involved in single-cell separation and transport is higher.

8) The BrdU incorporation assay detects cells that are in the S phase.

True. BrdU is taken up by newly synthesized DNA.

9) Necrosis is important for morphogenesis in developing tissues.

False. Apoptosis is important for morphogenesis while necrosis is brought about by injury or lack of nutrients.

10) Cell migration in a 3-D matrix usually requires matrix matalloproteinases.

*True *in vivo*. False *in vitro*. Migration can occur even without MMP depending on matrix components (hydrolysis) or pore size. Any reasonable explanation gets credit.

Part 3. (50 points) Essay and Quantitative Analysis. Show all steps and units.

1. A student has isolated some cells from the adult skin, and these cells look like fibroblasts based on the morphology. The cells are expandable, so you postulate that there are some stem cells in this population. However, there is no specific known marker for this type of stem cells.
a. Design an experiment to prove (or disprove) that there are stem cells in this population. (**10 points**)

-Accept answers involving differentiating into different cells found in the skin (eg. Dermal fibroblasts, keratinocytes) and other lineages (eg. Neurons, muscle cells and adipocytes). Expect to see multipotency to confirm they are adult stem cells.

-Reject answers on staining, teratoma

Telomerase activity could get partial credit, although it's not necessarily a sensitive method. Although adult stem cells have much lower telomerase activity than pluripotent stem cells, it is still a bit higher than differentiated cells.

-Injecting into blastocysts to obtain chimeras. Would have to explain how to identify the cells thereafter in the chimera, otherwise partial credit.

b. If you finally identify a cell surface marker for this type of stem cells, how can you isolate these stem cells from the mixture of many cell types in the culture? Describe one method. (**10 points**)

-Describe FACS or MACS using fluorescent-labeled antibody.

2. Your lab has recently purchased a spanking new stereolithographic set-up. Your boss needs you to prove your mettle before you can use the machines.
a. Describe the stereolithography procedure. (**5 points**)

-3rd-last slide of angiogenesis lecture.

b. Describe two variations of design properties of a 3D matrix that can be used to study how to improve cell migration in 3D. What do you expect to see and why? (**15 points**)

-Ligand density, stiffness variation, fiber alignment/density, pore size, etc and the relevant phenomenon eg. Chemotaxis, contact guidance, haptotaxis, etc

c. Your boss gives you the green light to begin some proliferation experiments on the 3D matrices. You seed some cells and notice that the number of cells had changed in two phases. In the first phase, cell number increases from 10^5 to 10^{10} within 10 days; in the second phase, cell number decreases from 10^{10} to 10^8 within 10 days. Assuming the rate of cell number change is proportional to the cell number (general equation $dX/dt = \mu X$; X(t) is the number of cells at time t), determine the rate constant μ for the 1st phase and 2nd phase respectively. (**10 points**)

$$\frac{dX}{dt} = \mu X$$
$$\int \frac{1}{X}\, dX = \int \mu\, dt$$
$$\ln X = \mu t + C$$

For 1st phase,

When t=0, $X = 10^5$, $C = \ln 10^5$
When t=10 days, $X=10^{10}$, $C=\ln 10^5$, $\boldsymbol{\mu = 0.5 \ln 10\ days^{-1} = 1.15\ days^{-1}}$

For 2nd phase,

When t=0, $X = 10^{10}$, $C = \ln 10^{10}$
When t=10 days, $X=10^8$, $C=\ln 10^{10}$, $\boldsymbol{\mu = -0.2 \ln 10\ days^{-1} = -0.46\ days^{-1}}$