Biochemistry
Team 434

Glycogen Metabolism

Musculoskeletal Block

Color index

Red= Important
Purple= Addition
Orange= Explanation

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Objectives:

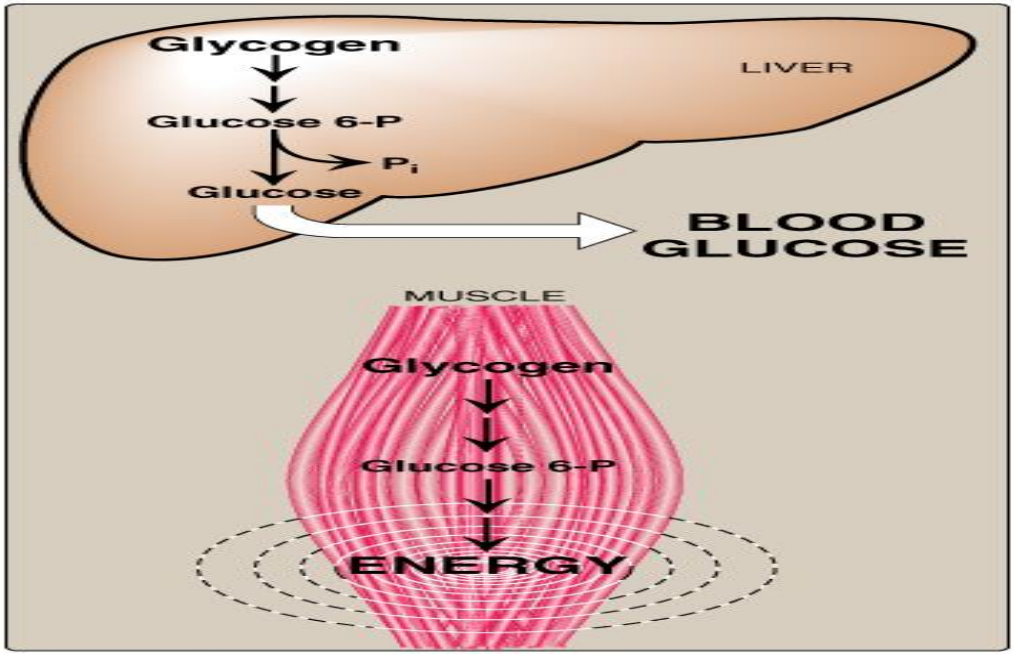
By the end of this lecture, students should be familiar with:

1. The need to store carbohydrates in muscle
2. The reason for carbohydrates to be stored as glycogen
3. An overview of glycogen synthesis (Glycogenesis)
4. An overview of glycogen breakdown (Glycogenolysis)
5. Key elements in regulation of both Glycogenesis and Glycogenolysis
6. Example of glycogen storage diseases

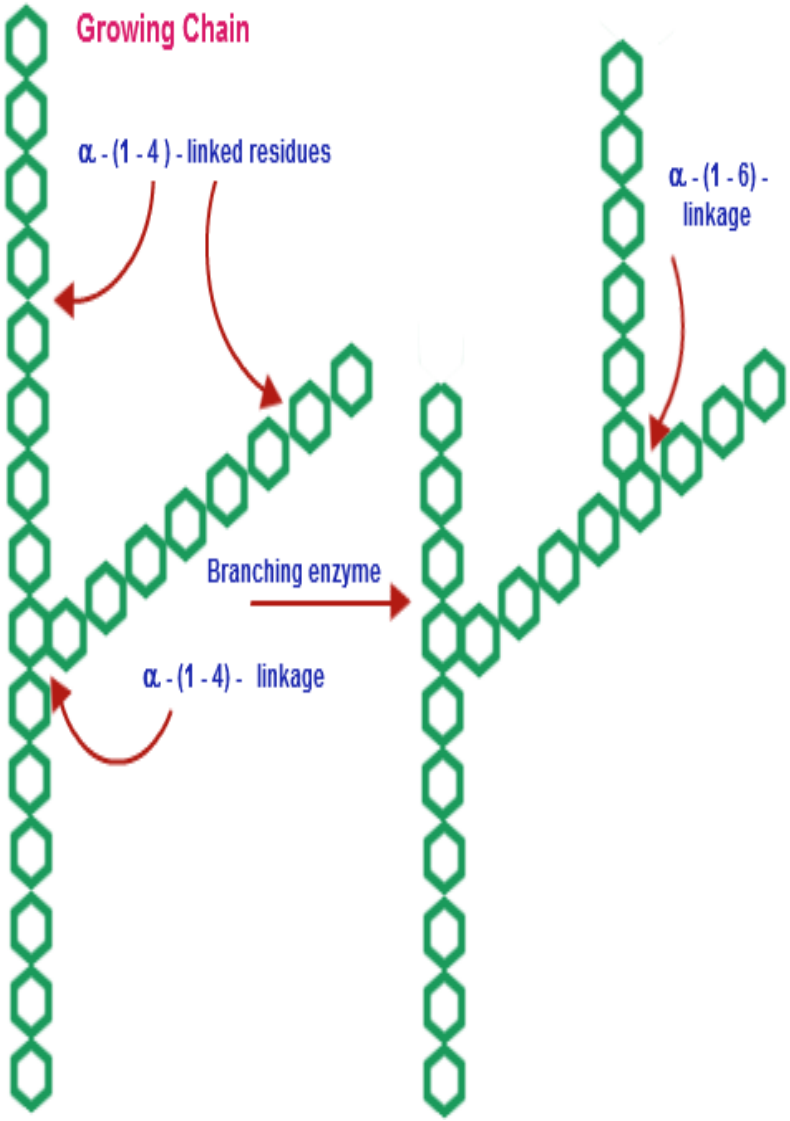
◆ Glycogen

It is found in the cytoplasm of muscle fibers (cells) and in the Hepatocytes of liver. In muscle fibers, glycogen is kept to provide fuel to the muscle during exercise. However, in the liver, it is used for gluconeogenesis and the glucose is transferred to the blood and to the whole body during fasting.
Muscles → 400g (1-2% of muscle at rest)
Hepatocytes → 100g (10% of a well-fed liver)

Note: In the body, muscle mass is greater than liver mass thus most of the body's glycogen is found in muscle.



◆ Glycogen Structure



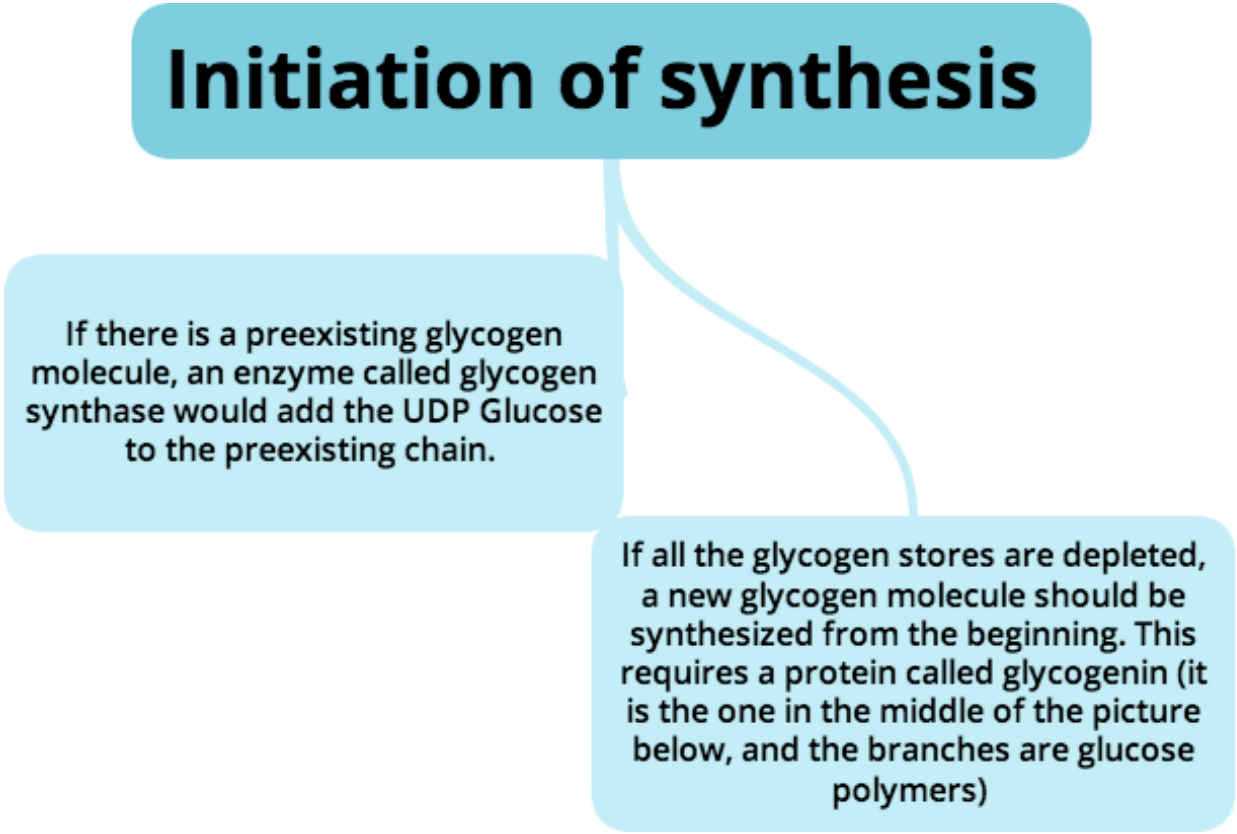
In this picture, the green building blocks resemble glucose (D-Glucose because it is the form found in humans). You can think of the glycogen polymer as **King Abdullah Road**. Let us say the main polymer is King Abdullah Road and it has alpha (1-4) glycosidic bonds. And the smaller branching glycogen polymers are also made of alpha (1,4) glycosidic bond; but their junction (تقاطع) with the main –long polymer of glucose has an alpha (1,6) glycosidic bond.

Extra information:
Why are these branches important?
Well, the enzymes that breakdown glycogen (called glycogen phosphorylase) can only attach to one end of each road; they can't break the polymer from the middle. Having all these branches will make more glycogen phosphorylase molecules work on it.

Note: we will talk about a disease where there is a problem in the branching process "Andersen Disease"

◆ Glycogenesis

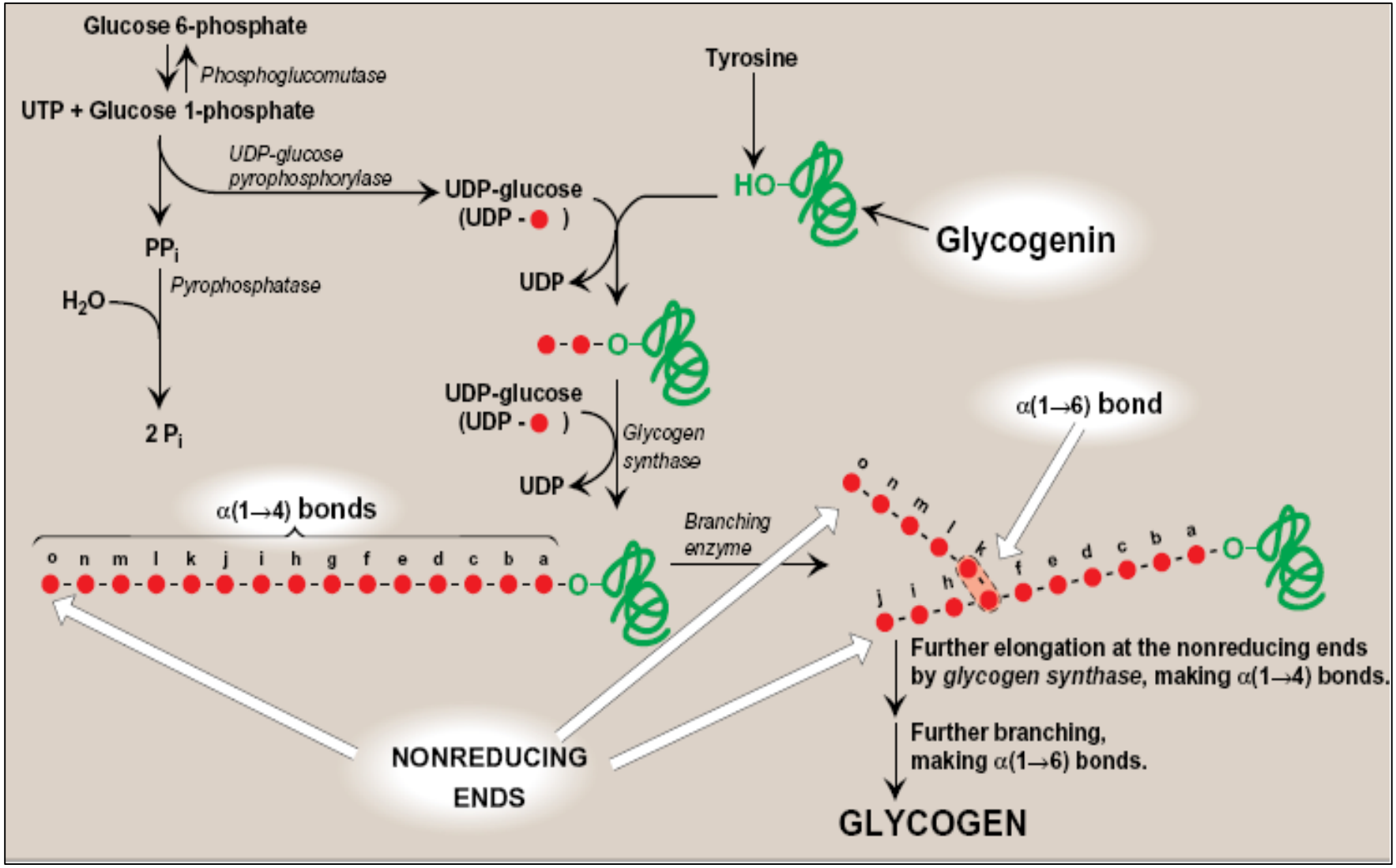
•The building blocks of glycogenesis are UDP Glucose (Uridine Diphosphate Glucose) (ATP اخو UTP)



•Glycogen synthase elongates the chain using alpha (1,4) Glycosidic bonds.

•The branching enzymes cuts some segments of the long chain and creates side chains with alpha (1,6) Glycosidic bond. Please look at the picture on the next slide to make it clear. So alpha (1,4) →Glycogen synthase / Alpha(1,6) →branching enzymes

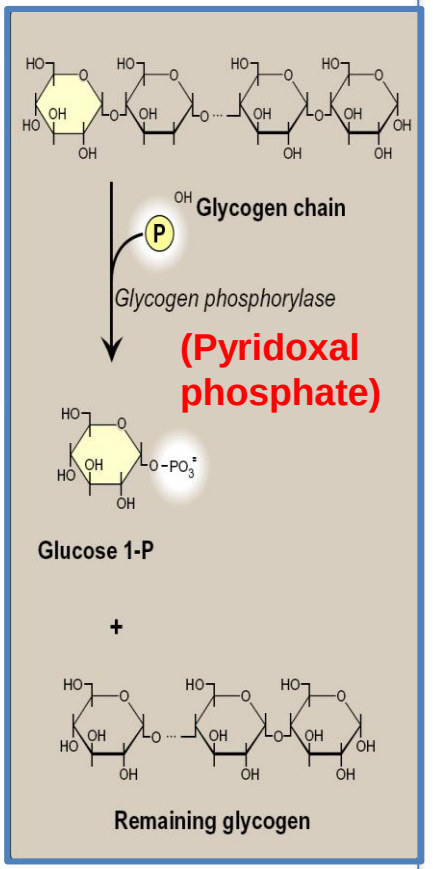
Synthesis of Glycogen



◆ Glycogenolysis

- **Glycogen phosphorylase** does the opposite of glycogen synthase; it breaks the alpha (1,4) glycosidic bond. This process releases Glucose 1P (one phosphate) and this glucose is then transformed to **Glucose 6P** via **mutase enzyme**. (remember G6P is a part of glycolysis)

- **Debranching enzyme** does the opposite of the branching enzyme (please don't get confused between them, "de" means remove as in "dephosphorylation", this enzyme removes the branches). This enzyme breaks the alpha (1,6) glycosidic bond at the branches which releases free glucose directly (in few quantities because the majority of the bonds are alpha (1,4) glycosidic bond)

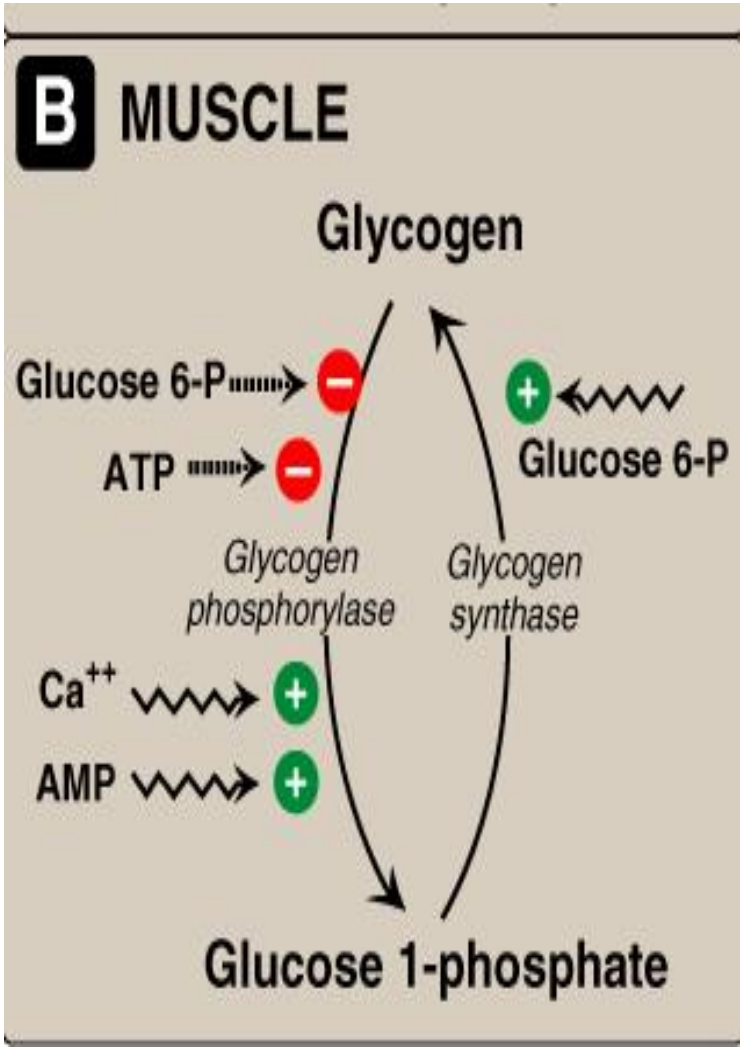


➢ **What happens to Glucose 6 Phosphate?**

Since the cell is breaking its stores of glucose it must be hungry. Therefore it wouldn't convert this G6P to glucose via gluconeogenesis, but instead
it will make G6P undergo glycolysis to produce energy in the cell.
It is broken down by the cell to produce energy.

◆ Regulation of Glycogen Metabolism

1)Allosteric Regulation



Try to understand it :
When the cell has lots of glucose (Glucose 6P), it has lots of energy, and this is why G6P would activate glycogen synthase; at the same time it would inhibit glycogen phosphorylase.
Under the same concept, when the cell has lots of ATP, the cell doesn't need glucose & ATP will inhibit glycogen phosphorylase.

On the other hand, high AMP levels indicate that the cell needs energy, and it will activate glycogen phosphorylase to produce Glucose 1 Phosphate via the process we have explained in the previous page.

Calcium: calcium is released during muscle contraction. As you know, calcium activates many enzymes when it is released. After it binds to **calmodulin**, it activates **glycogen phosphorylase**. Again this is obvious, because when you are lifting weights your muscles need all of the glycogen broken down for it to feed on glucose, the calcium that is released during muscle contraction does this.

2)Hormonal Regulation

we will put the steps that were mentioned in the slides in bold, you should know these. However, we'll include the whole process to tease your memory (we took these steps in the foundation block):

Epinephrine (due to muscle contraction) →Receptor on skeletal muscles (Gprotein coupled) → + Adenylyl Cyclase → **cAMP** (from ATP) → + Protein Kinase A (remember kinase means **it will phosphorylte enzymes**)

The enzymes that will be phosphorylated by PKA:

1)Glycogen synthase : this will make it

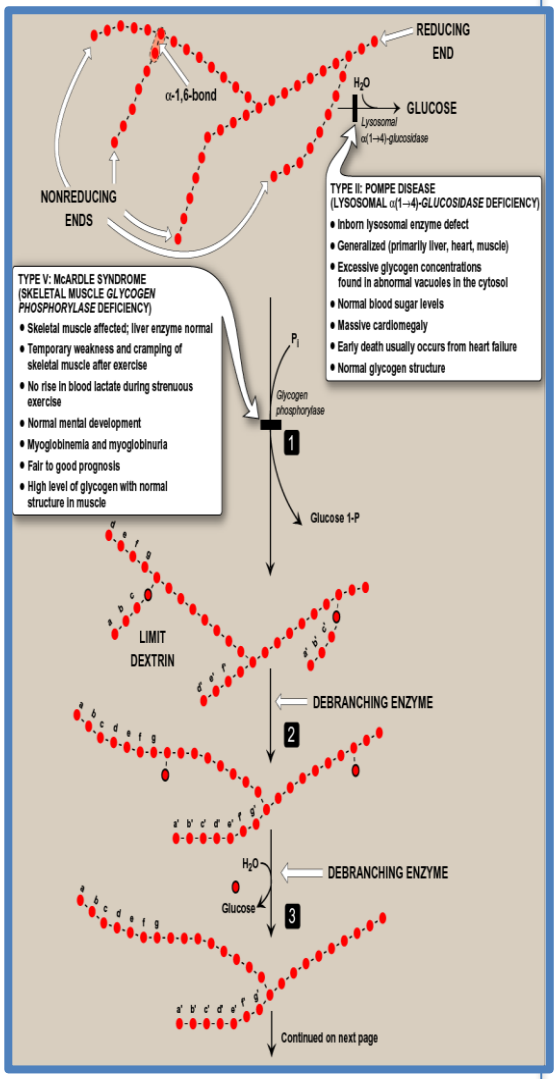
INACTIVE → inhibition of glycogenesis

2)Glycogen phosphorylase: this will make it

ACTIVE → activation of glycogenolysis

◆ Glycogen storage disease

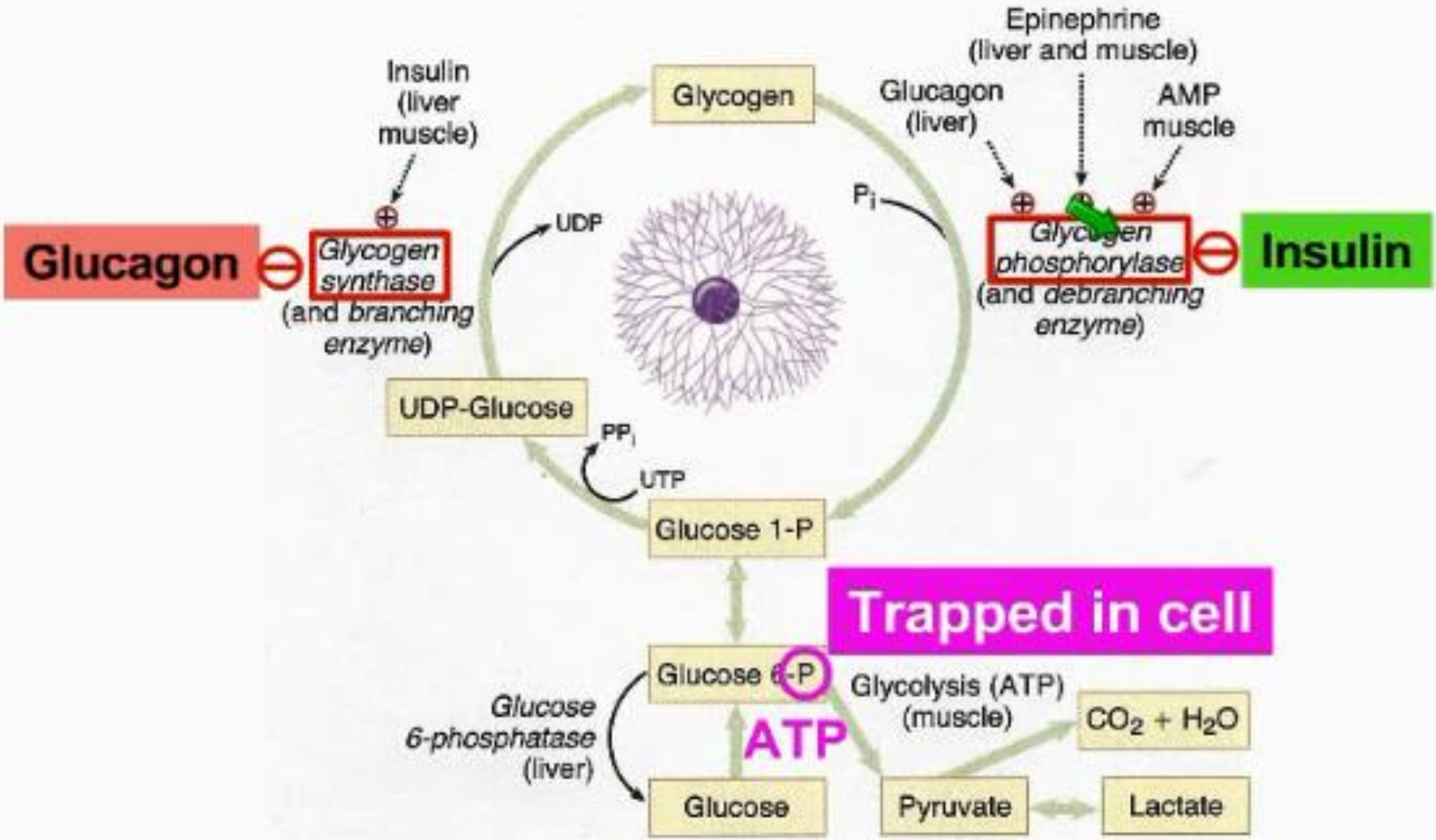
A group of genetic diseases that result from a **defect** in an enzyme required for glycogen **synthesis** or **degradation**.
They result in: Formation of **abnormal glycogen structure** OR **Excessive accumulation of normal glycogen** in a specific tissue
Example:
Glycogen storage disease type V : McArdle Syndrome:
deficiency in glycogen phosphorylase enzyme.



Extra information about this disease:

The enzyme glycogen phosphorylase is absent in the muscles.
At the beginning of exercise, patients can't break down glycogen.
This leads to cramps and some muscle fibers may die.
Dead muscle tissues release myoglobin, which is cleared by the kidney. This makes the urine dark after exercise.
It usually starts after the age of twenty.

Glycogen Metabolism



◆ **Helpful Links:**

Glycogenesis

http://www.youtube.com/watch?v=9doz-9w1RtI

Glycogenolysis

http://www.youtube.com/watch?v=vA42MK-fiAc

Quiz your self

https://www.examtime.com/en/p/1762076