Problem Set 8 (**Due April 1st**)

1. We have seen three different Carboxylase enzymes recently: pyruvate carboxylase, propionyl-CoA carboxylase, and acetyl-CoA carboxylase (ACC).
    a. What reaction does each of these enzymes catalyze and what process are they important in?
    b. Draw a mechanism for the acetyl-coA carboxylase catalyzed reaction.
    c. Acetyl-CoA carboxylase and pyruvate carboxylase both put the CO_2 group at the end of a carbon chain, but propionyl-CoA puts the CO_2 on a central carbon. What makes propionyl-CoA different? Show a mechanism or reaction intermediate that supports your answer.

2. How are dietary triacylglycerides transported to myocytes or adipocytes?

3. Ketone bodies can be produced from fatty acid degradation.
    a. Why are ketone bodies made?
    b. Show a reaction scheme for the biosynthesis of Acetoacetate and β-hydroxybutyrate (the two most common ketone bodies).

4. Draw a mechanism for the conversion of an 8 carbon fatty acid to a 10 carbon fatty acid. Please make sure to show what the fatty acid is anchored to at all times. Please identify what domain of FAS is responsible for carrying out each of these reactions.

5. Show a mechanism for the conversion of a 10 carbon fatty acid to an 8 carbon fatty acid. Please identify the enzyme that catalyzes each reaction. Please also explain how these reactions are similar to the conversion of succinate to oxaloacetate.

6. Consider Phosphatidylinositol-4,5-triphosphate (PIP_2).
    a. Where have we seen PIP_3 before? Please describe the role it played.
    b. Draw this molecule. Note that this molecule includes arachidonic acid and stearic acid at the appropriate positions on the glycerol backbone.
    c. What class of proteins can hydrolyze this molecule to produce free fatty acids?
    d. Describe the process of converting these free fatty acids to CO_2 and ATP. Note that the hydrolysis event (part c) occurs in the cytosol and β oxidation is in mitochondrial matrix.
    e. How many molecules of ATP can be generated from the complete oxidation of this molecule? Assume that the polar head group is recycled (so it does not get metabolized). Makes sure to consider the glycerol 3-phosphate backbone.

7. Odd chain fatty acids result in a product other than Acetyl-CoA. What is this product and how does it get metabolized? How many ATP are produced from oxidation of propionyl-CoA?

8. Fatty acids are synthesized in hepatocytes using glucose as a carbon and fuel source.
    a. Describe how glucose can be used to synthesize palmitic acid. Please be clear with the steps that you show (i.e. if you use acetyl-CoA in your process, which you should, make sure to state where it comes from.
    b. Oleic acid can be condensed with glycerol-3-phosphate to make a lysophosphatidic acid. The glycerol-3-phosphate also derives from glucose. Please describe how.
    c. Determine how much ATP energy is sacrificed to make this lysophosphatidic acid. Make sure to account for the energy that could be made from the glucose that are consumed, any ATP that is directly consumed in the process, as well as the ATP that is sacrificed to make the NADPH that gets consumed.

9. Fatty acid metabolism is controlled in a similar way that sugar metabolism is.
    a. Would you expect flux through each of the major pathways we've discussed (glycolysis, gluconeogenesis, glycogen synthesis, glycogen degradation, β oxidation, fatty acid synthesis) to increase or decrease when the ATP/ADP ratio is low? For each pathway, please justify why flux increases or decreases.
    b. Fatty acid synthesis and oxidation are regulated by hormone levels. In Chapteryou're your bood describes how glucagon and insulin are able to influence the activity of ACC. Please summarize these mechanisms.
    c. Please comment on how ACC activity influences fatty acid oxidation.