**Chemistry 4055 (Spring 2013)**

**Biochemistry I- Introduction to the Chemistry of the Animal Cell**

**HW Set 5 Assignment**

**PLEASE WRITE YOUR ANSWERS ON A SEPARATE SHEET OF PAPER OR USE THIS TEMPLATE AND ADD SPACES.**

**Chapter 14**

1. Glucose is frequently administered intravenously to patients as a food source. A new resident at a hospital where you are doing one of your rotations suggests administering glucose-6-phosphate instead. You recall from my lecture that the transformation of glucose to glucose-6-phosphate requires ATP and you consider the possibility that administering glucose-6-phosphate might save the patient energy. Should you use the resident’s suggestion?

2. Arsenate, AsO43-, acts as phosphate analog and can replace phosphate in the glyceraldehyde-3-phosphate dehydrogenase (GAPDH) reaction. The product of this reaction is 1-arseno-3-phosphoglycerate. It is unstable and spontaneously hydrolyzes to form 3-phosphoglycerate, as shown below. What is the effect of arsenate on cells undergoing glycolysis?



3. Red blood cells synthesize and degrade 2,3-bisphosphoglycerate (2,3-bpg) as a detour from the glycolytic pathway, as shown in the figure.



2,3-BPG decreases the oxygen affinity of hemoglobin by binding in the central cavity of the deoxygenated form of hemoglobin as you may recall from lecture. This encourages delivery of oxygen to tissues. A defect in one of the glycolytic enzymes may affect levels of 2,3-BPG. The following plot shows oxygen-binding curves for normal erythrocytes and for hexokinase- and pyruvate-kinase deficient erythrocytes. Identify which curve responds to which enzyme deficiency. Note that PGK stands for phosphoglycerate kinase.



4. Except during starvation, the brain burns glucose as its sole metabolic fuel and consumes up to 40% of the body’s circulating glucose.

a. Hexokinase catalyzes the primary rate-determining step of glycolysis in the brain. In tissues where glycogen is stored, phosphofructokinase catalyzes phosphorolysis and also catalyzes the rate determining step of glycolysis in these tissues. Why the difference?

b. Brain hexokinase has a KM for glucose that is 100 times lower than the concentration of circulating glucose (5 mM). What is the advantage of this low KM?

5. A liver biopsy of a four-year old boy indicated that the fructose-1,6-bisphosphatase enzyme activity was 20% of normal. The patient’s blood glucose levels were normal at the beginning of a fast but then decreased suddenly. Pyruvate level was elevated as was the glyceraldehyde-3-phosphate/dihydroxyacetone phosphate ratio. Explain the reason for these symptoms.

**Chapter 16**

1. The product of the pyruvate dehydrogenase complex, acetylCoA, is released in step 3 of the overall reaction. What is the purpose of steps 4 and 5?

2. We did not talk about this in class but citrate, the product of reaction 1 of the citric acid cycle, inhibits phosphofructokinase, which catalyzes the third reaction of glycolysis. Based on the importance of metabolic flux and the body meeting its metabolite needs, why is this important when there is an excessive buildup of citrate?

3. The compound S-acetonyl-CoA is an inhibitor of citrate synthase. Based on the Lineweaver-Burk plot below, what type of inhibitor (I) is S-acetonyl-CoA?



4. Administration of high concentrations of oxygen (hyperoxia) is effective in the treatment of lung injuries but at the same time can also be quite damaging.

a. It has been shown that lung aconitase activity is dramatically decreased during hyperoxia. How would the concentration of citric acid cycle intermediates be affected?

b. The decreased aconitase activity and decreased mitochondrial respiration in hyperoxia are accompanied by elevated levels of glycolysis and the pentose phosphate pathway. Explain why. (Clue: It has to do with the electron carrier cofactors.)

5. The ΔG°’ for the fumarase reaction is -3.4 kJ·mol-1, but the ΔG value is close to zero.

a. What is the ratio of fumarate to malate under cellular conditions at 37°C?

b. Is this reaction likely to be a control point for the citric acid cycle?

6. The crystal structure of isocitrate dehydrogenase shows that there is a cluster of highly conserved amino acids in the substrate binding pocket- three arginines, a tyrosine, and a lysine. What is a possible role for these amino acid side chains in substrate binding?

**Chapter 19**

1. Calculate the standard free energy change for the reduction of oxygen by cytochrome a3. Is this reaction spontaneous under standard conditions? Note: Your reduction potential does not change even if you have to multiply your reduction equation by a factor to balance the number of electrons being transported.

2. a. What is the Δε value for the oxidation of ubiquinol by cytochrome c when the ratio is QH2/Q is 10 and the ratio of cyt c (Fe3+)/cyt c (Fe2+) is 5?

Use the equation:

$$ε= ε°^{'}+ \frac{RT}{nF}ln\frac{\left[A\_{reduced}\right]}{[A\_{oxidized}]}$$

F is Faraday’s constant = 96,485 J·V-1mol-1

R is the gas constant = 8.3145 J·K-1mol-1

Assume T is 298 K.

b. Calculate ΔG for the reaction.

3. The sequence of events in electron transport was elucidated in part by the use of inhibitors that block electron transfer at specific points along the chain. For example, adding rotenone (a plant toxin) or amytal (a barbiturate) blocks electron transport in Complex I; antimycin A (an antibiotic) blocks electron transport in Complex III; and cyanide (CN-) blocks electron transport in Complex IV by binding to the Fe2+ in the Fe-Cu binuclear center.

a. What happens to oxygen consumption when these inhibitors are added to a suspension of respiring mitochondria?

b. What is the redox state of the electron carriers in the electron transport chain when each of the inhibitors is added separately to the mitochondrial suspension?

4. Calculate the free energy change for translocating a proton out of the mitochondrial matrix, where pHmatrix = 7.6, pHcytosol = 7.2, Δψ = 200 mV, and T = 37 ͦ C.

5. In ATP synthase, what promotes the conformational changes that facilitates the catalyzed reaction?

6. Let’s use glucose as the metabolic fuel for aerobic respiration.

a. How many ATPs would be formed if NAD+ were the sole electron carrier cofactor formed throughout the metabolic pathways of glycolysis, the citric acid cycle, and oxidative phosphorylation?

b. How many H+ would have to be pumped from the intermembrane space and into the matrix for the ATP synthase to generate all of these ATPs?

c. Answer part a and b but replace NAD+ with FAD.