TCA Cycle

History

Discovered by Hans Krebs in 1937

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

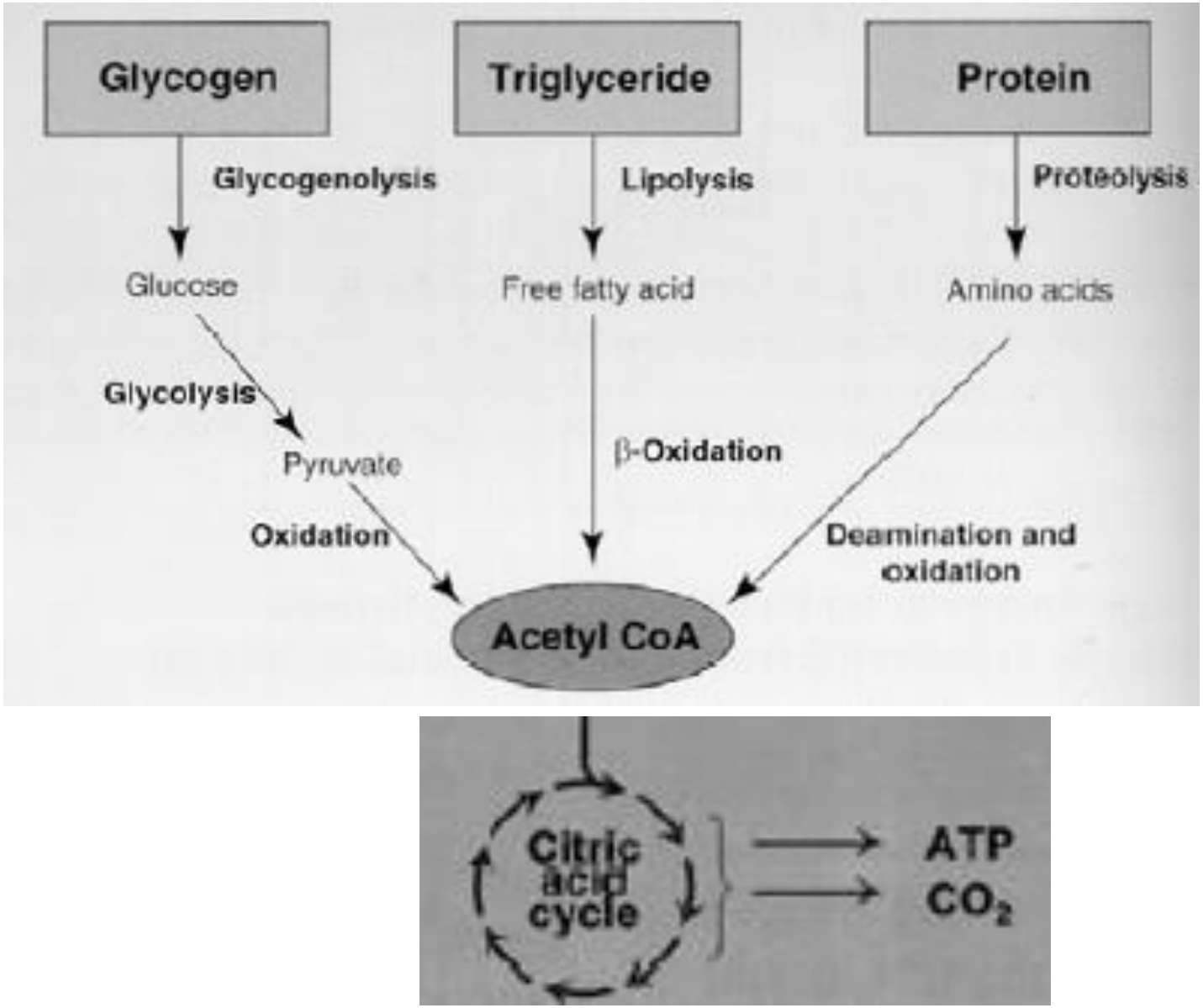
- Most of cells energy comes from oxidation of A.CoA in mitochondria

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

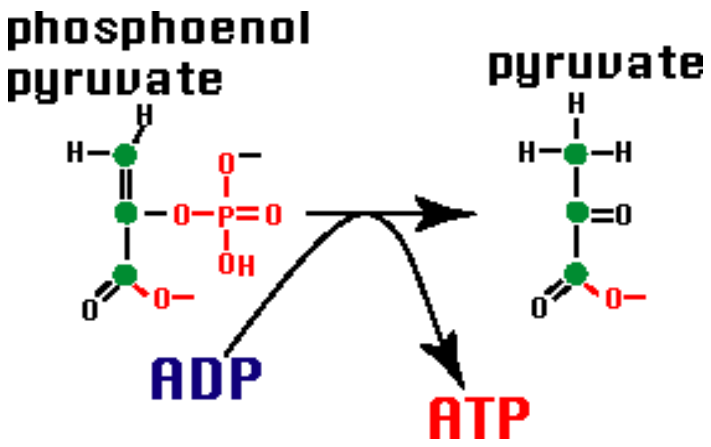
- Proteins and fatty acid are also broken down to yield A.CoA
- Acetyl units oxidized to CO2 in mitochondrial matrix by TCA cycle

- Energy released during oxidation captured by NAD+ and FAD

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

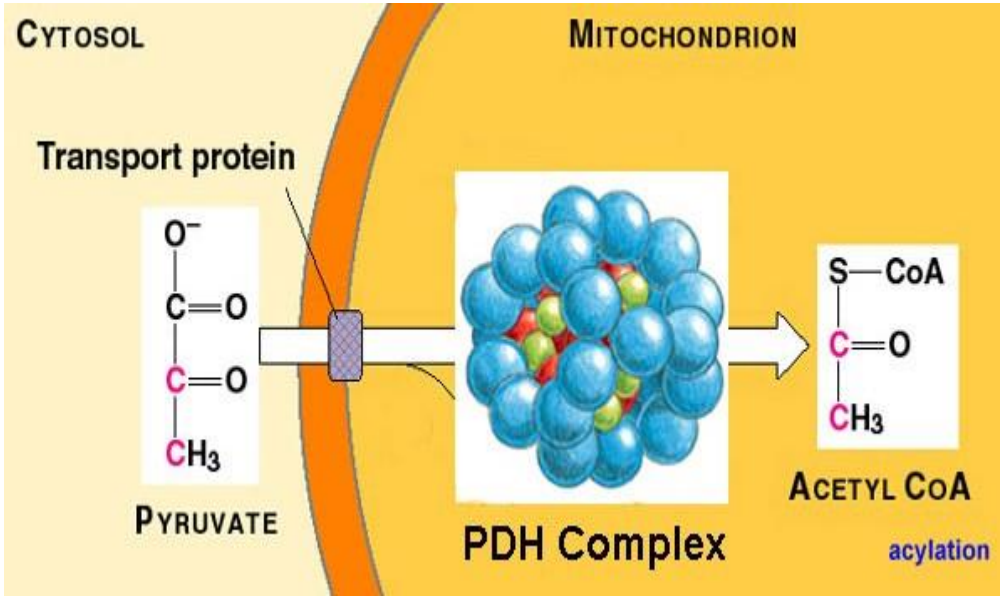

Glycogen
Triglyceride
Protein
Glycogenolysis
Lipolysis
Proteolysis
Glucose
Free fatty acid
Amino acids
Glycolysis
Pyruvate
β-Oxidation
Oxidation
Deamination and oxidation
Acetyl CoA
Citric acid cycle
ATP
CO_2

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

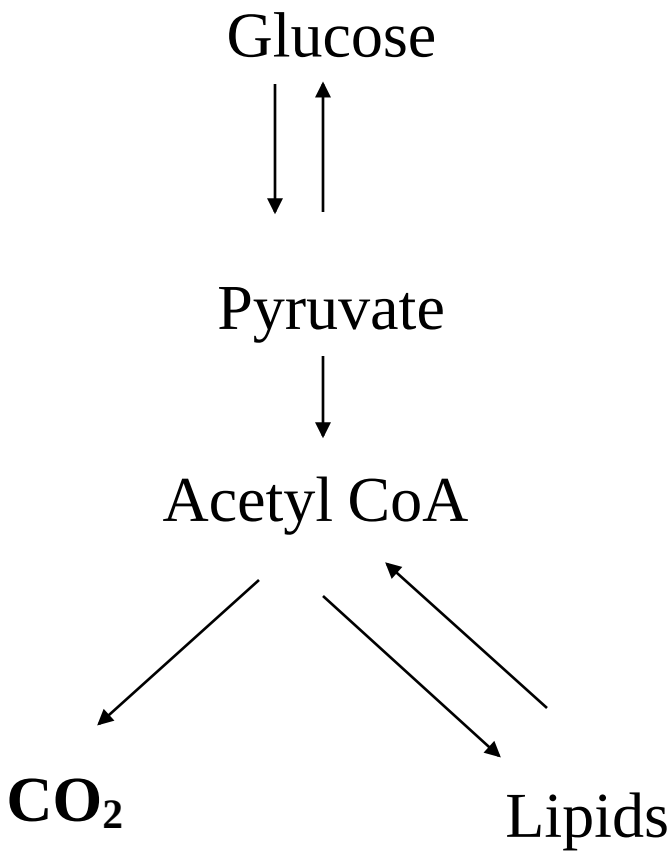
  >NAD^+ & CoA stimulate

- Regulation by energy charge

  > ATP : inhibit

  While

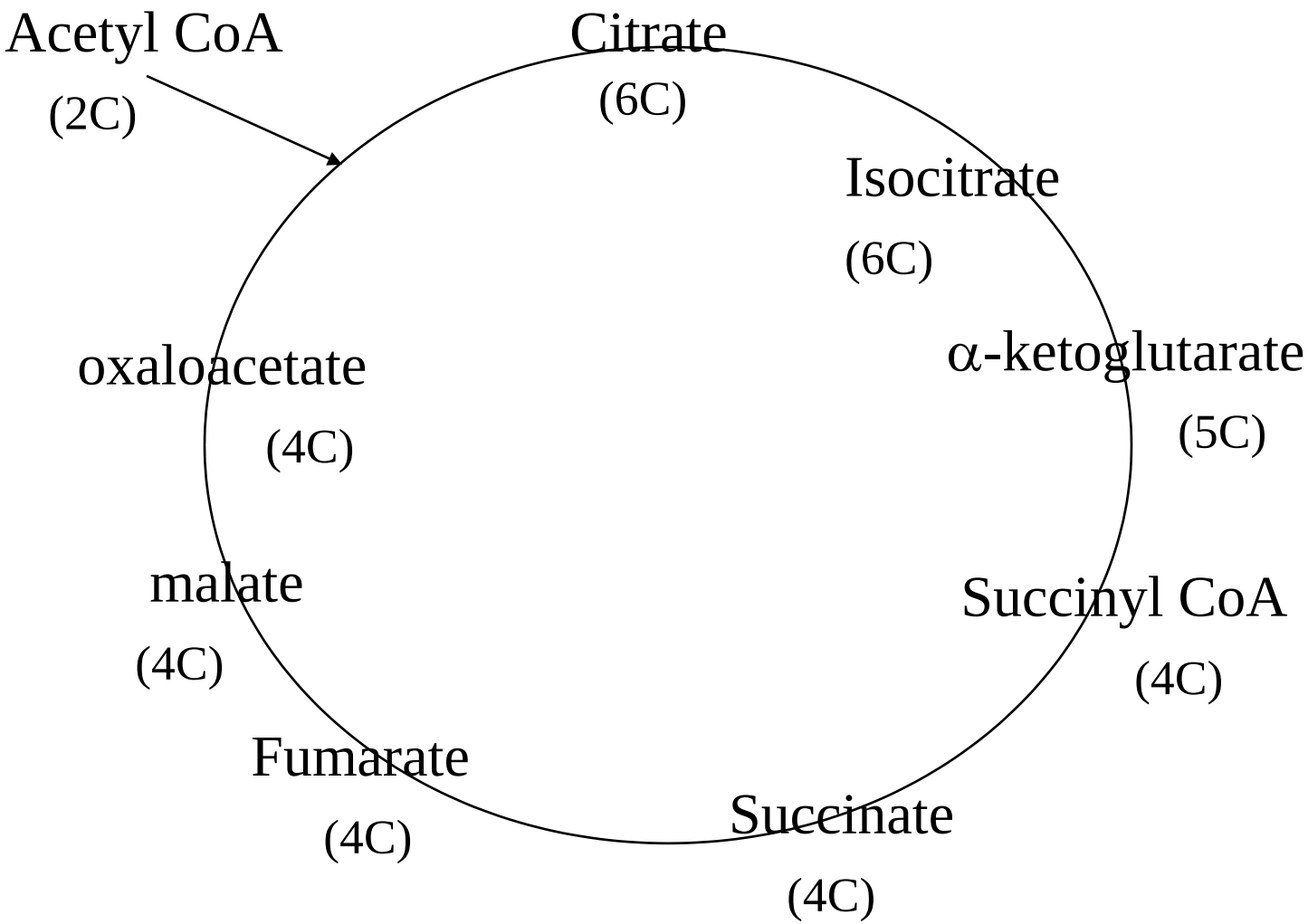
  > AMP: stimulate

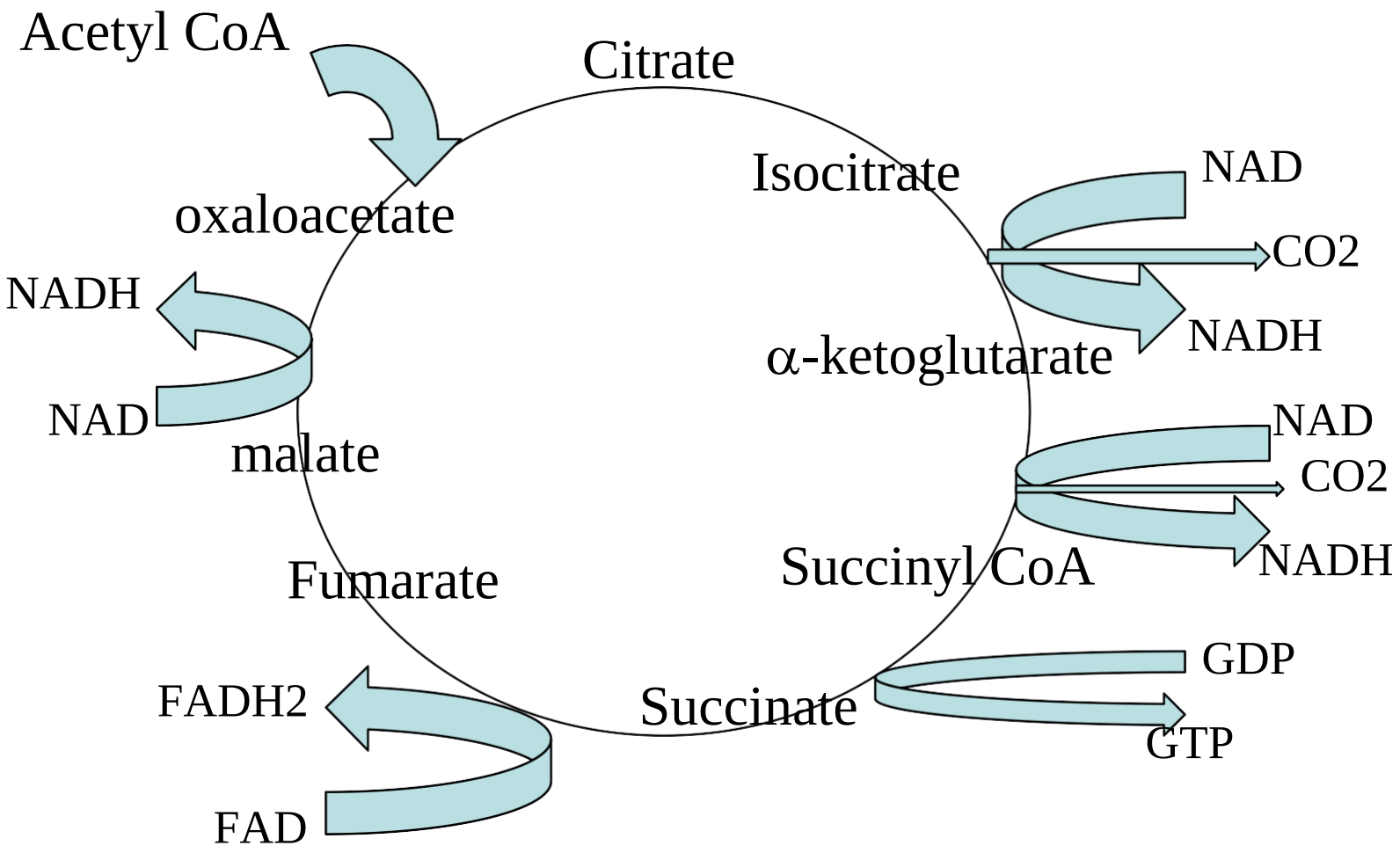

Glucose
Pyruvate
Acetyl CoA
CO2
Lipids

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)

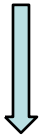

Acetyl CoA
Citrate
Isocitrate
NAD
CO2
NADH
α-ketoglutarate
NAD
CO2
NADH
Succinyl CoA
GDP
GTP
Succinate
FADH2
FAD
Fumarate
malate
NAD
NADH
oxaloacetate

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 ~~Succin~~yl 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
- S o NADH and FADH 2 carry energy in the form of electrons

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