Reductive TCA Pathway

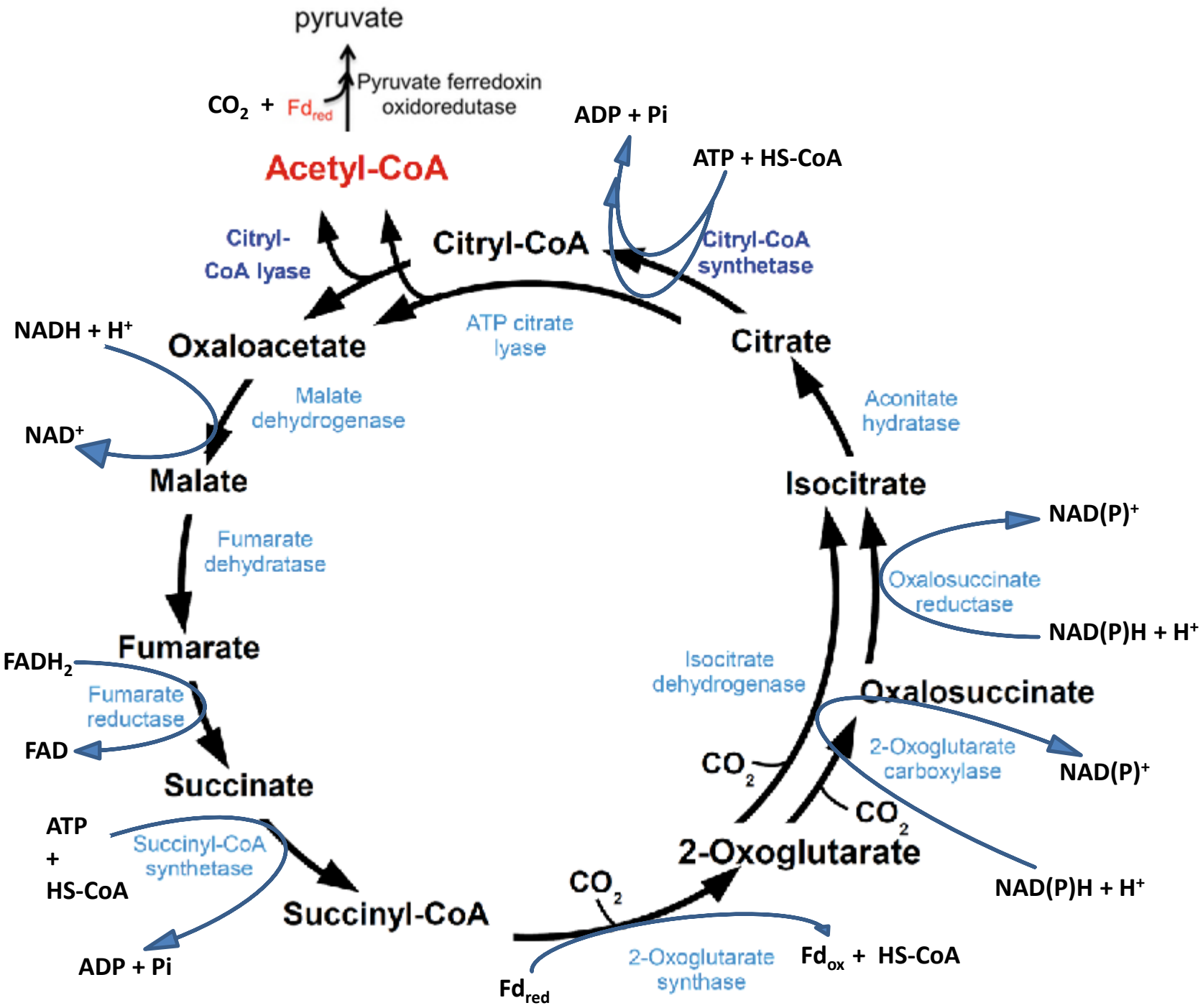
-Dr. Ekta Khare
Department of Microbiology
Institute of Biosciences & Biotechnology,
CSJM University, Kanpur

Reductive TCA Pathway

- The reductive TCA cycle appears to operate in phylogenetically diverse autotrophic bacteria and archaea, including:
  - genera of anoxic phototrophic bacteria (*Chlorobium*),
  - sulfate-reducing bacteria (*Desulfobacter*),
  - microaerophilic, hyperthermophilic hydrogen-oxidizing bacteria (*Aquifex* and *Hydrogenobacter*),
  - Sulfur reducing *Crenarchaeota* (*Thermoproteus* and *Pyrobaculum*)
- The reductive TCA cycle is essentially the oxidative TCA cycle running in reverse, leading to the fixation of two molecules of CO_2 and the production of one molecule of acetyl-CoA.
- Acetyl-CoA is reductively carboxylated to pyruvate, from which all other central metabolites can be formed.

r-TCA Enzymes

- Most of the enzymes of the two pathways are shared, with the exception of three key enzymes that allow the cycle to run in reverse:
  - ATP citrate lyase,
  - 2-oxoglutarate:ferredoxin oxidoreductase (2-oxoglytarate synthase/ α-ketoglutarate synthase),
  - fumarate reductase.
- 2-Oxoglutarate: ferredoxin oxidoreductase catalyzes the carboxylation of succinyl-CoA to 2-oxoglutarate (α-ketoglutatate),
- ATP citrate lyase the ATP-dependent cleavage of citrate to acetyl-CoA and oxaloacetate,
- Fumarate reductase the reduction of fumarate forming succinate


pyruvate
Pyruvate ferredoxin oxidoredutase
CO_2 + Fd_{red}
Acetyl-CoA
ADP + Pi
ATP + HS-CoA
Citryl-CoA lyase
Citryl-CoA
Citryl-CoA synthetase
ATP citrate lyase
NADH + H^+
Oxaloacetate
Citrate
Malate dehydrogenase
NAD^+
Aconitate hydratase
Malate
Isocitrate
Fumarate dehydratase
$NAD(P)^+$
Oxalosuccinate reductase
$NAD(P)H + H^+$
Fumarate
$FADH_2$
Isocitrate dehydrogenase
Oxalosuccinate
Fumarate reductase
FAD
2-Oxoglutarate carboxylase
$NAD(P)^+$
CO_2
CO_2
Succinate
ATP + HS-CoA
Succinyl-CoA synthetase
2-Oxoglutarate
$NAD(P)H + H^+$
CO_2
Succinyl-CoA
ADP + Pi
2-Oxoglutarate synthase
Fd_{ox} + HS-CoA
Fd_{red}