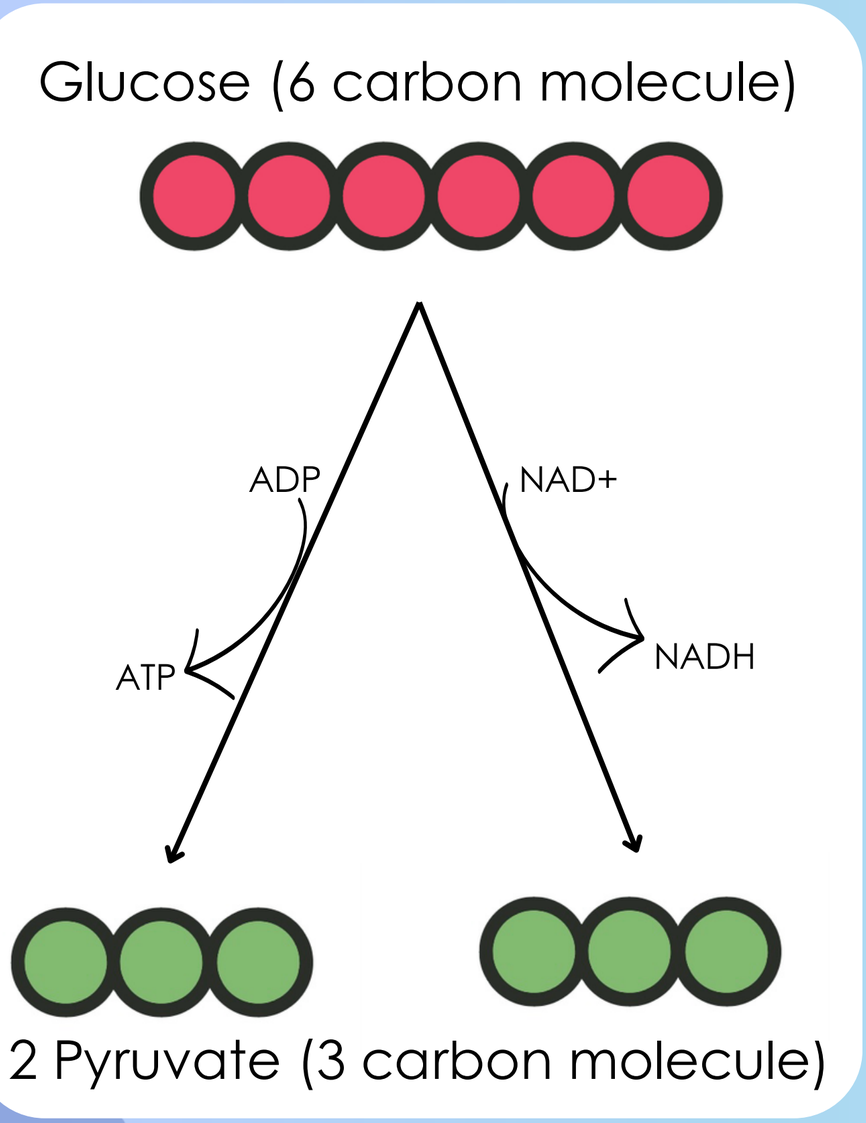
TCA Cycle & Oxidative Phosphorylation

By Sarah Cullen

Glucose is converted into Pyruvate



Glucose is converted from a 6 carbon fragment to a 3 carbon fragment named **pyruvate**

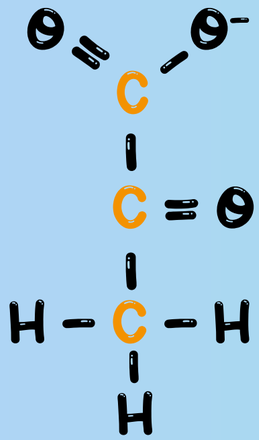
1 glucose = 2 pyruvate

2 NADH and 2 ATP are generated as a result

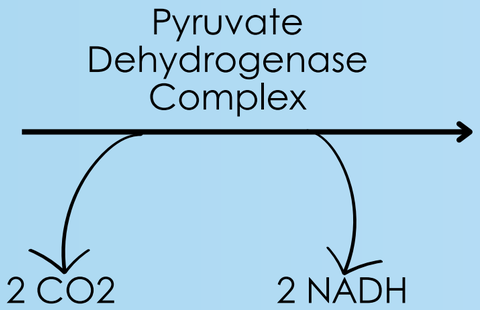
Pyruvate is then carried into the mitochondria if oxygen is present, where it enters a transition stage

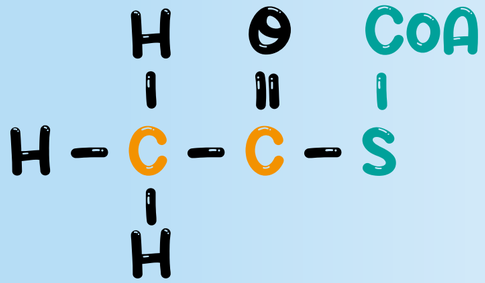
Acetyl-CoA

CoA is added to pyruvate, forming a 2 carbon molecule, Acetyl CoA through a p
rocess called decarboxylation



Pyruvate



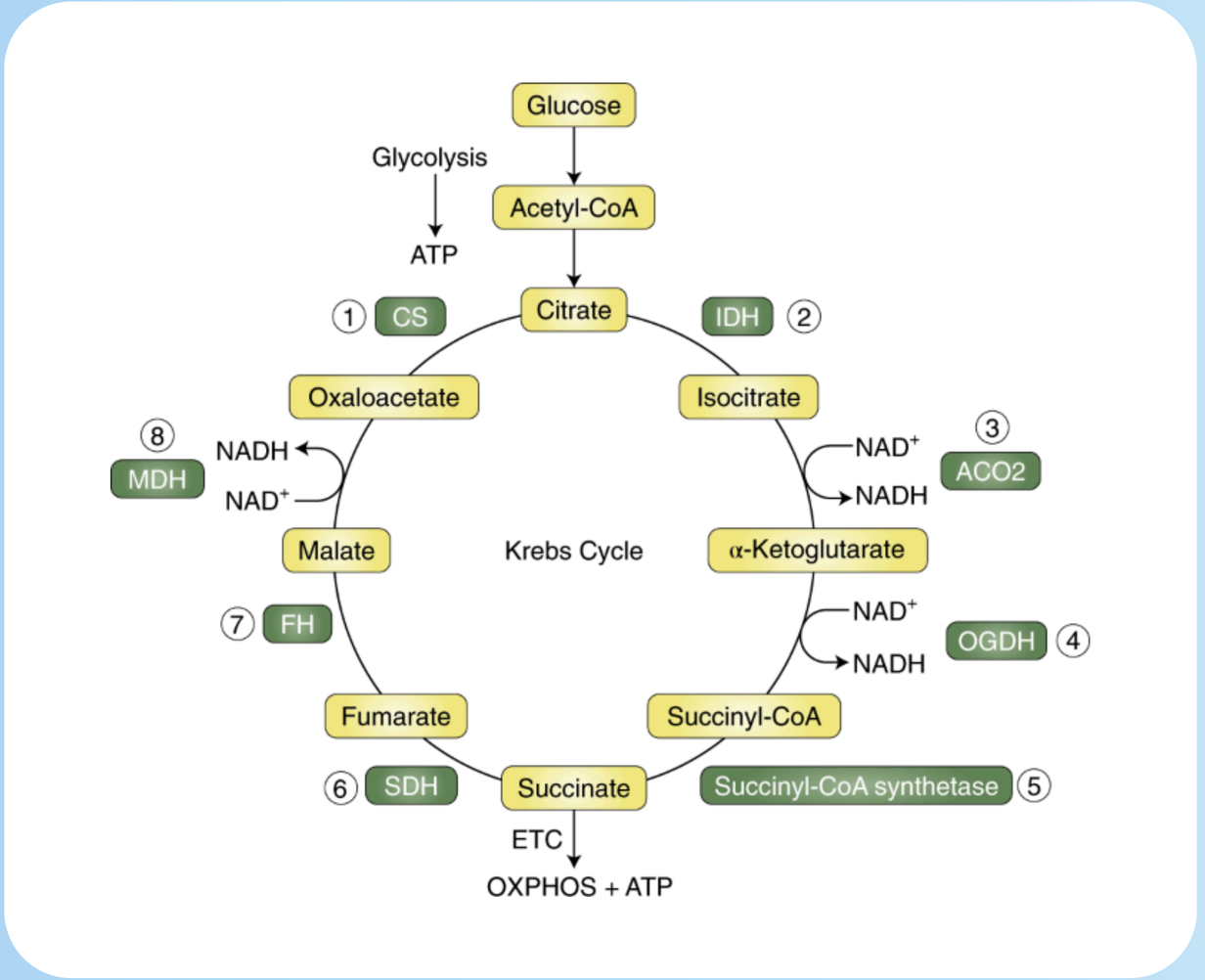


Acetyl-CoA

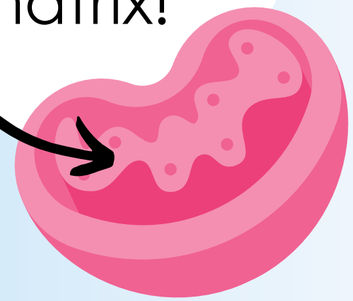
Generates:

2 CO2
2 NADH

TCA (Krebs cycle)



Takes place within mitochondrial matrix!



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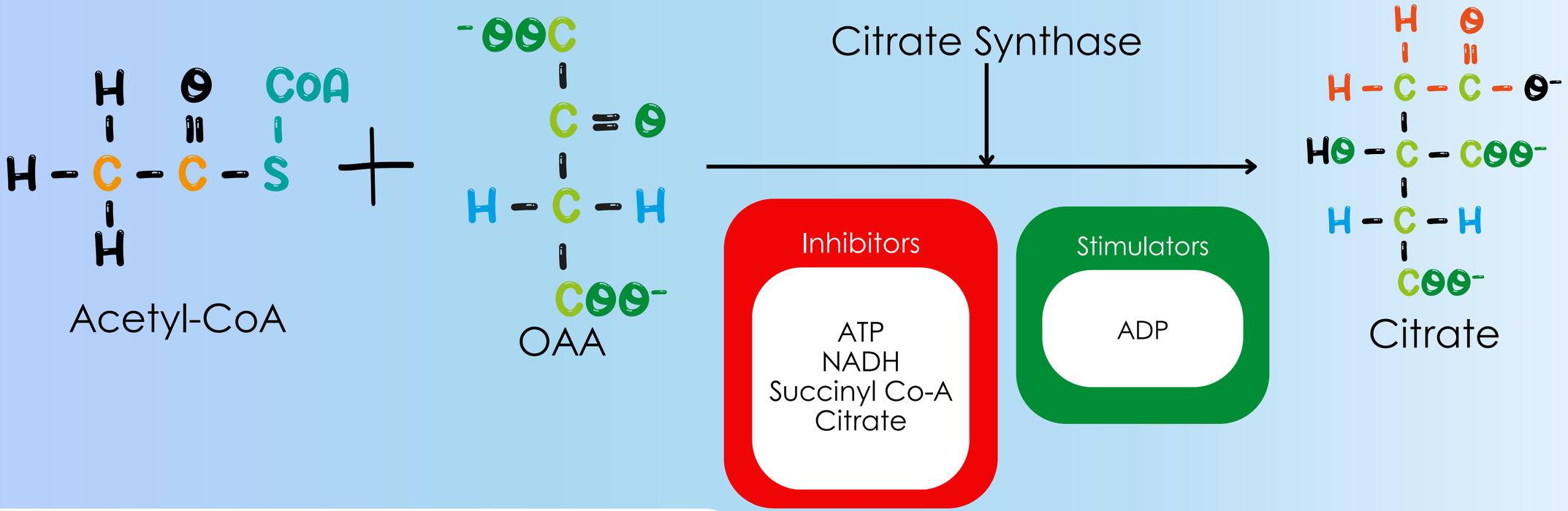
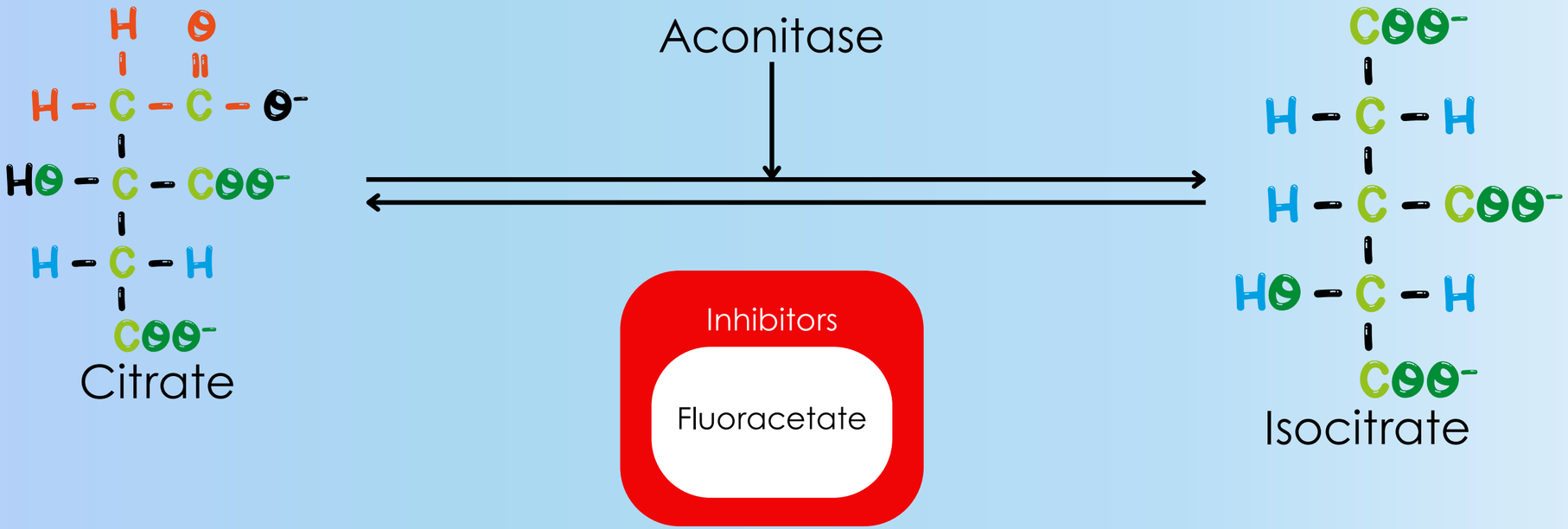
Citrate



Citrate synthase acts on Acetyl CoA and OAA to make Citrate

One way reaction - highly regulated and irreversible

Isocitrate



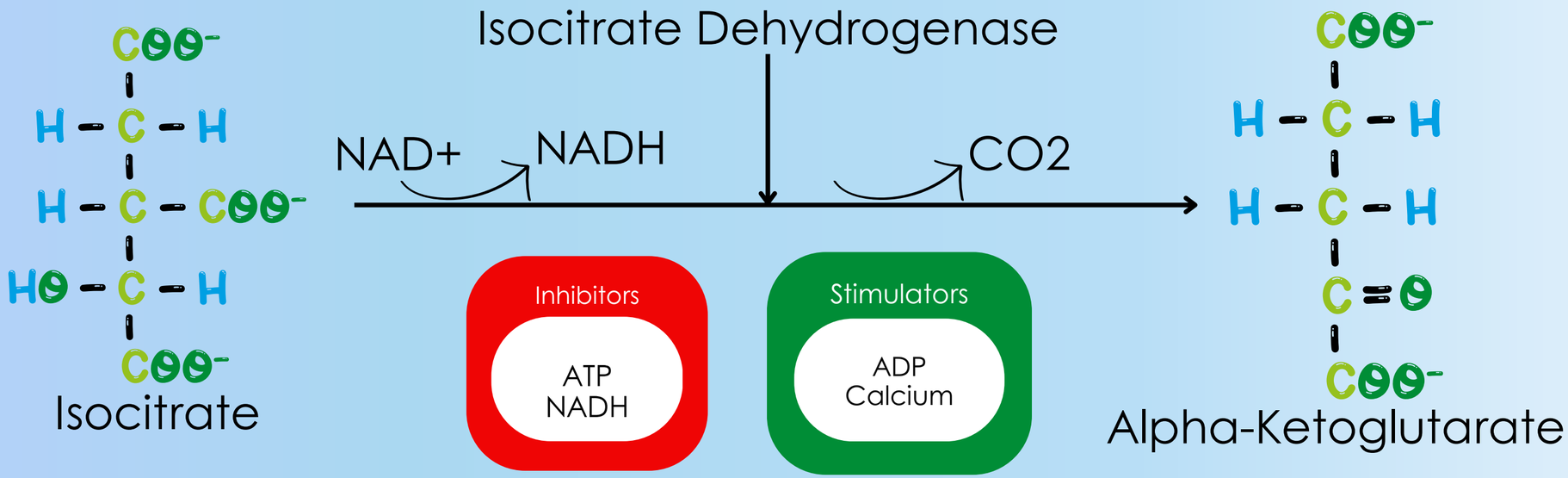
Isomerisation - Citrate is converted into Isocitrate

Enzyme: Aconitase

Reversible reaction

Fluoroacetate inhibits aconitase

Alpha-Ketoglutarate



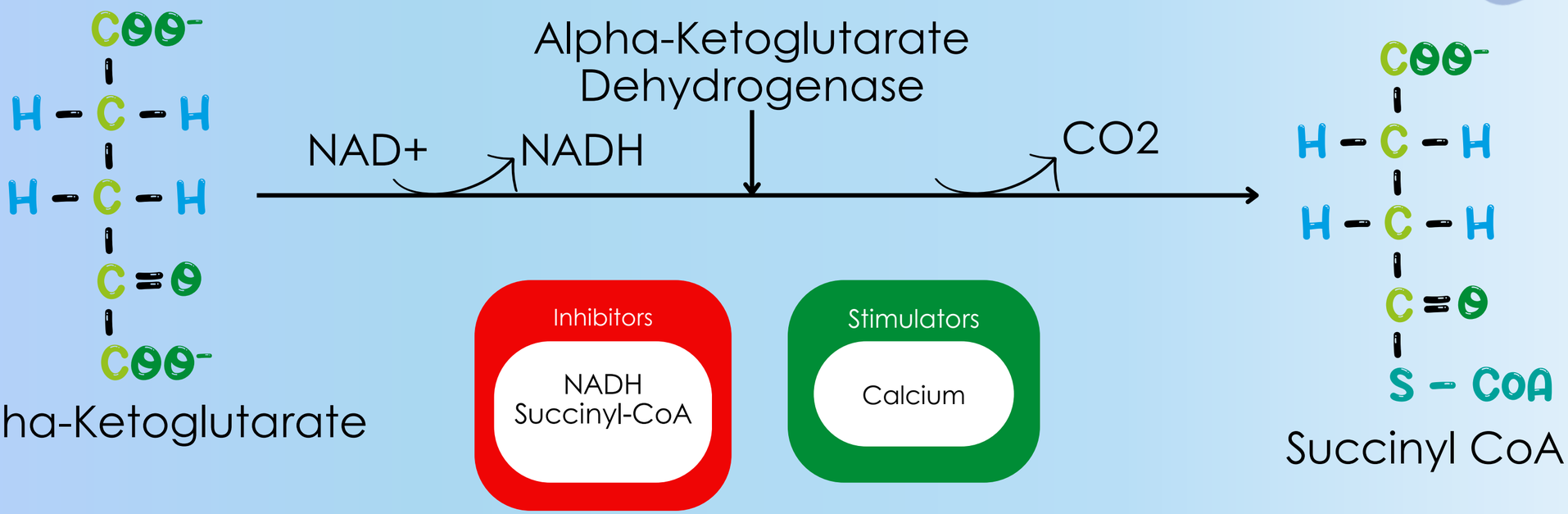
Decarboxylation - isocitrate is converted into alpha-ketoglutarate

Generates NADH and CO2

Enzyme: Isocitrate Dehydrogenase

Moves in one direction and is irreversible

Succinyl-CoA

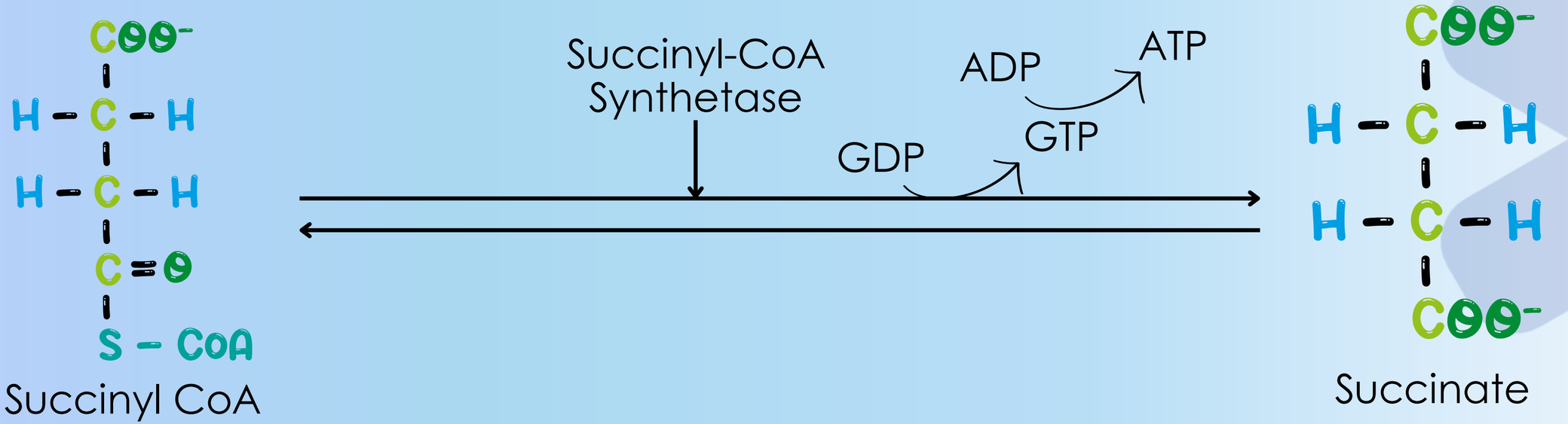


Decarboxylation - Alpha-ketoglutarate is converted into Succinyl CoA

Enzyme: alpha-keotglutarate dehydrogenase

Generates NADH and CO2

Succcinate



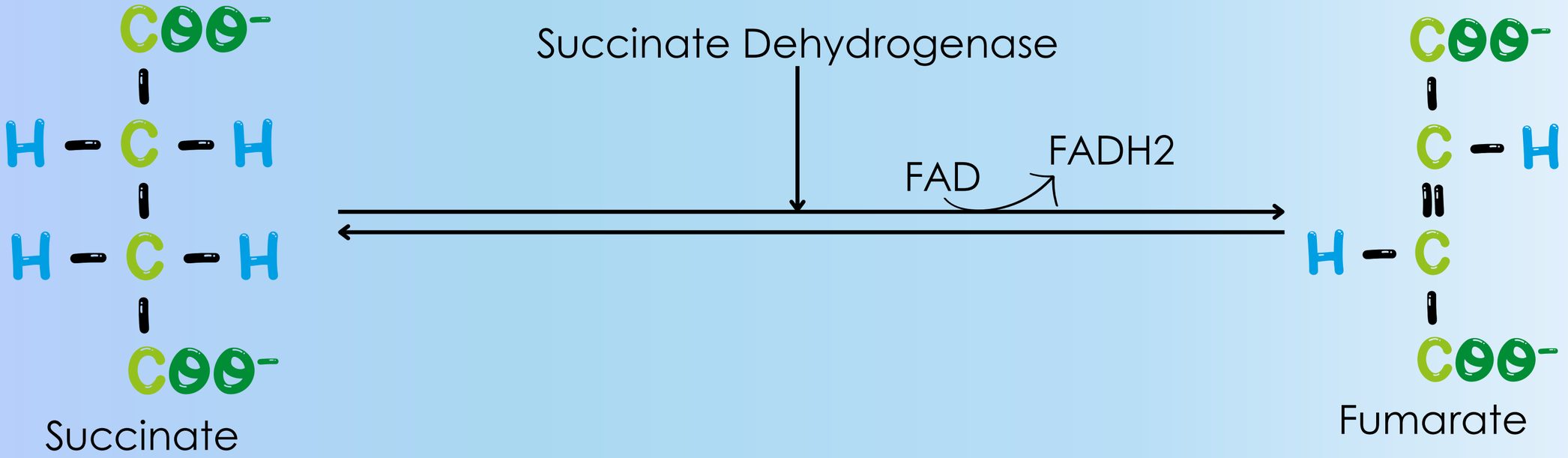
Succinyl-CoA is converted into succinate

GTP is generated from the energy of the reaction, ADP steals phosphate group to make ATP - substrate level phosphorylation (different from oxidative phosphorylation!)

Enzyme: Succinyl-CoA Synthesase

Reversible Reaction

Fumarate



Dehydrogenation - Succinate is converted into Fumarate

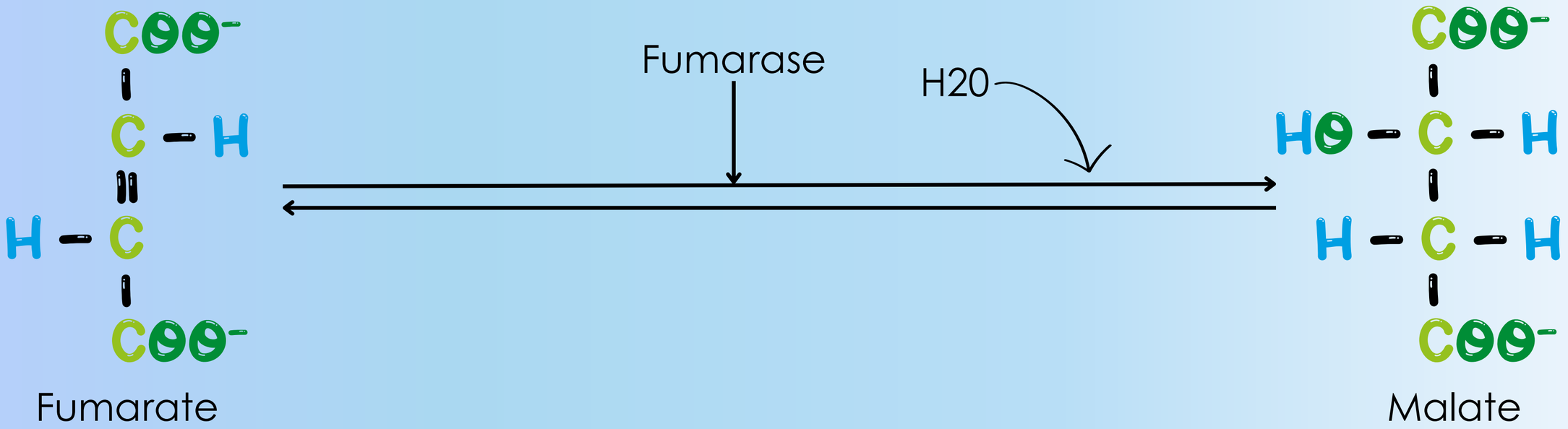
Enzyme: Succinate Dehydrogenase (located on cristae)

Products: FADH2

Reversible reaction

Clinical Correlation - Pheochromocytoma

Malate



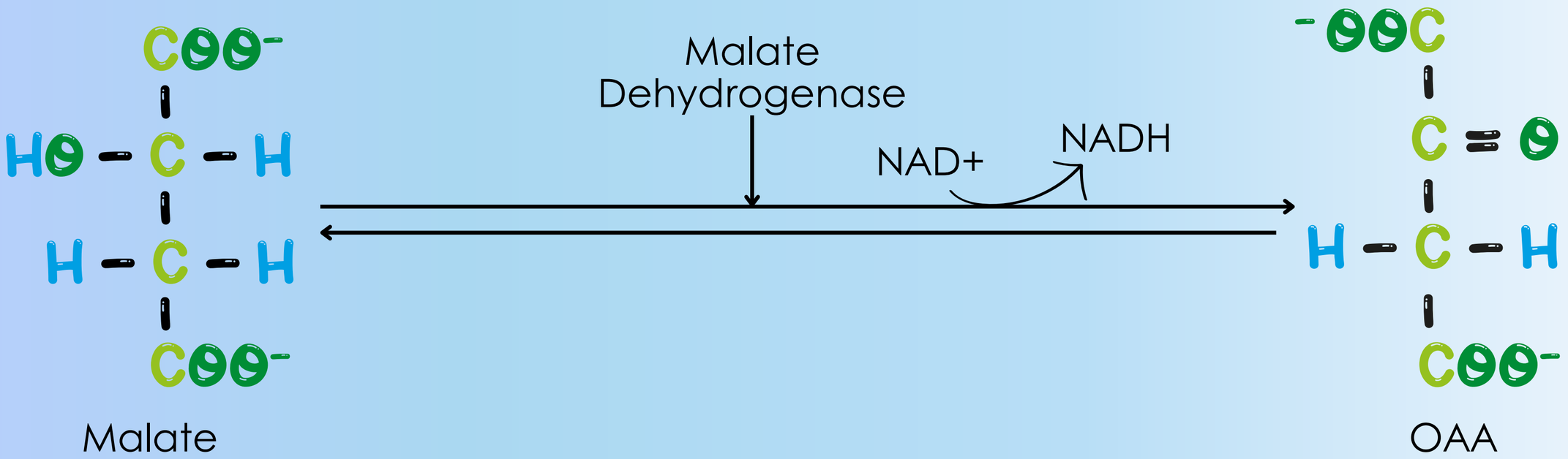
Fumarate is converted into Malate using H2O

Enzyme: Fumarase

Reversible reaction

Clinical Correlation: leiomas

OAA

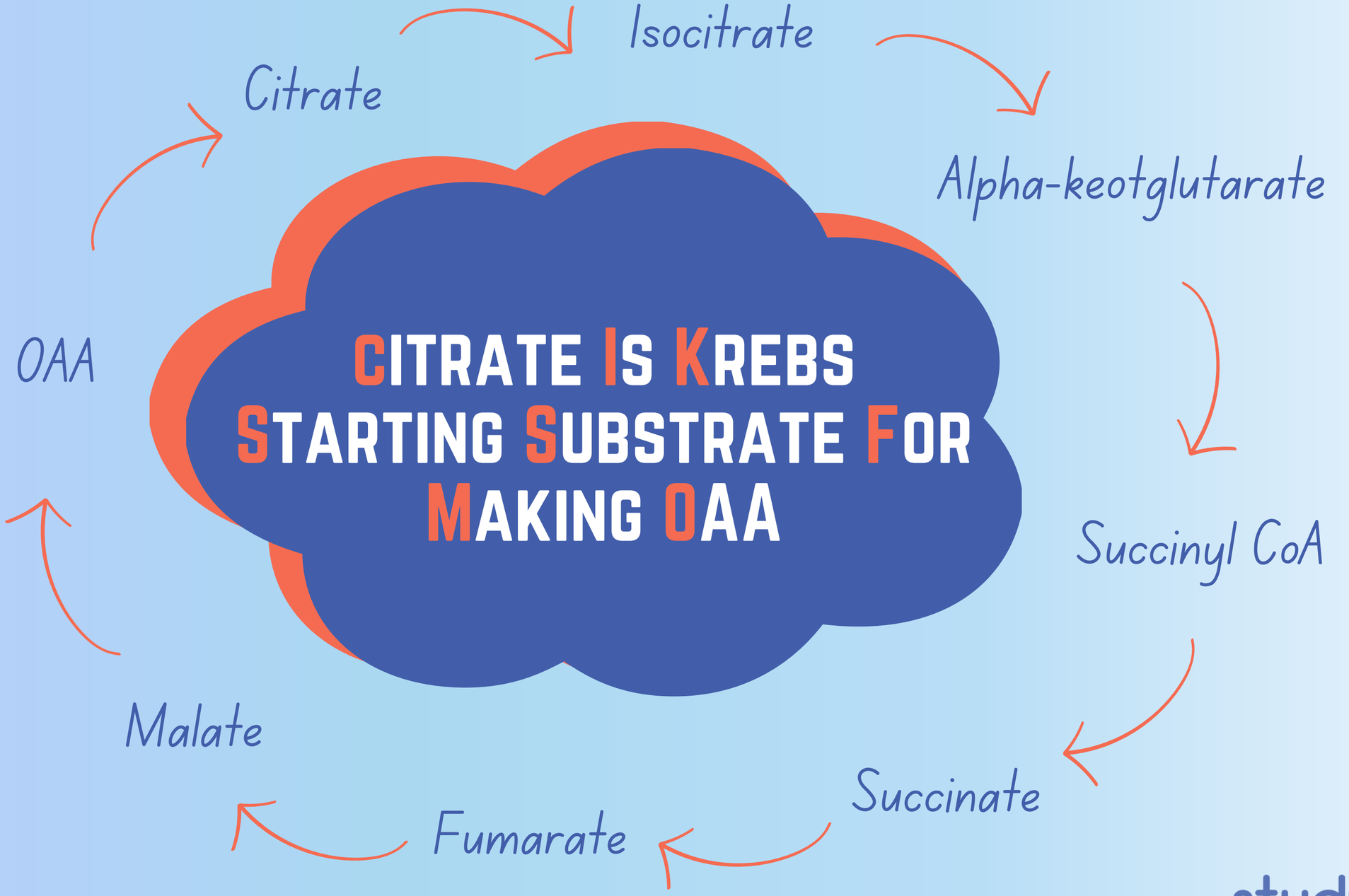


Dehydrogenation - Malate is converted into OAA

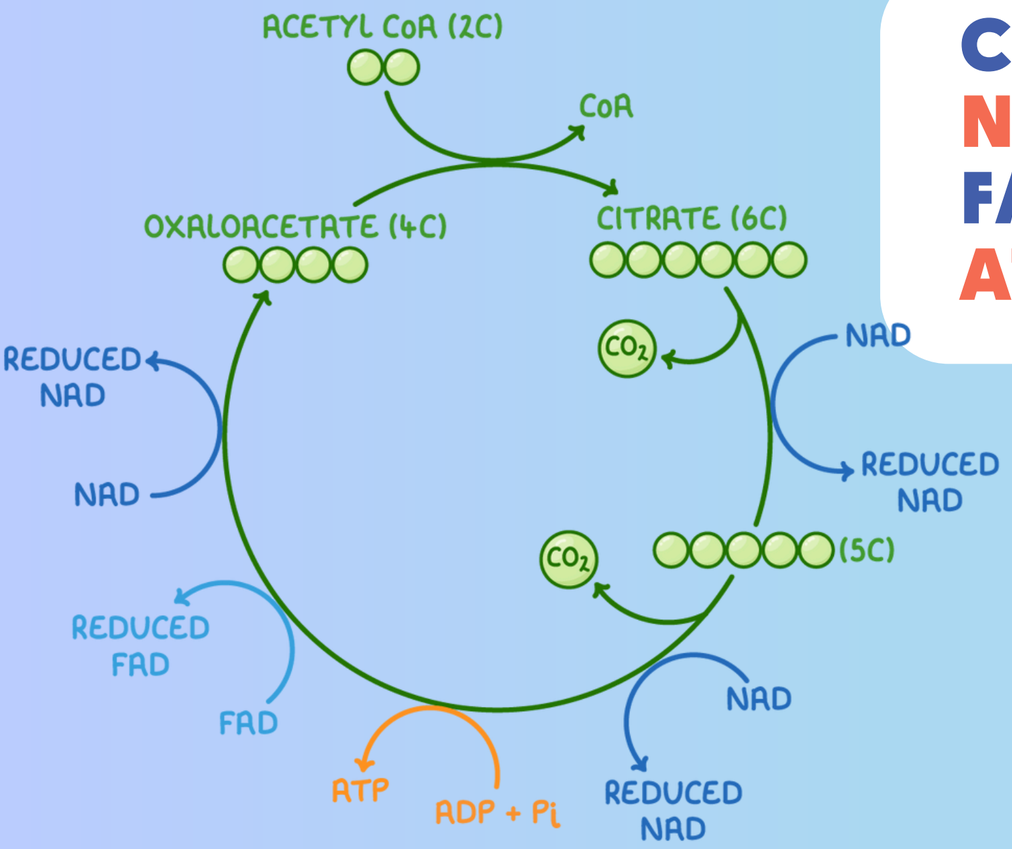
Enzyme: Malate Dehydrogenase

Products: NADH

Reversible reaction


Citrate
Isocitrate
Alpha-keotglutarate
Succinyl CoA
Succinate
Fumarate
Malate
OAA
CITRATE IS KREBS STARTING SUBSTRATE FOR MAKING OAA

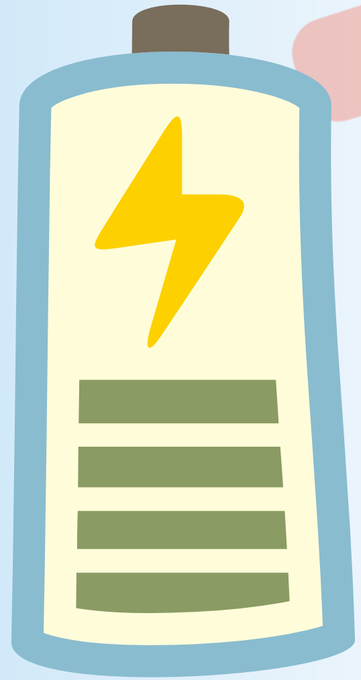
Total Products of the TCA Cycle



CO2: 2 x 2 = 4
NADH: 3 x 2 = 6
FADH: 1 x 2 = 2
ATP: 1 x 2 = 2

1 NADH = 2.5 ATP

1 FADH - 1.5 ATP



Total ATP per Cycle = 20

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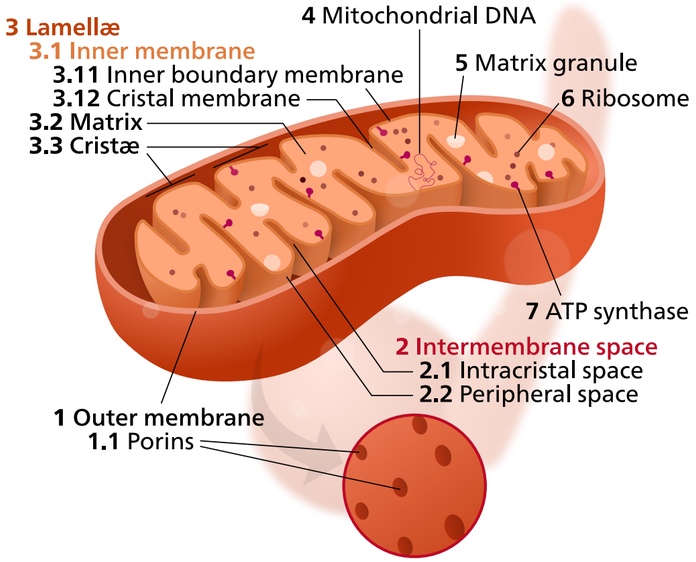
Oxidative Phosphorylation

Electron Transport Chain & Chemiosmosis

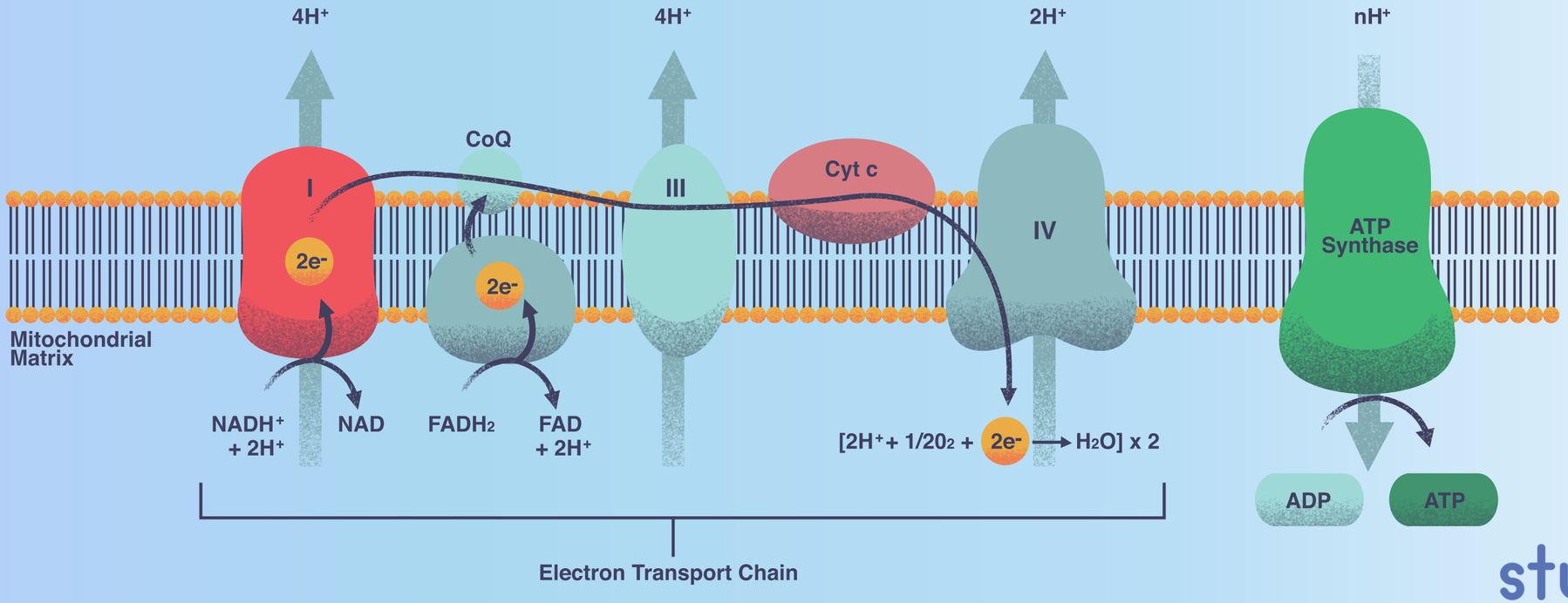
Location - cristae of the mitochondria + intermembrane space



Electron Transport Chain

Occurs on the inner mitochondrial membrane initially

NADH (8), FADH2 (2) and H+ act as shuttles to transport electrons through ETC



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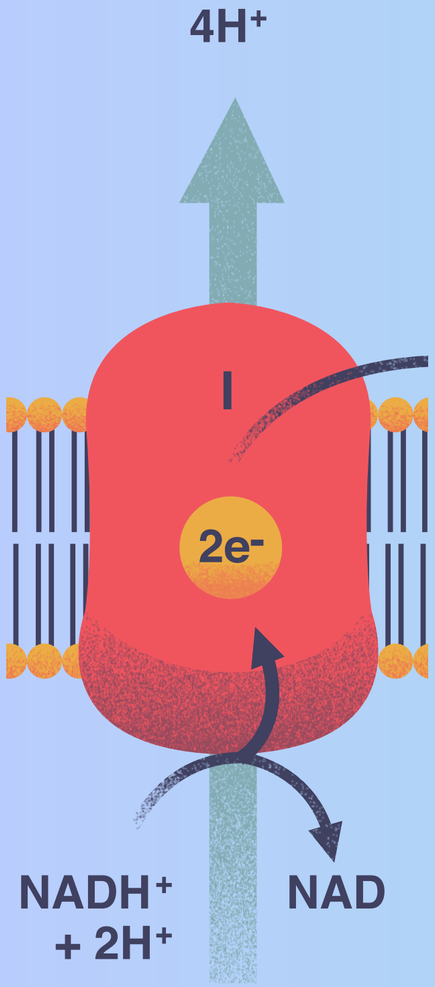
Complex I - NADH Dehydrogenase



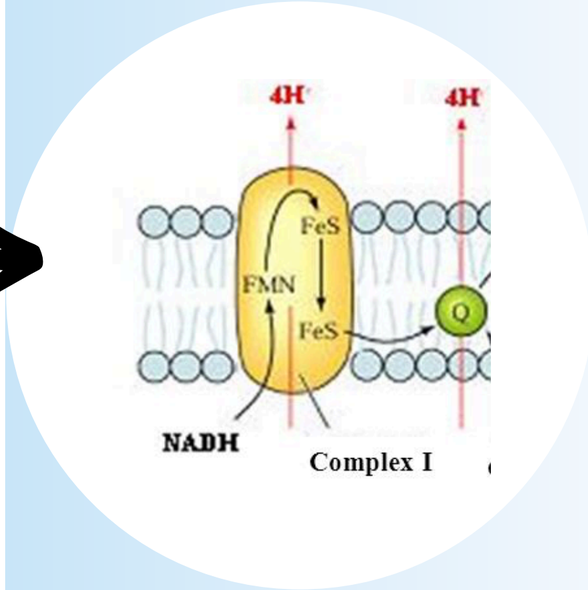
NADH is converted into NAD+, through the picking off of electrons by Flavin Mononucleotide (FMN)

FMN + H2 = FMNH2

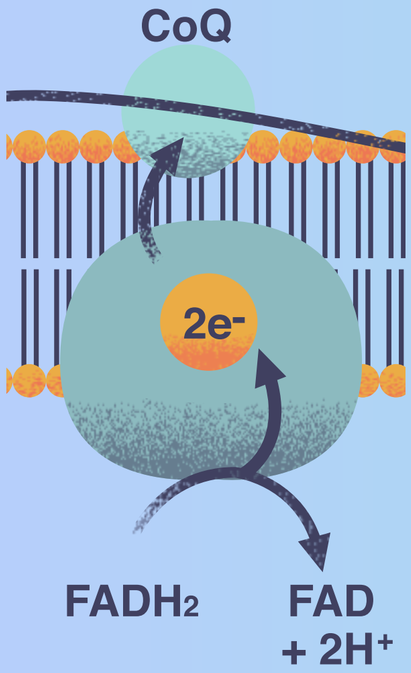
FMNH2 passes its electrons to Fe-S and then to CoQ

This reduced form is unstable and so the electrons are passed onto CoQ

Protons pumped into intermembrane space through a pore



Complex II - Succinate Dehydrogenase (Quinone)



FADH is converted into FAD
FMN picks up these electrons and is converted into it's reduced form FMNH2

Coenzyme Q takes electrons from FMNH2 and becomes reduced form QH2

Unstable state, passses these electron on to CoQ (Ubiquinone), this passes the electrons from complex I and II to complex III

Complex does not have a pump and therefore cannot pump out it's electrons

Complex III - Cytochrome bc1 Complex

Also known as CoQ-Cytochrome-b-Oxidoreductase

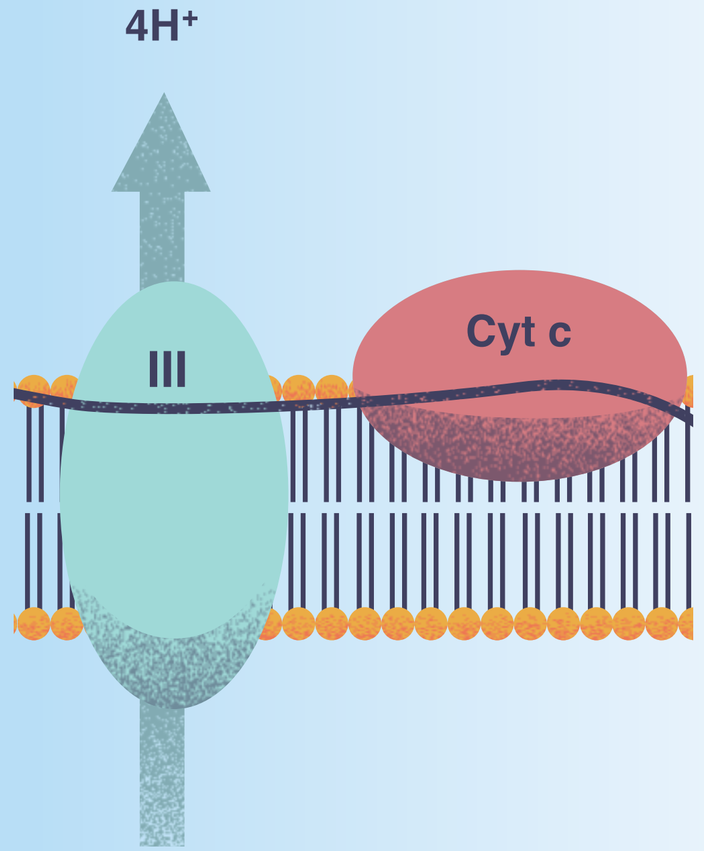
Contains Fe3+-CytB

Ubiquinone passes its electrons on to complex III

Electrons accepted and cytochrome becomes Fe2+-CytB

Unstable state and passes electrons on to Cytochrome C (CytC-Fe3+)

Pumps protons into intermembrane space via a pore



$$CytC\text{-}Fe3+ + e \longrightarrow CytC\text{-}Fe2+$$

Complex IV - Cytochrome Oxidase

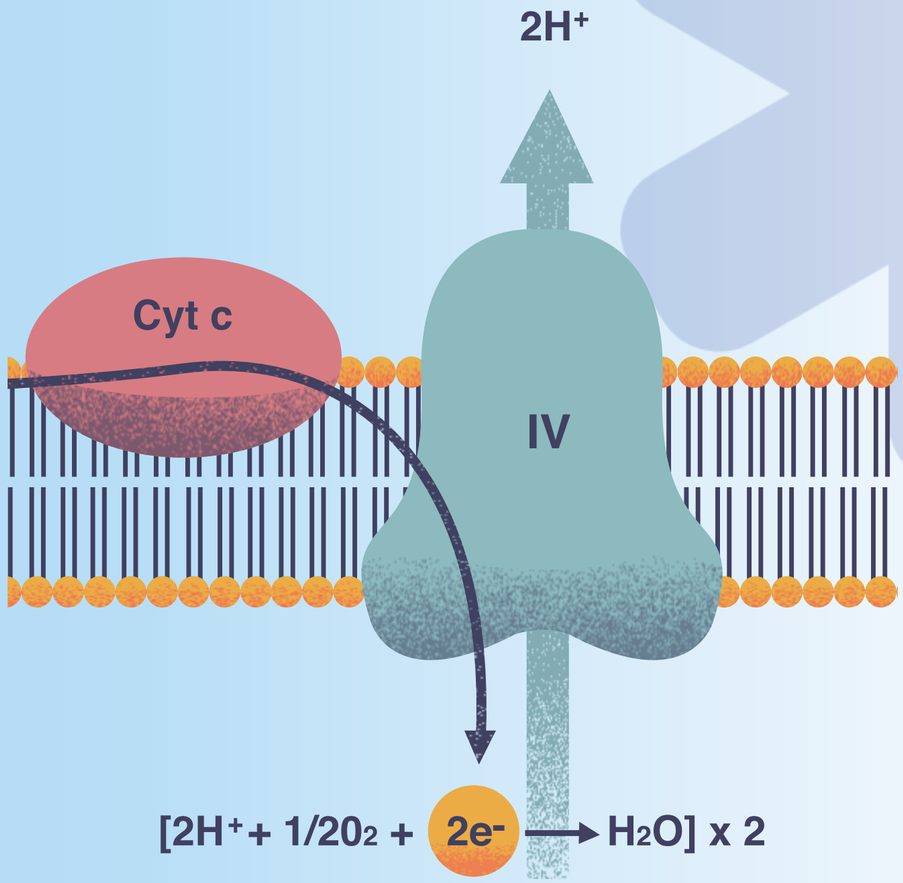
CytA-Fe3+ accepts electrons from CytC-Fe2+

Unstable state and so passes its electrons away.

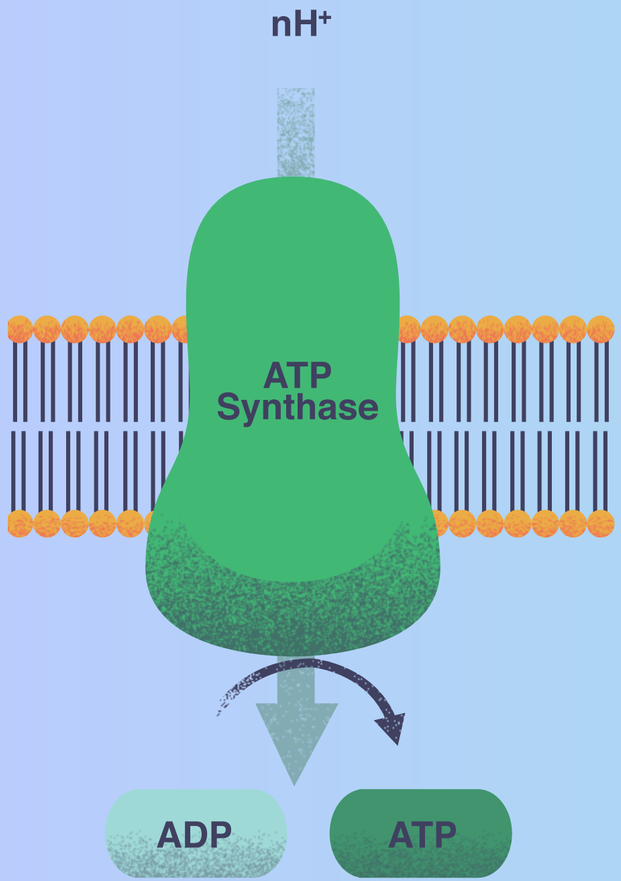
Energy is harvested into intermembrane space via a pump

Fe2+ donates its electrons to 1/2O2 located in the intermembrane space, also combining with 2 H+, forming water
1/2O2 + H2 + e = H2O

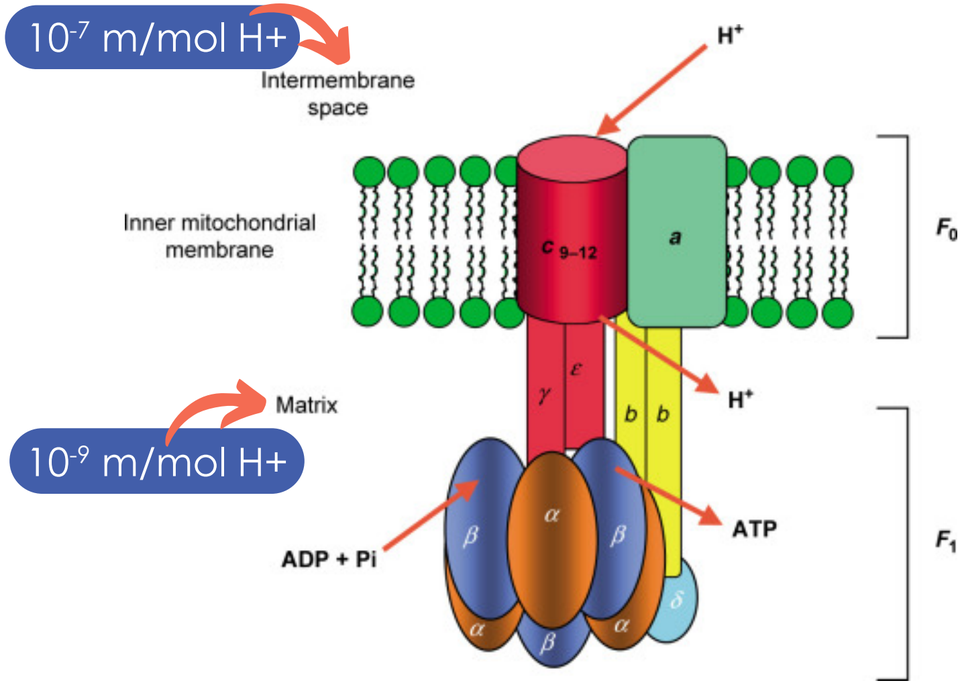
Clinial Correlation: Cyanide Poisoning



Chemiosmosis



Concentration Gradient - Proton concentration is much higher in intermembrane space compared to mitochondrial matrix after ETC



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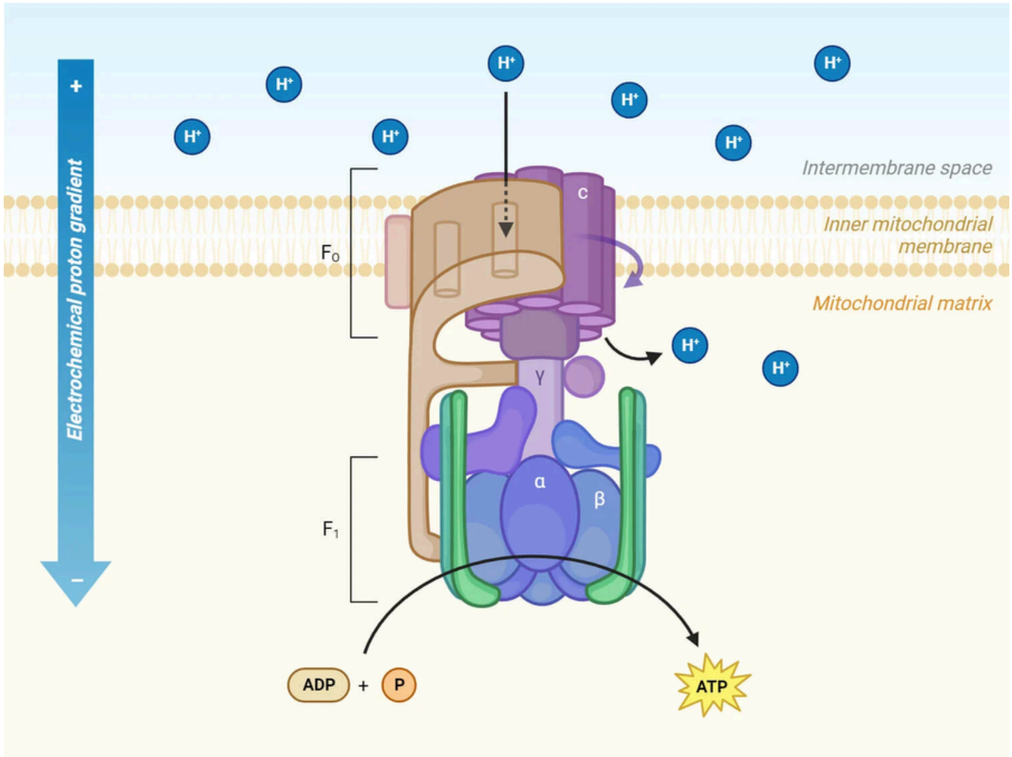
ATP Synthase

Component A - passive influx of protons

Arginine 2,10 - enzyme that facilitates transport from entry to exit

Component C + gamma protein - rotate generating proto-motor force

Beta-catalytic Subunit - uses protomotor force to make ATP



Generates much **larger** amounts of energy compared to substrate phosphorylation

Clinical Correlation - Weight loss drugs and oligomycin that can inhibit F0 subunit

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Electron Transport Chain Inhibitors

Complex I

Rotenone - inhibits transfer from Fe-S center to CoQ

Amytal - protects the heat generated during ischemia and reperfusion injury

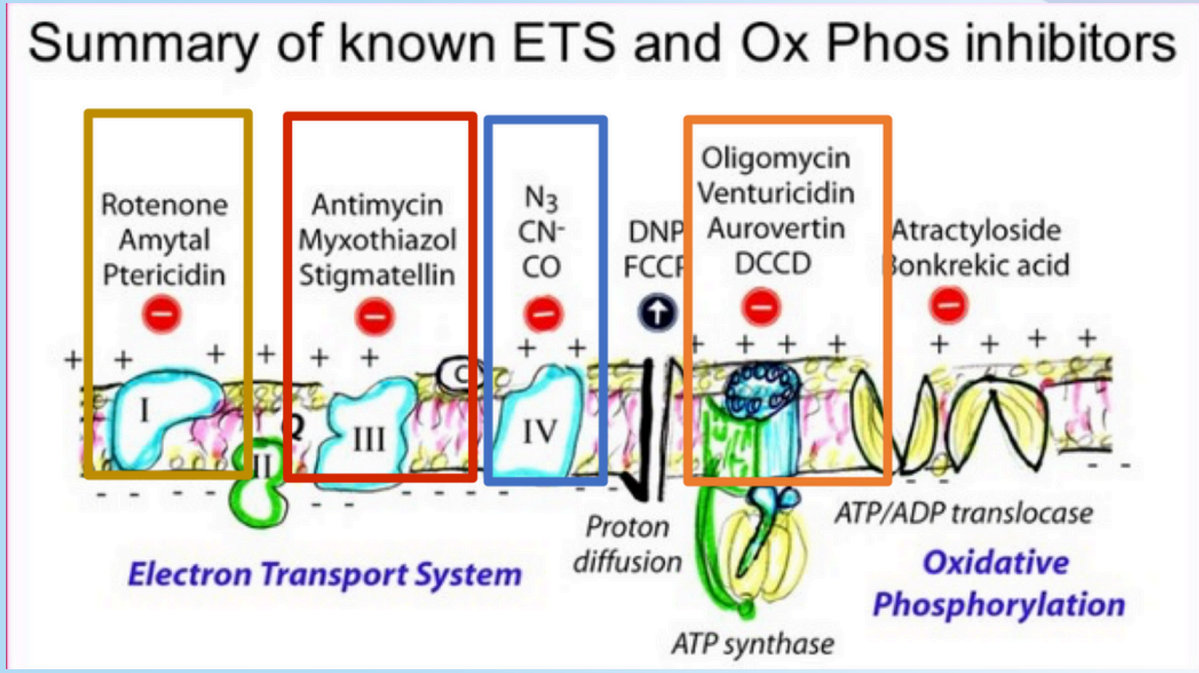
Complex III

Antimycin A and C - binds to quinone reduction site

Complex IV

Cyanide - binds to ferric ion which blocks the ETC causing cell death, hypoxia and lactic acidosis

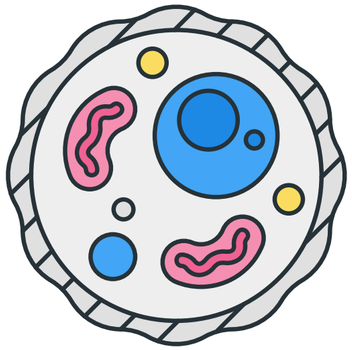
Carbon Monoxide - blocks electron flow between complex and O2, and also inhibits Fe2+



Total Energy Produced

Glycolysis	2 ATP (SP) + 2NADH (5ATP)
Transition Step	2 NADH (5ATP)
Krebs Cycle	6 NADH (15ATP), 2 FADH (3ATP), 2 ATP
Electron Transport Chain	1NADH (2.5ATP), 1 FADH (1.5ATP)

Total for both aerobic and anaerobic respiration:



38 ATP