Chemistry 5.07
Problem Set 7

Problem 1

1. This question gives you experience tracking a labeled atom through the catabolic pathways we have studied so far.

a. Carbon dioxide is lost in the pyruvate dehydrogenase step of respiration. Starting with glycogen, and working through glycolysis, please show which glycogen carbon(s) contribute to that CO_2 loss. Show pathway in sufficient structural detail so that we know that you know what you are doing.

b. Glycerol is the backbone of triacylglycerides. The middle carbon is C2. Please trace a label from C2 (e.g., a ^{14}C or ^{13}C that has been inserted at that site by a synthetic reaction) through glycolysis and indicate the first place where the labeled molecule escapes as CO_2. Again, draw the pathway in sufficient detail to show us that you know what you are doing.

c. In Part b., there may be an energy yield between entry of glycerol into catabolism and the first exit of CO_2 from glycerol metabolism. On your pathway of Part b., count consumed and generated NAD+/NADH, FAD/FADH2, ADP and ATP, etc. and let us know the value of this catabolic conversion. Consider one NADH to be worth 3 ATP and one $FADH_2$ to be worth 2 ATPs.

d. Look at your pathway in Part a. Trace the labeled carbon not to CO_2 (as before) but to alanine. Indicate any cofactor or energy needs for this transformation.

e. Look at your pathway of Part b. Trace the labeled carbon to the amino acid, glutamate. Indicate any cofactor or energy needs for this transformation.

f. Look once again at your pathway of Part b. Trace the labeled carbon to the amino acid, aspartate. Indicate any cofactor or energy needs for this transformation.

Problem 2

Heavy metal toxicology.

a. In ancient Rome, it was fashionable for men and women to have a pale complexion (e.g., a sun tan was not socially acceptable). A woman named Toffana made cosmetics

out of arsenate (AsO_4^{3-}), which gave the desired effect (it caused anemia). Based on what JoAnne Stubbe taught in class, draw the step in which arsenate primarily blocks catabolism. Please draw the reaction as it is supposed to occur, and how it occurs in the presence of this toxic metal. Based upon what you know about the structures (including compartments) of red blood cells circulating in the blood vessels of people using these cosmetics, come up with an hypothesis to explain why these people developed anemia (giving them the desired cosmetic effect). Eventually hundreds of people died (including Toffana) so do not try this at home.

b. *Treponema pallidum* is the causative organism of syphilis. In the days before antibiotics, an early treatment was arsenite (AsO_3^{3-}), which has the property of bonding with closely spaced sulfhydryl groups. Based on what you know about the details of the pathways you have studied so far, predict the step at which arsenite would be active. Do you think it would cause anemia, as did its cousin, arsenate?

Problem 3

While we usually think of glucose or fatty acids as the primary precursors for catabolic energy generating pathways, mammalian cells especially like to use glutamine and glutamate, which are excellent carbon and nitrogen sources.

a. Predict in detail how glutamine might be converted enzymatically to glutamate.

b. Predict, again showing structural details, how glutamate could be converted into a precursor for the TCA cycle, which is one of the catabolic pathways we have studied.

c. Follow one molecule of glutamate around one turn of the TCA cycle and let us know how much energy is yielded (in terms of the amount of ATP, GTP that could be made). As above, assume one NADH converts to 3 ATP and one FADH2 converts to two ATP equivalents.

Problem 4

Following is a list of hereditary or induced metabolic defects involving loss of single enzymes of catabolism, and a second list of possible consequences of such defects. Match each enzyme with its most likely consequence (only one) from the second list. Explain each answer by using, if appropriate, an abbreviated metabolic pathway.

Defects:

a. Lack of phosphoglucomutase (PGM)
b. Lack of UDP-glucose pyrophosphorylase (not studied yet so you need to look it up)
c. Lack of triose phosphate isomerase (TPI or TIM)
d. Lack of phosphofructokinse I (PFK-I)
e. Lack of alpha-1,6-glucosidase (read about glycogen structure)

Consequences:

1. Lower than normal production of glucose 1-P in response to a sudden, large increase in cAMP level (cAMP is part of the “signal” mentioned in John’s first lecture)
2. Lethal; prevents use of carbohydrates for ATP production
3. Inability to make glycogen unless galactose is available, with no effect on ability to use glycogen
4. Impaired ability to obtain energy from carbohydrates
5. Inability to use either glycogen or galactose as an energy source

5.07SC Biological Chemistry I
Fall 2013