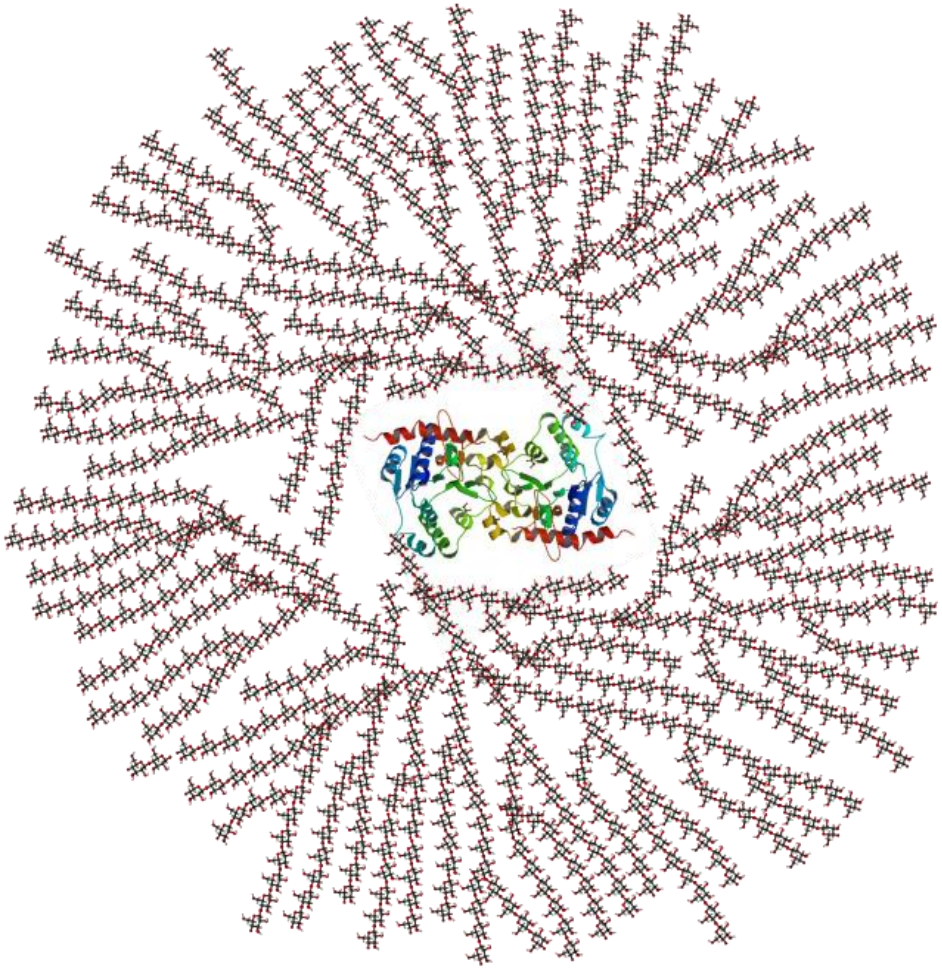



111

Glycogen Metabolism

Glycogenesis

By

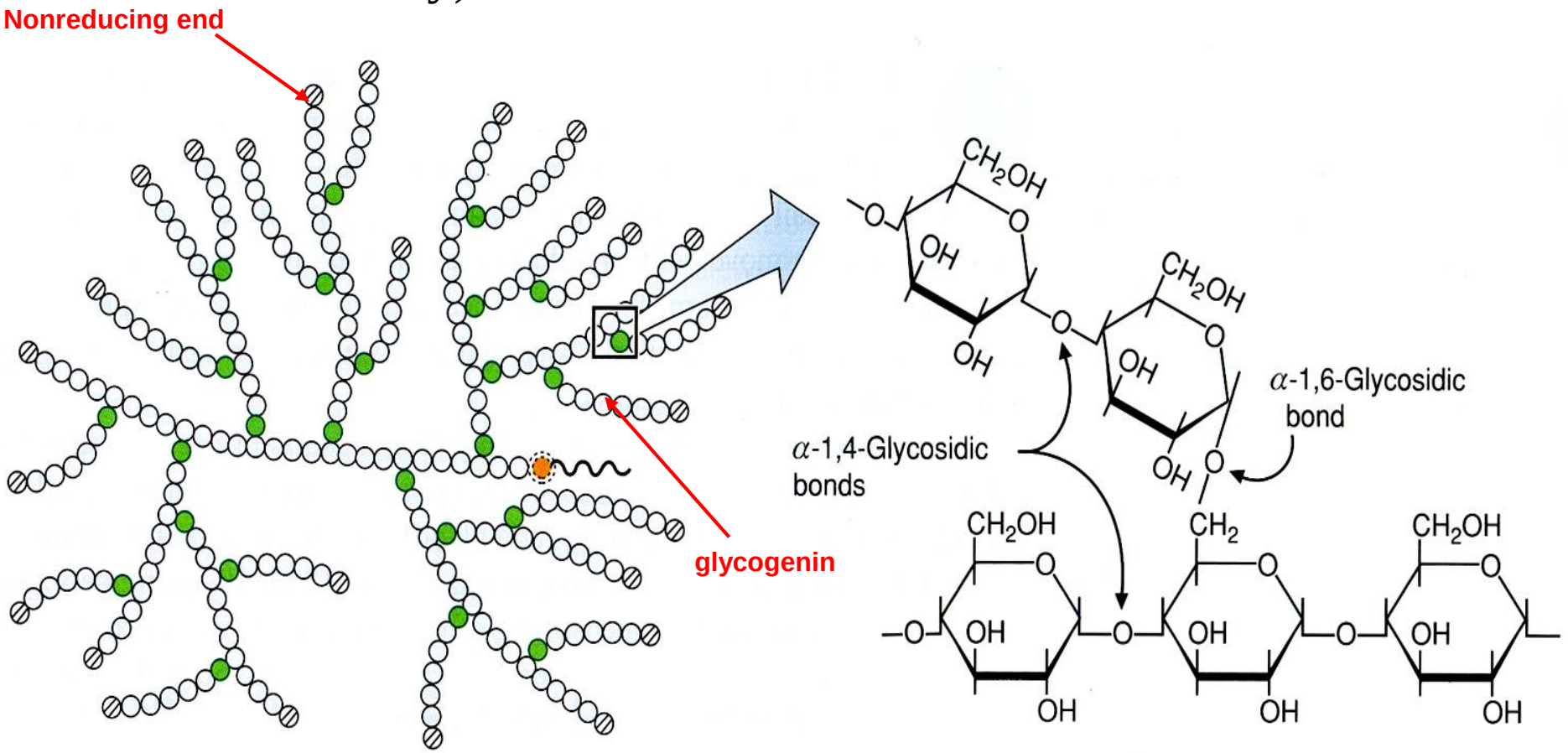
Dr Gulnaz Begum

Objectives

- Structure of glycogen
- Fluctuations of glycogen stores
- Biomedical importance
- Steps of glycogenesis
- Regulation of glycogenesis

Glycogen structure

- α-D-Glucose, α-1,4 and α-1,6 link (branching every 8-10 units)
- source of energy in animals (liver, muscles)
- highly branched structure (rapid degradation and synthesis, better solubility)



FLUCTUATION OF GLYCOGEN STORES:

- Liver glycogen stores are increased during well fed state and are depleted during fasting.

- MUSCLE glycogen stores are not affected by short period of fasting and moderately decreased in prolonged fasting(weeks).

BIOMEDICAL IMPORTANCE

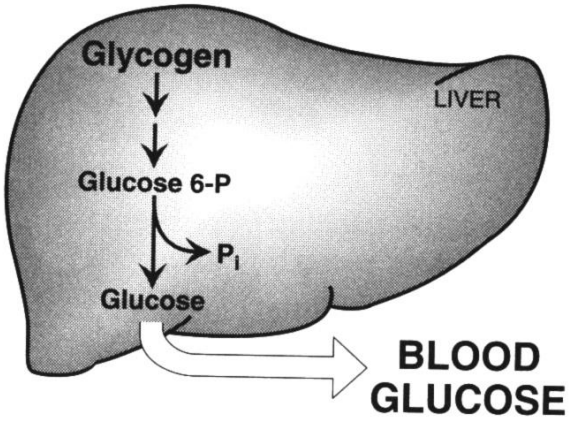
- Major storage CHO in animals-------starch in plants.
- Branched polymer of α-D glucose

- Occurs mainly in

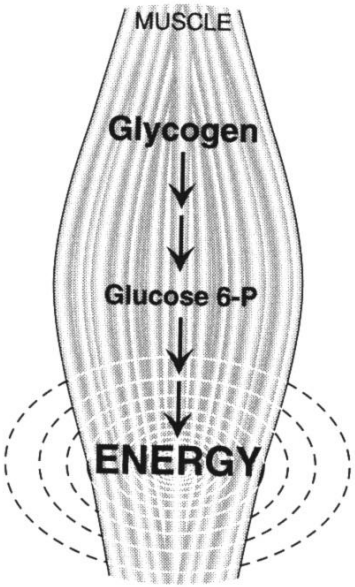
LIVER	6-8%
MUSCLE	1-2%

- Inherited deficiency of enzymes in the pathway produces certain inherited disorders.

different roles in liver and muscle



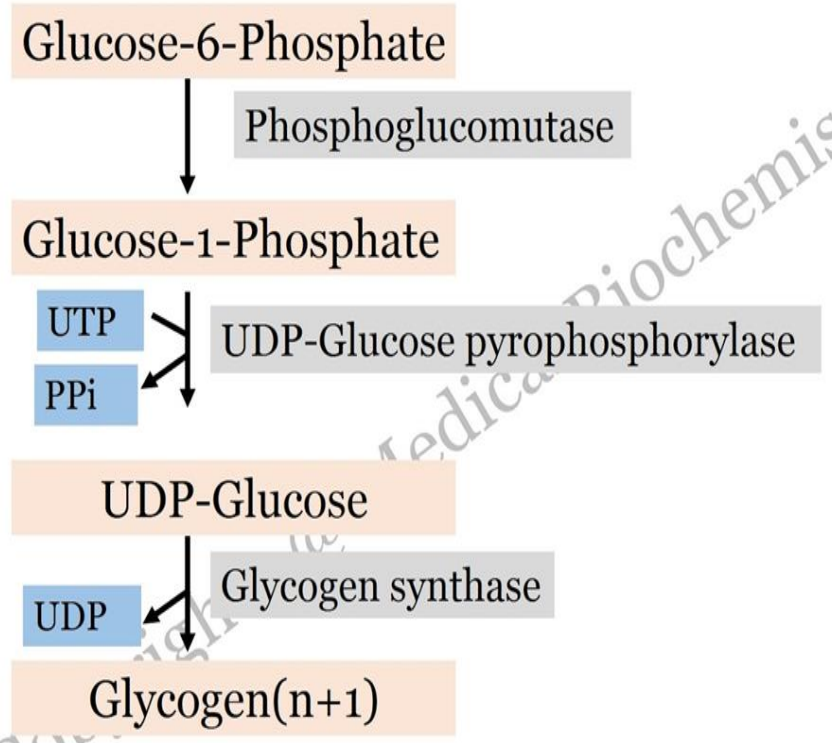
Liver glycogen stores exports glucose to maintain BLOOD GLUCOSE in between meals.



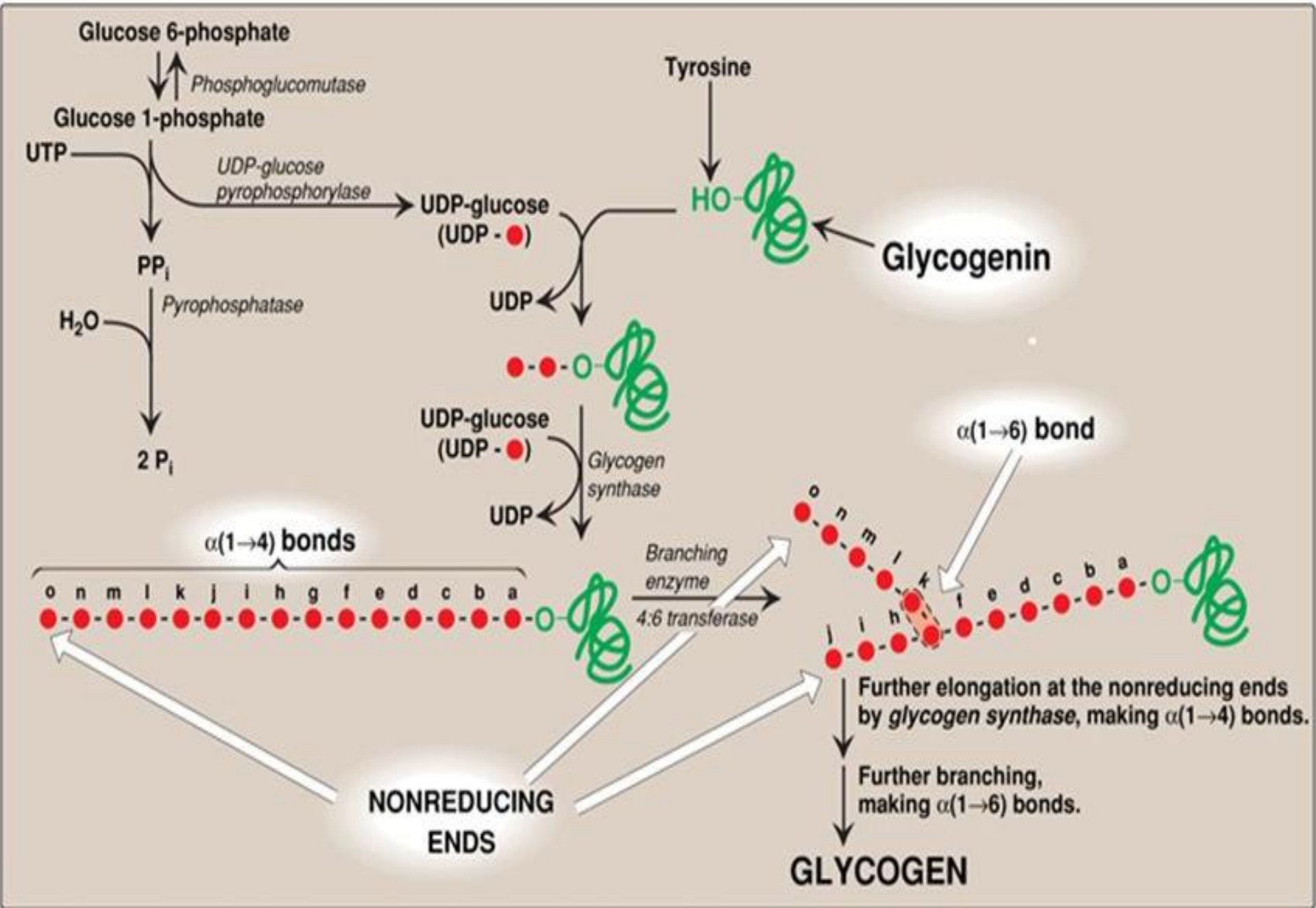
Muscle glycogen provides a readily available source of glucose for glycolysis within the muscle.

GLYCOGENESIS:

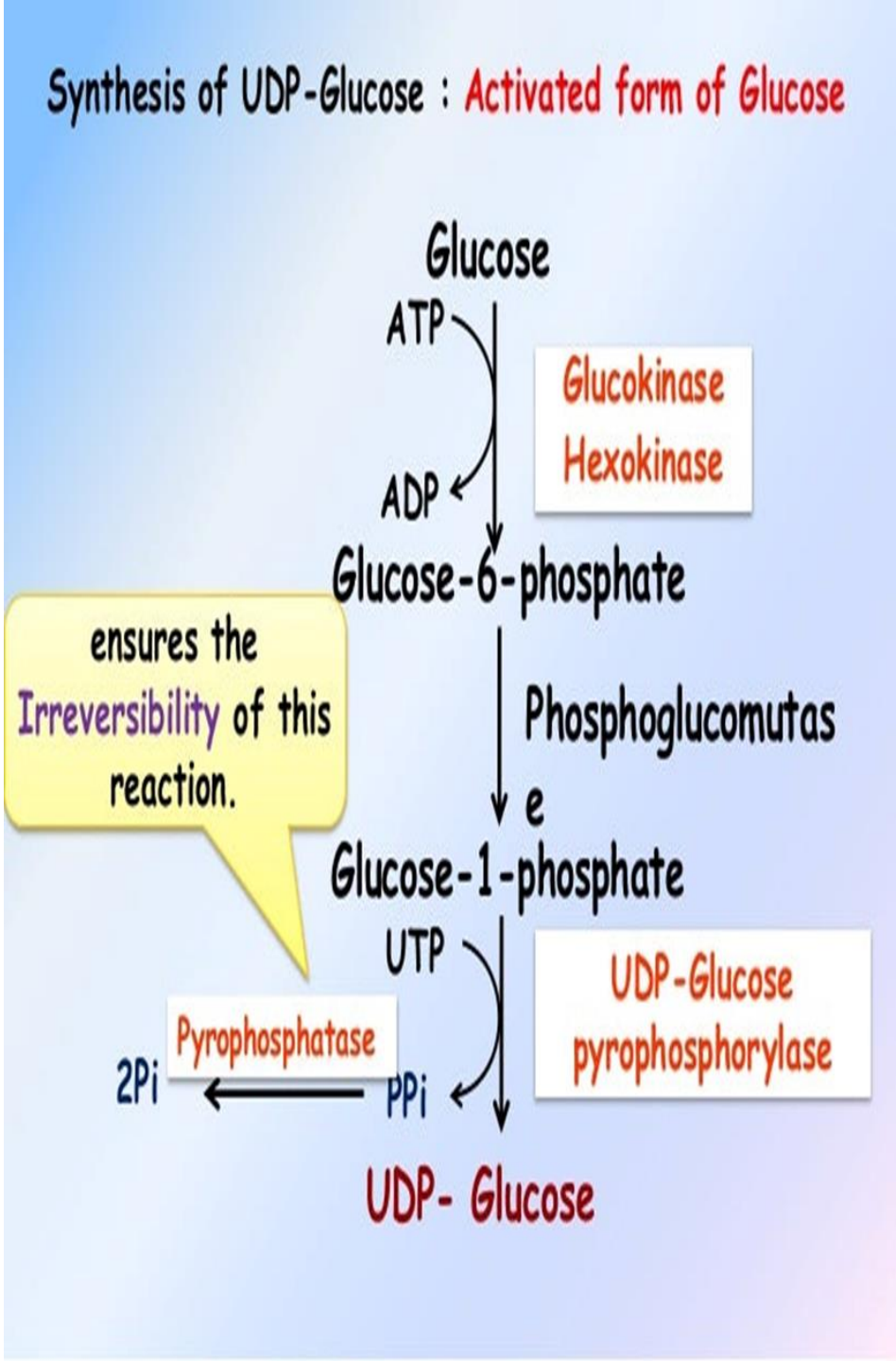
- Glycogenesis is the formation of glycogen molecule from alpha D-glucose.
- Site: liver & muscles , can occur in other tissues.
- The process occurs in cytosol and requires energy supplied by ATP and UTP.



GLYCOGENESIS

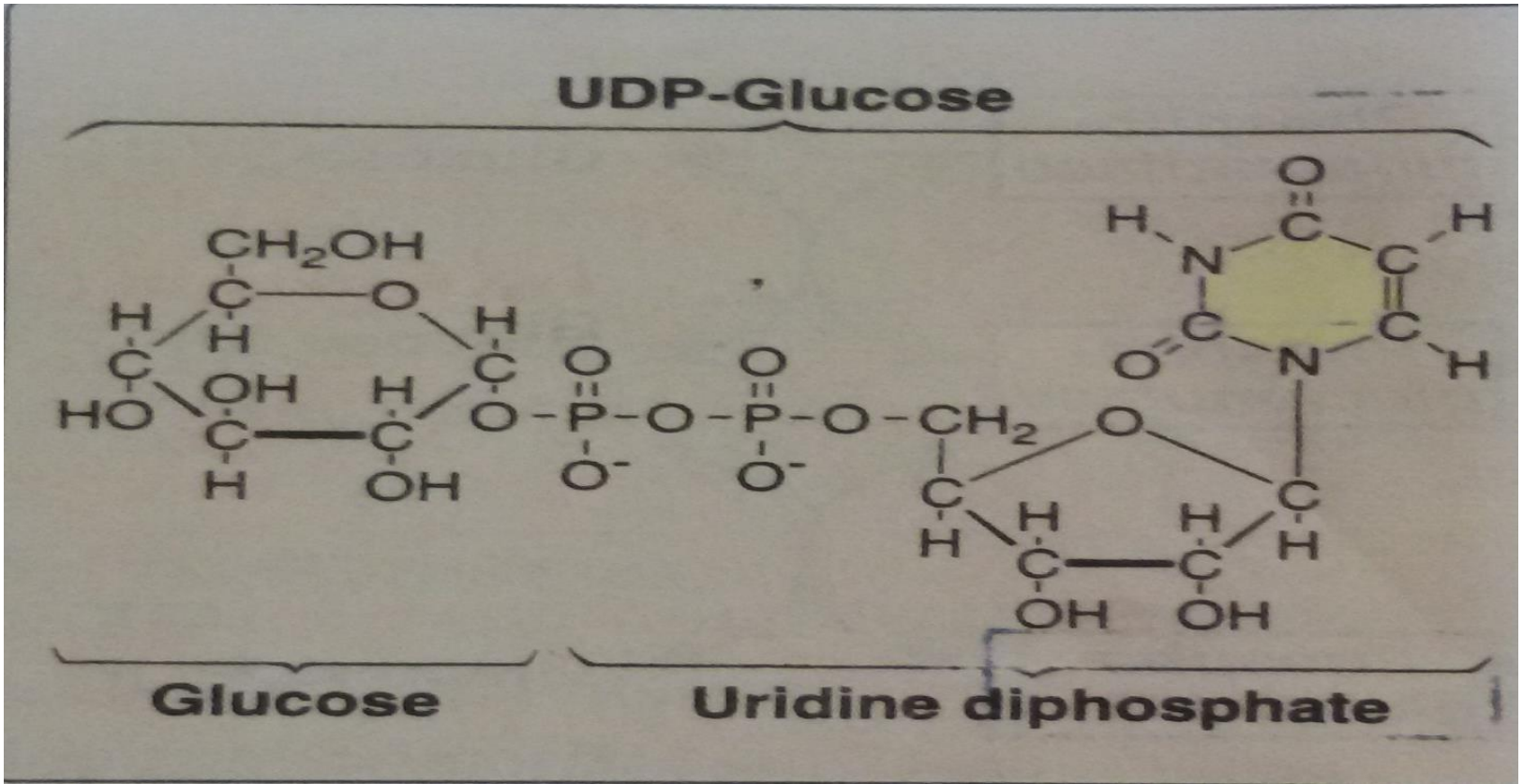


- Glucose-1-phosphate reacts with one molecule of UTP to form active metabolite UDP-Gucose.
- Enzyme: UDP-Glucose Pyrophosphorylase.
- Hydrolysis of pyrophosphate by pyrophosphatse drives the reaction to UDP-glucose production.



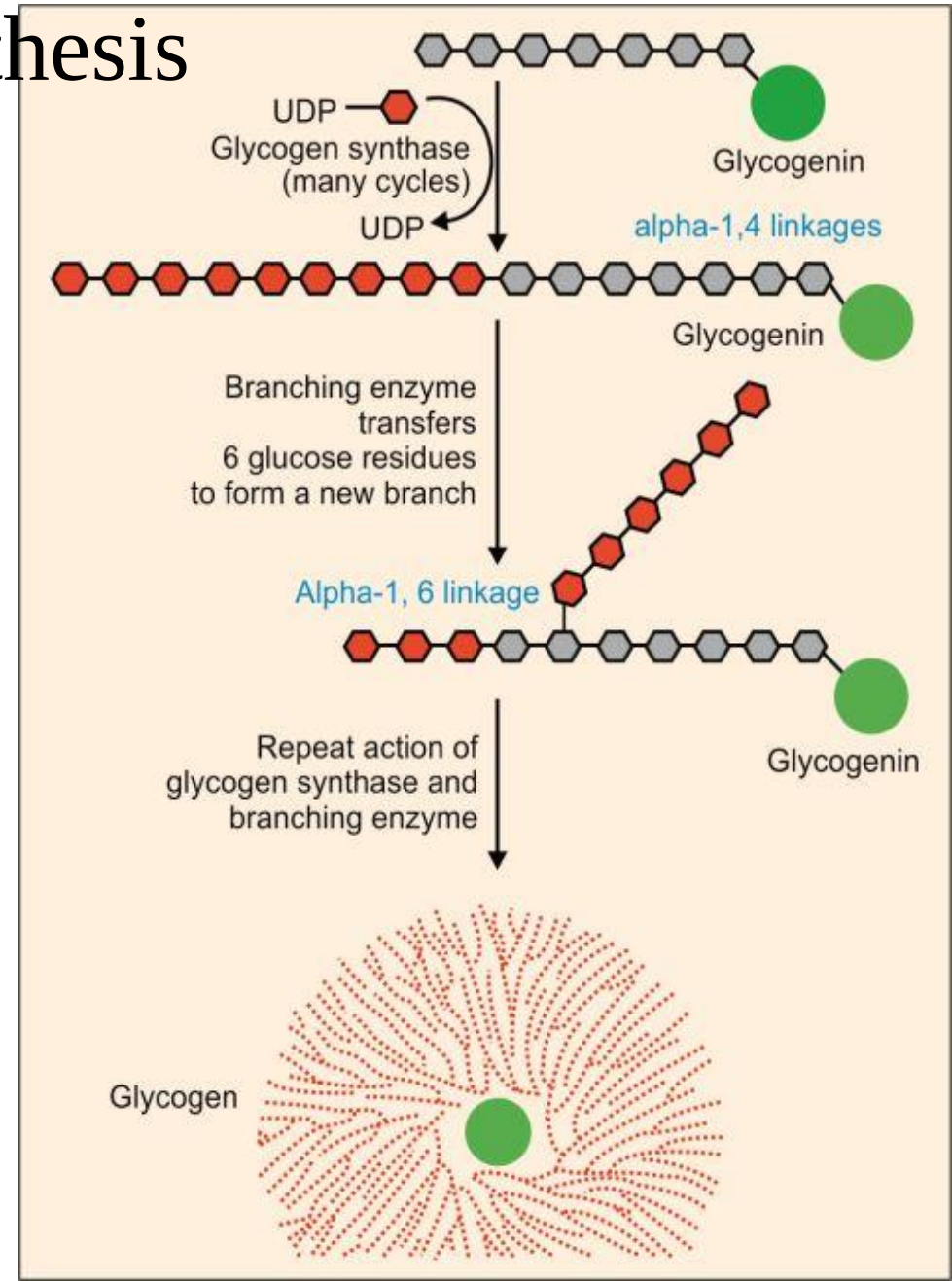
SYNTHESIS OF URIDINE DIPHOSPHATE GLUCOSE:

- ALPHA D-glucose attached to UDP is the source of all the glycosyl residue that are added to the growing glycogen molecule.



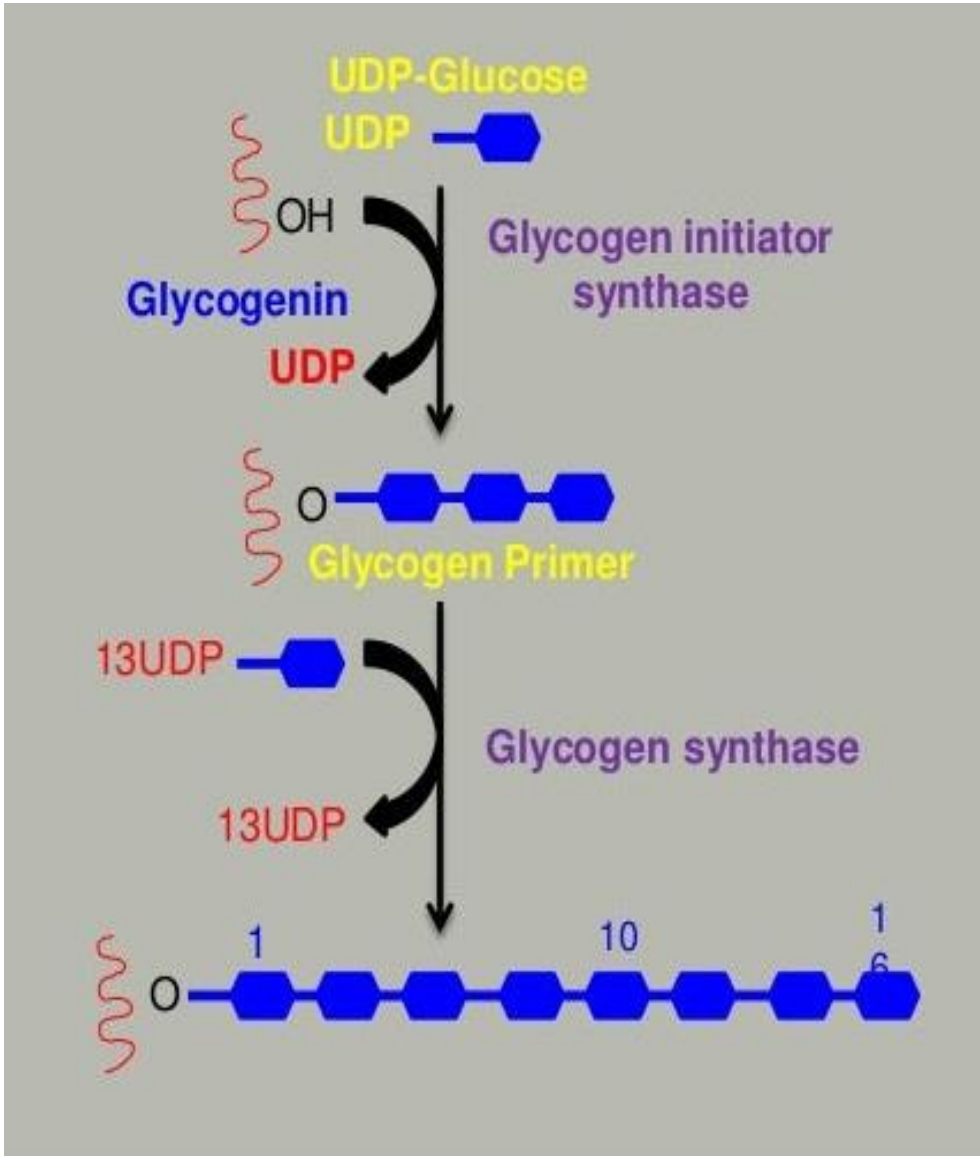
Synthesis of Primer to initiate Glycogen synthesis

- GLYCOGEN SYNTHASE makes the alpha 1-4 linkages in glycogen.
- This enzymes cannot initiate the chain synthesis using free glucose as an acceptor .
- Instead, it can only elongate the pre-existing chain of glucose.
- Glycogen fragment act as a primer in cells.



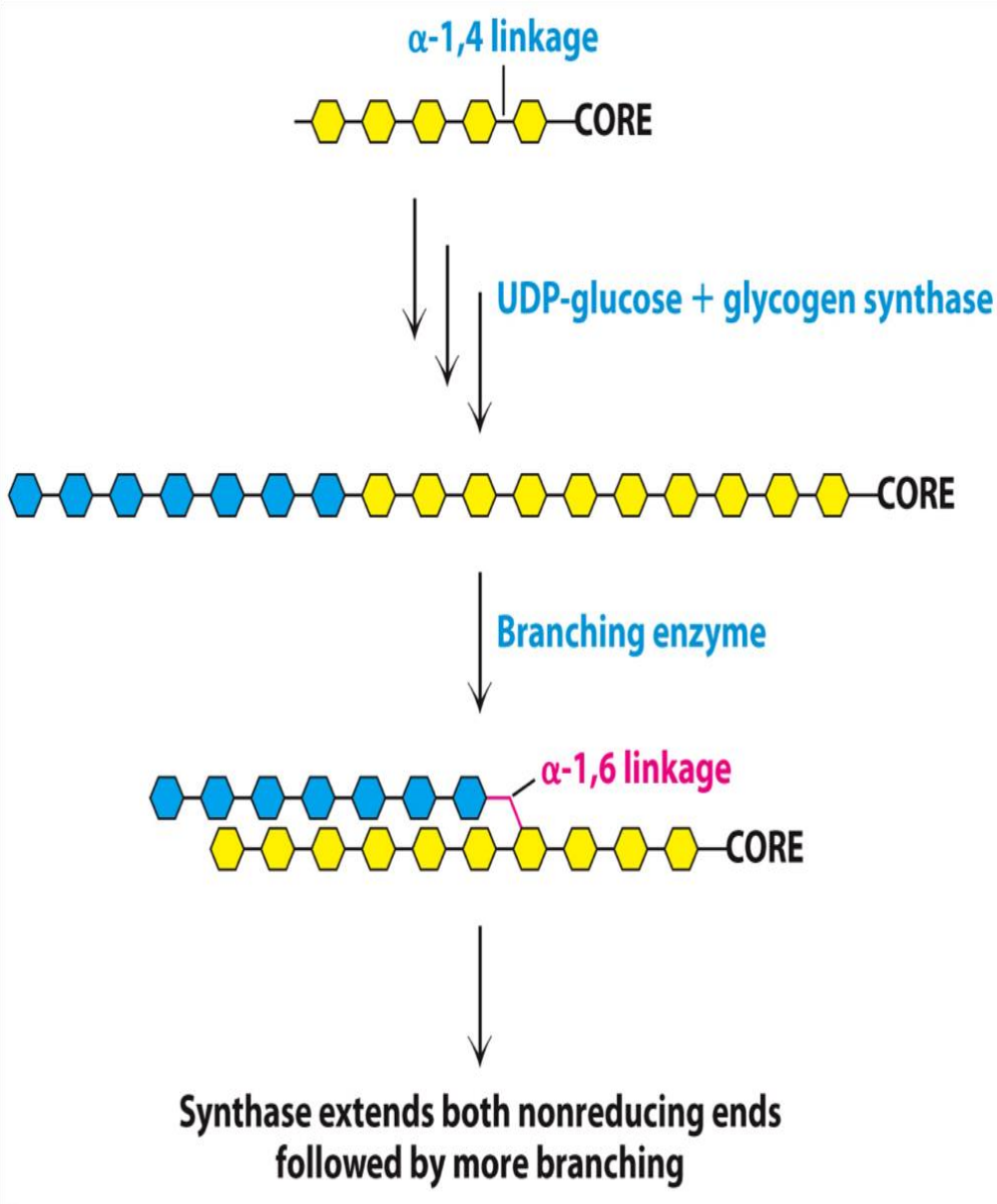
SYNTHESIS OF PRIMER TO INITIATE GLYCOGEN SYNTHESIS

- In the absence of glycogen fragment,a protein called glycogenin can serve as an acceptor of glucose residue from UDP-glucose.
- The OH group of tyrosine can serve as a site where initial glycosyl unit is attached.



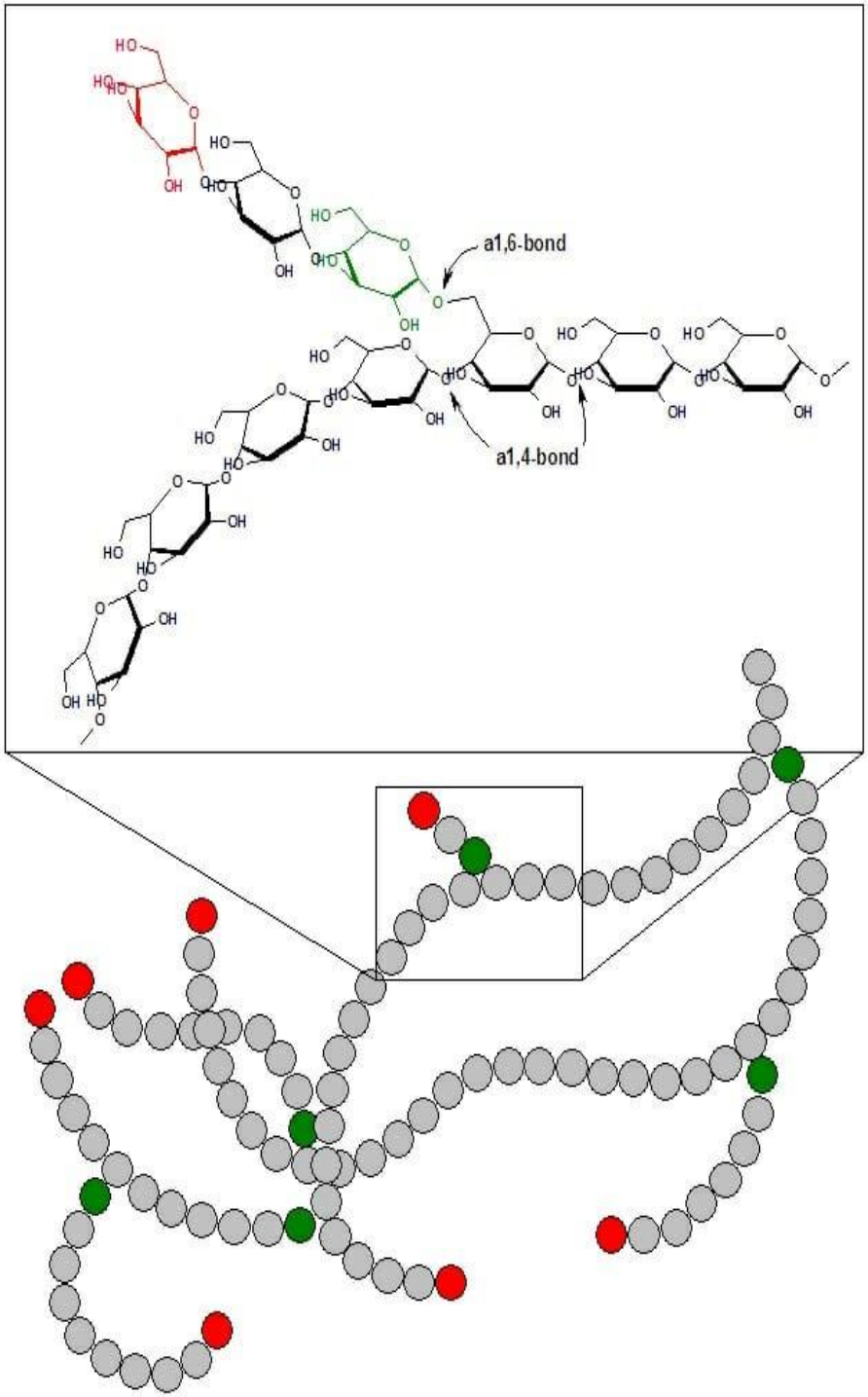
ELONGATION OF GLYCOGEN CHAIN

- Elongation of a glycogen chain involves the transfer of glucose from UDP-glucose to the nonreducing end of the growing chain by glycogen synthase.



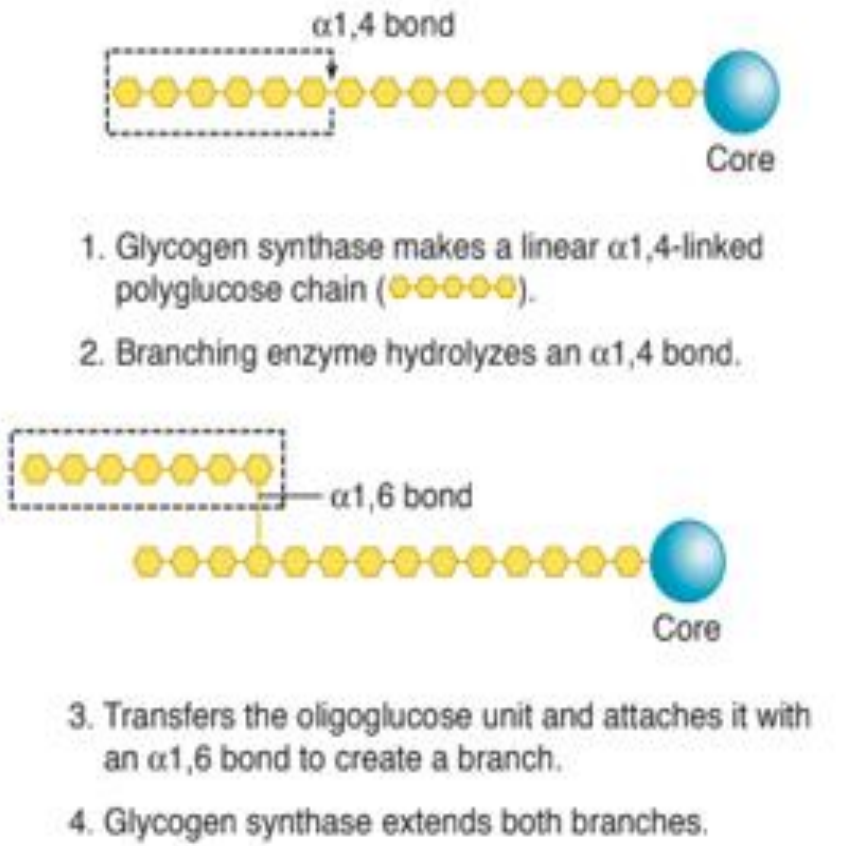
FORMATION OF BRANCHES IN GLYCOGEN:

- GLYCOGEN has branches located , on average, eight glycosyl residues apart, resulting in a highly branched tree like structure.
- Branches also increases the number of nonreducing ends to which new glycosyl residues can be added , thereby accelerating the rate at which glycogen synthesis can occur.

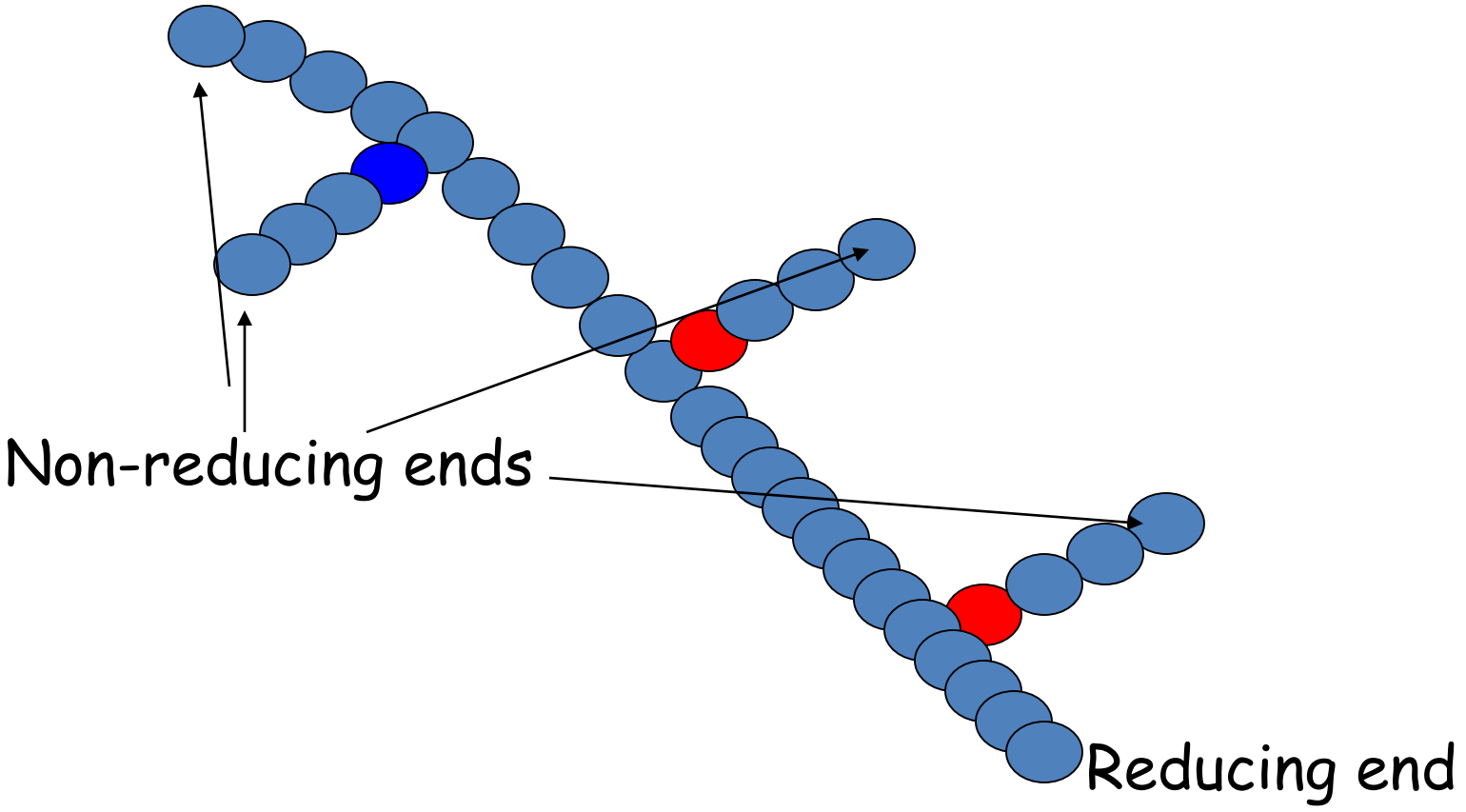


SYNTHESIS OF BRANCHES:

- The branching enzyme, amylo alpha(1-4)-(1-6) transglucosidase removes a set of six to eight glycosyl residues from non-reducing end of the glycogen chain(breaking an alpha 1-4 bond) and attaches it to a non terminal glycosyl residue by an alpha 1-6 linkages.

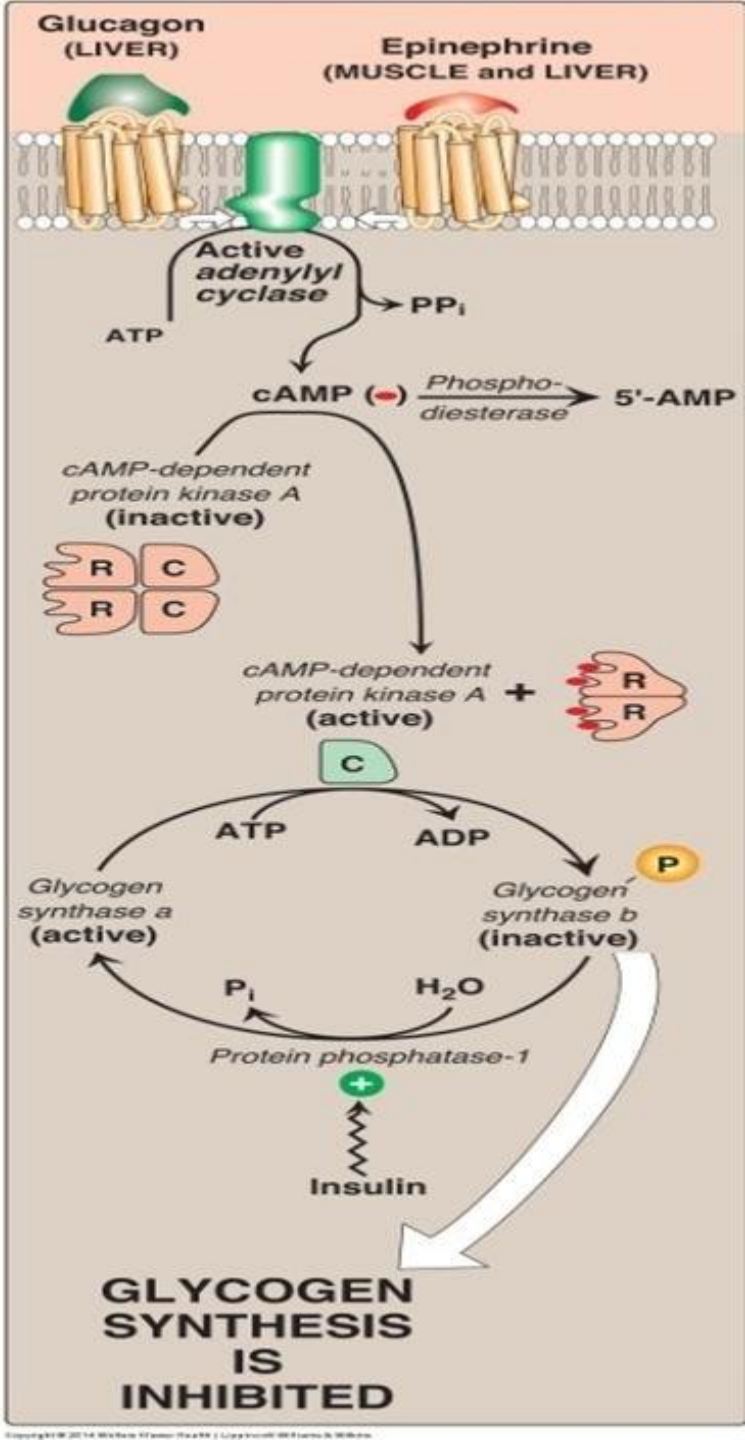


The resulting new non reducing end from which the six to eight residues were removed can now be further elongated by glycogen synthase.



Regulation of glycogenesis

- Glycogen synthase is key enzyme.
- Present in two forms
- Active form(GS ’a’) is converted to inactive form(GS’b’) by phosphprylation, modulated by cAMP dependent protein kinase.



- The interconversion of active to inactive form is controlled by

1. Substrate level

- High glucose conc↑ synthesis

2. End products

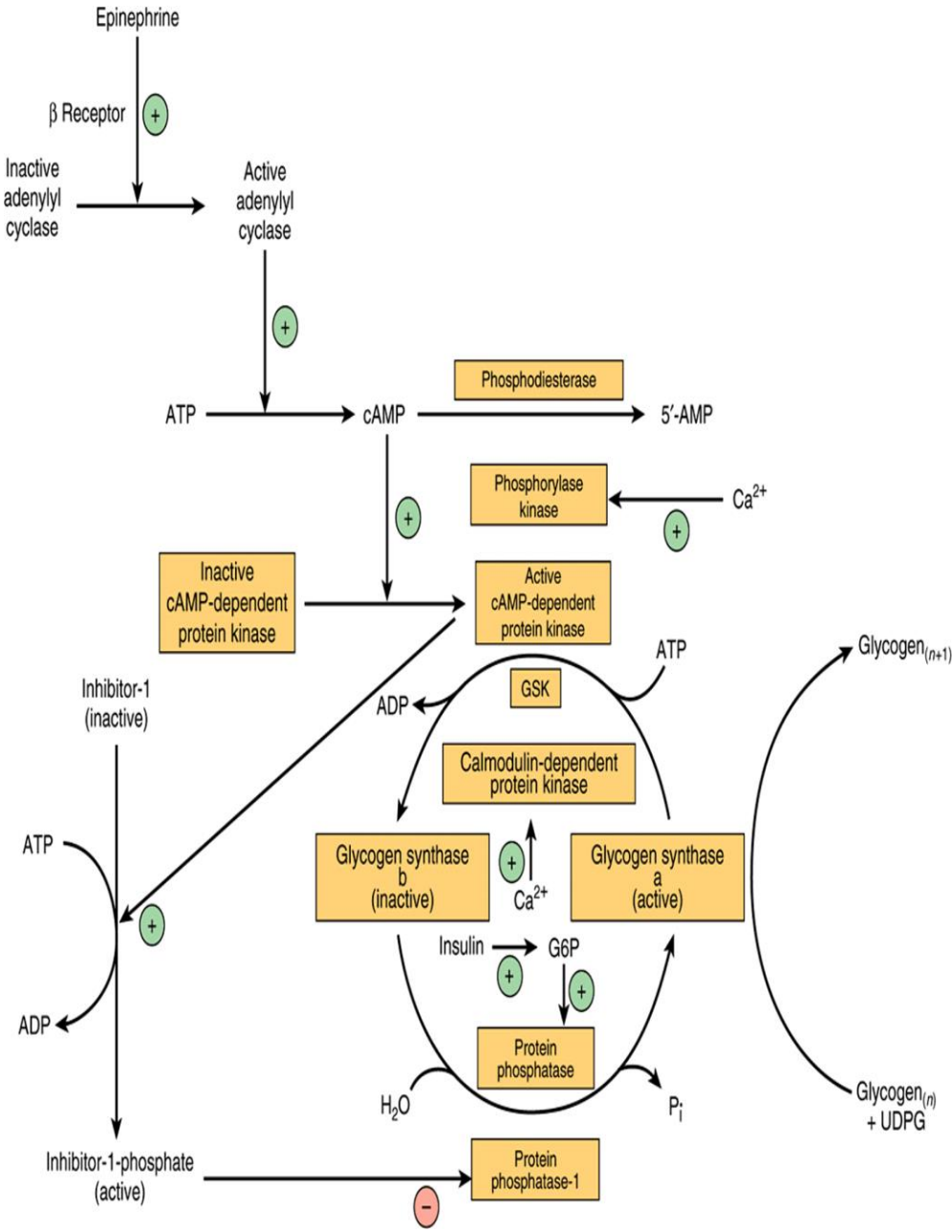
- ↑Glycogen conc inhibits glycogenesis.

3. Hormones

- Insulin increases glycogenesis
- Glucagon & epinephrine inhibit glycogenesis.

Role of cAMP dependant protein kinase

- Active protein kinase stimulates protein factor(inhibitor-1) & phosphorylates it to form ‘’active’’ inhibitor-1-p, which in turn inhibits protein phosphatase-1 thus conversion of inactive GS’b’ to active GS ‘a’ is inhibited.



References

- Chatterjea medical Biochemistry
- Lippincott’s illustrated review


Thank
You