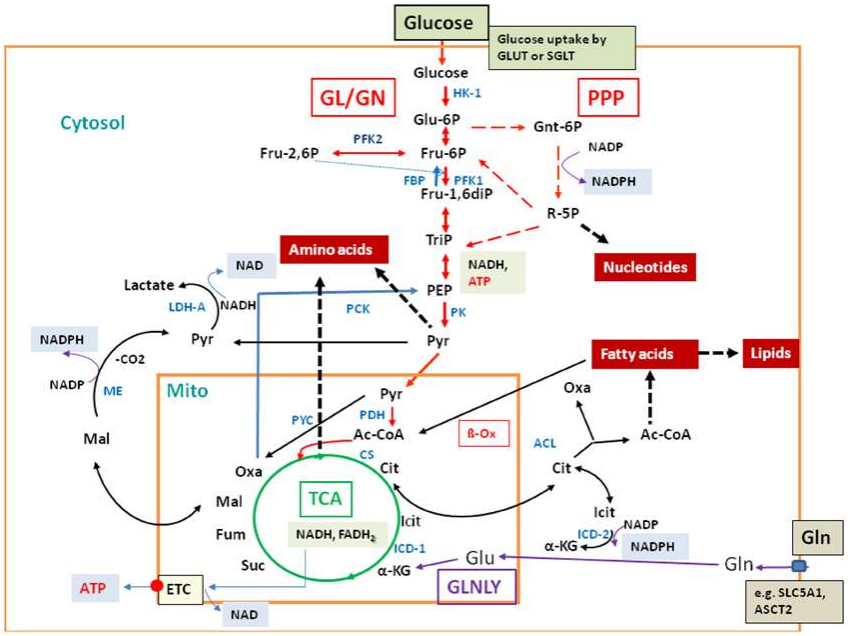
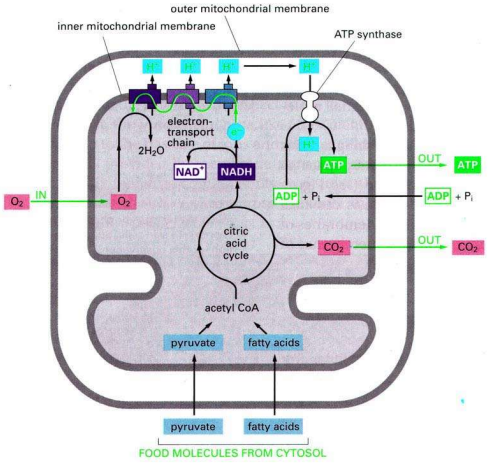
Krebs cycle
or
citric acid cycle



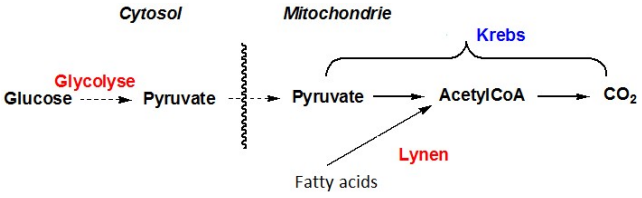
Cycle location



Krebs cycle : substrate balance

Krebs cycle is an aerobic metabolism allowing conversion of pyruvate (from glycolysis) or $CH_3COSCoA$ (from Lynen) into CO_2.pe

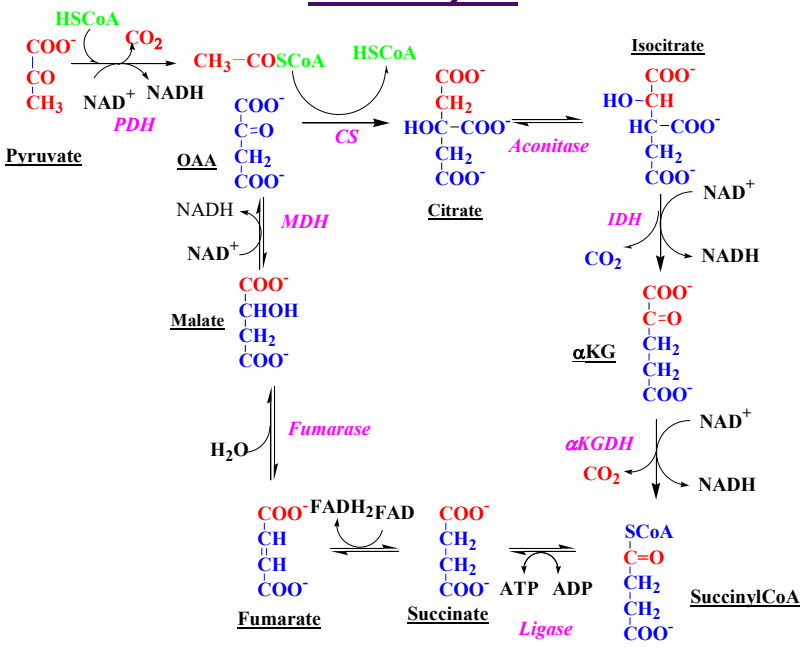
Krebs occurs in the mitochondria



Metabolic previsions

	Pyruvate	Acetyl-CoA
Oxidation	5	4
Squelette breakdow	2	1
Hydrolyse	0	1

Krebs cycle



Cycle analysis

This cycle allows catabolism of pyruvate or acetyl CoA, it forms 3 CO_2 from pyruvate or 2 CO_2 from acetyl CoA

The reactions that liberate CO_2 is a skeleton breakdowns called 'decarboxylation'

One important part of the cycle is directed to generat substrates required for decarboxylation.

It is very important to be able to identify these substrates, only some strutures can be decarboxylated:

α ketoacides

β ketoacides

β Hydroxyacides

Note :

Also the amino acids can also be decarboxylated but this occurs only when specific amines are synthetized in the anabolism.

Other decarboxylations occurs in aromatic compounds.

Attention : Decarboxylation is a subtype of skeleton breakdon reaction.

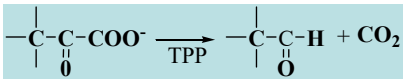
α Keto acids decarboxylation

Oxidative decarboxylation (enzyme: α ketoacide dehydrogenase)

In general, α ketoacids are converted to acyl-CoA by an oxidative decarboxylation involving 3 coupled reactions : « oxidation + skeleton breakdown, condensation + condensation ».

This complex reaction involves one enzyme and 5 coenzymes: Coenzyme A, NAD^+, FAD, thiamine pyrophosphate (TPP), and lipoic acid (LipSS) *(see diaporamA 9).*

Non oxidative decarboxylation (enzyme: α ketoacide decarboxylase)



This reaction is exceptional.

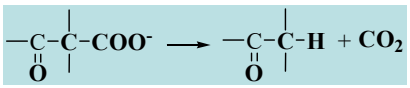
The reaction is a skeleton breakedown non red-ox.

This reaction involves one enzyme and one coenzyme: thiamine pyrophosphate (TPP)

Decarboxylations are all irreversible.

Decarboxylation reactions in Krebs

β Ketoacid decarboxylation (enzyme: β keto acide decarboxylase)

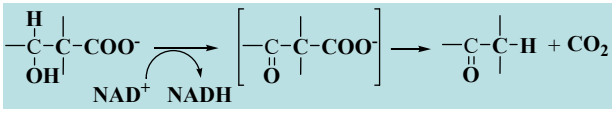


This is a skeleton non oxidative breakedown

NB : *In vitro, this reaction takes some hours*. However, decarboxylasee strongly accelerate the reaction.

β Hydroxyacid oxidative decarboxylation (enzyme: β hydroxyacide DH)

β Hydroxyacids are oxidated in β ketoacides that are then decarboxylated, this two reactions are assured by one enzyme (β ketoacide is not liberated).

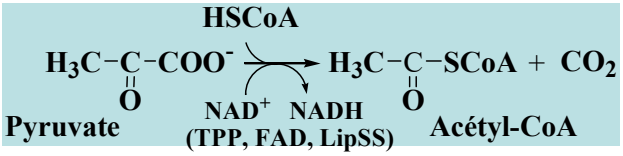


NB : The involved reactions are: skeleton breakdown and oxidation

Note : β alcohol MUST BE primary or secondary.

Krebs cycle analysis

Step 1 : Pyruvate → Acetyl-CoA + CO_2



(1)

Reaction type : **Oxidation + condensation + eskeleton breakdown**

Coenzyme : **HSCoA, NAD^+→NADH, FAD, TPP, LipSS**

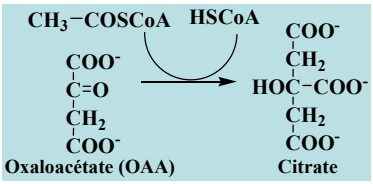
Enzyme : **Pyruvate DH**

Energetics : **Irreversible**

Comments :

1. It is an oxidative decarboxylation of an α ketoacid.

Step 2 : Acetyl-CoA + OAA → citrate



Reaction type : **Skeleton synthesis + hydrolysis (1)**

Coenzyme : ***Aucun***

Enzyme : **Citrate synthase (CS)**

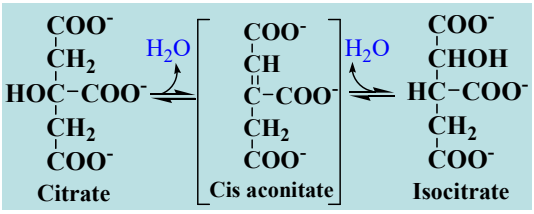
Energetics : **Irreversible (2)**

Comments :

(1) This synthesis is an aldolisation.

(2) Aldolisation is reversible but irreversible when coupled.

Step 3 : Citrate → Isocitrate



(1)

Reaction type : **Dehydration + hydration**

Coenzyme : ***Aucun***

Enzyme : **Isomerase (aconitase)**

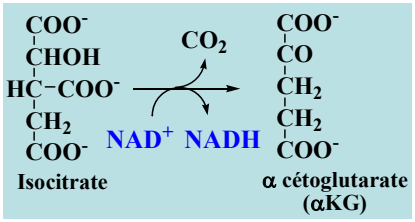
Energetics : **Reversible (2)**

Comments :

(1) Isomerisation.

(2) Evident !.

Step 4 : Isocitrate → αKG



(1)

Reaction type : **Oxidation + skeleton breakdown**

Coenzyme : **NAD^+ → NADH**

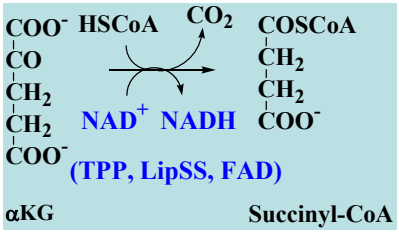
Enzyme : **DH**

Energetics : **Irreversible**

Comments :

(1) Isocitrate is a β hydroxyacide.

Step 5 : αKG → Succinyl-CoA



(1)

Reaction type : **Oxidation + skeleton breakdown + Condensation**

Coenzyme : **HSCoA, NAD^+ → NADH, TPP, LipSS, FAD**

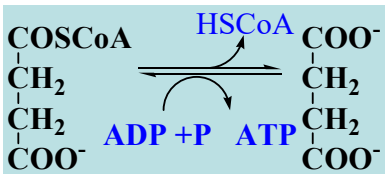
Enzyme : **DH**

Energetics : **Irreversible**

Commentaires :

(1) αKG is an α ketoacide.

Step 6 : Succinyl-CoA → Succinate



Reaction type : **Hydrolysis condensation (DT)**

Coenzyme : **ADP → ATP**

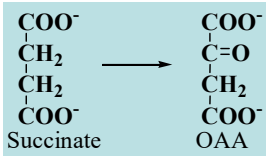
Enzyme : **Ligase**

Energetics : **Reversible**

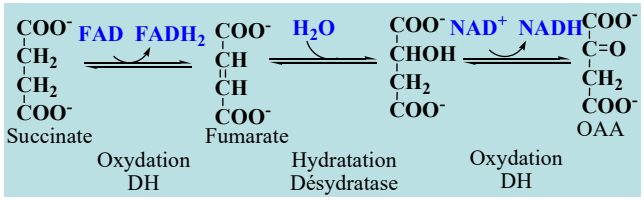
Comments :

NB Energy of oxidation is recovered in ATP

Steps 7 a 10 : Succinate →OAA (OAA regeneration)



- **-CH_2- need to be oxidized into ketone (-CO-).**
- **As in Lynen, we see the sequence:**



Comments : Two –COO^- results in mobile hydrogen : non activator co-enzyme needed

Substrate and energetic balance

From pyruvate

Pyruvate + 4 NAD^+ + FAD + ADP + P -----> 3 CO_2+ 4 NADH + $FADH_2$+ ATP

From acetyl-CoA

AcetylCoA+ 3 NAD^+ + FAD + ADP + P -----> 2 CO_2+ 3 NADH + $FADH_2$+ ATP

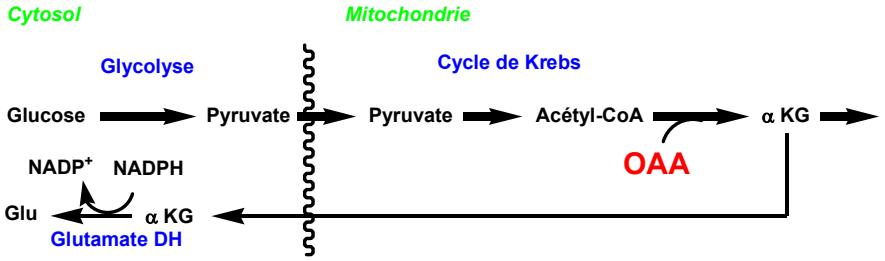
ATP (considering respiratory chain)

	From pyruvate		From acetyl-CoA	
	Regenerated Coenzymes	ATP formed	Regenerated Coenzymes	ATP formed
NADH	4	12	3	9
$FADH_2$	1	2	1	2
ATP	1	1	1	1
Total		15		12

Amphibolic character of CTA (Krebs) cycle

Krebs cycle intermediates are also precursors in anabolic reactions. They are exported to the cytosol in where anabolism takes place.

Example : Glutamate anabolism



Since Krebs is stopped after αKG synthesis, OAA is not regenerated.

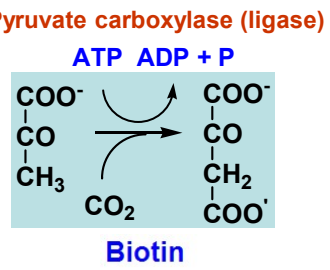
OAA is then produced from glycolysis. This OAA synthesis is called « anaplerotic reaction »

DPG1

Anaplerotic reactions

In animal cells

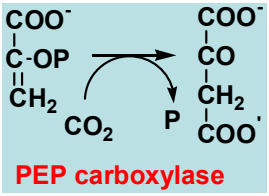
Oxaloacetate is synthetized from pyruvate by a carboxylation catalyzed by a pyruvate carboxylase and biotin as activator coenzyme.



Generality : Carboxylation reactions requires always ATP and biotin.

Cas des cellules végétales

Oxaloacetate is synthetized from PEP by a carboxylase that hydrolyze phosphate group. Biotin is not required.



Diapositive 19

DPG1 D PG; 16/11/2016