ANABOLISM

Gluconeogenesis and glycogen

Case of animal cells

ANABOLISM

(INTRODUCTION)

- **Anabolism is defined as the metabolism used to synthesize molecules that the body needs.**

- **As opposite to the catabolism, anabolism of aerobic systems proceeds in general by reduction reactions. The involved dehydrogenases very often use NADPH.**

INTRODUCTION ANABOLISM

- **The comparison of the catabolic and anabolic pathways highlights three different cases:**

  - **The anabolic and catabolic pathways are totally different.**

  - **Both use the same enzymes for all reversible reactions. Only the irreversible steps are different: Example glycolysis, gluconeogenesis**

  - **The metabolic steps are nearby, but many enzymes differ; In addition, the two metabolisms are located generally in different compartments.**
  - **Examples: anabolic and catabolic Lynen spirals example**

Gluconeogenesis

Balance - localisation

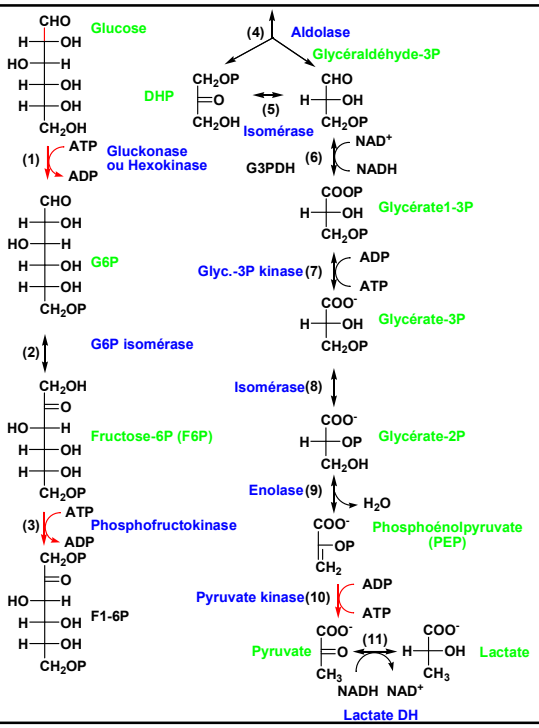
- The main source of substrate is pyruvate/lactate or
- Gluconeogenesis is localized in the cytosol
- This anabolism is very close to Glycolysis
  - Only irreversible steps are replaced by other reactions (or system of reaction) resulting from the point of view of the substrate to the inverse transformation (1).

Coment

- (1) it is obvious that the balance reaction is different.

Remeber glycolysis

(Irreversible steps in red)



Irréversible reactions in glycolysis

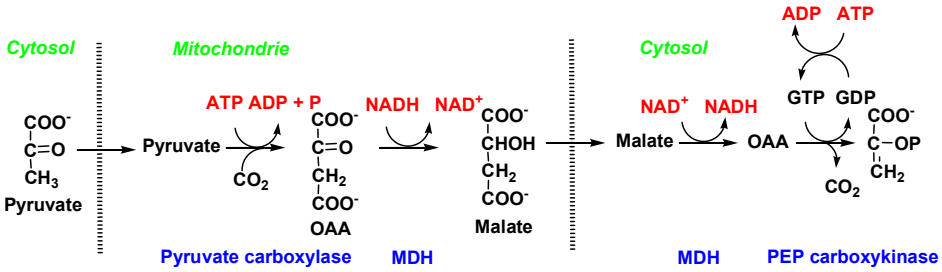
- Glucokinase (or hexokinase) : Glucose + ATP → G6P + ADP ($\Delta G'^{\circ}$= -15 kJ)
- Phosphofructokinase : F6P + ATP → F1-6P + ADP ($\Delta G'^{\circ}$= -15 kJ)
- Pyruvate kinase : PEP + ADP → Pyruvate + ATP ($\Delta G'^{\circ}$= -30 kJ)

- **Coments**
  - $\Delta G'^{\circ}$ values are approximative by simplification. The values are respectively-17, -14, -31 kJ.

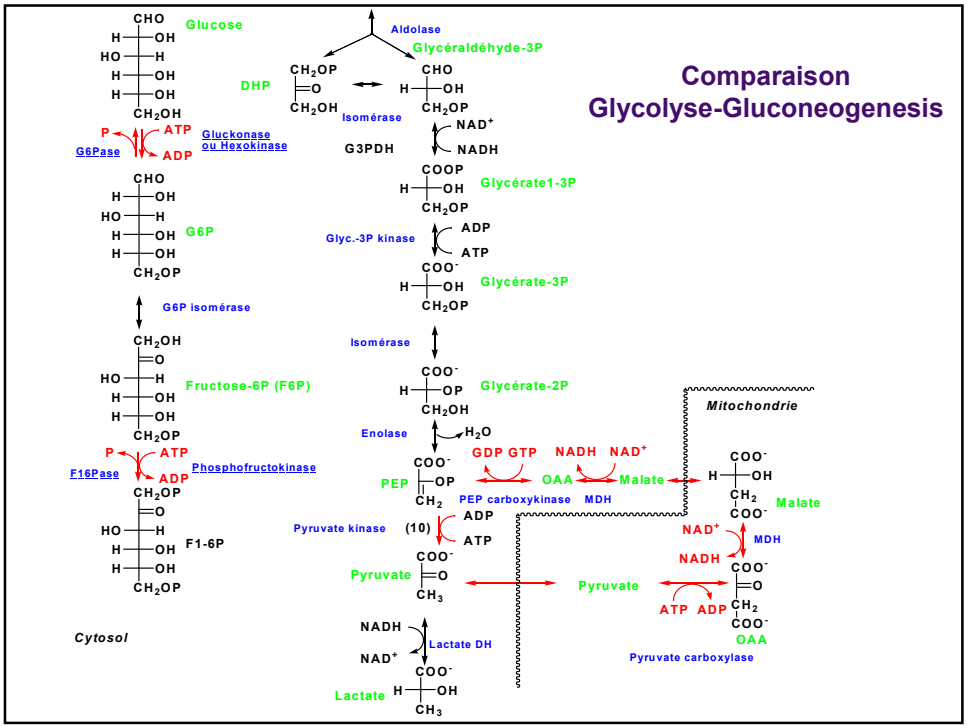
Corresponding reactions on gluconeogenesis

Glucose-6P → Glucose : G6P phosphatase (G6Pase) G6P → Glucose + P ($\Delta G'^{\circ}$= -15 kJ) (2)

Fructose1-6P → F6P : F1-6P phosphatase (F1-6Pase) F1-6P → F6P + P ($\Delta G'^{\circ}$= -15 kJ)



- Only malate and pyruvate are able to be transported, which explains the intervention of MDH in two compartments.



Comparaison Glycolyse-Gluconeogenesis

Regulation

•The activity of the enzymes controlling the irreversible steps (key enzymes) (GK, KFC, Pyruvate K) in glycolysis and gluconeogenesis (F1-6Pase, G6Pase) depends on the concentration of intracellular or extracellular substrates (hormones)

•This allows, according to the physiological state, to activate either Glycolysis or gluconeogenesis.

Example

A high concentration of ATP intracellular (ex: liver cell at rest) causes the activation of the G6Pase and F1-6Pase and inhibition of the GK, the KFC and the PK.

Inversely, a high concentration of ADP and AMP intracellular (liver cell late anabolic activity) causes inhibition of the G6Pase and F1-6Pase and the activation of the GK, the KFC, and the PK.

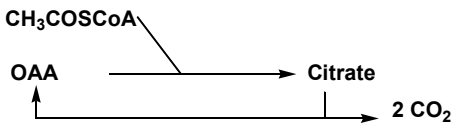
It results that:

– When the cell is in deficit of ATP (thus energy), glycolysis (and thus the Krebs cycle) are activated. When the cell has a high concentration of ATP, it triggers gluconeogenesis.

Other gluconeogenesis

Any substrate for the synthesis of malate can be used as a source of gluconeogenesis.

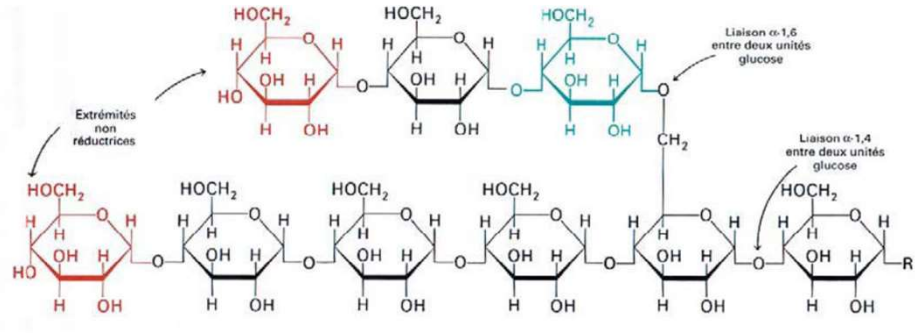
This is the case of the Krebs cycle except the AcetylCoA intermediaries since AcetylCoA enters the Krebs cycle only by reacting with OAA to form citrate..



➢There is no synthesis of OAA or malate. So it may not be of gluconeogenesis.

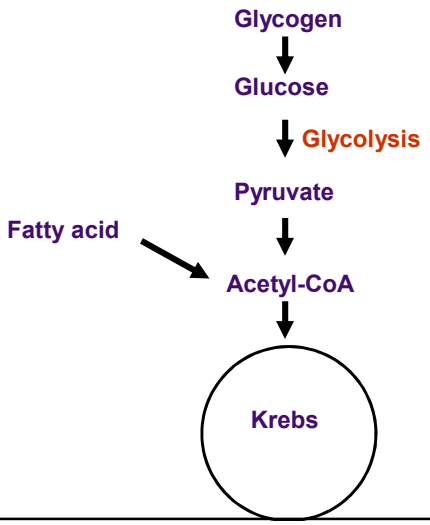
Synthesis of glycogen

- **Structure**



Synthesis of glycogen

- **Importance**



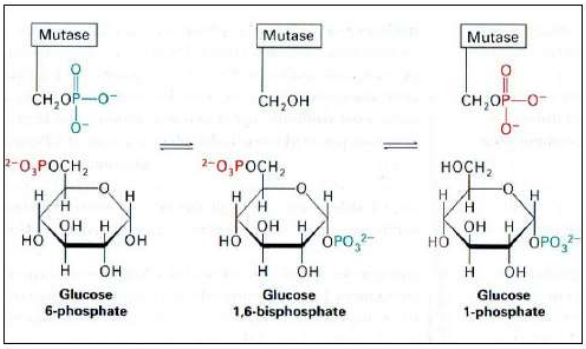
- Unlike glycogen, fatty acids cannot be converted into glucose.

- Fatty acids provide energy only in the presence of oxygen, glycogen can provide in the absence.

Synthesis of glycogen

- **Formation of glucose-1P**

Glucose-6P ⟶ **Glucose-1P**

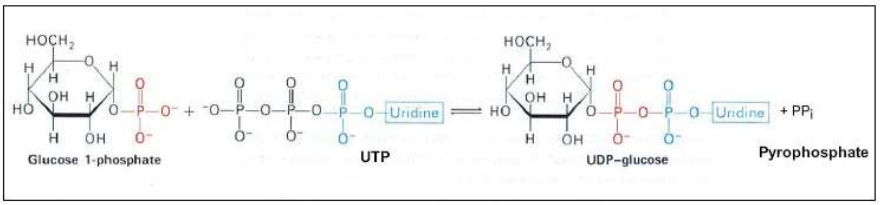


Enzyme: Phosphoglucomutase

Synthesis of glycogen

- **Formation of UDP-glucose**

Glucose-1P + UTP ⟶ **UDP-Glucose + PPi**

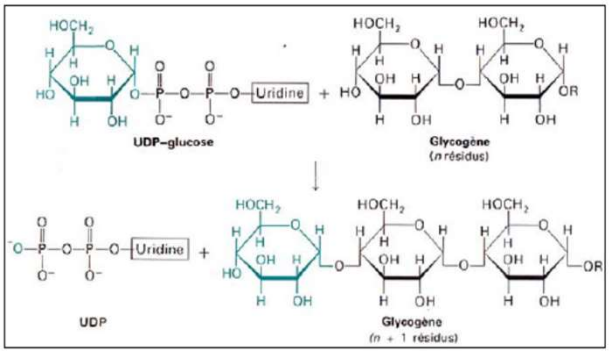


Enzyme: UDP-glucose pyrophosphorylase

Synthesis of glycogen

- **Glycosylation of the elongating glycogen chain**

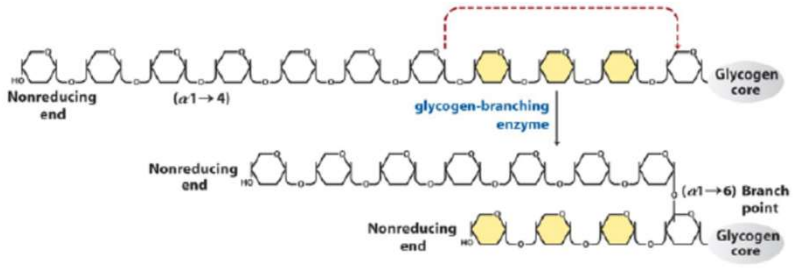
UDP-Glucose-1P + n glc → **UDP + (n+1) glc**



Enzyme: Glycogen synthase

Synthesis of glycogen

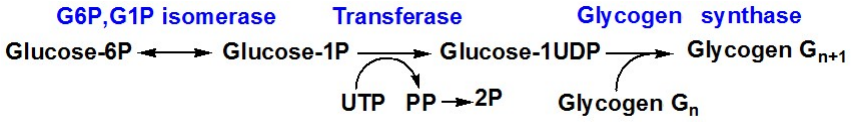
- **Ramification**



• The branches are formed by transferring glucose through links 1-6 at the end of chain.

Synthesis of glycogen

- **Lengthening of the chain by 1-4 links**



Note :

• The degradation of glycogen to the Glucose-1-P is irreversible. The synthesis replaces this step by a sequence of reactions that are transforming the glucose-1P in Glucose-UDP which serves as a source of glucose for glycogen. This allows the reversal of the sequence.