Location & Functions of Glycogen

- **Location of glycogen in the body skeletal muscle & liver**

400 g in muscles (1-2% of resting muscles weight)

100 g in liver (~ 10% of well-fed liver)

- **Functions of glycogen:**

Function of muscle glycogen: **fuel reserve (ATP) (during muscular exercise)**

Function of liver glycogen: **a source for blood glucose (especially during early stages of fasting)(the late stages will be by gluconeogenesis)**

Starting glycolysis from glucose 6-p how many net ATP will produced ?

9 ATP because it doesn't have enzyme that convert the glucose 6-p to glucose

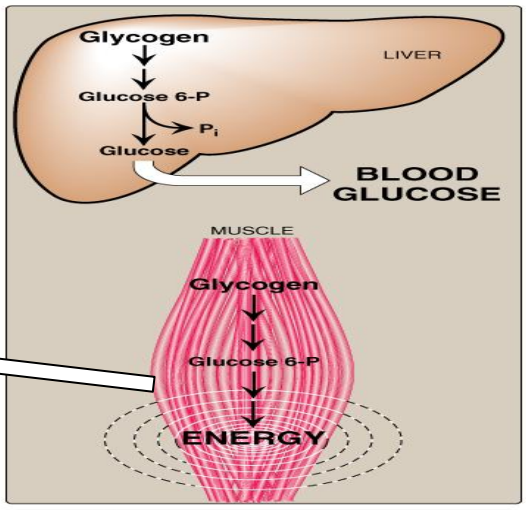
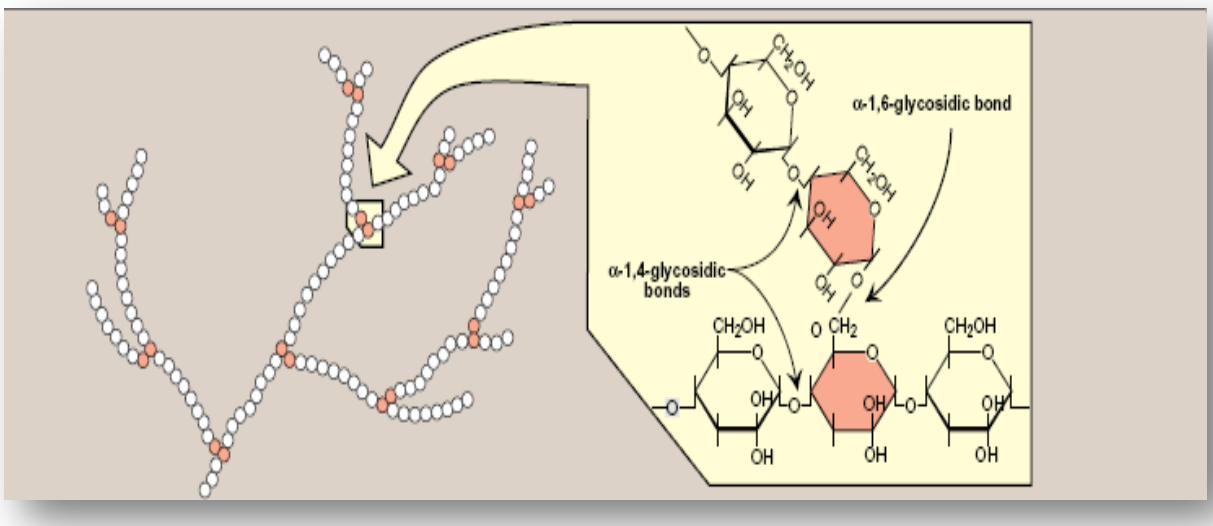


Figure 11.2
Functions of muscle and liver glycogen.

Structure of Glycogen

Homopolysaccharides are composed of a single type of sugar monomer. In glycogen is glucose

- **Glycogen is a branched-chain homopolysaccharide made exclusively from α- D-glucose**
- **Glucose residues are bound by α(1 - 4) glucosidic linkage**
- **Branches (every 8-10 residue) are linked by α(1-6) glucosidic linkage**
- Glycogen is present in the cytoplasm in the form of granules which contain most of the enzymes necessary for glycogen synthesis & degradation . (self sufficient).



Metabolism of Glycogen in Skeletal Muscle

Glycogenesis: Synthesis of Glycogen from Glucose

Glycogenolysis: Breakdown of Glycogen to Glucose-6-phosphate

Both processes happened in **cytosol** .

Cytosol is the fluid of cytoplasm

GLYCOGENESIS

(*Synthesis* of Glycogen in Skeletal Muscles)

1- **Building blocks:** UDP-GLUCOSE

Active form that **build** the chine

2- **Initiation of synthesis:**

Elongation of pre-existing glycogen fragment OR The use of glycogen primer (glycogenin)

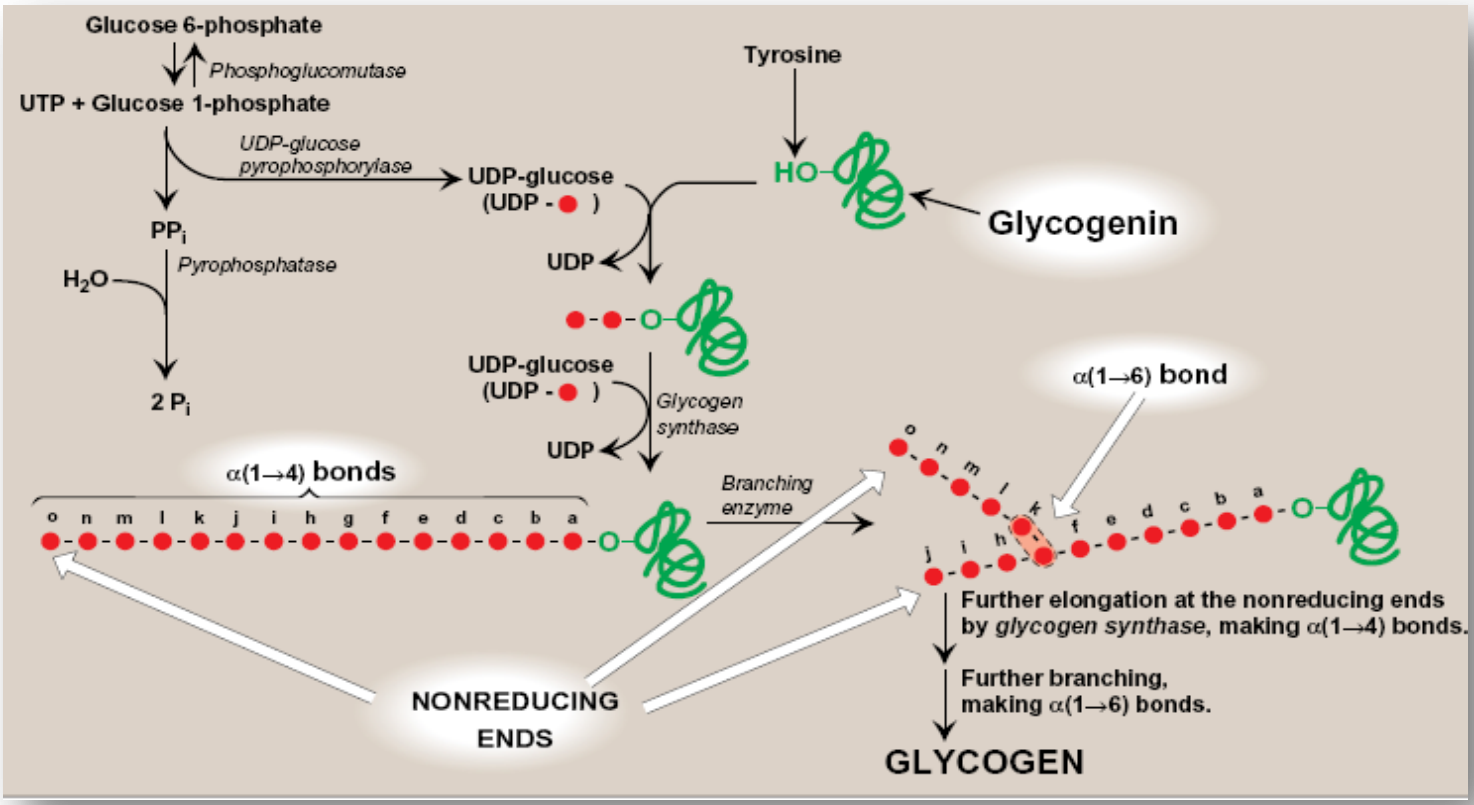
It's a protein that has the ability to add the first two glucose molecules in the chain; because it has a tyrosine amino acid which has a hydroxyl group on the side chain. This group will bind to the first glucose molecule and bring another glucose molecule to bind to it, and then the glycogen synthase can work by elongation.

3- **ELONGATION:** Glycogen synthase (for α1-4 linkages)
Glycogen synthase cannot initiate synthesis but only elongates pre-existing glycogen fragment or glycogen primer (glycogenin)

4- **BRANCHING:** Branching enzyme (for α1-6 linkages)

*This enzyme will remove the last small piece of the elongating chain
And add it in the middle by forming the α 1-6 glycosidic linkage.

Synthesis of Glycogen



This enzyme will break the bonds by adding a phosphate group to the glucose molecule but it does not get out of the cell because we need it for producing energy, except in the case of the liver. Where it produces free glucose molecules that get out from the cells into the blood stream to raise the glucose level in the blood when needed. (Blood Glucose)

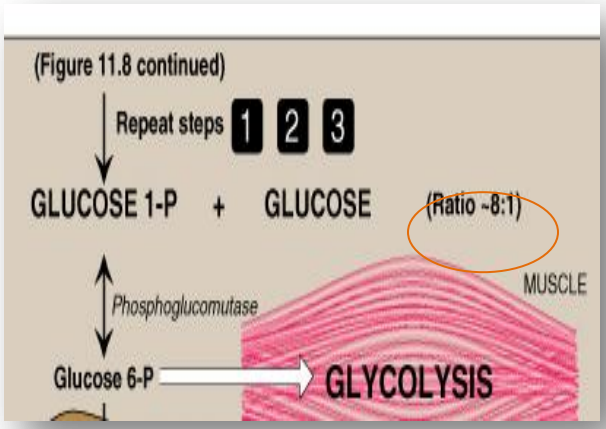
Glycogenolysis

(Breakdown of glycogen in skeletal muscles)

1- **Shortening of glycogen chain:** by **glycogen phosphorylase**
Cleaving of α(1-4) bonds of the glycogen chain producing glucose 1-phosphate
Glucose 1-phosphate is converted to **glucose 6-phosphate** (by mutase enzyme "Phosphoglucomutase")

2- **Removal of branches :** by **debranching enzymes**
Cleaving of α(1-6) bonds of the glycogen chain producing **free glucose (few)** → **Raito 8:1**

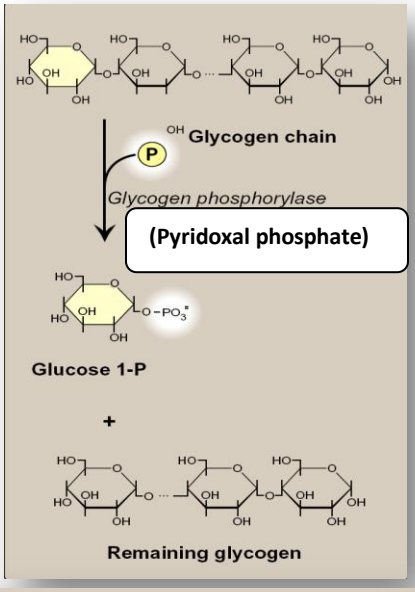
3- **Fate of glucose 6-phosphate (G-6-P):**
G-6-P is ***not*** converted to free glucose
It is used as a source of energy for skeletal muscles during muscular exercise (by anaerobic glycolysis starting from G-6-P step)



Glycogen phosphorlyase need :

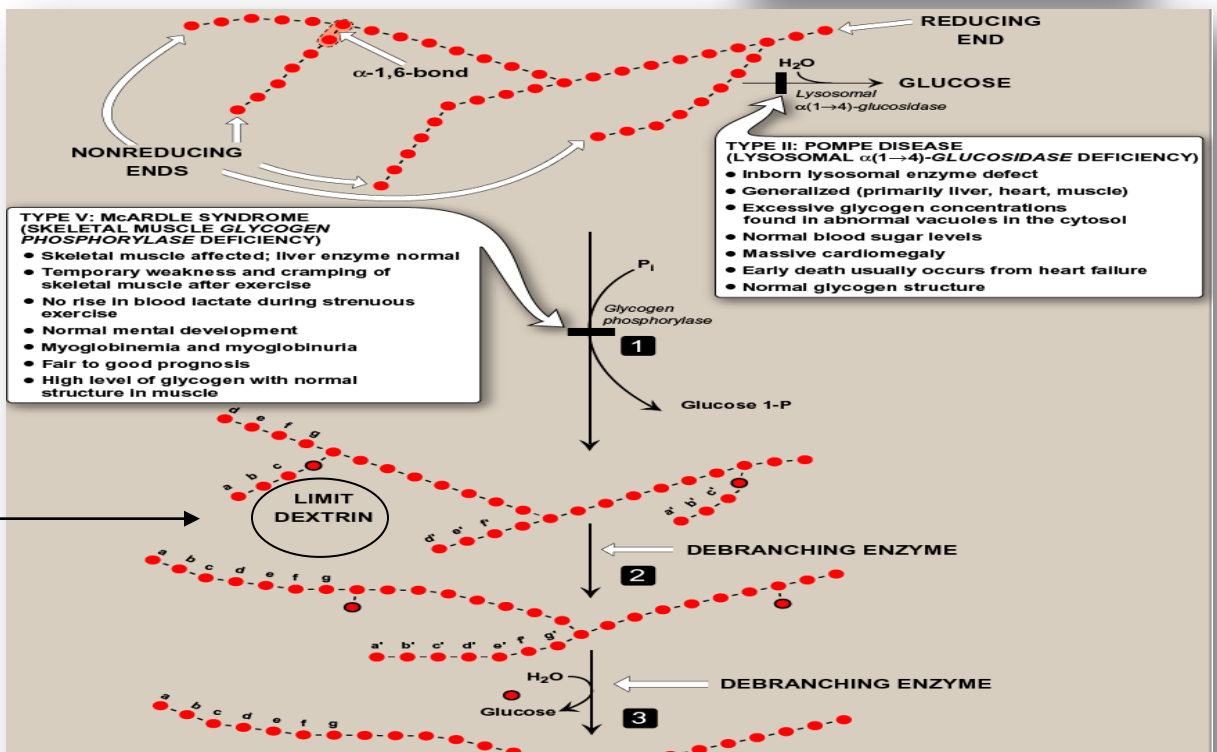
Pyridoxal phosphate it's coenzyme derived from

Vit B6 .



Limit dextrin is the part when you have four glucose molecules starting from each branching point. This phase limits the action of the glycogen phosphorylase.

The debranching enzyme will remove three glucose molecules to another end making the rest molecule bound by α 1-6 linkage clear to be removed by the same enzyme.



Regulation of Glycogen Metabolism

Synthesis & degradation of glycogen are tightly regulated

In Skeletal Muscles:

- Glycogen **degradation** occurs during **active exercise**
- Glycogen **synthesis** begins when the **muscle is at rest**
- **Regulation occurs by 2 mechanisms:**

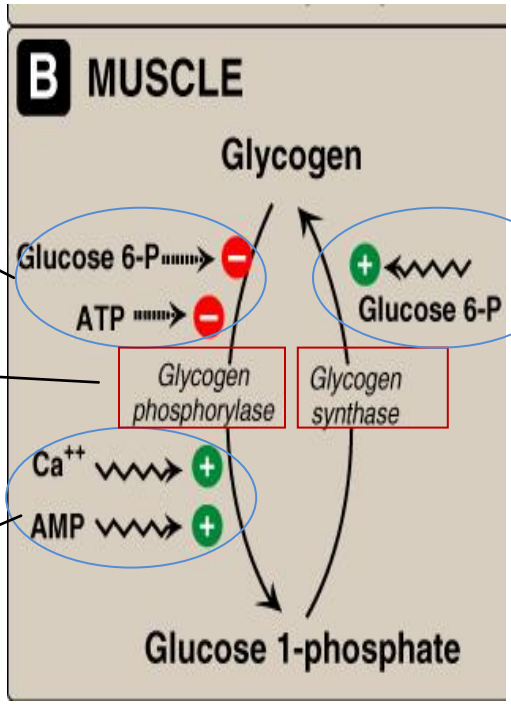
1- **Allosteric regulation**

2- **2- Hormonal regulation (Covalent modification)**

Regulation of Glycogen Metabolism

1. Allosteric Regulation

if there is an **increase** in **Glucose 6-p** or **ATP** the process will be **inhibited**



if there is an **increase** in **Glucose 6-p** the process will be **stimulated**

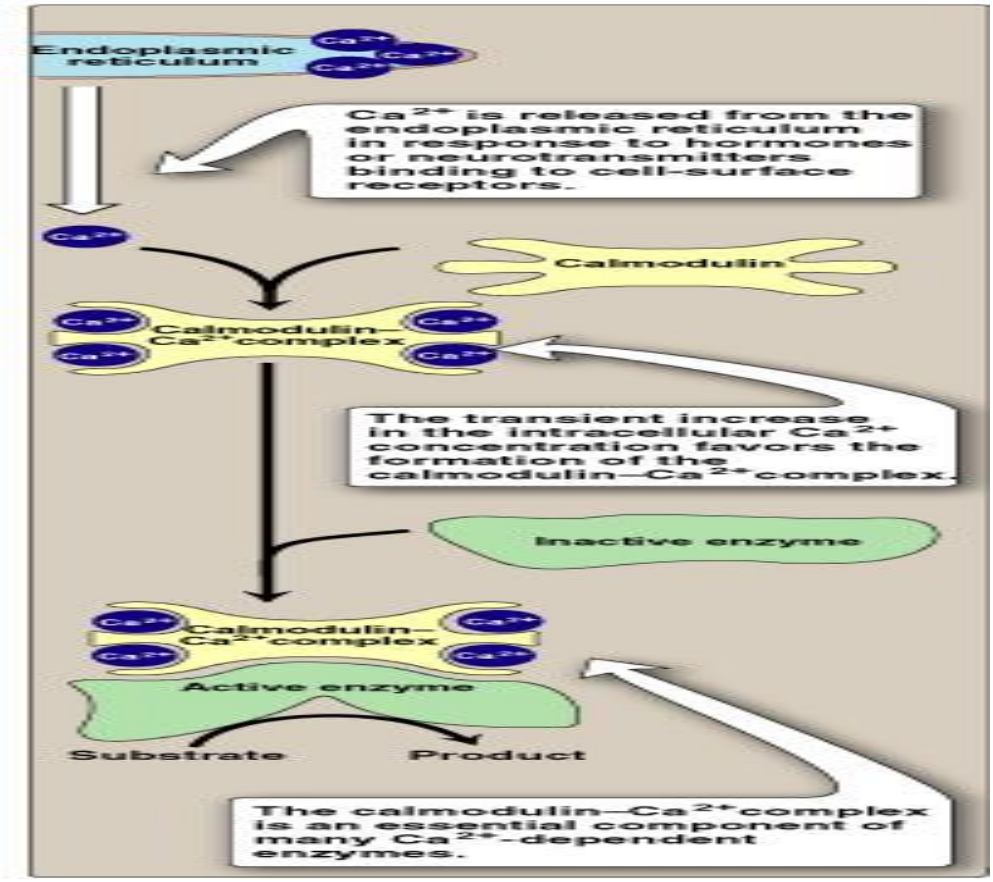
Glycogen break down

Glycogenolysis

Glycogen synthesis

GLYCOGENESIS

If there is an **increase** in **AMP** that means many **ATPs are being consumed**. So, it will **stimulate** the process



Regulation of Glycogen Metabolism

Increase of calcium during muscle contraction

Formation of Ca^{2+}-calmodulin complex

Activation of Ca^{2+}-dependent enzymes,

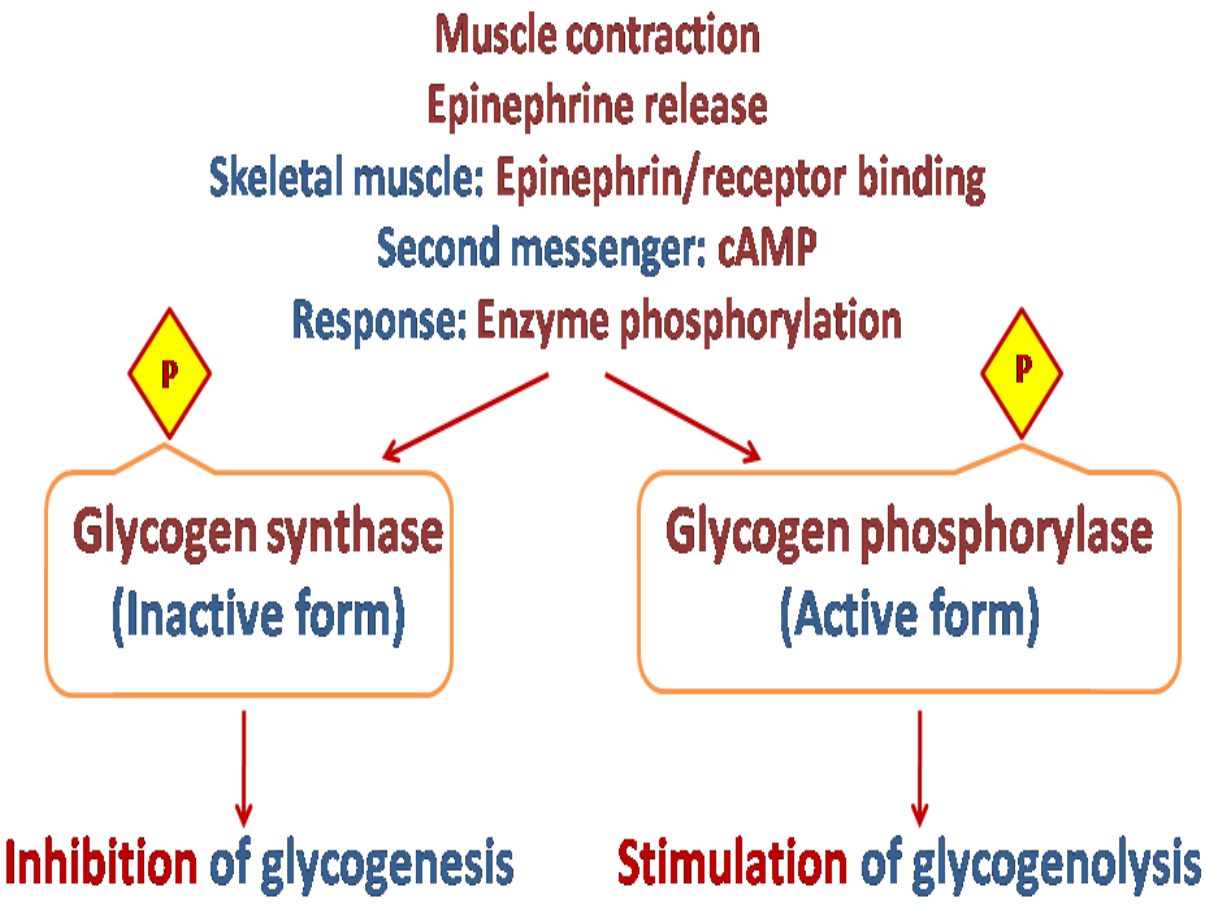
e.g., glycogen phosphorylase

Calmodulin(protein) stimulated in present of high level of Ca.

Calmodulin need 4 molecule of Ca to be active.

After activation Calmodulin , it will activate " inactive enzyme" (e.g glycogen phosphorylase)

Regulation of Glycogen Metabolism:
2. Hormonal Regulation by Epinephrine



Glycogen Storage Diseases *(Congenital diseases)

- **A group of genetic diseases that result from a defect in an enzyme required for glycogen synthesis or degradation.**
- **They result in:**
  - **Formation of abnormal glycogen structure**
  - **Excessive accumulation of normal glycogen in a specific tissue**

Glycogen Storage Diseases

GSD Type V (Mc Ardle Syndrome)

- **Deficiency of skeletal muscle glycogen phosphorylase**