C483 Exam 4
Summer 2016

Name Key Seat Number _____

Student ID _____ AI _____

The last page of this exam contains pKa values and other information you might find useful.
This exam contains 110 points. The highest score you may earn on this exam is 100 points.

1 _____/20pts

2. _____/10pts

3. _____/20pts

4. _____/10pts

5. _____/10pts

6. _____/10pts

7. _____/10pts

8. _____/10pts

9. _____/10pts

Total:

1. 20 pts Fill in the blanks (2 points each)

A. Fatty acids are activated in the cytosol by formation of the thioester high energy bond at the expense of two phosphoanhydride high energy bonds.

B. Processing of odd-carbon fatty acids requires the less-common vitamin cobalamine (B-12).

C. We do not have enzymes to make ω-3 or ω-6 fatty acids—they are termed essential fatty acids because we must obtain them through diet.

D. NADPH is a redox cofactor involved in fatty acid biosynthesis.

E. Glycine can be broken down by the glycine cleavage system to give a methylene group to the cofactor called THF.

F. Excess nitrogen is excreted in humans in the form of urea because it is less toxic and less basic than ammonia.

G. In addition to the liver, the other organ that does significant amounts of gluconeogenesis is kidney.

H. Lactate is recycled to glucose in the Cori cycle.

I. A ketone body is a water soluble form of acetyl CoA that forms in high concentrations in conditions such as diabetes and starvation.

J. In addition to carrying acetyl CoA into the cytosol, the citrate shuttle system also makes NADPH, which is essential for fatty acid synthesis, through the maleic enzyme.

2. 10 points True or false (1 point each)

A. True Besides the enzymes typically needed for β-oxidation, the catabolism of unsaturated fatty acids requires additional enzymes to help in the processing of the carbon-carbon pi bonds.

B. True Fatty acid degradation takes place in the mitochondrial matrix, but fatty acid synthesis takes place in the cytosol.

C. False Formation of HMG-CoA is the committed step of cholesterol synthesis.

D. False Lysine is a ketogenic amino acid because it is catabolized to succinate as an intermediate.

E. True Thymidylate synthase is a chemotherapy target.

F. False Synthesis of urea from bicarbonate and nitrogen sources costs a total of 3 high energy bonds.

G. False Insulin is an upregulator of gluconeogenesis.

H. True AMP-dependent kinase is a form of local regulation that works through covalent modification of catabolic and anabolic enzymes.

I. False Glycogen phosphorylase is covalently modified to upregulate glycogen synthesis.

J. False Branched fatty acids are a significant fuel for the liver.

3. (20pts) Short answer (5 points each)

A. Draw the reaction (starting material and final products) for the regulated step of fatty acid synthesis.

B. Match each amino acid to its catabolic intermediate: pyruvate, oxaloacetate, a-ketoglutarate, or more than one of these.

Alanine pyruvate

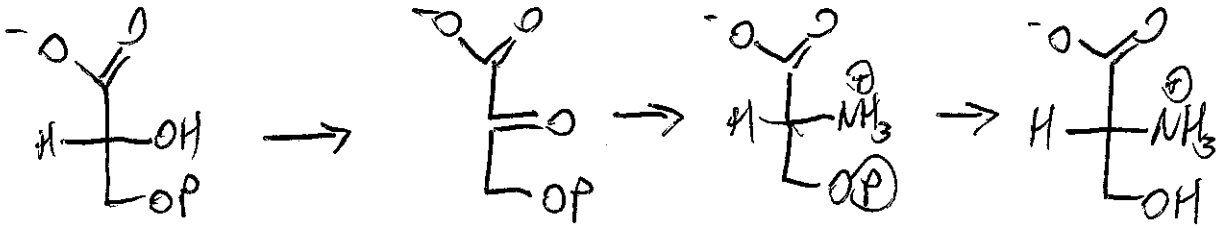
Histidine α-K.G

Asparagine OAA

Serine pyruvate

Glutamate α-KG

C. Give a three step synthesis of 3-phosphoglycerate to serine

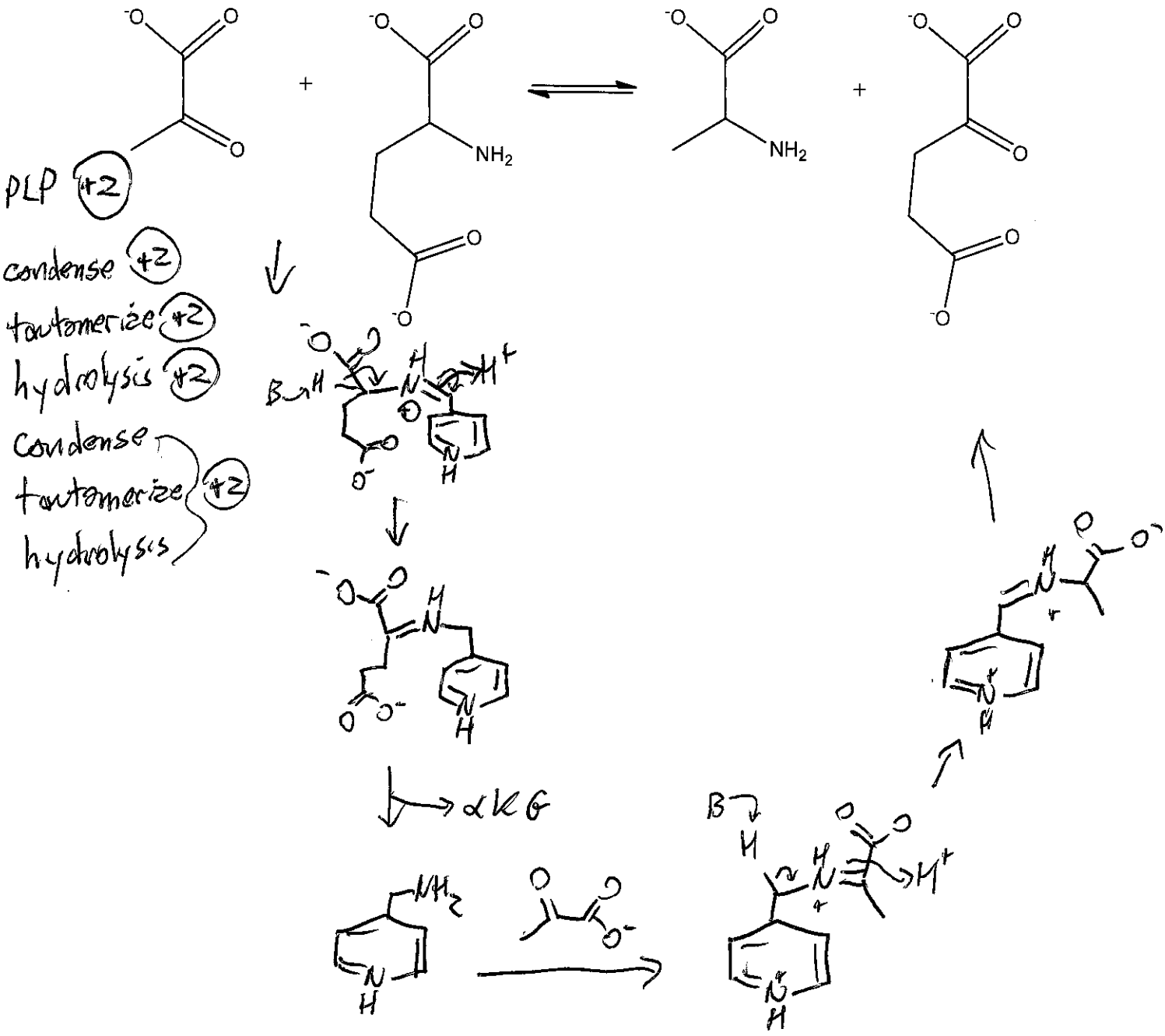


D. After several days of starvation, the ability of the liver to metabolize acetyl-CoA becomes severely compromised. Explain in 1-2 sentences.

With no dietary sugar, gluconeogensis increases, using up oxaloacetate. This reduces CAC intermediates, making acetyl CoA metabolism slow.

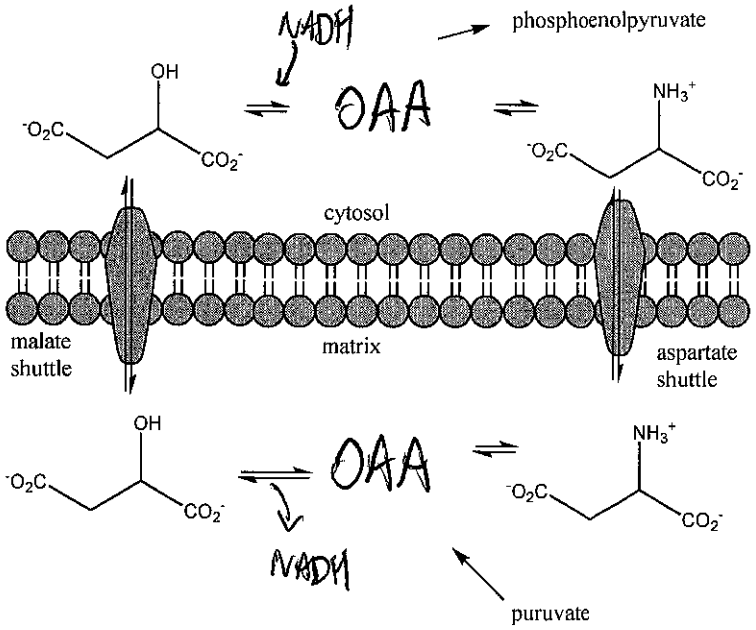
Problems (10pts each)

4. Provide an enzyme-mediated mechanism for this transamination. You do not need to write every step of Schiff base formation. (Which cofactor do you need?)



5. Part of the malate/aspartate shuttle is shown below. Finish the cycle with the missing compound..

+3



B. The shuttle is reversible. In one direction, it is part of one of the major pathways we have discussed? Which one? Explain.

+3

Gluconeogenesis - OAA From matrix is carried out to cytosol to be made into PEP

C. In the other direction, it serves as a reversible "NADH shuttle" even though no NADH crosses the membrane. Explain.

+2

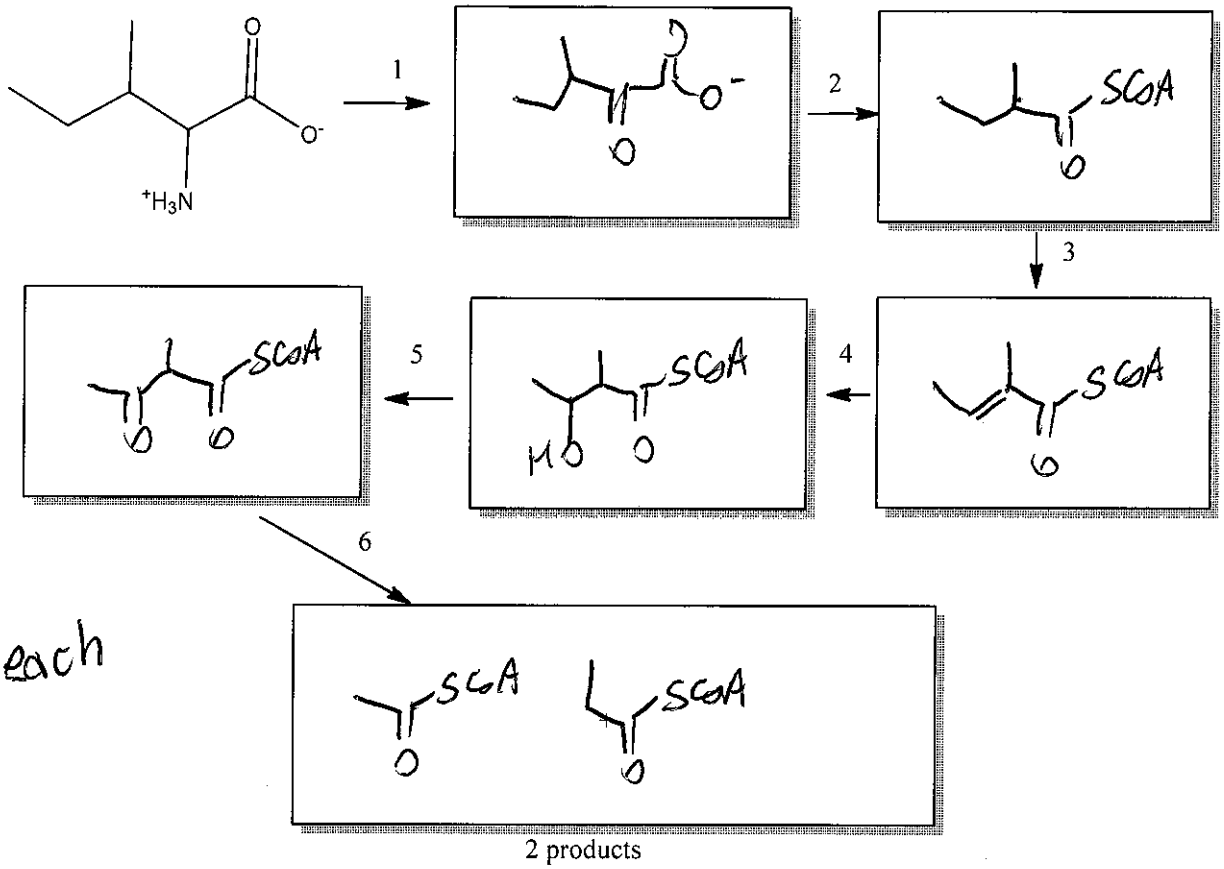
Malate $\rightleftharpoons$ OAA uses NADH in cytosol, but the reverse rxn then produces it in matrix

D. When this NADH shuttle is operational under aerobic conditions, how many ATP can be synthesized from the NADH made in glycolysis?

+2

2.5

6. Degradation of isoleucine involves a series of six steps. The first step is common to all amino acid degradation. The second step is analogous to pyruvate dehydrogenase. The last four steps are analogous to β-oxidation. Draw all intermediates and the final products of isoleucine degradation.



+1 each

Based on the products you drew, is isoleucine glucogenic, ketogenic, or both? Explain.

(+1) Both

acetyl CoA is ketogenic (+1)

propionyl CoA is glucogenic (+1)

7. Excess glucose can be transformed into acetyl CoA, which can go into long term storage as fatty acids. How many ATP equivalents need to be spent in producing a 16-carbon, saturated fatty acid from 8 acetyl CoA? (Assume that reduced cofactors are equivalent to 1.5 or 2.5 ATP as appropriate.) Show your reasoning.

Seven malonyl CoA = 7 ATP

Seven reverse β-oxidation x 2 NADPH = 14 NADPH = 35 ATP

Total = 42 ATP

How many equivalents of ATP can be produced from a 16-carbon saturated fatty acid through full b-oxidation and oxidative phosphorylation? Show your reasoning.

Seven β-oxidation = 7 QH_2 = 10.5 ATP
7 NADH = 17.5 ATP
= 80 ATP

Eight $\sim$SCoA

128 ATP
− 2 ATP initial activation
126 ATP

Based on your answers above, what is the net cost of storing fuel in the form of fatty acids?

Net cost = 14 ATP − storage = 42
− return of Box = 28
14 ATP

8. Under stress, muscle will tend to use various sources to obtain ATP. Some paths can be sued to produce a lot of ATP; some paths can be used to obtain ATP quickly. Fill in the table below with the appropriate paths from the list below:

Fuel source	ATP formation rate (mmol/s)	Total phosphorylations (mmol)
Muscle ATP	--	223
creatine phosphate	73.3	446
Anaerobic muscle glycogen	39.1	6700
Aerobic muscle glycogen	16.7	84,000
Aerobic liver glycogen	6.2	19,000
Aerobic adipose fat	6.7	4,000,000

-2

- Anaerobic oxidation of muscle glycogen
- Creatine phosphate
- Aerobic oxidation of adipose fatty acids
- Aerobic oxidation of liver glycogen
- Aerobic oxidation of muscle glycogen

Problem 19.47

9. (10pts Case study) The properties of acetyl-CoA carboxylase were studied in mice to see whether the enzyme might be a possible drug target to treat obesity. One isozyme is found in muscle and is upregulated by insulin. In addition to control mice, there was also a group of mice in which the gene for this enzyme is "knocked out."

A. Fatty acid oxidation was measured in muscle tissue samples collected from both control and knockout mice. Administration of insulin caused a 45% decrease in fatty acid oxidation in normal mice, but caused no change in the oxidation of fatty acids in the knockout mice. Explain.

+5

Normal mice - when treated with insulin, acetyl CoA carboxylase is activated, causing a rise in malonyl CoA, which is an inhibitor of fatty acid oxidation (carnitine transport)

Knockout mice will not produce malonyl CoA in response to insulin

B. Both knockout and normal mice were allowed access to as much food as they cared to eat. After 27 weeks, the knockout mice had consumed more calories but had accumulated less fat in the adipose tissue than normal mice. Explain.

+5

* Unable to synthesize fats, they have to mobilize them from adipose.
* There is no effective control of fatty acid oxidation, so fats quickly metabolized.