This exam will be taken apart for grading. Please PRINT your name on each page. If you do not have sufficient room for your answer in the space provided, please continue on the back of the page on which the question appears.

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<th>Earned Points</th>
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TOTAL 133

Score on:

Exam I Exam II Exam III Final Total*/3.3 = Course Avg.

NOTE: FULL CREDIT WILL BE GIVEN FOR THOSE ANSWERS WHICH CLEARLY ADDRESS ALL RELEVANT ASPECTS OF THE QUESTIONS IN THE CLEAREST AND MOST CONCISE MANNER.
1. [16 points; 2 points/correct response; 1 point off for each incorrect guess]
Illustrate your familiarity with heme metabolism [biosynthesis and catabolism] and intertissue cooperation by matching appropriate items in the list on the left with items from the list on the right.

1. Bone marrow. 
   _____a. Catalyzes the translocation of Δ-ALA from the cytosol to the mitochondrial matrix
   _____b. Principle site of red blood cell [RBC] production in adult humans.

2. Spleen. 
   _____c. Immature red blood cell; makes both globin and heme.
   _____d. Involved in transport of bilirubin from the spleen to the liver.

3. Liver 
   _____e. Degrades worn out RBC’s; part of the reticuloendothelial system.

4. Heart. 
   _____f. Required for removal of glucuronic acid residues from bilirubin diglucuronide.
   _____g. Converts bilirubin to the diglucuronide.

5. Ferritin 
   _____h. Produced by cleavage of the tetrapyrrrole ring and release of a molecule of CO. [as in class]

6. Δ-Aminolevulinic acid [Δ-ALA] synthase
   _____i. Produced by decarboxylation of protoporphyrin IX.

7. Reticulocyte
   _____j. Overproduction by dysfunctional liver causes brain damage and jaundice.
   _____k. Produced by SAM-mediated modification of a tetrapyrrrole

8. Transferrin
   _____l. Produced by SAM-mediated modification of a tetrapyrrrole

9. Bilirubin 
   _____m. Storage form of iron
NAME _____________________

II. [14 pts; 1 point/correct response; 1/2 point off for each incorrect guess]
Match each hormone in the left column with its properties, major target organ, and metabolic effects from the right column.

(a) Insulin  ____________________  
   (1) A catecholamine hormone  
   (2) A polypeptide hormone  
(b) Glucagon  ____________________  
   (3) Secreted by the α cells of the pancreas  
(c) Epinephrine  _________________  
   (4) Effects are mediated by cAMP  
   (5) Target organ is the liver  
   (6) Target organ is muscle  
   (7) Signals the fed state  
   (8) Secreted in response to low blood glucose levels  
   (9) Promotes storage of fuels  
   (10) Promotes the breakdown of stored fuels

III. [5 points; 1/2 point off for each incorrect guess]
Match the metabolic pathway in the left column with its major role in metabolism from the right column.

A) Glycolysis  ___________________________  
   1) Control of glucose levels in the blood
B) Gluconeogenesis  _________________  
   2) Formation of NADH and FADH₂
C) Pentose Phosphate Pathway  ____________  
   3) Storage of fuel
D) Glycogen Synthesis  _________________  
   4) Synthesis of NADPH and ribose-5-phosphate
E) Fatty acid degradation  ________________  
   5) Production of ATP and building blocks of molecules
IV. [16 points]
Describe the general fate of each of the following compounds in the mitochondria and in the cytosol of a liver cell:

<table>
<thead>
<tr>
<th>Cytosol</th>
<th>Mitochondrion</th>
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</thead>
<tbody>
<tr>
<td>A. Palmitoyl-CoA</td>
<td></td>
</tr>
<tr>
<td>B. Acetyl-CoA</td>
<td></td>
</tr>
<tr>
<td>C. Carbamoyl phosphate</td>
<td></td>
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<tr>
<td>D. Glutamate</td>
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</tbody>
</table>

V. [6 points]
Describe the major metabolic consequences of enzymatic deficiencies in:

1) Hexokinase in adipose tissue

2) Thiolase in brain

VI. [6 points]
The control of phosphofructokinase in the liver and muscle is different. In response to low blood glucose, epinephrine initiates responses in both tissues; however, epinephrine stimulates glycolysis in muscle, but inhibits glycolysis in liver. Explain in detail.

VII. [9 points]
We have discussed several examples of hormone-mediated regulation of enzymatic activity. Describe (in as much detail as you are able) the relevant biochemical events and the associated physiological context for the action of one hormone. Be as specific as possible. Begin by stating the dietary condition prevailing when the hormone is released, from which tissue it is released, and identifying the principal target tissue.

FULL CREDIT WILL BE GIVEN FOR ANSWERS WHICH MOST CLEARLY AND ACCURATELY ADDRESS ALL RELEVANT ASPECTS OF THE QUESTION IN THE MOST CONCISE MANNER.
VIII. [6 points]
ALA dehydratase from human RBC’s has a molecular weight of 280-kD, and is comprised of eight, apparently identical subunits; it contains no disulfide bonds. Each subunit contains one atom of Zn\textsuperscript{++}, and for full activity, a reducing agent such as 2-mercaptoethanol or glutathione must be included in the assay.

Using the principles of protein structure and function which you learned early in the course:

A. Postulate a role for Zn\textsuperscript{++} in ALA dehydratase (or any enzyme). [NOTE: Zinc ion does NOT undergo a change in oxidation state as part of the catalytic mechanism.]

B. Offer a rational explanation for the requirement of a reducing agent.

C. If you wanted to test the hypothesis you proposed in part B, what crucial information would you look for in the amino acid composition of the protein?

IX. [6 points] Answer A or B, but not both, only your first answer will be graded.

A.
As you know, the double bonds in naturally occurring fatty acids are of the cis configuration. Several recent reports have indicated a marked increase in the incidence of cardiovascular disease in individuals whose fat intake is comprised of a high proportion of trans fatty acids. The origin of these trans fatty acids is in the nature of the process used to partially reduce oils of plant origin, containing highly unsaturated fatty acids, for production of less liquid fatty foods like margarine. During partial reduction to increase the degree of saturation, some of the cis double bonds which are not reduced are converted to trans double bonds; hence foods containing these partially reduced fatty acids contain trans fatty acids.

The biochemical basis of the relationship between intake of trans fatty acids and heart disease is under investigation, you are not expected to provide a hypothesis to explain the clinical observations.

You are expected, however, to think about the structures, metabolism and functions of lipids which were discussed during the course and to suggest at least one line of investigation which might elicit significant metabolic or structural differences between triacylglycerols or phospholipids containing naturally occurring fatty acids and those containing trans fatty acids.

To help you get started, consider the following.

Suppose you had access to liposomes comprised of phospholipids containing a high proportion of trans fatty acids, as well as liposomes containing phospholipids having normal (cis) fatty acids. How might you use these preparations to explore possible differences in interactions among the hydrophobic tails in these preparations?
B.
Consider the following mechanism for an enzyme-catalyzed reaction (E represents the enzyme):

\[
\begin{align*}
E & \rightleftharpoons E^- + H^+ \\
E^- & + S^+ \rightleftharpoons E \cdot S^+ \\
E \cdot S^+ & \leftrightarrow E \cdot P^- \\
E \cdot P^- & \leftrightarrow E^- + P^+
\end{align*}
\]

What does this mechanism ‘say’, in words?

Would you expect the \( K_M \) for substrate to be pH-dependent? Explain.

Will the affinity for substrate increase or decrease as pH is lowered below the pK of the dissociable group indicated in the first line of the mechanism? Why?

X. [13 points]

Cytochrome c is a soluble heme protein that transfers individual electrons from the cytochrome reductase complex to the cytochrome oxidase complex during respiratory electron transfer.

(a) Acetylation of one or more surface exposed lysines in cytochrome c decreases both the rate of electron transfer during reduction and subsequent oxidation of this protein. What does this suggest concerning the operation of the electron transfer chain? [4 pts]

(b) What type of amino acid residues on the cytochrome reductase complex and the cytochrome oxidase complex would you expect to interact with cytochrome c? [3 pts]

(c) Describe (with a diagram) the role of two b hemes of cytochrome b in the cytochrome reductase complex during the Q-cycle. [6 pts]
XI. [5 points]
Histidine residues are found at the active sites of many enzymes and functional sites of many other proteins. Describe the special properties of His that make it such an important amino acid residue.

XII. [7 points]
Describe the role of ubiquitin in intracellular protein degradation.

XIII. [24 points]
(A) The CFTR protein is a member of ABC transporter superfamily. What does the term 'ABC' stand for? [2 pts]

(B) Each member of this family specifically transports one or a small number of ions, molecules or macromolecules. Which parts of an ABC transporter confer such specificities? [3 pts]

(C) What does the CFTR protein transport? [1 pt]

(D) The DF508 mutation is the most common lesion in the CFTR protein of cystic fibrosis (CF) patients. Describe the cellular and biochemical basis for the deleterious effects of this mutation. [6 pts]

(E) In your opinion, what will be the best strategy to cure a CF patient with the DF508 mutation? Why is your strategy better than at least one other strategy that you are aware of? [6 pts]

(F) What is a Prion disease? [2 pts] Explain with a diagram the possible mechanistic basis for the disease according to Prusiner and coworkers. [4 pts]