

Molecular Cell Biology 5068 In class Exam 3
December 16, 2014

Exam Number:

Please print your name: _____

Instructions:

Please write only on these pages, in the spaces allotted. Write your number on each page (not your name), so that we can split them up and grade them anonymously. There are a total of 6 pages including this cover page. You may not use any books or notes, and no electronic aids, including calculators.

Answer only in the space provided; short, concise answers are preferred and will be rewarded. Please be as neat as possible.

Answer the course evaluation at the end of the exam or pick up a take-home exam from the TA. The take-home exam is due Friday, December 19, 8:00 AM.

In Class Exam 3

Stewart Lecture (9 points)

1. Name one function of telomere. (1 Point)
2. Senescence is characterized by increased expression level of two genes. Name one of them. (1 Point)
3. According to “telomere hypothesis”, most normal cells will reach a stage called senescence. But, some of the cells can escape senescence to go into crisis phase, where the shortening of telomere can lead to cell death and genetic catastrophe. Cells can utilize either a mechanism or an enzyme to lengthen their telomere. Name both the enzyme and the mechanism. Be sure to put down the name of the enzyme, not its catalytic component. (2 Points)
4. (T or F) Overexpression of hTERT reduces cell’s resistance against apoptosis. (1 Point)
5. Discuss how SV40 ER and RAS lead to tumor formations. (3 Points)
6. (T or F) In the given tissue, there is a wide range of cell types, such as normal cells, premalignant cells, and tumor cells. (1 Point)

Huettner Lecture (8 points)

1. What are 3 types of stem cells? Briefly explain each of their characteristics. (3 Points)
2. In 2011 issue of *Nature Cell Biology*, a group of scientists managed to convert fibroblasts to cardiomyocytes without de-differentiating to an intermediate stage. Thus, this work is an example of what kind of reprogramming? (1 Point)

3. Which of the following accurately describes four genes required to induce pluripotent cells? Circle the correct answer choice. (1 Point)

(A) Oct3/4, Ras, CDK4, c-Myc

(B) Oct3/4, Sox2, Klf4, c-Myc

(C) Sox2, p53, EGFR, Klf4

(D) Oct3/4, Sox2, RB, Rab

(E) Sox2, Klf4, c-Jun, c-Myc

(F) Oct3/4, Sox2, Klf4, MKK4

4. Briefly, explain what SCNT is. Do not just write what it stands for. (1 Point)

5. In 2011 issue of *Nature*, a group of researchers used microRNAs to drive the conversion of fibroblasts to neurons. Based on what you have learned from this course, what technique/experiment could tell if the resulting populations of cells are indeed functionally neurons and not fibroblasts? Simply looking for the morphology is not an acceptable answer (this doesn't tell you about the functions). Be sure to support your reasoning. (2 Points)

Weihl Lecture (10 points)

1. There are 3 ways of protein degradation, which are autophagy, ubiquitin-proteasome system, and _____ . (1 Point)

2. Excluding the fact that ubiquitin/proteasome system happens more frequently than lysosomal processes, what is one major difference between these two ways of protein degradation? Explain your answer. (2 Points)

3. Ubiquitination is through a bond between C-terminal glycine of ubiquitin and ϵ -amino group of _____ on the substrate/protein. Blank refers to the name of an amino acid. (1 Point)

4. Name one way of autophagy. (1 Point)

5. How does ubiquitination work? Be sure to describe the role and official name of E1, E2, and E3, and discuss how this is regulated by an enzyme called DUB (what does it do?). (4 Points)

6. What signaling pathway is directly regulated by rapamycin? Name this pathway – note: I'm looking for a particular pathway, not a general process (i.e. protein synthesis). (1 Point)

Amarasinghe Lecture (9 Points)

1. (T or F) Elucidating structure of protein using NMR is a direct process. (1 Point)

2. Name one advantage and one disadvantage of using NMR to study biomolecules. (2 Points)

3. Choose the correct answer that lists the chronological order of steps (i.e. from the beginning to the end) used for protein structure determination (1 Point):

(A) Conformational restraint → Sequence specific resonance assignment → Calculate and refine structure

(B) Sequence specific resonance assignment → Conformational restraint → Calculate and refine structure

(C) Calculate and refine structure → Sequence specific resonance assignment → Conformational restraint

4. Deuteration is a frequently used tool in protein determination using NMR. Its advantage is that it is straightforward to do. But, it does come with a major disadvantage. Explain this disadvantage of deuteration. (2 Points)

5. Briefly, explain these two parameters used in NMR protein structure determination (2 Points):

(A) Coupling Constant (J)

(B) Dipolar Coupling Constant (D)

6. (T or F) It is not recommended to use the “average” NMR structure because it is a distorted structure that is not real. (1 Point)

Fremont Lecture (9 Points)

1. What are the first 3 steps for determining protein structure using X-ray crystallography? (3 Points)

2. How does MAD (multiple anomalous dispersion) work? Be sure to state whether this is an experimental or computational method for solving phase problem. Also, how can you use MAD to see if you have a correct crystal or not? (3 Points)

3. At what resolution (in angstrom) of electron density map do you begin to see the holes in aromatic rings of phenylalanine and tyrosine? (1 Point)

4. In 2011 issue of *Journal of Biological Chemistry*, a group of researchers tackled the problem of understanding how the recognition takes place between influenza virus A (IVA) and surfactant protein D (SP-D). Based on what you know about X-ray crystallography, how would you go about testing your crystal structure of surfactant protein D to explain this recognition? Explain your answer. (2 Points)

Oh lecture (12 points)

1) What are the 3 primary ways by which CDK activity is regulated to govern cell cycle progression? Briefly describe each regulatory mechanism you mention. (3 points)

2) What are the roles of SCF and APC in cell cycle control? (2 points)

3) Fully describe the Rb pathway in the control of S-phase initiation. Make sure to mention all the components involved. (5 points)

4) Excessive mitogenic stimulation of cell growth eventually leads to cell cycle arrest and/or cell death. Describe specifically how abnormally high levels of Myc result in cell cycle arrest and/or apoptosis. (2 points)

Weber Lecture [12 points]

1) List 3 genomic alterations by which proto-oncogenes can be activated. (3 points)

2) Because of its central location in various key pathways, mTOR is rarely an oncogene in cancer. However, other genes upstream and downstream of mTOR in translational regulation are often altered in cancer. List 2 proto-oncogenes and 1 tumor suppressor downstream of mTOR. (3 points)

3) List the 5 classical features of a tumor suppressor as discussed in class. (5 points)

4) Embryogenesis would generally favor loss of the tumor suppressor INK4A/ARF locus to prevent activation of Rb and p53 that could abrogate this process. What critical cellular process is generally thought to have contributed to evolutionary conservation of this locus? (1 point)

Miner Lectures [21 points]

1) List 3 biological functions mediated by the ECM. (3 points)

2) What 2 proteins does the heparan sulfate proteoglycan Perlecan bind to in the basement membrane? (2 points)

- 3) What is the function of the LG domain located on the C-terminal end of the Laminin alpha chain? (1 point)
- 4) List 4 primary components of all basement membranes. (4 points)
- 5) What is the role of Agrin at the neuro-muscular junction? From which cell type is the Z axon of Agrin derived? (2 points)
- 6) List 3 ECM-protein derived peptides from Matrix Metalloproteinase (MMP) activity that have anti-angiogenic function. (3 points)
- 7) Where are the Procollagen N- and C- proteinases located (cellular or extracellular space)? Why is this localization critical for cellular integrity? (2 points)
- 8) What structural feature makes Collagen IV more flexible than the Fibrillar (I, II, III, and V) collagens? (1 point)
- 9) What is Anoikis and why is it important in the setting of cancer? (2 points)

10) Name the protein that interacts with dystroglycan in a complex that allows the mediation of mechano-transduction between laminin in the basement membrane and the cell's actin cytoskeleton. (1 point)

Schlesinger Lecture [12 points]

1) List 2 ways in which apoptosis differs from necrosis. (2 points)

2) What is the fundamental difference between the intrinsic and extrinsic apoptotic pathways? List one apical/initiator caspase that is **typically** associated with each pathway. (3 points)

3) Starting with Bax activation by BID, describe the steps that lead to induction of apoptosis. Mention all components involved and their locations. (3 points)

4) BH3-only proteins are members of the BCL-2 family of proteins that can act as both activators and inhibitors of apoptosis. Describe the role of BH3-only proteins in **one of the following models** discussed in class. (3 points)

- a) Sensitizer BH3-only function
- b) Neutralization model
- c) De-repressor BH3-only function