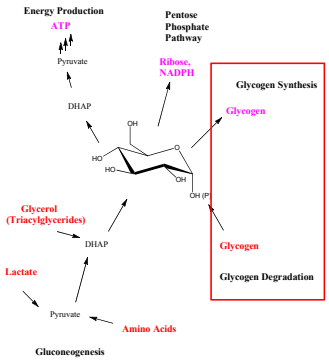
Glycogen Degradation

Chapter 24, Stryer Short Course

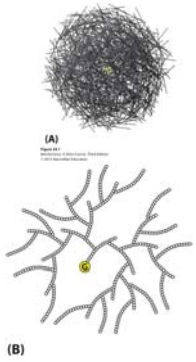
Glucose Metabolism Overview

- Gluconeogenesis
- Glycogen metabolism
- Pentose Phosphate Pathway



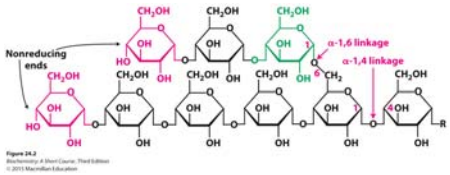
Glycogen

- Storage molecule
- Primer necessary
- Very large!
- Multiple ends allow for quick synthesis and degradation



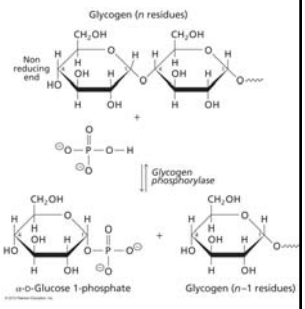
Four Degradation Enzymes

- Two enzyme debranching process
- Glycogen phosphorylase
- phophoglucomutase

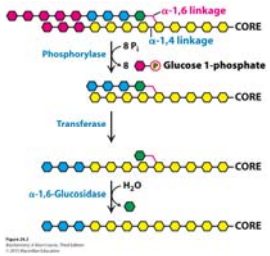


Chemistry of Degradation

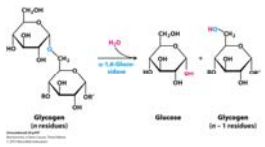
- Glycogen phosphorylase
- Key Regulation site
- Inorganic phosphate as a nucleophile
- Splits α(1→4) bonds
- Remake G-1-P with no ATP cost



Debranching

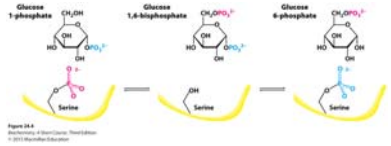


- Transfer branch
- α(1→6)glycosidase

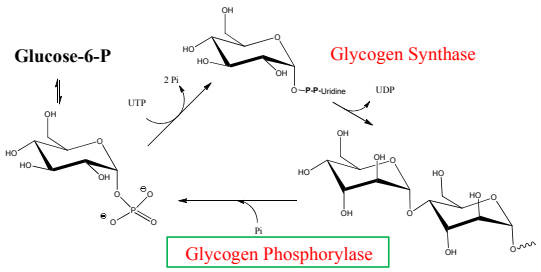


Mutase

- G-1-P to G-6-P with no energy expenditure
- Central metabolite
  - Muscle: glycolysis, pentose phosphate pathway
  - Liver: glycolysis, PPP, free glucose for blood

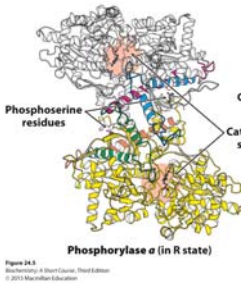


Key Regulatory Enzymes



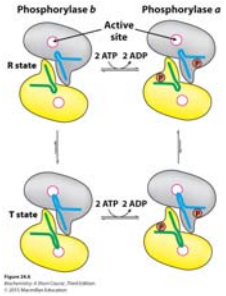
Glycogen Phosphorylase

- Dimeric
- Allosteric control
- Hormone level control
- Tissue isozymes
  - Muscle: Purpose it to release fuel for itself
  - Liver: Purpose is to release fuel for whole organism

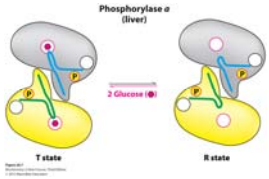


Covalent Modification

- Phosphorylase a
  - Phosphorylated
  - "usually active"
  - Default liver isozyme
- Phosphorylase b
  - Dephosphorylated
  - "usually inactive"
  - Default muscle enzyme



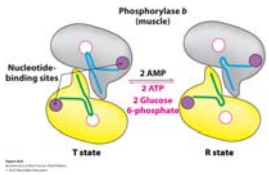
Liver Activity



- Physiological purpose: release of glucose
  - Default setting
- High glucose concentration favors T state in Phosphorylase *a*
- Turns off active glycogen degradation

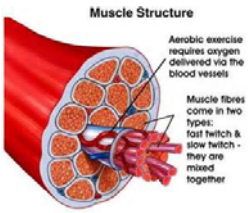
Muscle Activity

- Physiological purpose: conserve glycogen until a burst is needed
- Detection of energy charge
  - AMP shifts equilibrium to relaxed state



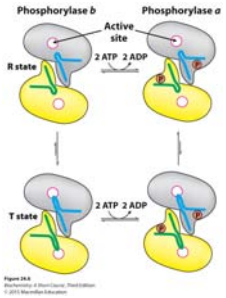
Muscle Fiber

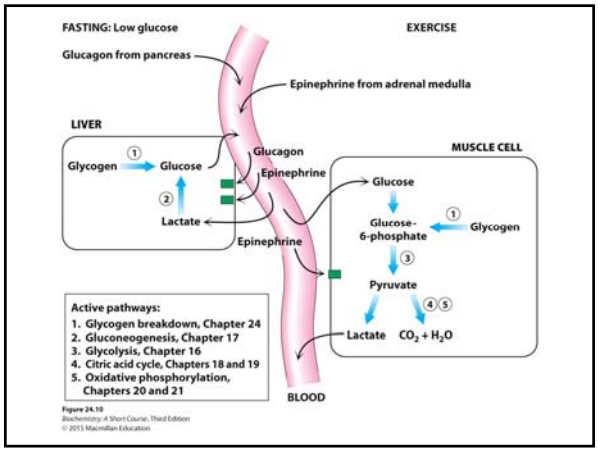
- Type I: Slow twitch
  - For endurance
  - use fats for aerobic catabolism
- Type IIb: Fast twitch
  - Burst of strength
  - Glycogen as main fuel source (anaerobic)
- Type IIa: Intermediate



Hormone Regulation

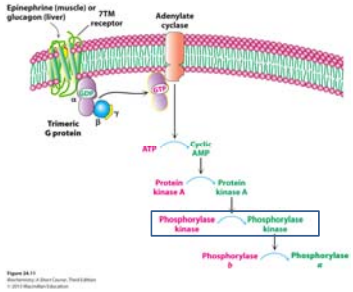
- Interconversion of "usually active" and "usually inactive" phosphorylase is hormone mediated
- Activation by glucagon and epinephrine





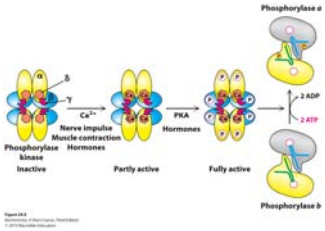
Signal Transduction

- Activation of cascade leads to active degradation of glycogen
- Epinephrine affects liver through IP_3 pathway



Regulating regulators

- Influx of calcium in active muscle partially activates kinase
- Hormone response fully activates



Glycogen Storage Diseases

Type	Enzyme Deficiency
I	Glucose-6-phosphatase
II	α-1,4-Glucosidase
III	Amylo-1,6-glucosidase (debranching enzyme)
IV	Amylo-(1,4 → 1,6)-transglycosylase (branching enzyme)
V	Muscle glycogen phosphorylase
VI	Liver glycogen phosphorylase
VII	Phosphofructokinase
VIII, IX, X	Phosphorylase kinase
XI	GLUT2 transporter
0	Glycogen synthase

Many disrupt glycogen breakdown in muscle and/or liver (hypoglycemia, enlarged liver, muscle cramps...)