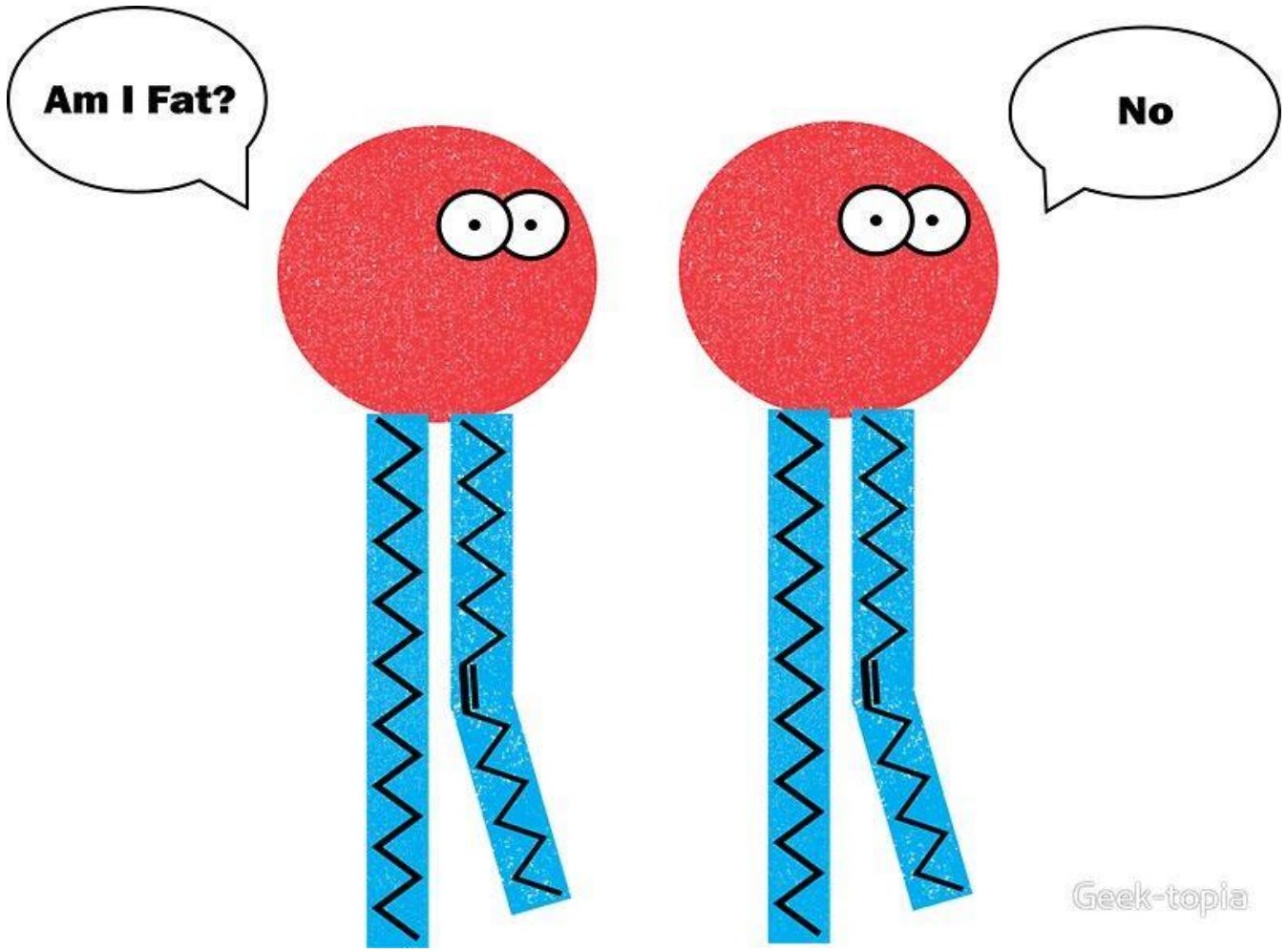
Metabolism of Glycerophospholipids

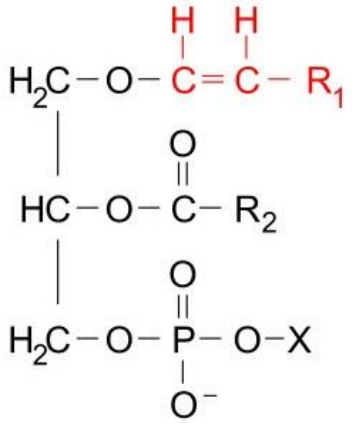


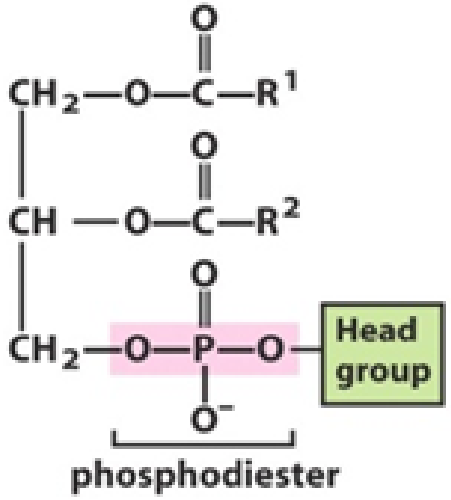
Dr. Diala Abu-Hassan

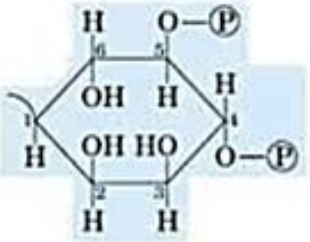
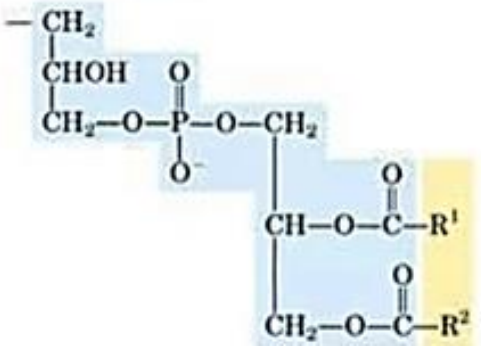
Lippincott's Biochemistry, Ch. 17

Structure and Classification of Glycerophospholipids

- Phosphatidic acids
- Phosphatidylcholine (lecithin)
- Phosphatidylethanolamine
- Phosphatidylserine
- Phosphatidylinositol
- Cardiolipin
- Plasmalogens



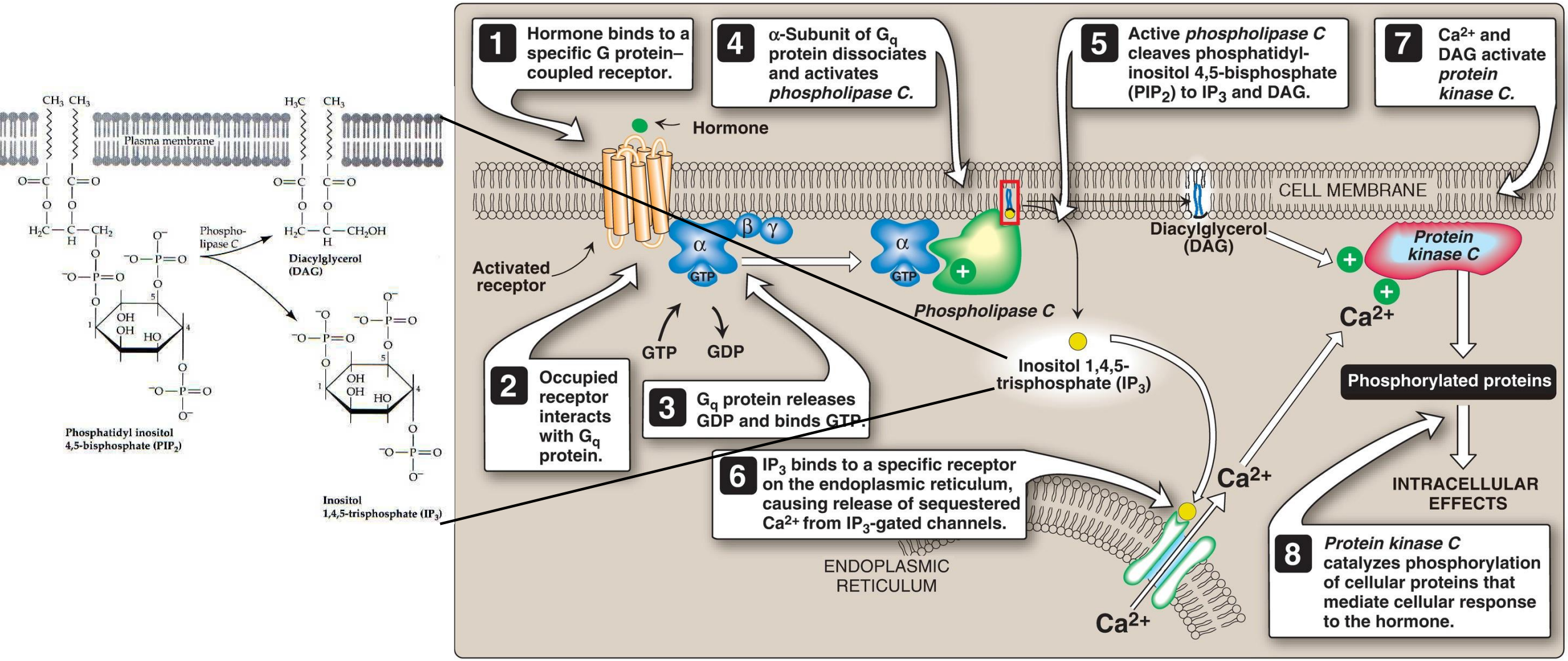


Phosphatidic acid	—	—H
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$
Phosphatidylserine	Serine	$-CH_2-\underset{COO^-}{CH}-\overset{+}{N}H_3$
Phosphatidylglycerol	Glycerol	$-CH_2-\underset{OH}{CH}-CH_2-OH$
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate	
Cardiolipin	Phosphatidyl-glycerol	

Why do we need to make glycerophospholipids?

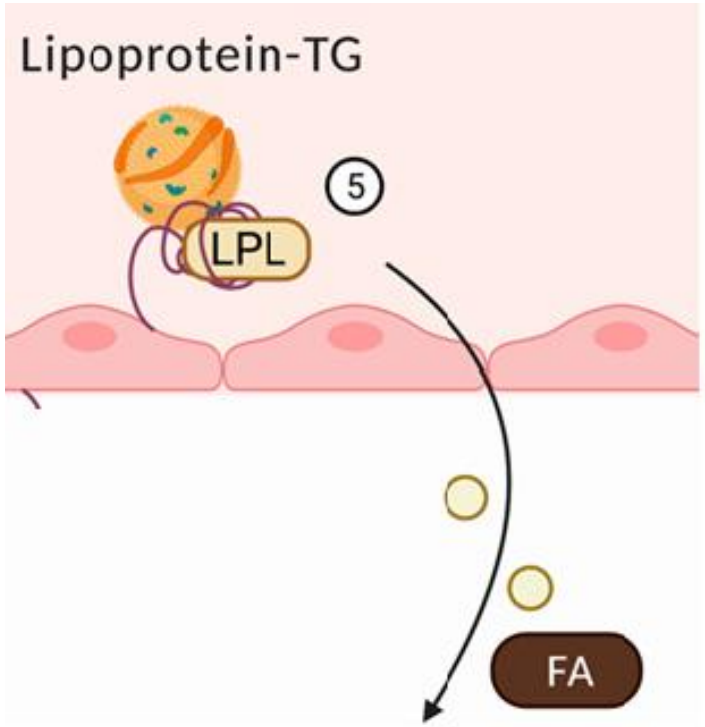
Important functions of glycerophospholipids other than their structural function in membranes

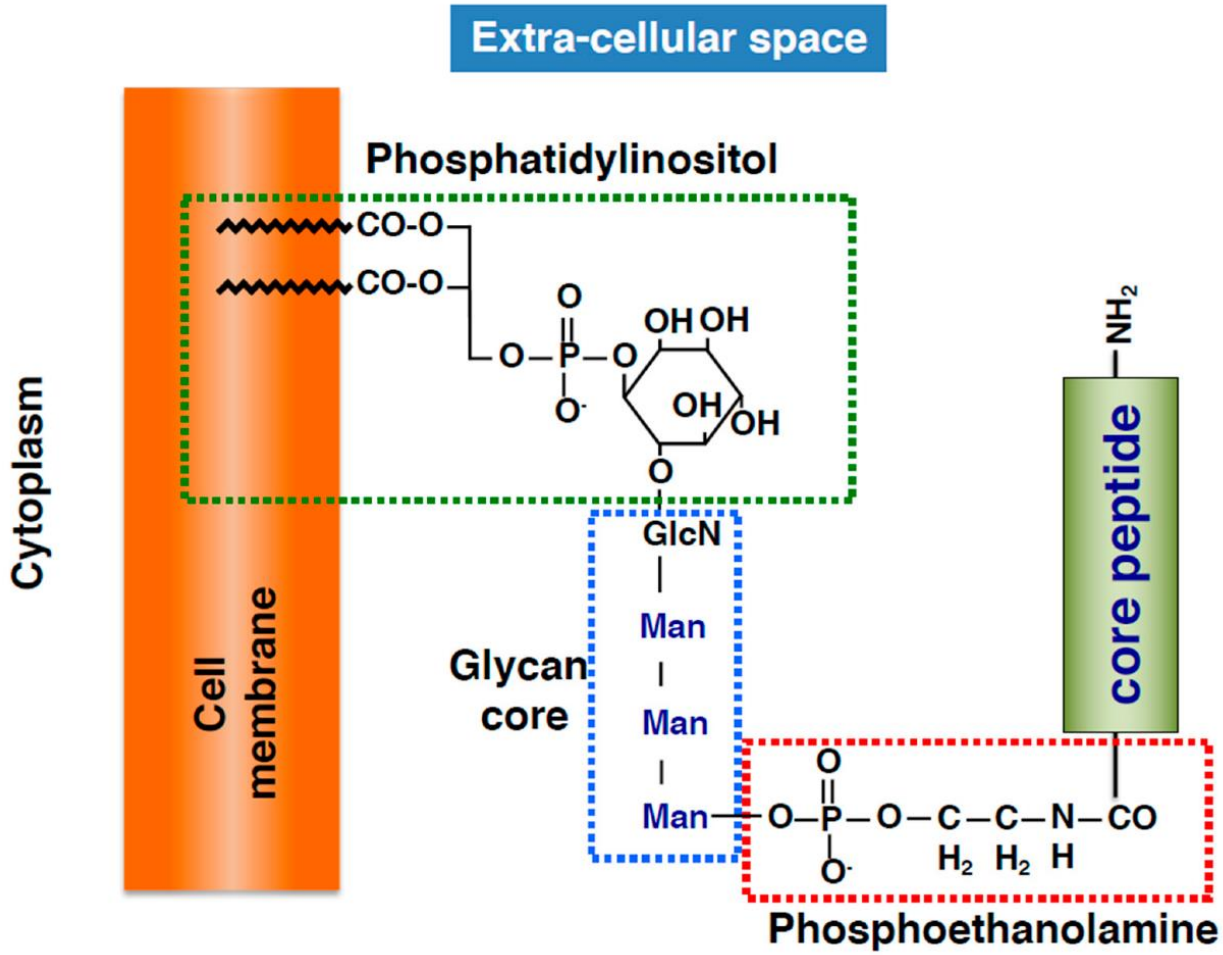
Signaling by PIP2 products



GPI for membrane attachment

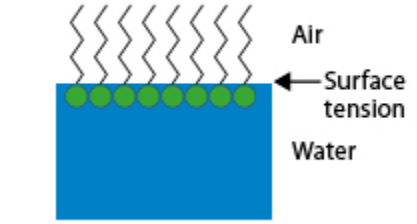
- Glycosyl phosphatidylinositol (GPI) attaches proteins to the plasma membrane.
- Advantage: lateral mobility
  - Example: lipoprotein lipase

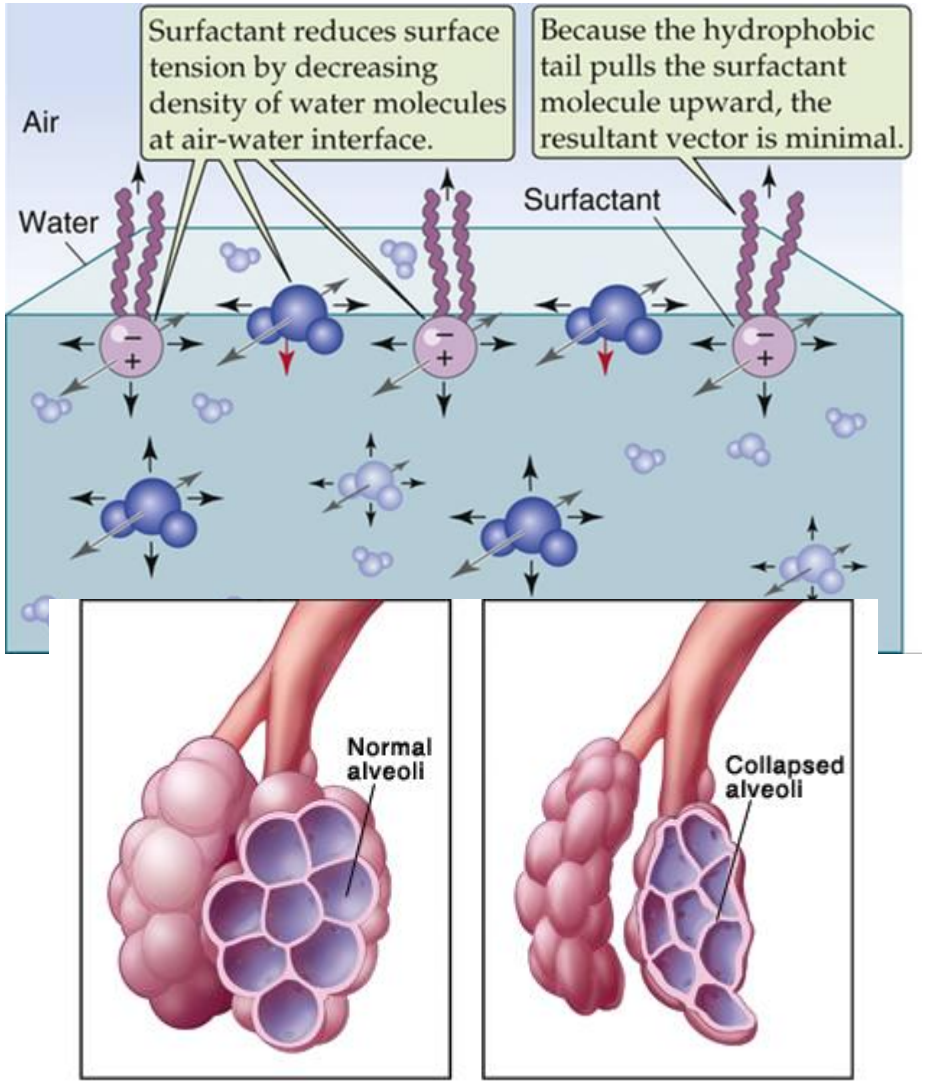




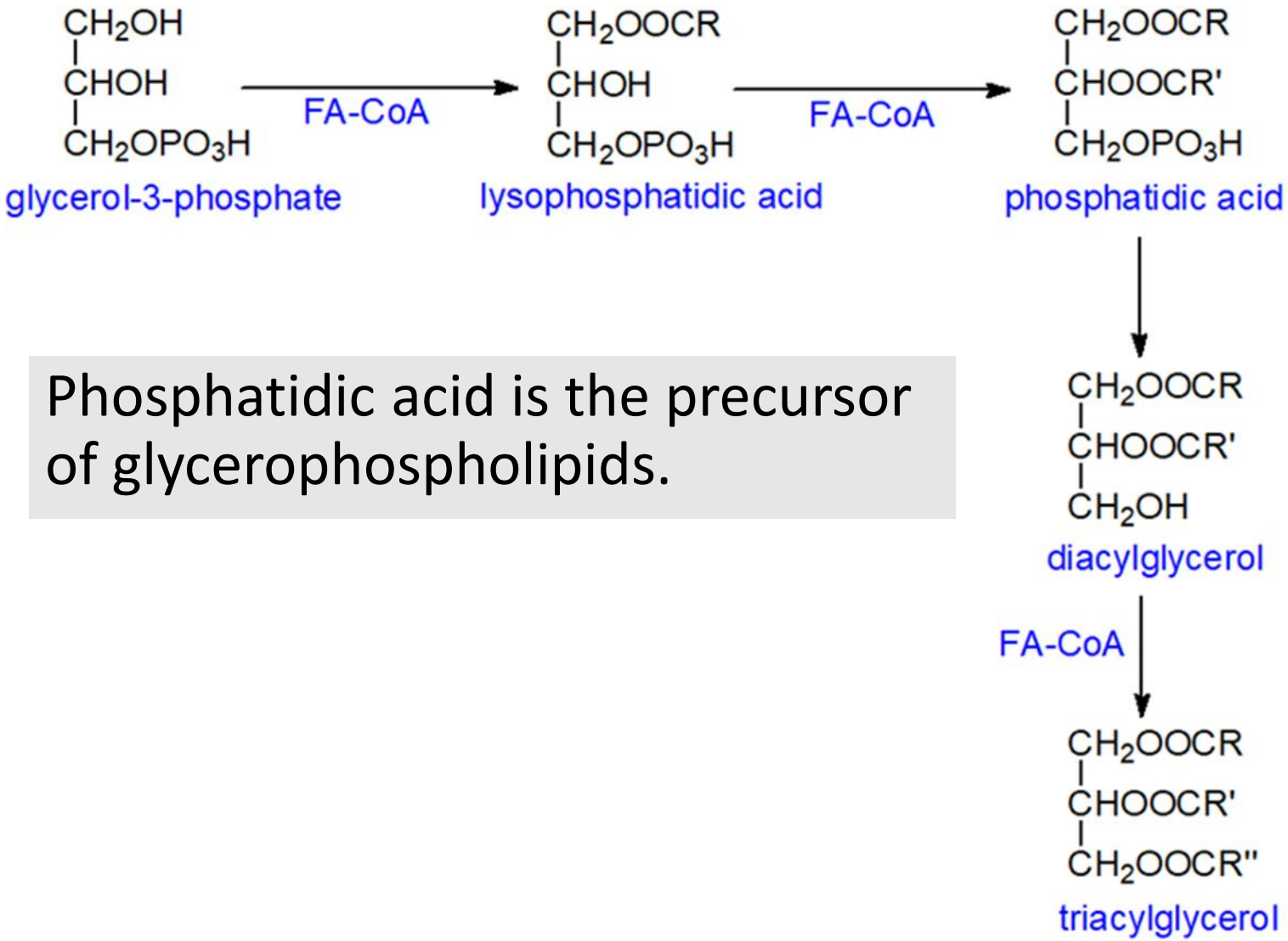
Application: Surfactants

- Surfactants are a complex mixture of lipids (90%) and proteins (10%) that make the extracellular fluid layer lining the alveoli and are secreted by type II pneumocytes in the lungs.
- Dipalmitoylphosphatidylcholine (DPPC) is the major lipid in surfactants.
- Surfactants serve to decrease the surface tension of the fluid layer allowing reinflation of alveoli and preventing alveolar collapse (atelectasis).
- Respiratory distress syndrome (RDS) in preterm infants is associated with insufficient surfactant production and/or secretion.
- Prenatal administration of glucocorticoids shortly before delivery to induce expression of specific genes.





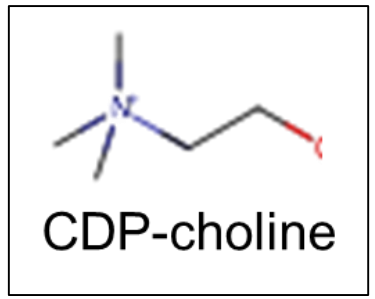
Synthesis of phosphatidic acid

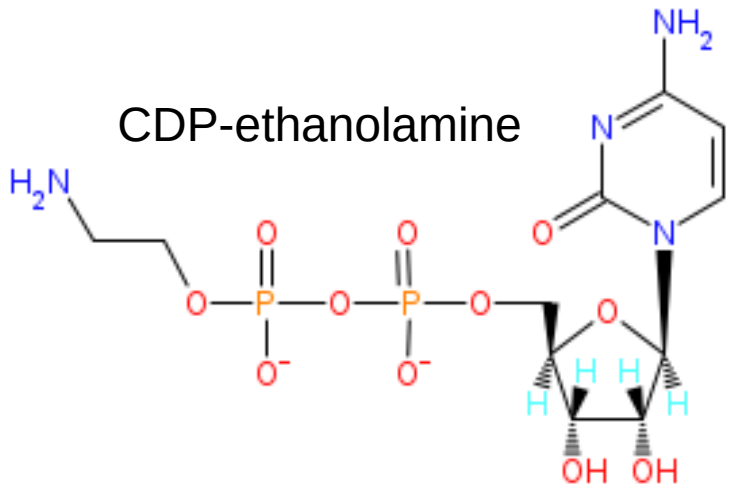


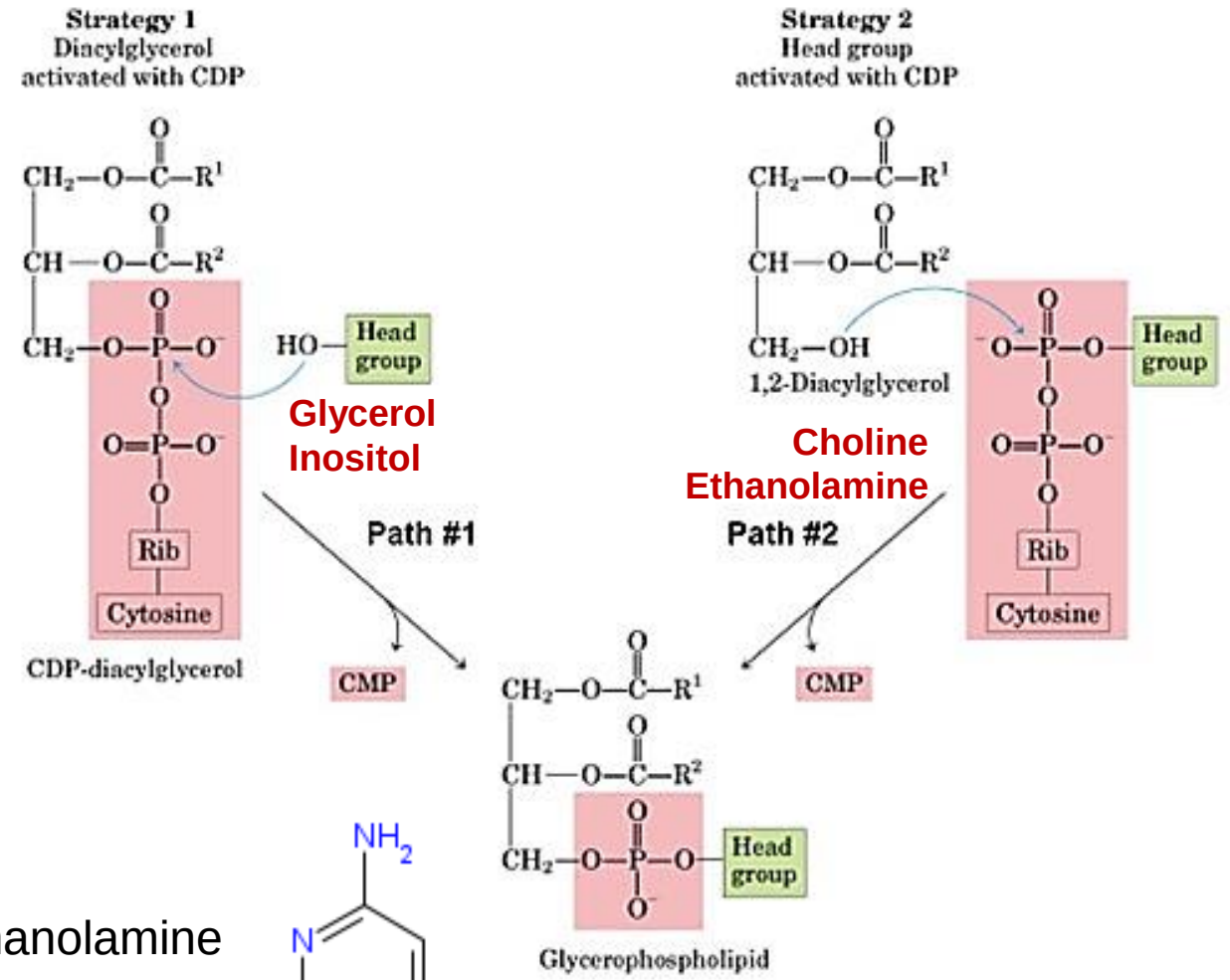
Phosphatidic acid is the precursor of glycerophospholipids.

Synthesis

- Location: smooth ER
  - Except for ether lipids
- Activation by CDP is necessary. Either:
  - CDP-DAG (glycerol, inositol)
  - CDP-alcohol (choline, ethanolamine)
- Sources of choline and ethanolamine
  - diet
  - synthesis
  - re-cycling from the turnover of pre-existing phospholipids
- Diet is still essential since demand > supply





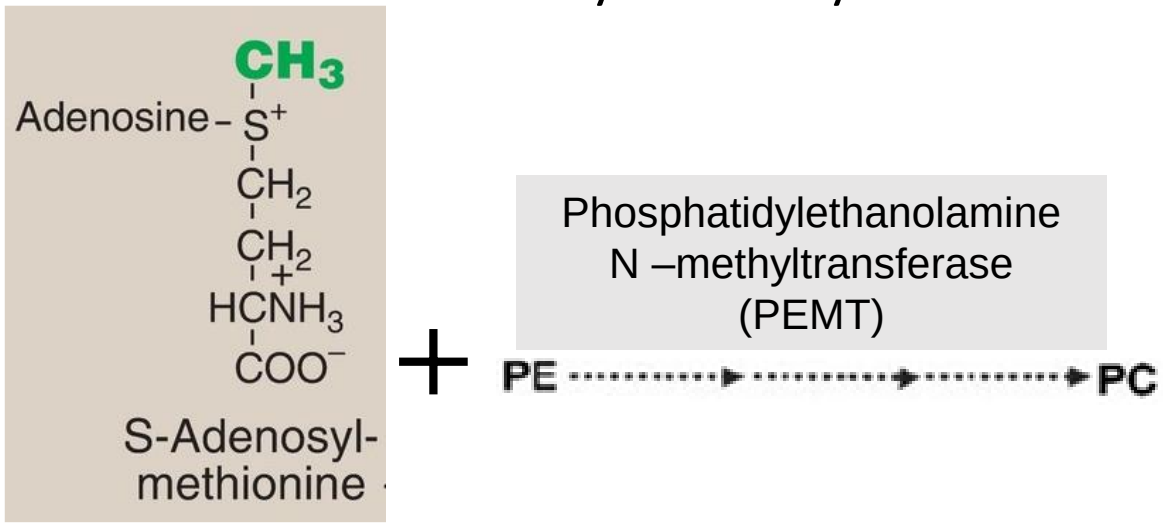


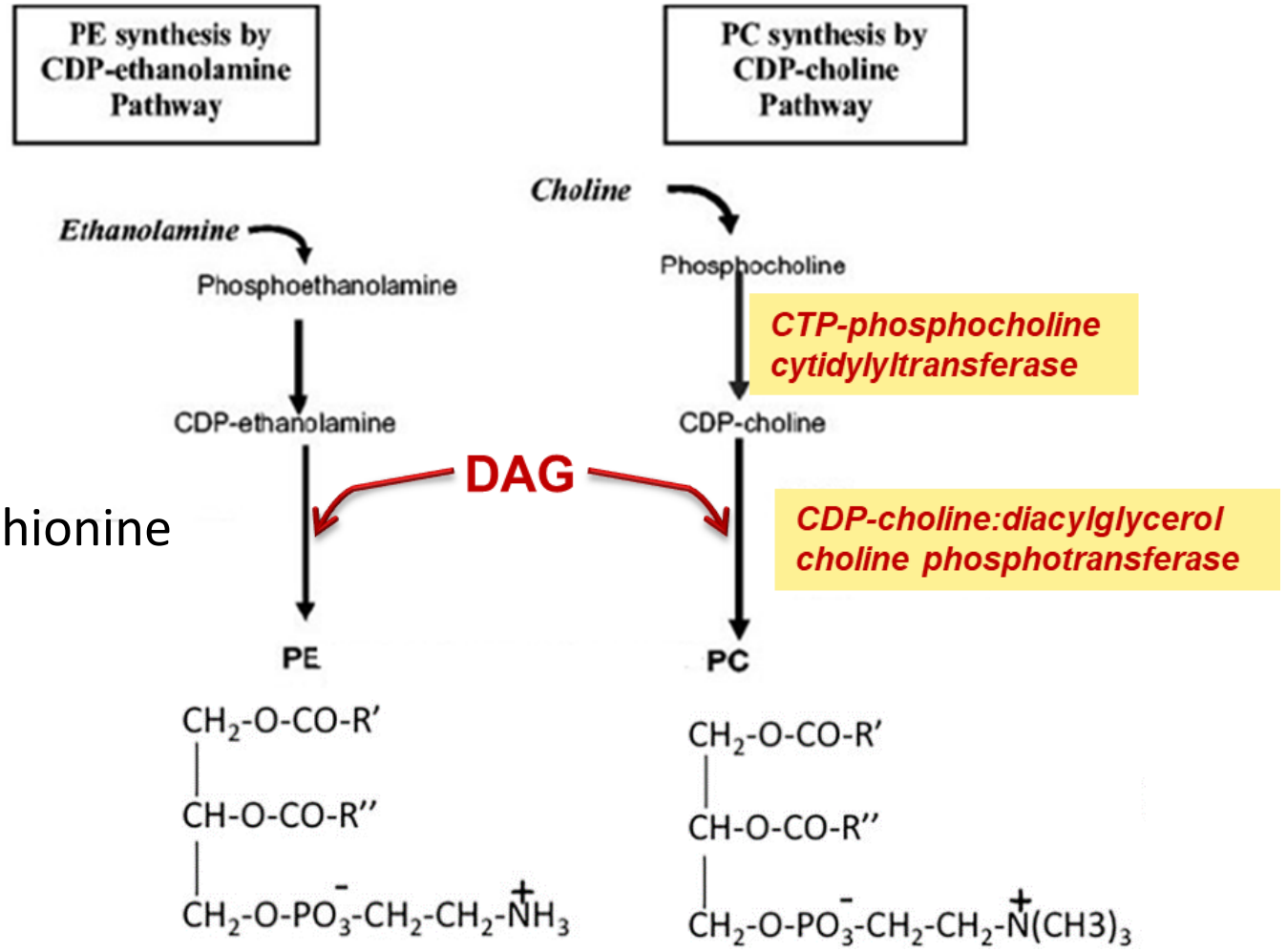
Synthesis of *ph*-choline and *ph*-ethanolamine

- Choline or ethanolamine are phosphorylated by *kinases*, then activated by *transferases* to form, CDP-choline or CDP-ethanolamine.
- Choline phosphate or ethanolamine phosphate is transferred from the nucleotide (releasing CMP) to DAG.

➢ Synthesis of ph-choline from ph-ethanolamine

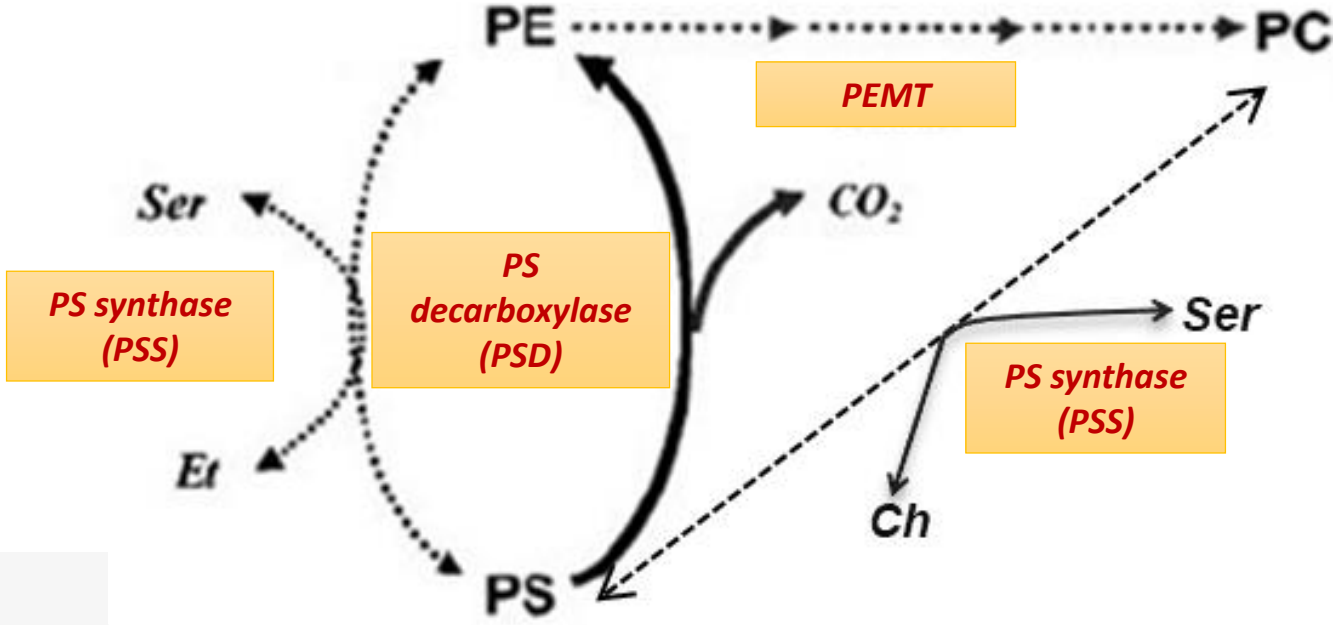
- Methyl groups are donated by S-adenosylmethionine to convert PE to PC by PE methyltransferase.

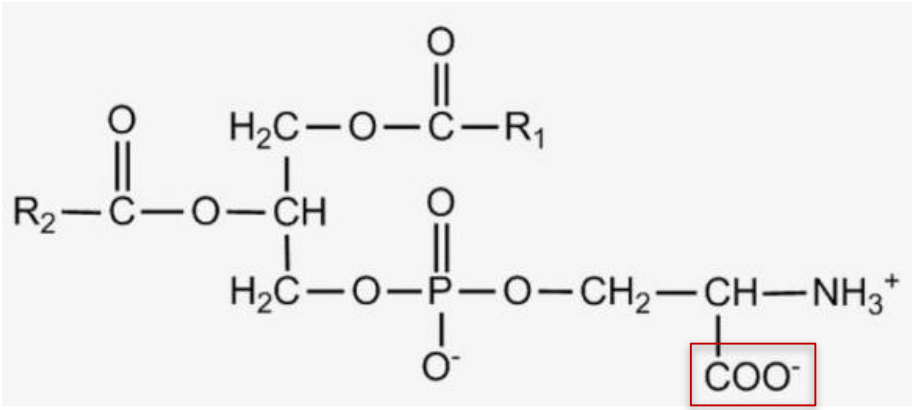




Synthetic pathways for and from ph-serine

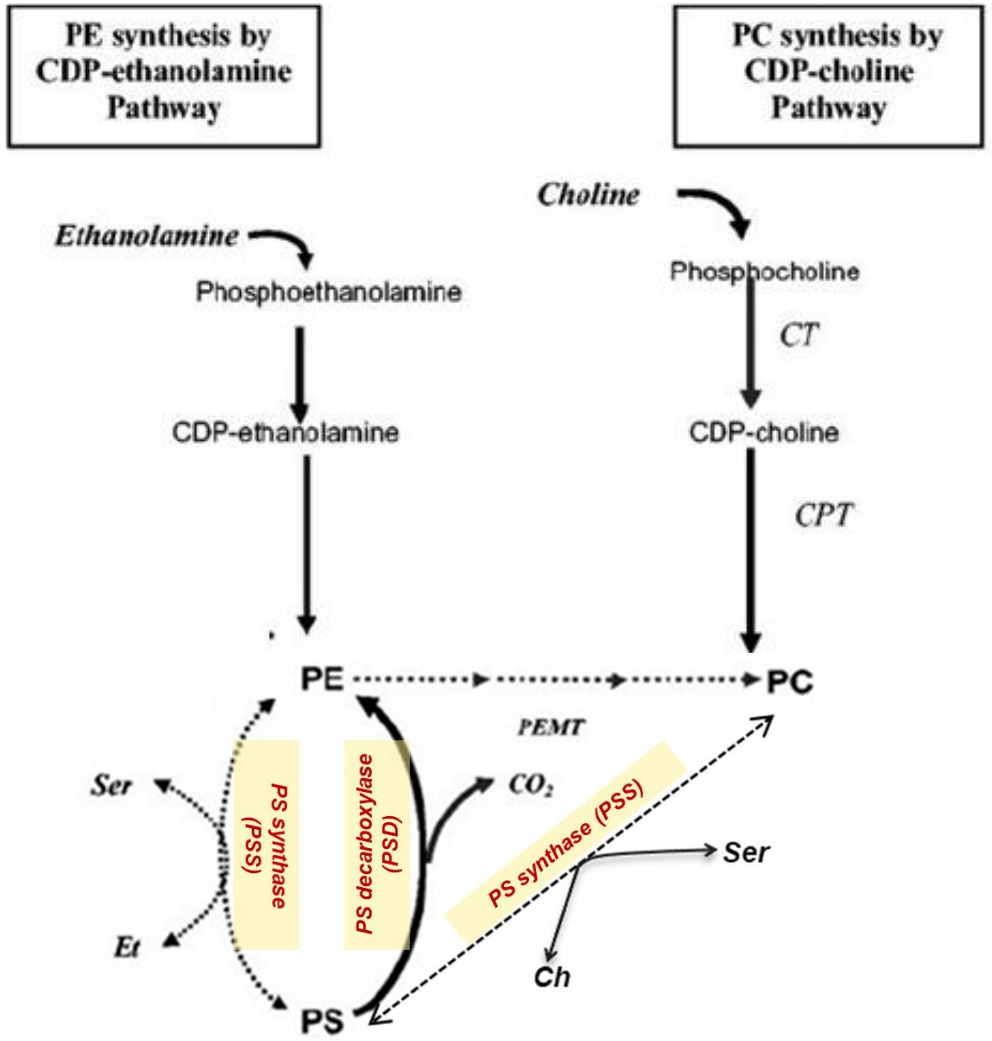
- The liver requires another mechanism to produce PC because it uses it to make bile and other plasma lipoproteins.
- PS is decarboxylated to PE by PS decarboxylase (PSD). It can be methylated by PEMT to PC
- PS is exchanged from PE or PC by PS synthases (PSS).





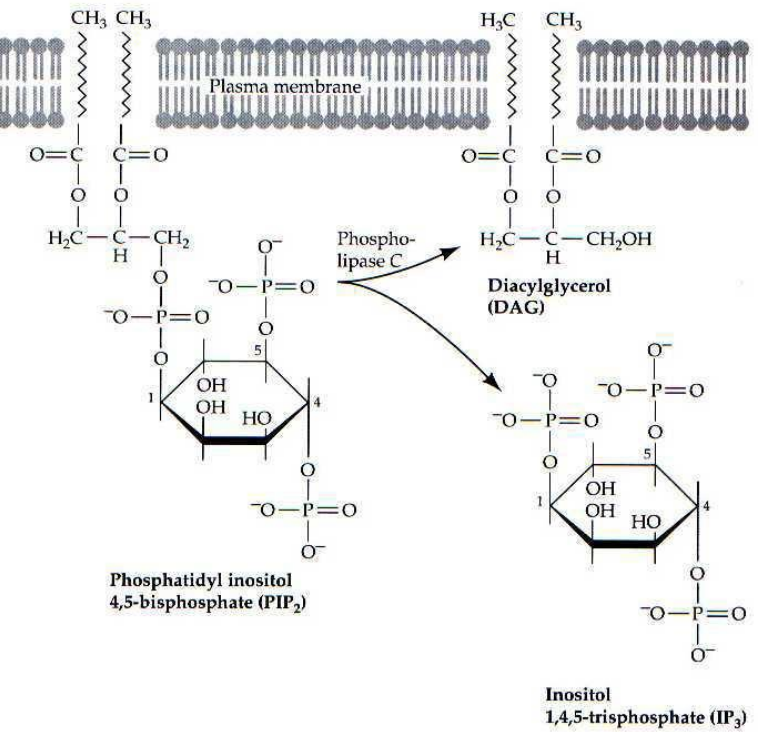
phosphatidylserine

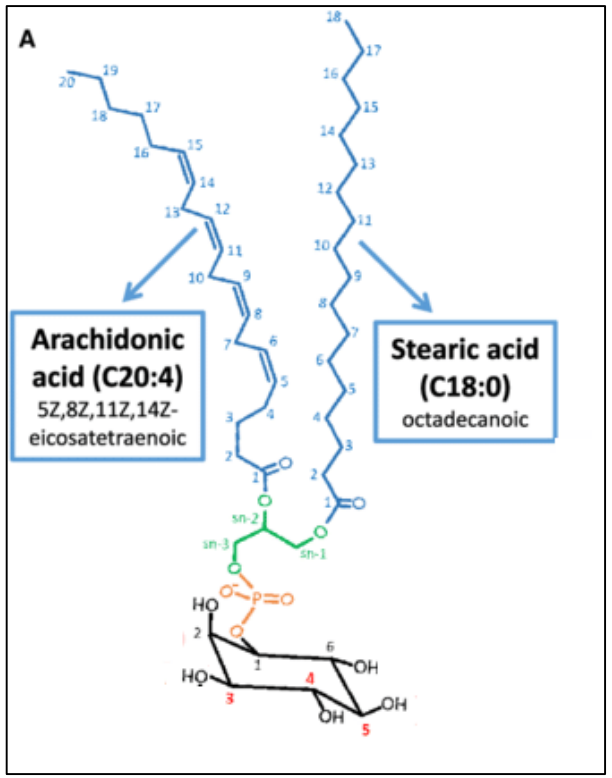
Summary of synthesis pf PE, PC, and PS

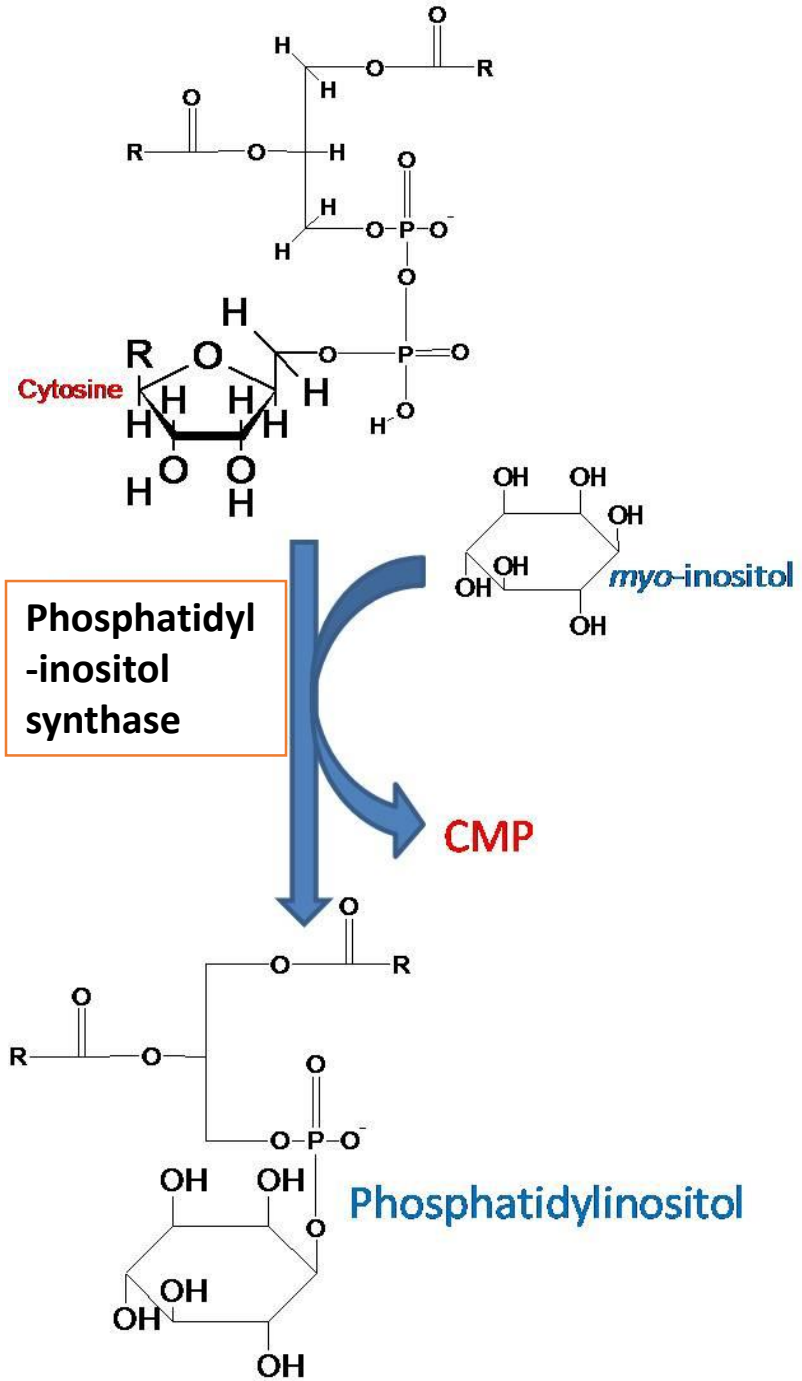


Synthesis of ph-inositol

- Inositol is combined with CDP-DAG by PI synthase to produce phosphatidylinositol.
- It is a reservoir of arachidonate.
- It also produces signaling molecules when cleaved by phospholipase C.

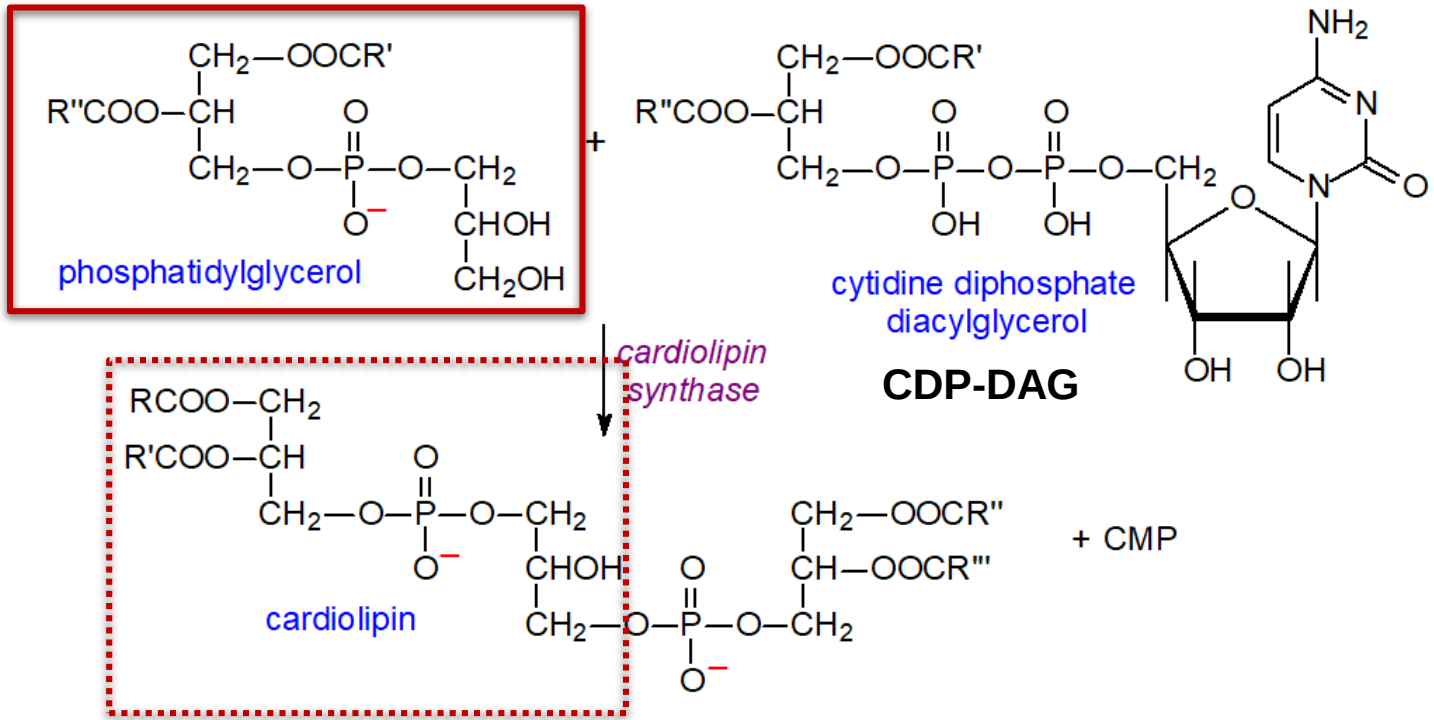


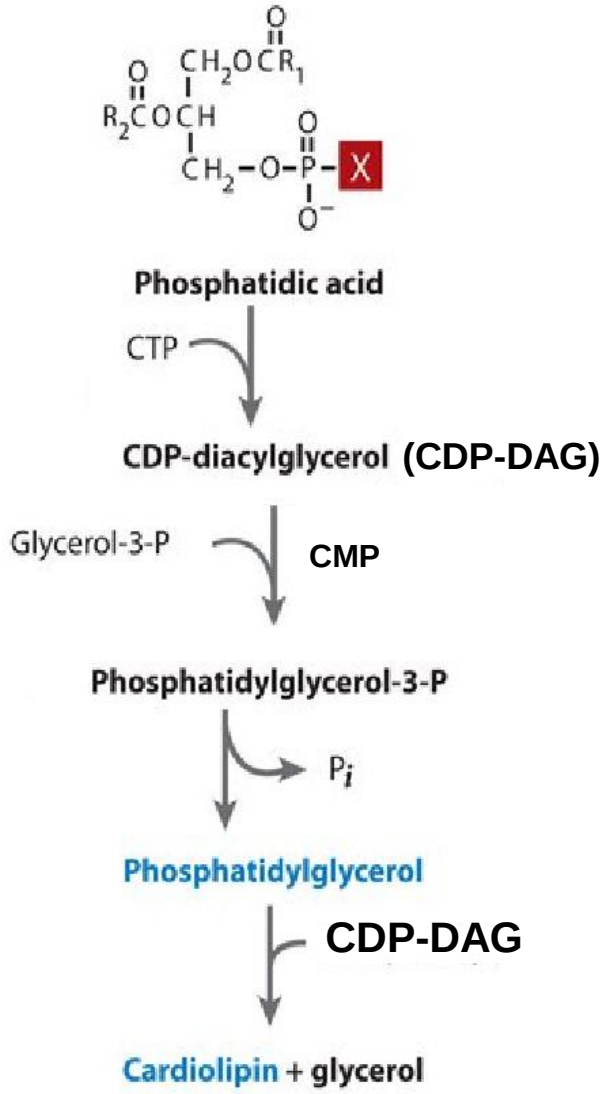




Phosphatidylglycerol and cardiolipin

- Phosphatidylglycerol is synthesized from CDP-DAG and glycerol 3-phosphate.
- Cardiolipin is synthesized by the transfer of DAG from CDP-DAG to a pre-existing molecule of phosphatidylglycerol.

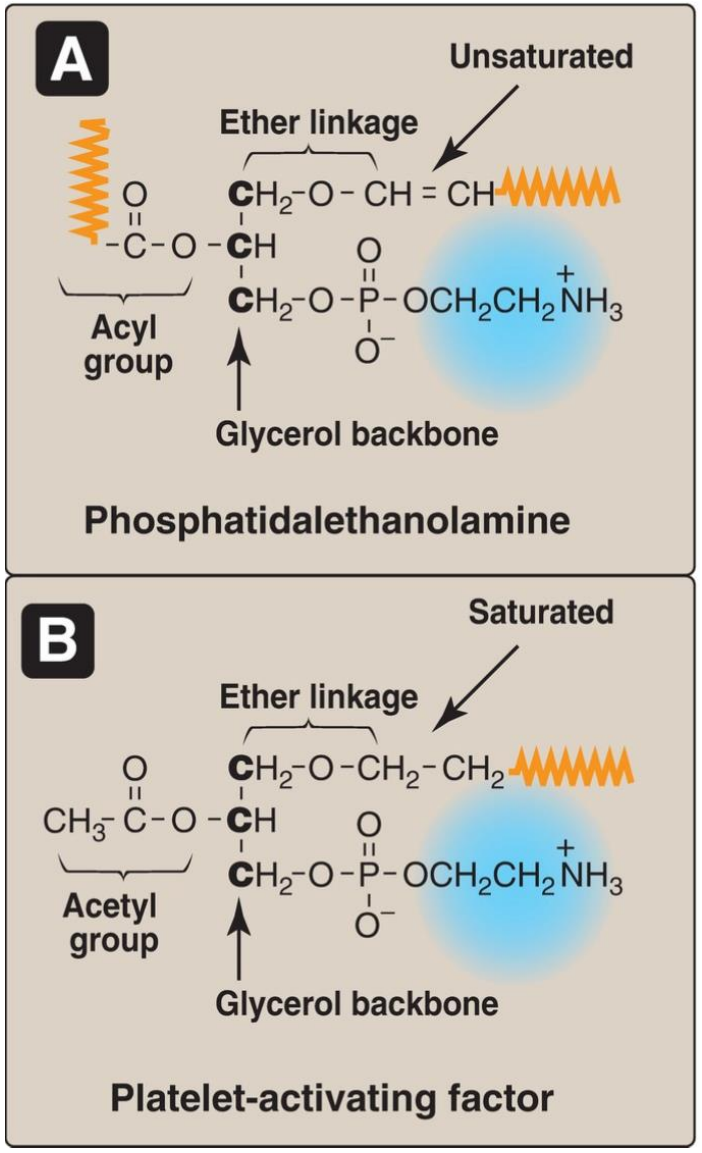




Ether glycerophospholipids

The FA at carbon 1 is replaced by an unsaturated alkyl group attached by an ether linkage.

- Plasmalogens: PhosphatidAlethanolamine (abundant in nerve tissue, is similar in structure to phosphatidylethanolamine.
  - Phosphatidalcholine (abundant in heart muscle) is another significant ether lipid in mammals.
- Platelet-activating factor has a saturated alkyl group in an ether link to carbon 1 and an acetyl residue at carbon 2 of the glycerol backbone.
  - Prothrombotic and inflammatory factor



Degradation of Phospholipids