Pyruvate Dehydrogenase Complex

**Pyruvate Dehydrogenase (PDH)**

**Overall Reaction:**

\[ \text{Pyruvate} + \text{NAD}^+ + \text{HS-CoA} \xrightarrow{\text{irreversible}} \text{Acetyl-CoA} + \text{NADH} + \text{CO}_2 \]

\[ \Delta G^\circ = -33.5 \text{ kJ/mol} \]

TCA cycle

Fatty Acid Biosynthesis

\(*\)

*This is why you will get fat if you eat sugar*
Note that the electrons in this bond came from glucose ... you should be able to find them and track them to NADH and then to oxygen – Follow the green arrows

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Irreversible reaction

TCA cycle

Fatty Acid Biosynthesis

Also …. Note similarity to the Pyruvate Decarboxylase (PDC) reaction JoAnne taught … in that reaction, the HO-ethyl-TPP is released as acetaldehyde … look at her notes
Pyruvate Dehydrogenase
I need you to think about
The electron flow (as well as
The carbon flow)

Note: Pyruvate moves from the cytoplasm to the mitochondrial matrix
In prokaryotes, this occurs in the cytoplasm, probably near the plasma membrane

Vitamin B1 (Thiamine)

Amino-pyrimididine activates red hydrogen … lowers pKa of thiazole proton … to about 18
Role of pyrimidine base in ylid formation: no GBC from protein in the vicinity of the thiazolium proton
From JoAnne’s Notes

Imine

Predominant form

Ylid

Steric clash

fast
Pyruvate Dehydrogenase (PDH)

- **Lipoic Acid**
  - "HO-C-C-N+R'" (E1)
  - "S-S" (E2)
- **Acetyl-CoA**
  - "CoA-S-C-CH3" (E2)
- **Actetyl-dihydrolipamide-E2**
  - "O-C-C-CH3" (E2)
  - "SH" (E2)
- **Reducing Equivalents**
  - "HS-HS" (E2)
  - "TPP" (E2, E3)
  - "SH" (E2, E3)
  - "FAD" (E3)

The diagram illustrates the steps of the PDH cycle, showing the conversion of pyruvate to acetyl-CoA and the role of lipoic acid and CoA in this process. The cycle involves multiple enzymes (E1, E2, E3) and coenzymes (TPP, FAD) to facilitate the transfer of electrons and the formation of acetyl-CoA.
Pyruvate Dehydrogenase (PDH)

Cys 43 and Cys 48 on the E3 subunit

reducing equivalents

HS

TPP

E1 E2 E3

FAD

E1 E2 E3

SH

TPP

E1 E2 E3

FAD

regenerated cofactor

NAD^+ + H^+

NADH