

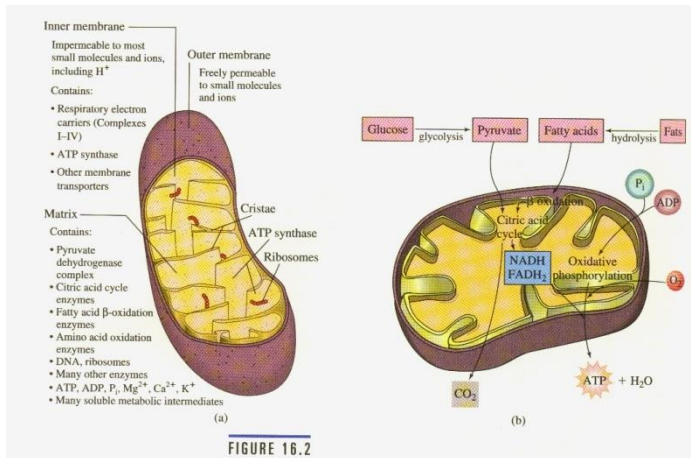
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Dr.M.S.MANJUNATH
ASSISTANT PROFESSOR AND HEAD
JSS COLLEGE OF ARTS, COMMERCE AND SCIENCE
OOTY ROAD, MYSORE

PYRUVATE DEHYDROGENASE COMPLEX

- The pyruvate dehydrogenase complex and the citric acid cycle enzymes exist in the matrix of the **mitochondrion** in eukaryotes
- Pyruvate is generated by glycolysis in the cytosol and needs to be moved into the mitochondria

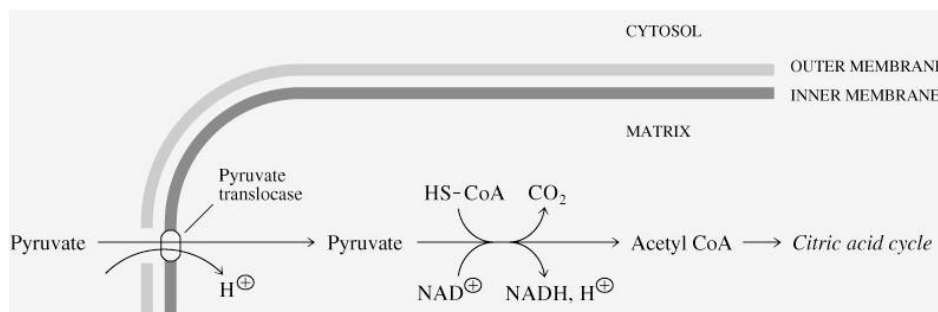
MITOCHONDRIAL STRUCTURE



- Mitochondria have a **TWO** membrane system

- **Outer Membrane:** Permeable to small molecules
- **Inner Membrane:** NOT permeable – Has specific integral membrane protein transporters
- Region between the two membranes = intermembrane space
- Inner membrane is highly folded and forms boundary to fluid filled interior = **MATRIX**
 - Matrix has a “gel-like” consistency
 - Contains the proteins of the TCA cycle
- Other proteins responsible for further aerobic metabolism are either in the matrix or are bound to the inner membrane

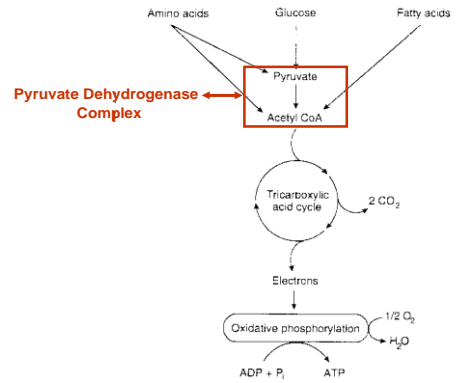
Pyruvate generated in Cytosol enters the Mitochondrion (Aerobic fate of Pyruvate)



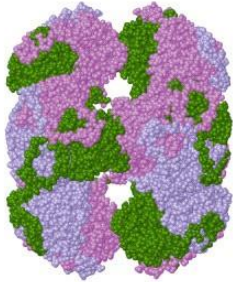
- Diffuses through the outer membrane
- **Pyruvate translocase** transports pyruvate **into** the mitochondria in **symport** with **H+**
 - Integral membrane protein in inner membrane

CONVERSION OF PYRUVATE TO ACETYL COA

The pyruvate dehydrogenase complex LINKS GLYCOLYSIS TO THE TCA CYCLE! - also occurs in mitochondria



(a)



- Pyruvate dehydrogenase complex (PDH complex) is a multienzyme complex containing:
 - 3 enzymes + 5 coenzymes + other proteins
 - (+ ATP coenzyme as a regulator)

E1 = pyruvate dehydrogenase

E2 = dihydrolipoamide acetyltransferase

E3 = dihydrolipoamide dehydrogenase

(b)

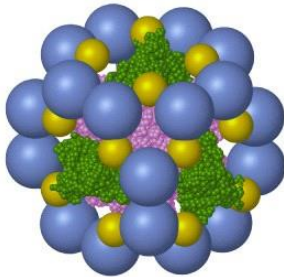


Table 16.1

Enzymes and coenzymes of the pyruvate dehydrogenase complex

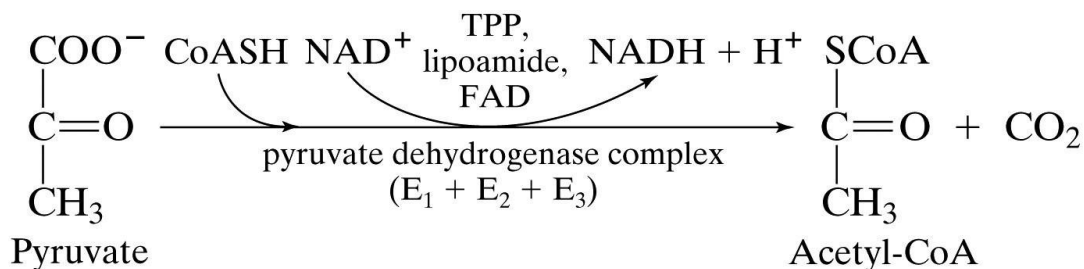
Enzyme	Abbreviation	Coenzyme
Pyruvate dehydrogenase	E ₁	Thiamine pyrophosphate (TPP)
Dihydrolipoyl transacetylase	E ₂	Lipoamide, coenzyme A (CoASH)
Dihydrolipoyl dehydrogenase	E ₃	Flavin adenine dinucleotide (FAD), nicotinamide adenine dinucleotide (NAD ⁺)

Table 16-1 Concepts in Biochemistry, 3/e
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Structure of the pyruvate dehydrogenase (PDH) complex

Overall reaction of pyruvate dehydrogenase complex

- Multienzyme Complex (36 subunits!)
- pyruvate + CoASH + NAD⁺ → acetyl-CoA + CO₂ + NADH + H⁺



Unnumbered figure pg 487 Concepts in Biochemistry, 3/e
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Roles of the coenzymes of the PDH complex

- TPP (thymine pyrophosphate)

- Active form of **thiamine**
 - **Vitamin B1**
 - Beans, green vegetables, sweet corn, egg yolk, liver, corn meal, brown rice
 - **Deficiency = beriberi**
- TPP often used for **decarboxylation** reactions

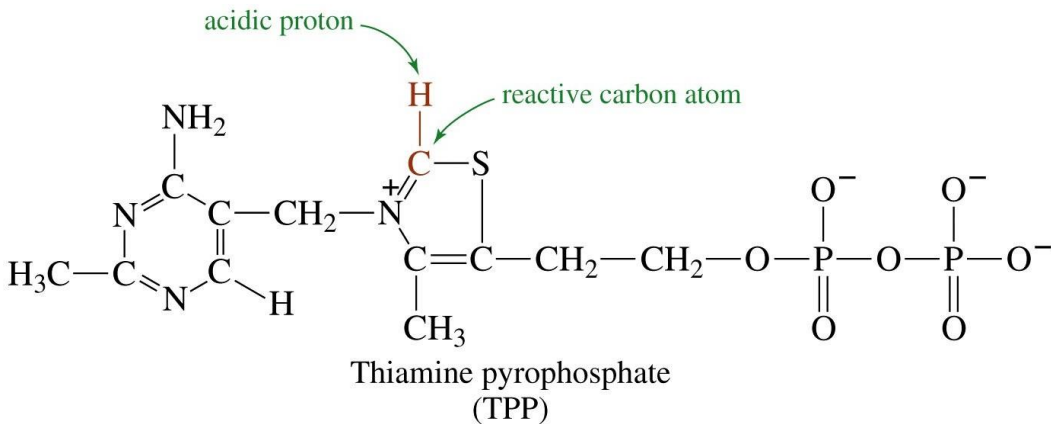


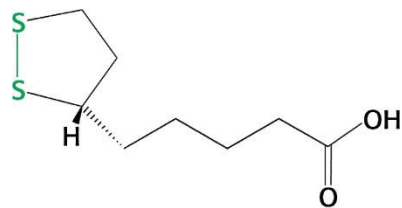
Figure 16-4 Concepts in Biochemistry, 3/e
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- Lipoic Acid

- Acetyl transfer and oxidation reactions

- FAD and NAD+

- Oxidizing agent/electron acceptors € Get reduced (will be later reoxidized)



Lipoic acid

- Coenzyme A (CoA-SH)

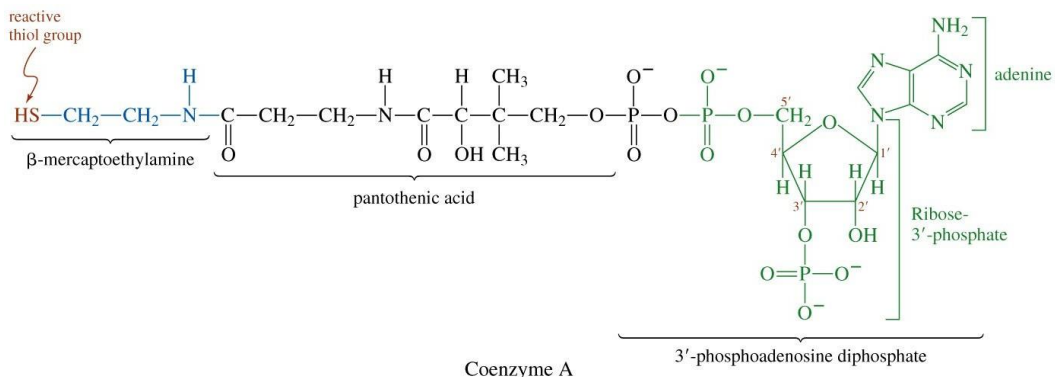
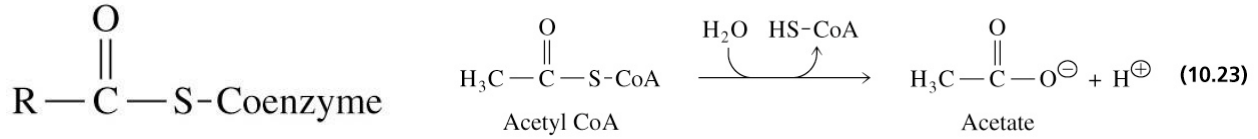


Figure 16-6 Concepts in Biochemistry, 3/e
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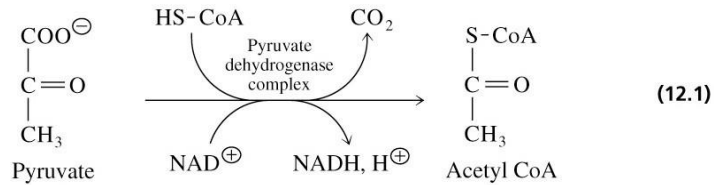
- Synthesized from the vitamin pantothenic acid
- Has a free thiol (-SH) group

- Coenzyme A has a free thiol group (CoASH) that can form **thioesters** which are **energy-rich compounds** (high free energies of hydrolysis - $\Delta G^{\circ} = -31 \text{ kJ/mol}$)
 - Energizes molecules
 - Makes more unstable and more prone to react and release energy



Thioester linkage
(joins thiol with carboxylic acid)

SUMMARY:



- Net reaction is **SIMPLE** – Process in **COMPLEX!**
- Pyruvate is now activated ready to enter the TCA cycle as Acetyl-CoA!