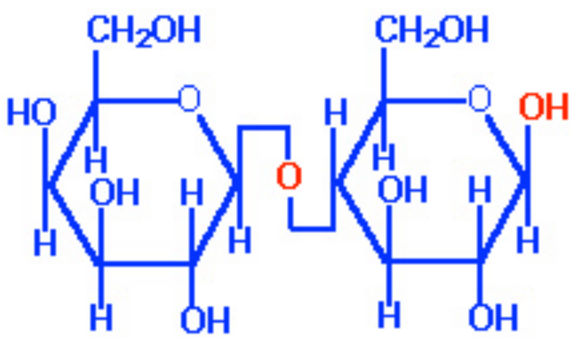
Name_______________________________

Chemistry 333
Principles of Biochemistry
Homework #3 (30 points)
Due Monday, November 23, 2009 (No later than 5pm!)

1. (14 points)

A. Your “favorite” TA, enjoys eating foods containing high levels of lactose and he wants to know how much ATP (in moles) is generated from the complete oxidation of one mole of lactose.

i. Draw the structure of lactose and name its constituent monosaccharides.



galactose glucose

ii. What enzyme is responsible for the degradation of lactose into its component parts?

Lactase or β-galactosidase

iii. As what molecule does each of the sugars enter glycolysis?

Glucose enters as glucose and must be phosphorylated by hexokinase.
Galactose is phosphorylated outside of glycolysis and enters as glucose-6-phosphate.

iv. Show all the work for the ATP calculation.

For 1 glucose molecule through glycolysis:

Step	ATP
Hexokinase	-1
Phosphofructokinase	-1
GAPDH	+5
Phosphoglycerate kinase	+2
Pyruvate kinase	+2
	7 ATP

For 1 galactose molecule through glycolysis

Step	ATP	
Entry of galactose into glycolysis	-1	
requires use of 1 mole ATP per mole galactose		
Phosphfructokinase	-1	
GAPDH	+5	
Phosphoglcerate kinase	+2	
Pyruvate kinase	+2	
	7 ATP	
For the 4 pyruvates		
4 pyruvate dehydrogenase	(NADH)	+10
4 Isocitrate Dehydrogenase	(NADH)	+10
4 α-ketoglutarate dehydrogenase	(NADH)	+10
4 Succinyl-CoA synthetase	(GTP)	+4
4 Succinate Dehydrogenase	(FADH2)	+6
4 Malate Dehydrogenase	(NADH)	+10
		50

TOTAL: 7+7+50= 64 ATP

(Hint: Be sure to account for energy used in activating the components of lactose so that they can enter glycolysis)

B. As a belated Halloween joke, you have decided to give Kevin a batch of cookies containing an inhibitor of some enzyme associated with metabolism. After eating these delectable cookies, Kevin finds that only **34** moles of ATP are being produced per mole of lactose.

For 1 lactose molecule through glycolysis:

Step		ATP	running total
Hexokinase		-2	-2
Phosphofructokinase		-2	-4
GAPDH		+10	+6
Phosphoglycerate kinase		+4	+10
Pyruvate kinase		+4	+14
For the 4 pyruvates			
4 pyruvate dehydrogenase	(NADH)	+10	+24
4 Isocitrate Dehydrogenase	(NADH)	+10	+34
4 α-ketoglutarate dehydrogenase	(NADH)	+10	
4 Succinyl-CoA synthetase	(GTP)	+4	
4 Succinate Dehydrogenase	(FADH2)	+6	
4 Malate Dehydrogenase	(NADH)	+10	
		64	

C. Where does the inhibitor act? Name the enzyme that is in inhibited and the pathway with which it is usually associated.

*Choose from enzymes in glycolysis, pyruvate dehydrogenase complex, and the TCA cycle. Assume electron transport and oxidative phosphorylation pathways are unaffected.

The inhibitor must act at <u>α-ketoglutarate dehydrogenase</u>, which is part of the <u>TCA cycle.</u>

2. (6 points) As a joke, Kalub made Chris a batch of "special" brownies containing an inhibitor of an enzyme associated with metabolism. After eating these delectable brownies, Chris finds that only moles of **48 ATP** are being produced per mole of sucrose. Which enzyme does the inhibitor act upon? Be sure to name the **inhibited enzyme** and the pathway with which it is usually associated.

Prior to entering TCA cycle, 24 ATP have been produced by glycolysis & PDH.

Glycolysis: 4 ATP & 4 NADH → 14 ATP
PDH: 4 NADH → 24 ATP

Enzyme	What's Produced	Total ATP
Isocitrate dehydrogenase	4 NADH	34
α-ketoglutarate dehydrogenase	4 NADH	44
Succinyl-CoA synthetase	4 GTP	48
Succinate dehydrogenase	INHIBITED!	TCA Cycle

3. (8 Points) You administer 360.32 grams of oral glucose to a patient. Calculate the amount of **ATP** your patient can generate under **aerobic** and **anaerobic** conditions with this glucose. Remember the different fates of pyruvate!

glucose MW=180.16 g/mol
(360.32g glucose)(mol/180.16g glucose) = 2.00 mol glucose

<u>AEROBIC</u>: (2.00mol glucose)(32ATP/mol glucose) = **<u>64 moles ATP</u>**

<u>ANAEROBIC</u>: (2.00mol glucose)(2ATP/mol glucose) = **<u>4 moles ATP</u>**

Under anaerobic conditions, 2 ATP are produced (net) per mole of glucose. 7 ATP are made per mole of glucose in glycolysis aerobically; but anaerobically, pyruvate is converted to lactate by lactate dehydrogenase at a cost of 2 NADH (5 ATP). Therefore 7 ATP - 5 ATP = 2 ATP. Since no O_2 is present for aerobic metabolism, any NADH produced (in glycolysis, PDH or TCA) cannot be used to make ATP.

NOTE: For this example, we assumed that the fate of pyruvate under anaerobic conditions ends with the production of lactate in muscles. As we will learn, lactate is recycled.)

4. (2 Points) In the hydrolysis of ATP to ADP and P_i, the equilibrium concentration of ATP is too small to be measured accurately. A better way of determining K'_{eq}, and hence $\Delta G^{\circ\prime}$ of this reaction, is to break it up into two steps whose values of $\Delta G^{\circ\prime}$ can be accurately determined. This has been done using the following pair of reactions (the first being catalyzed by glutamine synthetase):

(1) ATP + glutamate + $NH_3^+ \leftrightarrow$ ADP + P_i + glutamine + H^+ $\Delta G_1^{\circ\prime}$= -16.3 kJ/mol

(2) glutamate + $NH_3^+ \leftrightarrow$ glutamine + H_2O + H^+ $\Delta G_2^{\circ\prime}$= 14.2 kJ/mol

What is the $\Delta G^{\circ\prime}$ of ATP hydrolysis according to these data and is the **overall** reaction spontaneous?

In order to be able to achieve the overall ATP hydrolysis reaction from the two given reactions, you must reverse the 2nd equation and then add the ΔG's together. Note the sign of the 2nd ΔG changes to the negative value.

ATP + $H_2O \leftrightarrow$ ADP + P_i

Overall ΔG = -16.3 + -14.2 = **-30.5 kJ/mol**
The reaction is spontaneous