ANABOLISM II: Biosynthesis of Fatty Acids & Lipids

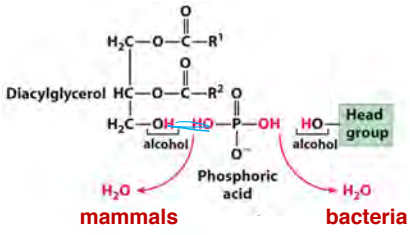
Lipid Biosynthesis

Biosynthesis of Membrane Phospholipds

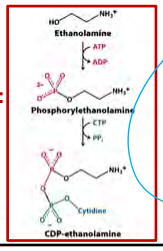
Glycerophospholipid Biosynthesis requires Activation by CTP

- Begin with phosphatidic acid (microorganisms) or 1,2 Diacylglycerol (mammals)
- Both activate precursors using CTP
- Bacteria use phosphatidate and attach head group to C-3 phosphate group
  - Make CDP-diacylglycerol from CTP and phosphatidic acid
- Mammals use CDP-alcohol and attach head group to diacylglycerol
  - Make CDP-alcohol from CTP and choline or ethanolamine

Attach head group by condensation here:



Example:



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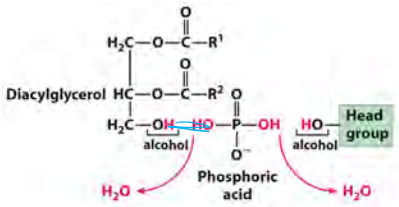

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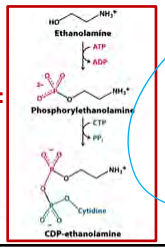

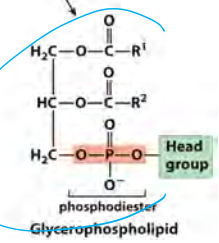

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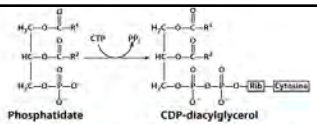
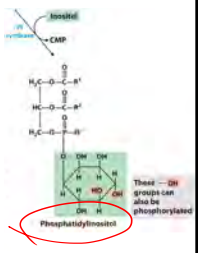


Glycerophospholipid Synthesis in *E. coli*

- For **Phosphatidylserine** and **phosphatidylinositol**, the free alcohol does a nucleophilic attack on the CDP-activated phosphatidate.
- Phosphatidylserine is decarboxylated to ***phosphatidylethanolamine.***
  - enzyme is phosphatidylserine decarboxylase
- Phosphatidylethanolamine acted on by *S*-adenosylmethionine (SAM) adds three methyl groups to amino group → ***phopshatidylcholine (lecithin).***
  - catalyzed by methyltransferase
- **Cardilipin** is from the condensation of two phosphatidyl glycerols, which are formed from glycerol 3-phosphate.



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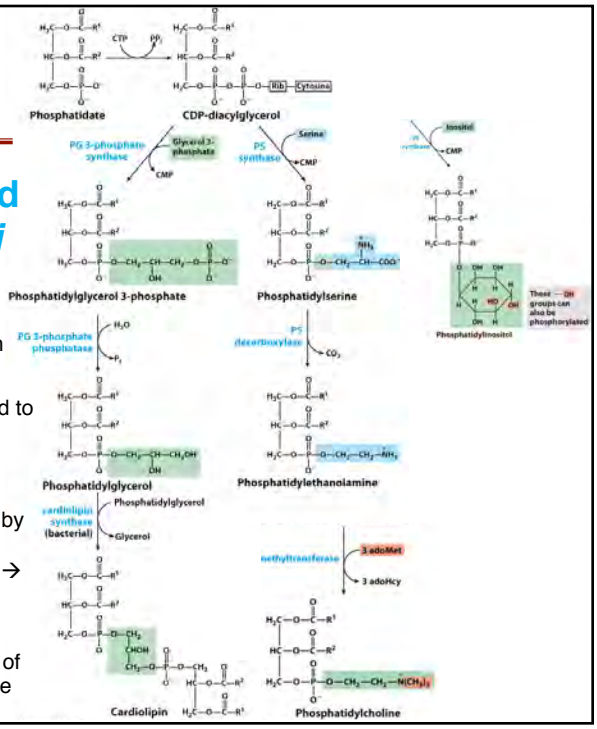
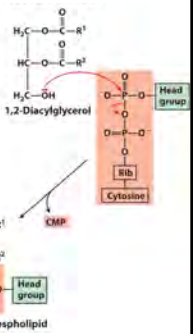


Lipid Biosynthesis

Synthesis of Phosphatidyl-choline, -ethanolamine, and -serine and in Mammals



- Either one of the alcohols is activated by attaching to CDP.
- CDP-alcohol is used to couple this to diacylglycerol

- Phosphatidyl-serine is made "backwards" from phosphatidyl-ethanolamine or phosphatidyl-choline via head-group exchange reactions.
  - catalyzed by specific synthases
  - pathway "salvages" the choline

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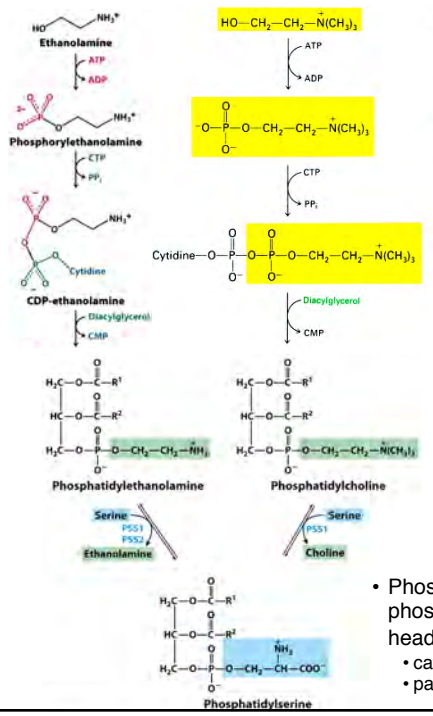

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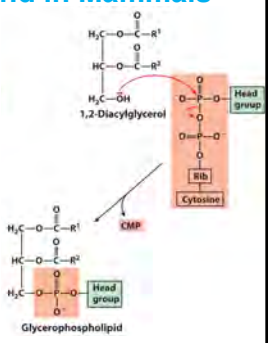

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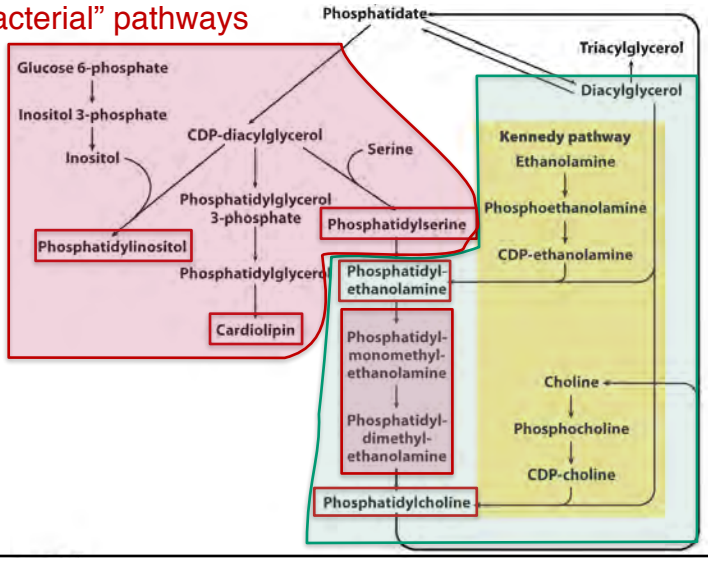
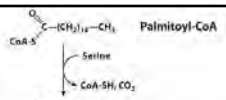
Lipid Biosynthesis

Synthesis of Phosphatidyl-choline, -ethanolamine, -serine, -inositol, and -diglycerol in Yeast

"Bacterial" pathways

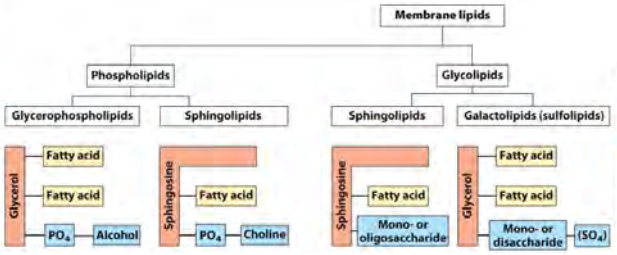


"Mammalian" pathways

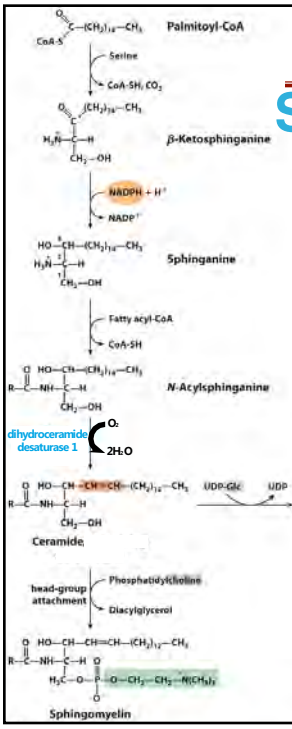


Lipid Biosynthesis

Synthesis of Sphingolipids



- Sphingosine comes from amino acids + fatty acids; serine + palmitate
- Condensation of palmitoyl-CoA and serine, forms β-ketosphinganine
- Reduction, acylation, oxidase yields N-acyl-sphinganine (a ceramide).



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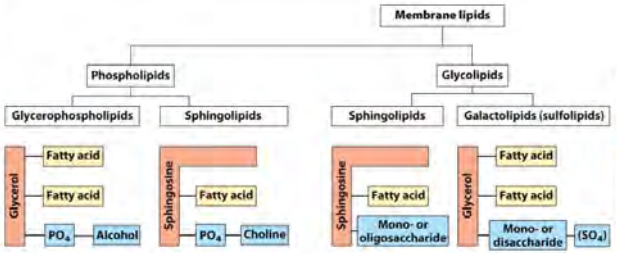

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