PYRUVATE DEHYDROGENASE COMPLEX

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

MITOCHONDRIAL STRUCTURE

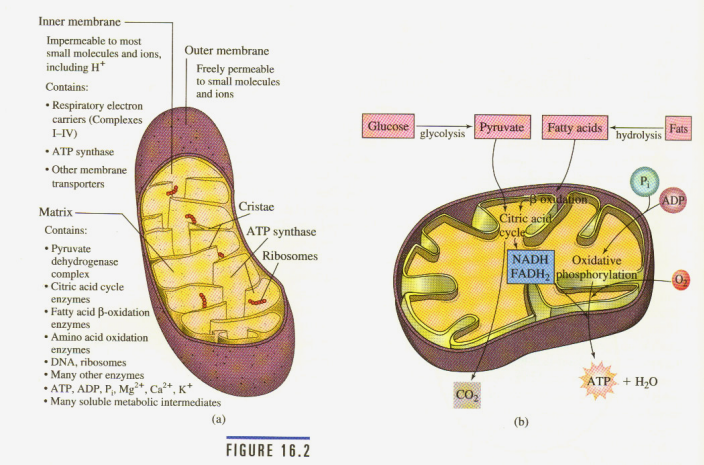
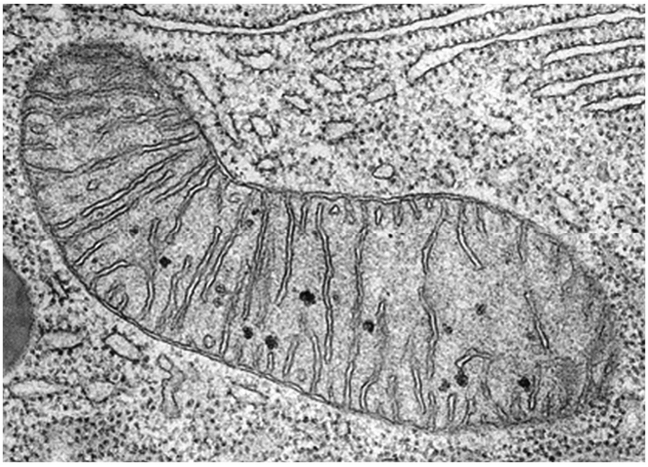
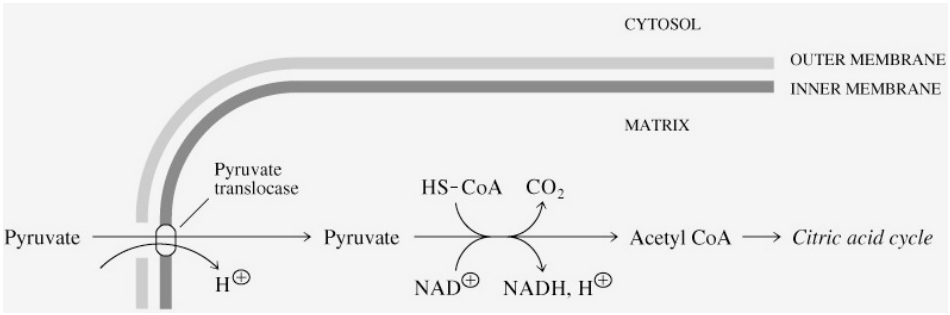


FIGURE 16.2



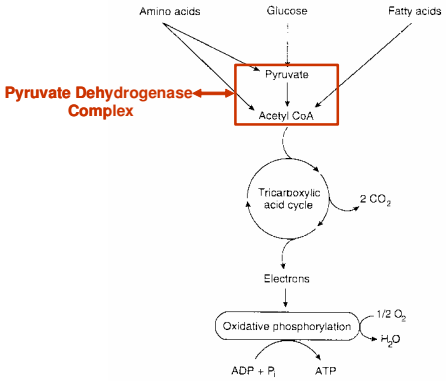
- Mitochondria have a **TWO** membrane system
  - **Outer Membrane:** Permeable to small molecules
  - **Inner Membrane:** NOT permeable – Has specific integral membrane protein transporters
  - Region between the two membranes = intermembrane space
  - Inner membrane is highly folded and forms boundary 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)



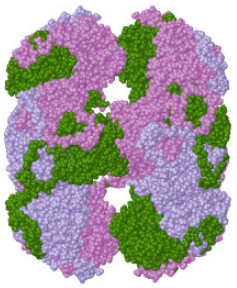
- Diffuses through the outer membrane
- **Pyruvate translocase** transports pyruvate **into** the mitochondria in **symport** with **H+**
  - Integral membrane protein in inner membrane

CONVERSION OF PYRUVATE TO ACETYL COA



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

(a)



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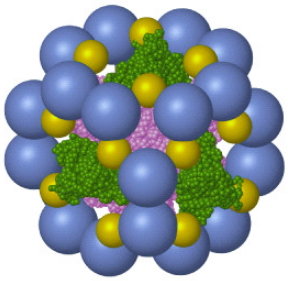


Structure of the pyruvate dehydrogenase (PDH) complex

- **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

Table 16.1

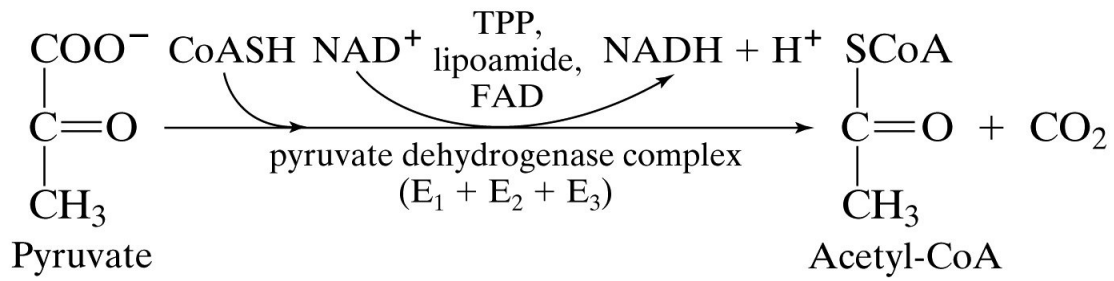
Enzymes and coenzymes of the pyruvate dehydrogenase complex

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

Overall reaction of pyruvate dehydrogenase complex

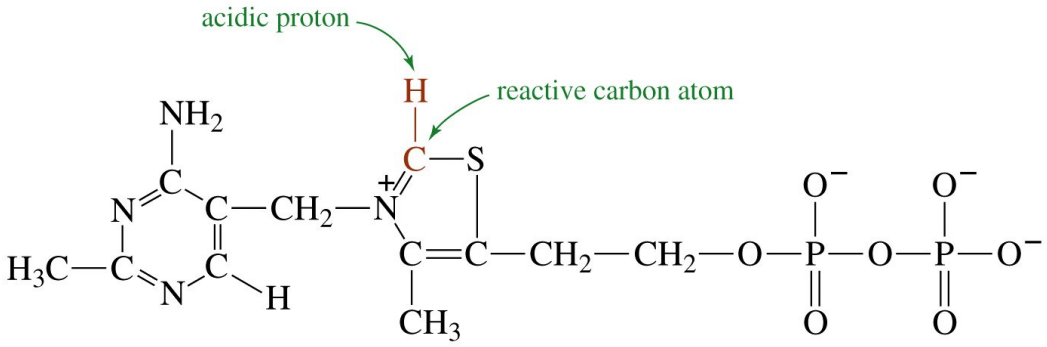
- **Multienzyme Complex (36 subunits!)**
- pyruvate + CoASH + NAD+ → acetyl-CoA + CO2 + NADH + H+



Unnumbered figure pg 487 Concepts in Biochemistry, 3/e

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



Thiamine pyrophosphate (TPP)

Figure 16-4 Concepts in Biochemistry, 3/e
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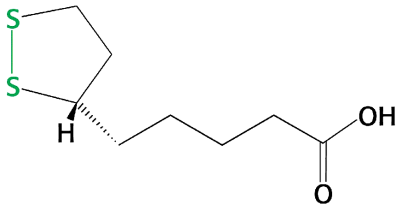
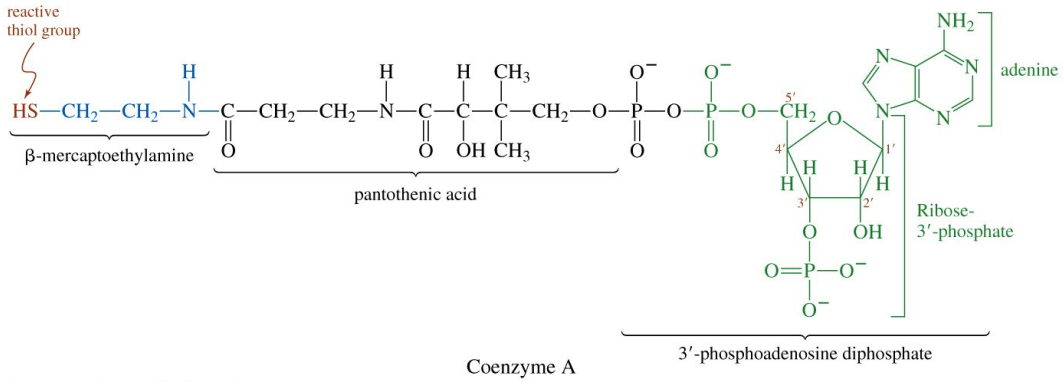
- **Lipoic Acid**
  - Acetyl transfer and oxidation reactions



Lipoic acid

- **FAD and NAD+**
  - Oxidizing agent/electron acceptors → Get reduced (will be later reoxidized)

- **Coenzyme A (CoA-SH)**



Coenzyme A

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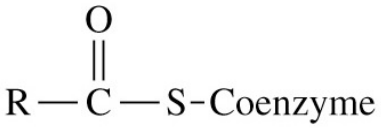
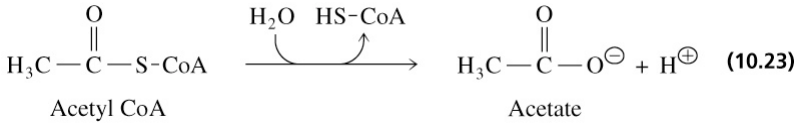
  - Synthesized from the vitamin pantothenic acid
  - Has a free thiol (-SH) group

- Coenzyme A has a free thiol group (CoASH) that can form **thioesters** which are **energy-rich compounds** (high free energies of hydrolysis **- ΔG°'** = -31 kJ/mol
    - Energizes molecules
    - Makes more unstable and more prone to react and release energy

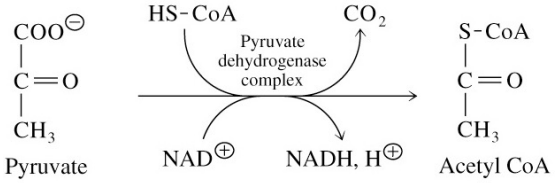




(10.23)

Thioester linkage
(joins thiol with carboxylic acid)

SUMMARY:



(12.1)

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