Multiple Choice (2 pts each) - Choose the single best answer.

1. An athlete whose urine tested positive for anabolic steroids requested that the urine sample be analyzed for DNA in order to prove that it was not hers. The nuclear DNA did not match the athlete, but the mitochondrial DNA was an exact match. What is the best explanation?
   A) The athlete had her identical twin sister take the drug test for her.
   B) The athlete substituted a maternal relative’s urine for her own.
   C) The scientist doing the drug test contaminated the urine with his own DNA.
   D) Because the mitochondrial DNA matched, it was definitely her urine sample.
   E) The DNA did not match, so she is clearly innocent of any wrongdoing.

2. Which of the following is not true about lipid rafts?
   A) They are enriched in sphingolipids.
   B) They are enriched in cholesterol.
   C) They have higher fluorescence anisotropy than normal membrane regions.
   D) They result in increased lateral diffusion of membrane proteins in the bilayer.
   E) They result in segregation of certain membrane proteins.

3. Facilitated diffusion for neutral metabolites is characterized by:
   A) Lineweaver-Burk plots that pass through the origin
   B) a large dependence on the membrane potential
   C) an upper limit in the transport velocity as the metabolite concentration increases
   D) a straight line plot of transport velocity versus the concentration of the metabolite
   E) the use of ATP to drive transport

4. The Hawaiian arrow poison palytoxin inhibits the Na⁺-K⁺ ATPase, locking it into such a position that it acts as a nonspecific ion channel. Which of the following is not true of the effects of palytoxin?
   A) K⁺ will exit the cell.
   B) Na⁺ will enter the cell.
   C) A great deal of secondary active transport will also be shut down.
   D) Its symptoms are probably similar to those of ouabain.
   E) Palytoxin is likely to result in rapid death for all organisms.

5. Phosphorylation plays an important role in signal transduction. Which of the following molecules would not be a regulator of phosphorylation in a major signaling pathway?
   A) An estrogen agonist
   B) A calcium channel blocker
   C) An uncompetitive inhibitor of GTP binding
   D) An irreversible inhibitor of Raf
   E) a competitive inhibitor of ATP binding
6. VEGFR, a receptor tyrosine kinase, is required for the formation of new blood vessels. Activity of VEGFR-mediated signaling is often high in tumors, enabling them to obtain the nutrients necessary for growth. Which of the following would be the best therapeutic strategy for inhibiting VEGFR-mediated signaling?

A) GTPγS, a non-hydrolyzable analogue of GTP
B) A drug that inhibits calmodulin
C) A drug that inhibits this pathway’s GAP
D) A drug that inhibits this pathway’s GEF
E) A drug that inhibits the receptor’s phosphatase

7. Which of the following is not involved in the signal transduction pathway that uses a cytosolic receptor guanylyl cyclase?

A) Grb2
B) GTP
C) cGMP
D) PKG
E) NO

8. What is the pH effect on the ΔG for the oxidation of glyceraldehyde 3-phosphate during glycolysis?

A) There is no effect on the ΔG.
B) The reaction becomes more favorable under acidic conditions.
C) The reaction becomes less favorable under acidic conditions.
D) The effect cannot be determined without knowing the ΔG°.
E) The ΔG remains the same, but the activation energy decreases.

9. Which of the following would not be a symptom of glucose 6-phosphatase deficiency?

A) hypoglycemia between meals
B) hyperglycemia right after eating
C) exercise intolerance
D) failure to thrive
E) enlarged liver

10. Your patient, Al Martini, is an adult presenting with symptoms that suggest glucose-6-phosphate dehydrogenase deficiency as a result of taking a sulfa drug. He has never been diagnosed with this disease before, but is now suffering from hemolysis after being prescribed the drug for a kidney infection. You feel certain that the following statements are true EXCEPT

A) Al has a fairly common genetic mutation.
B) This is probably the first time Al’s system has been swamped with reactive oxygen species.
C) Al has some glucose-6-phosphate dehydrogenase activity but less than normal.
D) Al probably has some innate malarial resistance.
E) Al’s red blood cells have no trouble making reduced glutathione but cannot oxidize it.
Short Answer Questions – You must show your work for full credit.

11. (9 pts) During the 2007 Rowing World Cup, a local resident reported seeing a team official discard a plastic bag containing medical waste. The International Rowing Federation (FISA) requested that the Swiss Laboratory for Doping Analyses perform an analysis to investigate a potential anti-doping rule violation. Traces of blood were found on needles and tubing, allowing DNA analysis of the samples.

a) Panel A shows partial results from one of the needles. What kind of DNA analysis was done and why was it a good choice?

![Panel A](image)

b) What is the most informative finding revealed by Panel A for tracking down the guilty athlete?

c) Eight different profiles were found on various needles and tubing. How would the Swiss Laboratory be able to determine which athletes were involved in this incident?

12. (4 pts) Rusty Johansson, a plant breeder, has developed a new frost-resistant variety of tomato plant. He is ready to start raking in the money, but when temperatures climb above 95°F, this frost-resistant variety dies, whereas the standard variety continues to grow. Consider the membrane only and provide a likely explanation for the biochemical basis of increased tolerance to cold and increased susceptibility to heat of this new tomato plant variety.
13. (12 pts) Poinsettias contain toxic phorbol esters, which interfere with normal signaling pathways involved in the inflammation response. Scientists are studying these compounds to determine how they exert their biological effects.

a) A representative structure of a phorbol ester is shown here. In general, where in the cell would you predict these compounds to end up? Explain.

b) A series of experiments was performed to determine the effects of phorbol esters on histamine release from mouse mast cells. First, adding Ca$^{2+}$ alone to the cells induced spontaneous histamine release in the absence of an inflammation signal. What signaling pathway(s) does this finding suggest might be at work?

c) The following data were obtained for histamine release in the presence of various combinations of the phorbol ester TPA, Ca$^{2+}$, and EDTA, a chelating agent that sequesters Ca$^{2+}$.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% histamine release</th>
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<tbody>
<tr>
<td>control</td>
<td>1.4 ± 0.2</td>
</tr>
<tr>
<td>+Ca$^{2+}$ only</td>
<td>7.1 ± 1.5</td>
</tr>
<tr>
<td>+ TPA only</td>
<td>34.0 ± 4.5</td>
</tr>
<tr>
<td>+ Ca$^{2+}$ and TPA</td>
<td>59.9 ± 4.9</td>
</tr>
<tr>
<td>+ TPA and EDTA</td>
<td>32.8 ± 3.2</td>
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</table>

Propose a mechanism by which TPA leads to histamine release, including information about its molecular target.

d) What information does the experiment with TPA and EDTA provide?
14. (11 pts) The $\text{H}^+/\text{K}^+$ ATPase (aka the gastric acid pump) pumps $\text{H}^+$ from the parietal cells of the stomach in exchange for $\text{K}^+$. These cells have an internal pH of 7.0, an internal $\text{K}^+$ concentration of 160 mM, and a membrane potential of -60 mV. Parietal cells secrete $\text{H}^+$ at a concentration of 0.18 M, and the extracellular concentration of $\text{K}^+$ is 12 mM.

a) If the pump transports one $\text{H}^+$ and one $\text{K}^+$ ion per cycle, what is the total energy cost per cycle? (Don’t forget to show your work!)

c) How much ATP is required for one cycle of the pump?

15. (12 pts) The gastric acid pump is the molecular target for the class of antisecretory drugs called the proton-pump inhibitors (PPIs), which are useful to treat gastric ulcers. You are characterizing several potential new PPIs, measuring the rate of hydrolysis of ATP by the pump in the presence and absence of inhibitors.

a) The first potential inhibitor is SC3265, which yields the adjacent Lineweaver-Burk plot. What can you conclude about the mechanism of inhibition? You should address all possibilities.

b) The second potential inhibitor is PSB143, which yields the adjacent Lineweaver-Burk plot. What can you conclude about the mechanism of inhibition? You should address all possibilities.

c) What is a potential problem with inhibiting the gastric acid pump therapeutically?

d) The half-life of the pump is about 50 hours. How does this impact the choice of drug?
16. (19 pts) Another potential therapeutic strategy for excess gastric acid secretion is to interfere with the signaling pathway that triggers acid release. Signaling results in activation of proteins responsible for bringing the H⁺/K⁺ ATPase to the plasma membrane from cytoplasmic vesicles. The signaling pathway is triggered by the presence of food in the stomach, which results in release of gastrin, histamine, and acetylcholine (ACh).

a) Identify the major players indicated by the numbers in the schematic below of the signaling pathway for gastric acid secretion. (Note that there may be some small inconsistencies in this schematic; e.g., 3 should be in the membrane.)

<table>
<thead>
<tr>
<th>1:</th>
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<tr>
<td>2:</td>
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<tr>
<td>3:</td>
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<tr>
<td>4:</td>
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<tr>
<td>5:</td>
</tr>
</tbody>
</table>

b) For each signal, name the pathway by which it operates in the gastric acid secretion process. (One word, or less, is sufficient.)

Histamine:

Acetylcholine (Ach):

Gastrin:

c) If your goal were to synthesize a therapeutic inhibitor of this signaling pathway, what molecule(s) would you target? Explain.
17. (9 pts) A two-year-old Caucasian male presents to the emergency department with a history of six days of fever and acute onset of red-colored urine. Birth history, past medical history, and family history are unremarkable. There has been no recent travel, and he has taken no medication. He was seen by his primary care physician approximately five days prior for evaluation of cough and runny nose. The only notable physical exam findings are an enlarged spleen and hemoglobin of 9.4 g/dL (normal, 11-13 g/dL). His blood glucose and response to glucagon were normal.

a) Hemolytic anemia makes you suspect an inherited disorder in an enzyme related to glycolysis. Explain why.

b) Based on your suspicions, you order further blood tests. Concentrations of some key glycolytic intermediates were measured in the patient’s red blood cells as follows.

<table>
<thead>
<tr>
<th>Glycolytic intermediate (nmol/mL red blood cells)</th>
<th>G6P</th>
<th>F6P</th>
<th>F1,6-BP</th>
<th>DHAP</th>
<th>3-PG</th>
<th>pyruvate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td>212</td>
<td>66</td>
<td>4780</td>
<td>1307</td>
<td>43</td>
<td>389</td>
</tr>
<tr>
<td>Normal</td>
<td>113-119</td>
<td>35-37</td>
<td>45-51</td>
<td>62-68</td>
<td>74-81</td>
<td>168-173</td>
</tr>
</tbody>
</table>

What specific single-enzyme defect best accounts for these lab results? Explain.

c) At first, you wonder whether your patient will also have problems in skeletal muscle, and then you realize he will not. Explain.

18. (4 pts) Given caffeine’s effects on cAMP levels, what you would advise a marathon runner who is trying to maximize her glycogen stores prior to competition about drinking coffee? Explain. Be specific.