Oxidative Decarboxylation and Krebs Cycle

Foundation block..

دعاء قبل المذاكرة

اللهم انى اسالك فهم النبيين وحفظ
المرسلين والملائكة المقربين
اللهم اجعل السنتنا عامرة بذكرك
وقلوبنا بخشيتك واسرارنا بطاعتك
انك على كل شىء قدير
وحسبنا الله ونعم الوكيل

دعاء بعد المذاكرة

اللهم انى استودعك ما
قرأت وما حفظت وما
تعلمت فرده عند حاجتى
اليه انك على كل شىء
قدير وحسبنا الله ونعم
الوكيل

Fates of Pyruvate

Anaerobic Occurs in yeast and some bacteria (intestinal flora)

Reduction

Decarboxylation by Thiamine pyrophosphate

Alanine

ALT

PLP

αKG

Glutamate

Non essential amino acid

Intermediates for Krebs cycle

4 Carbons

Krebs cycle begins when

Oxaloacetate + Acetyl CoA = citrate

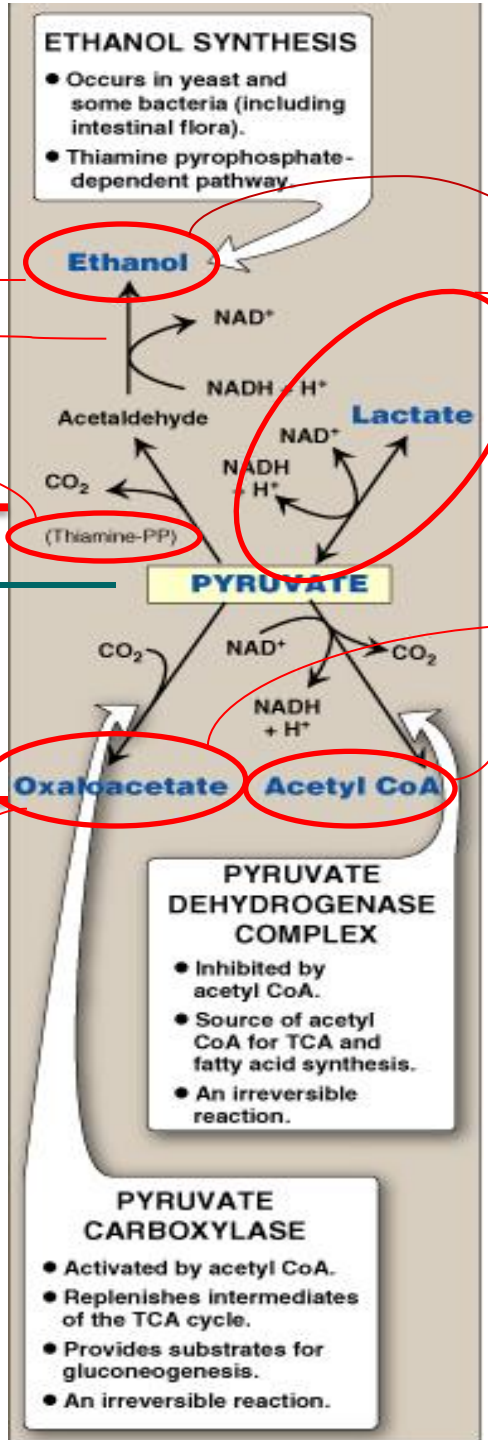
4 Carbons 2 Carbons

synthesis of glucose by the lactate to pyruvate then **Oxaloacetate**

That's why its important

Reversible reaction

irreversible steps



Fates of Pyruvate

1. Oxidative decarboxylation into Acetyl CoA: the enzyme is pyruvate dehydrogenase complex (PDH). It occurs in mitochondria. It is irreversible. Acetyl CoA can enter the Krebs cycle to produce energy, or acts as a building block for fatty acid synthesis. Inhibited by Acetyl CoA and NADH +H.

2. Carboxylation into oxaloacetate (OAA): the enzyme is pyruvate carboxylase. It occurs in mitochondria. It is irreversible. It needs biotin and ATP. OAA replenishes the Krebs cycle intermediate & provides substrate for gluconeogenesis.

3. Reduction to lactate: the enzyme is lactate dehydrogenase. (LDH). Important in anaerobic glycolysis and in gluconeogenesis. Reversible reaction.

4. Reduction to ethanol: it occurs in 2 steps: decarboxylation then reduction. Decarboxylation occurs in yeast and some micororganisms and in intestinal bacterial Flora. The enzyme requires thiamine pyrophohsphate (TPP) as a coenzyme.

5. Conversion to Alanine by alanine aminotransferase (ALT): an amino group is transferred from glutamate to pyruvate, resulting in the formation of alpha ketoglutarate (αKG) and alanine. The enzyme requires the coenzyme pyridoxal phosphate (PLP: vit B_6 derivative) as a coenzyme. The reaction is reversible.

Oxidative Decarboxylation of Pyruvate

Occurs in the mitochondria and produce energy

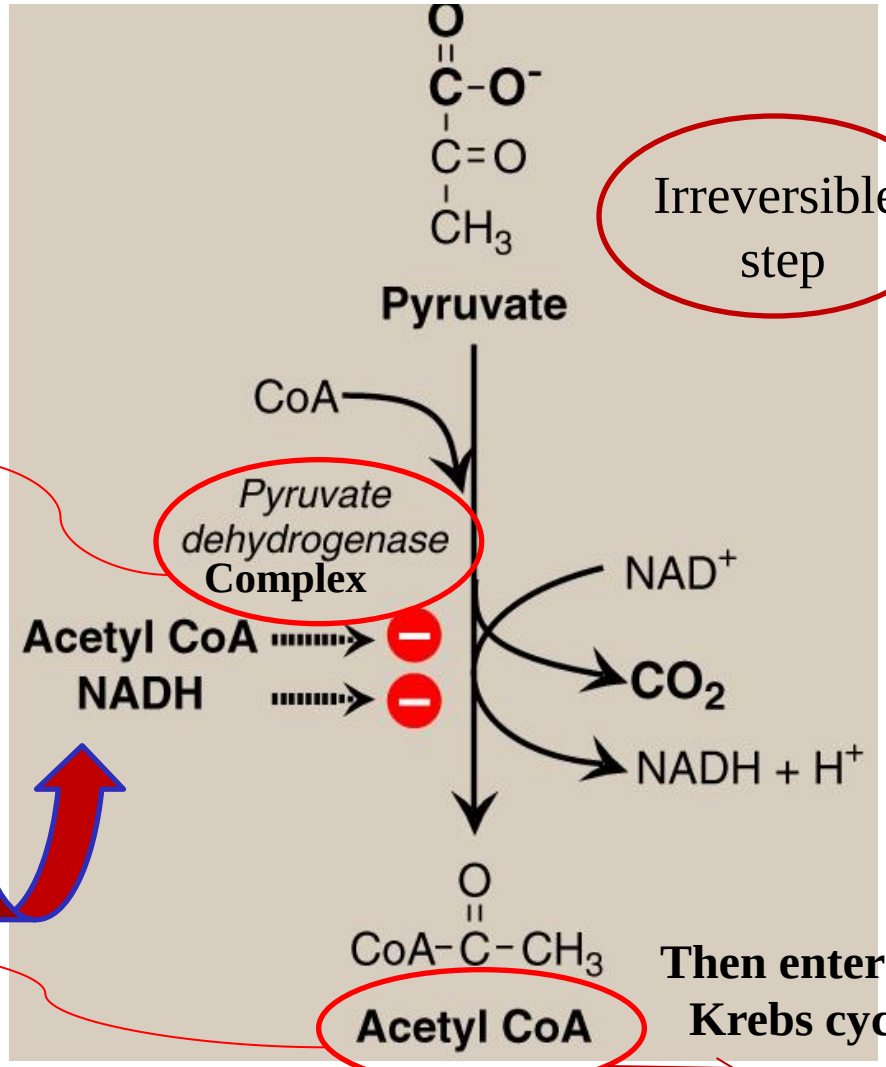
irreversible

Not only 1 enzyme

If there is many <u>Acetyl CoA</u> It Inhabits the pyruvate dehydrogenase complex

At the same time **stimulate the pyruvate carboxylase**

Allosteric Regulation

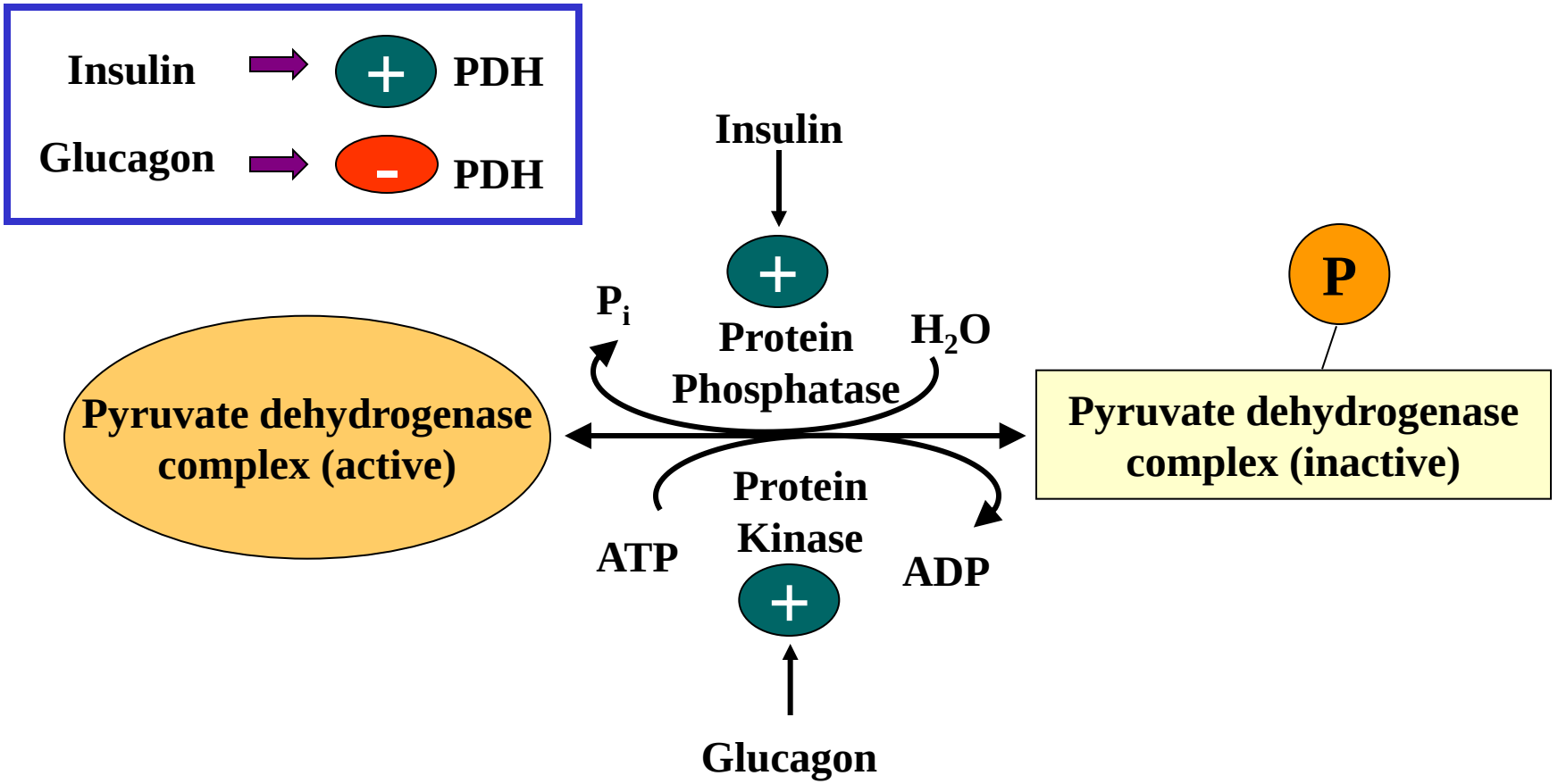


Fatty acid synthesis (non essential) our bodies can produce it

Oxidative Decarboxylation of Pyruvate

The endproduct of aerobic glycolysis (Pyruvate) is transported to mitochondria
to be Oxidatively decarboxylated to Acetyl CoA.
The enzyme is pyruvate dehydrogenase complex (PDH).
PDH is not part of the glycolysis nor of TCA cycle.
It occurs in mitochondria.
It is irreversible.
The endproduct (Acetyl CoA) can enter the Krebs cycle, or be used in fatty acid synthesis.

PDH Complex: Covalent Regulation



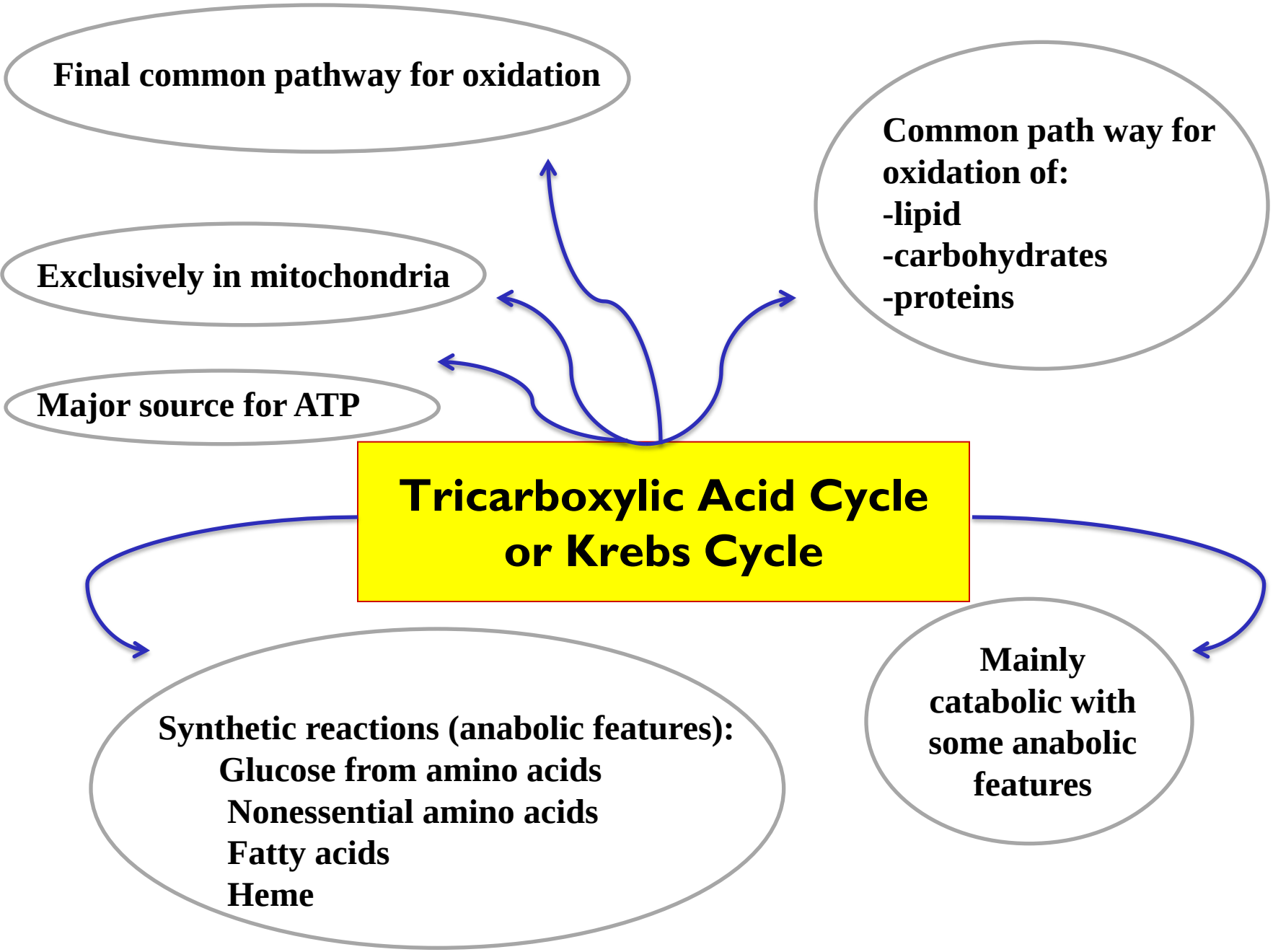
Regulation of PDH Complex:

Allosteric inhibition by Acetyl CoA and NADH

Covalent regulation by a kinase and a phosphatase enzymes (phophorylated form of PDH is inactive, and dephosphorylated form is active)

Insulin activates PDH complex (by stimulating the phosphatase enzyme), and Glucagon inhibits PDH complex (by stimulating the kinase enzyme).

Calcium ions activates the PDH complex, which is particularly important in skeletal muscle contraction.

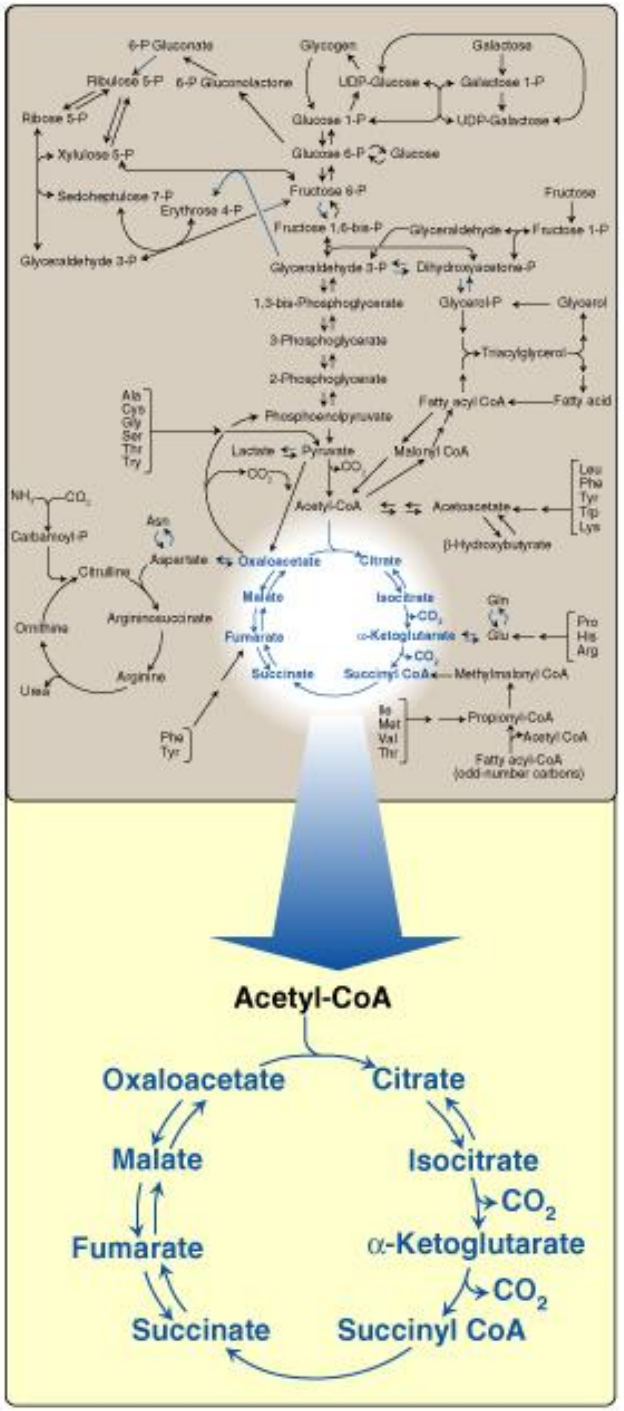

Final common pathway for oxidation
Common path way for oxidation of:
-lipid
-carbohydrates
-proteins
Exclusively in mitochondria
Major source for ATP
Tricarboxylic Acid Cycle or Krebs Cycle
Synthetic reactions (anabolic features):
Glucose from amino acids
Nonessential amino acids
Fatty acids
Heme
Mainly catabolic with some anabolic features

Krebs Cycle

Krebs cycle: there must be mitochondria and o_2

There is no Krebs cycle in RBCs

It is Aerobic pathway
It is a major source for ATP



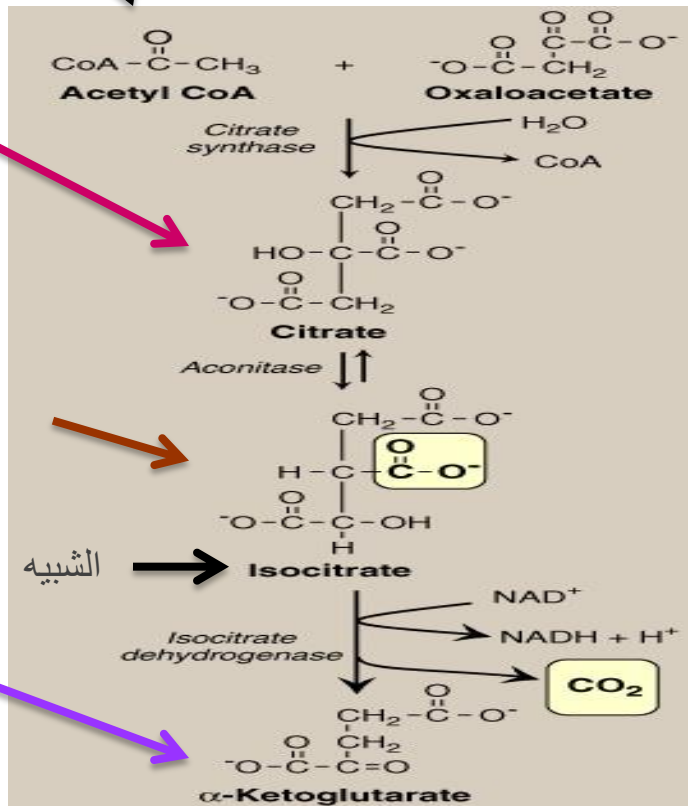
Krebs Cycle Reactions (1)

From pyruvate

-Synthesis of citrate (from acetyl CoA + OAA): the enzyme is citrate synthase. Citrate inhibits PFK-1 (The rate limiting step in glycolysis)

-Isomerization of citrate to isocitrate by aconitase enzyme

- Oxidation & decarboxylation of Isocitrate to αKG by isocitrate dehydrogenase. The reaction releases CO_2 and NADH



Krebs Cycle Reaction (2)

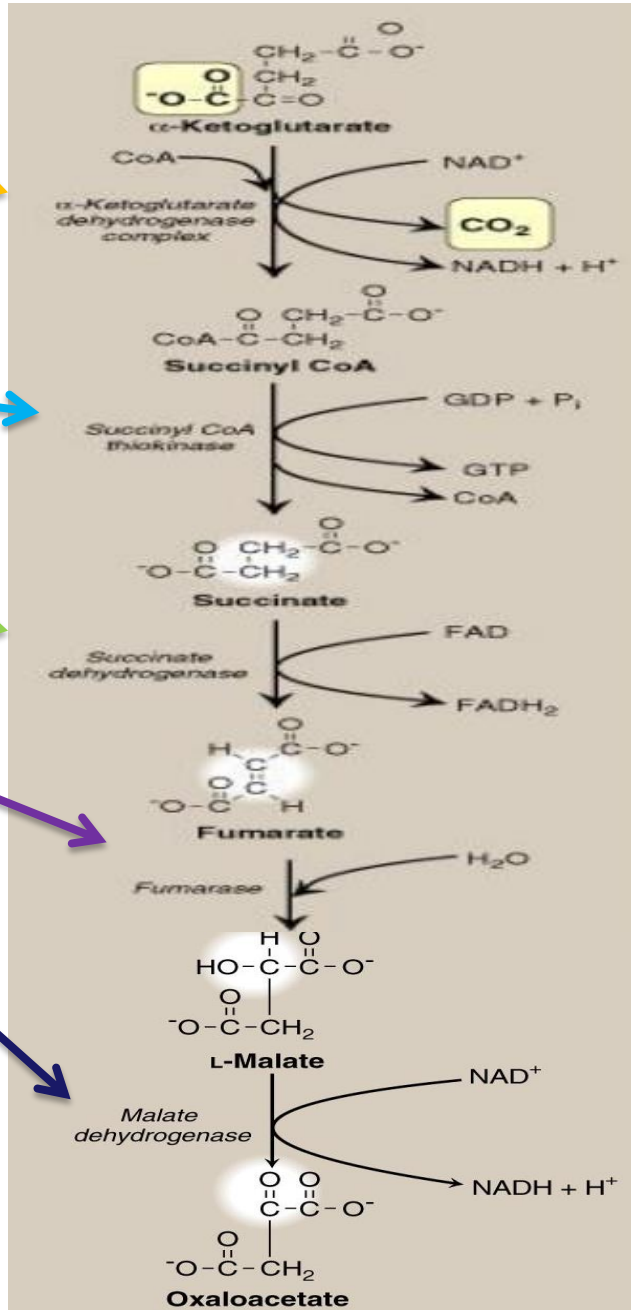
-Oxidation & decarboxylation of αKG to succinyl CoA(by αKG dehydrogenase complex). The reaction releases CO_2 and NADH.

-Cleavage of succinyl CoA into succinate (by succinate thiokinase). The reaction produces GTP (which can be converted to ATP). This is substrate-level phosphorylation > (NO need for o2 and/or mitochondria).

-Oxidation of succinate to fumarate (by succinate dehydrogenase). The reaction produces $FADH_2$

-Hydration of fumarate to L-malate (by fumarase)

- -Oxidation of L-malate to OAA by malate dehydrogenase.
- The reaction releases NADH.



Important:

1.When NADH is oxidized in the ETC → 3 ATP molecules, (this is oxidative phosphorylation).

2.which when FADH oxidized in the ETC → 2 ATP (this is oxidative phosphorylation).

3. In substrate-level phosphorylation NO need for o2 and/or mitochondria.. And we have only one reaction in krebs cycle can do it (which is the blue one)

4.Oxidative = dehydrogenation

5.Multiply by X2 at the end NOT now

didn't get it? Maybe this will help you..

Enzyme	Between who?	Action
Citrate synthase	Acetyl CoA+ Oxaloacetate and Citrate	-irreversible -Citrate inhibits PFK-1 (The rate limiting step in glycolysis)
Aconitase	Citrate and isocitrate	-Isomerization
Isocitrate dehydrogenase	Isocitrate and αKG	-Oxidation & decarboxylation -reaction releases CO_2 and NADH (this is oxidative phosphorylation)
αKG dehydrogenase complex (multiple enzymes)	αKG and succinyl CoA	-Oxidation & decarboxylation -reaction releases CO_2 and NADH (this is oxidative phosphorylation)
Succinate thiokinase	succinyl CoA and succinate	-Cleavage -The reaction produces GTP> ATP (substrate-level phosphorylation)
Succinate dehydrogenase	succinate and fumarate	-Oxidation -reaction produces $FADH_2$
Fumarase	Fumarate and L-malate	-Hydration.
Malate dehydrogenase	L-malate and OAA	-Oxidation -reaction releases NADH

Krebs Cycle: Energy yield

Energy-producing reaction	Number of ATP produced
3 NADH ⟶ 3 NAD^+	9
$FADH_2$ ⟶ FAD	2
GDP + P_i ⟶ GTP	1
	12 ATP/acetyl CoA oxidized

Oxidative phosphorylation

Substarte-level phosphorylation

Of 1 acetyl CoA = 12 ATP

Net ATP production by complete glucose oxidation:

Aerobic glycolysis = 8 ATP
Oxidative decarboxylation = 2 x 3 = 6 ATP

Krebs cycle: 2 x 12 = 24 ATP

Net = 38 ATP

Summary:

-Pyruvate is oxidatively decarboxylated by PDH to acetyl CoA inside the mitochondria

-glycolysis is both aerobic and anaerobic but krebs cycle is only aerobic

-Krebs cycle:

- -Final common pathway for the oxidation of carbohydrates, fatty acids and amino acids
- -occurs in the mitochondria
- -Aerobic
- -Mainly catabolic, with some anabolic reactions

-The complete oxidation of one glucose molecule results in a net production of 38 ATP molecules

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