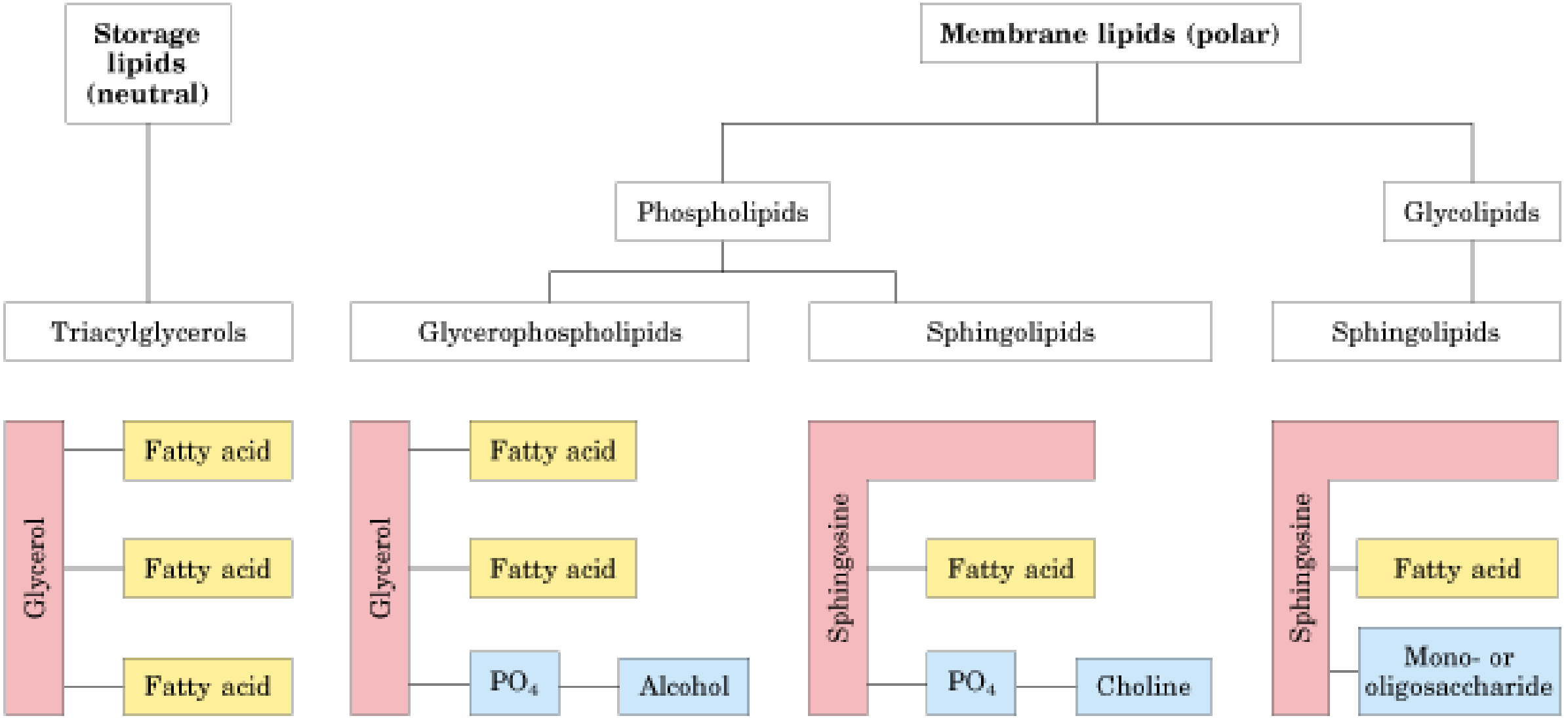
Metabolism of lipids V:
Glycerophospholipids

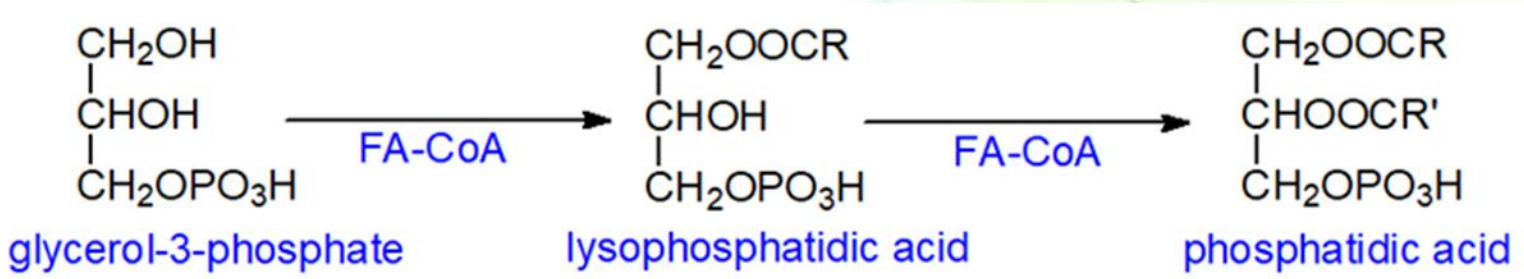
Prof. Mamoun Ahram

Resources

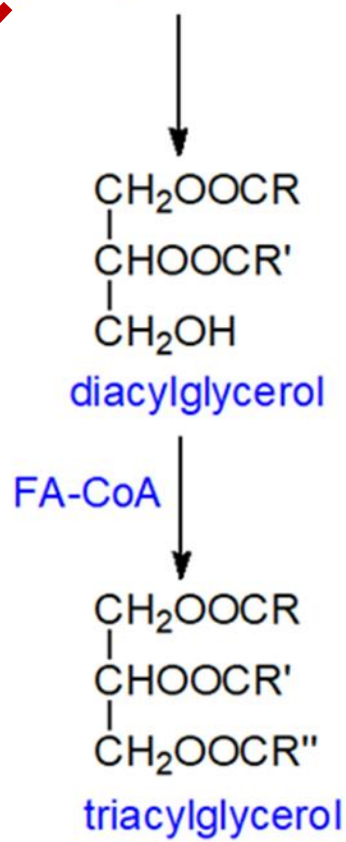
- This lecture
- Lippincott's Biochemistry, Ch. 17


Storage lipids (neutral)
Membrane lipids (polar)
Phospholipids
Glycolipids
Triacylglycerols
Glycerophospholipids
Sphingolipids
Sphingolipids
Glycerol
Fatty acid
Fatty acid
Fatty acid
Glycerol
Fatty acid
Fatty acid
PO_4
Alcohol
Sphingosine
Fatty acid
PO_4
Choline
Sphingosine
Fatty acid
Mono- or oligosaccharide

Phosphatidic acid

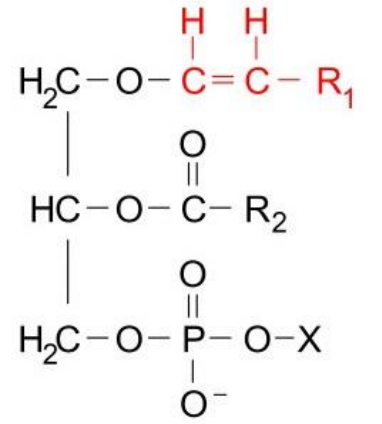


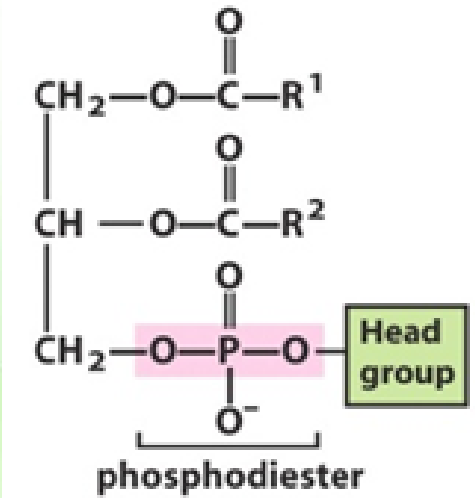
- Phosphatidic acid is the precursor of glycerophospholipids.

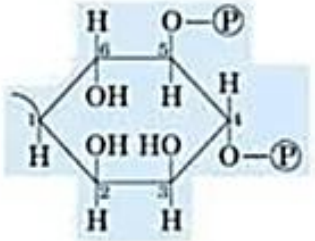
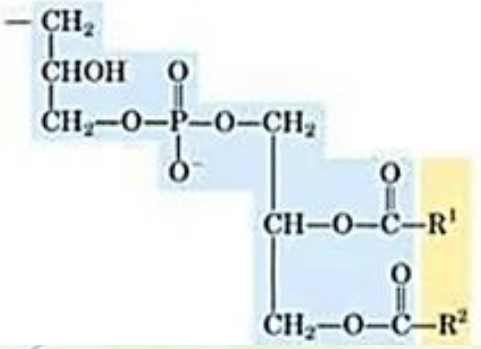


Classification of Glycerophospholipids

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

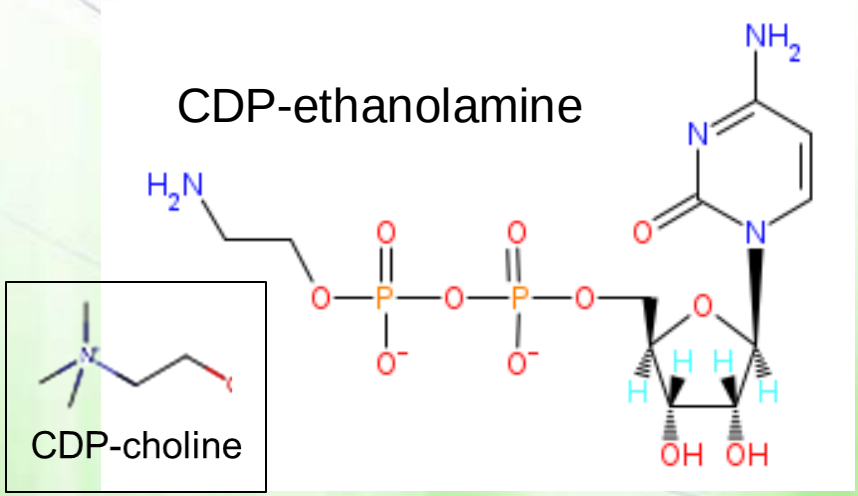


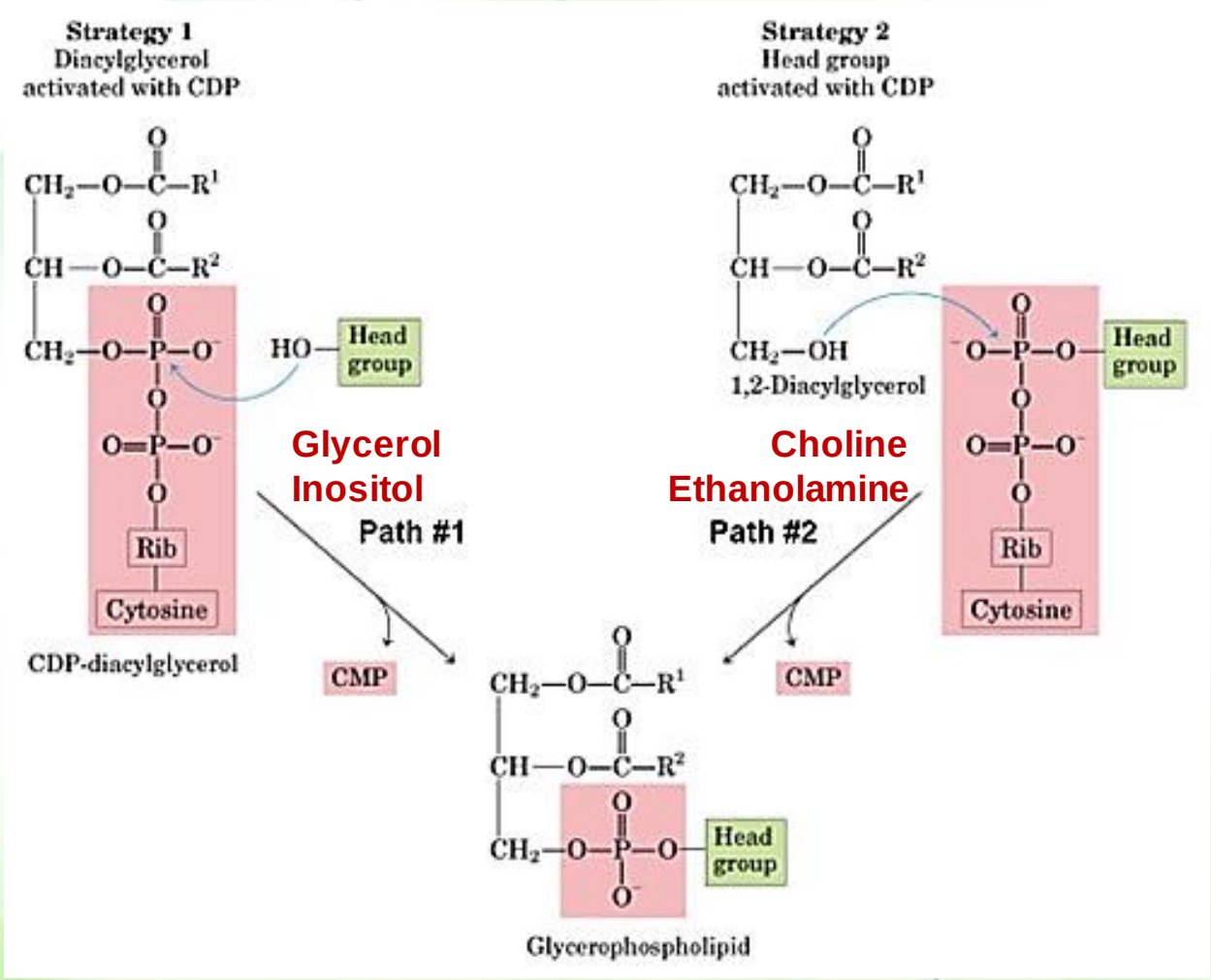


Phosphatidic acid	—	—H
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$
Phosphatidylserine	Serine	$-CH_2-\underset{COO^-}{CH}-\overset{+}{N}H_3$
Phosphatidylglycerol	Glycerol	$-CH_2-\underset{OH}{CH}-CH_2-OH$
Phosphatidylinositol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

Synthesis

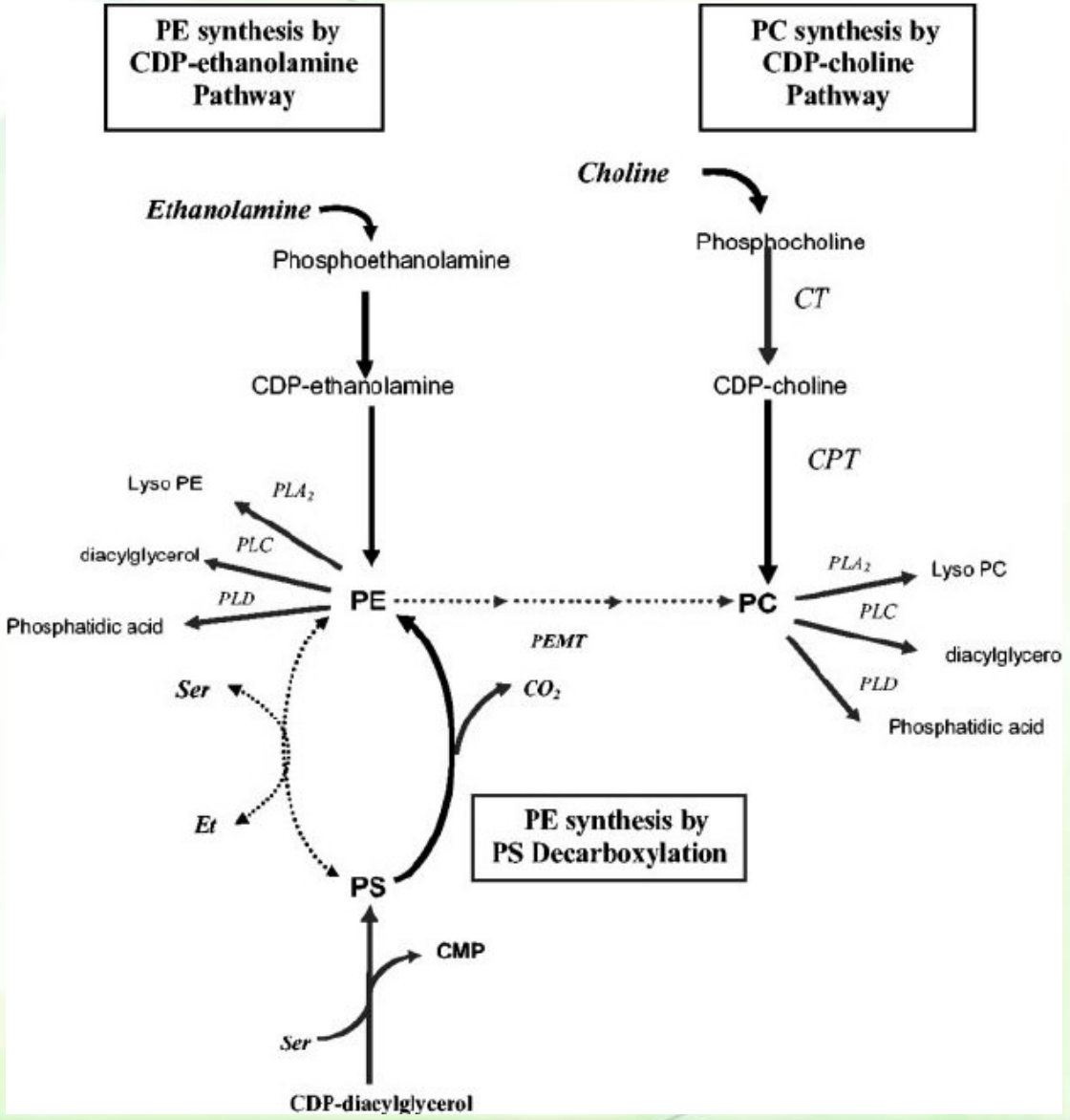
- Location: smooth ER
  - Except for ether lipids
- Activation by CDP is necessary. Either:
  - CDP-DAG
  - CDP-alcohol





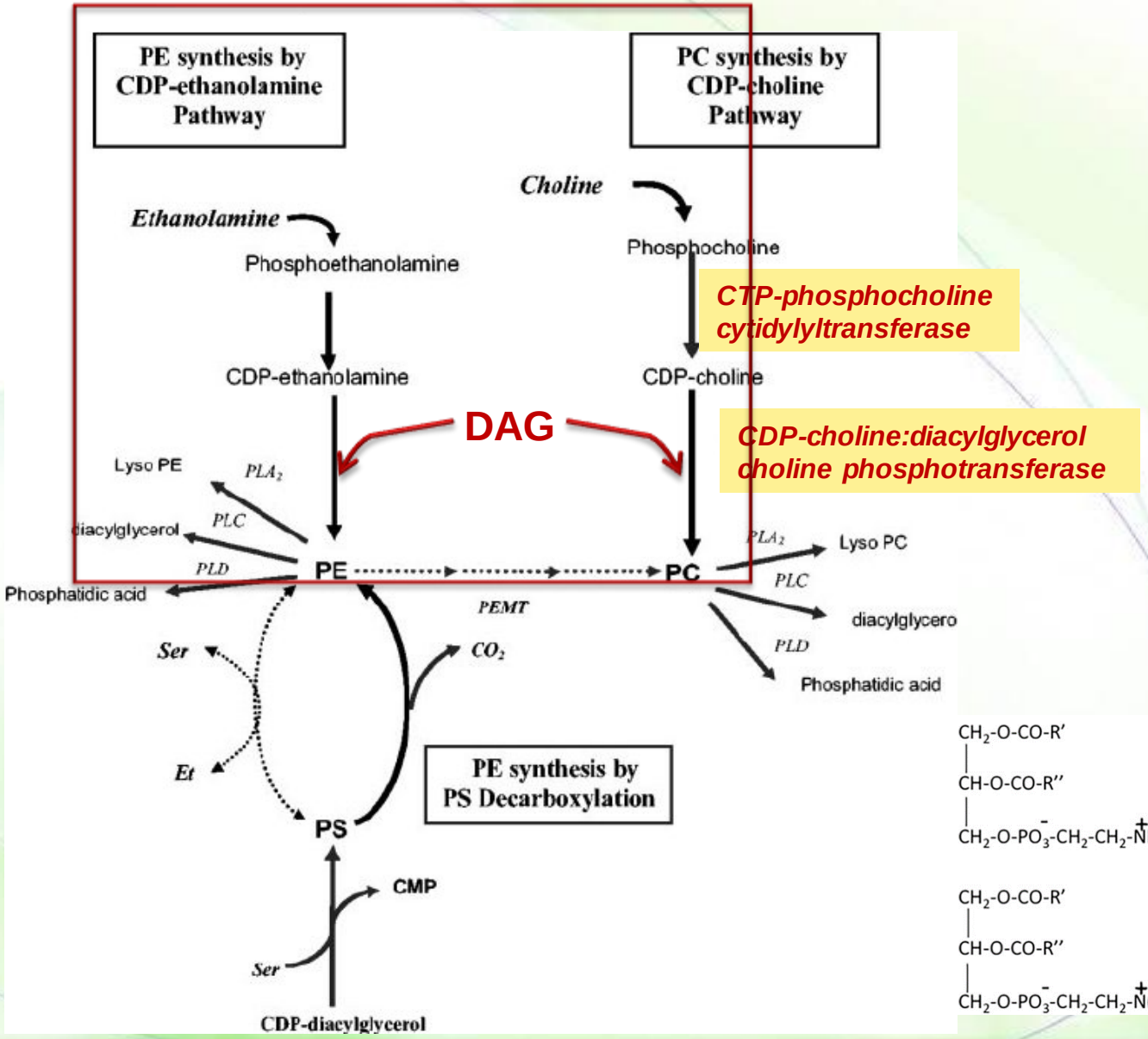
Sources of choline and ethanolamine

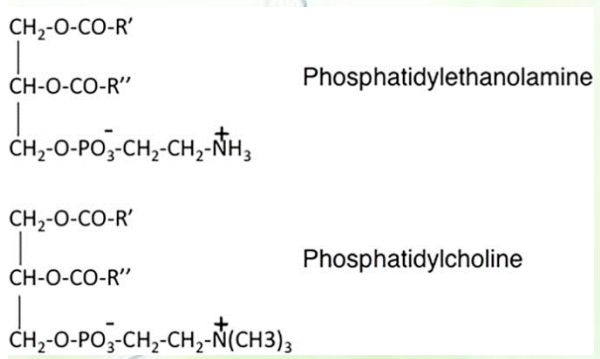
- Choline and ethanolamine are
  - obtained from diet,
  - synthesized, or
  - re-cycled from the turnover of pre-existing phospholipids
- Diet is still essential since demand > supply



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

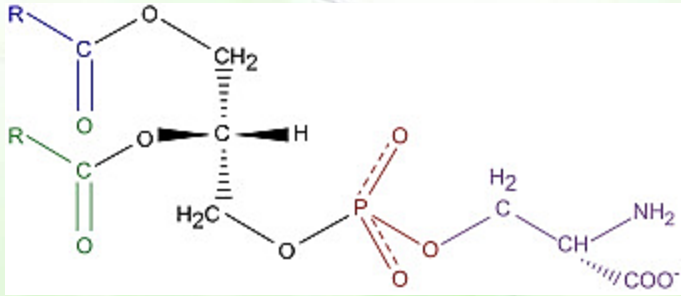
- Choline or ethanolamine are phosphorylated by *kinases*, then activated by *transferases* to form, CDP-choline or CDP-ethanolamine.
- Choline phosphate or ethanolamine phosphate is transferred from the nucleotide (releasing CMP) to DAG.



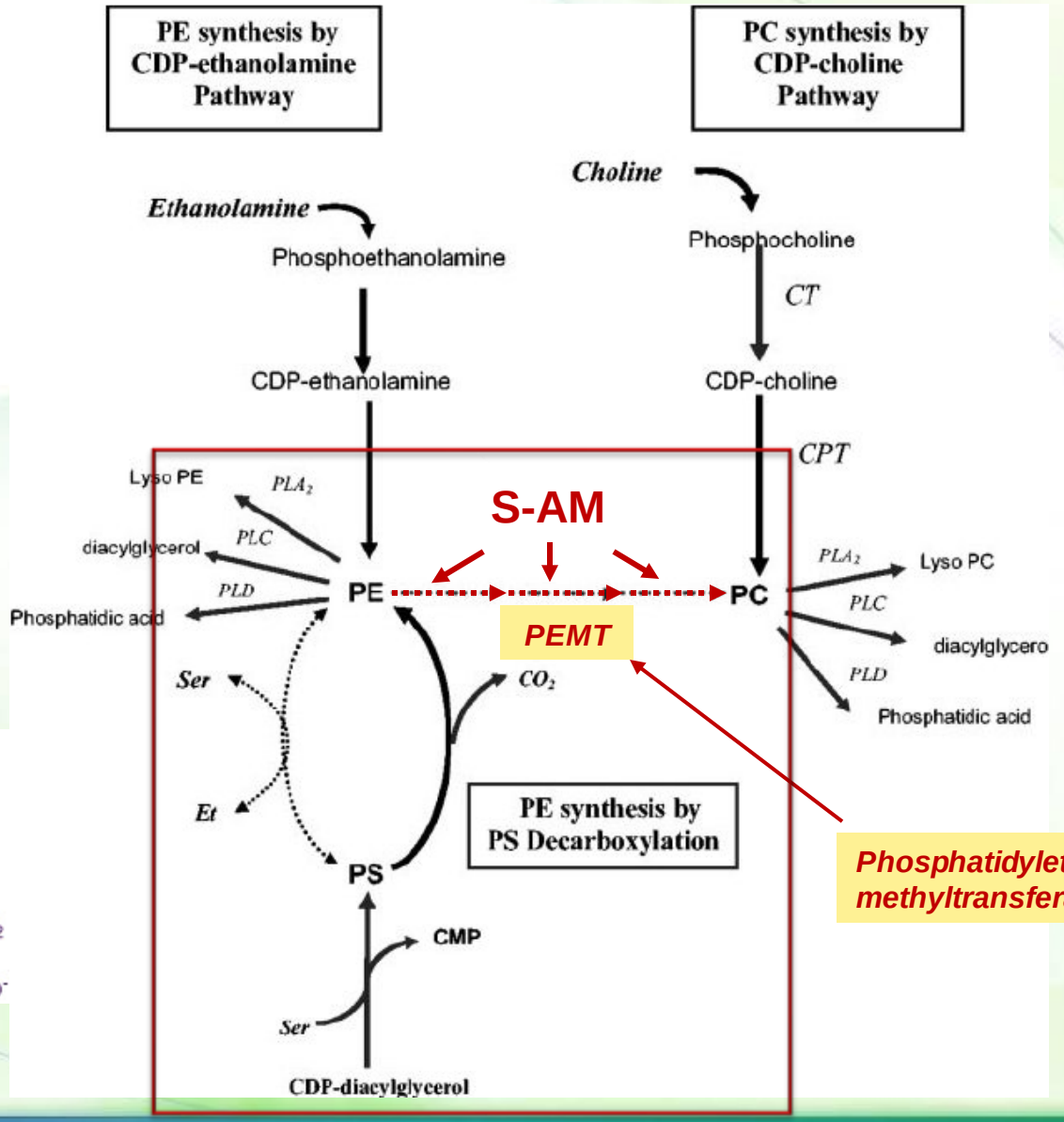


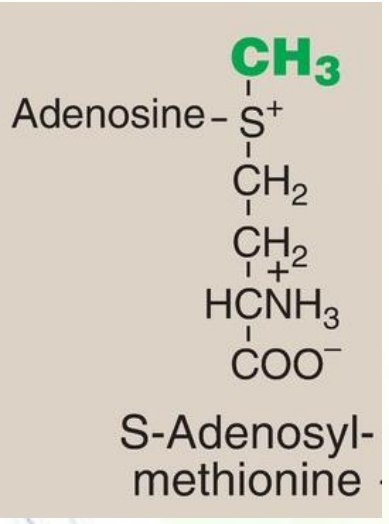
Ph-choline synthesis from ph-serine

- The liver requires a mechanism for producing PC because it uses it for production of bile and other plasma lipoproteins.
- PS is decarboxylated to PE by PS decarboxylase.
- PE is methylated from S-adenosylmethionine.



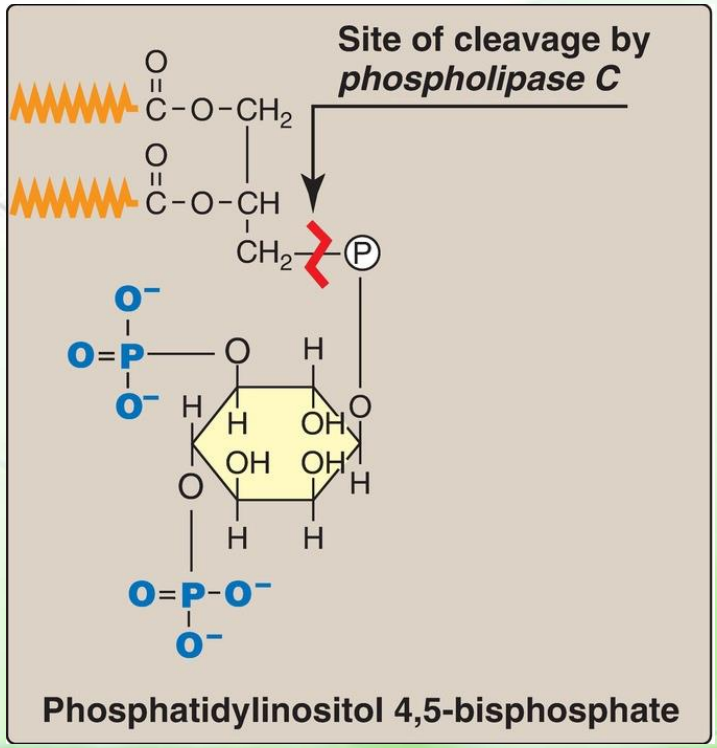
phosphatidylserine

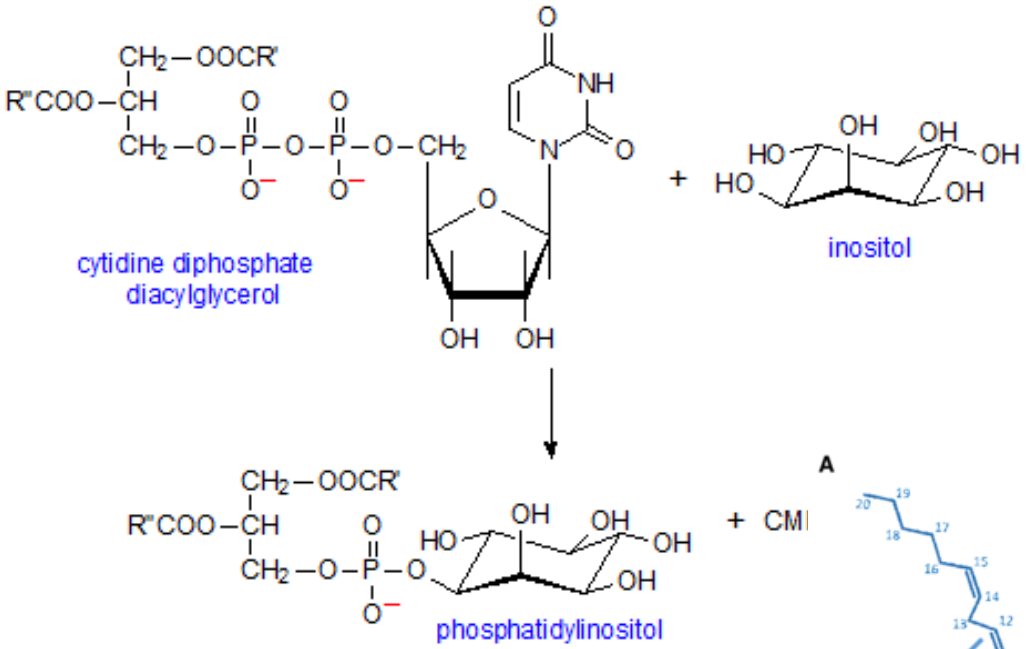


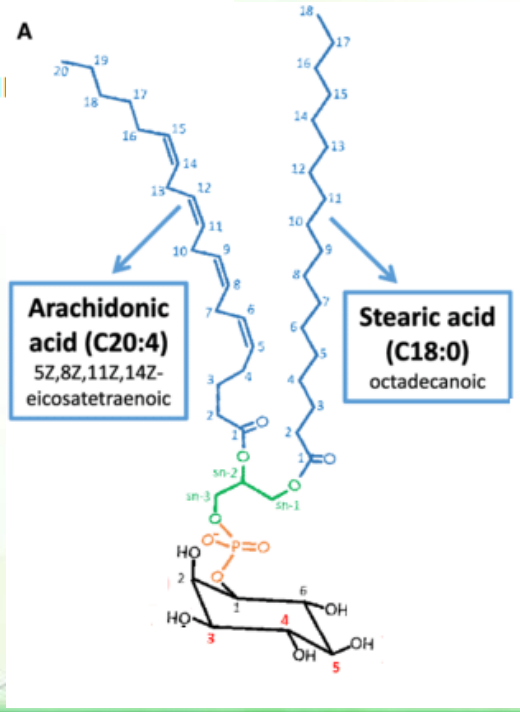


Synthesis of ph-inositol

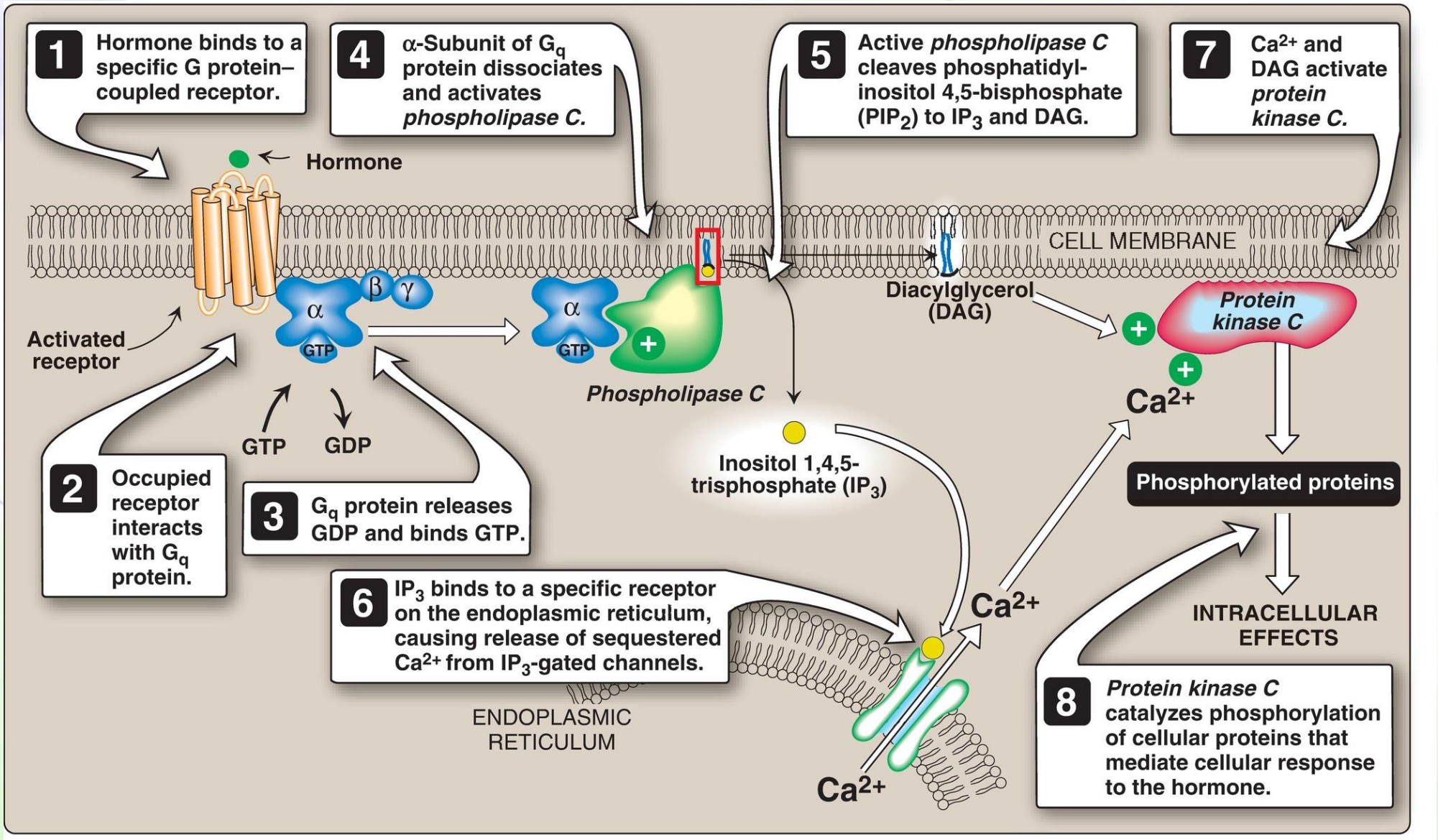
- ph-inositol is a reservoir of arachidonate.
- It produces signaling molecules when cleaved by phospholipase C.





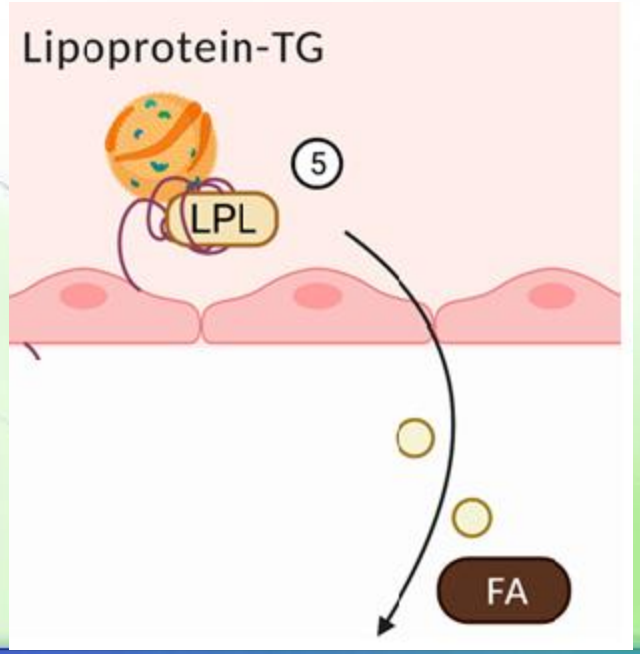


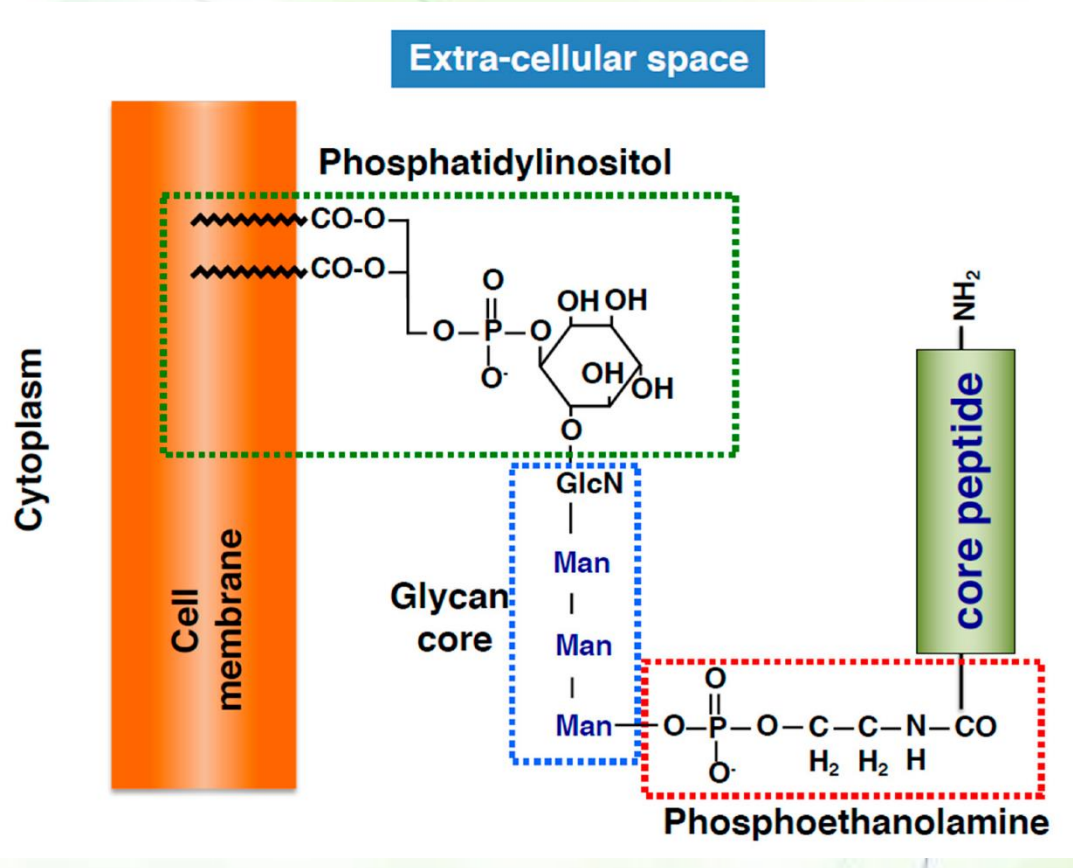
Signaling by PIP2 products



GPI for membrane attachment

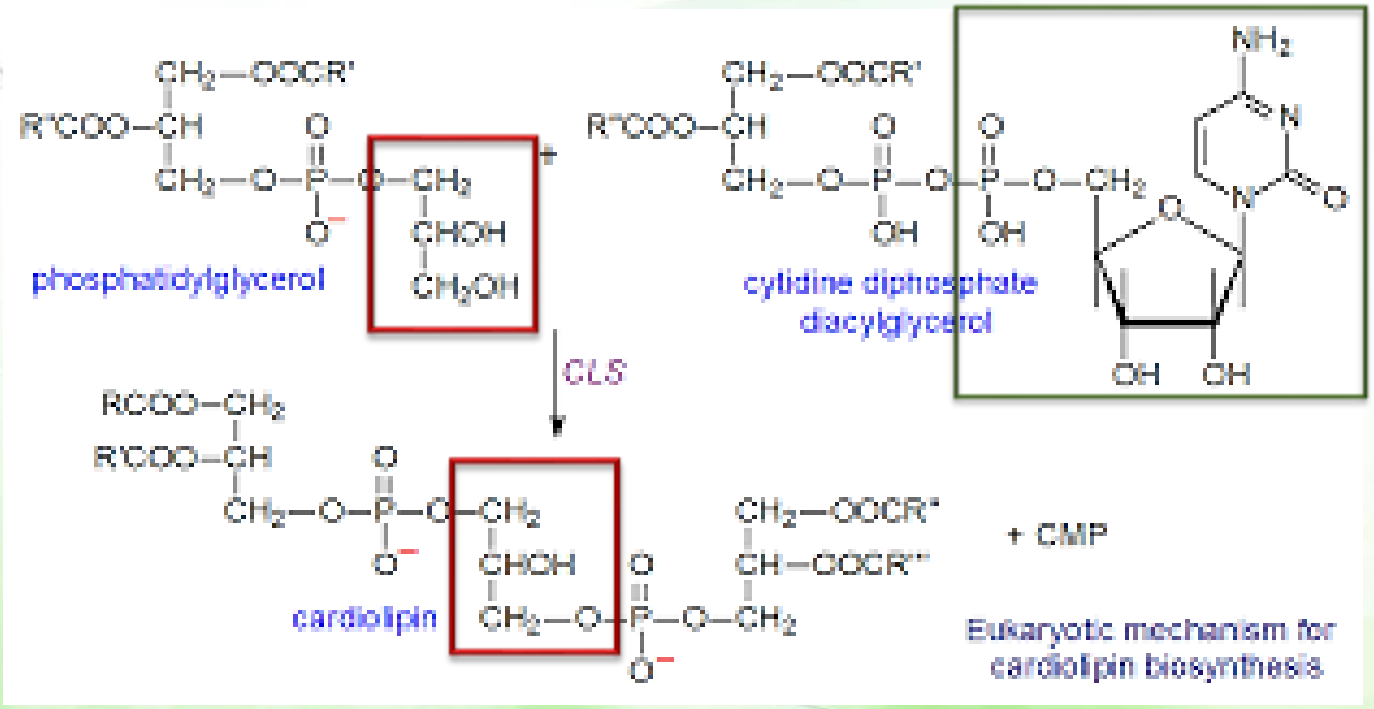
- glycosyl phosphatidylinositol (GPI) is used to attach proteins into the plasma membrane.
- Advantage: lateral mobility
- Example: lipoprotein lipase

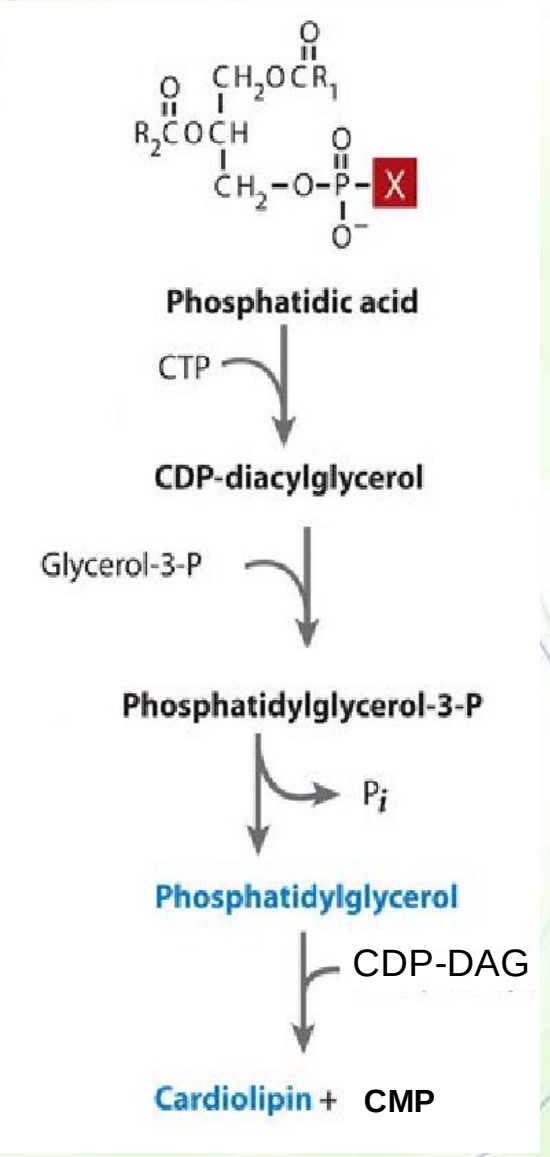




Phosphatidylglycerol and cardiolipin

- 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.

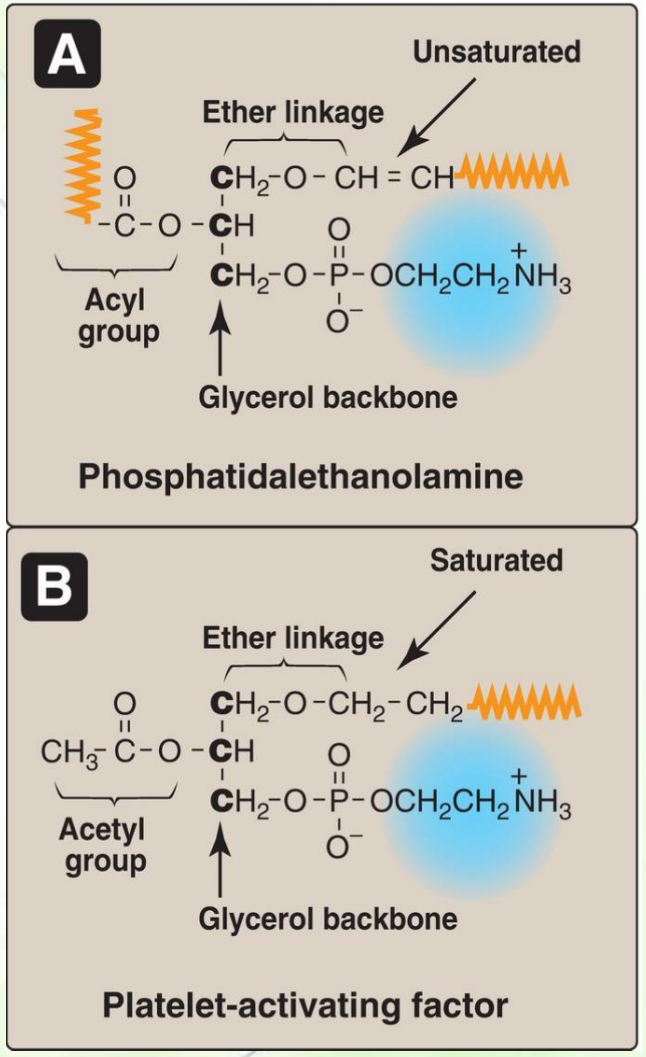




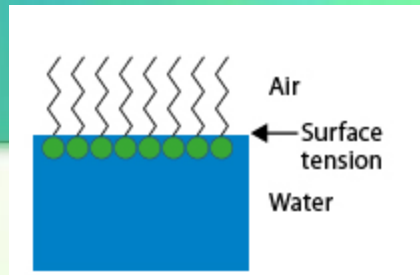
Ether glycerophospholipids

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

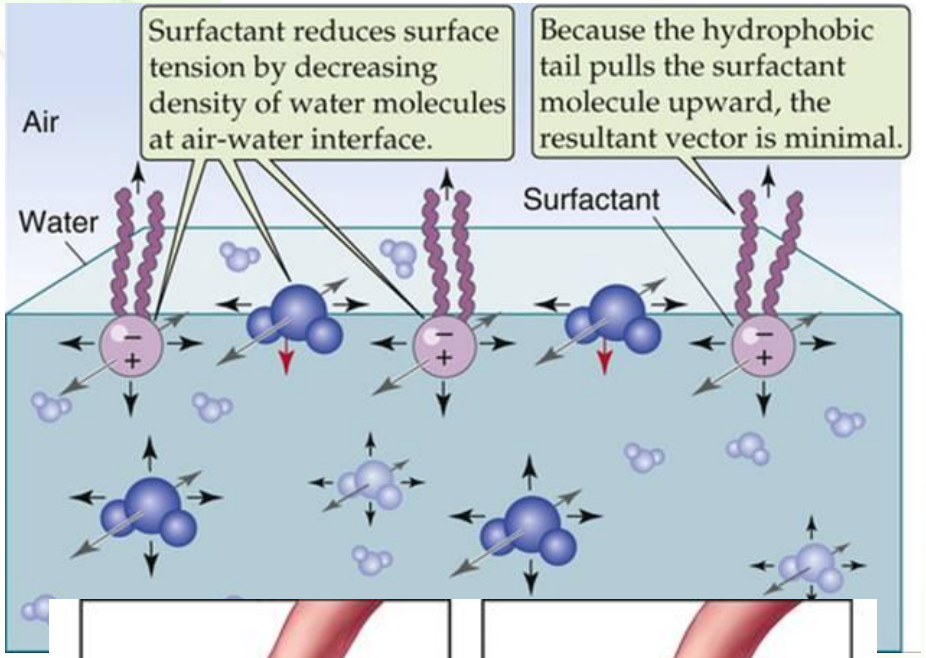
- Plasmalogens: PhosphatidAlethanolamine (abundant in nerve tissue, is similar in structure to phosphatidylethanolamine.
  - Phosphatidalcholine (abundant in heart muscle) is the other quantitatively significant ether lipid in mammals
- Platelet-activating factor: has a saturated alkyl group in an ether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



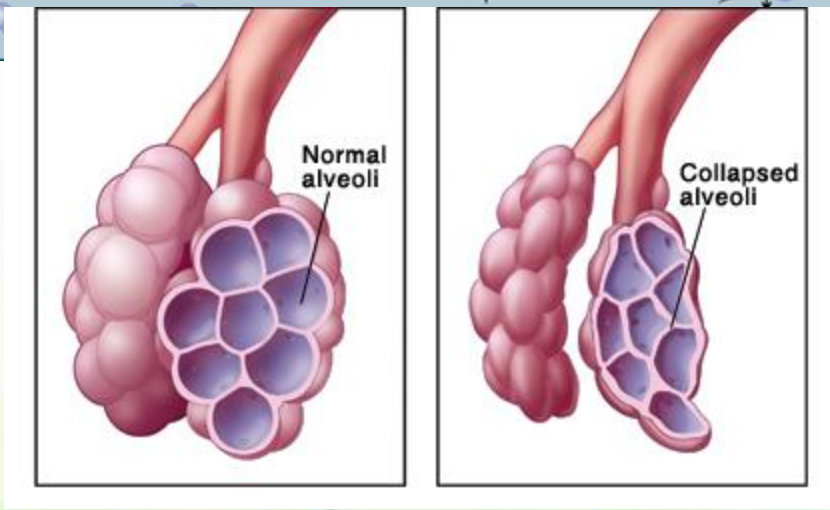
Surfactants



- 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.



Degradation of Phospholipids

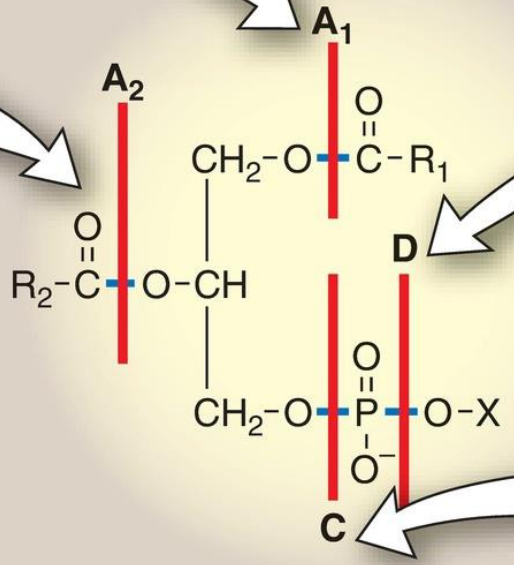
The role of phospholipases

PHOSPHOLIPASE A_2

- *Phospholipase* A_2 is present in many mammalian tissues and pancreatic juice. It is also present in snake and bee venoms.
- Pancreatic secretions are especially rich in the *phospholipase* A_2 proenzyme, which is activated by *trypsin* and requires bile salts for activity.
- *Phospholipase* A_2, acting on phosphatidyl-inositol, releases arachidonic acid (the precursor of the eicosanoids).
- *Phospholipase* A_2 is inhibited by glucocorticoids (for example, cortisol).

PHOSPHOLIPASE A_1

- *Phospholipase* A_1 is present in many mammalian tissues.



PHOSPHOLIPASE D

- *Phospholipase D* is involved in signal transduction, generating phosphatidic acid (PA) and choline from phosphatidylcholine and diacylglycerol from PA.

PHOSPHOLIPASE C

- *Phospholipase C* is found in liver lysosomes and the α-toxin of clostridia and other bacilli.
- Membrane-bound *phospho-lipase C* is activated by the PIP_2 system and, thus, plays a role in producing second messengers.