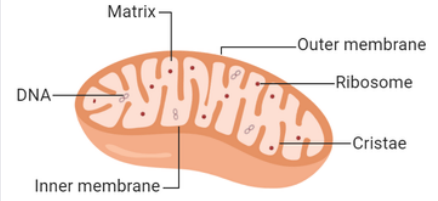
#10: Citric Acid Cycle

BIOCHEM2280

Mitochondrion

- 2 membranes
  - Outer → pores allow small molecules to cross
  - Inner → impermeable to small polar molecules → need channel/receptors for transport
    - Folded to increase surface arena for cristae (**lots of chemical reactions** occur in this area)
- Matrix - space enclosed by the inner membrane
  - Many soluble proteins
- 37 genes in mitochondrial genome
- IM can extend into middle of mitochondria, separated from the matrix by the inner membrane



Sourced from https://www.ahmadcoaching.com/2020/10/what-is-a-mitochondria-structure-function.html

Coenzyme A

- Pantothenic acid residue from vitamin B5
- A = adenosine (nucleotide)
- SH = thiol group
- Important for function, adds molecules via ester linkage
- Thiosester bond broken = energy released
- Therefore the group added is in its active form
- Fatty acids commonly joined

Cellular Respiration

- Pyruvate oxidized to CO_2
- O_2 reduced to H_2O
- ADP phosphorylated to ATP

2 Components: Decarboxylation of pyruvate + Citric Acid Cycle

Pyruvate Decarboxylation

- Pyruvate = made in the cytosol
- ⅓ of pyruvate carbon atoms are fully oxidized
  - e^- go to NAD^+ → make NADH
- ⅔ carbons added to coenzyme A → acetyl-coA formed
  - Acetate = 2 fatty acids
  - Coenzyme A removed acyl groups
- 2 CO_2 = 1 CoA per Acetyl-CoA

Overall Reaction:
Pyruvate + CoA + NAD^+ -(*pyruvate dehydrogenase*)→ Acetyl-CoA + CO_2 + NADH

Regulation of Pyruvate Dehydrogenase

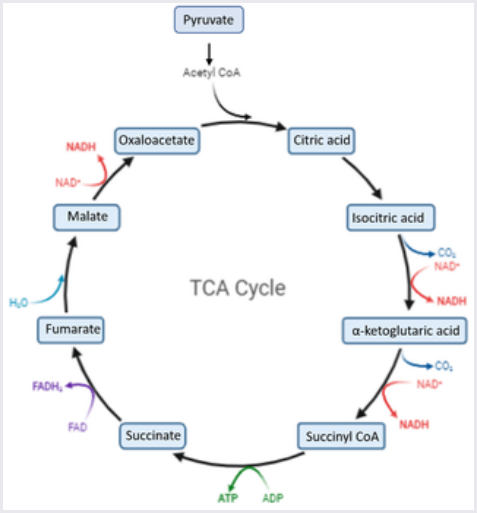
- Active form promoted by pyruvate + insulin
- Inactive form promoted by acetyl-coA + NADH
  - Competitive inhibitors, compete with CoA and NAD^+

Enzyme Activity
Pyruvate dehydrogenase = active
Pyruvate dehydrogenase-Ⓟ = inactive

Citric Acid Cycle

- Unidirectional Process
- Carbon oxidized → CO_2
- e^- transferred, make NADH
- Last 3 reactions are oxidation (e^- removed from carbon)
- 3 irreversible reactions makes the cycle unidirectional
- 4 pairs of e^- lost from carbon
- 3 NADH, 1 QH_2 → 4 e^- carriers made
- 1 GTP → GDP + Pi
- 2 CO_2

Overall Reaction:
Acetyl-CoA + 3 NAD^+ + Q + GDP + P → 2 CO_2 (waste) + CoA (recycled) + 3 NADH (e^- transport, must generate NAD^+ and Q) + QH, + GTP (becomes ATP, useable energy)



Sourced from https://www.purposegames.com/game/citric-acid-cyclekrebs-cycle-enzyme-quiz

Regulation of Citric Acid Cycle

- Availability of substrate
- Competitive inhibition by products
- Allosteric regulation
  - e.g. increased ADP = low energy = activate cycle
  - Increased NADH, succinyl-CoA = slow down cycle

Precursors for Synthesis

- Biosynthetic pathways and intermediates are used as raw material to make a variety of biological molecules
  - Citrate → Fatty acids, cholesterol
  - Oxaloacetate → Glucose
  - Malate → Pyruvate
  - Alpha-Ketoglutarate → Amino acids, nucleotides
  - Succinyl-CoA → Heme

Proteins as an Energy Source

- Proteins can be degraded to make ATP
  - Providing energy is **NOT** their major function
  - Nitrogen atoms discarded as urea during amino acid catabolism
    - Pyruvate, amino acids → Oxaloacetate
    - Amino acids → Fumarate
    - Amino acids, odd-chain fatty acids → Succinyl-CoA
    - Amino acids → Alpha-ketoglutarate
- Some intermediates are used to synthesize amino acids
- Requires acetyl-CoA to be directed away from energy metabolism
- ATP obtained is **lower** than the theoretical maximum

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-The WebStraw team

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Note: Marvin was used for drawing, displaying and characterizing chemical structures, substructures and reactions, Marvin 24.4.1, Chemaxon (https://www.chemaxon.com)

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