2024
SUMMARY

METABOLISM

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ARKAN ACADEMY

Pyruvate Oxidation

⇝ by pyruvate dehydrogenase complex (PDH)

↳ 3 enzymes + 5 coenzymes

Enzymes		Co-enzymes
E_1: Pyruvate dehydrogenase	⇝	TPP (vitamin B_1)
E_2: Dihydrolipoyl transacetylase	⇝	lipoic acid , CoA
E_3: Dihydrolipoyl dehydrogenase	⇝	NAD^+ , FAD

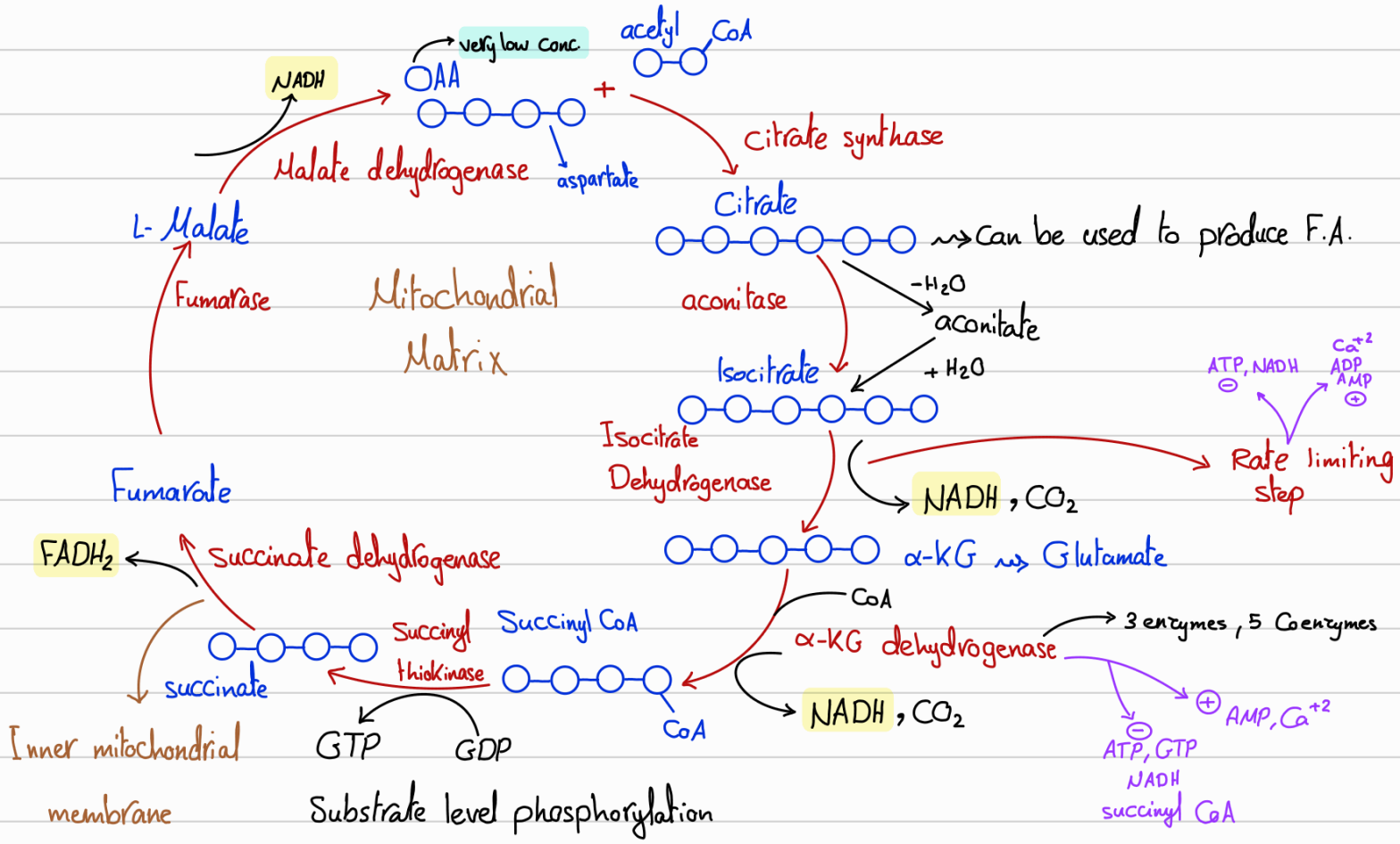
Net production = 1 CO_2 , 1 NADH , Acetyl CoA

E_1 deficiency, Arsenic Poisoning
- ⇝ affect the brain due to lactic acidosis
- ⇝ TPP suplementary reduce symptoms

- ☆ ↑ energy (ATP, NADH, Acetyl CoA) ⇝ activate kinase ⇝ inhibition
- ☆ ↓ energy (ADP, NAD^+) ⇝ Activate Phosphatase ⇝ activation
- ☆ Pyruvate ⇝ inhibit kinase ⇝ activation
- ☆ Ca^{+2} ⇝ activate phosphatase ⇝ activation

PDH
P ⊖ ↔ ⊕ X P

TCA Cycle (Krep's, Citric acid cycle)



Products: $2CO_2$, 1 GTP , 3 NADH , 1 $FADH_2$

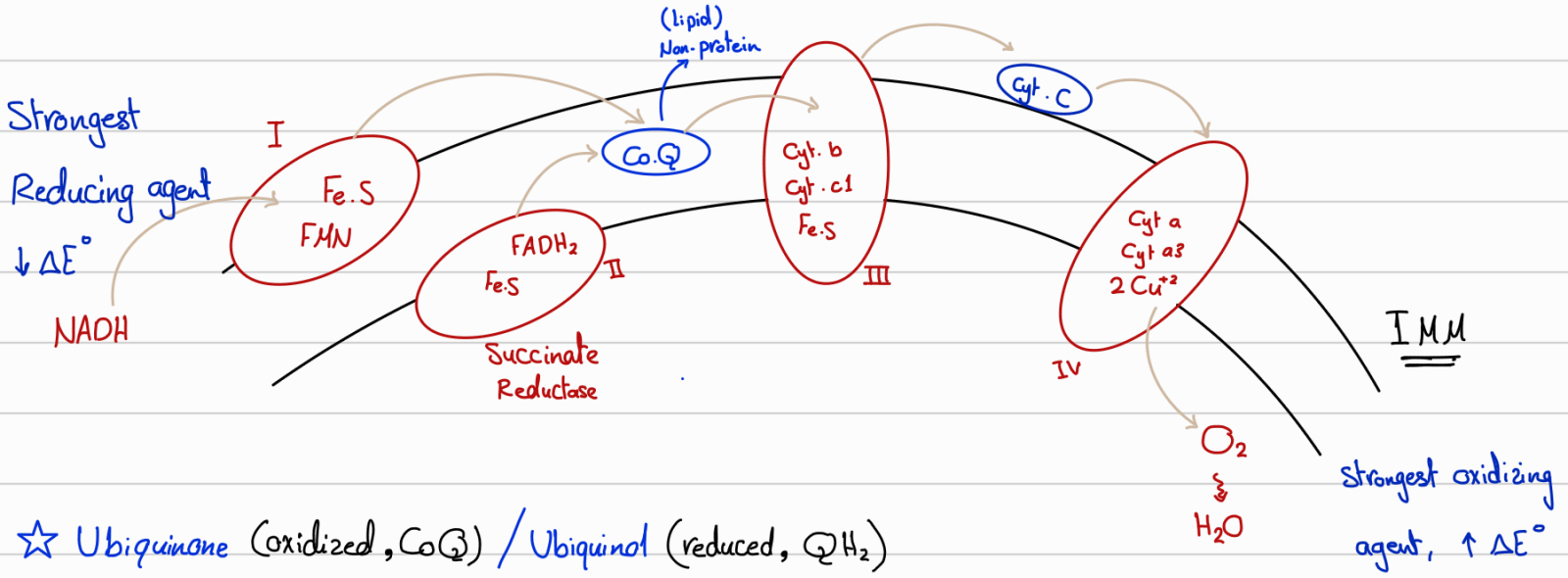
Organic inhibitors ⇝ Flouroacetate ⇝ ⊖ aconitase
- Arsenite ⇝ ⊖ α-kg DH
- Malonate ⇝ ⊖ Succinate DH

Mitochondrial Membrane
- Outer ⇝ Permeable , ↑cholesterol , ↓cardiolipin
- Inner ⇝ Impermeable, ×cholesterol, ↑cardiolipin

⇝ Anaplerosis: maintained metabolic intermediates

⇝ Amphibolic: Catabolic + Anabolic

- Succinyl CoA ⇝ Heme
- Citrate ⇝ FAs
- Malate ⇝ Gluconeogenesis
- α-kg ⇝ Glutamine, GABA
- OAA ⇝ asparagine



☆ Ubiquinone (oxidized, CoQ) / Ubiquinol (reduced, QH_2)

☆ $FADH_2$, NADH ⇝ transfer $2e^-$

☆ Cytochrome ⇝ heme protein
- a, b, c are differentiated by α-band
- 4 pyrrole rings with iron Center ⇝ ferrous or ferric
- Can accept only $1e^-$

☆ Co.Q , NADH , $FADH_2$ → Transfer $2e^-$

☆ Under normal (aerobic) conditions ⇝ all carriers are oxidized

☆ Anaerobic conditions ⇝ all carriers are reduced

☆ Addition of inhibitors ⇝ downward (oxidized), upward (reduced)
- Complex I : amytal (sedative), Rotenone (insecticide)
- Complex III : Antimycin A
- Complex IV: CO, Cyanide (amygdalin), Azide
- Complex V: Oligomycin

Chemiosmosis: The utalization of proton gradeint to do a work (ATP production)

☆ Protons are pumped from the matrix into the intermembranous space (complex I, III, IV)
- I, III: $4H^+$
- IV: $2H^+$

☆ Protons flow back (ATP synthase) into matrix

ATP Synthase

- F_o
  - a: entry, exit Point
  - C: Rotation
- F_1
  - α: structural
  - β: Catalytic
  - γ: Connect F_o to F_1

☆ β has 3 conformation:

L → T → O
- L: inactive
- T: Produce ATP
- O: Release ATP

☆ ETC and ATP synthase are highly coupled
- ADP is the most important regulator

☆ DNP (2,4-dinitrophenol) ⇝ uncoupling agent by collapsing the proton gradient
- The energy of proton gradient is dissipated as heat
- DNP is used for wieght-losing

Inhibitors cause
- ↑ O_2 consumption
- ↓ ATP synthesis

☆ Uncouplers: relieve the inhibition of O_2 consumption

☆ Uncoupler protein: Produce heat
- ☆ UCP1 (thermogenin): brown adipose, infants
- ☆ UCP2 in most cells
- ☆ UCP3 in skeletal muscles
- ☆ UCP 4,5 in the brain

DNA

- mitochondrial
  1) maternal inheritance
  2) Replicative segregation and heteroplasmy
- Nuclear

Mitochondrial DNA mutations:
- (LHON) Lebers hereditary optic neuropathy (complex I)
- Sporadic myopathy (complex III, IV)
- Encephalomyopathy (Complex IV)
- (NARP) Neuropathy, ataxia, retinitis pigmentosa (V)

Nuclear DNA Mutations
- Leigh syndrome (Complex I, II, 4)

NADH shuttling from cytosol → Mitochondria

1) Glycerol 3P shuttle
   - by Glycerol 3P Dehydrogenase
   - Muscle, Brain

2) Malate - aspartate shuttle
   - Malate Dehydrogenase
   - ⇝ Reversible
   - Kidney, liver, heart

ATP shuttle

- ATP translocase
  - 1 : 1
    ATP : ADP

ARKAN

ACADEMY

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