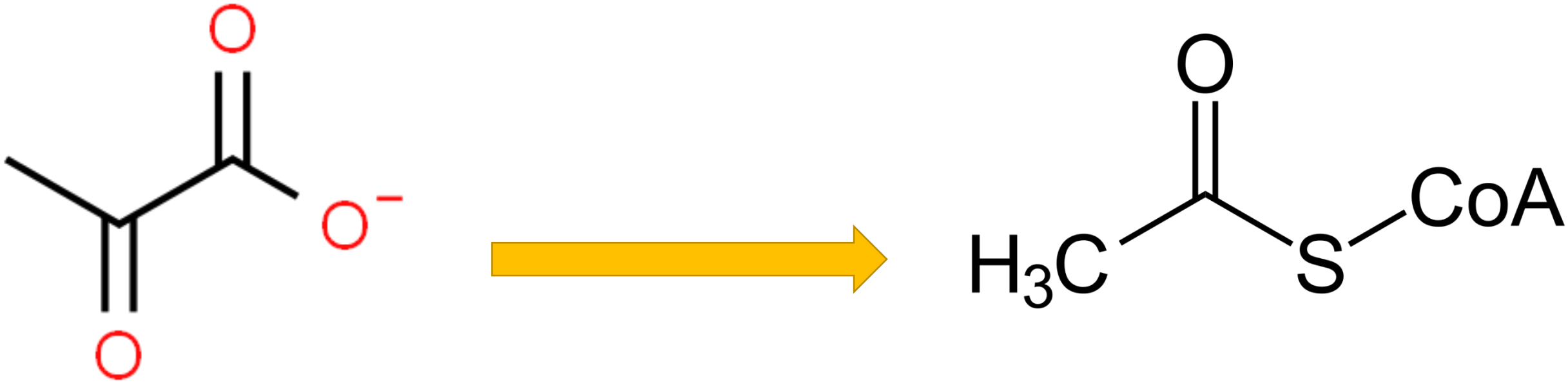


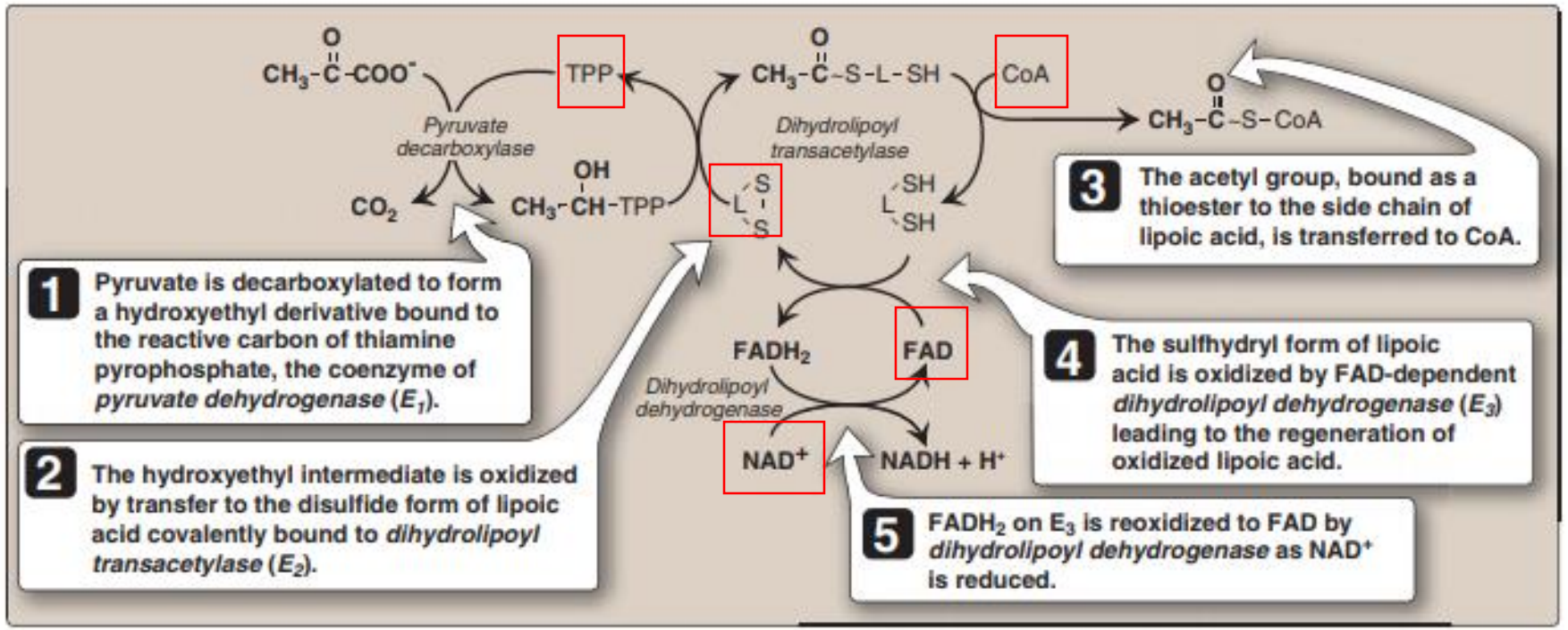
After Glycolysis: From Pyruvate to Acetyl-CoA

Dr. Diala Abu-Hassan, DDS, PhD

From Pyruvate to Acetyl-CoA

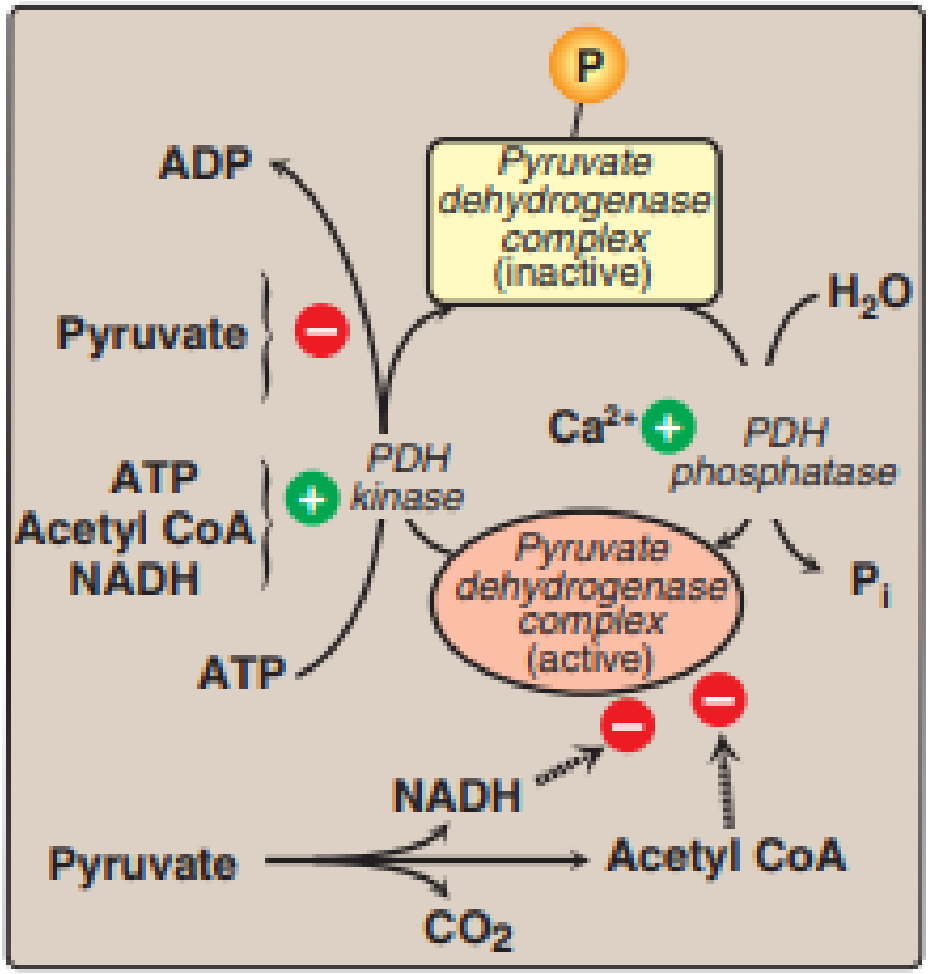
Oxidative decarboxylation of pyruvate

- ✓ 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

- ✓ Rare deficiency in the E1 component of the PDH complex
- ✓ However, the most common biochemical cause of congenital lactic acidosis.
- ✓ This enzyme deficiency results in an inability to convert pyruvate to acetyl CoA, causing pyruvate to be shunted to lactic acid via lactate dehydrogenase
- ✓ Affected tissues: brain, relies on the TCA cycle for most of its energy, and is particularly sensitive to acidosis.
- ✓ Symptoms are variable and include neurodegeneration, muscle spasticity and, in the neonatal onset form, early death.
- ✓ X-linked dominant
- ✓ No proven treatment
- ✓ Dietary restriction of carbohydrate and supplementation with TPP may reduce symptoms in select patients.