# Highlights Glycogen III

1. Reversing phosphorylations causes glycogen breakdown to cease and glycogen synthesis to begin. Remember that insulin is released in response to an increase in blood sugar and it stimulates cells to take up glucose. Thus, when the cells take up glucose, the glycogen synthesis system is stimulated to put it into glycogen and this occurs because insulin stimulates the activity of Protein Phosphatase (PP1), which is capable of removing phosphates from all the proteins described above.

2. Thus, when insulin binds the cell surface receptor, glycogen synthesis is stimulated (glycogen synthase is converted from the 'b' form to the 'a' form) and glycogen breakdown is inhibited (glycogen phosphorylase is converted from the 'a' form to the 'b' form). In addition, PP1 removes the phosphate from glycogen phosphorylase kinase, which stops it from phosphorylating additional glycogen phosphorylase enzymes.

3. Insulin is capable (via binding to a cell surface receptor) of reversing the action of the phosphorylation system. It does this by stimulating the activity of Protein Phosphatase I (PP1). This, in turn, causes ALL OF THE EARLIER PHOSPHORYLATIONS TO BE REVERSED.

4. By contrast, the protein kinase A phosphorylation system simultaneously activates glycogen breakdown (by making GPa) and inhibits glycogen synthesis (by making GSb), it also INACTIVATES the enzyme that removes phosphates (PP1).

5. PP-1 binds to a protein called $G_M$ (in muscle) or $G_L$ (in liver). When bound to $G_L$, PP-1 is held close to the glycogen phosphorylase, which is useful because this allows easy access to dephosphorylate it and turn it off.

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7. Activation of PKA by epinephrine or glucagon causes $G_M$ to be phosphorylated, which, in turn, causes PP-1 to be released in a less active form. PKA also phosphorylates the PP-1 inhibitor, which then binds PP-1 and inactivates it. Thus, the phosphorylation system shuts down the dephosphorylation system and vice versa, depending on which hormone has bound to the cell surface receptor.

8. GPa normally binds PP-1-$G_L$ tightly and acts as a glucose sensor in liver cells. PP-1 is inactive when bound to GPa if GPa is in the R state. Increasing glucose concentration causes GPa to flip into the T state. When GPa is in the T state, PP-1-$G_L$ is released from GPa, becomes active, and dephosphorylates GPa, forming GPb. Freed from GPa, can then PP-1 dephosphorylate GSb, forming GSa. Thus, glycogen synthesis is NOT activated until glycogen breakdown is first

stopped.

9. Thus, the experiment I showed in class where addition of glucose to purified GPa and GSb causing conversion of GPa to GPb and GSb to GSa makes sense in that addition of glucose causes GPa to flip into the T state, which causes it to release PP-1-$G_L$ to begin dephosphorylation of the two enzymes.

That's all folks. I have enjoyed working with you this term and look forward to working with you again next term.