Glycogen and Regulatory Cascade

1. The name for the group of enzymes that catalyze the removal of a phosphate from molecule is \textit{phosphatase}.

2. The name for the group of enzymes that catalyze the addition of a phosphate to a molecule is \textit{kinase}.

3. In the diagram below, label which elements of the regulatory cascade are phosphorylated using a \textit{P}.

   \textbf{DURING EXERCISE OR FASTING}

   | Glucagon (liver) or epinephrine (muscle and liver) | Adenylate cyclase |
   | ATP | Cyclic AMP |
   | Protein kinase A | Protein kinase A |
   | Phosphorylase kinase | Phosphorylase kinase |
   | (P) Glycogen synthase | Glycogen synthase |
   | Phosphorylase b | Phosphorylase a |
   | Glycogen_n | \textit{Glycogen}_n-1 |
   | Glucose 1-phosphate |

4. List each element that is phosphorylated in the diagram above, what enzyme is responsible for its phosphorylation, and whether it is active or inactive when phosphorylated.

   \textit{phosphorylase kinase} - phosphorylated by \textit{protein kinase A} \hspace{1cm} \textit{active}

   \textit{phosphorylase a} - phosphorylated by \textit{phosphorylase kinase} \hspace{1cm} \textit{active}

   \textit{glycogen synthase} - phosphorylated by \textit{protein kinase A} \hspace{1cm} \textit{inactive}
5. The activity of protein kinase A is not controlled by phosphorylation. What activates protein kinase A?

binding of cyclic AMP (cAMP)

6. What effect do epinephrine or glucagon on:
   a. glycogen synthesis?
      inhibits
   b. glycogen breakdown?
      activates
   c. Are these effects consistent with glycolysis or gluconeogenesis?
      gluconeogenesis

7. What effect do you expect insulin will have on:
   a. glycogen synthesis
      activates
   b. glycogen breakdown?
      inhibits
   c. Are these conditions consistent with glycolysis or gluconeogenesis?
      glycolysis
8. In order to prevent a futile cycle, glycogen synthesis and breakdown are reciprocally regulated. When insulin binds the cell surface receptor, glycogen synthesis is stimulated and glycogen breakdown is inhibited.

a. Do the effects of insulin on glycogen synthesis and glycogen breakdown make sense in terms of physiology? Why or why not?

Insulin signals a fed state so there is a lot of glucose around which is toxic. Glycogen is a way to store all of this glucose. Glycogen synthesis is activated. There is abundant glucose already so we do not need to break glycogen down (would release more glucose—unnecessary).

b. Considering the diagram on the first page, what has to be done in order for insulin to have the desired effect?

*all of these phosphorylations must be reversed*

c. What type of enzyme do you think is responsible for the effects of insulin/reversal of the effects of glucagon or epinephrine?

*phosphatase*  
*(in this case protein phosphatase I)*
Challenge Question: Glycogen and Regulatory Cascade

Group Members

Individuals with McArdle disease have a total deficiency of muscle glycogen phosphorylase. As a result, they cannot exercise strenuously due to muscle cramping and exertion by these patients leads to much greater cellular levels of ADP and Pi than normal. Furthermore, lactic acid does not accumulate in the muscles of these patients as it does in normal individuals.

Explain the chemical imbalances involved in McArdle disease.

Glycogen phosphorylase is required for glycogen breakdown. Without glycogen phosphorylase, glycogen cannot be broken down so glycogen cannot be mobilized into glucose as an energy source.

Insufficient glucose prevents the production of ATP by glycolysis. ATP (necessary for muscle contraction) is not replenished so ADP and Pi accumulate. Lack of ATP results in muscle cramping.

Lactic acid does not accumulate because little pyruvate is produced (pyruvate → lactate) from glycolysis (no glucose available from glycogen).

There is little glucose so any lactic acid will quickly be taken away to the liver for the Cori Cycle (makes glucose).