2020 Spring Cell Biology Midterm Exam (10:10am~1:00pm, Apr. 9th, 2020)

1. Provide your answers on the answer sheet provided. Be sure to fill in your name and student ID number. Send your answer sheet to T.A. via email by 1:00pm, Apr. 9th, 2020.
2. Questions 1~45: Select the best answer unless instructed otherwise. (Questions 1~36 are 1 point each; Questions 37~45 are 2 points each.) Questions 46~53 are short-answer/essay questions. The full score of the exam is 100.

1. All cells …
   A. have membrane transport proteins.
   B. synthesize proteins on the ribosome.
   C. replicate their genome by DNA polymerization.
   D. transcribe their genetic information by RNA polymerization.
   E. All of the above.

2. To trace family relationships between distantly related organisms such as humans, algae, bacteria, and archaea, one should compare their genomes in regions …
   A. that evolve rapidly.
   B. that have a higher mutation rate.
   C. that code for proteins.
   D. where mutations are hardly tolerated.
   E. where most mutations are selectively neutral.

3. A mutation in the *cdc28* gene in the budding yeast *Saccharomyces cerevisiae* causes cell-cycle arrest, giving rise to unbudded cells that look like "dumbbells." Treatment of wild-type cells with nocodazole, a drug that destabilizes some cytoskeletal polymers, leads to a similar phenotype. Based only on these observations, which statement is true regarding *cdc28*?
   A. c*dc28* codes for a master regulatory kinase that phosphorylates other proteins.
   B. Nocodazole binds to the protein coded by the *cdc28* gene.
   C. The product of the *cdc28* gene is responsible for resistance to nocodazole.
   D. The product of the *cdc28* gene is involved in cell cycle regulation.
   E. The product of *cdc28* destabilizes the same cytoskeletal polymers that nocodazole also destabilizes.

4. Mitochondria and chloroplasts are thought to have evolved from free-living aerobic bacteria that were engulfed by an ancestral anaerobic cell and established a mutually beneficial (symbiotic) relationship with it. Which of the following statements is NOT true about these organelles?
   A. They are similar in size to small bacteria.
   B. They have their own circular genomic DNA.
   C. They have their own ribosomes.
   D. They have their own transfer RNAs.
   E. They are found in all eukaryotes.

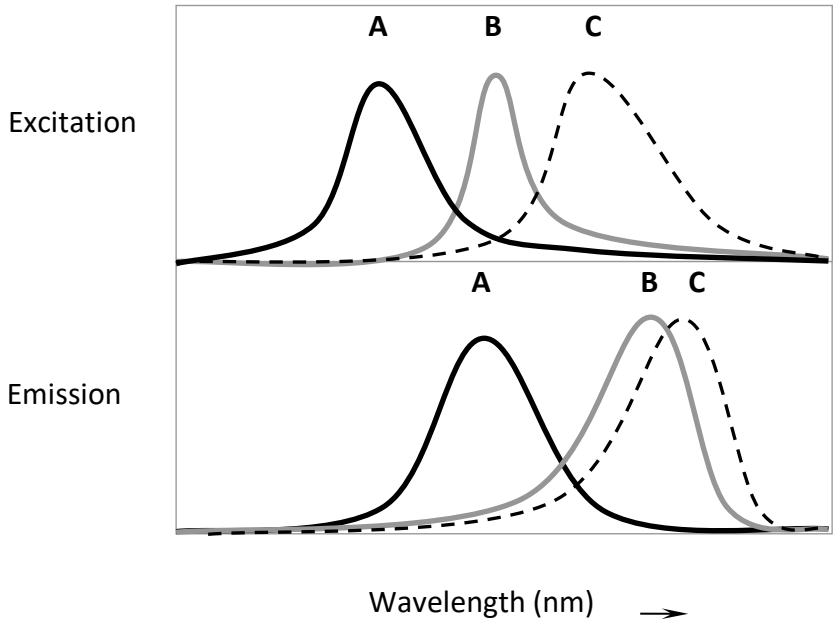
5. It is a model organism used to study various eukaryotic cell and developmental processes such as cell division and cell death. Its hermaphrodite adult is composed of exactly 959 somatic (non-germ) cells, the lineage of each of which has been worked out with great precision. It is approximately 1 mm long. Which of the following describes this organism?

A. It is a vertebrate.
B. It is a plant pathogen that destroys many crops.
C. Its genome codes for a few thousand genes.
D. It can fly.
E. It can be frozen indefinitely in a state of suspended animation.

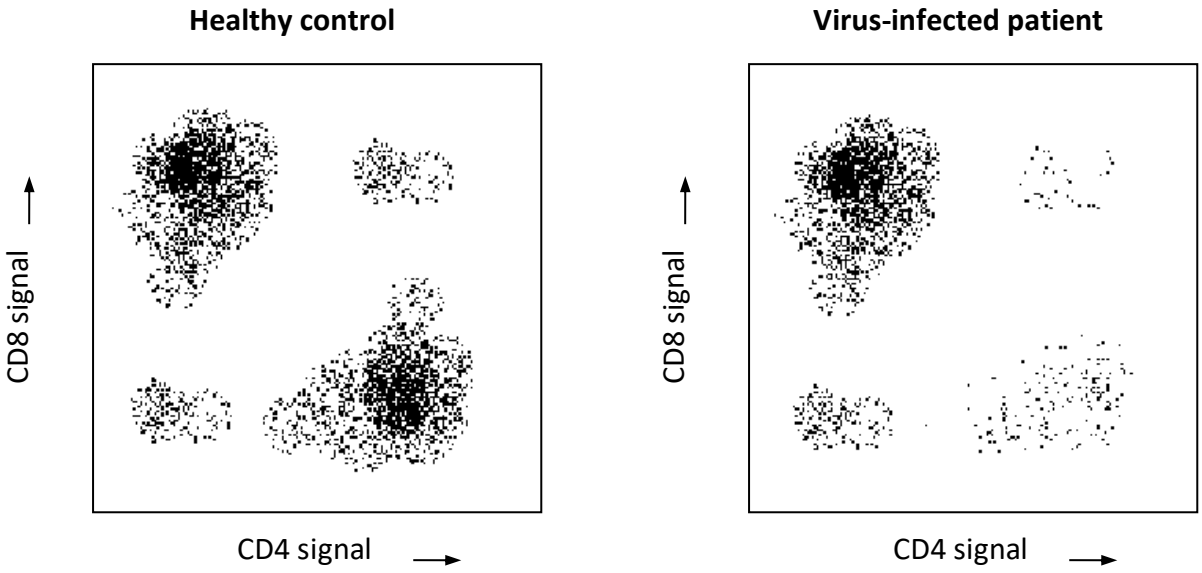
6. The light used to excite a fluorescent molecule carries … energy and has a … wavelength compared to the light that is then emitted from the molecule.

A. greater; longer
B. greater; shorter
C. the same amount of; shorter
D. less; longer
E. less; shorter

7. Given the absorption and emission spectra of three fluorescent dyes in the simplified diagrams below, which pair of dyes is better suited for a fluorescence resonance energy transfer (FRET) study? Write down AB, BC, or AC as your answer.



8. You have used fluorescence-activated cell sorting to separate blood T lymphocytes from a healthy person and a patient infected with a virus. To sort the cells, you used antibodies against two cell-surface receptors, CD4 and CD8, each conjugated to a different fluorescent dye. Based on the results below, which cell type do you think is depleted by the viral infection: CD4+ helper T cells (H) or CD8+ cytotoxic T cells (C)? In these dot plots, each cell is represented by a dot whose coordinates are the intensities of CD4 and CD8 signals. Write down H or C as your answer.



9. How are antibody-producing hybridoma cell lines immortalized to provide an unlimited source of monoclonal antibodies?

A. By ectopic expression of telomerase
B. By transformation with a retrovirus
C. By cell fusion
D. By overproduction of introduced oncogenes
E. By irradiation

10. Which of the following is normally NOT found in a eukaryotic membrane?

A. Cholesterol
B. Phosphatidylinositol
C. Sphingomyelin
D. Ganglioside G_{M1}
E. Octylglucoside

11. The motion of lipid molecules in a synthetic bilayer can be studied by various techniques. Which of the following has been observed in these systems?

A. Phospholipids diffuse rapidly within and between the two leaflets of a bilayer.
B. An average lipid molecule can diffuse the length of about 2 micrometers in a fraction of a millisecond.
C. The flip-flops are very rare for phospholipids but cholesterol molecules flip-flop more often.
D. Within a bilayer, lipid molecules rarely rotate about their long axis, but diffuse laterally at very high rates.
E. All of the above.

12. Transmembrane proteins …

A. are typically exposed only to one side of the membrane.
B. can be released from the membrane by a gentle extraction procedure such as salt treatment.
C. are often further attached to the membrane via a GPI anchor.
D. are sometimes covalently attached to a fatty acid chain that inserts into the membrane.

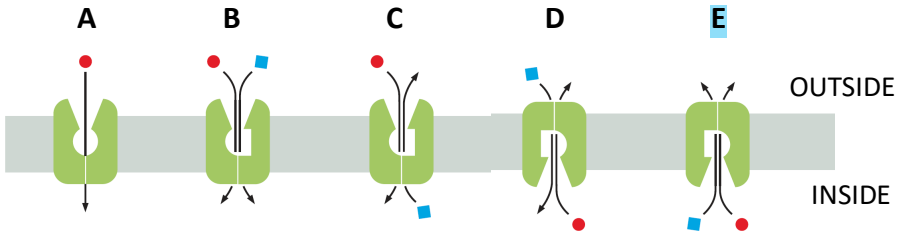
E. cannot contain β sheets in the part of their structure that interacts with the membrane interior.

13. Why do cells not have membrane transport proteins for O_2?
A. Because they need to keep the oxygen concentration low inside the reducing environment of the cell.
B. Because oxygen can dissolve in water and leak in via water channels.
C. Because oxygen can dissolve in the lipid bilayer and diffuse in and out rapidly without the need for a transporter.
D. Because oxygen is transported in and out of the cell in special oxygen-carrying proteins such as hemoglobin.
E. Because oxygen transport across a membrane is energetically unfavorable.

14. In contrast to transporters, the channel proteins in cellular membranes …
A. interact strongly with the solute(s) that they transport.
B. undergo a conformational change every time they transport a solute.
C. can only mediate passive transport.
D. form pores that are always open.

15. A potassium channel conducts K^+ ions several orders of magnitude better than Na^+ ions, because …
A. the Na^+ ion is too large to pass through the channel pore.
B. the hydrated Na^+ ion occupies a larger volume compared to the hydrated K^+ ion, and is too large to pass through the channel pore.
C. the Na^+ ion is too small to interact with the channel in a way that facilitates the loss of water from the ion.
D. the Na^+ ion cannot bind to the high-affinity K^+-binding sites in the channel pore.

16. Which of the following transporters mediates primary active transport when transporting the solutes in the directions indicated? The concentration of both solutes (shown as small *circles* and *squares*) is higher outside of the cell.



17. Many amino acids in our diet are absorbed via the transcellular transport pathway by the intestinal epithelial cells. This process requires ATP hydrolysis by …
A. the Na^+–amino acid symporters in the apical domain of the plasma membrane.
B. the Na^+–amino acid antiporters in the apical domain of the plasma membrane.
C. the Na^+-K^+ pumps in the basal and lateral domains of the plasma membrane.
D. the amino acid carriers in the basal domain of the plasma membrane.
E. F-type ATPases in the apical domain of the plasma membrane.

18. This family of ATPases is structurally related to the turbine-like pumps that acidify lysosomes and vesicles; however, they usually function in reverse, generating ATP from ADP and P_i using proton gradients across membranes. What are they called?

A. P-type pumps
B. ABC transporters
C. V-type pumps
D. F-type pumps
E. Permeases

19. Imagine a protein that has been engineered to contain a nuclear localization signal, a nuclear export signal, a C-terminal peroxisomal targeting sequence, and a canonical endoplasmic reticulum (ER) signal sequence. With all of these signals, where would you expect to find the protein after its synthesis?

A. Cytosol
B. Nucleus
C. Shuttling between the cytosol and the nucleus
D. Peroxisomes
E. Endoplasmic reticulum

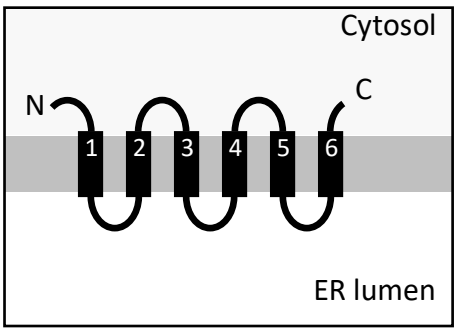
20. According to the model for nuclear transport described in this chapter, what do you think would happen if you could artificially limit all Ran-GAP activity to the nucleus and all Ran-GEF activity to the cytosol?

A. Proteins containing an NLS would be actively exported from the nucleus, while NES-containing proteins would be actively imported.
B. Both import and export of nuclear proteins would be stalled, as they lose their directionality.
C. Protein import into the nucleus would be reversed, but export would be unaffected.
D. Protein import into the nucleus would be stalled, but export would be unaffected.
E. Nothing would change; this is the normal Ran-GAP and Ran-GEF distribution.

21. Certain cysteine-containing proteins of the mitochondrial intermembrane space are imported from the cytosol with the help of the Mia40 protein via a disulfide relay system. What drives the unidirectional import of these proteins? Are these proteins reduced or oxidized at their cysteine residues upon import?

A. ATP hydrolysis; oxidized
B. The electron-transport chain; oxidized
C. ATP hydrolysis; neither oxidized nor reduced
D. ATP hydrolysis; reduced
E. The electron-transport chain; reduced

22. The following diagram depicts the topology of a multipass transmembrane protein in the endoplasmic reticulum (ER) membrane. Which set of helices act as stop-transfer signals in this protein?

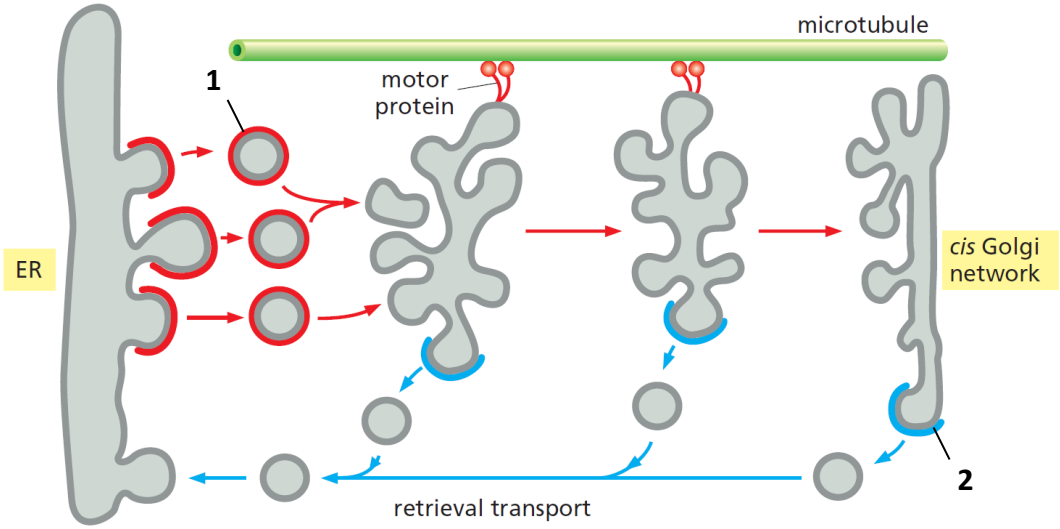


A. 1, 2, 3
B. 4, 5, 6
C. 1, 3, 5
D. 2, 4, 6
E. 1, 6

23. Misfolded proteins in the ER may actively undergo any of the following EXCEPT ...
A. binding to chaperones such as BiP to allow unfolding and refolding.
B. binding to chaperones such as calnexin to prevent aggregation.
C. being transported back to the cytosol for degradation.
D. being expelled to the Golgi apparatus for disposal.
E. being glycosylated and binding to lectins.

24. Sort the following events to reflect the order in which they occur during vesicle docking onto a target membrane, starting with an inactive Rab in the cytosol. Your answer would be a four-letter string composed of letters A to D only, e.g. DACB.
(A) Rab is bound to its effector (tethering protein) on the target membrane.
(B) Rab is bound to its Rab-GDI.
(C) Rab is bound to the membrane in its GTP-bound form.
(D) Rab dissociates from the membrane.

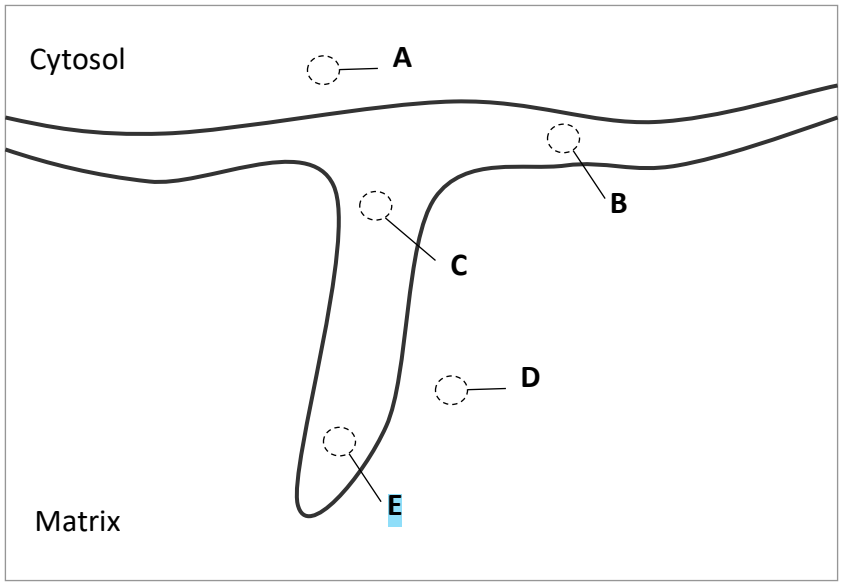
25. In the following schematic diagram depicting the formation of vesicular tubular clusters between the ER and the CGN, what major coat proteins are indicated by 1 and 2, respectively?



A. COPI; COPII
B. COPI; clathrin
C. COPII; COPI
D. COPII; clathrin
E. Clathrin; COPII

26. Which of the following pathways does NOT directly deliver materials to lysosomes?
A. Endocytosis
B. Exocytosis
C. Phagocytosis
D. Autophagy
E. Macropinocytosis

27. In actively respiring mitochondria, where in the following schematic drawing of the inner and outer mitochondrial membranes would you expect to find the lowest local pH?



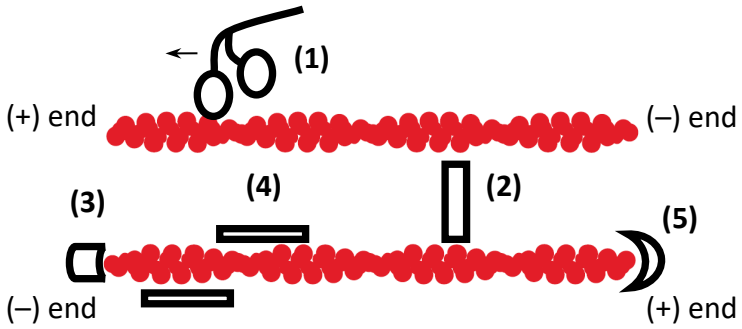
28. The synthetic toxin 2,4-dinitrophenol can uncouple ATP synthesis from mitochondrial respiration by decreasing the permeability of the inner membrane to protons. What would be the effect of dinitrophenol treatment on the amount of ATP produced by mitochondria and on the rate of ATP transport across the inner membrane, respectively?
A. Positive; positive
B. Positive; negative
C. Negative; positive
D. Negative; negative

29. The water-splitting step in photosynthesis …
A. occurs on the stromal side of the thylakoid membrane.
B. is catalyzed by an iron–sulfur cluster.
C. consumes H^+ and therefore contributes to the proton gradient across the thylakoid membrane.
D. generates all the O_2 in the Earth's atmosphere.
E. All of the above.

30. Bacteria contain homologs of cytoskeletal filament subunits …
   A. except those of the intermediate filaments.
   B. but these homologs are incapable of nucleotide binding and hydrolysis.
   C. that are less diverse in their function relative to their eukaryotic counterparts.
   D. that can have different functions to those of their eukaryotic counterparts.
   E. that are dispensable for cell growth and proliferation.

31. In the polymerization *in vitro* of actin filaments and microtubules from their subunits, what does the "lag phase" correspond to?
   A. Nucleation
   B. Reaching steady state
   C. Nucleotide exchange
   D. ATP or GTP hydrolysis
   E. Treadmilling

32. Which of the actin-binding proteins (1 to 5) in the following schematic drawing represents tropomyosin, α-actinin, Arp 2/3 complex, CapZ, and myosin, respectively? Your answer would be a five-digit number composed of digits 1 to 5 only; e.g. 15324.



33. In contrast to growing microtubules, shrinking microtubules …
   A. have a GTP cap at their plus end.
   B. have strong lateral interactions at their plus ends.
   C. have curved protofilaments at their plus ends.
   D. cannot be rescued unless microtubule-stabilizing proteins bind and inhibit depolymerization.
   E. All of the above.

34. What is the major microtubule-organizing center in animal cells?
   A. The γ-tubulin ring complex
   B. The centrosome
   C. The cell cortex
   D. The primary cilium
   E. The spindle pole body

35. These proteins are found in the budding yeast *Saccharomyces cerevisiae*; they form "neck filaments" between a mother cell and its growing bud, and help polarize protein distribution between the two. These proteins ...
   A. can polymerize to form filaments and sheets.
   B. bind GTP.

C. are also involved in contractile ring formation during cytokinesis in animal cells.
D. form filaments that are thought to be nonpolar.
E. All of the above.

36. SUN and KASH proteins embedded in the nuclear envelope provide connections between the organization of the nucleus and the cytoplasm. Which of the following pairs of proteins DO NOT bind directly to each other in these connections?

A. Nuclear lamina and SUN proteins
B. Plectins and KASH proteins
C. KASH proteins and microfilaments
D. KASH proteins and SUN proteins
E. SUN proteins and cytoplasmic intermediate filaments.

37. Indicate true (T) and false (F) statements below regarding the mitochondrial protein import system. Your answer would be a four-letter string composed of letters T and F only, e.g. TTTF.

( ) Mitochondrial proteins should fold natively twice: once in the cytosol and once inside the organelle.
( ) β-barrel proteins that are abundant in the mitochondrial outer membrane are imported from the cytosol independently of the TOM complex.
( ) Signal sequences that target precursor proteins to the mitochondrial matrix form an α- helix in which positively charged residues cluster near its N-terminus, while uncharged or hydrophobic residues cluster near the other side.
( ) At least two signal sequences are required to direct proteins to the mitochondrial matrix.

38. Indicate true (T) and false (F) statements below regarding peroxisomal proteins. Your answer would be a four-letter string composed of letters T and F only, e.g. TTTF.

( ) All peroxisomal proteins are encoded in the nucleus.
( ) Some peroxisomal proteins are synthesized by ribosomes attached to the rough endoplasmic reticulum.
( ) All peroxisomal proteins reach the organelle after their synthesis is completed.
( ) Peroxisomal proteins have to be unfolded before import.

39. Indicate true (T) and false (F) statements below regarding *N*-linked glycosylation of proteins. Your answer would be a four-letter string composed of letters T and F only, e.g. TTTF.

( ) *N*-linked glycosylation can be carried out co-translationally, possibly at multiple asparagine residues on the same protein molecule.
( ) *N*-linked glycosylation is a gradual process, with step-by-step addition and trimming events that commence with the addition of *N*-acetylglucosamine to an asparagine side chain.
( ) Most proteins synthesized in the rough ER are *N*-glycosylated, and some of them require this modification for their correct folding.
( ) Once a protein is properly folded in the ER, its attached oligosaccharides are quickly removed by an *N*-glycanase, although it may be glycosylated again later.

40. Indicate whether each of the following descriptions better applies to COPI- (1), COPII- (2), or clathrin- (3) coated vesicles. Your answer would be a four-digit number composed of digits 1 to 3 only, e.g. 1322.

( ) They mediate transport from the ER to the *cis* Golgi network.
( ) Their coat protein forms a three-legged structure called a triskelion.
( ) They are pinched off from their donor compartment by a dynamin collar.
( ) They are involved in retrograde transport in the Golgi apparatus.

41. Indicate true (T) and false (F) statements below regarding glycosylation of proteins in the endoplasmic reticulum and the Golgi apparatus. Your answer would be a four-letter string composed of letters T and F only, e.g. TTTF

( ) Glycosylation can promote protein folding.
( ) The glycosylation state of a protein can determine its fate along the secretory pathway.
( ) Glycosylation makes a protein more accessible to proteases and other proteins.
( )Glycosylated proteins are generally more flexible.

42. Indicate true (T) and false (F) statements below regarding receptor-mediated endocytosis of LDL particles. Your answer would be a four-letter string composed of letters T and F only, e.g. TTTF.

( ) LDL receptors are normally degraded in the lysosome along with their LDL ligands.
( ) LDL receptors that do not bind to extracellular LDL cannot be internalized in clathrin-coated vesicles.
( ) A mutation that impairs the attachment of an LDL receptor to a clathrin-coated pit would cause depletion of blood LDL levels.
( ) LDL receptors at the plasma membrane are usually concentrated in clathrin-coated pits.

43. Indicate true (T) and false (F) statements below regarding the genetic systems of mitochondria and chloroplasts. Your answer would be a four-letter string composed of letters T and F only, e.g. TFTT.

( ) Most proteins in these organelles are encoded by the organelle's genome.
( ) Mammalian mtDNA can make up less than 1% of the total cellular DNA.
( ) In some highly specialized animal cells, mtDNA can comprise as much as 99% of the cellular DNA.
( )The genetic systems of these organelles are most similar to extremophilic archaea.

44. Indicate whether the location of each of the following is topologically equivalent to the cytosol (C) or the extracellular space (E). Your answer would be a five-letter string composed of letters C and E only, e.g. CCECE.

( ) Ribosomes
( ) Chromatin
( ) Lysosomal hydrolases
( ) Calcium ions in the ER
( ) Peroxisomal catalase

45. Indicate whether each of the following descriptions better matches the rough (R) or the smooth (S) endoplasmic reticulum (ER). Your answer would be a five-letter string composed of letters R and S only, e.g. SRSRR.

( ) It mostly has a tubular appearance.
( ) It contains the transitional ER.
( ) It is coated by ribosomes.

( ) It can be specialized for functions such as detoxification and lipid metabolism.
( ) Sarcoplasmic reticulum in muscle cells is one of its specialized forms.

Questions 46~53 are short-answer/essay questions.

46. An acid hydrolase is an enzyme that works best at acidic pHs. It is commonly located in lysosomes.
(a) What type of endoplasmic reticulum (ER) is an acid hydrolase synthesized in? (2%)
(b) After the synthesis, what are the organelles and type(s) of vesicles involved in its transport to the lysosome? (Please list the organelles and the vesicle types in the order of transport, i.e., ER→…→ lysosome.) (6%)
(c) Why is an acid hydrolase not enzymatically active during the transport process? (2%)

47. It is presumed that mitochondria were primitive aerobic prokaryotes that were engulfed in mutualism by primitive anaerobic eukaryotes, receiving protection from these beings and offering energy to them. This hypothesis is called the "endosymbiotic hypothesis" on the origin of mitochondria.
(a) What are the molecular facts that support the hypothesis? Please name two facts. (4%)
(b) To which other cellular organelles the hypothesis can also be applied? (1%)

48. What are the functions of (a) SNARE proteins (b) Rab proteins during vesicular transport? (6%)

49. What is the mechanism underlying the directionality of nuclear transport? (8%)

50. How is glucose transported from intestinal lumen to extracellular fluid (blood)? (Please describe the transporters involved and the mechanisms of operation.) (8%)

51. (a) What is the difference between pinocytosis and phagocytosis? (3%)
(b) Please name one example for each of them. (2%)

52. What are the motor proteins that function with actin filaments and microtubules, respectively? (2%)

53. Where are F-ATPases located and what is their function? (2%)