

Biosynthesis of Heme

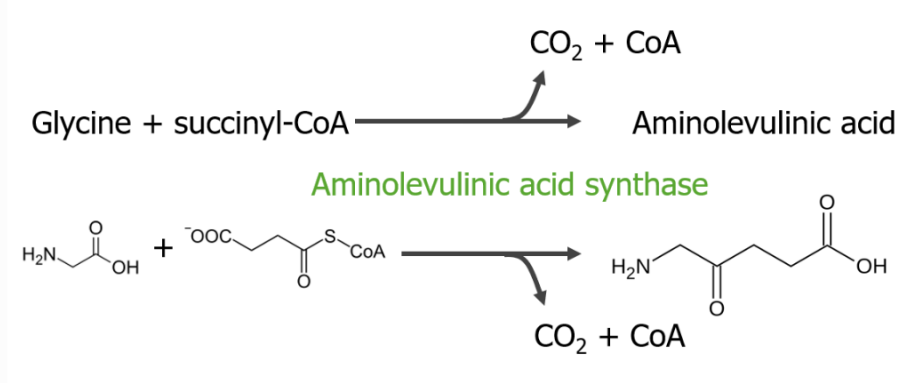
• Step 1 ↓↓

Is the synthesis of Amino-levulinic acid.

Condensation of glycine & succinyl-CoA → forming delta amino-levulinic acid (ALA)

- Enzyme name → Aminolevulinic acid synthase ALA synthase (Rate limiting step)
- Coenzyme → pyridoxal phosphate.
- Site → Mitochondria

With loss of 1CO₂ (Decarboxylation)
And removal of Co A

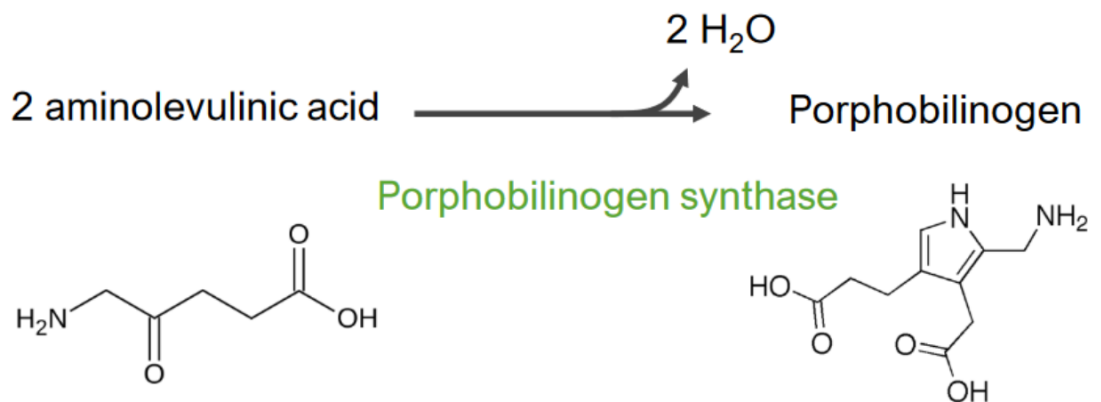


• Step 2

Formation of porpho-bilinogen PBG.

Moving out to the cytosol, 2 molecules of aminolevulinic acid condense to form PBG (a pyrrole), removing 2 molecules of water in the process (Dehydration reaction)

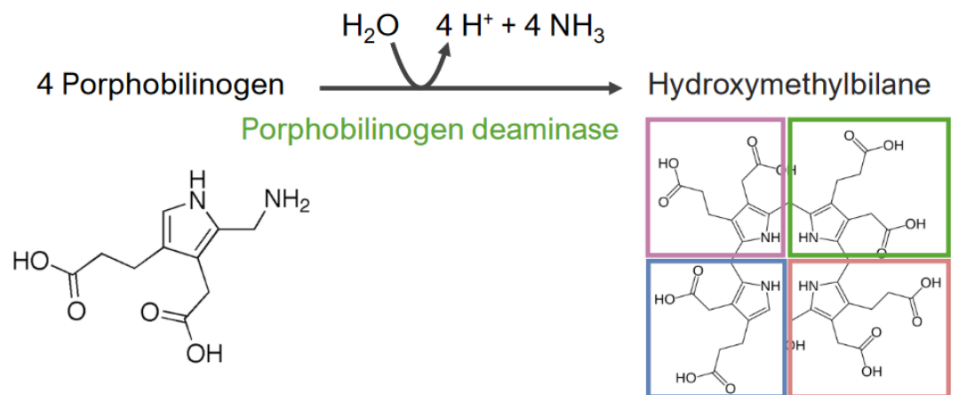
- Enzyme → **PBG synthase (porphobilinogen synthase)/ ALA dehydratase**
- Site → cytosol
- This step is affected by lead poisoning. (Aminolevulinic acid dehydratase is inhibited by lead.)



- **Step 3**

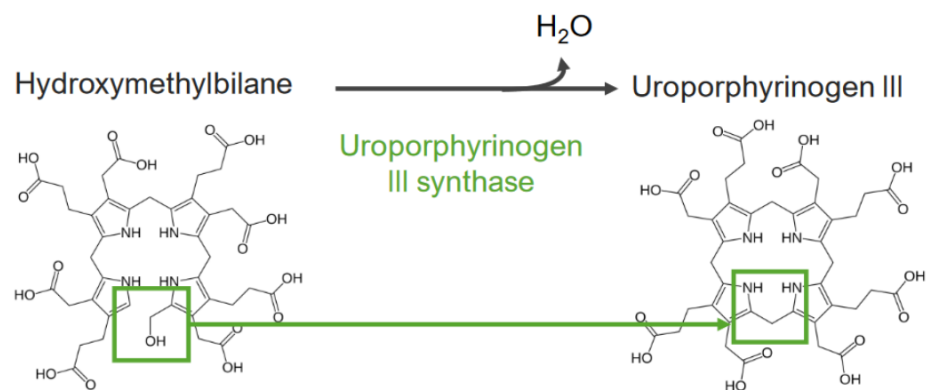
Is the formation of Hydroxy-methyl-bilane HMB (Linear molecule) .

- 4 molecules of porphobilinogen PBG condense to form HMB
- Enzyme name → Porphobilinogen deaminase / HMB synthase
- Site → cytosol
- Molecules are joined through elimination of an amino group.



- **Step 4**

- Step 4 is the formation of **uroporphyrinogen (UPG)**.
- **HMB (a linear compound) is converted to UPG III cyclic :**
 - Enzyme: UPG III synthase.
 - Coenzyme: UPG III cosynthase
 - Site: cytosol
- **Cyclization of the linear HMB to forms UPG III , the 1st cyclic intermediate of the pathway.**



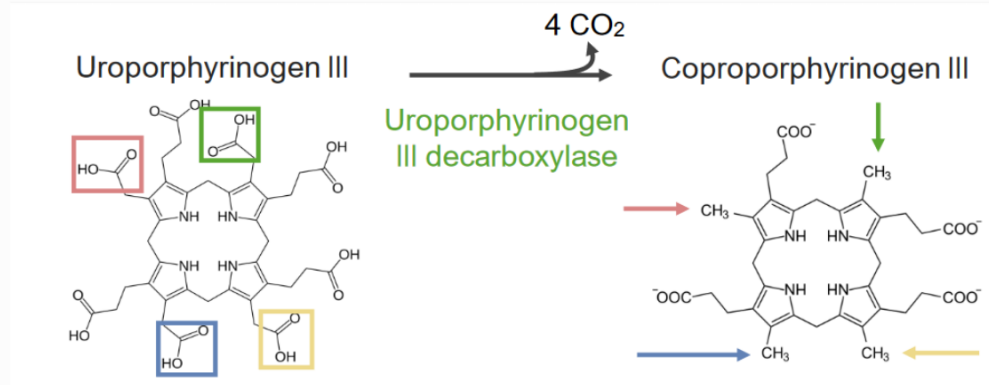
- Step 5

Synthesis of coproporphyrinogen (CPG) III.

Involves the decarboxylation of UPG III to CPG III with the elimination of 4 CO₂ molecules.

All 4 acetyl side chains are decarboxylated to methyl groups.

- Enzyme: uroporphyrinogen decarboxylase.
- Site: cytosol

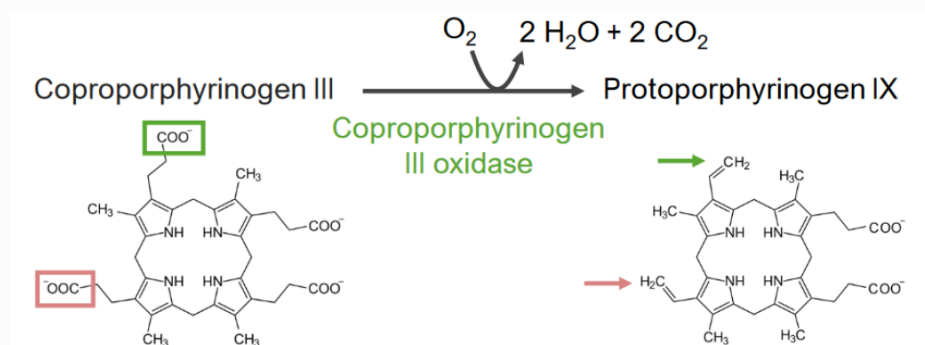


- Step 6

Synthesis of protoporphyrinogen (PPG)

Oxidative decarboxylation converts 2 of 4 propionyl side chains to vinyl groups (catalyzed by Coproporphyrinogen oxidase)

- Molecular oxygen is required for this reaction.
- Enzyme: CPG oxidase (CPOX)
- Site: mitochondria

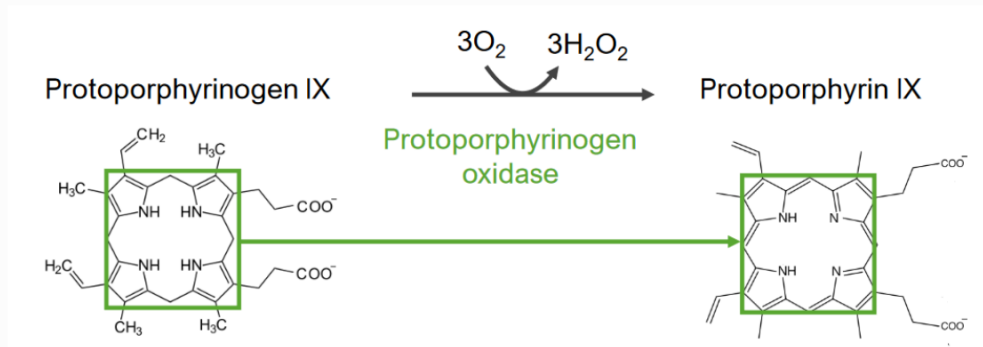


Step 7

Generation of protoporphyrin (PP).

PPG IX is converted to PP IX by oxidation.

- Oxidation adds double bonds
- Enzyme: PPG oxidase (PPOX)
- Site: mitochondria



Step 8

Step 8 is the generation of heme.

Fe^{++} is added to protoporphyrin IX (PP) :

The ferrous ion is inserted in the middle of the porphyrin ring

- Enzyme: ferrochelatase (FECH)/heme synthase.
- A homodimeric enzyme containing 2 iron-sulfur clusters
- Site: mitochondria

