BIS103-001 (Spring 2009)  
Final Exam (June 6)  
Name_____________________________________

Instructor: Abel  
Student ID #_______  

ANSWER KEY

Pls., check appropriate box below.

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<th>Undergraduate Student</th>
<th>Completing Incomplete</th>
<th>Open Enrollment Student</th>
<th>Graduate Student</th>
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This exam consists of 5 questions. A maximum of 100 points can be earned. Partial credit will be given. There are a total of 13 pages, including the cover page and one blank sheet at the end for notes. However, do not use the blank sheet for your final answers. If you need more space, use the back of pages 2-12. Write your name on top of each page! Petitions for regarding will be considered only if you have used permanent ink, unless an addition error has occurred.

*IT IS YOUR RESPONSIBILITY TO WRITE LEGIBLE!  
No extra effort will be made to decipher your handwriting.

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<th>Question</th>
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I, ________________________________, authorize the University to distribute publicly this graded exam (e.g., handed out in class or left in a bin for pick up).

I am aware of the fact that violations of the Academic Code of Conduct\(^1\) may be reported to UC Davis Student Judicial Affairs.

\(^1\)Examples of academic misconduct include: receiving or providing unauthorized assistance on examinations, using unauthorized materials during an examination, altering an exam and submitting it for re-grading, or using false excuses to obtain extensions of time (http://sja.ucdavis.edu/cac.htm).

Signature________________________________________  Date____________________________
1. (26 pts) Questions related to fatty acid metabolism.

a) The citrate shuttle, which can be viewed as an indirect transporter of acetyl groups, provides the acetyl-CoA units required for fatty acid biosynthesis. What is the cost of this transport process in ATP equivalents per acetyl group? (2 pt)

ATP per acetyl group: ___ 1 ATP _____

b) Acetyl-CoA is the precursor in fatty acid biosynthesis. However, for most of the reactions, acetyl-CoA needs to be further activated by a biotin-dependent enzyme before it can be used by the fatty acid synthase complex.

Write the balanced reaction of acetyl-CoA activation and give the enzyme name. (4 pts)

Reaction:   

    Acetyl-CoA + HCO_3^- + ATP → Malonyl-CoA + ADP + Pi

Enzyme:  

    Acetyl-CoA Carboxylase


c) The synthesis of fatty acids and their breakdown by β-oxidation occurs by separate pathways. Compare the two pathways in animals by filling the blanks below. (7 pts)

<table>
<thead>
<tr>
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<th>Synthesis</th>
<th>β-oxidation</th>
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<tbody>
<tr>
<td>Cellular Compartment</td>
<td>Cytosol</td>
<td>Mitochondria</td>
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<tr>
<td>Carbon-units added/removed</td>
<td>Malonyl-CoA</td>
<td>Acetyl-CoA</td>
</tr>
<tr>
<td>Required redox cofactors</td>
<td>NADPH</td>
<td>NAD^+</td>
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<tr>
<td></td>
<td></td>
<td>FAD</td>
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d) Activated fatty acids (i.e. acyl-CoA) are both the substrates of β-oxidation and the end products of fatty acid synthesis. Briefly describe how the simultaneous degradation and synthesis of fatty acids in the same cell is prevented. (4 pts)

Malonyl-CoA, an intermediate of fatty acid synthesis, inhibits carnitine-acyl transferase I and thus the uptake of acyl-CoA into the mitochondria.

e) Assume that the synthesis of a 14:2 fatty acid is accomplished by the fatty acid synthase complex using acetyl-CoA units initially produced by the PDH complex, and by a fatty acid desaturase to introduce the double bonds (the position of the double bonds is not important for this problem). Calculate how many moles of ATP and NADPH are required for the synthesis of the 14:2 acid. You must show your work for full credit. (6 pts)

I. Transport of 7 acetyl-CoA from mitochondria to cytosol: 7 ATP  
II. Activation of 6 acetyl-CoA to 6 malonyl-CoA: 6 ATP  
III. Two reduction steps (2 NADPH) per round (6 rounds) 12 NADPH  
IV. Each of the two desaturation reactions requires 1 NADPH 2 NADPH  

Moles of ATP: 13 ATP  Moles of NADPH: 14 NADPH

f) Six colonies of fruit flies are cultured in jars containing only one of the following organic acids as the sole source of carbon. Three of the six colonies survive. Which ones? Circle. (3 pts)

β-hydroxybutyrate  succinate  acetate  propionate  serine  glycine
2. (24 pts) Questions related to amino acid metabolism.

a) Once proteins are hydrolyzed to free amino acids, what initial reaction catabolizes the amino acids? Give a specific example for alanine. Draw the chemical structure of alanine into the left box and provide the chemical structures and full names of the other reactants. Further, provide the specific name of the enzyme that catalyzes this reaction and the full name of its required co-factor. (9 pts)

Reactants: See booklet for structures

Alanine $\alpha$-Ketoglutarate Pyruvate Glutamate

Specific enzyme name: ______ Alanine Aminotransferase

Full name of co-factor: ______ Pyridoxal-phosphate

b) Describe in one sentence the purpose of urea production in humans. (1 pts)

To excrete excess nitrogen.

c) In what organ is urea synthesized? Circle. (1 pt)

Muscles Brain Liver Kidneys Bladder Pancreas

d) Which intracellular compartments participate in the production of urea? Circle all correct. (2 pts)

Cytosol Nucleus Mitochondria Peroxisome Chloroplast
e) Draw the chemical structure of urea and name the precursor molecules of its N and C atoms that enter the urea cycle. (4 pts)

Carbamoyl-P and Aspartate

f) Name the two sulfur-containing protein amino acids and circle the one that is essential for humans. (3 pts)

Cysteine and Methionine


g) Tyrosine (Tyr) is derived from phenylalanine (Phe). Circle the correct enzyme name and the required co-factor. (2 pts)

Oxidase  Dehydrogenase  Monooxygenase  Dioxygenase

\[\text{FMNH}_2, \text{NADPH, NADH, Tetrahydrofolate}\]

h) Histamine acts as neurotransmitter and triggers the inflammatory response. Histamine is derived from histidine by its decarboxylation. Which one of the following co-factors is required by the enzyme histidine decarboxylase? Circle. (1 pt)

Biotin  TPP  PLP  THF  SAM  Coenzyme A

i) Glycine (Gly) can be generated from serine (Ser) in a single reaction by eliminating the “hydroxymethyl” (-CH$_2$OH) group. Which co-factor “rescues” this group? Circle. (1 pt)

Biotin  TPP  PLP  THF  SAM  Coenzyme A
3. (12 pts) Reactions related to nucleotides and reactive oxygen species (ROS).

a) Theobromine, a compound related to caffeine, is derived from xanthine by successive methylation (see below). Theobromine belongs to what compound class and which co-factor is the most likely donor of the two methyl groups? (2 pts)

![Diagram of Xanthine to Theobromine conversion]

- Compound class (circle):  
  - Pyrimidines
  - Purines

- Co-factor (full name):  
  - S-Adenosylmethionine

b) The carbon atom of the methyl groups of theobromine does most likely originate from what biochemical pathway? Circle. (1 pt)

- Glycolysis
- Pentose-P Pathway
- TCA cycle
- β-oxidation

c) Riboucleotides contain a ribose unit. How is the ribose unit activated for nucleotide biosynthesis (provide a balanced equation of the reaction)? Briefly describe the major difference between de novo synthesis of pyrimidine and purine nucleotides in regards to ribose attachment. (4 pts)

Ribose activation:  

\[
\text{Ribose-5-P} + \text{ATP} \rightarrow 5'-\text{phosphoribosyl-1-pyrophosphate (PRPP)} + \text{AMP}
\]

Difference between pyrimidine and purine nucleotide synthesis:

- **The purine nucleobase is assembled step-by-step on the activated ribose (PRPP) platform whereas the pyrimidine ring structure is first formed and then transferred to PRPP.**
d) Briefly explain the term “reactive oxygen species” (ROS) and give one specific example for a ROS molecule. (3 pts)

ROS are partially reduced compounds derived from oxygen. Examples are superoxide, hydrogen peroxide or the hydroxyl radical.

e) A major source of ROS is the mitochondria and the chloroplasts in plants. What pathways in these organelles generate accidentally ROS? (2 pts)

Mitochondria: Electron Transport Chain (ETC)

Chloroplasts: Photosynthesis (Light reactions)
4. (16 pts) The diagram below shows a hypothetical catabolic pathway in amino acid metabolism. Assume that compound A is a protein amino acid that is degraded to product F (fumarate) and to product I (pyruvate) via the intermediates B, D, E, G, and H.

The $\Delta G^\circ$ values for each reaction (1-8) are as follows:

1. (A to B) = $+2.2$ kJ mol$^{-1}$
2. (B to D) = $-46.8$ kJ mol$^{-1}$
3. (D to G) = $+1.1$ kJ mol$^{-1}$
4. (G to H) = $-29.4$ kJ mol$^{-1}$
5. (B to C) = $-0.5$ kJ mol$^{-1}$
6. (G to E) = $-32.7$ kJ mol$^{-1}$
7. (H to I) = $-2.8$ kJ mol$^{-1}$
8. (E to F) = $+1.8$ kJ mol$^{-1}$

a) Which of the eight enzymatic reactions (1-8) are essentially irreversible under physiological conditions and which are reversible? Insert arrow heads in the graph above: double arrows for reversible reactions and single arrows for irreversible reactions. (3 pts)

**Irreversible: 2, 4, 6**

**Reversible: 1, 3, 5, 7, 8**

b) Compounds A, C, F, and I are allosteric regulators of the pathway. Indicate which of the four compounds are most likely allosteric inhibitors and allosteric activators. (4 pts)

Activators: _______ A and C

Inhibitors: _______ F and I

c) The amino acids degraded by this pathway can be referred to as: (1 pt) Circle one.

**glucogenic**    **ketogenic**    **gluco- and ketogenic**
d) Predict the effect of each of the following hormones on this pathway. Circle. (3 pts)

- Adrenaline: Activation
- Glucagon: Activation
- Insulin: Activation

Inhibition

e) What is your reasoning of your choice for adrenaline? (2 pts)

The action of glucagon prevents a serious decline in blood glucose concentration by activating pathways that generate glucose. As the degradation of amino acids A and C leads to fumarate and pyruvate (products I and F), which can be used in gluconeogenesis, this pathway is likely activated by glucagon secretion.

f) Which one of the eight enzymes is most likely to be regulated by covalent modification in response to these hormones? (1 pt)

Enzyme No.: 2

g) Briefly describe the difference between allosteric regulation and covalent modification of enzymes. (2 pts)

**Allosteric regulation:** Metabolites that are not substrates (so-called effectors, or activators and inhibitors) bind to a regulatory site of the enzyme, which is different from the catalytic site and true substrate binding site. This “allosteric” interaction rapidly alters protein conformation and kinetic properties of the enzyme.

**Covalent modification:** Covalent but reversible addition of a group (very often a phosphate group from ATP) to an enzyme in response to a regulatory signal (e.g., a hormone), which alters protein conformation and kinetic properties of the enzyme.
5. (22 + 3 pts) Multiple-choice questions. **Circle the best answer.** There is **only one best answer** per question. Each question is worth 2 pts.

a. High blood concentrations of urea suggest consumption of one of the following diets:
   
   i. A gallon of Classic Coca Cola (16.25% sucrose) watching a game. 
   
   ii. Ten pieces of cake topped with whipped cream at the “Konditorei”. 
   
   iii. Two pounds of greasy French fries at home. 
   
   iv. **Two large T-bone steaks at the “Buckhorn”**. 
   
   v. A plate of cereals topped with fruits from the “Farmers Market”

b. Biological oxidation-reduction reactions always involve:
   
   i. Peroxisomes 
   
   ii. Formation of water and carbon dioxide 
   
   iii. Transfer of hydrogen 
   
   iv. Use of molecular oxygen 
   
   v. **Transfer of electrons**

c. The coenzyme that can carry a one-carbon (C1) unit at the highest oxidation state is:
   
   i. **Biotin** 
   
   ii. Tetrahydrofolic acid 
   
   iii. Tetrahydrobiopterin 
   
   iv. Lipoic acid 
   
   v. **S-Adenosylmethionine**

d. NADPH is NOT a reactant in one of the following processes:
   
   i. Pentose-P pathway 
   
   ii. Photosynthesis 
   
   iii. Detoxification of ROS 
   
   iv. Hydroxylation Reactions 
   
   v. **Methyl Cycle**
e. Which one of the following enzymes is NOT part of the glyoxylate cycle?
   i Malate Dehydrogenase
   ii Malate Synthase
   iii Aconitase
   iv Isocitrate Dehydrogenase
   v Isocitrate Lyase

f. Glutathione is best described as:
   i a carbohydrate
   ii a peptide
   iii a lipid
   iv a protein
   v an amino acid

g. What is the most immediate biosynthetic precursor to an “isoprenoid” compound?
   i glucose
   ii pyruvate
   iii acetyl-CoA
   iv carbamoyl-phosphate
   v propionyl-CoA

h. Uric acid, falling from the sky onto your head, is:
   i an intermediate of the urea cycle
   ii a purine compound
   iii a highly oxidized amino acid
   iv a pyrimidine compound
   v the polymeric form of urea
i. What is the most likely source of propionyl-CoA in metabolism (as discussed in class)?

- a product of glycolysis
- a product of the PDH reaction
- a product of fatty acid degradation
- a product of ketone body degradation
- a product of the pentose phosphate pathway

j. Which one of the following free organic acids is a potent allosteric regulator of enzymes involved in the aerobic catabolism of glucose?

- acetic acid
- lactic acid
- pyruvic acid
- citric acid
- malonic acid

k. Which one of the following enzymes is most likely NOT regulated by ATP availability?

- phosphofructokinase
- pyruvate dehydrogenase
- triose-P isomerase
- $\alpha$-ketoglutarate dehydrogenase
- pyruvate kinase

l. **Bonus question (3 extra points)!** Nuclear gene expression is regulated by the acetylation of histones (a process known as chromatin remodeling). The acetylation of lysine residues of histone proteins is catalyzed by histone acetylases, which use acetyl-CoA as a substrate. Which one of the following enzymes is most likely to provide the acetyl-CoA for histone acetylation?

- ATP-Citrate lyase
- Acyl-CoA synthetase
- Pyruvate dehydrogenase
- Thiolase
- Serine-hydroxymethyl transferase