Problem Set 5

MCDB 108B

1. You are studying a patient with McArdle's disease which is characterized by a deficiency in glycogen phosphorylase in muscle but not in liver. Explain how the following would be altered (in comparison to a normal patient) upon analysis:

a) fasting levels of blood glucose
b) liver glycogen content
c) muscle glycogen content
d) blood lactate levels after vigorous exercise
e) blood glucose levels after administration of glucagon
f) blood glucose levels after administration of epinephrine

2. At low pyruvate concentrations, pyruvate is preferentially shunted to the TCA cycle as opposed to being reduced to lactate. But at high pyruvate concentrations, proportionally greater flux to lactate occurs. Draw the predicted graphs of reaction velocity vs [pyruvate] for both TCA cycle and lactate dehydrogenase that would explain this phenomenon. Indicate the significant parmeters obtained from the curves. (8).

3. **a)** The substrates for the TCA cycle are oxaloacetate and acetyl-CoA. Explain how the levels of these metabolites are balanced so that increased levels of acetyl-CoA are constantly matched by oxaloacetate (2).

b) (4) During starvation and diabetes, the main route for acetyl-CoA is the formation of acetoacetate and ketone bodies. Explain the biochemical mechanisms which largely prohibit oxidation of acetyl-CoA and its conversion to free fatty acids, two other major fates of acetyl-CoA metabolism (4).

c) (4) Why is oxaloacetate formation so critical for survival during, for example, starvation? Give two reasons (4).

d) Answer true or false and explain. The following can serve as a source of oxaloacetate during starvation (4):

___ 1) amino acids such as alanine
___ 2) fatty acids through the formation of acetyl CoA.

4. (6) If the appropriate cell type is treated with the following hormones, will the following be increased (↑), decreased (↓) or unaffected (un) by the respective hormone treatment? (fill in the blanks) (7)

	glucagon	epinephrine	Insulin
F6P → F1,6 BP in:			
liver	_____	_____	_____
muscle	_____	_____	
pyruvate → acetyl CoA			_____
acetyl CoA → malonyl CoA	_____		_____
glycogen → Glucose 1P	_____		
TAG → FFAs + glycerol	_____		_____
cAMP levels	_____		_____
HMG CoA → mevalonate	_____		

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5. Palmitate is degraded to acetyl-CoA by β-oxidation. Starting with the acyl-CoA form of palmitate, explain the chemical strategy involved in one cycle of the β-oxidation process. Show all cofactors, reactants and products involved. (6)

6. Explain the requirement for HCO_3^- in fatty acid synthesis (4). What is the point of carboxylation of acetyl-CoA when the same carboxyl group is subsequently removed later in the same cycle?