

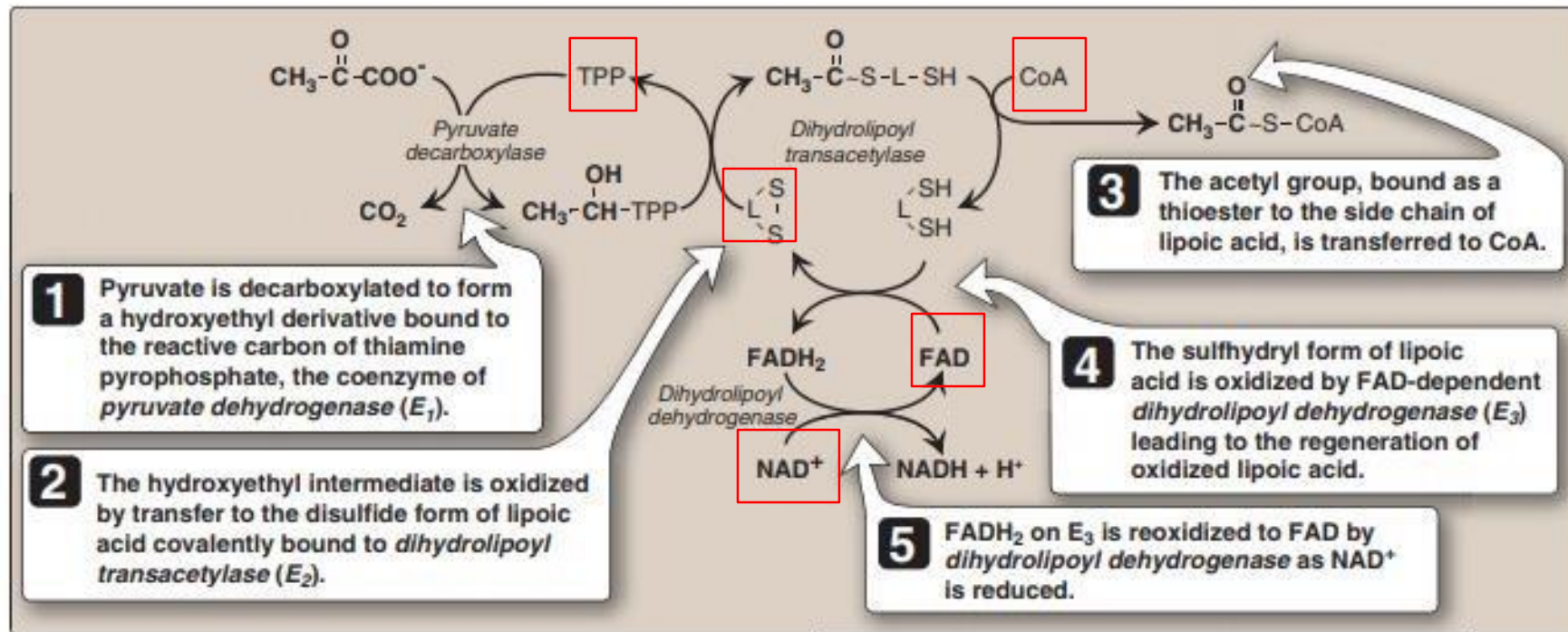
After Glycolysis: From Pyruvate to Acetyl-CoA

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From Pyruvate to Acetyl-CoA

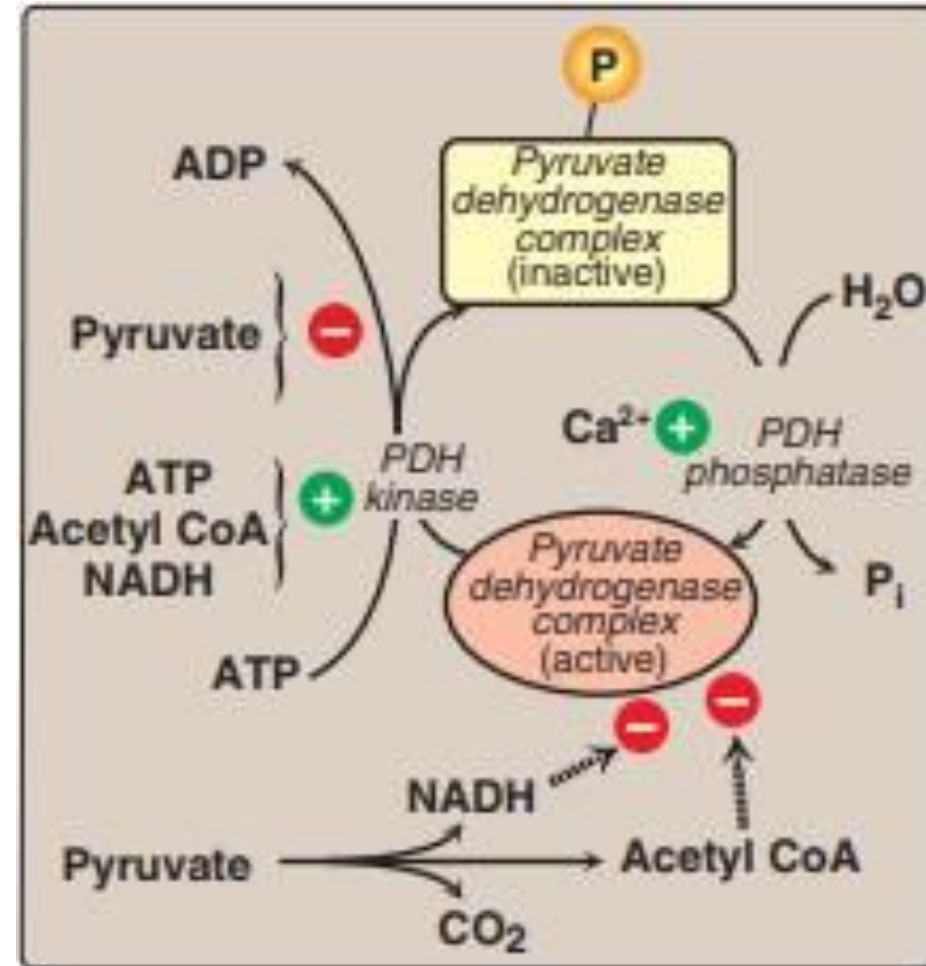
Oxidative decarboxylation of pyruvate

- ✓ Pyruvate is produced in the cytosol and needs to be transported to the mitochondria by a specific pyruvate transporter
- ✓ Once in the matrix, pyruvate is converted to acetyl CoA by the pyruvate dehydrogenase (PDH) complex, which is a multienzyme complex made of 3 enzymes, E1 (decarboxylase), dihydrolipoyl transacetylase (E2), and dihydrolipoyl dehydrogenase (E3).



Regulation of PDH Complex

- ✓ The complex also contains two tightly bound regulatory enzymes, PDH kinase and PDH phosphatase



Clinical Application: PDH deficiency

- Component enzymes
- Coenzymes
- Regulation of the pyruvate dehydrogenase complex
 - Pyruvate dehydrogenase deficiency: A deficiency in E₁ component is the most common biochemical cause of congenital lactic acidosis (X-linked, no treatment)
- Affected tissues: brain, relies on the TCA cycle for most of its energy, and is sensitive to acidosis.
- Symptoms are variable and include neurodegeneration, muscle spasticity and, in the neonatal onset form, early death.
- Dietary restriction of carbohydrate and supplementation with TPP may reduce symptoms in select patients.
- Mechanism of arsenic poisoning**

