

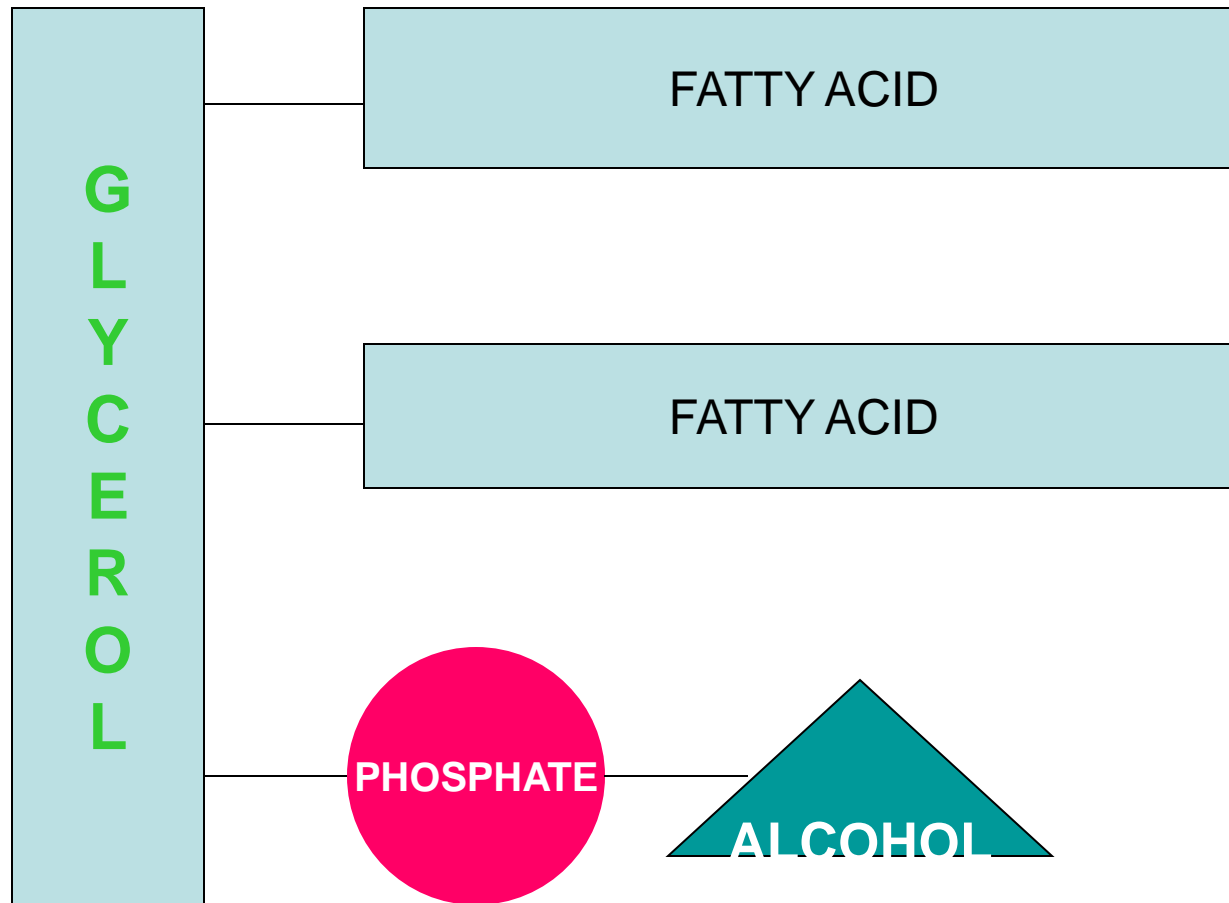
Biosynthesis of Glycerophospholipids

also known as

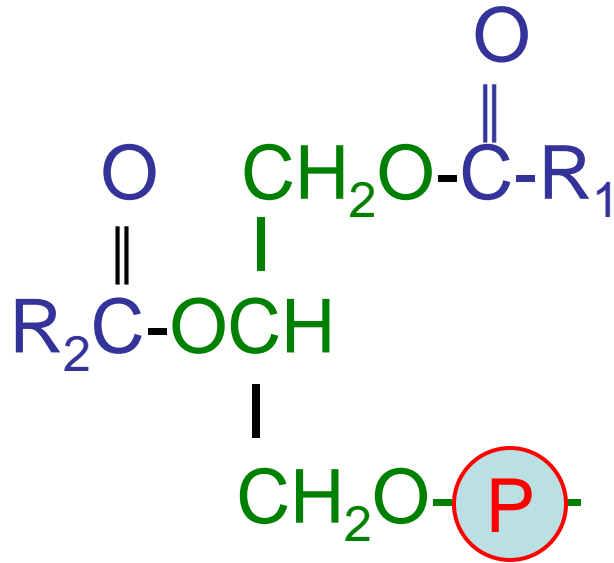
Phosphoglycerides or

Phosphoacylglycerol

Lippincott's Ch 17



PHOSPHOACYLGLYCEROL



Phosphatidic Acid

Can Form Ester with Alcohol:

- Serine
- Ethanolamine
- Choline
- Inositol
- Glycerol

Phosphatidyl -



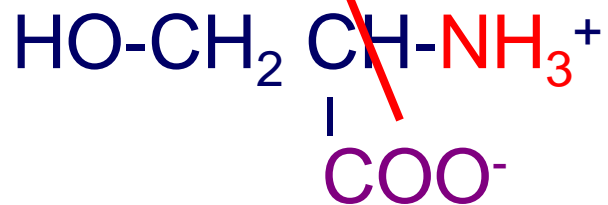
Ethanol



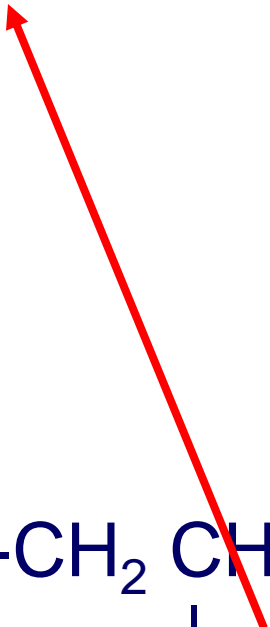
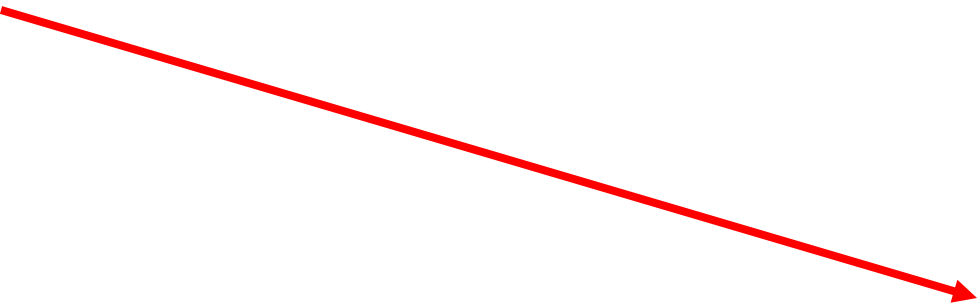
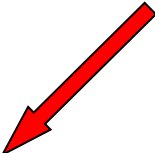
Ethanolamine

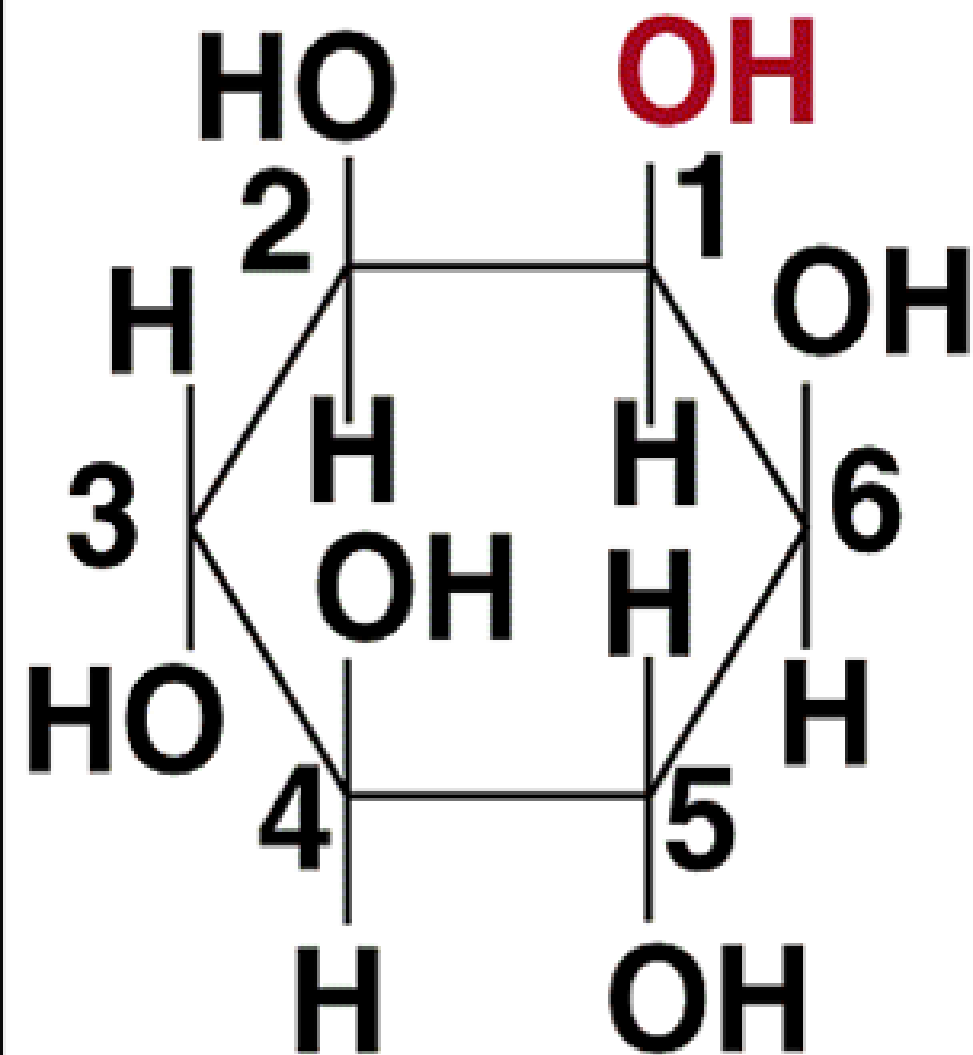


Choline

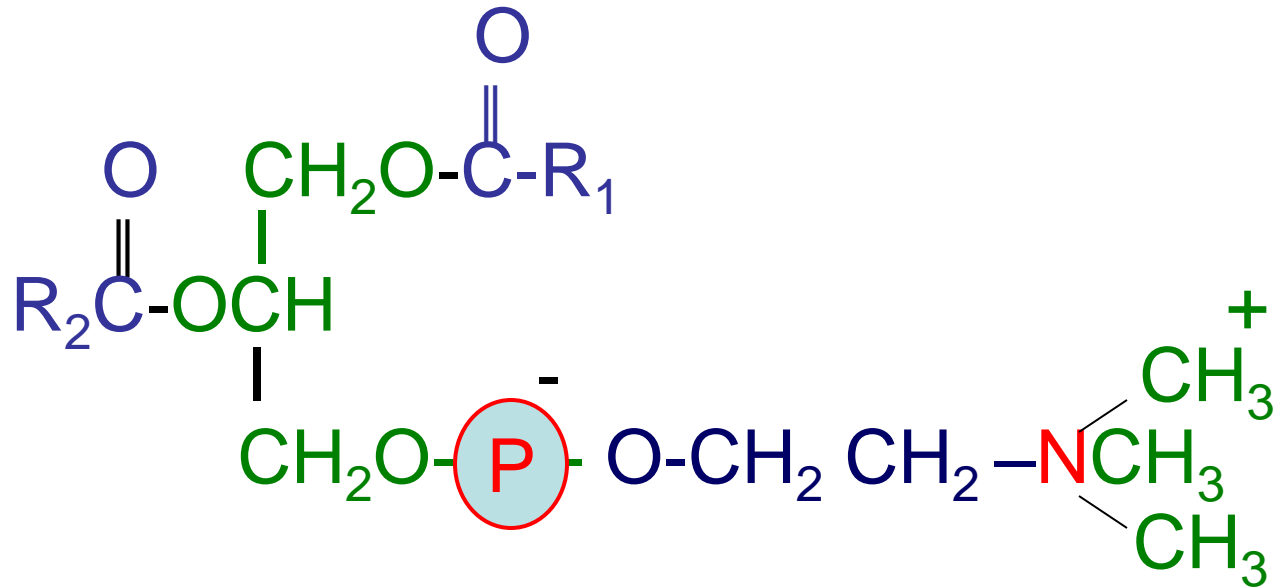


Serine





myo-Inositol



Phosphatidyl Choline (Lecithin)

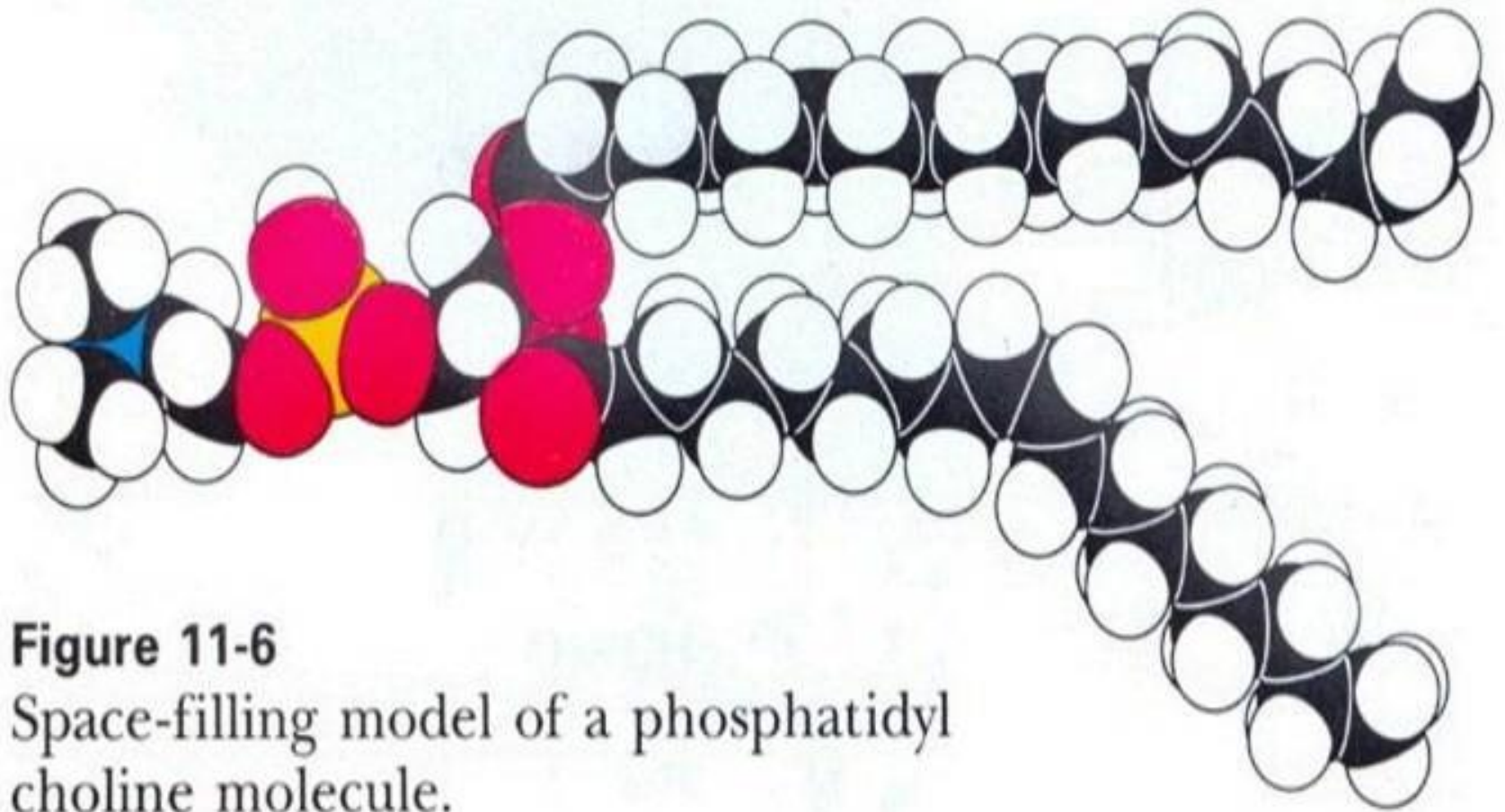


Figure 11-6

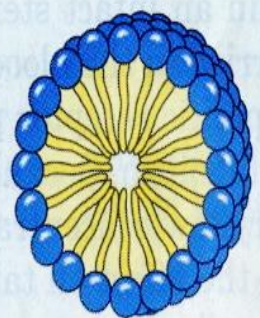
Space-filling model of a phosphatidylcholine molecule.



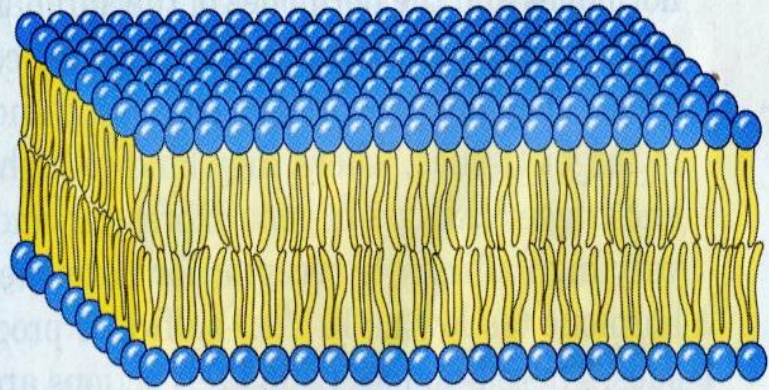
Individual units are wedge-shaped (cross-section of head greater than that of side chain)



Individual units are cylindrical (cross-section of head equals that of side chain)

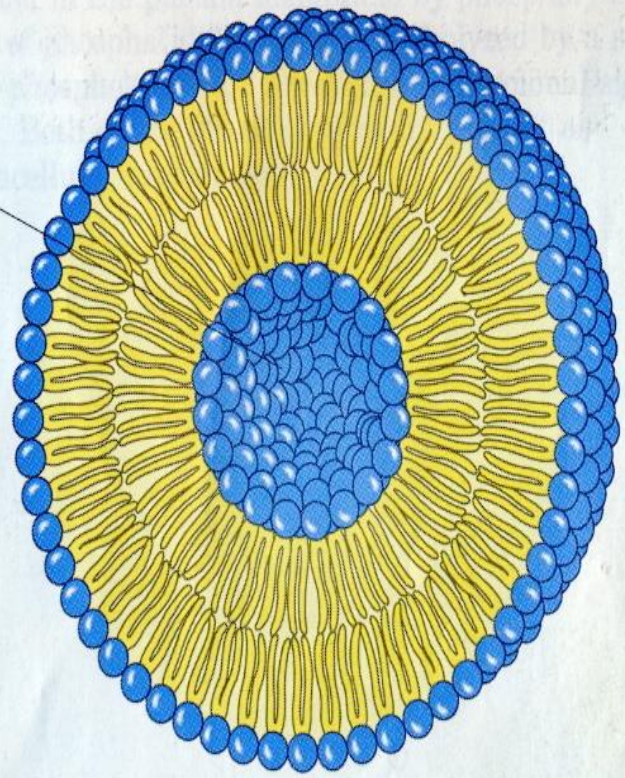


(a)

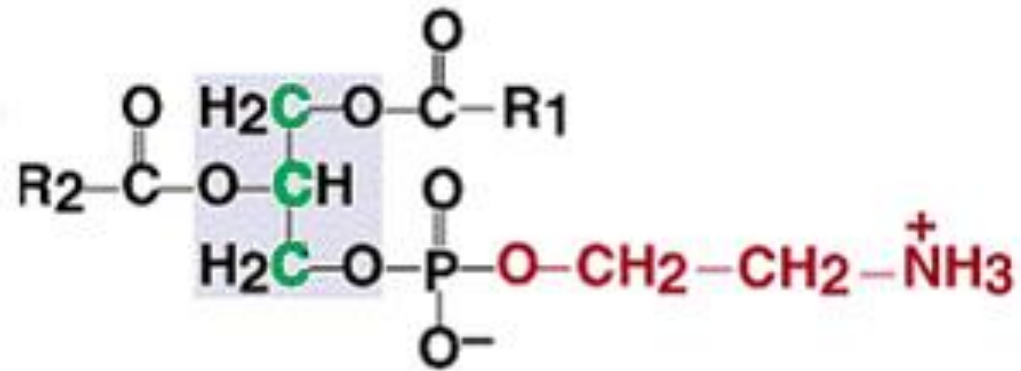


(b)

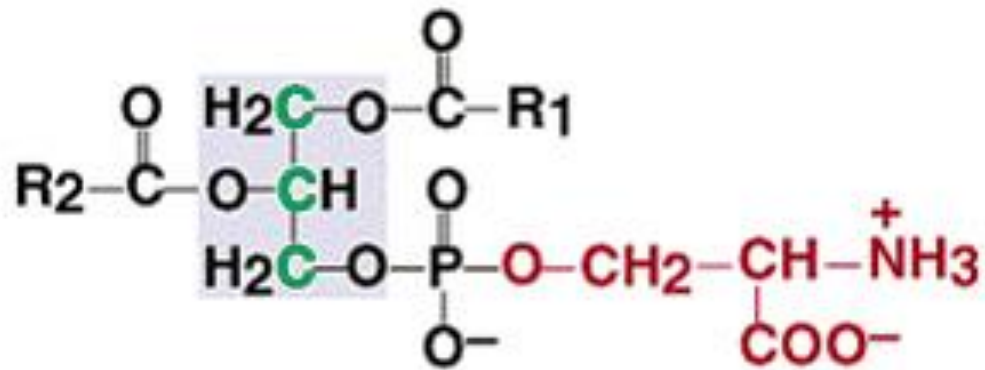
Aqueous cavity



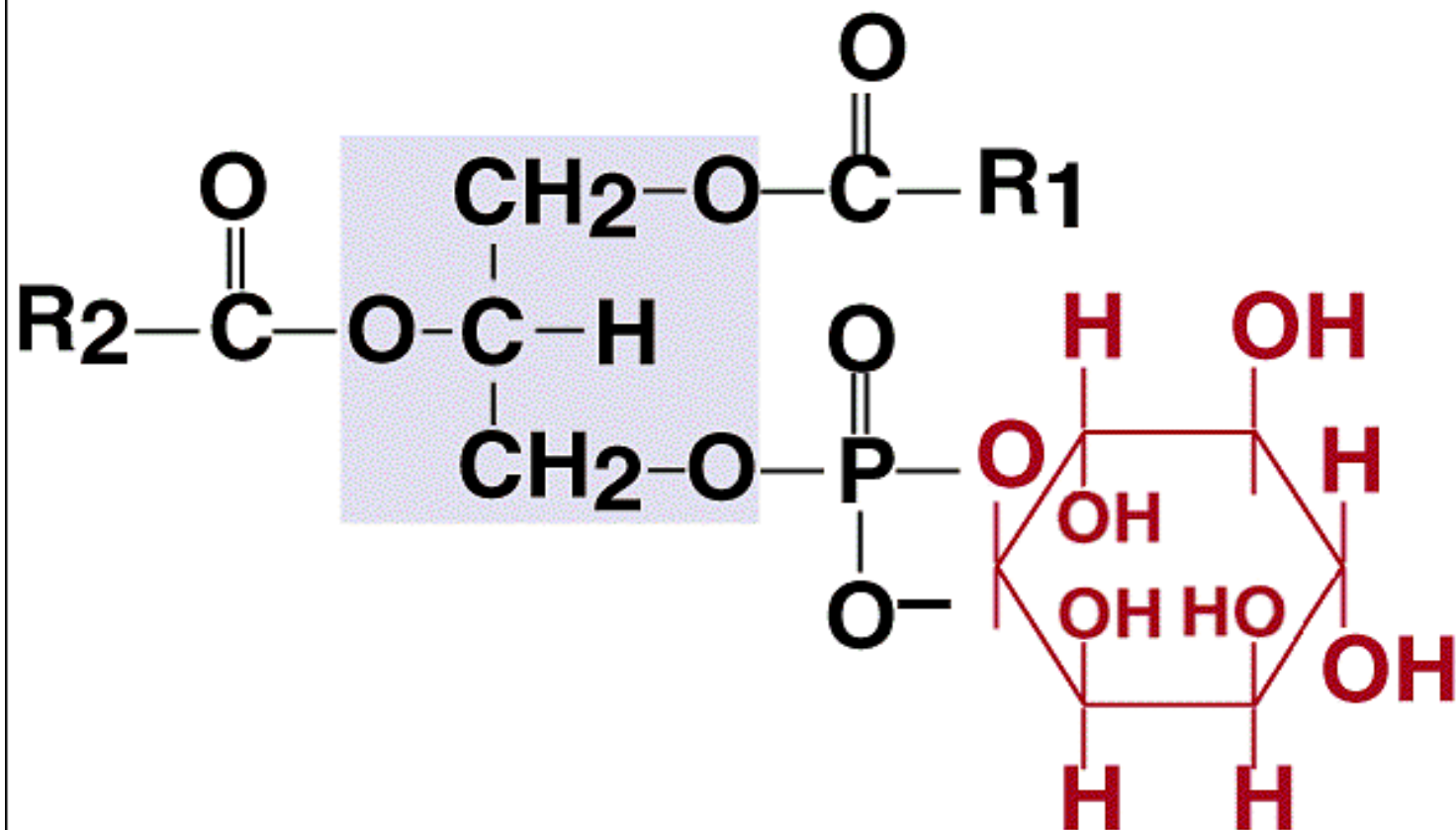
(c)



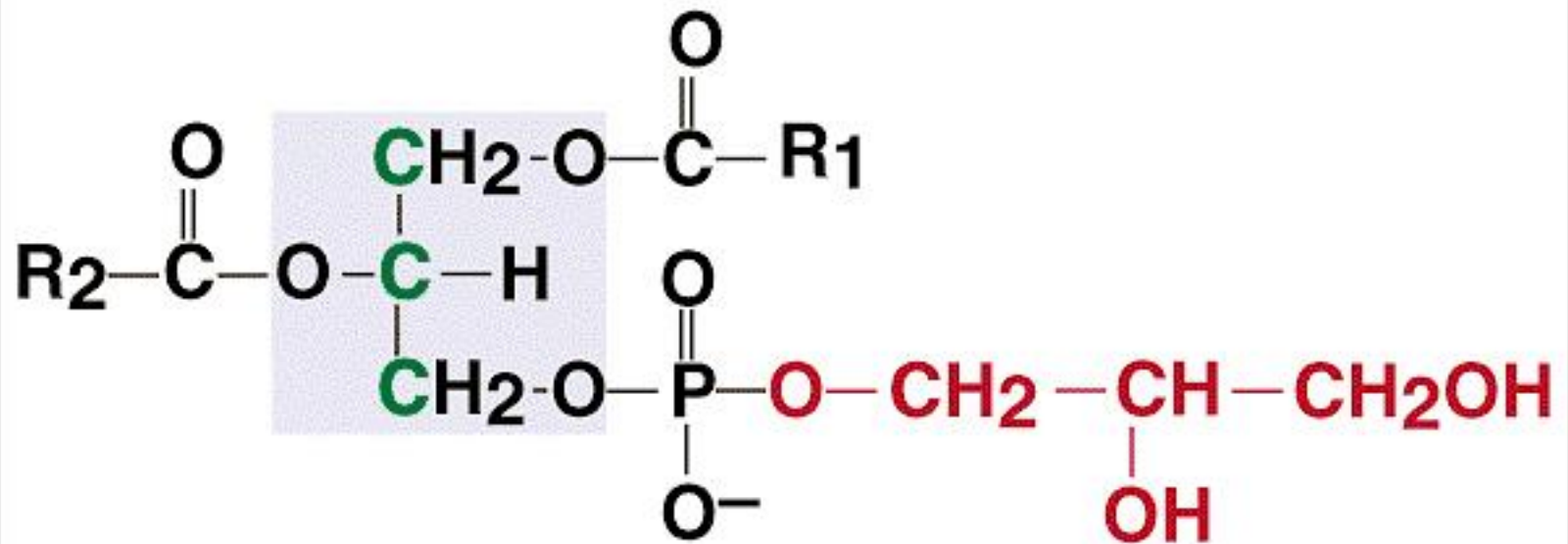
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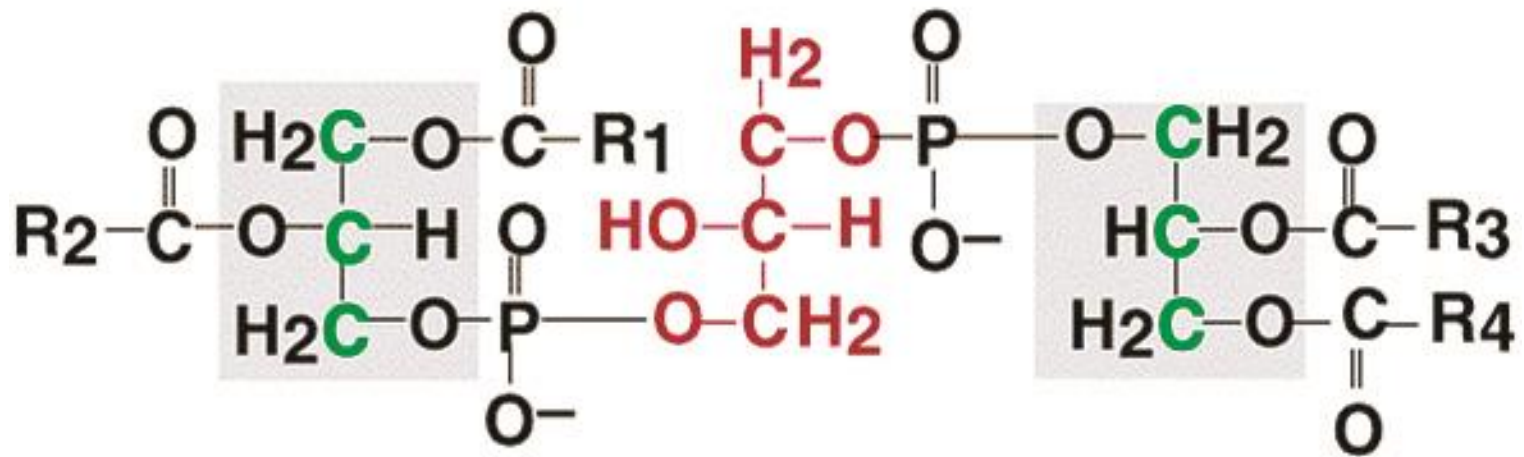
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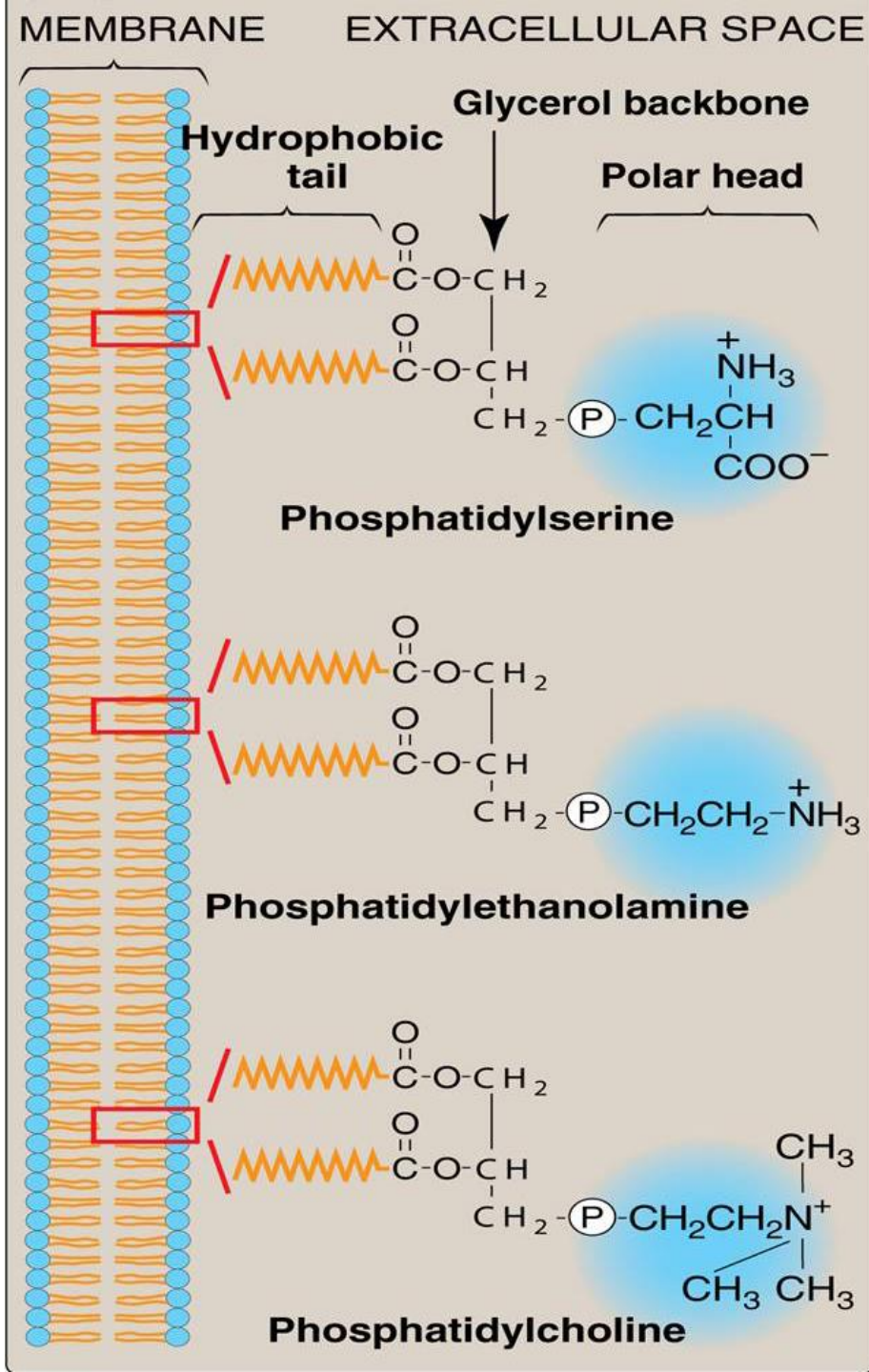
Phosphatidylinositol

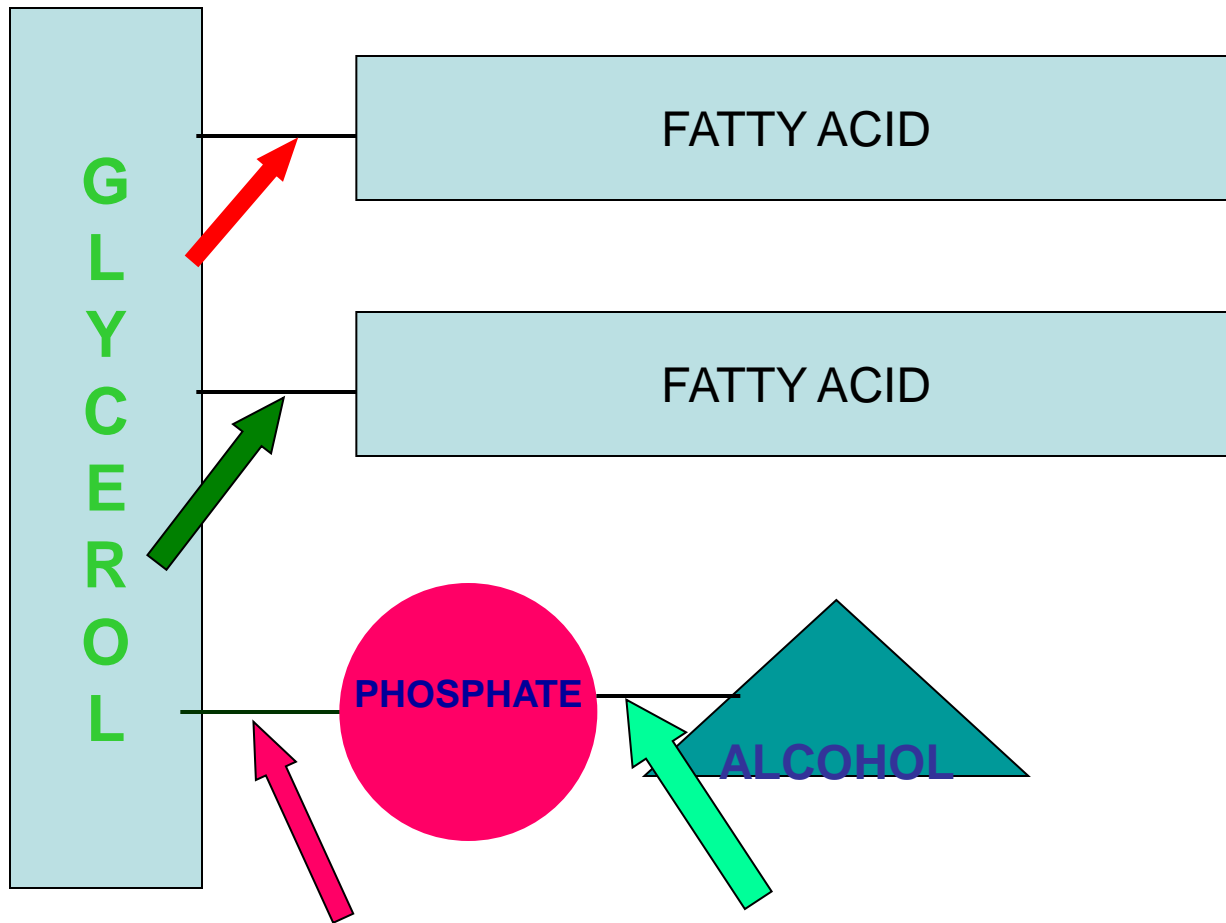


Phosphatidylglycerol



Cardiolipin: Two molecules of Phosphatidic Acid
Connected through **Glycerol**





Degradation of Phospholipids:

Phospholipase A₁

Phospholipase A₂

Phospholipase C

Phospholipase D

Degradation of Phospholipids

PHOSPHOLIPASE A_2

- *Phospholipase A_2* is present in many mammalian tissues and pancreatic juice. It is also present in snake and bee venoms.
- *Phospholipase A_2* , acting on phosphatidylinositol, releases arachidonic acid (the precursor of the prostaglandins).
- 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* is inhibited by glucocorticoids (for example, cortisol).

PHOSPHOLIPASE A_1

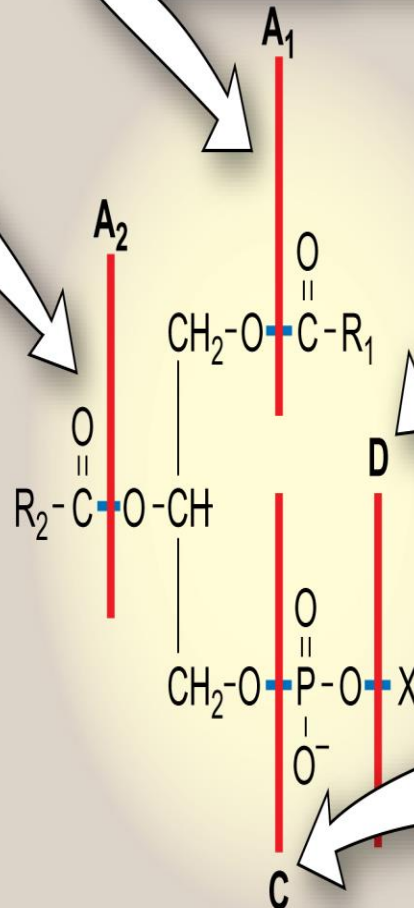
- *Phospholipase A_1* is present in many mammalian tissues.

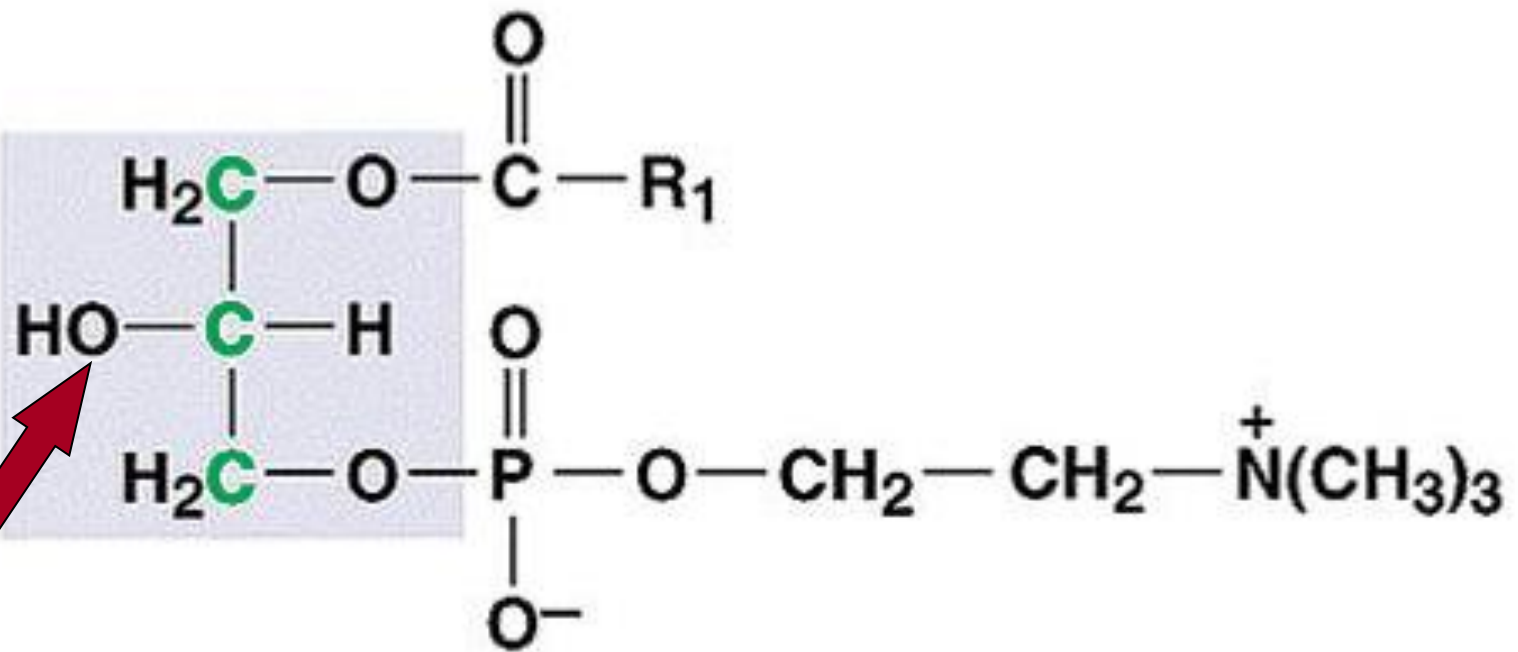
PHOSPHOLIPASE D

- *Phospholipase D* is found primarily in plant tissue.

PHOSPHOLIPASE C

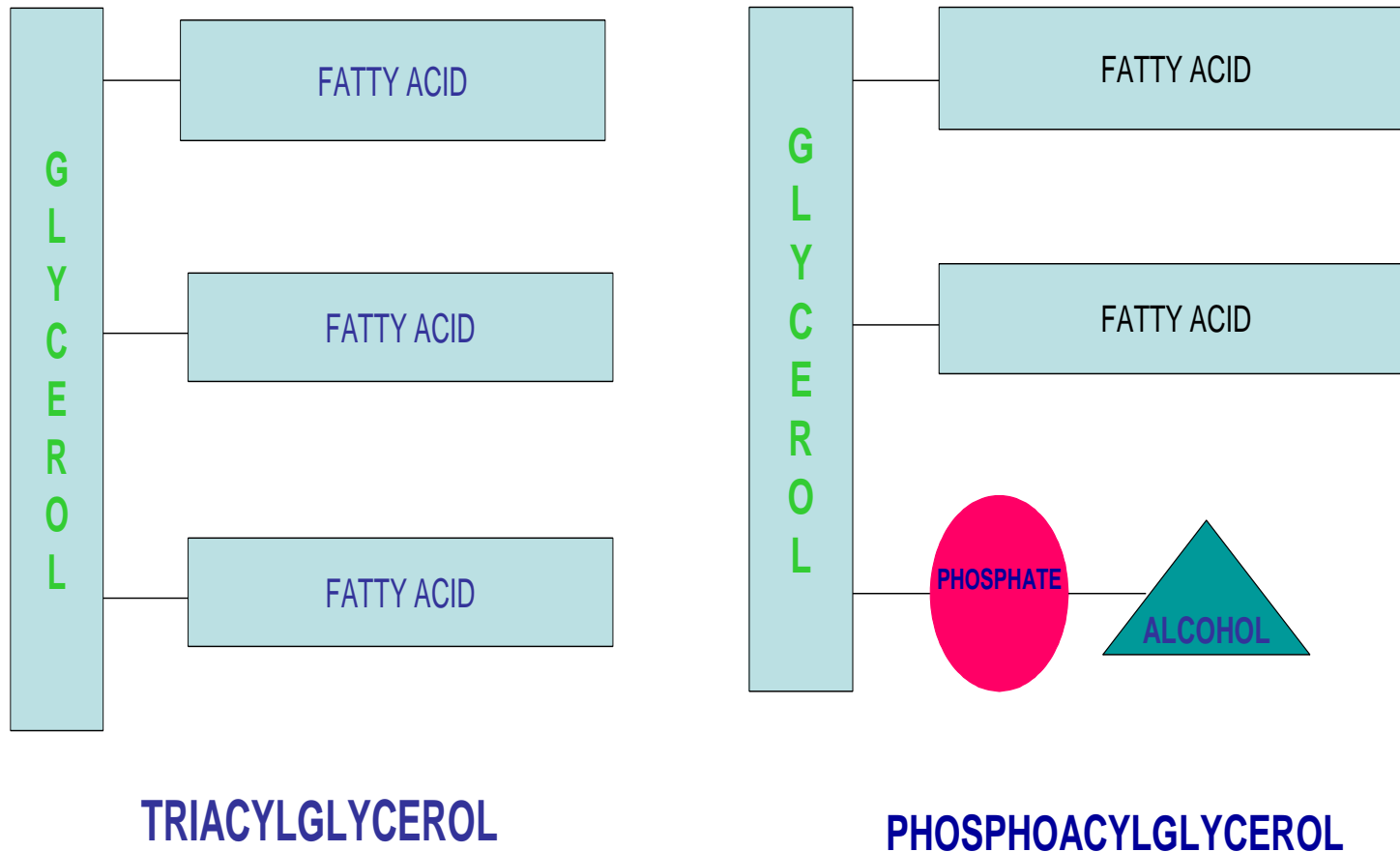
- *Phospholipase C* is found in liver lysosomes and the α -toxin of clostridia and other bacilli.
- Membrane-bound *phospholipase C* is activated by the PIP_2 system and, thus, plays a role in producing second messengers.



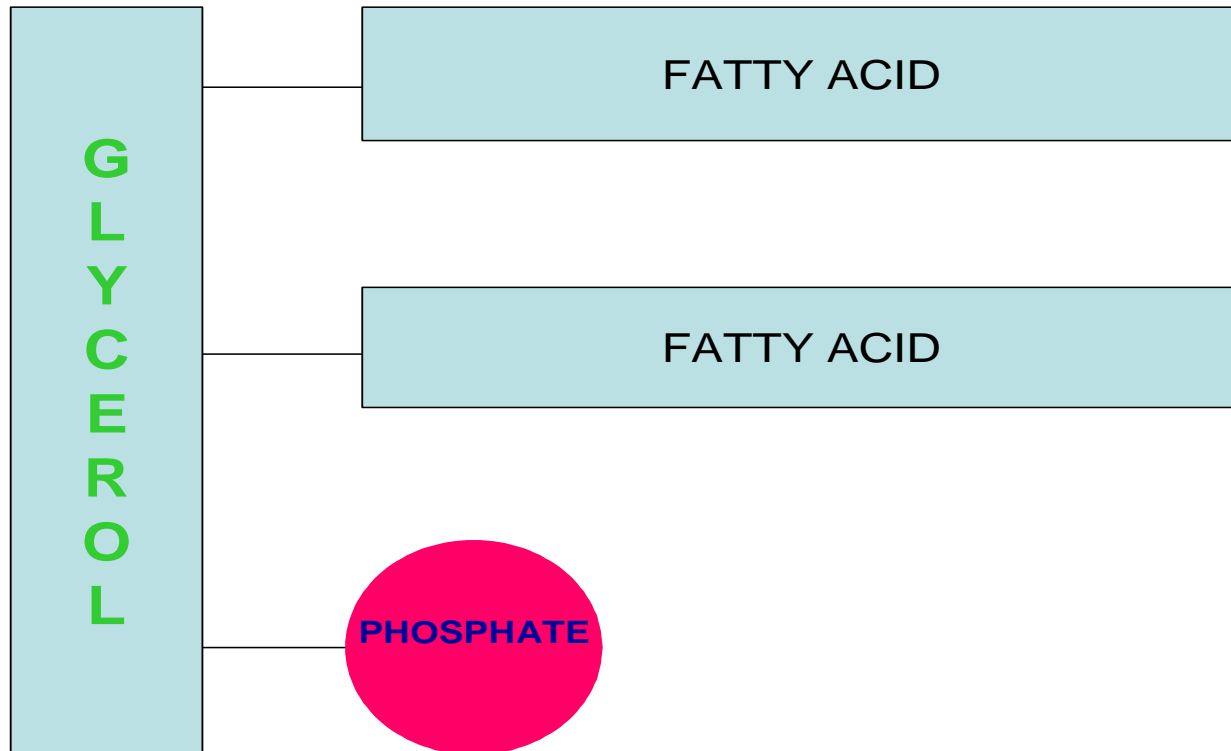


Lysophosphatidylcholine

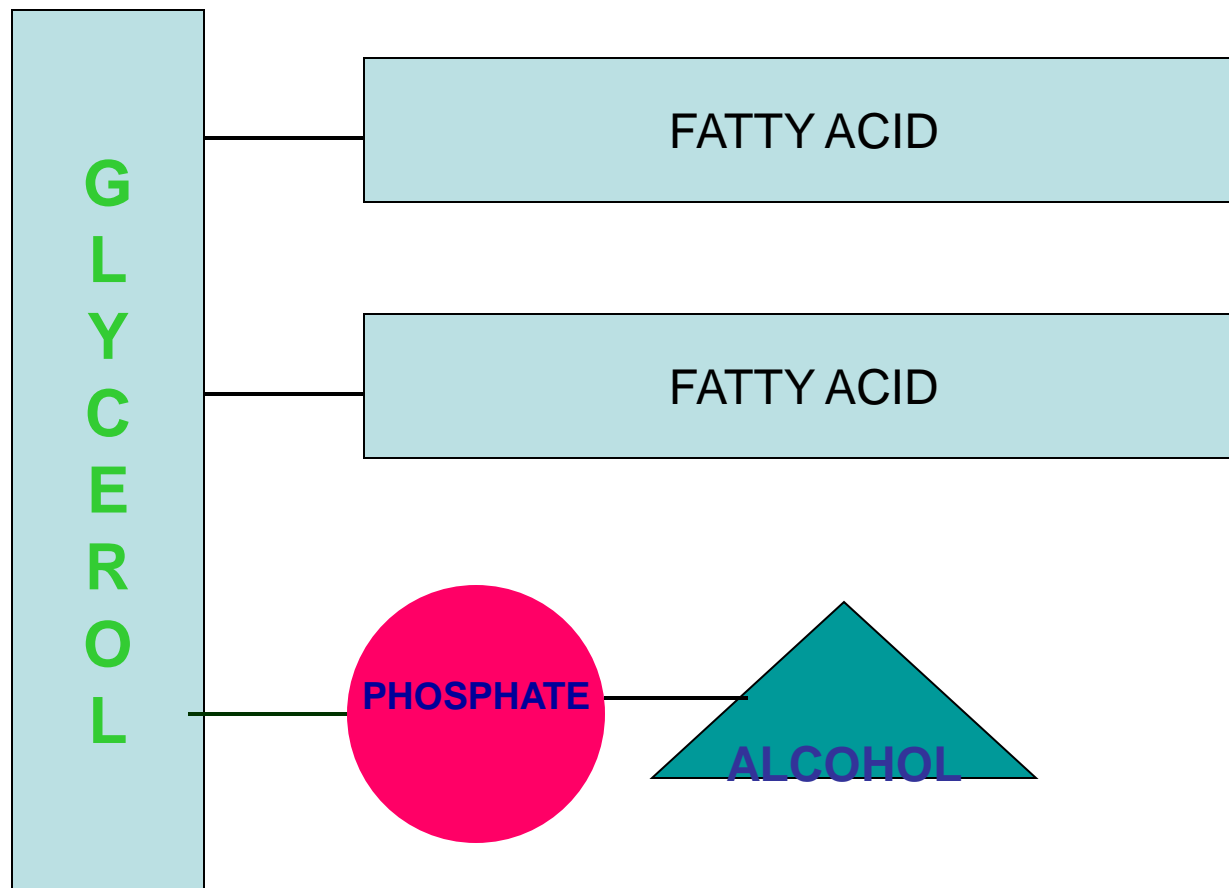
Biosynthesis of Triacylglycerol & Phosphoacylglycerol



Phosphotadic Acid is Common Intermediate



PHOSPHOACYLGLYCEROL



Biosynthesis of glycerophospholipids

Alcohol₁

Phosphate

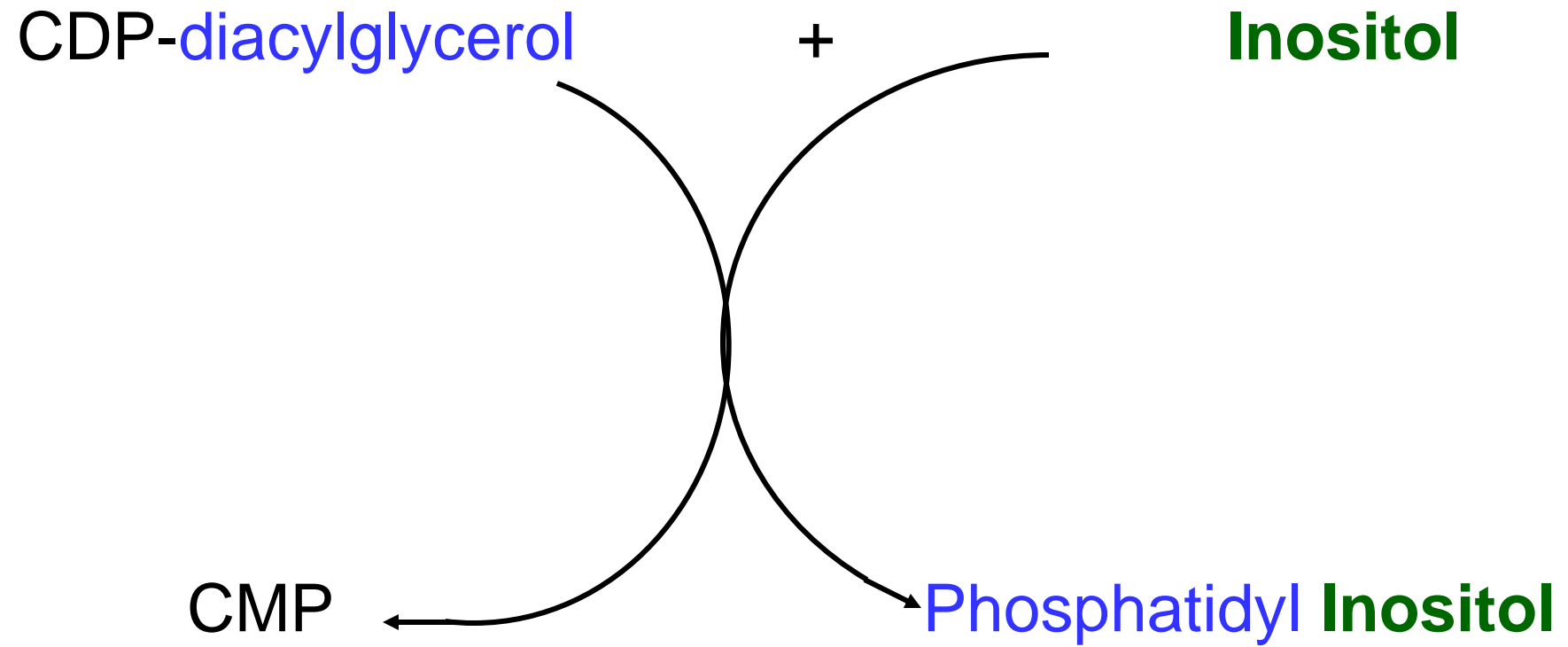
Alcohol₂

Transfer $\sim(\text{Phosphate-Alcohol}_1)$ to Alcohol₂ or

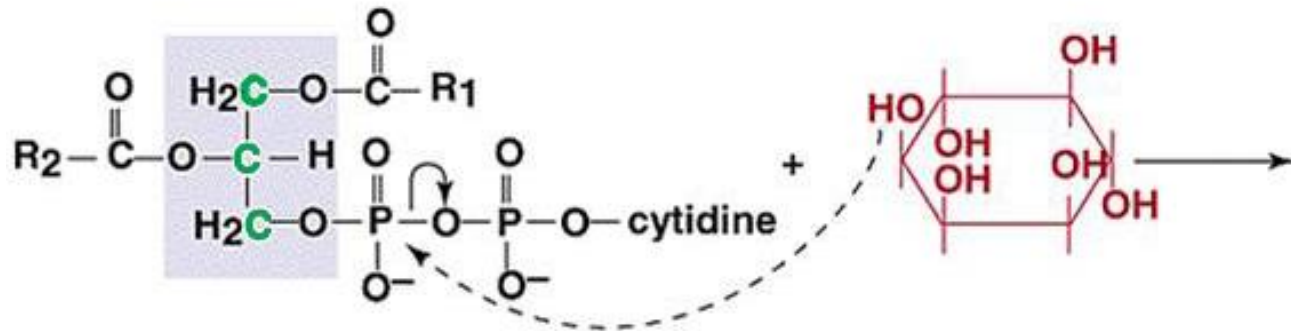
Transfer $\sim(\text{Phosphate-Alcohol}_2)$ to Alcohol₁

Synthesis of Phosphatidyl Inositol

Transfer of Phosphatidic acid to Inositol

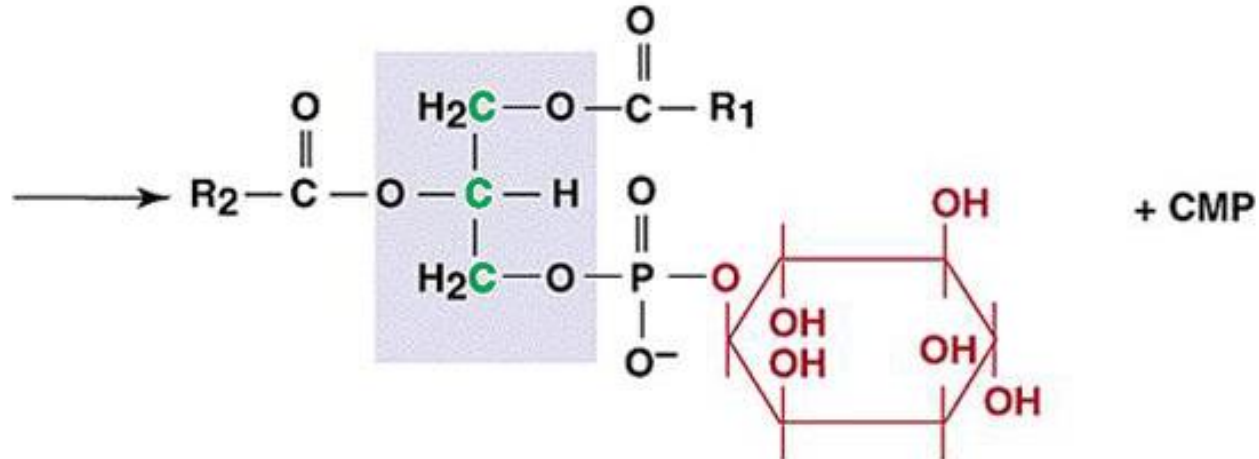


Synthesis of Phosphatidyl Inositol



CDP-diacylglycerol

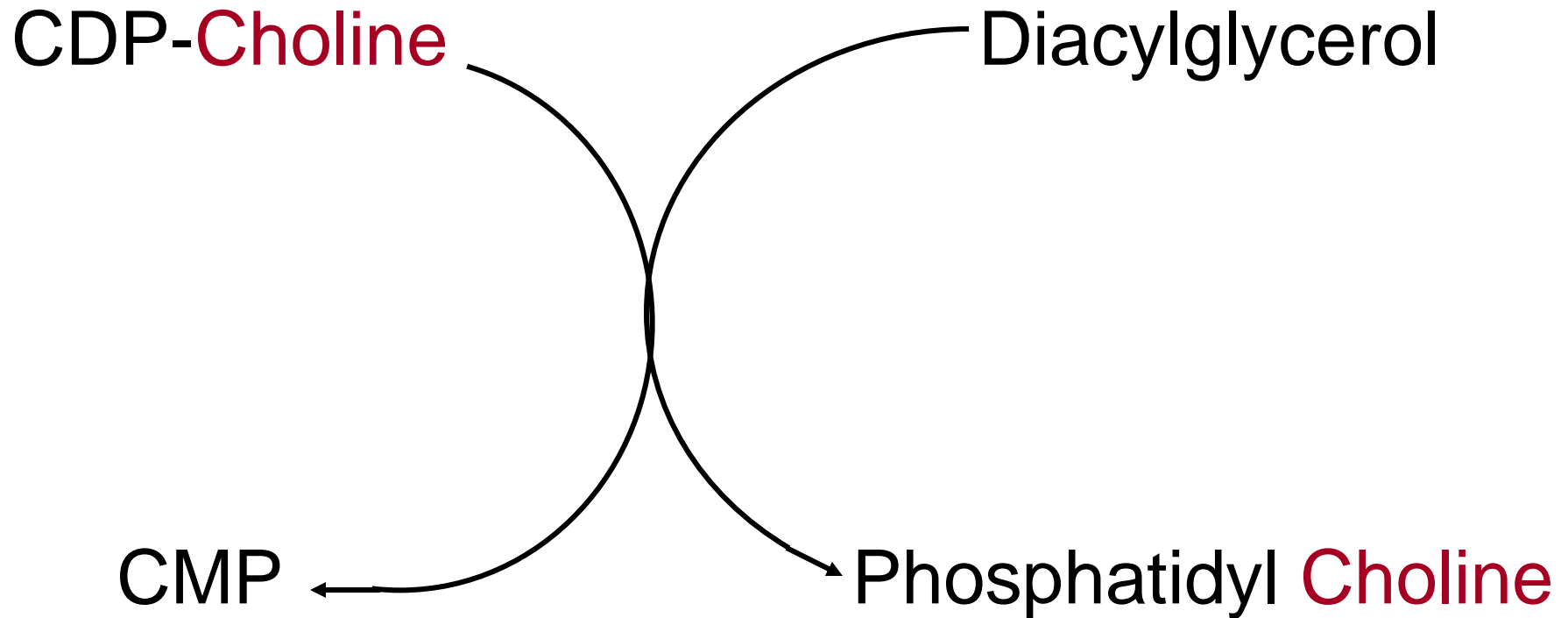
Inositol



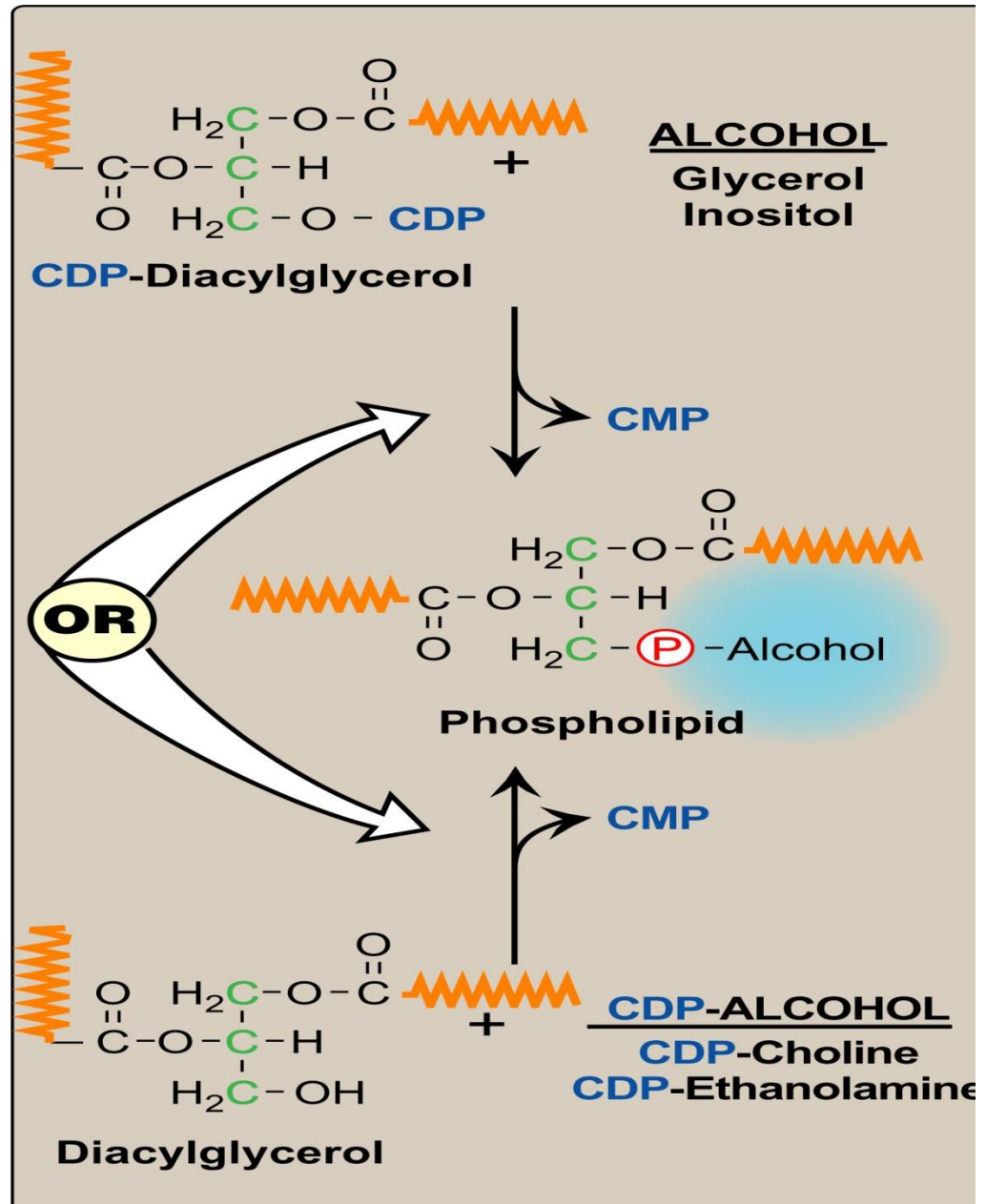
Phosphatidylinositol

Synthesis of Phosphatidyl Choline

Transfer of Phosphocholine (Ethanolamine) to Diacylglycerol

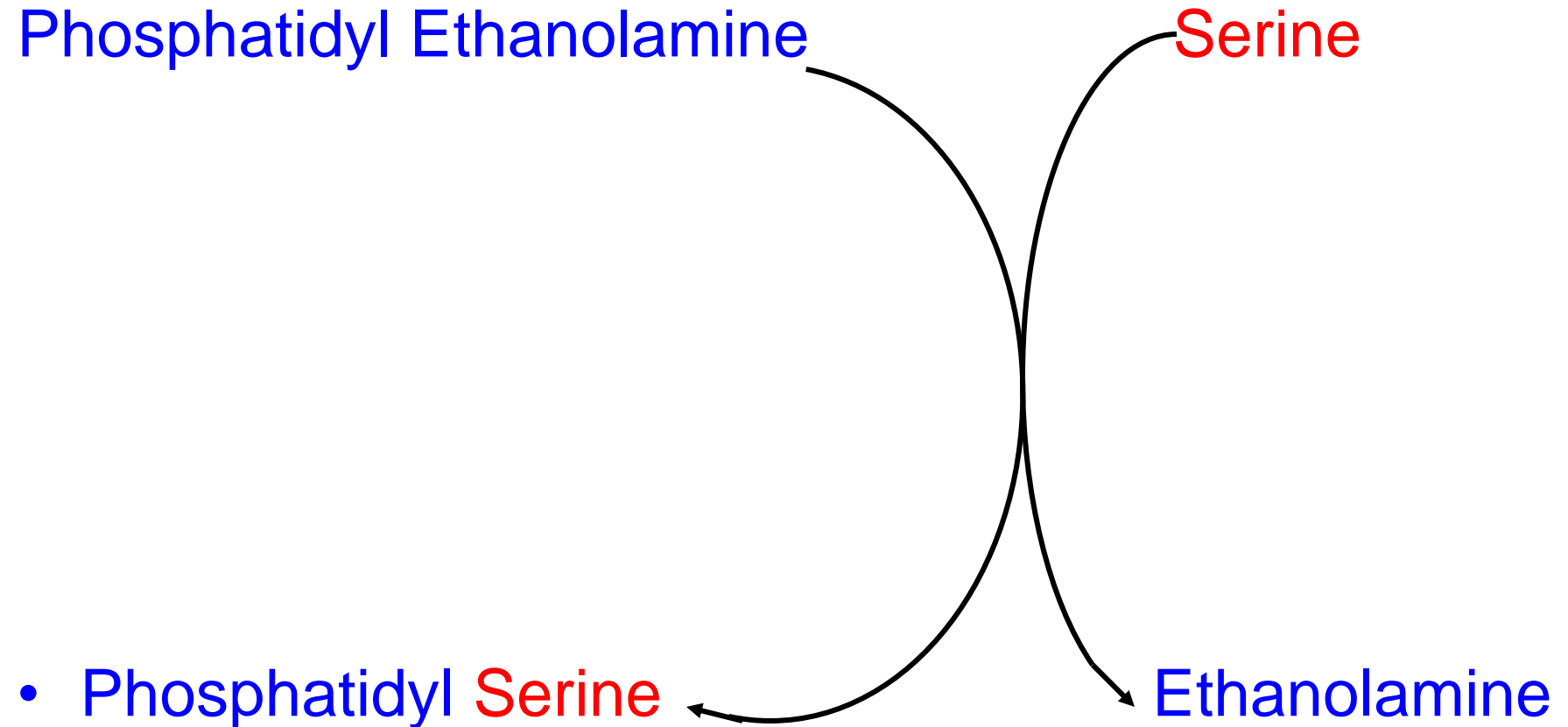


Synthesis of Phospholipids



Alteration of Polar Head Group

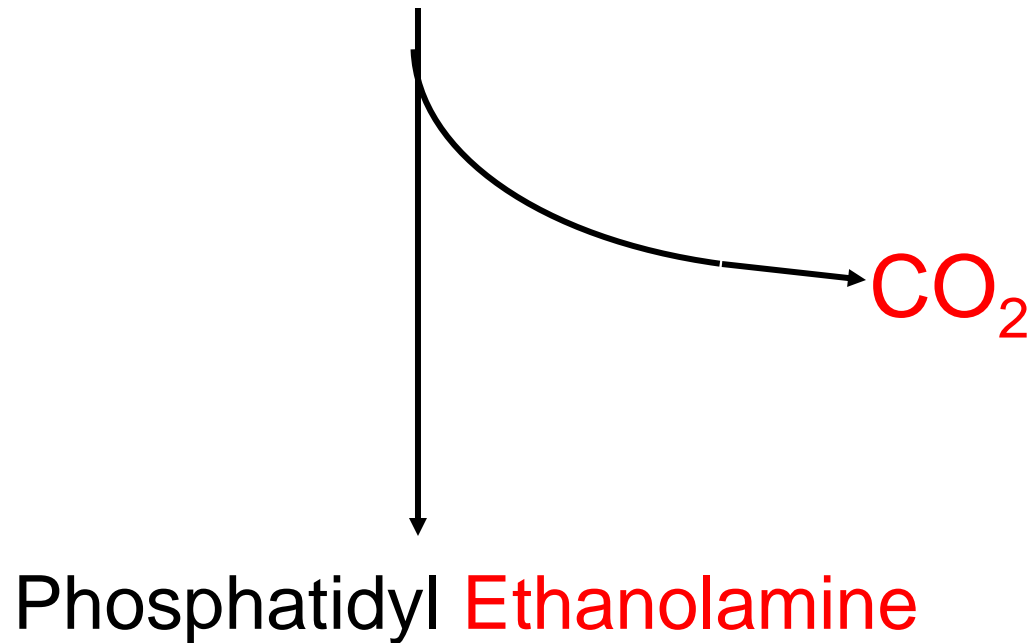
- Exchange of the Polar Head Group



Alteration of Polar Head Group

- Decarboxylation of Phosphatidyl Serine

Phosphatidyl Serine

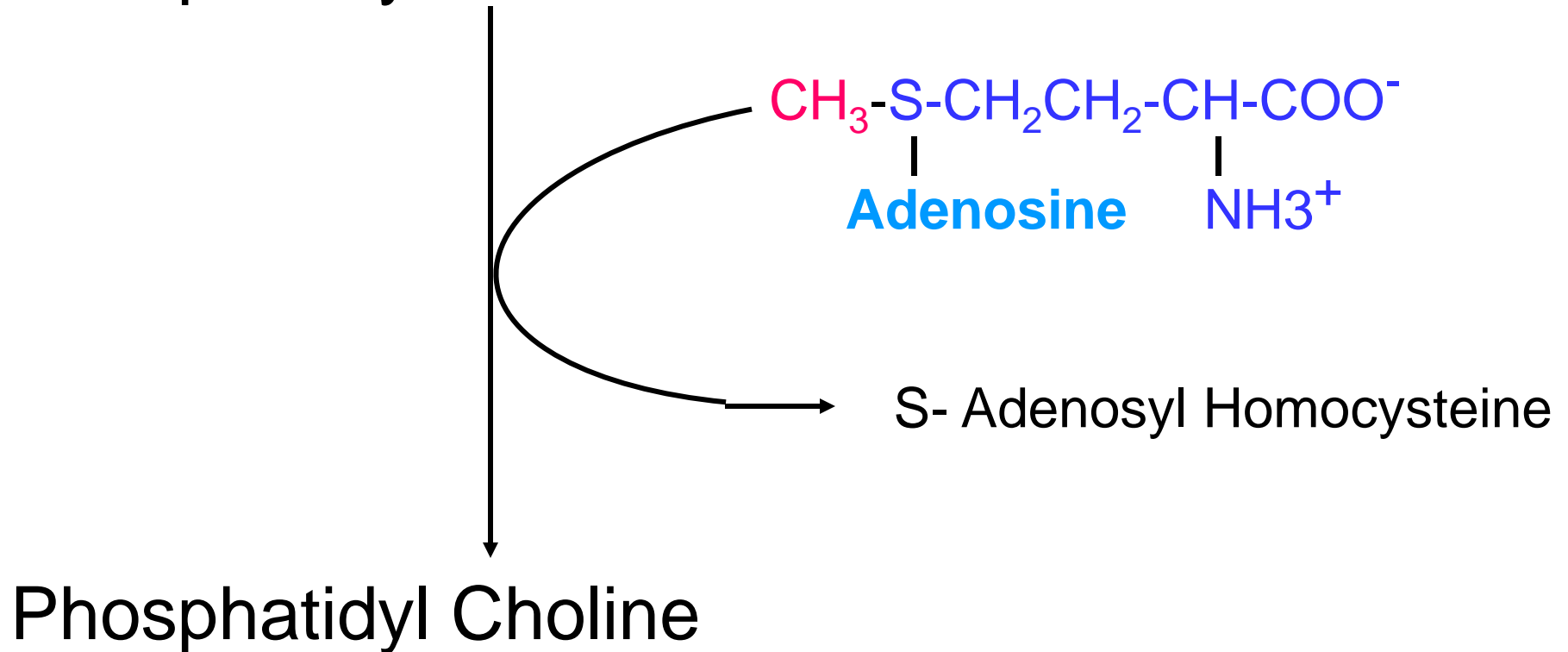


Alteration of Polar Head Group

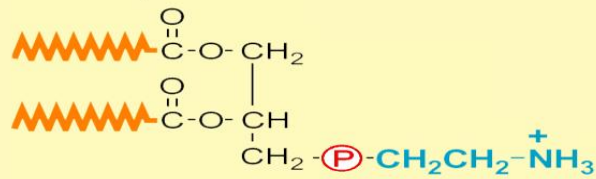
- Methylation of Phosphatidyl Ethanolamine**

S- Adenosyl Methionine (SAM); Methyl donor

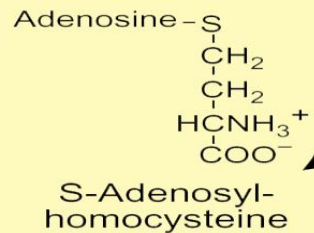
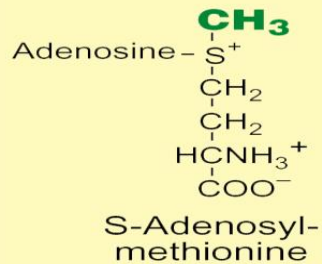
Phosphatidyl **Ethanolamine**



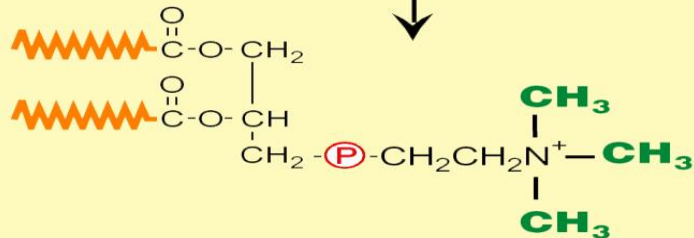
Synthesis of Phosphatidylcholine



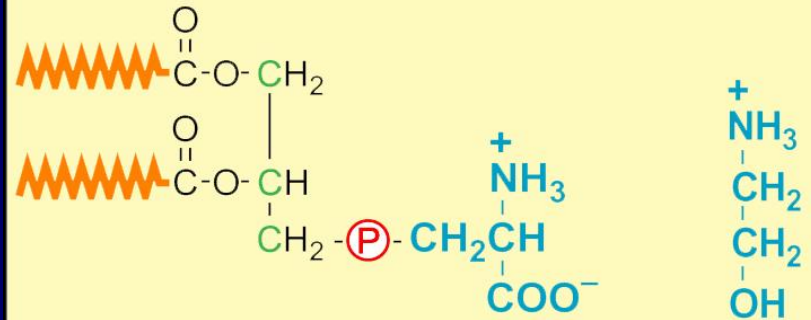
Phosphatidylethanolamine



N-Methyltransferase



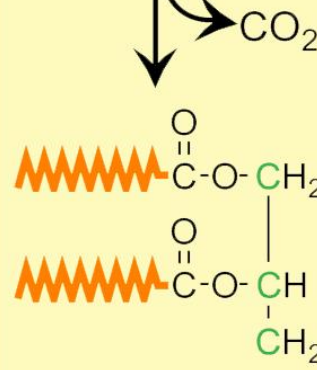
Phosphatidylcholine



Phosphatidylserine

Ethanolamine

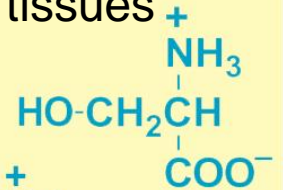
Phosphatidylserine
decarboxylase
Liver



Phosphatidylethanolamine

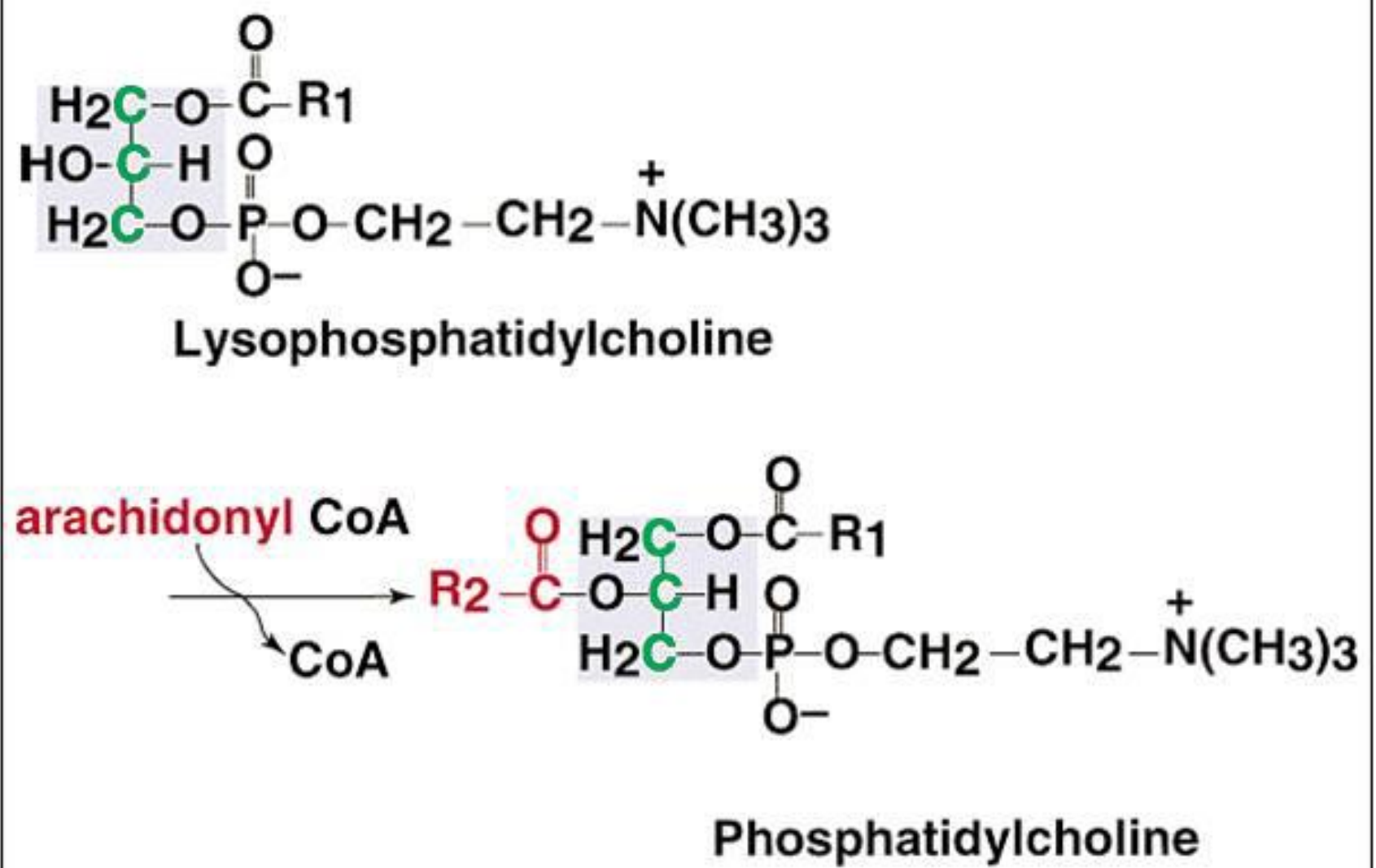
Phosphatidylethanolamine-serine
transferase
(base exchange
reaction)

Other tissues

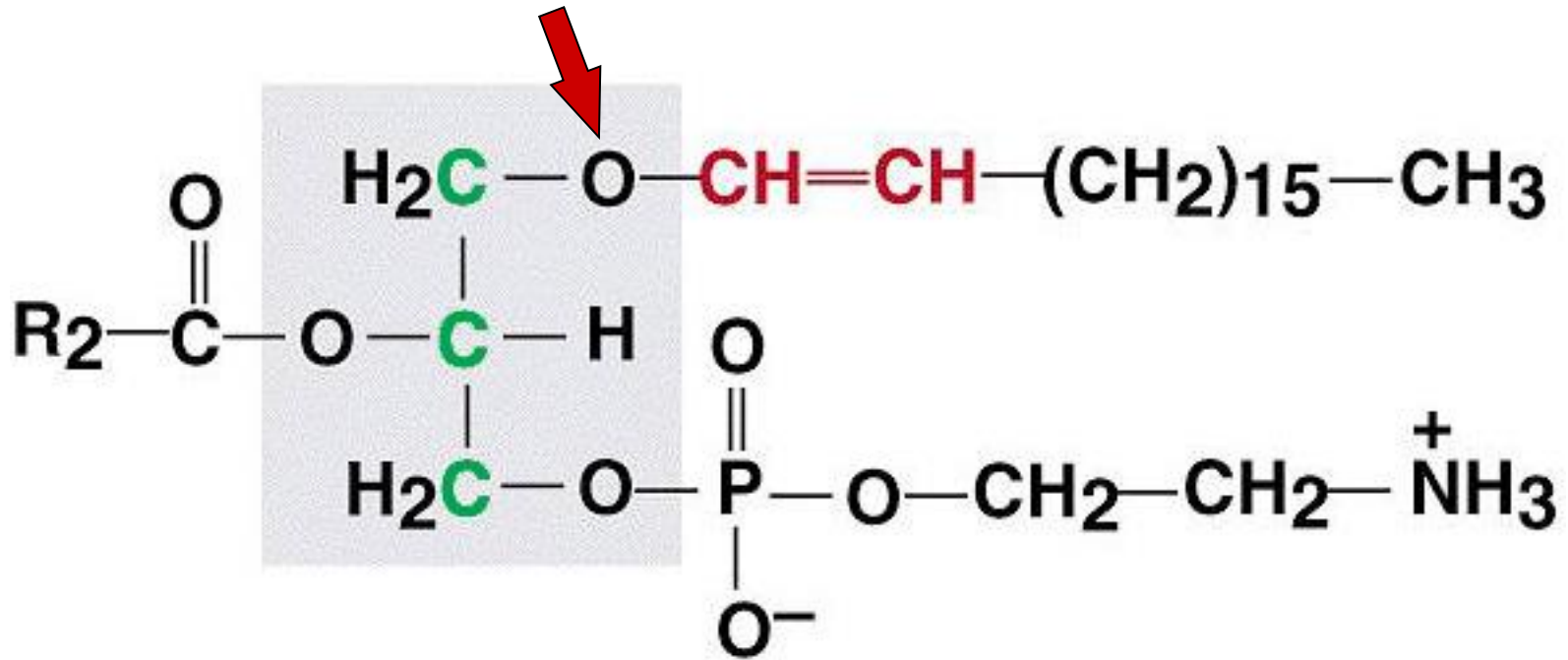


Serine

Remodeling Phospholipids: Changing the Fatty Acid



Plasmalogens



Ether Glycerophospholipids

Phosphatid**al**choline (heart muscle)

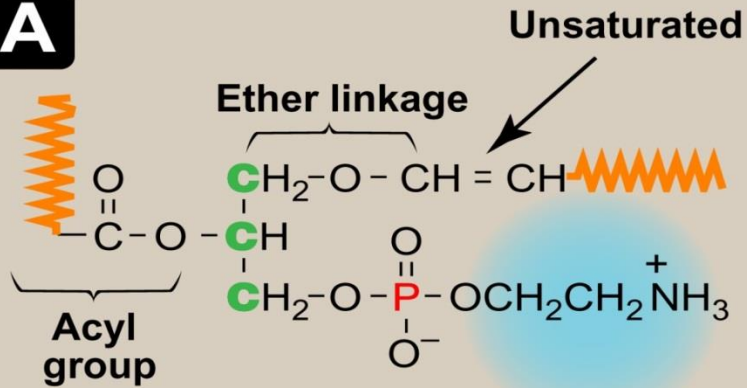
Phosphatid**al**ethanolamine (nerve tissue)

CC(=O)OCC(COP(=O)([O-])OCC[N+](C)(C)C)OCCCCCCCCCCCCCCCC

- ✓ Thrombotic and acute inflammatory events
- ✓ Released by different types of cells

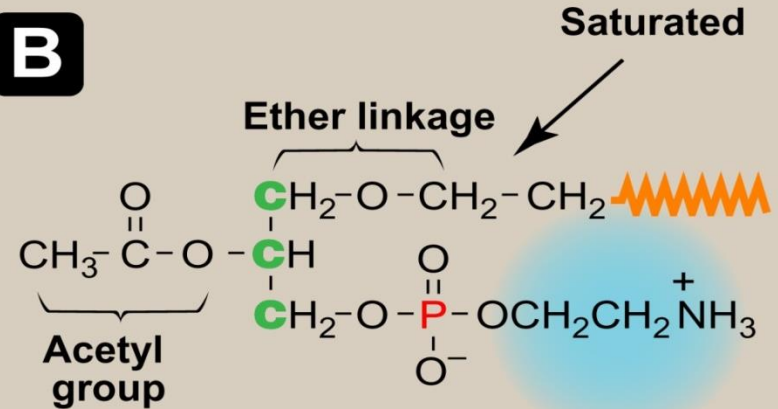
Ether Glycerophospholipids

A



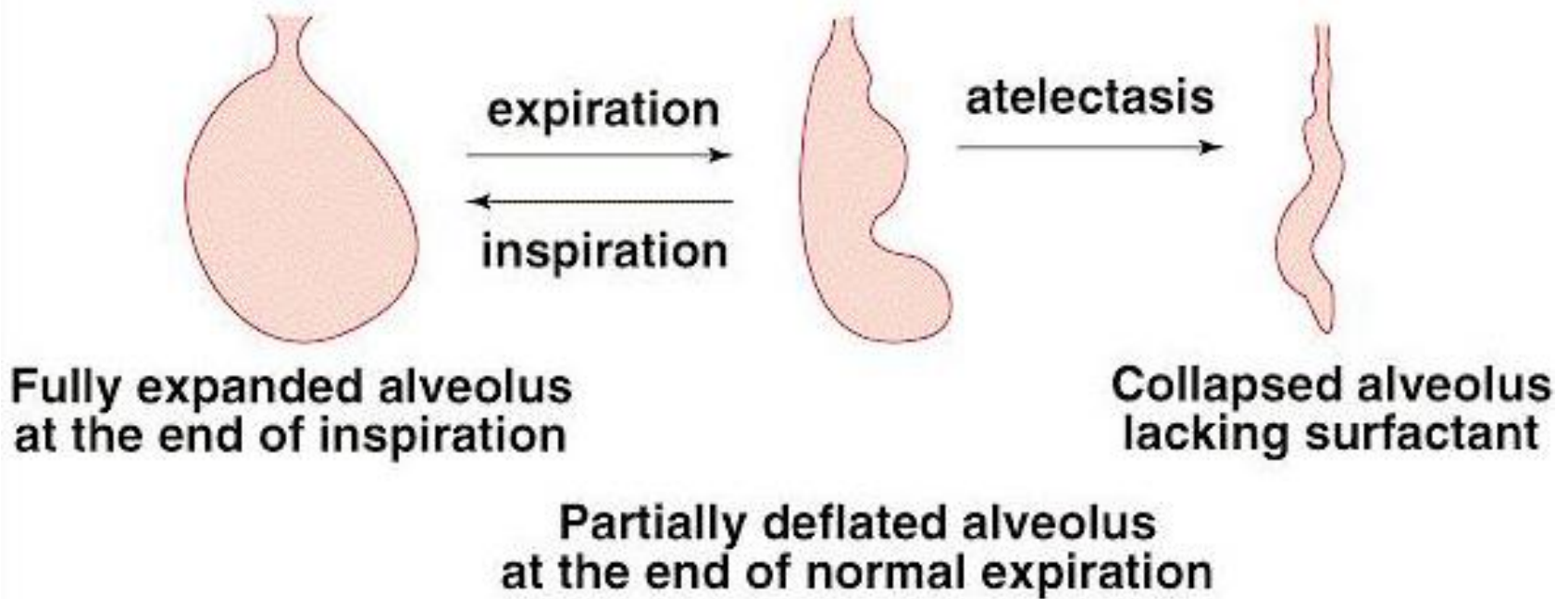
Phosphatidylethanolamine

B



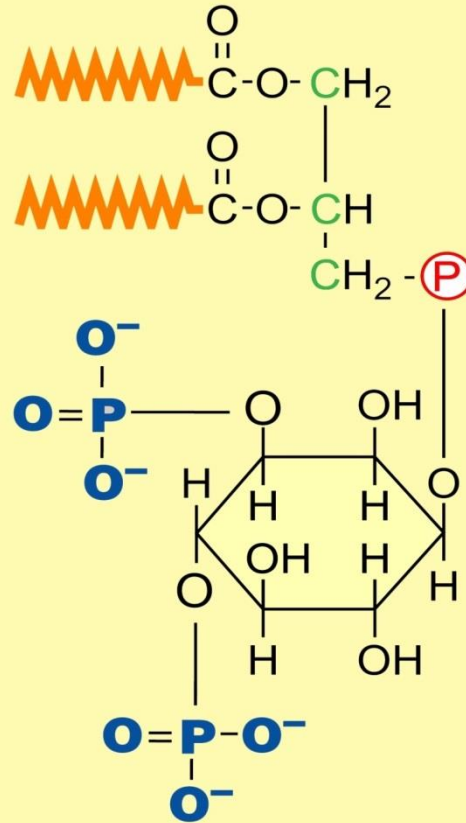
Platelet-activating factor

Surfactant Action of Phospholipids



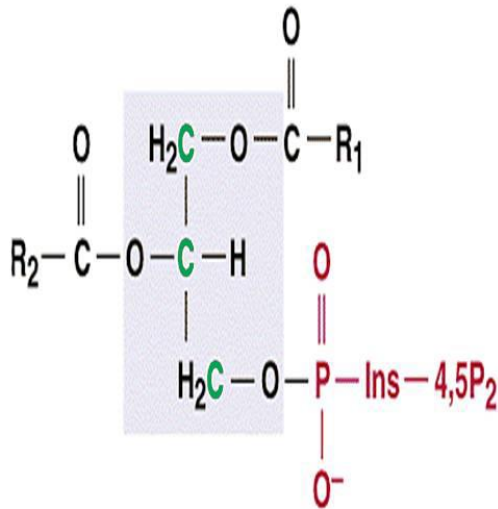
- ✓ DPPC (dipalmitoylphosphatidylcholine) by type II pneumocytes
- ✓ Decrease surface tension and reduce pressure needed to reinflate
- ✓ Prevents alveolar collapse or atelectasis
- ✓ RDS: insufficient surfactant production or secretion
- ✓ DPPC/Sphingomyelin (L/S) in amniotic fluid > 2 indicates maturity (32 weeks)

PI and signaling

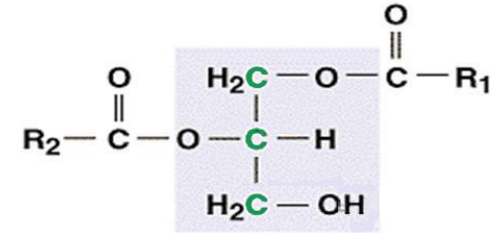
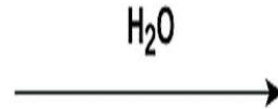


Phosphatidylinositol 4,5-bisphosphate

Phospholipase action on PIP2

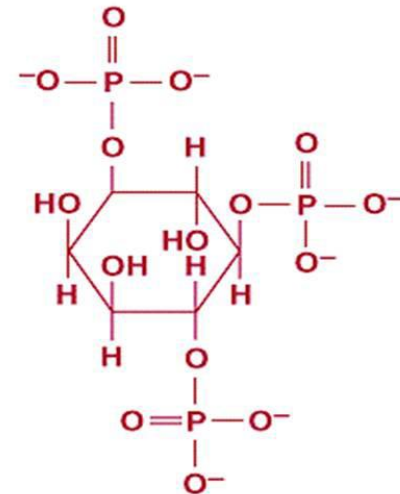


Phosphatidylinositol 4,5-bisphosphate



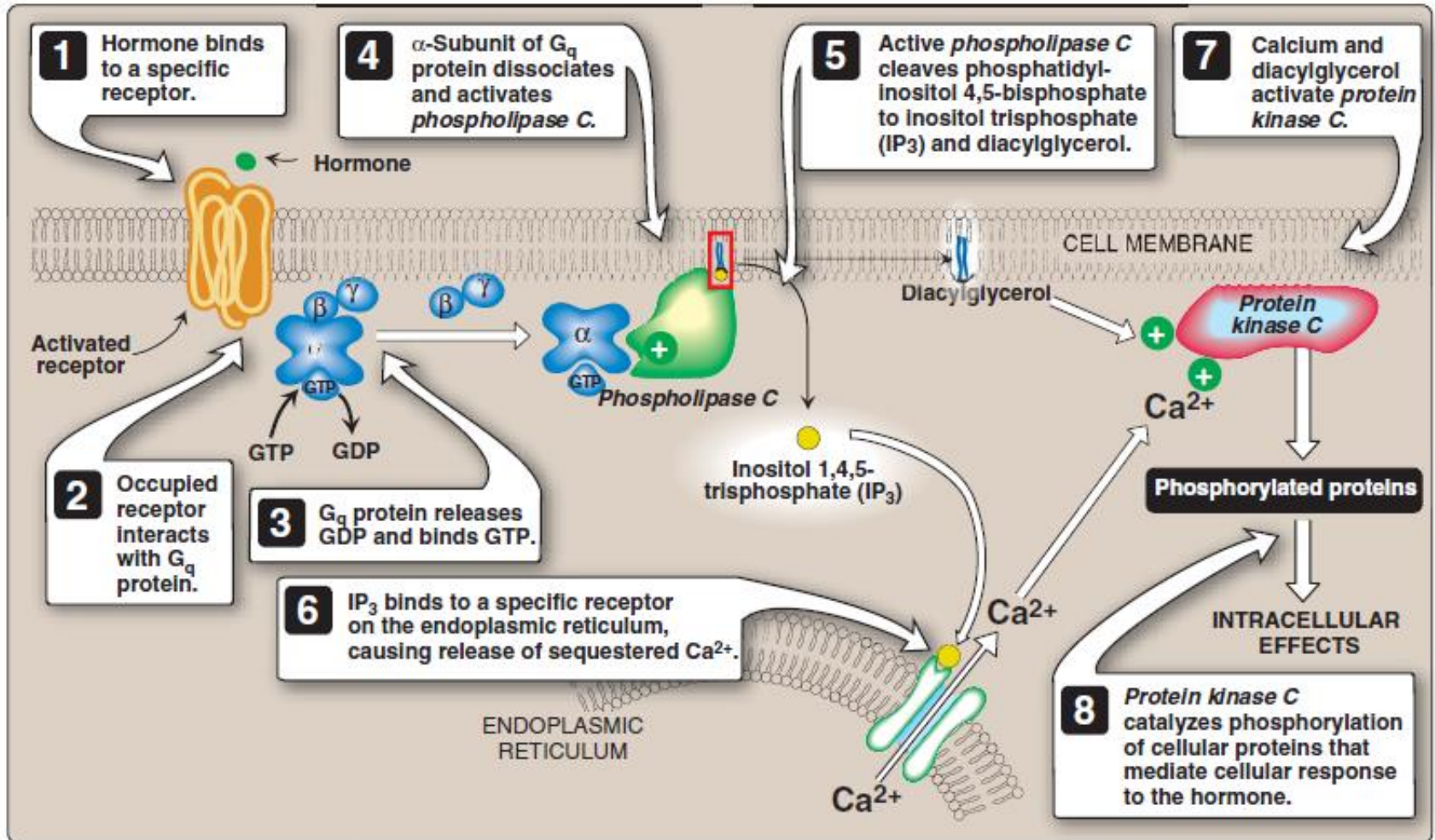
Diacylglycerol

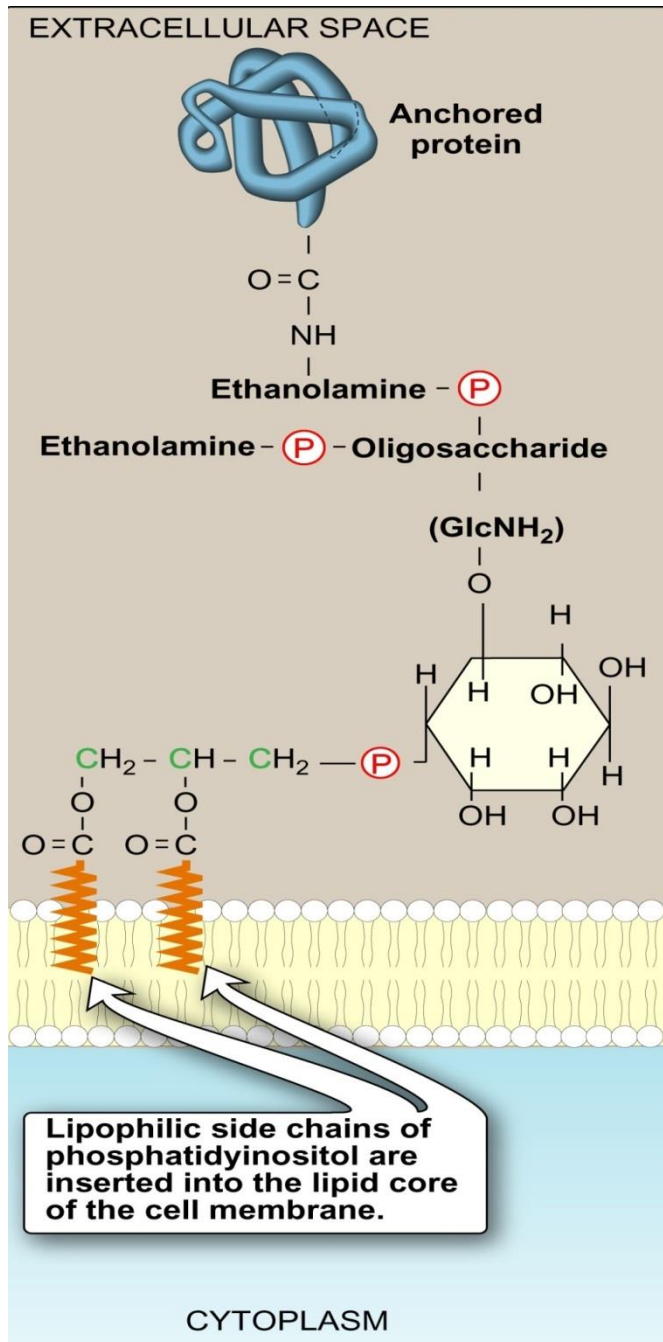
+



Inositol
1,4,5-trisphosphate

PI and signaling





GPI Anchors

- ✓ Phospholipase C can cleave protein from GPI anchors.
- ✓ Deficiency in GPI anchor synthesis in hematopoietic cells results in paroxysmal nocturnal hemoglobinuria hemolytic disease