السلام عليكم ورحمة اللّه وبركاته ...

هذه عبارة عن سلايدات الدكتور
عمرو معاد ترتيبها و مضاف
إليها نوتات ، إضافة إلى توضيح
النقاط المهمة في المحاضرة
الأولى وحذف بعض النقاط التي
قال عنها الدكتور أنها غير مهمة..

نسأل اللّه الإعانة للجميع ..

تيم البيو ٤٣٠ --- MSK --- قروب B

1ST lecture

Glycogen Metabolism

TEEM 430

- **Why do we need to store carbohydrates in muscle?**

- To use it when we need ..

- **Why carbohydrates are stored as glycogen?**

- To take little space with large amount ..

NOTE: The branching makes glycogen more soluble, it increases the speed of glycogen degradation and synthesis… as a result, glycogen can be readily used when needed

Location of Glycogen

skeletal muscle & liver

400 g in muscles (1-2% of resting muscles weight)
100 g in liver (~ 10% of well-fed liver)

- أعتقد أنه مو ذاك الأهمية

Functions of Glycogen

Function of muscle glycogen: وهذا يهمنا أكثر

generation of ATP during muscle exercise.

Function of liver glycogen:
Generation of glucose for blood during fasting.

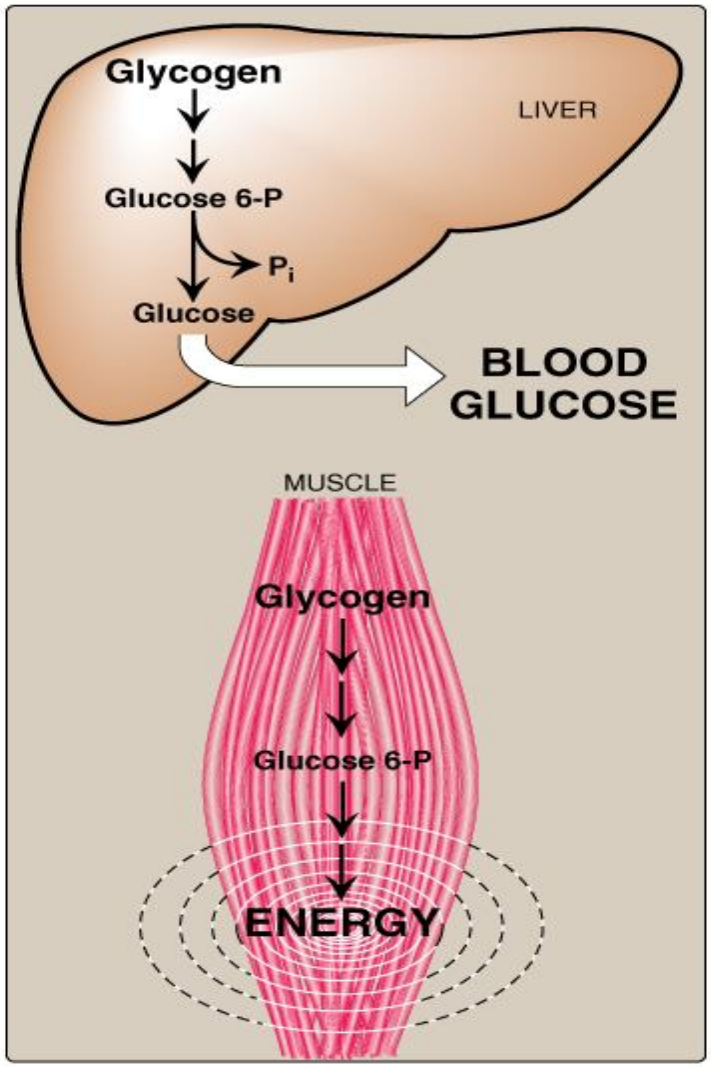


Figure 11.2
Functions of muscle and liver glycogen.

هنا في معلومة مهمة:

In muscles there's **NO** glucose-6-phosphatase , then it don't give glucose >>

Glucose-1-p

↓ directly

Glucose-6-p

نستفيد منها أننا ما نستخدم ATP

Structure of Glycogen

Glycogen is a branched-chain homopolysaccharide made exclusively from α- D-glucose

Glucose residues are bound by α(1 - 4) glucosidic linkage

يعني أن الجلوكوز الذي يكون في اللونق شين (السلسلة) يرتبط مع بعضه بهذه الرابطة

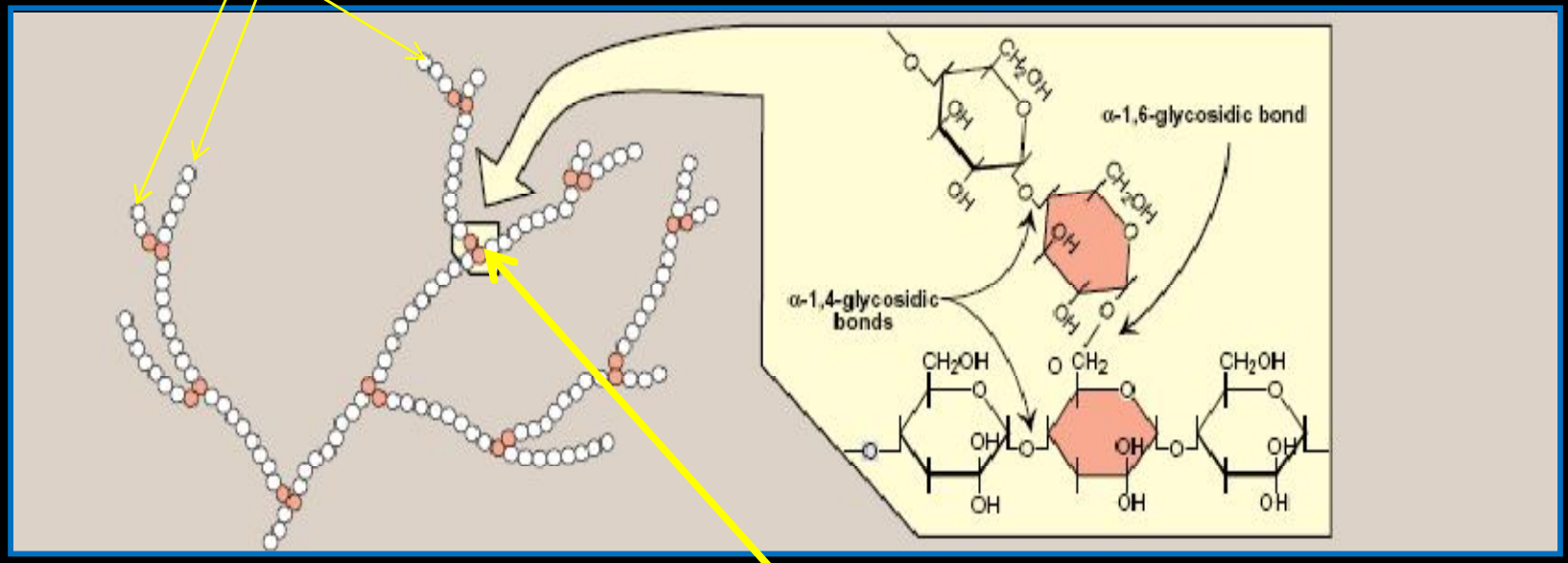
Branches (every 8-10 residue) are linked by α(1-6) glucosidic linkage

هذه الرابطة تكون بين الجلكوز الذي في السلسلة والجلوكوز الآخر الذي يبدأ التفرع

- Glycogen is present in the **cytoplasm** in the form of granules which contain most of the enzymes necessary for glycogen synthesis & degradation

Structure of Glycogen

Nonreducing end ; they are the point of addition and removal



α(1-6) glucosidic linkage

Metabolism of Glycogen in Skeletal Muscle

Glycogenesis:

Synthesis of Glycogen from Glucose

Glycogenolysis:

Breakdown of Glycogen to Glucose-6-phosphate

GLYCOGENESIS

(*Synthesis* of Glycogen in Skeletal Muscles)

1- Building blocks: UDP-GLUCOSE

2- Initiation of synthesis:

The use of glycogen primer (glycogenin)

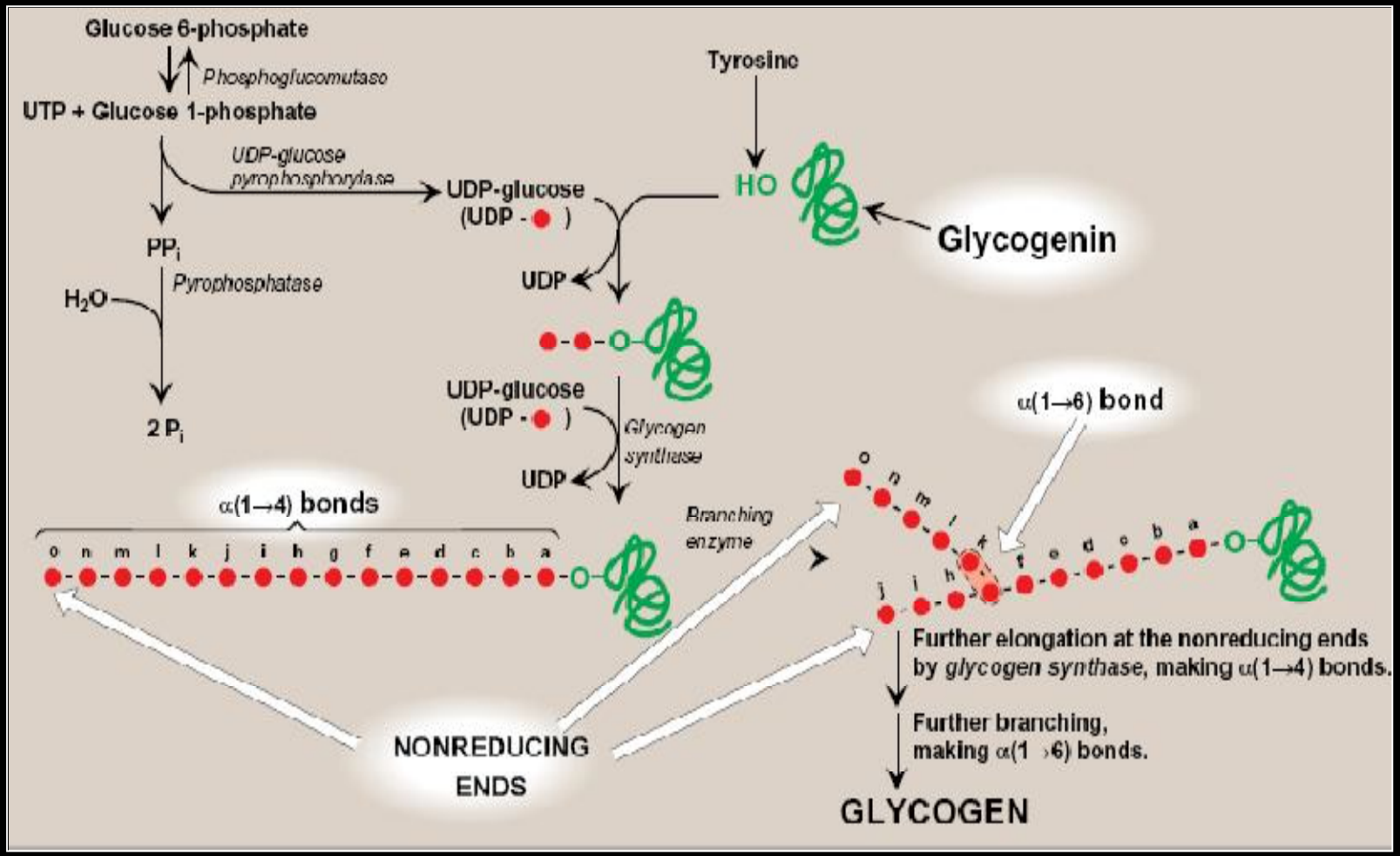
Glycogenin: is auto-catalytic (becouse it will give UTP by cleaving UDP-glucose), it can add few glucose molecules then the process will continue by glycogenesis.

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)

Synthesis of Glycogen



هذي السلايد للفهم ،،، بدون حفظ الإنزيمات ما عدا اللي في السلايد السابق

Glycogenolysis

(Breakdown of glycogen in skeletal muscles)

1- **Shortening of glycogen chain:**

by **glycogen phosphorylase** (begin from nonreducing end)

Cleaving of α(1-4) bonds of the glycogen chain producing glucose 1-phosphate

Then Glucose 1-phosphate is converted to glucose 6-phosphate (without being glucose) and **pyridoxal phosphate** is required as a co-enzyme.

glycogen phosphorylase → Glucose 1-phosphate

2- Removal of branches :

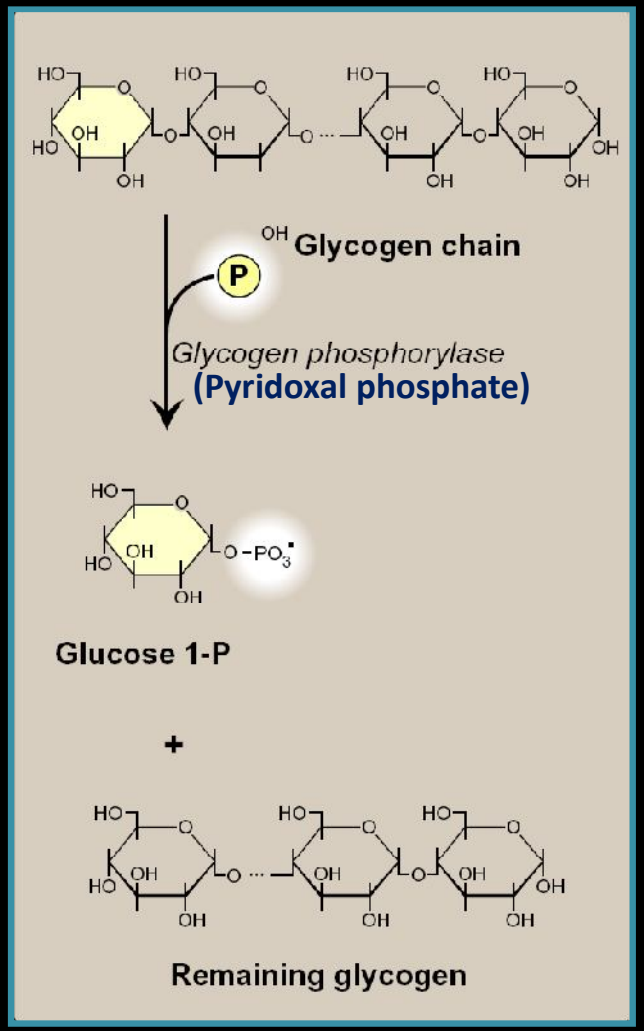
by **debranching enzymes** Cleaving of α(1-6) bonds of the glycogen chain producing **free glucose (few)**

debranching enzymes ⟶ free glucose

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)) glycolysis يعني تبدأ عملية الـ

Glycogenolysis



لاحظ إنه قاعد يبدأ من
Nonreducing end

(Pyridoxal phosphate) is coenzyme

Regulation of Glycogen Metabolism

In Skeletal Muscles:

Glycogen **degradation** occurs during **active exercise**

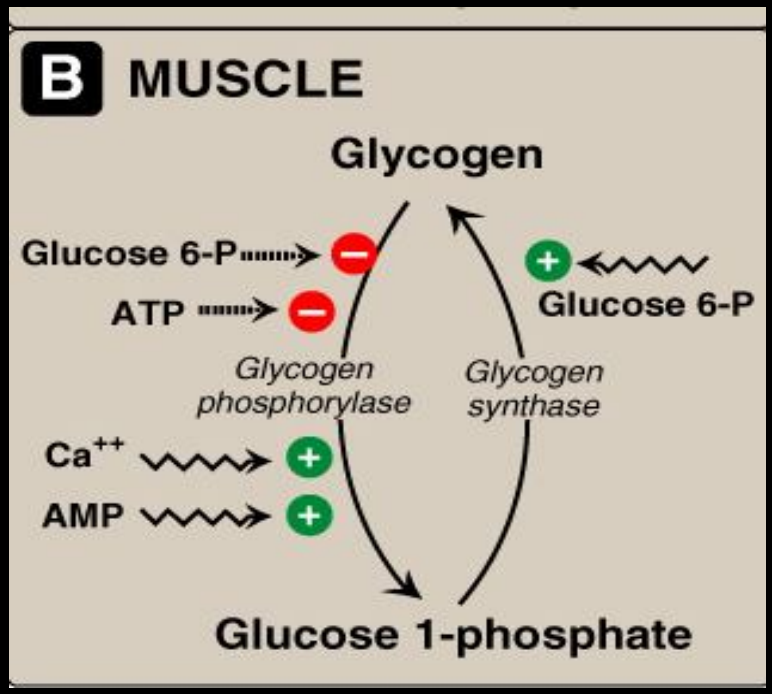
Glycogen **synthesis** begins when the **muscle is at rest**

Regulation occurs by 2 mechanisms:

1- **Allosteric regulation**

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

Regulation of Glycogen Metabolism
1. Allosteric Regulation



Ca++ & AMP **stimulate** Glycogen phosphorylase at **Allosteric Regulation.**

Glucose-6-p & ATP **inhibit** Glycogen phosphorylase at **Allosteric Regulation.**

Glucose-6-p & ATP **stimulate** Glycogen synthase at **Allosteric Regulation.**

Glycogen synthase does NOT has **Allosteric site** for Ca++ , AMP & ATP**.**

Regulation of Glycogen Metabolism

Increase of calcium during muscle contraction

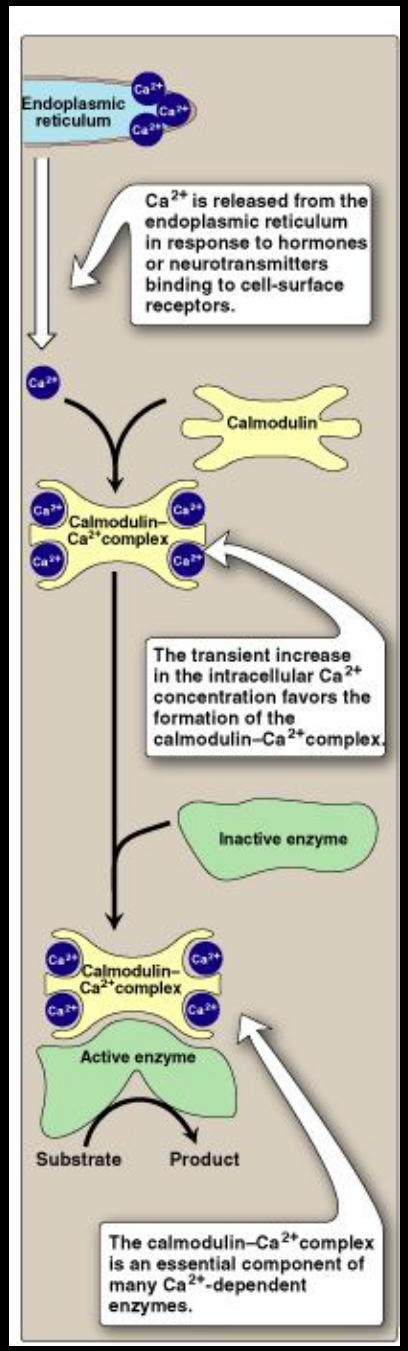
↓

Formation of Ca^{2+} -calmodulin complex

↓

Activation of Ca^{2+} -dependent enzymes,
e.g., glycogen phosphorylase

بالعربي : صار عندك مجهود على عضلة ما ، فيزيد الكالسيوم ومن ثم يرتبط مع بروتين ليكون Ca^{2+}-calmodulin complex ، ليذهب للانزيم الفسفرة ويحفزه



Regulation of Glycogen Metabolism:
2. Hormonal Regulation by Epinephrine

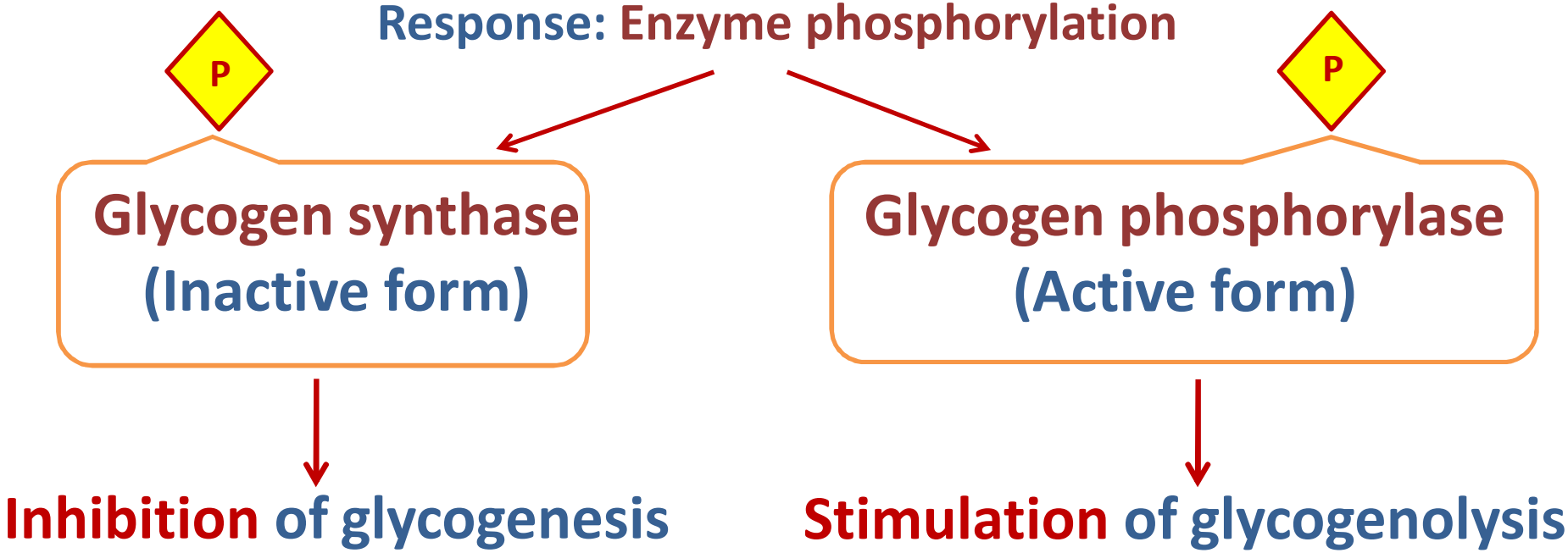
Muscle contraction

Epinephrine release

Skeletal muscle: Epinephrin/receptor binding

Second messenger: cAMP (protein kinase ويرتبط في cAMP يروح)

Response: Enzyme phosphorylation



Glycogen Storage 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

OR

Excessive accumulation of normal glycogen in a specific tissue **(Mc Ardle Syndrome)**

Glycogen Storage Diseases
GSD Type V (Mc Ardle Syndrome)

Deficiency of skeletal muscle glycogen phosphorylase , But liver glycogen phosphorylase are normal.

fasting blood glucose level is normal becouse liver glycogen phosphorylase is normal

Excessive glycogen because of Deficiency of skeletal muscle glycogen phosphorylase.

No rise in blood lactate during hard exercise.

Myoglobinemia (low blood sugar) in blood , and myoglobinuria in urine.

Weakness and cramping at exercise.

fair to good prognosis.

Normal mental development.

http://www.rpi.edu/dept/bcbp/molbiochem/MBWeb/mb1/part2/glycogen.htm

موقع مفيد كمرجع للمحاضرة ...