MCB 102: Pantea's Sxn **Chapter 16 Problem Set Answer Key**

1) **Page: 603 Ans: A**

Which of the following is *not* true of the reaction catalyzed by the pyruvate dehydrogenase complex?

A) **Biotin participates in the decarboxylation.**
B) Both NAD^+ and a flavin nucleotide act as electron carriers.
C) The reaction occurs in the mitochondrial matrix.
D) The substrate is held by the lipoyl-lysine "swinging arm."
E) Two different cofactors containing —SH groups participate.

2) Page: 603 Ans: E

Which combination of cofactors is involved in the conversion of pyruvate to acetyl-CoA?

A) Biotin, FAD, and TPP
B) Biotin, NAD^+, and FAD
C) NAD^+, biotin, and TPP
D) Pyridoxal phosphate, FAD, and lipoic acid
E) **TPP, lipoic acid, and NAD^+**

3) Page: 607 Ans: B

Malonate is a competitive inhibitor of succinate dehydrogenase. If malonate is added to a mitochondrial preparation that is oxidizing pyruvate as a substrate, which of the following compounds would you expect to decrease in concentration?

A) Citrate
B) Fumarate
C) Isocitrate
D) Pyruvate
E) Succinate

4) Page: 607 Ans: B

Oxaloacetate uniformly labeled with ^{14}C (i.e., with equal amounts of ^{14}C in each of its carbon atoms) is condensed with unlabeled acetyl-CoA. After a single pass through the citric acid cycle back to oxaloacetate, what fraction of the original radioactivity will be found in the oxaloacetate?

A) all
B) **1/2**
C) 1/3
D) 1/4
E) 3/4

5) Page: 610 Ans: E

The reaction of the citric acid cycle that is most similar to the pyruvate dehydrogenase complex-catalyzed conversion of pyruvate to acetyl-CoA is the conversion of:

A) citrate to isocitrate.
B) fumarate to malate.
C) malate to oxaloacetate.
D) succinyl-CoA to succinate.
E) α-ketoglutarate to succinyl-CoA.

6) Page: 612 Ans: B
The standard reduction potentials ($E'°$) for the following half reactions are given.

Fumarate + $2H^+$ + $2e^-$ → succinate	$E'° = +0.031$ V
FAD + $2H^+$ + $2e^-$ → $FADH_2$	$E'° = –0.219$ V

If succinate, fumarate, FAD, and $FADH_2$, all at l M concentrations, were mixed together in the presence of succinate dehydrogenase, which of the following would happen *initially*?

A) Fumarate and succinate would become oxidized; FAD and $FADH_2$ would become reduced.
B) **Fumarate would become reduced; $FADH_2$ would become oxidized.**
C) No reaction would occur because all reactants and products are already at their standard concentrations.
D) Succinate would become oxidized; FAD would become reduced.
E) Succinate would become oxidized; $FADH_2$ would be unchanged because it is a cofactor, not a substrate.

7) Page: 614 Ans: A
Which of the following intermediates of the citric acid cycle is prochiral?

A) Citrate
B) Isocitrate
C) Malate
D) Oxaloacetate
E) Succinate

8) Page: 621 Ans: E
Citrate synthase and the NAD^+-specific isocitrate dehydrogenase are two key regulatory enzymes of the citric acid cycle. These enzymes are inhibited by:

A) acetyl-CoA and fructose 6-phosphate.
B) AMP and/or NAD^+.
C) AMP and/or NADH.
D) ATP and/or NAD^+.
E) **ATP and/or NADH.**

9) Page: 602
Briefly describe the relationship of the pyruvate dehydrogenase complex reaction to glycolysis and the citric acid cycle.

Ans: The pyruvate dehydrogenase complex converts pyruvate, the product of glycolysis, into acetyl-CoA, the starting material for the citric acid cycle.

10) Pages: 602-605
Describe the enzymes, cofactors, intermediates, and products the pyruvate dehydrogenase complex.

Ans: The pyruvate dehydrogenase complex consists of multiple copies of each of three enzymes. The first enzyme to act is pyruvate dehydrogenase (E_1), which converts pyruvate to CO_2 and the hydroxyethyl derivative of thiamine pyrophosphate (TPP). The same enzyme then oxidizes the hydroxyethyl group to an acetyl group attached to enzyme-bound lipoate through a thioester linkage. The second enzyme, dihydrolipoyl transracetylase (E_2), transfers the acetyl group to coenzyme A, forming acetyl-CoA. The third enzyme, dihydrolipoyl dehydrogenase (E_3), oxidizes the dihydro-lipoate to its disulfide form, passing the electrons through FAD to NAD^+. (See Fig. 16-6, p. 605.)

11) Page: 605
Match the cofactors below with their roles in the pyruvate dehydrogenase complex reaction.

Cofactors:
A. Coenzyme A (CoA-SH)
B. NAD^+
C. Thiamine pyrophosphate (TPP)
D. FAD
E. Lipoic acid in oxidized form

Roles:
_______ Attacks and attaches to the central carbon in pyruvate.
_______ Oxidizes $FADH_2$.
_______ Accepts the acetyl group from reduced lipoic acid.
_______ Oxidizes the reduced form of lipoic acid.
_______ Initial electron acceptor in oxidation of pyruvate.

Ans: C; B; A; D; E

12) Page: 605
What is the function of FAD in the pyruvate dehydrogenase complex? How is it regenerated?

Ans: FAD serves as the electron acceptor in the re-oxidation of the cofactor dihydrolipoate. It is converted to $FADH_2$ by this reaction and is regenerated by the passage of electrons to NAD^+.

13) Page: 606
The human disease beriberi is caused by a deficiency of thiamine in the diet. People with severe beriberi have higher than normal levels of pyruvate in their blood and urine. Explain this observation in terms of specific enzymatic reaction(s).

Ans: Thiamine is essential for the synthesis of the cofactor thiamine pyrophosphate (TPP). Without this cofactor the pyruvate dehydrogenase complex cannot convert pyruvate into acetyl-CoA, so the pyruvate produced by glycolysis accumulates.

14) Page: 607
Draw the citric acid cycle *from isocitrate to fumarate only*, showing and naming each intermediate. Show where high-energy phosphate compounds or reduced electron carriers are produced or consumed, and name the enzyme that catalyzes each step.

Ans: This part of the citric acid cycle includes the reactions catalyzed by isocitrate dehydrogenase, the α-ketoglutarate dehydrogenase complex, succinyl-CoA synthetase, and succinate dehydrogenase. (See Fig. 16-7, p. 607.)

15) Page: 607
Show the structures of the reactants and products for two of the four redox reactions in the citric acid cycle. Indicate where any cofactors participate, and label the reactants, products, and cofactors as oxidants or reductants in the reaction.

Ans: The four oxidation-reduction reactions are those catalyzed by isocitrate dehydrogenase, the α-ketoglutarate dehydrogenase complex, succinate dehydrogenase, and malate dehydrogenase. (See Fig. 16-7, p. 607.)

16) Page: 613

Explain in quantitative terms the circumstances under which the following reaction can proceed.

L-Malate + NAD^+ → oxaloacetate + NADH + H^+ $\Delta G'^\circ = +29.7$ kJ/mol

Ans: A reaction for which $\Delta G'^\circ$ is positive can proceed under conditions in which the actual ΔG is negative. From the relationship

$$\Delta G = \Delta G'^\circ + RT \ln \frac{[\text{product}]}{[\text{reactant}]},$$

it is clear that if the concentration of product is kept very low (e.g., by its removal in a subsequent metabolic step), the logarithmic term becomes negative and the actual ΔG can then have a negative value. (See also Chapter 13.)