Biochemistry 463, Summer II **Your Name:** _____

University of Maryland, College Park **Your SID #:** _____

Biochemistry and Physiology **Prof. Jason Kahn**

Final Exam (150 points total) **August 16, 2013**

You have 90 minutes for this exam.

Exams written in pencil or erasable ink will not be re-graded under any circumstances.

Explanations should be concise and clear. I have given you more space than you should need. There is extra space on the last page if you need it.

You will not need a calculator for this exam, and no other study aids or materials are permitted.

Partial credit will be given, *i.e.*, if you don't know, guess.

Honor Pledge: At the end of the examination time, please write out the following sentence and sign it, or talk to me about it:

"I pledge on my honor that I have not given or received any unauthorized assistance on this examination."

1. (15 pts) TCA Cycle Energetics and Regulation

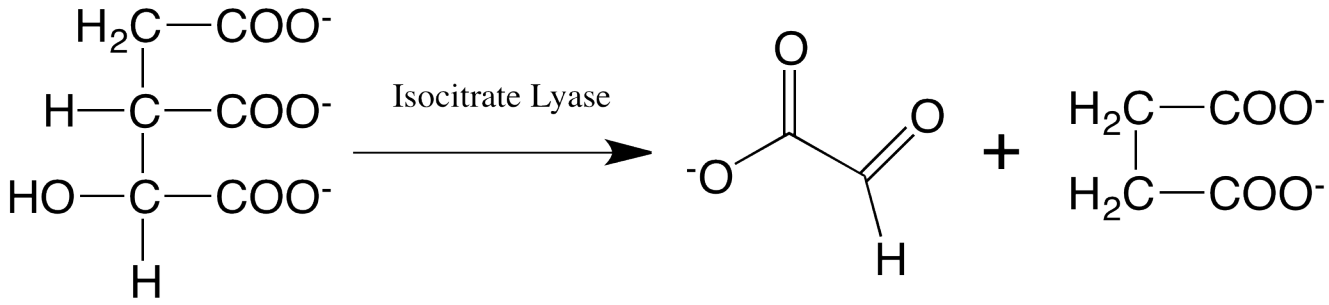
   Citrate synthase condenses oxaloacetate (OAA) and acetyl-CoA. Draw the structure of OAA and indicate the electrophilic carbon. What is the biochemical function of the final hydrolysis step of the mechanism, which appears to be just a waste of a thioester? Explain why the concentration of citrate actually decreases when the flux through the TCA cycle increases upon removal of NADH.

Score for the page_____

2. (15 pts) Enzyme Mechanisms

Mammals cannot incorporate net carbon from acetyl-CoA into glucose. Why not, biochemically?

Other organisms have a glyoxylate shuttle, in which the enzyme isocitrate lyase converts isocitrate into succinate plus glyoxylate and then glyoxylate is condensed with acetyl-CoA to give malate. This allows net conversion of acetyl-CoA into OAA and hence glucose. This seems like a useful trick to me – it would let us avoid using ketone bodies. The isocitrate lyase mechanism resembles the Class II aldolase mechanism of glycolysis (the one with an enolate intermediate rather than a Schiff's base). Propose a retro-aldol (actually formally a retro-Claisen) mechanism for isocitrate lyase. Include AH+ and B: groups as needed.



3. (8 pts) Glycogen

Name a glycogen storage or breakdown disease and briefly describe the biochemical defect..

Score for the page_____

4. (15 pts) Metabolic Nodes

Glucose-6-phosphate is an important control point metabolite. Draw its structure in the chair form. List three of the four possible fates for G6P in liver cells, and indicate which pathways will be stimulated by insulin.

5. (15 pts) Regulation

Sketch the bicyclic phosphorylation cascade that shuts off glycogen synthesis and activates glycogenolysis. Don't worry about the phosphatase side of things. Why is glycogen synthase also independently inhibited by other kinases like GSK-3β?.

Score for the page_____

6. (8 pts) Hormone regulation

How does insulin stimulate glucose uptake by muscle cells? Why does it make physiological sense that muscle cells do not respond to glucagon?

7. (6 pts) Metabolite Pools

Why do cells maintain separate pools of NADH/NAD+ and NADPH/NADP+ even though the cofactor pairs have identical redox properties? Name an enzyme (or draw the reaction) that reduces NADP+ to give NADPH.

8. (12 pts) Commitment to Fat

Draw the reaction (not the mechanism, just reactants and products), name the enzyme, and name the cofactor for the committed step for fatty acid biosynthesis. Where else have we seen a carboxylate installed just to be decarboxylated and provide a driving force for the following uphill reaction?

Score for the page_____

9. (8 pts) Building Fat

Mammalian and yeast fatty acid synthases are both megasynthases, protein complexes with many linked active sites. What is the biochemical rationale for this? What speculative reason did we give for the fact the two complexes have very different architectures?

10. (16 pts) Utility of Fat

Starting with palmitoyl (saturated C16)-CoA, draw the intermediates in the sequential oxidation, hydration, oxidation, and retro-Claisen reactions of one cycle of β-oxidation, with names of cofactors, abbreviations for enzymes, but no mechanisms.

Score for the page_____

11. (18 pts) Connections

Succinate dehydrogenase is uniquely situated among TCA cycle enzymes. How so, and what is its other name? What cofactors does it use, and why doesn't it use NADH? SDH deficiency can predispose cells to cancer. What was our speculation on how this works (a bird's eye view, not specific targets)?

Score for the page_____

12. (14 pts) Transport

We described two fundamentally different ways that protons are pumped protons across membranes in the ETC. Sketch them briefly (no need to describe the theory of relativity or the Q cycle in detail).

Page	Score
1	/15
2	/23
3	/30
4	/26
5	/24
6	/18
7	/14
Total	**/150**

Score for the page_____