Part I. (20 points total)

The following diagram shows the various intracellular compartments involved in the biosynthetic-secretory, endocytic, and retrieval pathways.
1. (11 points) Identify various COMPARTMENTS in the diagram from A to K.
2. (9 points) Indicate on the arrows whether they are part of the biosynthetic-secretory pathway (L), the endocytic pathway (M), or a retrieval pathway (N).

1. 
   A. Endoplasmic Reticulum
   B. Cis Golgi Network
   C. Cis Cisterna
   D. Medial Cisterna
   E. Trans Cisterna
   F. Trans Golgi Network
   G. Vesicle
   H. Early Endosome
   I. Late Endosome
   J. Lysosome
   K. Nuclear Envelope
Part II. (70 points total)

Multiple choice. Circle ALL correct answers (there may be more than one). 2 points each question.

1. Which of the following is not associated with clathrin-coated pits?
   A. trans Golgi network ⭕
   B. endoplasmic reticulum
   C. LDL–LDL receptor complex ←
   D. triskelion ✓

2. The movement of a motor protein along a cytoskeletal filament is most analogous to:
   A. a locomotive rolling along a railroad track
   B. a truck driving along the highway
   C. a person on crutches walking down a sidewalk
   D. a jet plane in flight

3. The C-terminal 40 amino acids of three ER-resident proteins – calnexin, calreticulin, and HMG CoA reductase – are shown as below.

   **Calnexin**
   . . . KDQGDEEEGEEKLEEKQKSDAEBEEGTVSEQBEEDRPKAEDEIILRNPRRNKRPE

   **Calreticulin**
   . . . KQDEEQLKEEEEDKKRKEEEAEEDKEDDEEDKDEEDEEDKEDEEEDVPGQAQKDEL

   **HMG CoA reductase**
   . . . PGENARQLARVCGTVMAELSLMAAAALAGHLKSHMHLRNRSKINLQDLQGACTKSKTA

   Which of the following is true?
   A. Calnexin and HMG CoA reductase are transmembrane proteins; Calreticulin is a soluble protein.
   B. HMG CoA reductase and calreticulin are transmembrane proteins; Calnexin is a soluble protein.
   C. Calnexin and calreticulin are transmembrane proteins; HMG CoA reductase is a soluble protein.
   D. HMG CoA is a transmembrane protein; Calnexin and calreticulin are soluble proteins.

4. The NSF-SNARE complex contains
   A. homotypic SNARE proteins associated with different membrane compartments
   B. different SNARE proteins associated with different membrane compartments
   C. homotypic SNARE proteins associated with the same membrane compartments
   D. different SNARE proteins associated with same membrane compartments
5. GTPase-activating proteins (GAP) can turn the Rab GTPases into a state that favors the hydrolysis of bound GTP to form bound GDP. Which of the following will happen in a cell line overexpressing a Rab-specific GAP protein?
   A. The vesicle transport will not be affected because guanine nucleotides remain bound to the Rab proteins.
   B. The vesicle transport will be enhanced because the Rab proteins are now predominantly bound to GDP.
   C. The vesicle transport will be weakened because the GDP-bound Rab proteins will not promote the docking of vesicles.
   D. The vesicle transport will not be affected because the GDP-bound Rab proteins can promote the docking of vesicles but not the fusion of the vesicles.

6. Which of the following can convert ATP energy into the mechanical movement of actin microfilaments?
   A. kinesins
   B. dyneins
   C. keratins
   D. myosins

7. The disassembly of actin filaments can be facilitated by
   A. cofin
   B. gelsolin
   C. profilins
   D. thymosin-β4

8. Which of the following is true?
   A. The secretory proteins become more concentrated in the secretory vesicles than in the Golgi apparatus.
   B. The concentration of the secretory proteins remains constant in either the secretory vesicles or the Golgi apparatus.
   C. The secretory proteins become less concentrated in the secretory vesicles than in the Golgi apparatus.
   D. The concentration of the secretory proteins could be higher or lower than that in the Golgi apparatus.

9. Which one of the following changes take place when a skeletal muscle contracts?
   A. Z-discs move farther apart.
   B. Actin filaments contract.
   C. Myosin filaments contract.
   D. Sarcomeres become shorter.

10. Transcytosis occurs in
    A. fibroblasts
    B. polarized epithelial cells
    C. lymphocytes
    D. smooth muscle cells
11. Which of the following is the step taken by soluble ER proteins that are destined to be secreted?

B. They stay as membrane-bound until they move into secretory vesicles and are cleaved of their signal peptides in these vesicles to become soluble.

C. They are cleaved of their signal peptides in ER and move into the vesicles by binding to the vesicle coating proteins.

D. They are cleaved of their signal peptides in ER and move into the vesicles by incorporating into the membrane through their hydrophobic amino acid stretches.

E. They are cleaved of their signal peptides in ER and move into the vesicles by binding to ER membrane proteins.

12. Electron micrographs show that mitochondria in heart muscle have much higher density of cristae than mitochondria in skin cells. That is because

A. it is made this way by nature without particular functional meaning

B. cristae are portions of the mitochondrial outer membrane that contains transport proteins needed for heart muscle function

C. cristae are portions of the mitochondrial inner membrane that contains respiratory chain and ATP synthase, the essential components for producing energy that is needed for the contraction of heart muscle but not for skin function

D. cristae are portions of the mitochondrial inner membrane that contains respiratory chain and ATP synthase, the essential components for producing energy that is needed more for the continuous contraction of heart muscle but not less for skin function

13. The first step in the movement of myosin II along actin microfilaments is:

A. ATP hydrolysis of the F-actin-bound myosin II and the detachment of myosin II from F-actin.

B. ATP binding to the F-actin-bound myosin II and the detachment of myosin II from F-actin.

C. the detachment of ADP-bound myosin II from F-actin

D. ATP binding and ATP hydrolysis of the F-actin-bound myosin II followed by the detachment of myosin II from F-actin.

14. The citric acid cycle generates NADH and FADH2, which are then used in the process of electron transfer through respiratory chain. If cells are deprived of oxygen, which of the following is most likely to occur?

A. The citric acid cycle will be unaffected because it does not require oxygen.

B. The citric acid cycle will soon stop because oxygen is one of the substrates.

C. The citric acid cycle will soon stop because NAD and FAD are not available.

D. The citric acid cycle will be unaffected because it needs NAD and FAD but not oxygen.
15. If complex IV were incorporated into an artificial lipid vesicle in order to demonstrate its proton translocating ability in isolation, which of the following would be an appropriate electron donor?
A. cytochrome bc1 complex
B. ubiquinone
C. cytochrome a
D. cytochrome c

16. Which of the following best describes microtubules?
A. Microtubules have more β-tubulins than α-tubulins
B. Microtubules have more α-tubulins than β-tubulins
C. Microtubules have the equal amount of α-tubulins and β-tubulins
D. Microtubules have only tubulin dimers; they do not have α- tubulins or β- tubulins

17. Electron transfer along the respiratory chain is coupled with one of the following in mitochondria:
A. Lower pH in the matrix than in the intermembrane space and reduced mitochondrial membrane potential
B. Higher pH in the matrix than in the intermembrane space and reduced mitochondrial membrane potential
C. Lower pH in the matrix than in the intermembrane space and increased mitochondrial membrane potential
D. Higher pH in the matrix than in the intermembrane space and increased mitochondrial membrane potential

18. Which of the following can both initiate the assembly of actin filaments from monomeric actin subunits and support the growth of more filament branches?
A. gelsolin
B. Arp 2/3
C. both gelsolin and Arp 2/3
D. tropomodulin

19. The influence of stathmin on microtubule structure is due to
A. the shrinking pool of the tubulin dimers
B. the increased pool of the tubulin dimers
C. the inability for stathmin to bind microtubules
D. the inability for stathmin to bind tubulin dimers

20. Which of the following will result in oxidative stress?
A. The products generated from reactions catalyzed by catalases can not be consumed by reactions catalyzed by peroxisomal oxidases.
B. The products generated from reactions catalyzed by peroxisomal oxidases can not be consumed by reactions catalyzed by catalases.
C. The enzymatic activities of superoxide dismutases and catalases are both increased.
21. Which of the following electron carrier is found in NADH dehydrogenase?
A. Copper atoms
B. Heme groups
C. Flavin mononucleotide
D. Flavin adenine dinucleotide

22. The growth rates at the plus and minus ends of actin filaments as a function of actin concentration are shown in the figure below. If you add actin filaments of defined length to a solution of actin monomers at the concentration indicated as A, B, C, D, or E, which concentration of the solution will let you control the growth of actin filaments at the plus end but not the minus end?
A. Concentration at A or B
B. Concentration at B or C
C. Concentration at C or D
D. Concentration at D or E

Growth rate
(molecules per second)

23. Dinitrophenol partially uncouples the electron transfer and the generation of proton gradient. It was once prescribed as a diet drug to aid in weight loss. What is the most likely explanation for the use of dinitrophenol in weight loss?
A. It changes the energy generation because the electron transfer is blocked.
B. It generates the same amount of energy requiring more electron donors.
C. It speeds up the energy generation because electron transfer does not lead to the generation of proton gradient.
D. It generates the same amount of energy requiring less electron donors.
24. Dynamic instability caused microtubules either to grow or shrink rapidly. If an individual microtubule is in its shrinking phase, which of the following is true?
   A. Both ends of the microtubule are in the GDP-bound form.
   B. Both ends of the microtubule are in the GTP-bound form.
   C. The end with α-tubulin is GDP-bound and the end with β-tubulin is GTP-bound.
   D. The end with α-tubulin is GTP-bound and the end with β-tubulin is GDP-bound.

25. Taxol and vinblastine are two drugs that have the opposite influence on the microtubule organization. Taxol stabilizes the microtubules whereas vinblastine inhibits polymerization of microtubules. Which of the following is true?
   A. Both taxol and vinblastine can inhibit cell division.
   B. Taxol but not vinblastine inhibits cell division.
   C. Vinblastine but not taxol inhibits cell division.
   D. Neither taxol nor vinblastine can inhibit cell division.

26. Free radicals generated in mitochondria and peroxisomes could lead to oxidative stress. Which of the following is true?
   A. The mitochondrial complex I can both transfer electrons and be a direct source of free radicals.
   B. The mitochondrial complex III can both transfer electrons and be a direct source of free radicals.
   C. The mitochondrial complex IV can both transfer electrons and be a direct source of free radicals.
   D. Free radicals are only generated by the nonprotein mitochondrial electron carrier and the peroxisomal enzymes.

27. Which of the intermediate filament proteins is defective in the blistering diseases?
   A. Vimentin
   B. Keratin
   C. Desmin
   D. Neurofilament protein-L

28. Which of the following best describes intermediate filaments?
   A. Intermediate filaments (IFs) are different from microtubules or microfilaments because IFs are more heterogeneous than the other two. That means each individual IFs are composed of more types of protein subunits.
   B. Intermediate filaments (IFs) are similar to microtubules or microfilaments because all three types of filaments have structural polarity.
   C. Intermediate filaments (IFs) are different from microtubules or microfilaments because the building blocks of IFs do not have polarity.
   D. Intermediate filaments (IFs) are similar to microtubules or microfilaments because all three types of filaments are found in only a small number of cell types.
29. A typical time course of polymerization of actin filaments from actin subunits sequentially includes
A. steady-state phase, rapid growth phase, and nucleation nucleation, rapid growth phase, and steady-state phase
B. rapid growth phase, steady-state phase, and nucleation
C. nucleation, steady-state phase, and rapid growth phase

30. Which of the following is true?
A. G-actin subunits are mostly associated with ATP whereas the majority of F-actin subunits are ADP-bound.
B. G-actin subunits are mostly associated with ADP whereas the majority of F-actin subunits are ATP-bound.
C. Bound ATP in G-actin subunits can exchange for ADP before G-actin is incorporated into actin filaments.
D. Bound ADP in F-actin subunits can exchange for ATP during the filament elongation.

31. Mitochondria have the ability to synthesize proteins and also contain proteins synthesized in the cytosol. How do cytosolic proteins become integrated in the inner membrane of mitochondria?
A. The outer membrane translocator TOM complex and the inner membrane translocator TIM 22/23 complex in the mitochondria allow the import of cytosolic proteins into the matrix. The proteins are inserted into the inner membrane through the OXA complexes.
B. The outer membrane translocator TOM complex and the inner membrane translocator TIM 23 complex in the mitochondria bind the cytosolic proteins. The proteins are inserted into the inner membrane through the TIM 23 complexes.
C. The outer membrane translocator TOM complex and the inner membrane translocator TIM 22 complex in the mitochondria bind the cytosolic proteins. The proteins are inserted into the inner membrane through the TIM 22 complexes.
D. The outer membrane translocator TOM complex and the inner membrane translocator OXA complex in the mitochondria bind the cytosolic proteins. The proteins are inserted into the inner membrane through the OXA complexes.

32. In cells that have defective GlcNAc phosphotransferase, which of the following is most likely to occur?
A. Accumulation of undigested substance in the lysosomes and secretion of lysosomal enzymes to the extracellular space
B. Failure to attach the precursor oligosaccharide en bloc to the Asn in proteins
C. Accumulation of undigested substance in the lysosomes only
D. Secretion of lysosomal enzymes to the extracellular space only
33. Phalloidin tagged with fluorescent dyes has been extensively used in visualizing the actin filaments in cell motility. This application of phalloidin in research is based on the ability of phalloidin
   A. to bind G-actin subunits
   B. to bind F-actin subunits
   C. to be tagged by fluorescent dyes
   D. to present the actin polymerization

34. If cells were treated with a weak base such as ammonia or chloroquine that raises the pH of organelles toward neutrality, the trafficking of lysosomal proteins from the Golgi apparatus to the lysosome will be impaired because
   A. M6P receptor fails to bind the lysosomal proteins in the Golgi apparatus.
   B. M6P receptor fails to move beyond the Golgi apparatus
   C. M6P receptor does not release the associated lysosomal proteins in the late endosome
   D. M6P receptor carries the lysosomal proteins to the extracellular environment

35. Dynamin function was discovered from the neurobiological studies in *Drosophila*. Shibire mutant flies, which carry a mutation in the dynamin gene, are rapidly paralyzed when the temperature is elevated. They recover quickly once the temperature is lowered. The complete paralysis at the elevated temperature suggested that synaptic transmission between nerve and muscle cells was blocked. Which of the following is most likely to be defective in the mutant flies?
   A. Endocytosis of neurotransmitters by muscle cells
   B. Exocytosis of neurotransmitters by the nerve terminals
   C. Both endocytosis of neurotransmitters by muscle cells and exocytosis of neurotransmitters by the nerve terminals
   D. Neither endocytosis of neurotransmitters by muscle cells nor exocytosis of neurotransmitters by the nerve terminals. Something else must be defective.
Part III. (10 points total)

Fill-in the blanks. 2 points each question.

Several mutant cell lines that are defective in their ability to have proper N-glycosylated proteins. Suppose you have analyzed the sugar monomers on a protein that carries only N-linked complex oligosaccharides purified from different mutant cells. Your results are listed in the table below. Each mutant is unique in the kinds and numbers of different sugars contained in its N-linked oligosaccharides.

<table>
<thead>
<tr>
<th>Cell line</th>
<th>Man</th>
<th>GcNAc</th>
<th>Gal</th>
<th>NANA</th>
<th>Glc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wild type</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Mutant A</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mutant B</td>
<td>3</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mutant C</td>
<td>9</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Mutant D</td>
<td>9</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mutant E</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mutant F</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mutant G</td>
<td>8</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mutant H</td>
<td>9</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Abbreviations: Man = mannose; GcNAc = N-acetylglucosamine; Gal = galactose; NANA = N-acetylmuramic acid, or sialic acid; Glc = glucose.

Numbers indicate the number of sugar monomers in the oligosaccharide.

Based on the steps in the pathway for processing N-linked oligosaccharides as illustrated in next page, please fill in the blanks.

1. The mutants \[A, B, C, D, E, F, G, H\] are defective in processing steps that occur in the Golgi.

2. The mutant F is most likely defective in the enzyme \[\text{galactose transferase}\].

3. The order of the mutants that corresponds to the steps from ER to the Golgi is \[A, B, C, D, E, F, G, H\].

4. If a new mutant Y is defective in NANA transferase, fill in the number of sugar monomers in the oligosaccharide on the protein purified from this mutant:
   Man \[9\]; GcNAc \[0\]; Gal \[3\]; NANA \[0\]; Glc \[3\].

5. The N-linked oligosaccharide is attached to the amino acid Asn in the sequence \[Glc\text{N Ac}, Glc, GcNAc, Gal, NANA}\].
The diagram illustrates the process of glycoprotein assembly in the endoplasmic reticulum (ER) and the Golgi apparatus. The key enzymes and molecules involved are shown at various stages.

1. **ER lumen**
   - **Asn**: Asparagine residue
   - **Glycosylation enzymes**
   - **ER mannosidase I**

2. **Golgi lumen**
   - **Asn**: Asparagine residue
   - **GlcNAc transferase I**
   - **UDP**
   - **UDP**
   - **CMP**

3. **Complex oligosaccharide**
   - **Endo H sensitive**
   - **Endo H resistant**

**KEY:**
- ○ = N-acetylgalactosamine (GlcNAc)
- ● = mannose (Man)
- ○ = galactose (Gal)
- ○ = N-acetylgalactosamine (GalNAc)
- ○ = N-acetylneuraminic acid (sialic acid, or NANA)