open.michigan

Author(s): Aken Desai, Michael Mathis, 2008

Glycogen

Friday, January 11, 2008
10:00 AM

25. What are the structural features of glycogen?
    a. Mostly in liver and muscle
    b. Glucose molecules in alpha(1-->6) and alpha (1-->4) linkages
    c. Alpha(1-->6) linkages are branch points
    d. End with freely converted to open form carbon is called reducing end and is bound to glycogenin
    e. Other ends are non-reducing
    f. Reactions take place at non-reducing ends
26. How is glucose-1-P formed from glycogen?
    a. Glycogen Phosphorylase
        i. Breaks alpha 1-->4 bonds w/ phosphate
        ii. Products are glucose-1-p and remainder of glycogen chain
        iii. Requires pyridoxal phosphate (niacin)
        iv. Reacts at non-reducing end
    b. Debranching enzyme
        i. Breaks alpha 1-->4 bonds adjacent to branch point
        ii. Forms new alpha 1-->4 bond w/ other chain
        iii. Releases free glucose (alpha1-->6 bound) from branch
27. How is glycogen synthesized? What is the role of glycogenin?
    a. Phosphoglucomutase: Glucose-6-P --> Glucose-1-P
    b. Glucose-1-P uridylyltransferase: Glucose-1-P + UTP --> UDP-Glucose + Ppi
    c. Glycogen synthase: UDP-Glucose + (Glucose)n --> UDP + (Glucose)n+1
    d. Branching enzyme: Breaks alpha (1-->4) and forms alpha (1-->6) bonds
    e. Glycogenin
        i. Self glucosylates w/ 8 UDP-Glucose at Tyr residue
        ii. Once primed, glycogen synthase and branching enzyme can do their thing
28. What is the role of debranching and branching enzymes and how do they operate in the synthesis and breakdown of glycogen?

- 26b and 27e

29. How is phosphorylase regulated?
    a. T form/phosphorylase b is inactive
        i. Partially activated by AMP binding allosterically to R/phosphorylase b
        ii. R/phosphorylase b inactivated by ATP or G6P
    b. Phosphorylase kinase: T form + 2ATP --> phosphorylated but inactive
    c. Conformational change makes phosphorylase a (fully active)
    d. Allosteric glucose binding to phosphorylase a causes inactivation
    e. PPP can dephosphorylate
        i. Insulin activated kinase activates PPP
        ii. Glucagon/EPI --> cAMP --> PPI inhibition of PPP
30. How is glycogen synthase regulated?
    a. Active form is dephosphorylated
    b. Primed by casein kinase II phosphorylation
    c. Glycogen synthase kinase 3 phosphorylates at 3 serine residues to inactivate
        i. Can also by phosphorylated at other residues by PKA, phosphorylase kinase, calmodulin-dependent kinase. Each phosphorylation decreases activity.
        ii. GSK3 inhibited by phosphorylation by insulin activated kinase
    d. PPP can dephosphorylate inactive glycogen synthase
        i. Insulin activates PPP
        ii. Glucagon and epinephrine activate PPI --> inhibit PPP --> keep glycogen synthase inactive

iii. G6P can allosterically bind to glycogen synthase to make it a better substrate for PPP
iv. Glucose because it acts to inactivate phosphorylase a pushes reaction to glycogen synthesis

31. How does glucagon and insulin affect glycogen metabolism? What are the mechanisms involved in the regulatory cascade? How does glucose function as a sensor?
    a. Glucagon enhances glycogen break down
    b. Insulin enhances glycogen synthesis
    c. Glucose functions as a sensor by binding to allosteric sites on phosphorylase a and inactivating it therefore inhibiting glycogen breakdown and pushing the system to glycogen synthesis
32. How is calcium connected to the regulation of glycogen metabolism?
    a. Increases activity of phosphorylase b kinase --> activates phosphorylase a
    b. Thus increases glycogen breakdown