* β oxidation of fatty acids

- Oxidation & splitting of two carbon unit
  ↓
  at β carbon atom

→ preparative steps of β-oxidation :-

Coenzyme A → contain B complex
pantothenic acid
β-mercaptoethanolamine

① Activation of fatty acids :-

- occur in cytoplasm

- Activated to their Coenzyme A derivative

- ATP → AMP + PPi

Enzyme - Thiokinase / fatty acyl CoA Synthetase

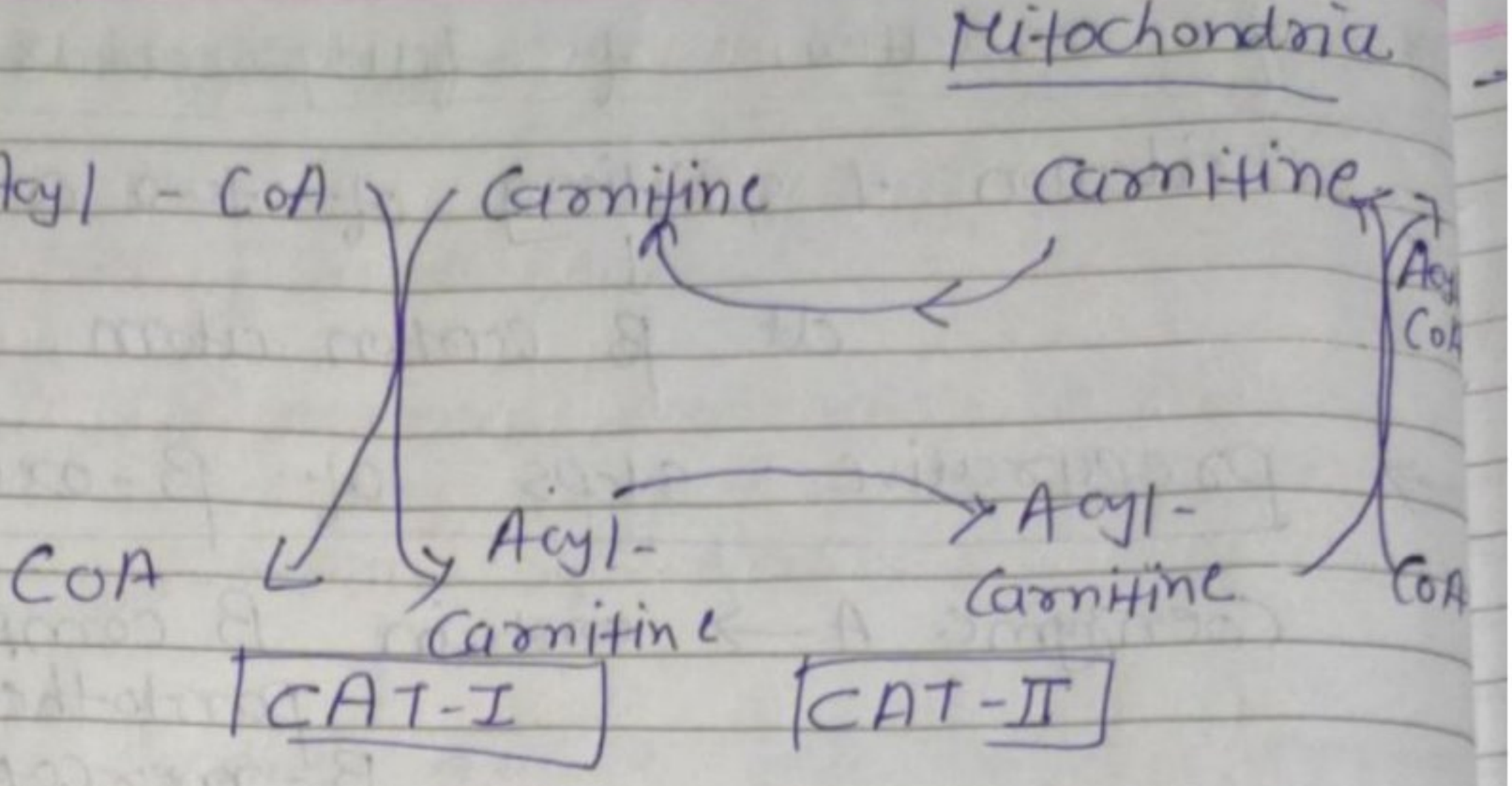
for Small chain fatty acid - thiophorase

② Carnitine : Synthesis from lysine & methionine in liver & kidney

function : Act as a transporter for transport of long chain fatty acid from cytoplasm to inner mitochondrial membrane

③ Carnitine acyltransferase

CAT-I



(4) Translocase

- Acyl carnitine
  ↓ translocase
  from cytosol to mitochondria
- Carnitine returned back to cytosolic side by translocase.

→ Energy production from beta - oxidation

e.g. palmitic acid (C 16 C)

7 cycle of β-oxidation
8 molecule of Acetyl - CoA
1 TCA cycle - 10 ATP

- 7 FADH x 1.5 = 10.5
- 7 NADH x 2.5 = 17.5
- 8 acetyl CoA x 10 = 80

2 ATP Total = 108 ATP - generated
2 ATP used

Net yield = 106 ATP

β oxidation of fatty acids

→ Fatty acid —(Synthetase / thiokinase)→ Fatty acyl CoA

ATP → AMP + PPi

Cytoplasm

Mitochondria

Fatty acyl CoA

(1) FAD → FADH2 — Acyl CoA dehydrogenase

1.5 ATP

Trans - Enoyl CoA

(2) H2O — Enoyl - CoA hydratase

L - β - Hydroxyacyl - CoA

(3) β hydroxyacyl CoA dehydrogenase — ~~Enoyl CoA~~ by NAD+ → NADH + H

2.5 ATP

β Keto acyl - CoA

(4)

Acyl CoA

Acetyl CoA

TCA Cycle (10 ATP)

* Regulation of beta-oxidation :-

(1) Availability of free fatty acid

Glucagon - ↑ FFA
Insulin - ↓ FFA

(2) CAT - I - Entry of FA into mitochondria

- Malonyl CoA ⊖ CAT - I activity
- During de novo synthesis → β-oxidation inhibited

* Defects in Beta - oxidation :-

- Deficient energy production by oxidation of long chain fatty acids.

features : Hypoketotic hypoglycemia
Hyperammonemia
Skeletal muscle weakness
Liver diseases.

Dx - ↑ Acylcarnitine — transferase I/translocase deficient

Rx - Dietary supplementation of carnitine.

* Organic aciduria :-

- Disorder of metabolism of branched chain amino acid, aromatic amino acids & citric acid cycles.

- Accumulation of organic acid in body

↓

Organic acid excreted in urine.

clf - Acidosis
vomitting
convulsion
coma
mental & physical retardation.

Diagnosis - presence of organic acid in urine by chromatography.

Treatment - Dietary restriction
Cofactor therapy
Substrate removal

e.g (1) methyl malonic acidemia
Deficiency of methyl malonyl CoA mutase or B12 coenzyme

(2) propionic acidemia - propionyl - CoA Carboxylase

(3) MCADH deficiency - MCADH

(4) LCADH deficiency - LCADH

(5) Glutaric aciduria - Glutaryl - CoA dehydrogenase

* **Oxidation of odd chain fatty acids :-**

→ 3 C - propionyl Co-A

→ metabolism of propionic acid :

Propionyl CoA + CO_2 —(ATP, Biotin, ADP; Propionyl CoA carboxylase)→ D-methylmalonyl CoA

D-methylmalonyl CoA —(Racemase)→ L-methylmalonyl CoA

L-methylmalonyl CoA —(Adenosyl B12, mutase)→ Succinyl CoA

Succinyl CoA → TCA cycle → Oxaloacetate

→ propionic acid derived from -

metabolism of odd chain fatty acid
- Isoleucine
- Valine

→ FA not used for gluconeogenesis.

→ odd chain FA used for gluconeogenesis

↓

enter in TCA cycle after CO_2 elimination steps

present in cow's milk. - odd chain F.A.

→ Inborn error of propionate metabolism :-

① propionyl CoA carboxylase deficiency
↓
propionic acidemia
ketoacidosis
Developmental abnormalities.

② Methylmalonic aciduria :-
↓
- Defective formation of adenosyl B12 & deficient mutase activity.
↓
- Accumulation of methylmalonate
↓
metabolism in brain affected
↓
mental retardation.

* Alpha oxidation of fatty acid :-

- Removal of carbon atom from Carboxyl end & cause oxidation of FA
- Important in brain
- No activation of ~~acetyl~~ CoA FA required
- Occur in endoplasmic reticulum
- Does not generate energy.

Fatty acid

↓

Hydroxylation at α-carbon

↓

α keto acid

↓ Decarboxylation

CO_2 + FA with 1 carbon less

use - FA which has methyl group at β carbon - block beta oxidation

- Dietary methylated FA - phytanic acid (milk)

- Refsum disease :- Lack of α hydroxylase (phytanic acid oxidase)

- Accumulation of phytanic acid

↓

Severe neurological symptom - polyneuropathy, retinitis pigmentosa, nerve deafness, cerebellar ataxia.

R. - Restrict dietary intake of phytanic acid

- Infantile refsum disease - peroxisomal disorder

- Accumulation of phytanic acid + VLFA.

* Omega oxidation :

- occur in mitochondria

- Use NADPH & cytochrome P450.

- CH_3 Hydroxylase CH_2OH. $\xrightarrow{NAD^+ \; NADH}$ COOH

Imp - When β oxidation defective &
Dicarboxylic acid excreted in urine
↓
dicarboxylic aciduria