Krebs Cycle
or
TCA Cycle

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History

Discovered by Hans Krebs in 1937

He received the Nobel Prize in physiology or medicine in 1953 for his discovery

Forced to leave Germany prior to WWII because he was Jewish

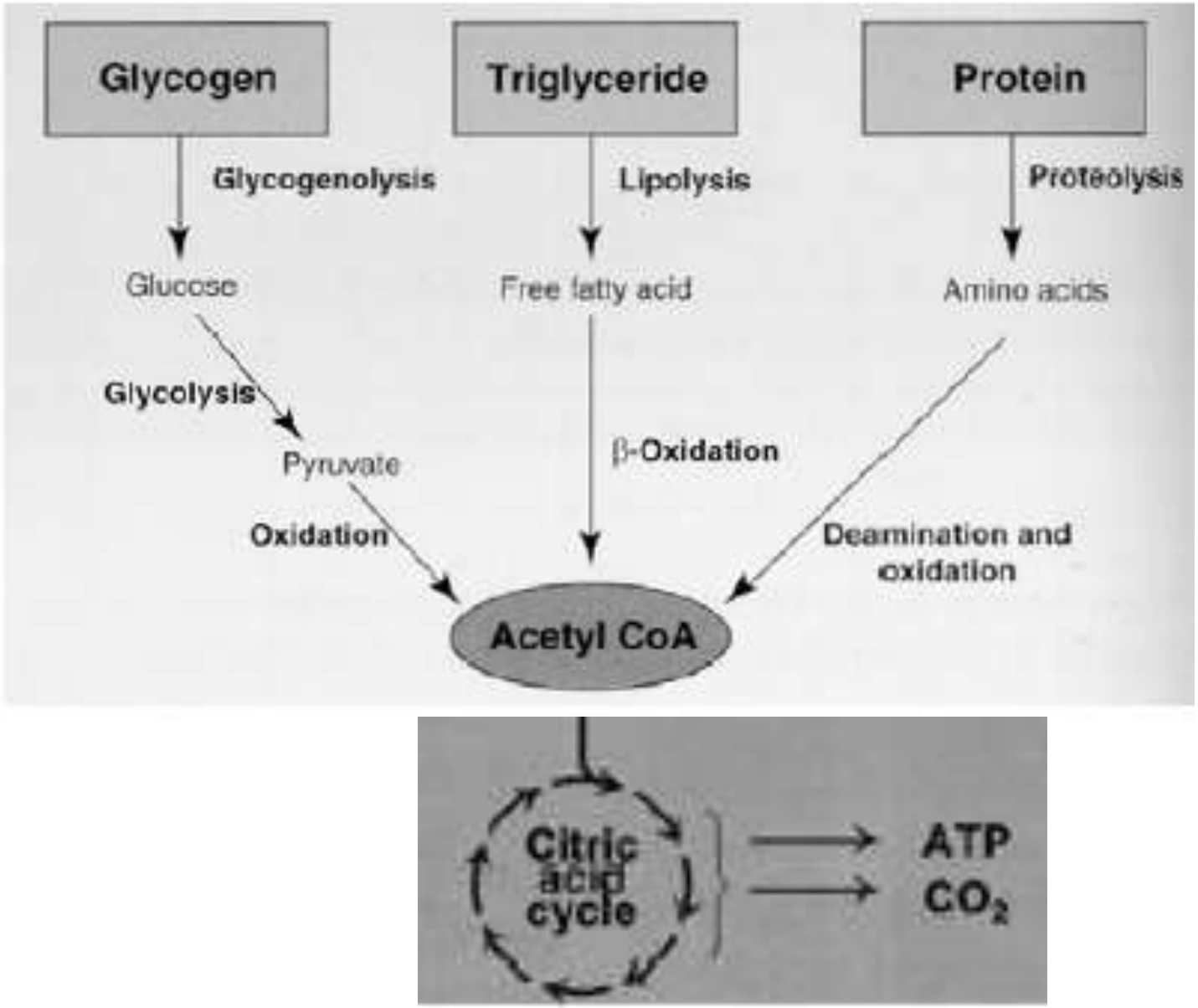
- Most of cells energy comes from oxidation of A.CoA in mitochondria

- Glycolysis oxidizes sugar to pyruvate which is converted to A.CoA in mitochondria

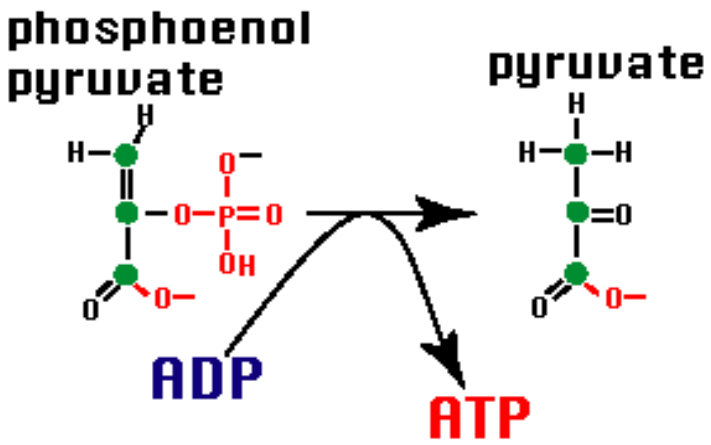
- Proteins and fatty acid are also broken down to yield A.CoA
- Acetyl units oxidized to CO2 in mitochondrial matrix by TCA cycle

- Energy released during oxidation captured by NAD+ and FAD

> Carried to ETC for synthesis of ATP (oxidative phosphorylation)

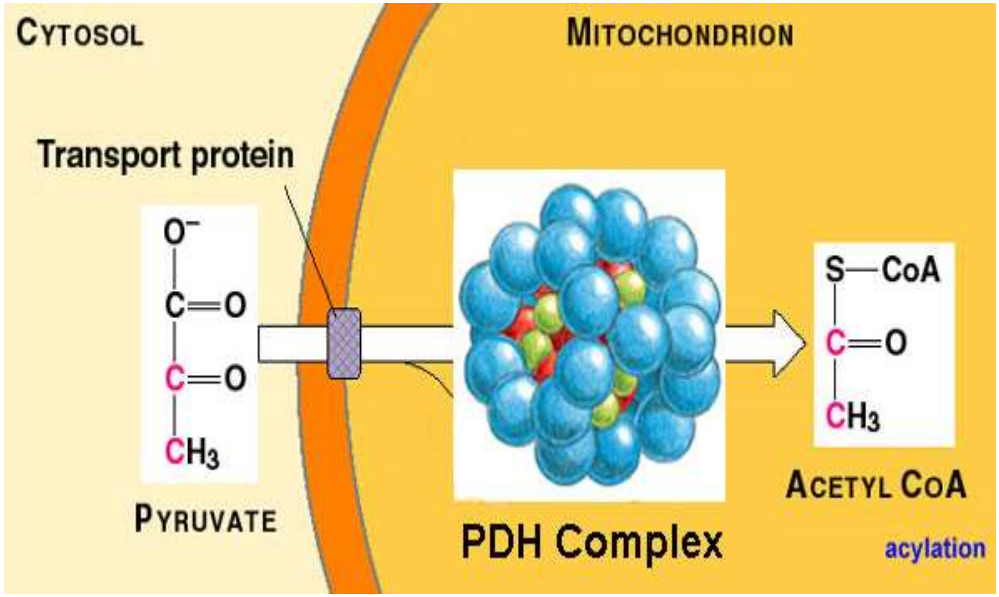

Glycogen
Triglyceride
Protein
Glycogenolysis
Lipolysis
Proteolysis
Glucose
Free fatty acid
Amino acids
Glycolysis
Pyruvate
β-Oxidation
Oxidation
Deamination and oxidation
Acetyl CoA
Citric acid cycle
ATP
CO_2

RXN 10 Glycolysis



Pyruvate produced from glycolysis must be decarboxylated to A. CoA before it enters TCA cycle

Catalyzed by large enzyme
-Pyruvate dehydrogenase complex (mitochondrial matrix)



$$\text{Pyruvate} + \text{CoA} + NAD^+ \longrightarrow \text{A. CoA} + CO_2 + NADH + H^+$$

Control of the Pyruvate Dehydrogenase complex

- Regulation by its products

  > NADH & Acetyl-CoA : inhibit

  While

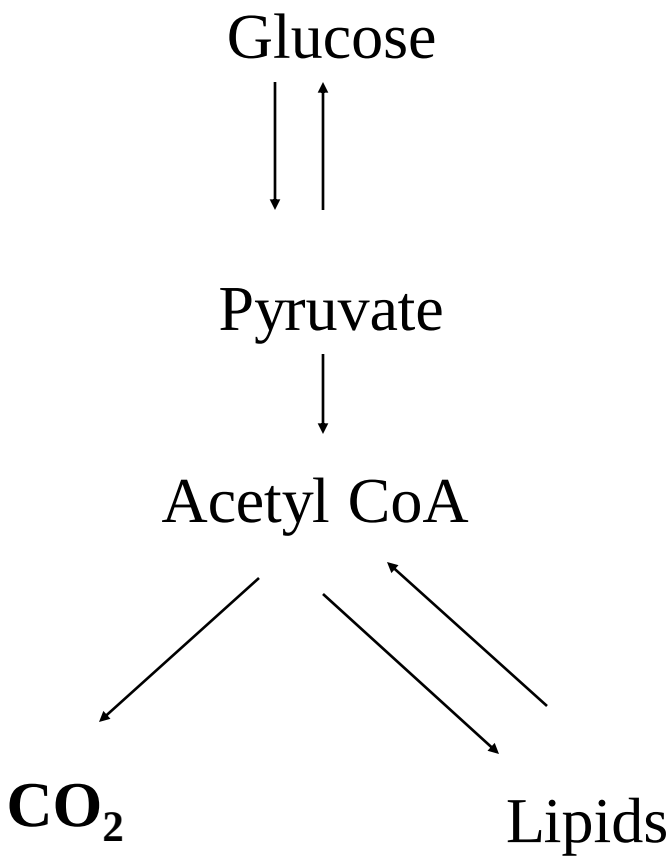
  >NAD^+ & CoA stimulate

- Regulation by energy charge

  > ATP : inhibit

  While

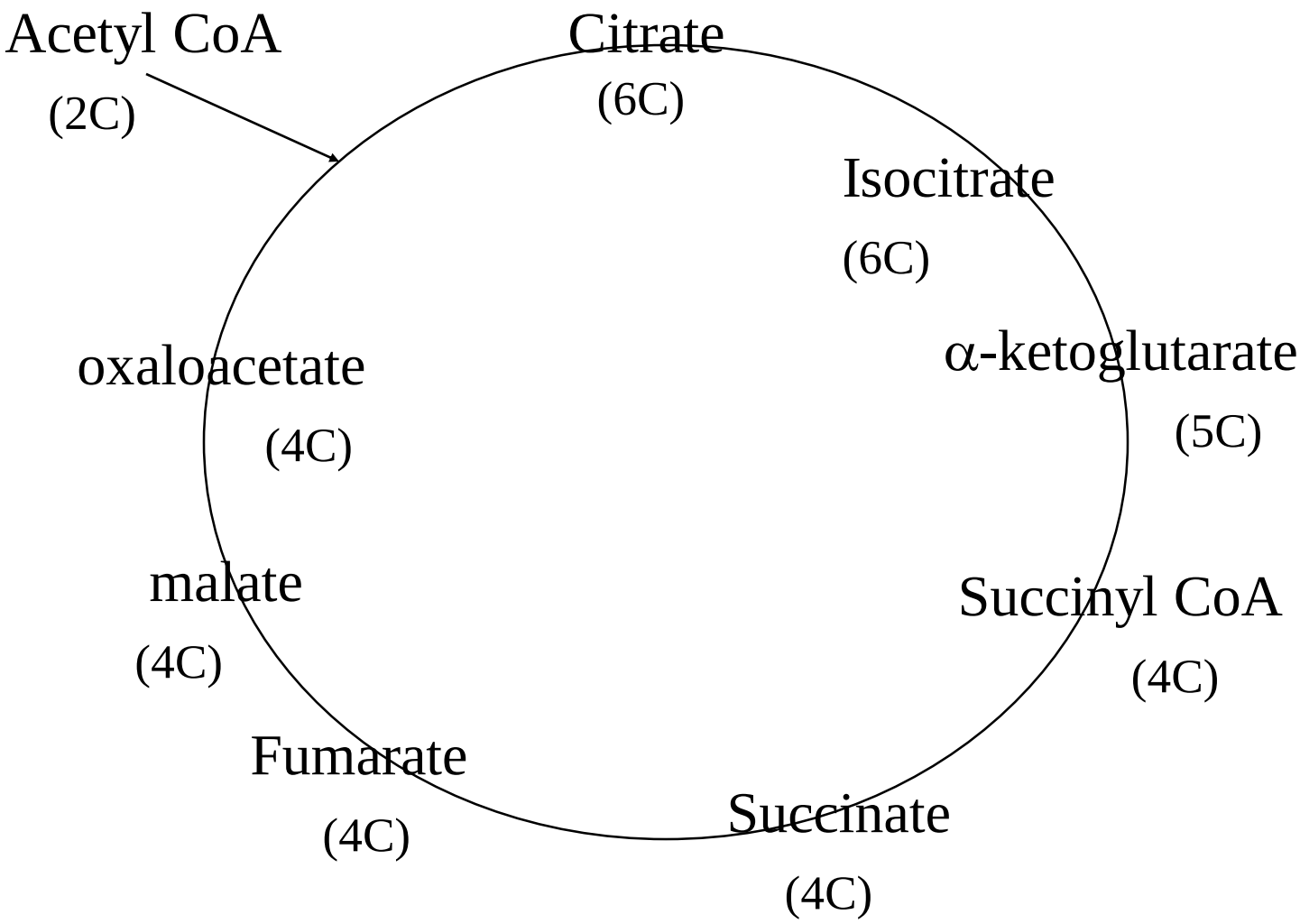
  > AMP : stimulate

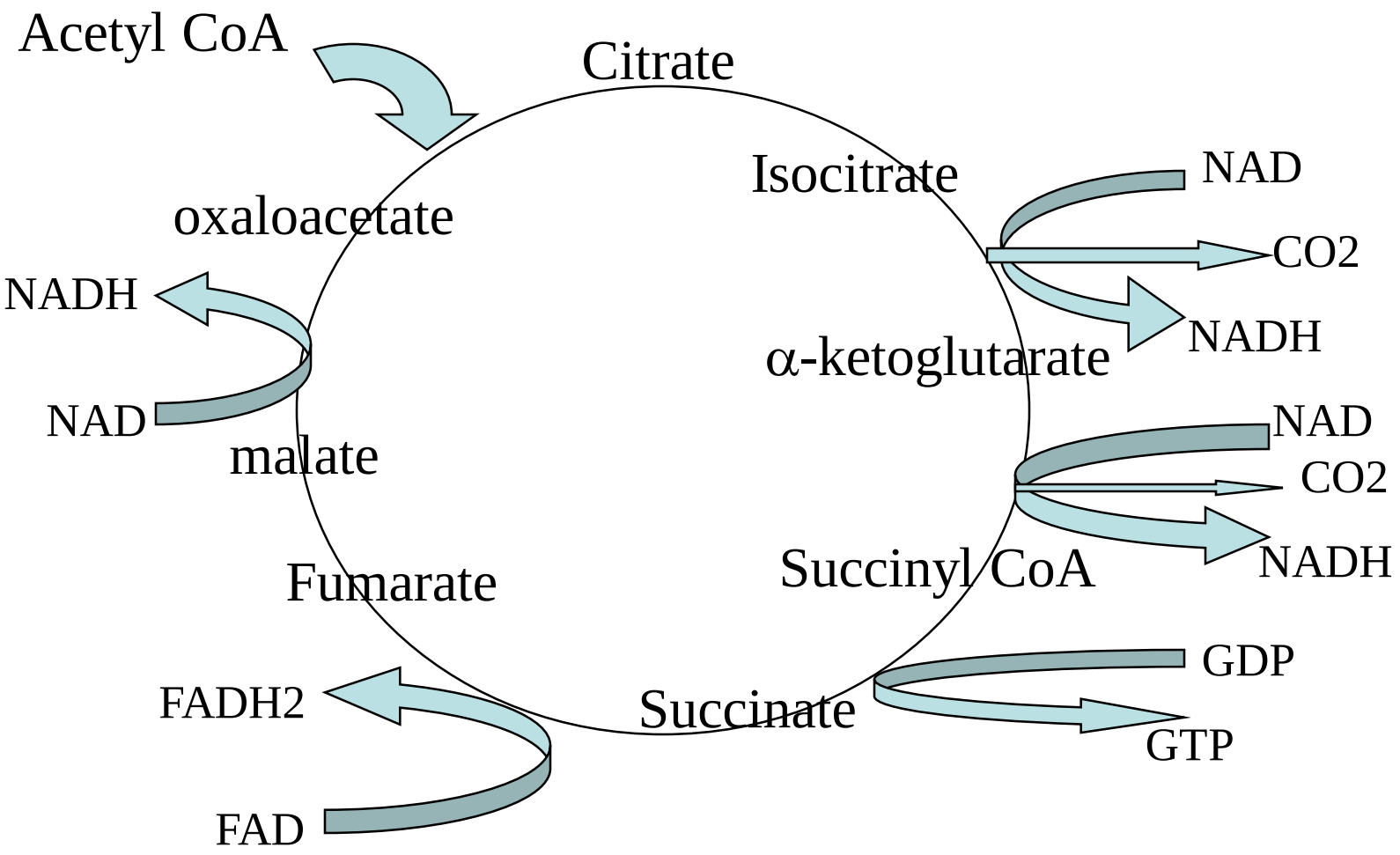

Glucose
Pyruvate
Acetyl CoA
CO_2
Lipids

Overall rxn

- Acetyl CoA + $3NAD^+$ + FAD + GDP + Pi + $2H_2O$

- $2CO_2$ + CoA + 3NADH + $FADH_2$ + GTP + H^+


Acetyl CoA
(2C)
Citrate
(6C)
Isocitrate
(6C)
α-ketoglutarate
(5C)
Succinyl CoA
(4C)
Succinate
(4C)
Fumarate
(4C)
malate
(4C)
oxaloacetate
(4C)

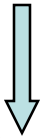

Acetyl CoA
Citrate
Isocitrate
NAD
CO2
NADH
α-ketoglutarate
NAD
CO2
NADH
Succinyl CoA
GDP
GTP
Succinate
FADH2
FAD
Fumarate
malate
NAD
NADH
oxaloacetate

Regulation of Citric Acid Cycle

- 3 Control sites

Regulation of Citric Acid Cycle con't
Site 1 - rxn 1

Acetyl CoA + Oxaloacetate



Citrate

- Enzyme: citrate synthase
- Inhibited by ATP

Regulation of Citric Acid Cycle con't
Site 2 - rxn 3

- Isocitrate ⟹ α-Ketoglutarate

- Enzyme: isocitrate dehydrogenase
- Inhibited by ATP & NADH
- Stimulated by ADP & NAD^+

Regulation of Citric Acid Cycle con't
Site 3 - rxn 4

- α-Ketoglutarate ⟹ Succinyl CoA

- Enzyme: α-Ketoglutarate dehydrogenase
- Similar to PDH complex
- Inhibited by Succinyl CoA & NADH also high-energy charge.

Regulation of Citric Acid Cycle Summary

- IN GENERAL THE TCA CYCLE IS INHIBITED BY A HIGH ENERGY CHARGE AND STIMULATED BY LOW ENERGY CHARGE

Overview

- Glycolysis produces pyruvate by oxidation of glucose
- The pyruvate is than oxidized to A.CoA in the mitochondria
- The acetly units are oxidized to CO2 by TCA cycle in the mitochondrial matrix
- Energy released during both the oxidation rxns are collected by NAD+ and FAD
- So NADH and FADH2 carry energy in the form of electrons

Where do all the NADH's and FADH2's Go