

BCMB 8020  
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### Glycogen

Most common storage form of glucose in animals, bacteria (yeast)

Branched polymer of  $\alpha$ 1,4- &  $\alpha$ 1,6-linked glucose

Similar to amylopectin; but with smaller and more frequent branching: branching every 8-12 residues

In animals glycogen is stored largely in the liver and muscle

In mammals glycogen can make up ~10% liver mass & 2% of muscle mass

### Glycogen use in animals

Insulin

glucagon or adrenaline  
(fasting) (flight or fight)

Excess Glucose  $\rightarrow$  GLYCOGEN  $\rightarrow$  replenished glucose  
(i.e. after feeding)

glycogen synthesis

glycogenolysis

In vertebrates ~ 2/3 of dietary glucose is converted to glycogen

transported in blood

Food  $\rightarrow$  Glucose  $\rightarrow$  intestine  $\rightarrow$  cells  $\rightarrow$  converted to Glc-6-P  
absorbed hexokinase

liver (GLUT1)  
muscle (\*GLUT4, GLUT 1)  
\*insulin stimulated

The stimulation of glycogen synthesis is one of the major physiological responses modulated by insulin

The exact mechanism by which insulin stimulates glycogen synthesis is not known

Insulin:

\* Controls uptake and transport of glucose (GLUT4)

\* Regulates phosphorylation and activation state of glycogen biosynthetic and catabolic enzymes (glycogen synthase; glycogen phosphorylase)

### Steps in Glycogen Synthesis

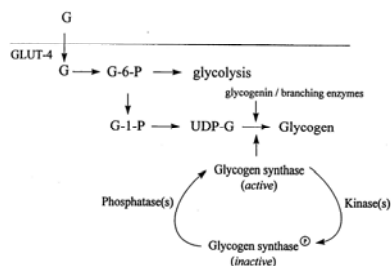
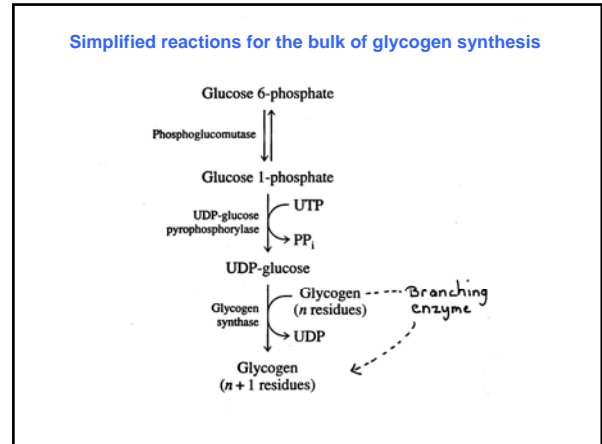
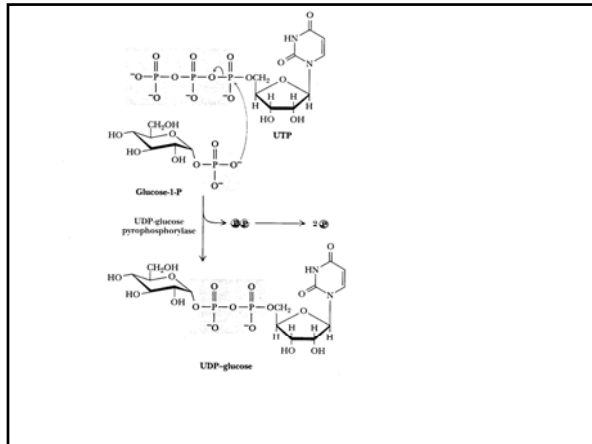


Fig. 7. Schematic model showing sequential steps of glycogen synthesis. Glucose (G) enters the cells of insulin-sensitive tissues by a facilitative transport process mediated by insulin-sensitive glucose transporters present, GLUT 4. GLUT 4 is translocated from cytosol to the plasma membrane in response to insulin. G is then converted to glucose-6-phosphate (G-6-P) by hexokinase, which then either enters into glycolysis and/or is converted to glucose-1-phosphate (G-1-P) by phosphoglucomutase. G-1-P, in the presence of UTP and UDP-glucose pyrophosphorylase is converted to UDP-G, an active glucose donating molecule, which donates glucosyl residue to glycogen molecule. Glycogen synthase catalyzes the transfer of glucosyl units from UDP-glucose to the nonreducing ends of glycogen molecule. Glycogen branching enzymes help add glucose to growing chain of glycogen molecule. Glycogen synthase itself cycles between an active and inactive state. Phosphorylation by protein kinase(s) leads to decrease in glycogen synthase activity (i.e. inactive form) whereas dephosphorylation catalyzed by protein phosphatase(s) causes activation of the enzyme (i.e. active state).

Synthesis of the chemically activated substrate for glycogen synthesis, UDP-Glc, by UDP-Glc pyrophosphorylase

(Luis Leloir, discovered NDP-sugars)

The synthesis of UDP-Glc is driven by the subsequent hydrolysis of pyrophosphate



The question of how glycogen synthesis was initiated remained open for many years. It is now known that glycogen synthesis begins by the Mn<sup>++</sup>-dependent self glucosylation of glycogenin on Tyr194 to form a glycogenin with an average glucan chain of DP 8 (maltooctose).

**Steps in glycogen synthesis**

**Self-glucosylation of glycogenin (~37 kD) on Tyr-194 in a glycosidic linkage**

**UDP-Glc + Proglycogen Synthase + Branching Enzyme → Proglycogen (~ 400,000 daltons; ~DP 2470)**

**Proglycogen + UDP-Glc + Macroglycogen Synthase + Branching Enzyme → Macroglycogen (~ 10<sup>7</sup> daltons; ~DP 61,728)**

