

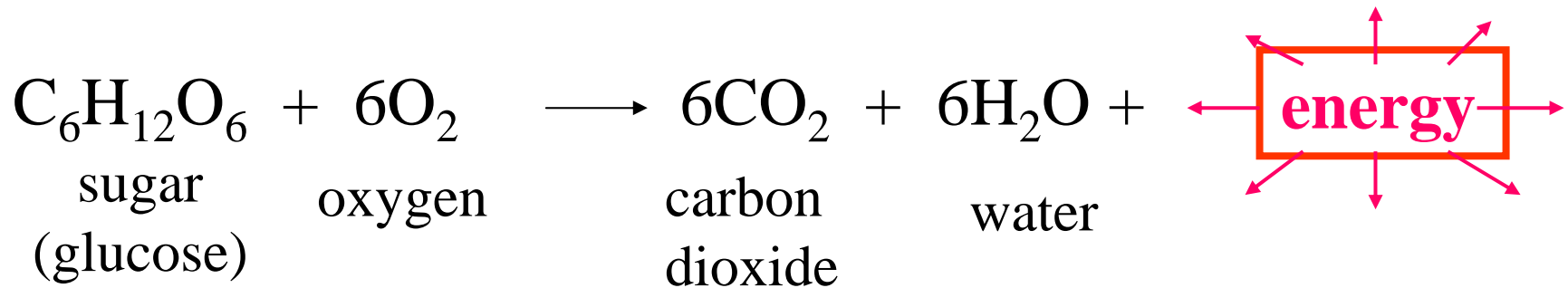
# **Posforilasi Oksidasi – Respirasi Sel**

Blok 1.2

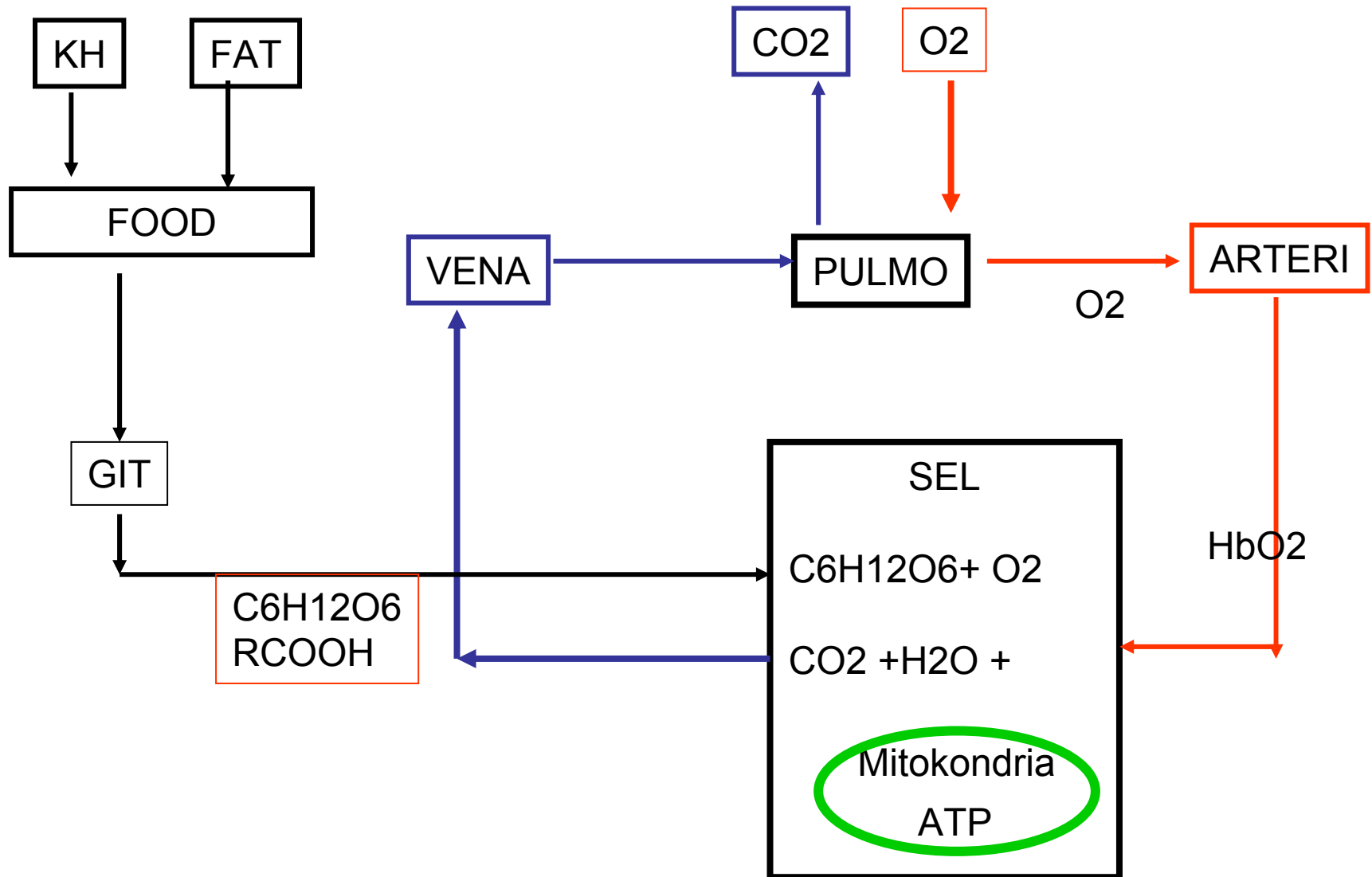
Biokimia Fk-Unand

# Respirasi Sel

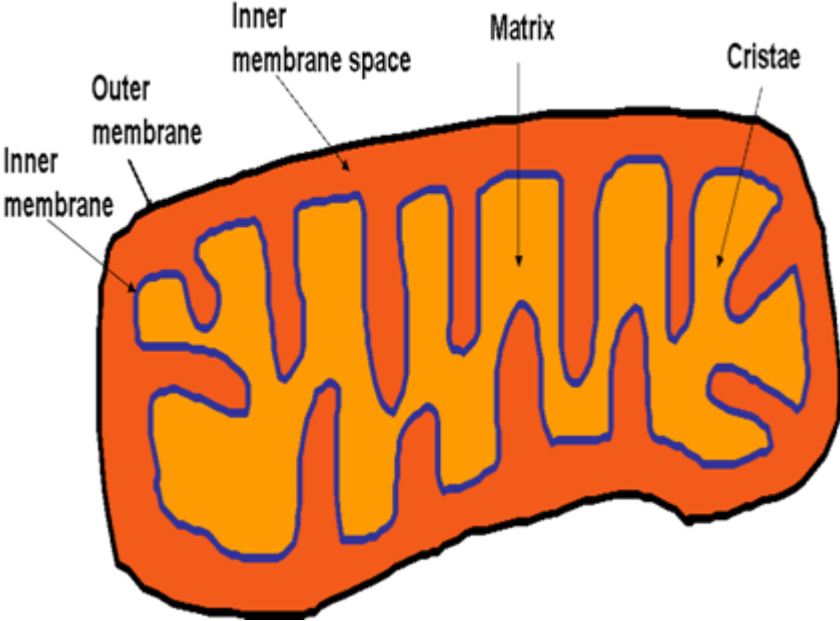
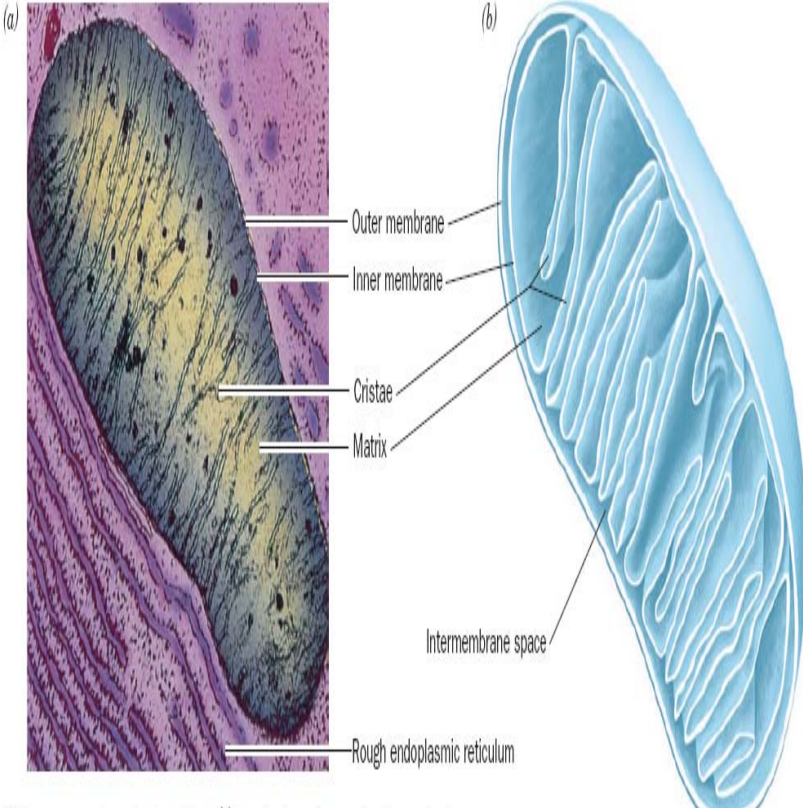
- Reaksi kimia pada sel hidup antara atom C, H dengan O<sub>2</sub> menghasilkan CO<sub>2</sub>, H<sub>2</sub>O dan ENERGI
- C,H : makanan, O<sub>2</sub> : udara / air
- Energi berguna: reaksi kimia pada sel



# Pencernaan - Pernapasan – Metabolisme - Respirasi Sel



# Mitochondria



# Proses Pemindahan Electron

- Biologi oksidasi: Oksidasi senyawa makromolekul pada sel dengan bantuan enzim intrasel.
- Transport Electron : Electron dibawa oleh *reduced coenzymes* (NADH atau  $\text{FADH}_2$ ) melalui suatu rantai pada membran dalam mitokondria atau *electron transport chain* tdd: protein dan coenzymes ke  $\text{O}_2$

# Proses...

- Oxidative Phosphorylation: Coupling elektron ( $e^-$ ) yang dibawa ke membran dalam mitokondria dengan  $O_2$ ), pembentukan ATP (Phosphorylation) .
- Sumber posfat in-organik pada metabolisme aerob
- Enzim: Oxidoreductase pada respirasi
  - oxidase acceptor H :  $O_2$
  - Dehydrogenase acceptor H : NAD dan FAD

# Oksidasi

- Oxidation: pelepasan electron dari subsrat dan reduksi pada penerima elektron
- Enzim: oxidase, dehydrogenase, hydroperoxidase, dan oxygenase

# Oksidase

- oxidase : oxygen sebagai hydrogen acceptor
- Produk: H<sub>2</sub>O atau H<sub>2</sub>O<sub>2</sub> .
- Cytochrome oxidase (cyt a<sub>3</sub>):
  - Hb, mioglobin
  - Cu
  - Comp IV ETC
- Flavoprotein enzymes
  - FAD dan NAD (CoE, prosthetic groups enzim oksidase) mis: xanthine oxidase



# Dehidrogenase

- Acceptor e<sup>-</sup>: NAD dan FAD
- *NAD-linked dehydrogenase* : satu atom hydrogen dibebaskan dari substrat sebagai hydrogen dengan *two electrons* (hydride ion, H<sup>-</sup> )
  - Glikolisis, TCA, B-oksidasi
  - *succinate dehydrogenase, acyl-CoA dehydrogenase, and mitochondrial glycerol-3-phosphate dehydrogenase*
- Ribovlavin-*linked dehydrogenase*: dihidrolipoyl dehydrogenase
- Cytochrome : kecuali Cyt a3

# Hydroperoxidase

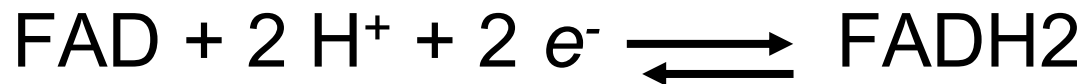
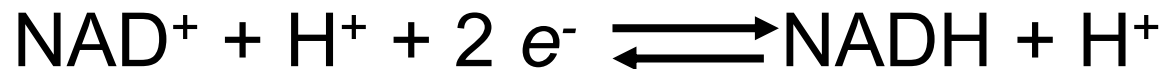
- Peroxidase
  - Substrat  $H_2O_2$
  - Acceptor : ascorbate, quinone, cytochrome c.
  - Milk, leukocytes, platelets, metabolit eicosanoid
  - Erytrosit : glutathione peroxidase, selenium as a prosthetic group
    - *Protector membran lipid dan erytrosit dari oksidasi peroksida*
- Catalase
  - $H_2O_2$  : substrat atau acceptor e-
  - blood, bone marrow, mucous membranes, kidney

# Elektron

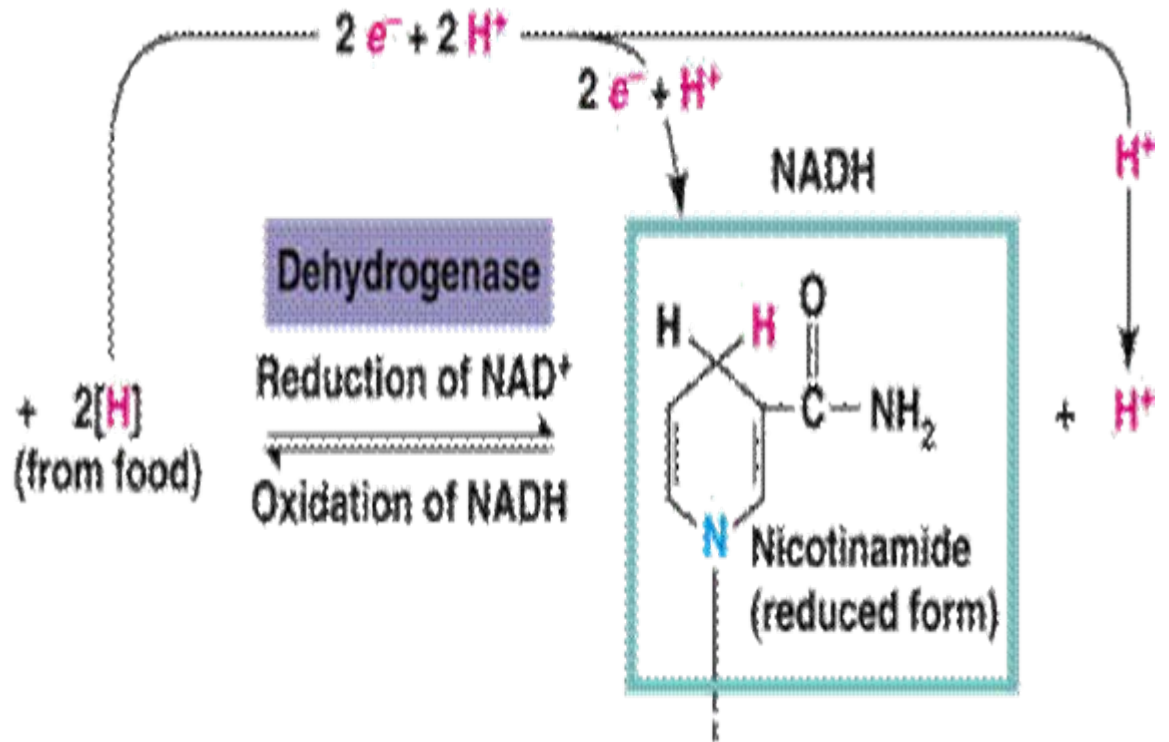
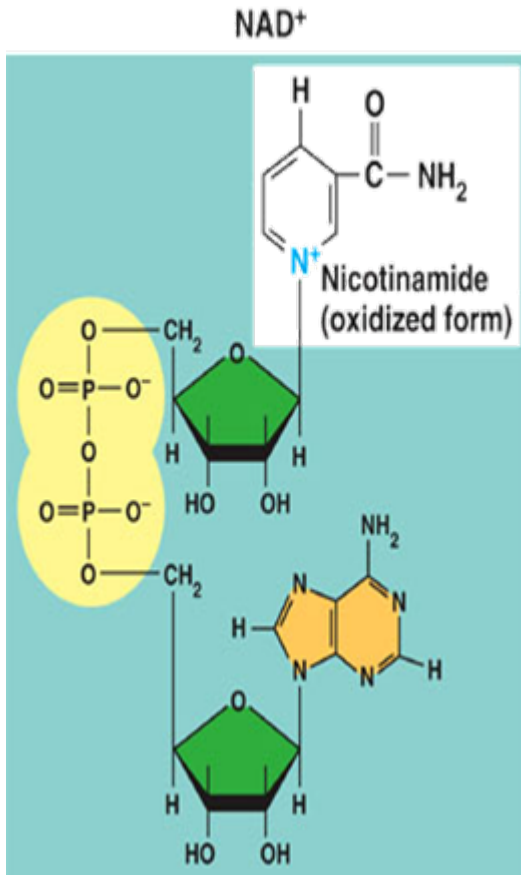
- Sumber : metabolisme senyawa makromolekul pada sitoplasma dan mitokhondria melalui proses oksidasi dan reduksi (REDOK)
  - Glikolisis
  - Siklus Krebs
  - B-oksidasi asam lemak
- Acceptor elektron :
  - NAD dan FAD (  $\text{NADH} + \text{H}^+$  dan  $\text{FADH}_2$  )

# NAD<sup>+</sup> & FAD

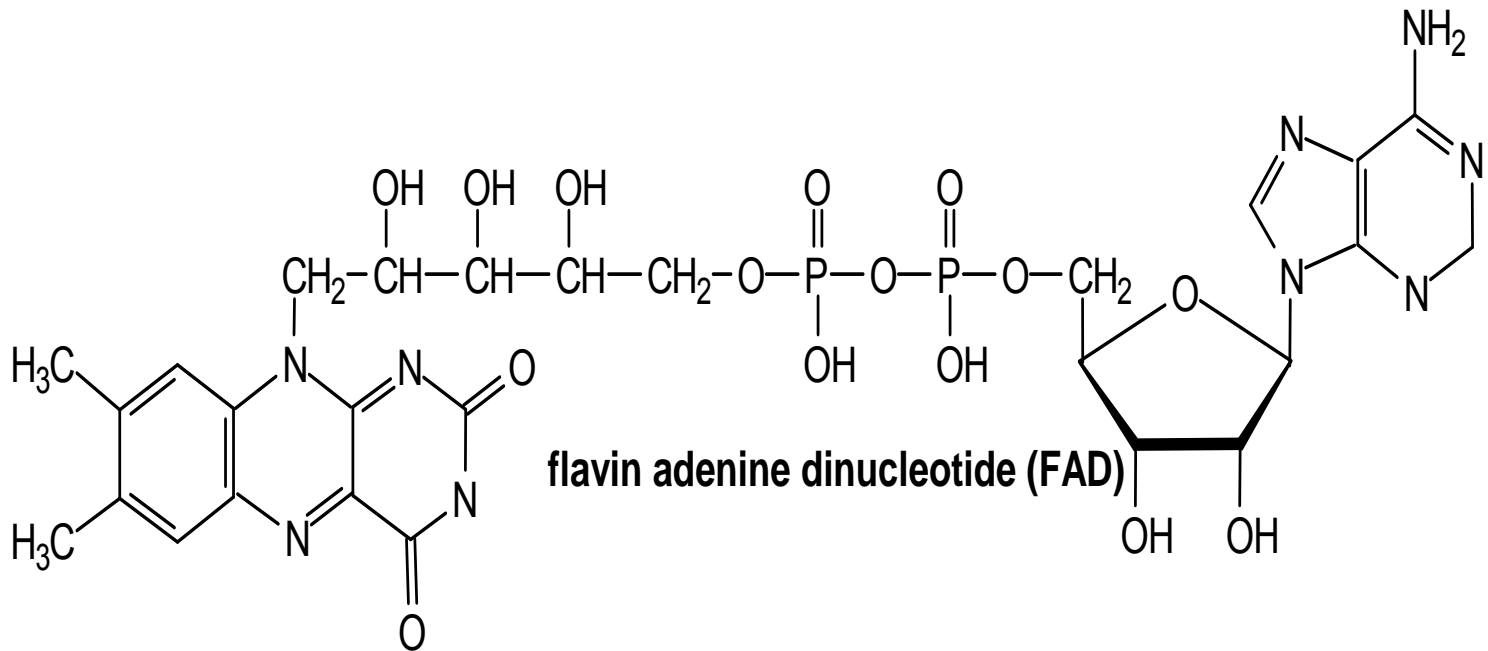
- electron carrier
- nucleotide coenzyme
- nicotinamide adenine dinucleotide (NAD<sup>+</sup>)
- flavin adenine dinucleotide (FAD)
- Transfer hydride ion (H<sup>-</sup> ; a proton with two electrons)
- Enzim: Dehidrogenase



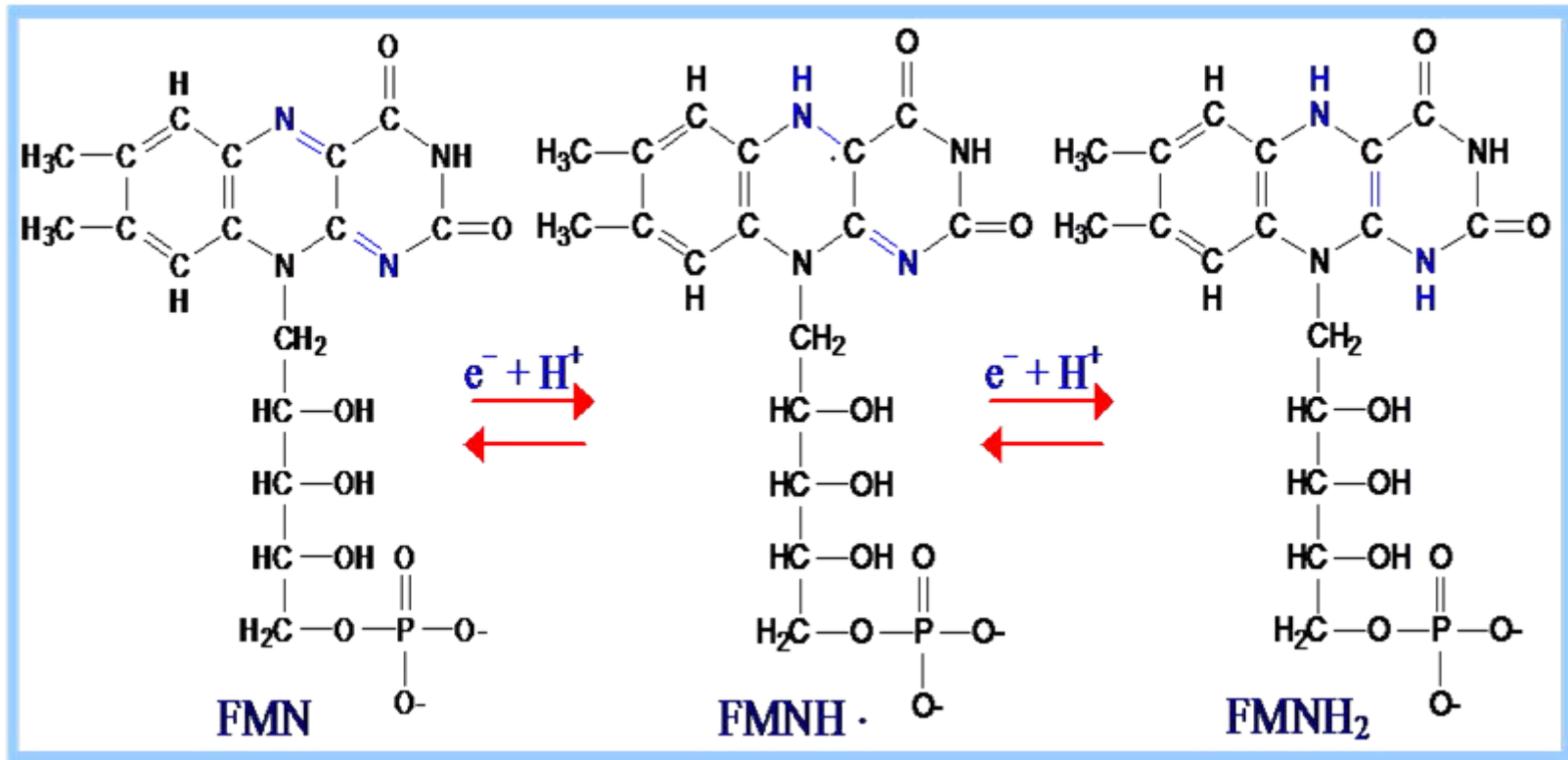
# NAD<sup>+</sup> dan NADH



# FAD



# FMN



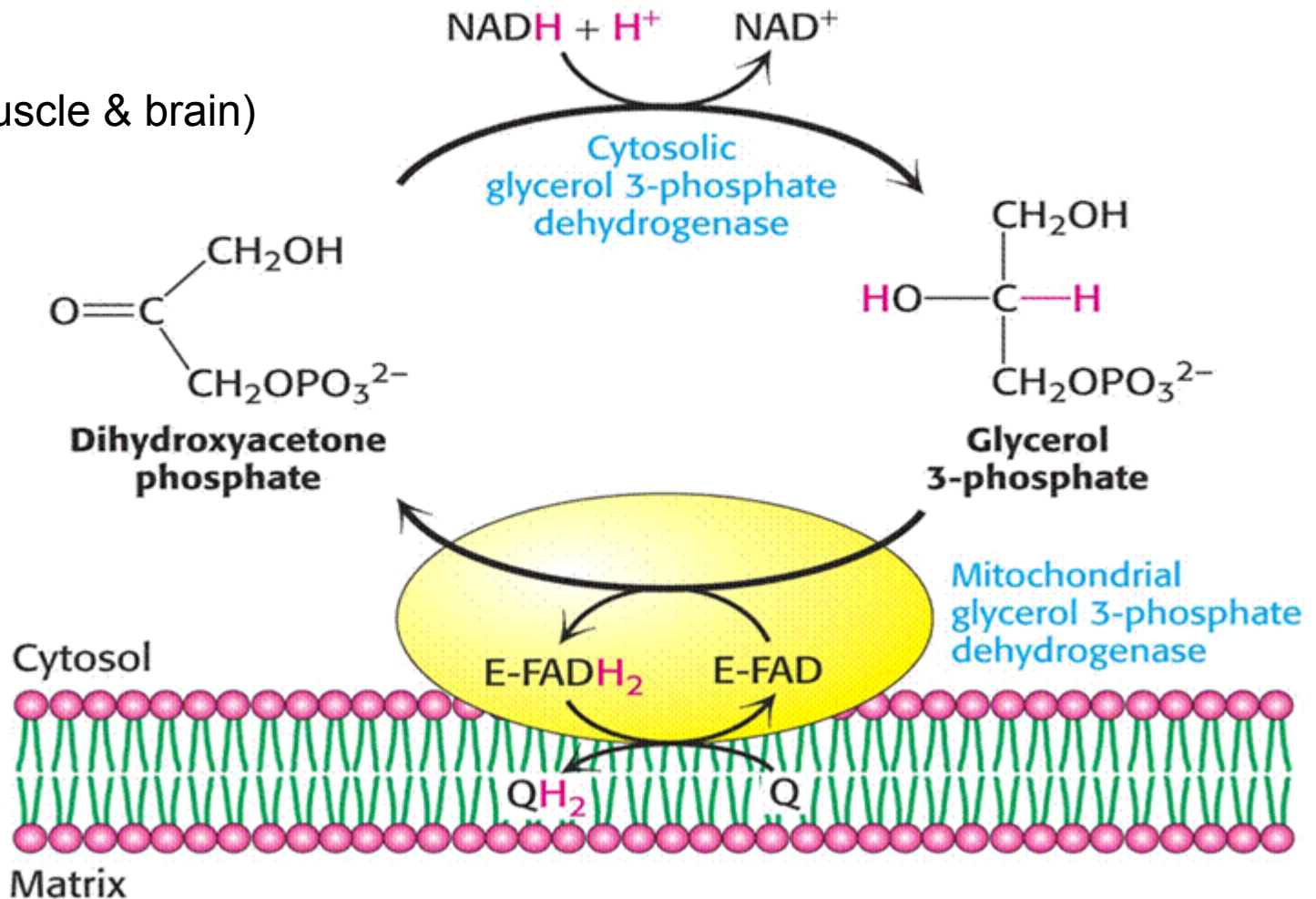
# Sumber NADH dan FADH

- Glikolisis aerob : 2 NADH
- Piruvat  $\longrightarrow$  Acetil CoA: 2NADH
- Siklus Kreb's : 3 NADH dan 1 FADH<sub>2</sub>



# Glycerol 3-phosphate shuttle: ( $\text{NADH} \xrightarrow{2e^-} \text{FADH}_2$ )

(skeletal muscle & brain)

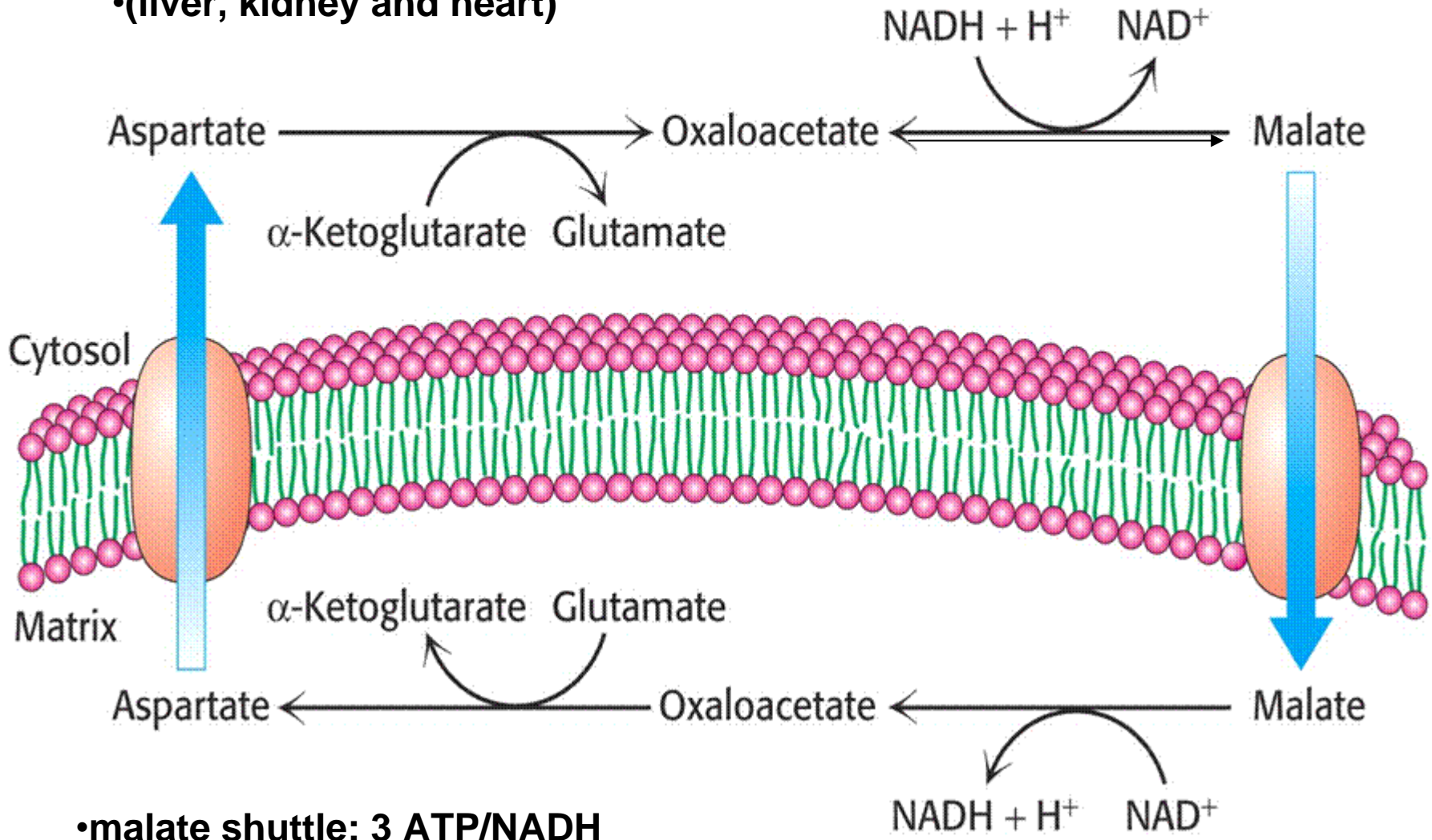


**Glycerophosphate shuttle : 2 ATP/NADH**

ATP synthesis

- Malate-aspartate shuttle: ( $\text{NADH} \xrightarrow{2e^-} \text{NAD}^+$ )

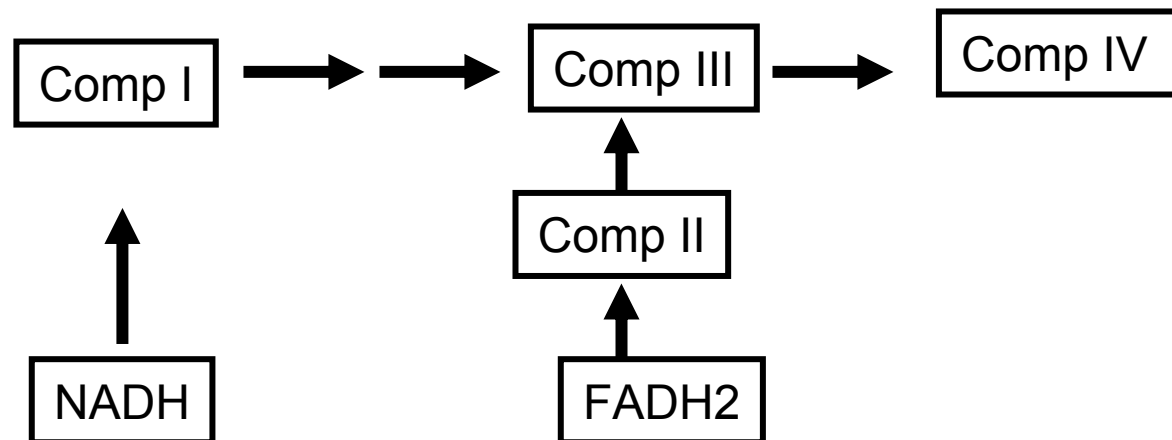
•(liver, kidney and heart)



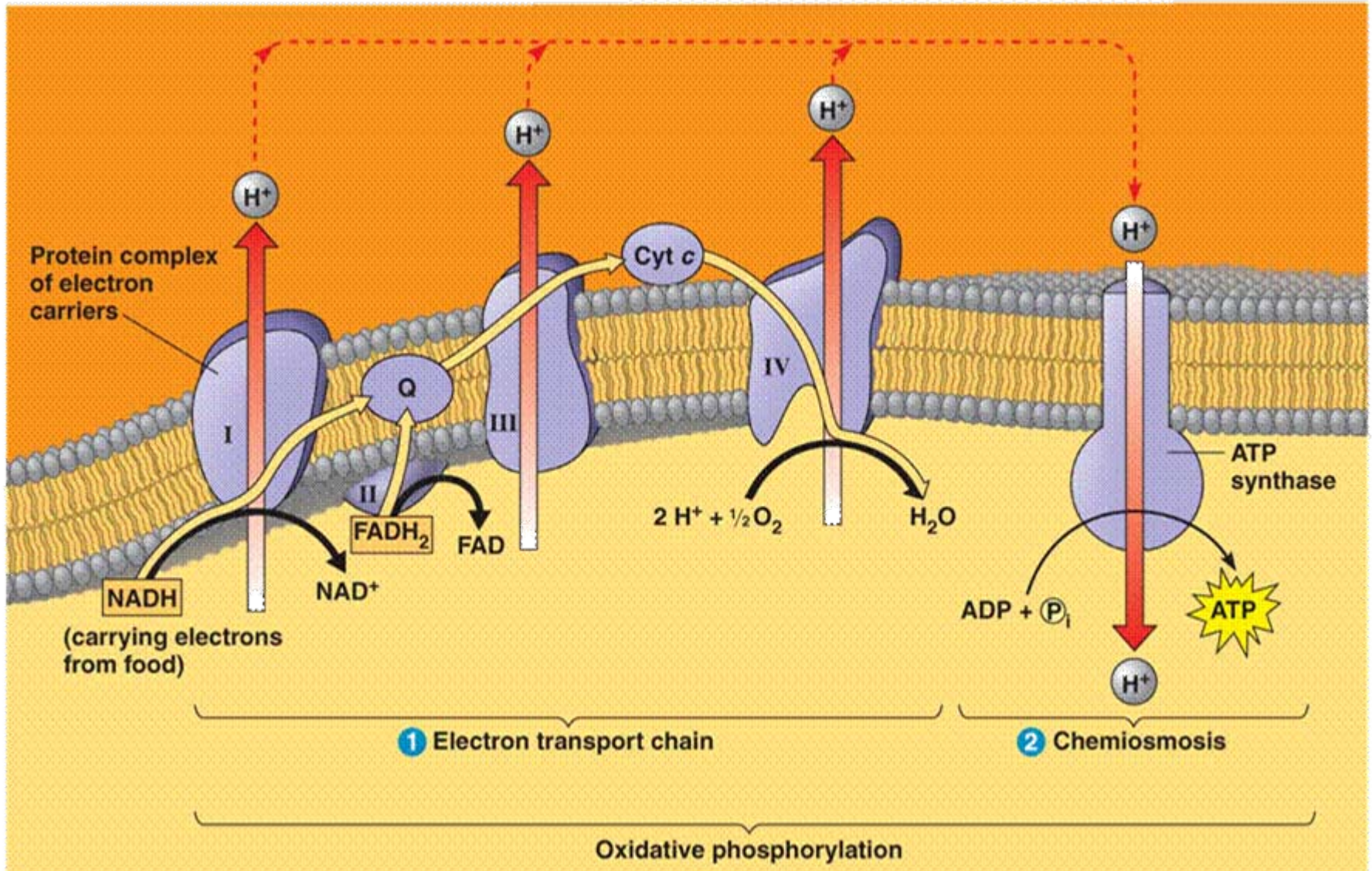
•malate shuttle: 3 ATP/NADH

# *Electron Transport chain (respiratory chain)*

- *inner mitochondrial membrane*
- Empat protein complex (I, II, III, IV).
- Coenzyme (Q) larut dalam lemak dan protein (cyt c) larut dalam air (shuttle between protein complexes)
- Electrons transfer:



# ETC



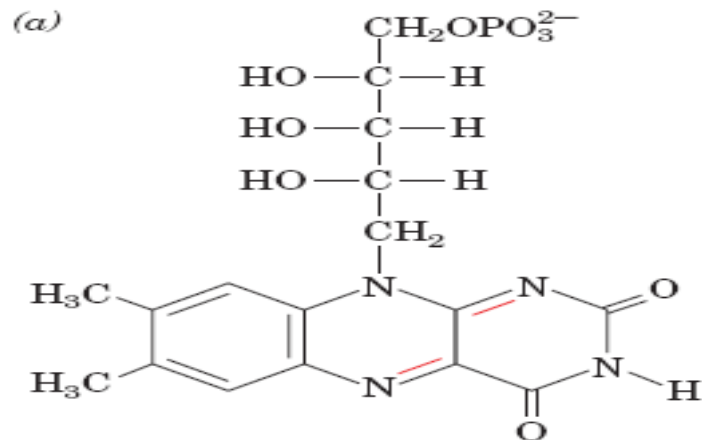


# ETC....

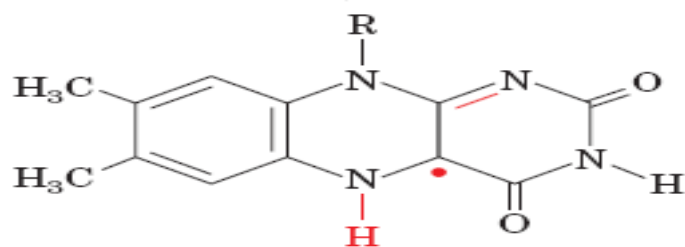
- Complex I dan II menerima electron dari sumber yang berbeda
  - NADH : Comp. I
  - FADH<sub>2</sub>: Comp.II
    - Carier e- dari Comp I & II ke Comp III: CoQ (ubiquinon)
  - Complex III: Cyt b dan c
  - Complex IV:
    - carier e- Cyt C membawa e- ke comp IV
    - butuh 4 e-, terdiri : Cu dan Fe

# Complex I

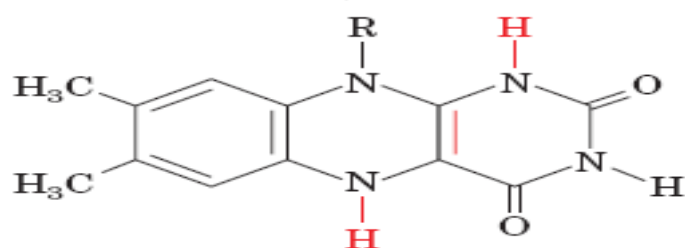
- Menerima e- dari NADH
- NADH-coenzyme Q oxidoreductase
- (FMN)Flavin mononucleotide
  - **iron-sulfur clusters : [2Fe-2S] dan [4Fe-4S] clusters**
- e- dibawa ke Co Q (ubiquinon)
- Tranlokasi 4 proton (H<sup>+</sup>) dari *matrix* ke *intercellular membrane*



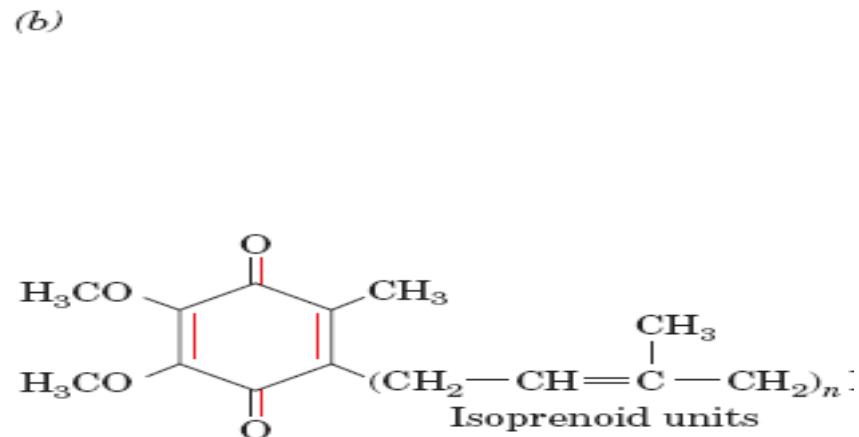
**Flavin mononucleotide (FMN)**  
(oxidized or quinone form)



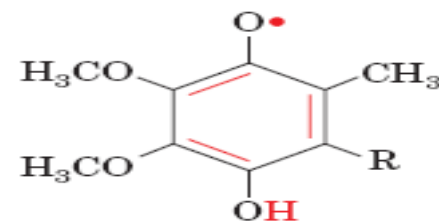
**FMNH• (radical or semiquinone form)**



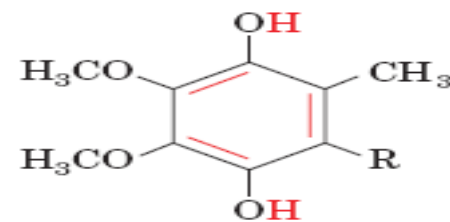
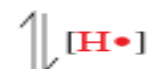
**FMNH<sub>2</sub> (reduced or hydroquinone form)**



**Coenzyme Q (CoQ) or ubiquinone**  
(oxidized or quinone form)



**Coenzyme QH• or ubisemiquinone**  
(radical or semiquinone form)



**Coenzyme QH<sub>2</sub> or ubiquinol**  
(reduced or hydroquinone form)

# Complex II

- succinate–coenzyme Q oxidoreductase
  - succinate dehydrogenase
  - Membawa e- dari succinat (FADH<sub>2</sub>) ke Co Q
  - Membawa e- dari *glycerophosphate shuttle*
- Redox Cofactor
  - Cytochromes : CybL , CybS
    - protoporphyrin IX : Hb dan mioglobin
  - Heme : Redox ETC Fe(II) → Fe(III)



# Complex III

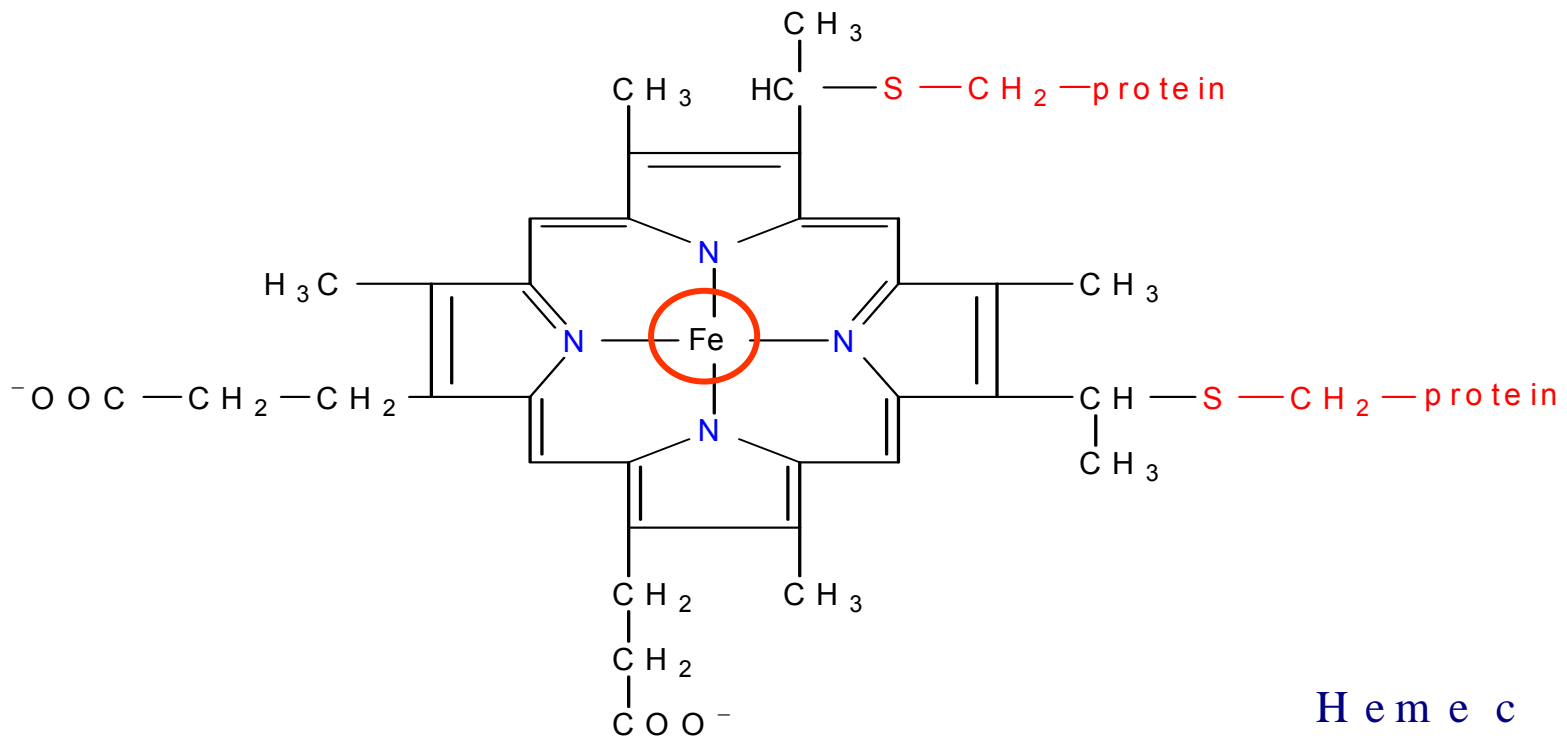
- coenzyme Q–cytochrome *c* oxidoreductase (cytochrome *bc*1)
- 2 Cyt.b, 1 cyt.c1 dan 1 [2Fe–2S] cluster
- Q-Cycle

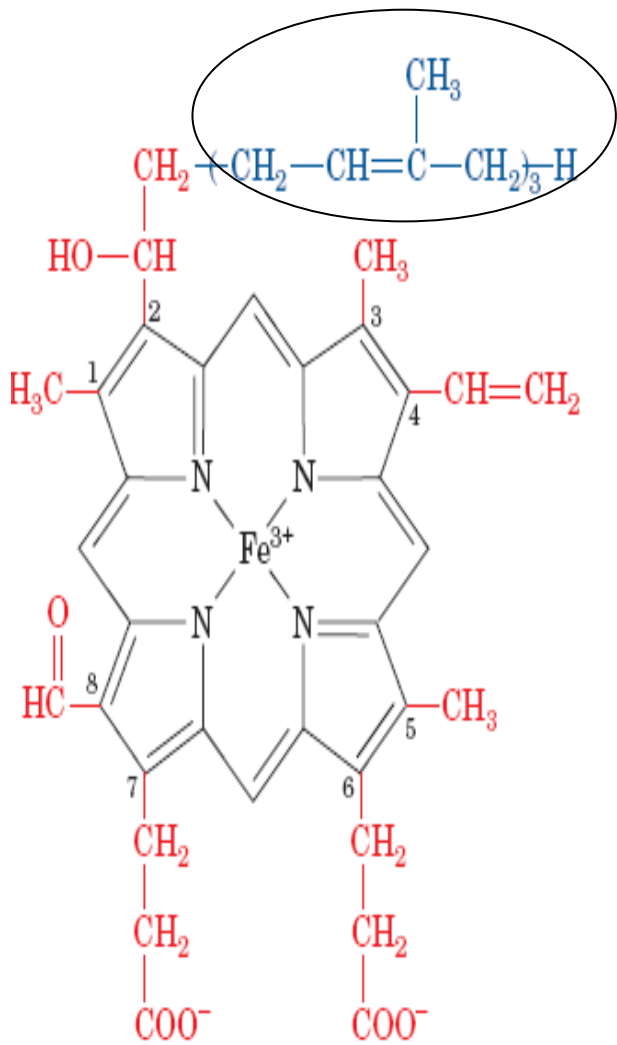
# Cytochrome

**Cytochrome** : electron carrier, tdd heme

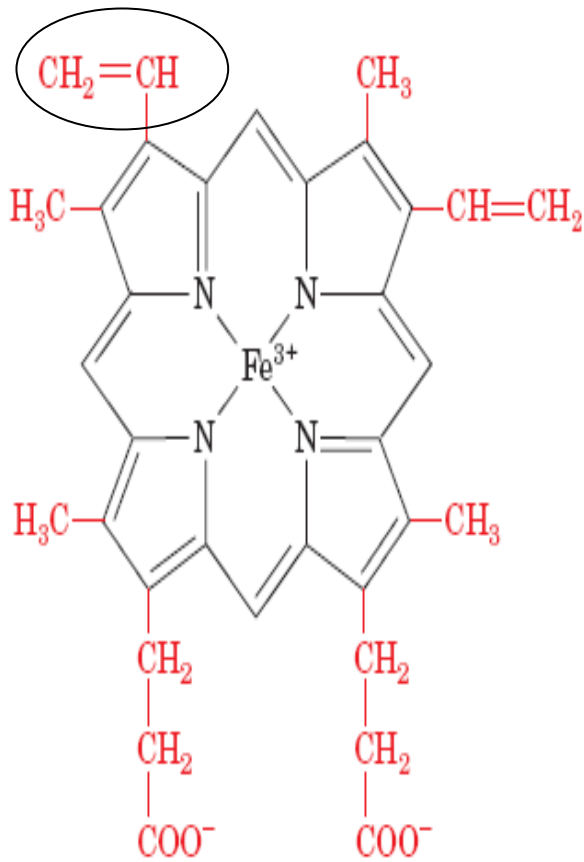
Heme: cytochrome (a, b, c) perbedaan pada *porphyrin ring*.

**Cytochrome c** : small, water-soluble protein.

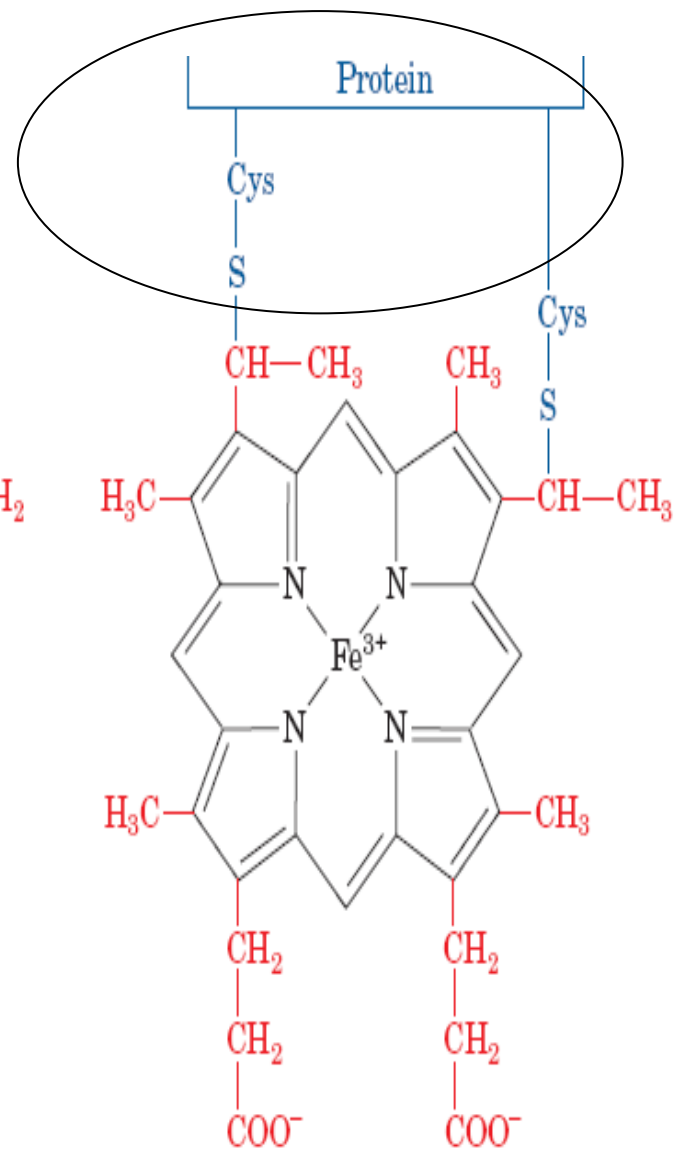




Heme *a*



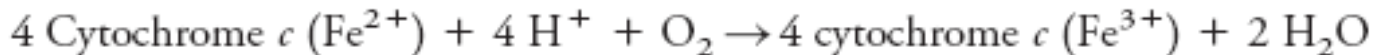
Heme *b*  
(iron-protoporphyrin IX)



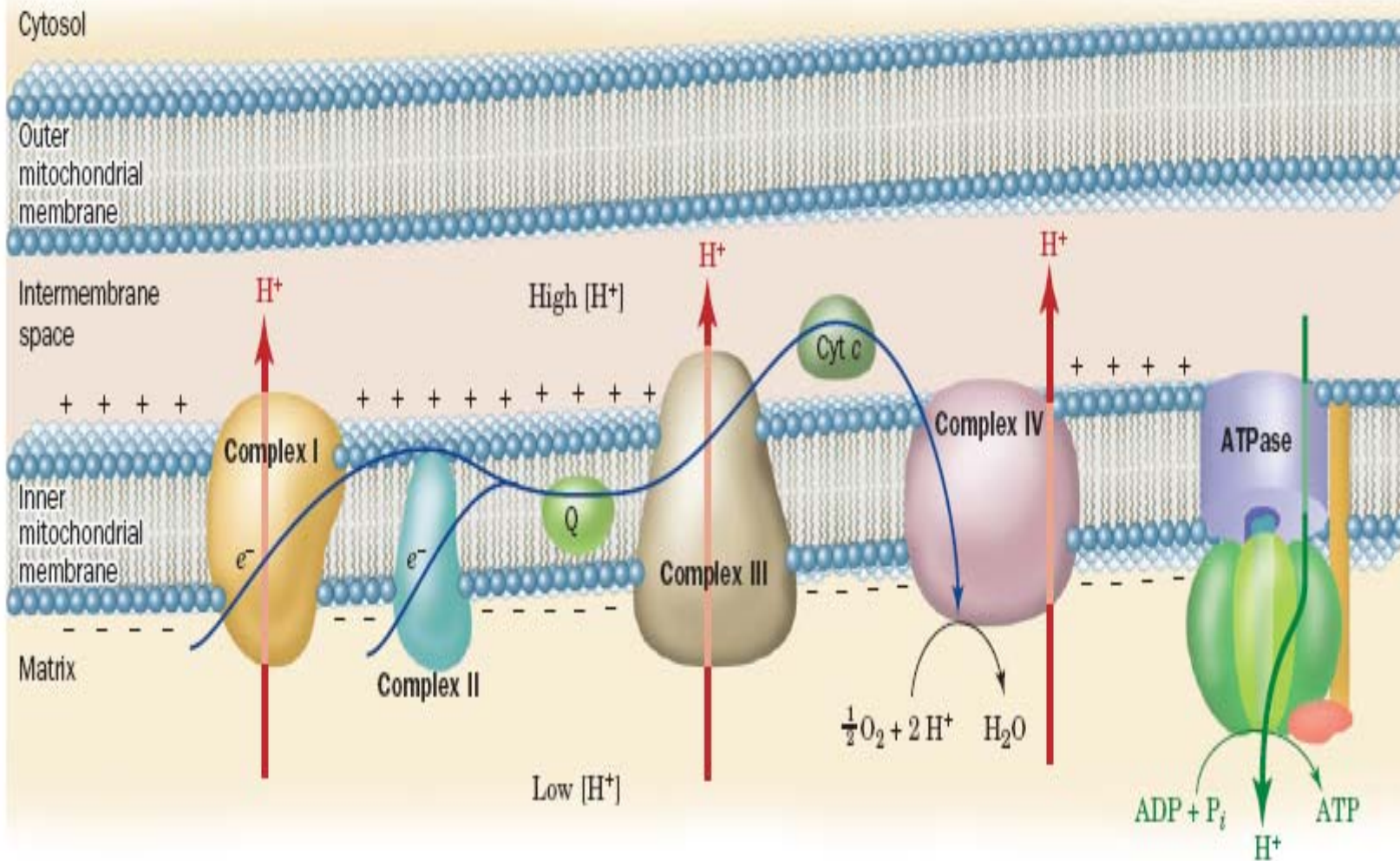
Heme *c*

# Complex IV

- acceptor ion H adalah O<sub>2</sub>
- Cytochrome *c* oxidase
- 4 redok center : cytochrome *a*, cytochrome *a*<sub>3</sub>, CuB dan CuA



- Ion H *intermembrane space* masuk ke matrix :
  - Pi + ADP → ATP (ATP-sintase)



# Inhibitor ETC

- Complex I : Rotenon, Amytal dan Piericidin A
- Complex III : Actimicycyn A
- Complex IV: Cyanida, Carbon monoxide
  - ion Cyanide berkompetisi dengan O<sub>2</sub> untuk berikatan dengan *cytochrome c oxidase* pada *oxygen-binding site*.
  - *ATP synthase* : Oligomycin
  - ADP/ATP translocase: Atractyloside, Bongkrekate

## Pembentukan ATP

- 2 electron (NADH) melewati Complex I, III, IV menghasilkan 10 proton ( $H^+$ ) pada *intermembran space*: menghasilkan 3 ATP
- 2 electron  $FADH_2$  melewati complex II, III, IV menghasilkan 6 proton pada *intermembrane space* : 2 ATP
- Energi bebas yang dibutuhkan untuk sintesis satu ATP: 40-50 kJ/mol
- Butuh ion 2-3  $H^+$  /1 ATP

# Referensi

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