Editing file

Phospholipids of clinical significance

Respiratory Block

- Main text
- Important
- Girls Slides
- Boys Slides
- Doctor Notes
- Extra

objectives

- Identify the types and functions of phospholipids
- Discuss the physiological importance of phospholipids
- Understand the role of glycerophospholipids in lung surfactant and their clinical implications in respiratory distress syndrome (RDS)
- Identify the classes and physiological functions of phospholipase enzymes

phospholipids

IMPORTANT!

Definition

Phospholipids are polar (amphipathic), ionic compounds that contain an alcohol group attached either to:

1- Diacylglycerol (Diacylglycerol + Phospholipid = Glycerophospholipids)

2- Sphingosine (Sphingosine + Phospholipid = Sphingophospholipids)

Classes

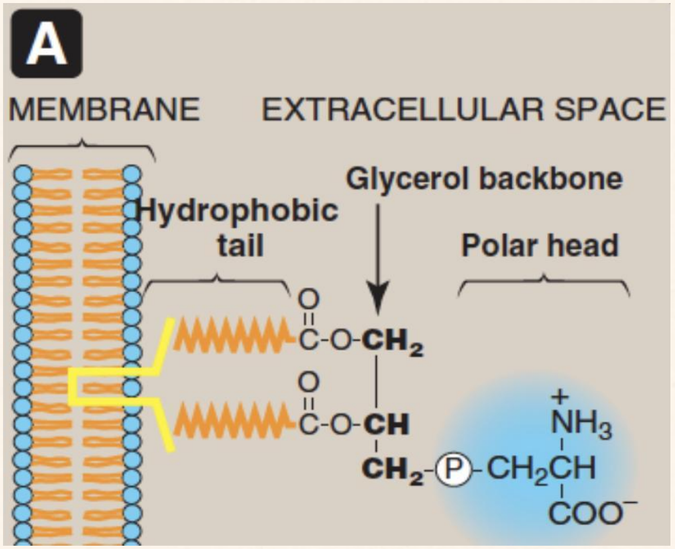
They are the major lipids of cell membranes, Two classes:

1-Glycerophospholipids
2-Sphingophospholipids

Properties

Their hydrophobic (nonpolar) portion is attached to the membrane

Their hydrophilic (polar) portion extends outward interacting with the aqueous environment



- Phospholipid is an amphipathic
- The alcohol part gives polarity to the group

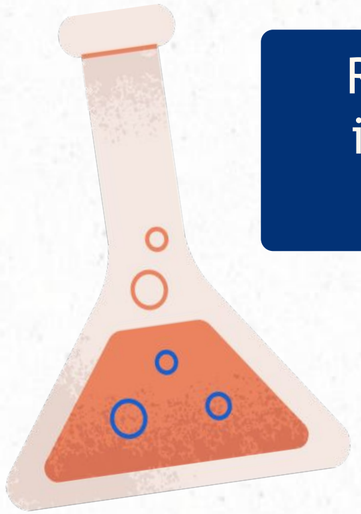
phospholipids

Functions

→ Other than it forms the cell membrane

Membrane bound phospholipids

- Anchors to cell membranes
  - Anchors: proteins that are attracted to the surface (outside the cell membrane.)
- Reservoir for intracellular messengers



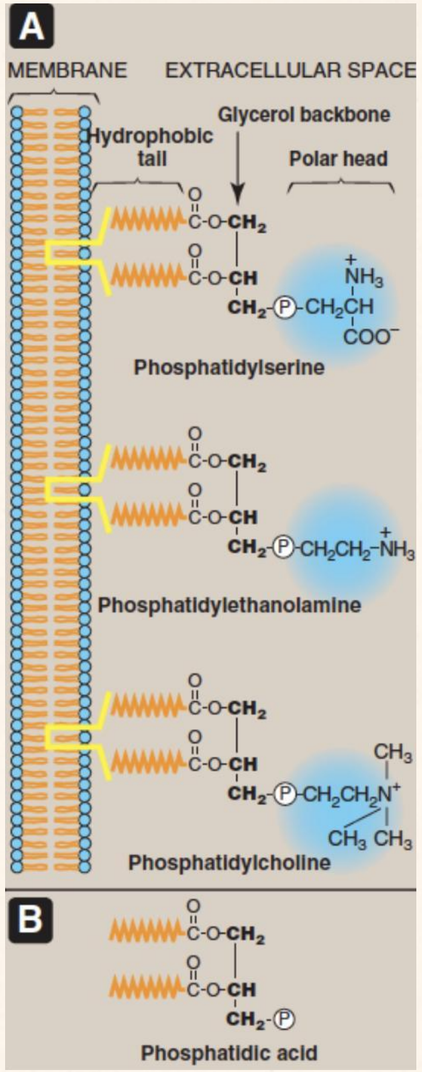
Non-Membrane bound phospholipids

- **Lung surfactant**
- Components of bile (as detergents to solubilize cholesterol)
  - Bile is produced by liver to facilitate fat absorption

Glycerophospholipids

Glycerophospholipids (phosphoglycerides)

- A major class of phospholipids
- Contain **glycerol**
- All contain phosphatidic acid (PA)
- PA is the simplest phospholipid



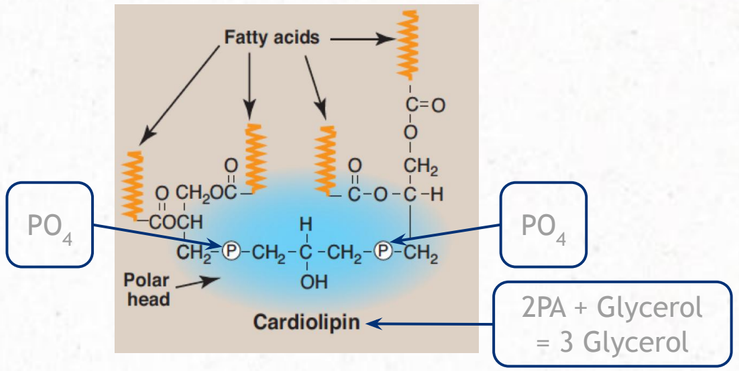
Phospholipids are derived from PA such as:

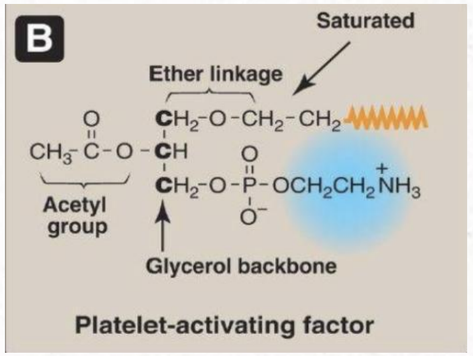
Serine + PA	Phosphatidyl**serine** (PS)	Cell signaling, Blood clotting
Ethanolamine+PA	Phosphatidyl**ethanolamine** (PE) (common name cephalin)	Cell membrane
Choline + PA	Phosphatidyl**choline** (PC) (common name lecithin)	Lung surfactant
Inositol + PA	Phosphatidyl**inositol** (PI)	Cell signaling
Glycerol + PA	Phosphatidyl**glycerol** (PG)	Lung surfactant

Glycerophospholipids

Some Examples of Glycerophospholipids

	Cardiolipin	Platelet activating factor (PAF)
Structure	Two molecules of PA joined to an additional molecule of glycerol through PO_4 groups	One Fatty acid attached to glycerol by **Ether linkage**, and instead of having fatty acid at carbon No.2 it has an acetyl group
Location	in the inner mitochondrial membrane	Binds to cell surface receptors
Function	maintenance of respiratory complex of electron transport chain	Triggers thrombotic and acute inflammatory reaction Activate platelets so they can stick together





Role of PC in lung Surfactant

- Alveolar cells of the lungs are lined by the extracellular fluid layer
- Alveolar cells type 2 secrete **DPPC** (a major lung surfactant)

Lung surfactant

Consist of

Lipids (90%) including Dipalmitoylphosphatidylcholine **(DPPC)** You can write the abbreviation

Proteins (10%)

Functions

- Decreases the surface tension of the fluid layer
- Reduces pressure needed to re-inflate alveoli
- Prevents alveolar collapse (atelectasis)

Respiratory distress syndrome (RDS)

In **Preterm infants** due to deficiency of lung surfactant

A Major cause of neonatal death

Treatment: Glucocorticoids to mother to promote lung maturation

In **Adults** due to damaged alveoli by infection or trauma

By decreasing the surface tension of the fluid layer and reducing pressure needed to re-inflate alveoli.

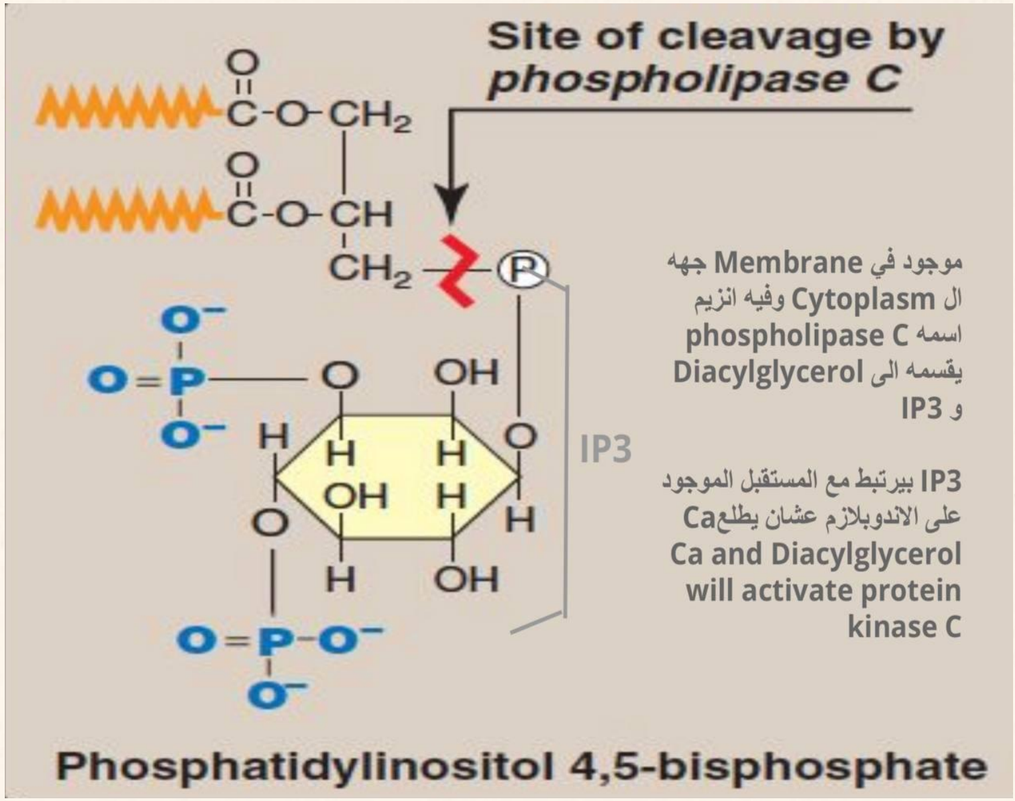
Roles of Phosphatidylinositol(PI)

Foundation block — cell signaling lecture

In Cell Signaling:

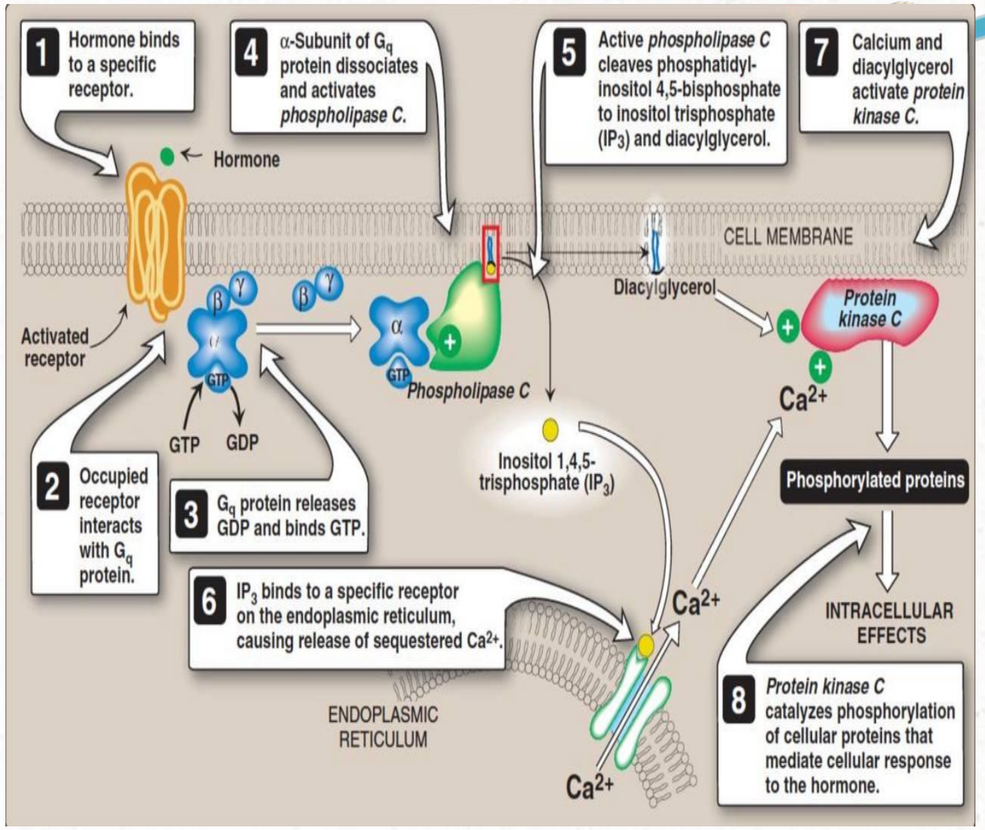
Plays important role in intracellular signaling

PI is part of Calcium-phosphatidylinositol system



Roles of PI

1. Hormone or neurotransmitter binds to a specific receptor
2. Occupied receptor interacts with **Gq protein**
3. Gq protein releases GDP and binds GTP
4. α subunit of Gq protein dissociates and activates phospholipase C (enzyme attached to the cell membrane)
5. Active phospholipase C cleaves phosphatidylinositol 4,5-bisphosphate to inositol trisphosphate (IP_3) and diacylglycerol

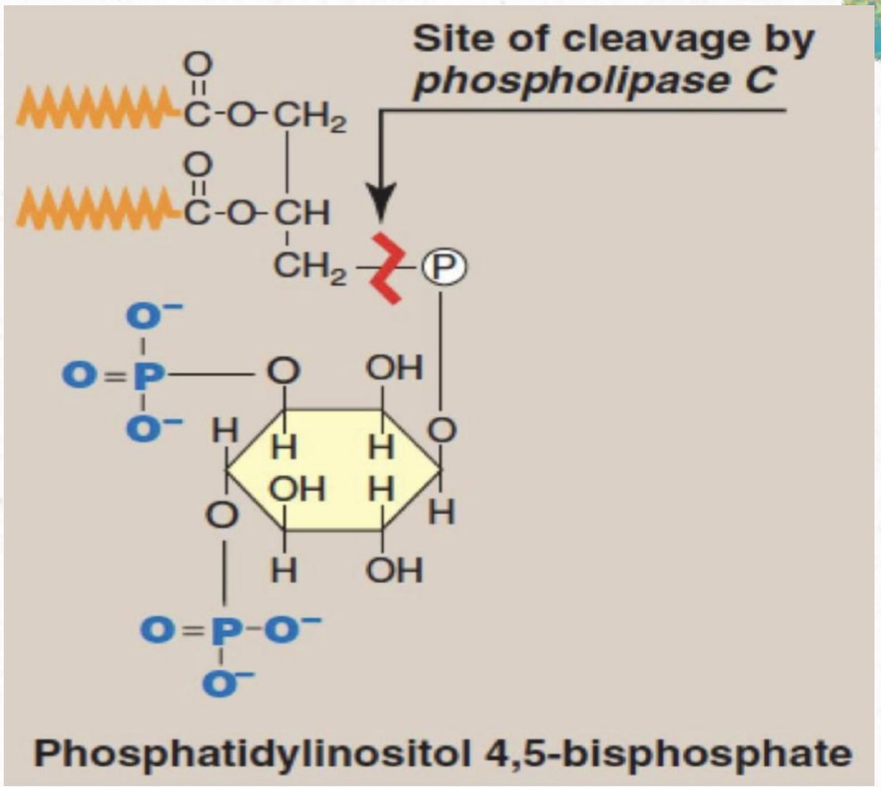


Roles of PI

6. IP_3 binds to a specific receptor on the endoplasmic reticulum causing release of sequestered Ca^{2+}

7. Calcium and diacylglycerol activate **protein kinase C**

8. Protein kinase C catalyzes phosphorylation of cellular proteins that mediate cellular response to the hormone



Roles of PI

In Membrane **protein** Anchoring:

- Anchoring of proteins to membranes through Carbohydrate-PI bridge EC space→protein-carbohydrate-PI→cell membrane
- Anchoring proteins can be cleaved by Phospholipase C enzyme

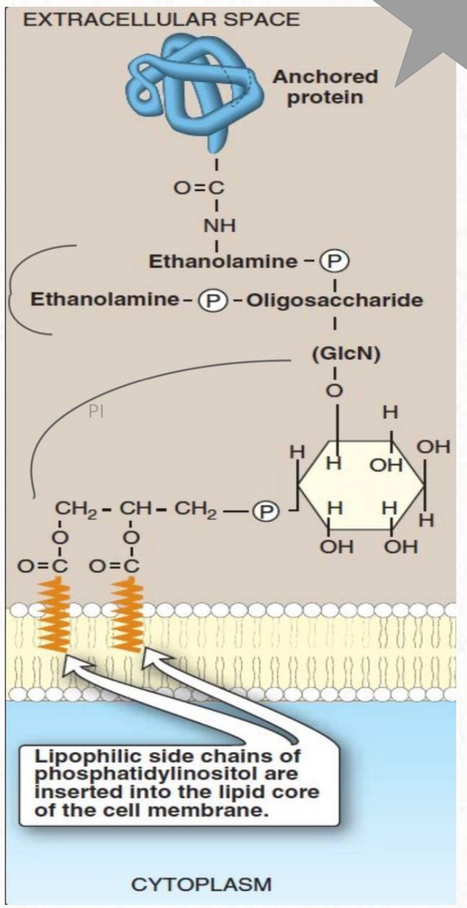
Examples:

- Alkaline Phosphatase:

(on the surface of small intestine)

- Acetylcholine esterase:

(on postsynaptic membrane of neurons)

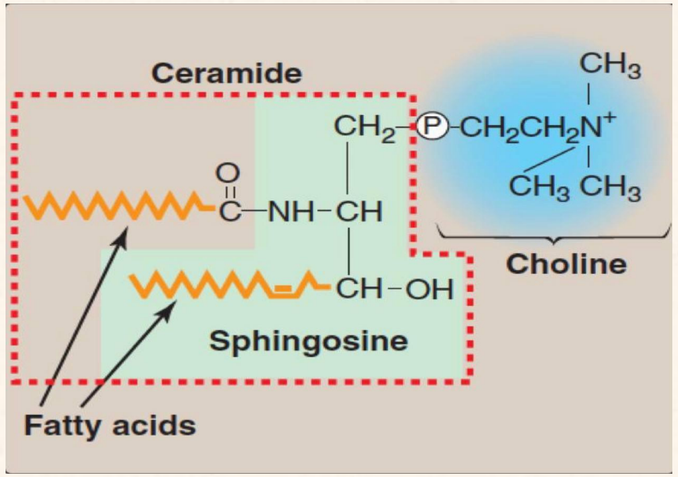


كل واحد منهم يرتبط مكان البروتين (مثل الازرق اللي بالصورة) بعد ما يخلصون شغلهم يروحون

Sphingophospholipids

Definition

- A long-Chain Fatty acids attached to Sphingosine → Ceramide
- Ceramide + phosphorylcholine → sphingomyelin



Example

Sphingomyelin

Function

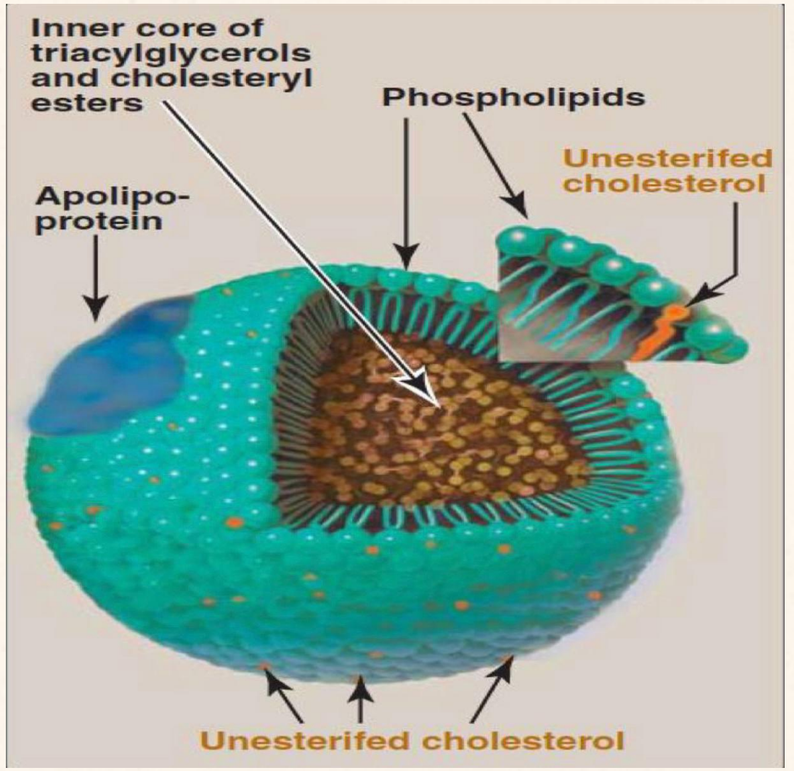
An important component of myelin that protects and insulates nerve fibers

Phospholipids in lipoprotein particles

The outer core of lipoprotein particles is **hydrophilic**, contains phospholipids and free cholesterol

Allows transport of core Lipids in aqueous plasma

The outer core **Hydrophilic** (protein)
The inner part **Hydrophobic** (lipid)



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

مهمة في نقل lipids ، كيف تنقل lipids في محلول مائي؟ لازم يكون حول lipids جزء hydrophilic فراح يكون حوله phospholipids لأن جزء منها محب للماء وهو على برا وجزء كاره للماء وهو داخل

Phospholipases

- Phospholipids are degraded by phospholipase enzymes
- Present in all tissues including **pancreatic juice**
- Glycerophospholipids are degraded by phospholipase A1, A2, C, D
- Sphingophospholipids are degraded by sphingomyelinase

Functions of phospholipases:

- Digestion of phospholipids by pancreatic juice
- Important for remodeling of phospholipids
- Production of second messengers (DAG and IP_3)
- Pathogenic bacteria produce phospholipases to dissolve cell membranes and spread infection

IMPORTANT!

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.
- *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).

+ has Role in infflamation

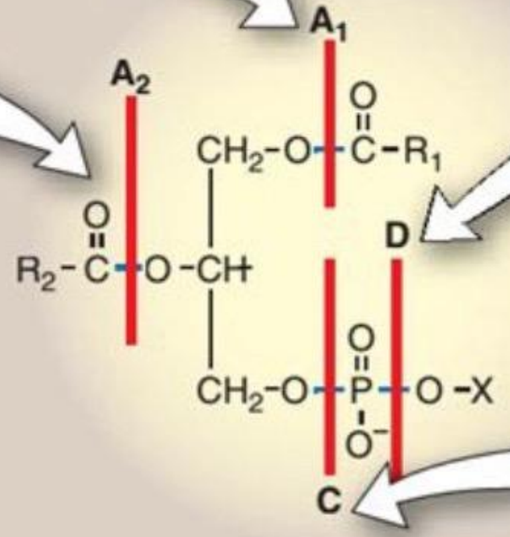
PHOSPHOLIPASE A_1

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

PHOSPHOLIPASE D

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

→ cell signaling



PHOSPHOLIPASE C

- *Phospholipase C* is found in liver lysosomes and the α-toxin of clostridia and other bacilli.

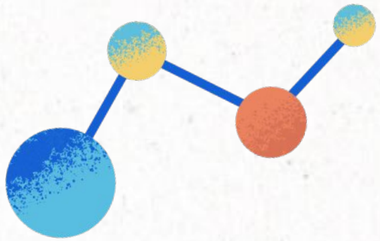
+bacteria

- Membrane-bound *phospholipase C* is activated by the PIP_2 system and, thus, plays a role in producing second messengers.

Take Home Messages

- Phospholipids are complex lipids that perform important physiological functions in the body
- Membrane-bound phospholipids are involved in cell signaling, protein anchoring and myelin protective functions
- Non membrane-bound phospholipids function as lung surfactant and as detergent in the bile
- Phospholipases are enzymes that degrade phospholipids
- They are important for remodeling of phospholipids

References: Lippincott's Illustrated Reviews, Biochemistry, 6th Edition, Denise R. Ferrier, Lippincott Williams & Wilkins, USA, pp 201-207.



MCQ

Q1) Which of the following is the simplest glycerophospholipids?			
A-PG	B-PC	C-PI	D-PA
Q2) The inner mitochondrial membrane is rich in?			
A-Cephalin	B-Cardiolipin	C-PAF	D-PI
Q3) Which of the following plays a role in cell signaling?			
A-Phosphatidylcholine	B-Phosphatidylinositol	C-Phosphatidylglycerol	D-Phosphatidylethanolamine
Q4) The outer part in lipoproteins is.			
A- Hydrophilic	B- Hydrophobic	C- Amphipathic	D- All of the above
Q5) Which of these PI's is present on postsynaptic neurons?			
A- Acetylcholin esterase	B- Alkaline phosphatase	C-Acetylcholine phosphatase	D- Alkaline esterase

Answers: 1-D 2-B 3-B 4-A 5-A

SAQ

Q1) Name 3 phospholipids that are derived from PA and their function?

Q2) Enumerate functions of

Phospholipase A2

Q3) Write one example of

Sphingophospholipid

Answers

Q1)

slide 5

Q2)

Slide 15

Q3)

Sphingomyelin

Biochemistry Team

Leaders

Lama Alahmari

Faisal Bakri

Members

Ghaida Alotaibi

Reema Aldhabaan

Norah Albahily

Khalid Alghamdi

Osama Alhenaki

Faisal Alghamdi

Nasser Alabdulsalam