Molecular Cell Biology 5068 In Class Exam 1 **Exam Number: _____**
September 29, 2015

Please print your name: _____

Instructions:

Please write only on these pages, in the spaces allotted and not on the back. 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 8 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.

When you are finished, turn this in to the TA and pick up the take-home portion.

Exam Number:_____

MCB 5068 Exam 1 September 29, 2015

Dr. Mueckler's Lectures (30 Points)

1. List 2 major functions of the plasma membrane in cells. [2 points]

2. What property of phospholipids makes it thermodynamically favorable to form a bilayer? Why is the formation of a sealed compartment by this phospholipid bilayer energetically favorable? [2 points]

3. Name 2 ways that phospholipids are involved in signal transduction. [2 points]

4. Explain the difference between the scramblase and flippase enzymes based upon the membranes with which they are associated, the symmetry of these membranes, and their energy requirements. [4 points]

5. List the steps involved in signal-mediated targeting of proteins to the rough ER. Be sure to include all components involved. [6 points]

6. Based upon the charge difference rule, draw the expected topology of the following transmembrane protein. [2 points]

7. What protein is responsible for the formation of disulfide bonds? Where does this occur? [2 points]

8. What are the two translocons responsible for importing proteins into the matrix of the mitochondria? Does the protein traverse these translocons in a folded or unfolded state? (3 points)

9. Describe one of the three routes a protein may travel in order to be inserted into the inner membrane of the mitochondria. Make sure to mention all the components necessary. [3 points]

10. Describe how the Ran-GDP/GTP concentration gradient is established in order to confer directionality on nuclear transport by the keryopherins. Make sure to mention all the components necessary for this cycle to occur, including the locations of Ran-GAP and Ran-GEF. [4 points]

Dr. Hanson's Lectures (30 Points)

1. True or false. If false, please correct: the smooth ER is involved in lipid metabolism and sodium sequestration / release. (1 point)

2. What type of coat proteins mark transitional ER, also known as ER exit sites _____. (1 point)

3. Briefly explain how chaperone proteins interact with nascent proteins in the ER. Is this an active or passive process? (4 points)

4. The oligosaccharide that is added *en bloc* to nascent proteins during ER folding is composed of a particular pattern of sugar residues. Please explain how this oligosaccharide is modified when a nearly folded glycoprotein intermediate requires another round through the Calnexin/Calreticulin cycle. (2 points)

5. Briefly explain the strategy employed by Schekman et al. to screen for and isolate yeast mutants with defects in secretion. (4 points)

6. Some members of the Clostridium genus of bacteria have evolved toxins that can cause paralysis in animals (like humans). Using your knowledge that membrane trafficking plays an important role in the function of nerve terminals like the neuromuscular junction, please explain how these toxins cause paralysis. (2 points)

7. NEM sensitive factor (NSF) forms a complex with SNAP and SNARE proteins. What is the role of NSF in membrane trafficking? (2 points)

8. True or false; if false, please correct: synaptotagmin is the calcium sensing protein responsible for vesicle fusion with the plasma membrane, as in the case of synaptic vesicles and the axon terminal plasma membrane. (1 point)

9. What receptor is responsible for the retrograde recycling of ER resident proteins from the Golgi to the ER? In your response, please be sure to include the name of the coat protein this receptor binds to as well as the sequence of the motif it recognizes on ER resident proteins (either the yeast or higher eukaryote sequence will suffice). (3 points)

10. Briefly describe how newly synthesized enzymes are targeted to lysosomes. In your response, please be sure to mention: the sorting signal, where is the signal receptor located, i.e. where is the sorting signal recognized, and the trafficking coat system utilized? (4 points)

11. True or false; if false, please correct: the Rab family of proteins are key determinants for determining organelle identity. (1 point)

12. True or false. If false, please correct: Membrane trafficking requires that transport intermediates undergo fission from the donor compartment and fusion with the target compartment in a highly regulated series of molecular reactions. (1 point)

13. Answer either A or B. (4 points)

A. How does intravesicular / lumenal pH change through the endocytic pathway? Briefly describe why this is important for receptor recycling during endocytosis.

B. Of the LDL, Transferrin, and EGF receptor trafficking pathways discussed in class, choose your favorite and briefly outline its itinerary through the endocytic pathway. Please be sure to comment on the fate of the receptor and cargo.

Drs. Greenberg, Mahjoub, and Morley Lectures (35 Points)

1. Name two potential in vivo functions of intermediate filaments, then highlight how your favorite intermediate filament fulfills one of these functions. (3 points)

2. Please list two ways in which intermediate filaments are unique from actin and microtubule filaments. (2 points)

3. Please list three advantages of assembling filaments from small protein subunits. (3 points)

4. Directionality of polymerization occurs in 2 of the 3 filament types discussed in class. Briefly outline the mechanism of the directionality. Please be sure to comment on how this mechanism impacts the relative critical concentrations of either end of the filament. (2 points)

5. True or false; if false please correct: The "treadmilling" of a filament requires net addition at one end and net loss at the other end. (1 point)

6. Which microtubule motor protein discussed in class is responsible for the motility of motile cilium. [1 point]

7. True or false; if false please correct: Formins are Rho-GTPase effector proteins that function as nucleators during actin polymerization. [1 point]

8. Contrast actin and microtubule filaments in terms of subunits, nucleotide energy source, and the amount of elastic energy stored within the filament. Answers in the form of a table are preferred. (3 points)

9. Cancers are characterized by uncontrolled cell division. Paclitaxel is a taxol chemotherapeutic drug used to treat a variety of cancers. Its mechanism of action is the stabilization of microtubules. Using your knowledge of the microtubule filament kinetics and the role of microtubules in the cell, please speculate as to why taxols can be used to treat cancers. (2 points)

10. Please list the two microtubule motor proteins discussed in class and the direction they move along microtubules. Are these active or passive processes? If active, what nucleotide is utilized? (4 points)

11. Microtubules play diverse roles in cells. List three ways in which the heterogeneity of microtubule function is regulated. [3 points]

12. Please name two functions of the protein Profilin in the rapid remodeling of the actin cytoskeleton. [2 points]

13. _____ is the primary contractile element in all muscles and is the only known motor protein to act on actin filaments. Most proteins in this superfamily processively move towards the _____ end of the filament. [2 points]

14. Answer <u>either</u> A or B. (2 points)

A. Name your favorite Ras-related small GTP-binding protein involved with actin cytoskeletal remodeling and briefly describe a role for subcellular structure it forms.

B. Rigor mortis is one of the recognizable signs of death in which the muscles of the body are stiffened. On a cellular level, death is characterized by the inability to replenish depleted intracellular ATP stores. Using your knowledge of the power stroke process that occurs between actin and the primary contractile element in all muscles, please briefly explain why rigor mortis occurs.

Bonus Question:

15. Canada is the USA's largest single-country trading partner. What is the capital of Canada? (1 point)

A. Ottawa

B. Montreal

C. Toronto

D. Vancouver

16. Answer <u>either</u> A, B or C. (4 points)

A. Cell motility is dependent on the rapid remodeling of the actin cytoskeleton. Choose either the leading or trailing edge of the moving cell and briefly list: the type of actin structure involved, the direction of the actin filaments (parallel, anti-parallel, or branched) as well as one protein that is important for this process.

B. Briefly describe how Ras-related proteins can be activated or inactivated. Be sure to mention the role of the two proteins involved in this process.

C. In Wiskott Aldrich Syndrome, the body's lymphocytes (defense cells) exhibit abnormal motility. The Wiskott Aldrich Syndrome protein (WASP) is involved in cell motility through interactions with a Ras-related small GTP binding protein and a protein involved in the rapid remodeling of the actin cytoskeleton. Please list these two proteins and briefly state how they function in conjunction with WASP to promote cell motility.

Bonus Question:

16. Hypertrophic cardiomyopathy (HCM) is the leading cause of sudden death in people < 35 years of age. Variants in _____ filaments are associated with this disease. (1 point)