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Hormonal Control

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1. What are the overall effects of insulin and glucagon? How are blood levels of these hormones regulated? What cell types produce glucagons and insulin?
    a. Insulin
        i. Decreases blood sugar by
            1) Promotes uptake of glucose into muscle and adipose tissue by activating GLUT transporters
            2) Promotes storage of glucose --> glycogen, glucose --> FA and FA --> triglycerides
            3) Inhibits secretion of glucagon and transcription of glucagon gene
        ii. Insulin levels increase w/ increased blood sugar
        iii. Produced by beta/B-cells of pancreas in Islets of Langerhans
    b. Glucagon
        i. Promotes conversion of glycogen to glucose, gluconeogenesis, release of FA from adipose and FA oxidation
        ii. Levels increase w/ decreased blood sugar and epinephrine stimulation
        iii. Produced by A-cells of pancreas
2. What is the mechanism for the action of glucagons on metabolism?
    a. Glucagon triggers the synthesis of cAMP by binding to a receptor on liver and adipose cell membranes
        i. This g-protein coupled receptor causes GTP hydrolysis which activates adenylyl cyclase
        ii. Adenylyl cyclase converts ATP --> cAMP
        iii. cAMP can activate PKA via binding to the regulatory subunit and releasing the catalytic subunits
        iv. PKA will then phosphorylate certain proteins
        v. This phosphorylation can be activating or deactivating
    b. Epinephrine follow a similar pattern in muscle, liver and adipose
3. How are the levels of cAMP regulated?
    a. cAMP levels are regulated by the above mechanism (increases cAMP) as well as cAMP phosphodiesterase (PDE) (decreases cAMP)
    b. PDE causes the conversion of cAMP to AMP
    c. PDE is activated by PKA (feed-forward regulation) and by the insulin activated kinase
    d. Thus, insulin leads to a decrease in cAMP levels and decreased PKA activity
4. What are the structured features of phosphoprotein phosphatase?
5. How is phosphoprotein phosphatase activity regulated?
    a. Structure of PPP: constant catalytic subunit and variable regulatory subunit that regulates activity and cell location
    b. Regulation of PPP: phosphorylation of the regulatory subunit
        i. Liver PPP acts on proteins that are phosphorylated on serine or threonine
        ii. PPP is activated by phosphorylation by insulin activated kinase by a huge cascade of reactions --> amplification
        iii. PPP causes dephosphorylation of the protein
        iv. There is also a PPP inhibitor
            1) PPI is activated by phosphoryation by PKA (cAMP)
            2) PPI binds to PPP to inhibit its activity
            3) PPI causes cAMP signal to remain ON