Biochemistry

Phospholipids of clinical significance

Nothing is ever wrong.
We learn from every step we take. Whatever you did today was the way it was meant to be.
Be proud of you !

- Important.
- Extra Information.
- **Doctors slides**

Revised by
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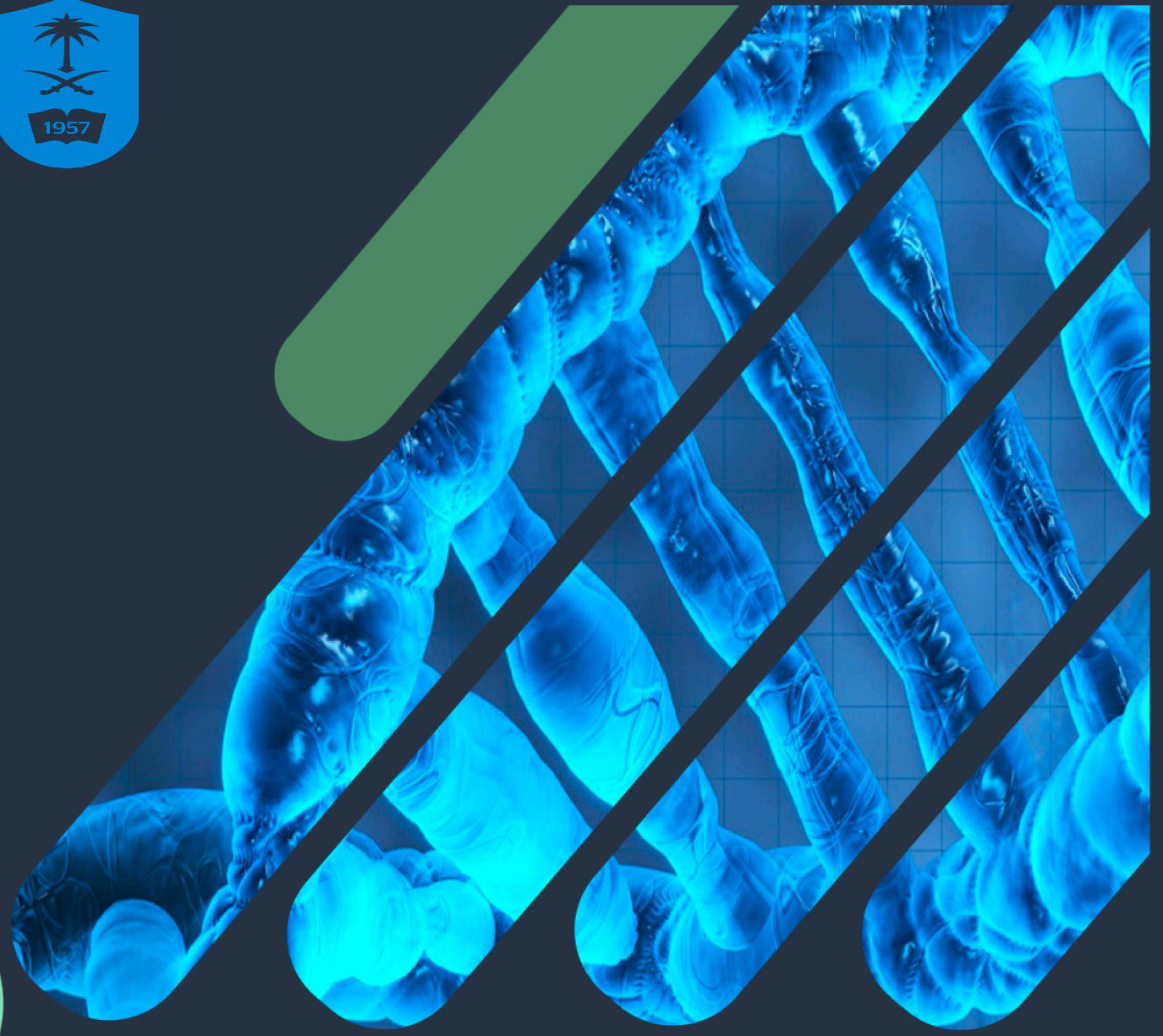

436 Biochemistry team

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Objectives:

By the end of this lecture the students will be able to:

1-Identify the types and functions of phospholipids

2-Discuss the physiological importance of phospholipids

3-Understand the role of glycerphospholipids in lung surfactant and their clinical implications in respiratory distress syndrome (RDS)

4-Identify the classes and physiological functions of phospholipase enzymes

Overview

- Types and functions of phospholipids
- Glycerophospholipids : Types, functions and role in lung surfactant, cell signaling and protein anchoring
- Respiratory distress syndrome (RDS)
- Sphingophospholipids
- Phospholipids in lipoprotein particles
- Phospholipases: Types and functions

Phospholipids

Major lipids of cell membranes

- Phospholipids are polar, ionic compounds that contain an alcohol group attached either to:
  - Diacylglycerol
  - Sphingosine

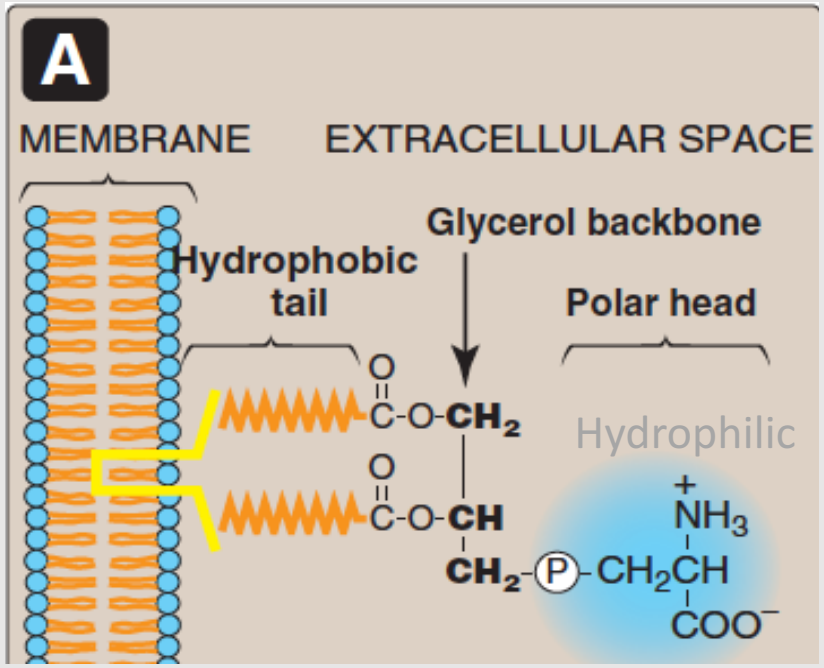
  It's an amino alcohol

When the backbone of alcohol is diacylglycerol we call it glycerophospholipids, when it is sphingosine we call it sphingophospholipids

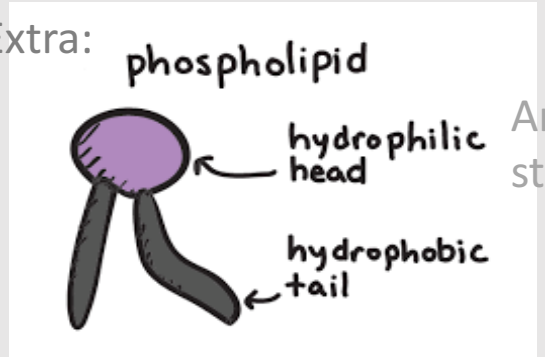
CLASSIFICATIONs OF PHOSPHOLIPIDS:

- Glycerophospholipids — When phosphate group attached to Diacylglycerol
- Sphingophospholipids — When phosphate group attached to Sphingosine

- ➢ Their hydrophobic (non-polar) portion of is attached to the membrane.
- ➢ Their hydrophilic (polar) portion extends outward interacting with the aqueous environment.



Extra:



Amphipathic structure

You know all of these information from the foundation block, aren't you smart ?!

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Functions of phospholipids:

Membrane-bound phospholipids

- Reservoir for intracellular messengers (cell signaling)
  - Ex: kinase C Anchors; hold proteins and stabilize them
- Anchors to cell membranes
  - Holding or Attaching some proteins to membranes

Nonmembrane-bound phospholipids

- Lung surfactant
  - works as a coat that surround cholesterol "lipid" to solubilize it and make it able to leave the body.+ helps in digestion of phospholipids
- Components of bile (as detergents to solubilize cholesterol)

Team435/Detergents:
مثل مساحيق الغسيل عندما تقوم بتذويب البقع الدهنية ، فهنا يساعد على تذويب الليبدز من أجل أهداف معينة.

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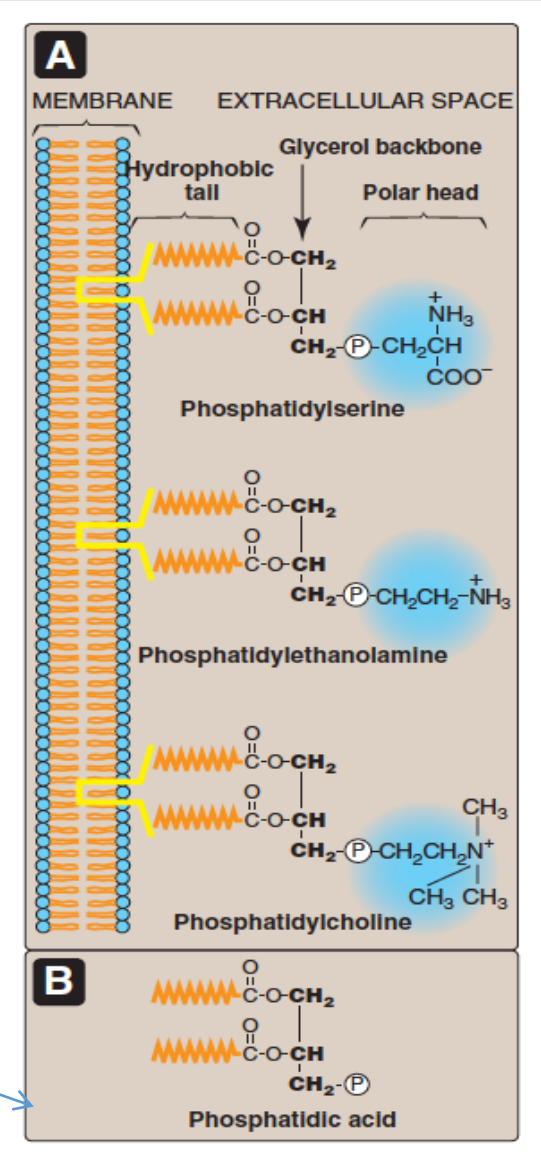
Glycerophospholipids: ⟷ Also called phosphoglycerides

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

الصورة من اليسار توضح تركيب الفوسفوليبيد والي شرحناه في السلايد رقم 2.
الصورة من ليمين توضح انواع الكحول الي راح تنضاف عليها وبناءً على النوع يتحدد اسم المركب ووظيفته, الشرح التفصيلي في السلايد القادمة.

The structure of phosphatidic acid: it's a DAG with a phosphate group on carbon 3



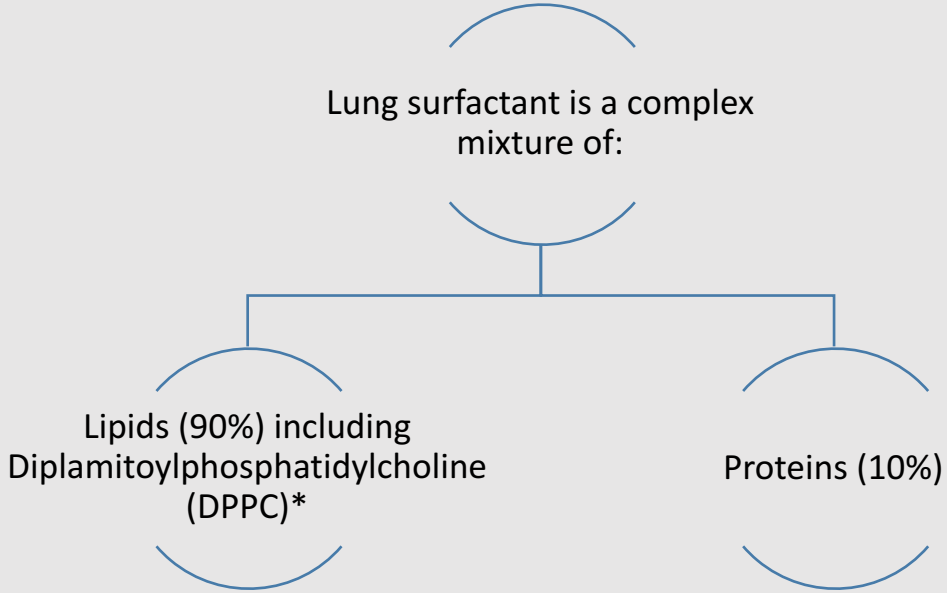
Glycerophospholipids :

1-Phospholipids are derived from PA such as:

Serine + PA	Phosphatidylserine (PS)	Cell signaling Blood clotting
Ethanoliamine+PA	Phosphatidylethanolamine (PE) (cephalin)	It's present in heart & brain
Choline + PA	Phosphatidylcholine (PC)(lecithin)	Lung surfactant
Inositol + PA	Phosphatidylinositol (PI)	Cell signaling
Glycerol + PA	Phosphatidylglycerol (PG)	Lung surfactant

Role of PC (phosphatidylcholine) in lung surfactant:

- Alveolar cells of the lungs are lined by the extracellular fluid layer.
- Alveolar cells (pneumocyte type2) secrete DPPC (a major lung surfactant)



*(the major lipid in lung surfactant is phosphatidylcholine present in a different form)

Role of PC (phosphatidylcholine) in lung surfactant:

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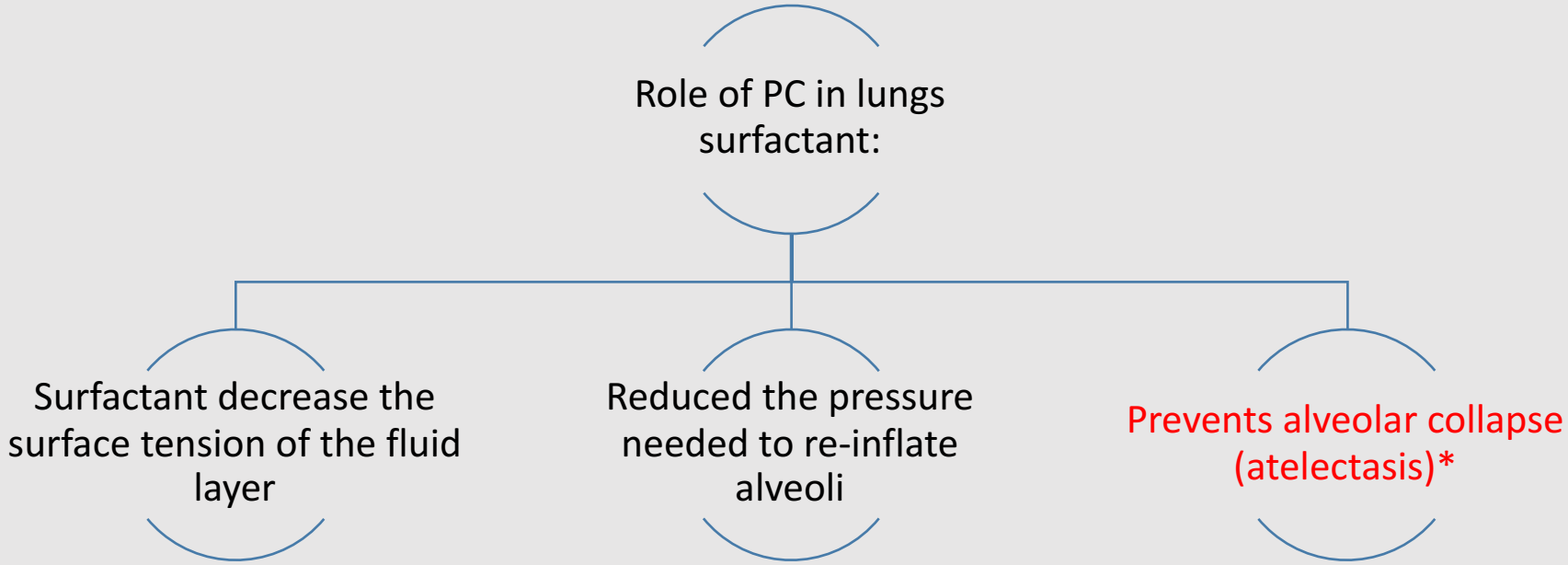


*If the lung surfactant is not there the alveoli will collapse and not be able to re-inflate which leads to Respiratory distress syndrome.

Respiratory Distress Syndrome (RDS):

Respiratory distress syndrome (RDS) **(also called new born respiratory distress syndrome)**

- In preterm infants due to deficiency of lung surfactant.
- A major cause of neonatal death.
- Preventation : glucocorticoids to mother to promote lung maturation.*
- In adults due to damaged alveoli by infection or trauma.**

Dr.Sumbul and lippincot explanation about the RDS:

- How to measure if the lung is having respiratory distress syndrome or not?
  - By measuring the ratio between Sphingomylein and Lecithin, if the ratio is 2 or more that means the person is healthy, if less that means the person is having respiratory distress syndrome.

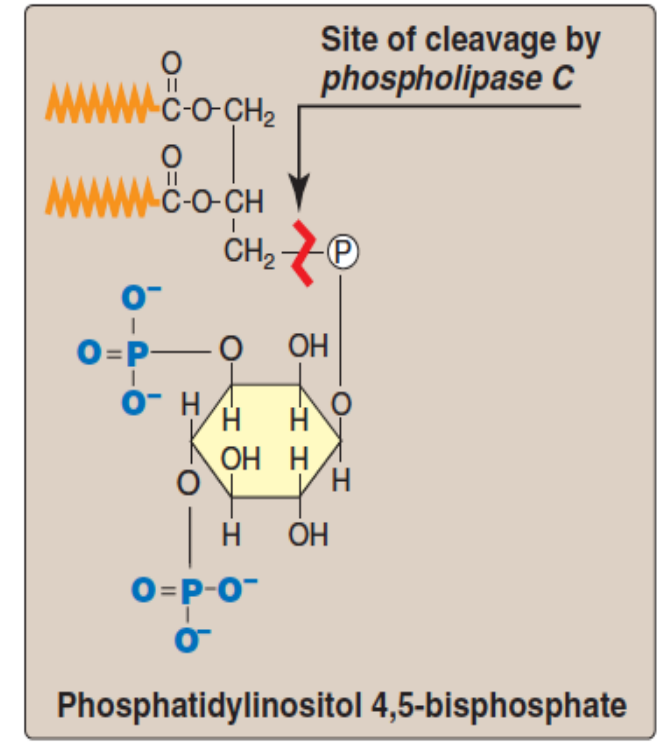
***It is actually a preventive method, if there's any complication in the mother or the baby leading to earlier delivery we give the mother glucocorticoids (by injection) which activates specific enzymes leading to earlier production of lung surfactants. But the actual treatment is giving the early born child an intratracheal lung surfactants (either natural or synthetic)**

****Can also happen to heavier chronic smokers because smoking causes inflammation which leads to accumulation of water in lungs.**

Role of PI (phosphatidylinositol) In Cell signaling:

- Plays an important role in intracellular signaling.
- PI is a part of calcium-phosphatidyl inositol system.
- PI is present in the membrane and it gets phosphorylated at two positions, and it is the target for phospholipase C enzyme.

Phospholipase C cleaves phosphatidylinositol 4,5-bisphosphate and give inositol triphosphate (IP3) soluble, and diacylglycerol (DAC)



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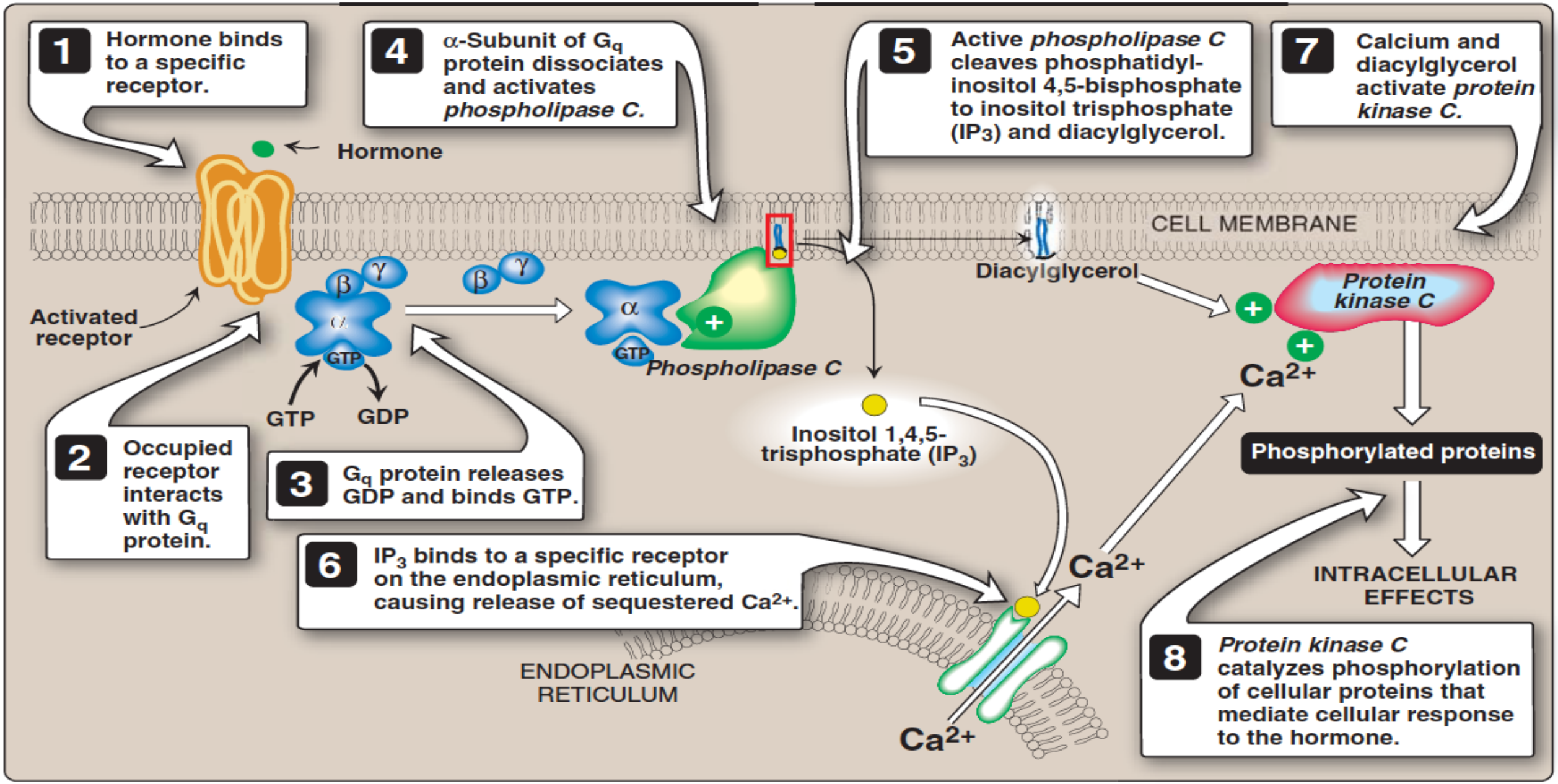


Figure 17.8
Role of inositol trisphosphate and diacylglycerol in intracellular signaling.

1. Binding

- Hormone/neurotransmitter binds to G-protein coupled receptor.
- e.g. “Antidiuretic hormone (ADH), Acetylecholine”

2,3. Receptor Interaction

- Receptor will Interact with G-protein Which will lead to replacing GDP with GTP.

4. Dissociation

- α-subunit dissociates from β & γ subunits, and activates Phospholipase C.

5. Breaking Down

- Phospholipase C break phosphatidylinositol 4-5trisphosphate into DAG + inositol 4-5 bisphosphate

6. Ca Releasing

- ER stores Calcium Which released to the cytoplasm when IP3 binds. (IP3: Inositol 1,4,5 triphosphate)

7. Kinase C Activation

- Calcium and DAG activate protein kinase C

8. Responding to Action

- Protein kinase C catalyze protein phosphorylation. These proteins will give the response of the hormone or neurotransmitter.

Role of Phosphatidylinositol (PI) in membrane protein anchoring

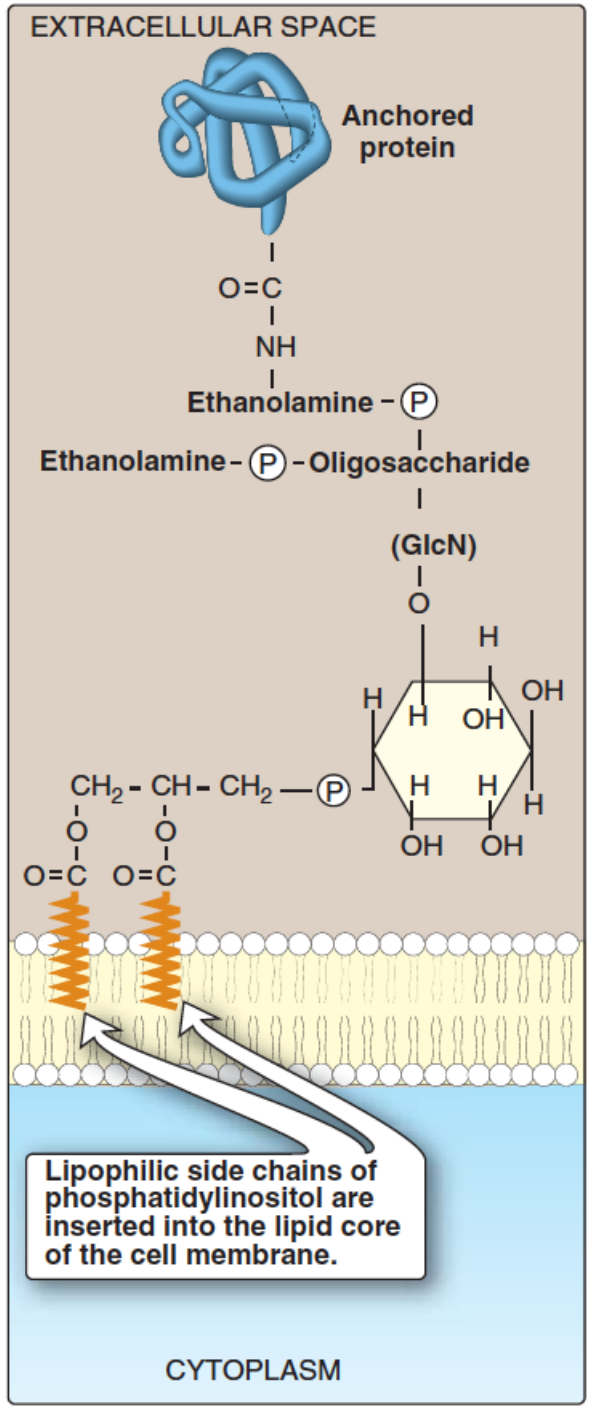
- Anchoring (holds proteins there) of proteins to membranes is done through: carbohydrate-PI bridge.

Examples of anchored proteins

- **Alkaline phosphatase**
  (present on the surface of small intestine)
- **Acetylcholine esterase**
  (present on postsynaptic membrane of neurons)

- Anchoring proteins can be cleaved by phospholipase C enzyme.

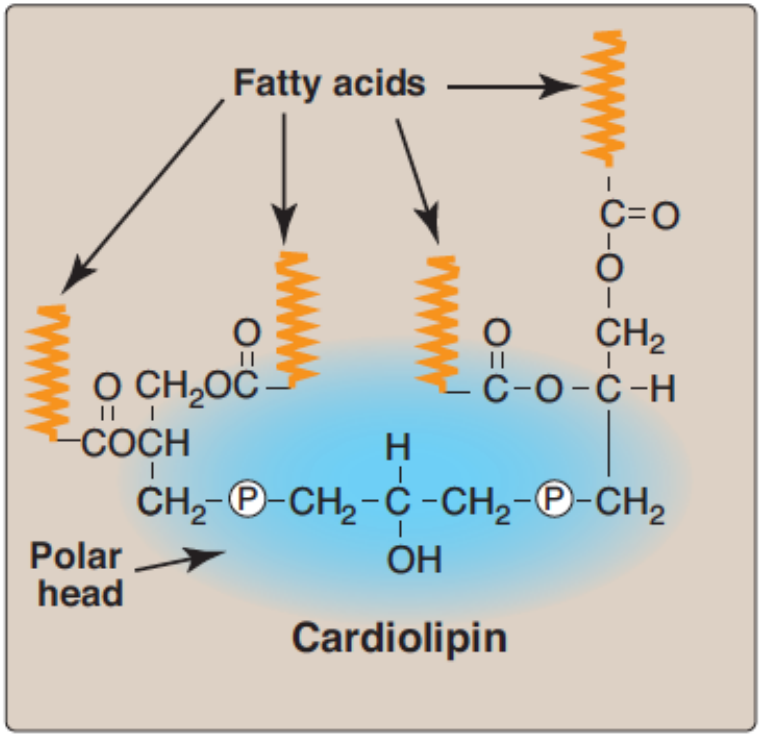
When anchoring proteins it needs the help of carbohydrates that makes a bridge between the protein and anchor



Some examples:

Cardiolipin

- Two molecules of PA joined to an additional molecule of glycerol through PO4 groups
- In the inner mitochondrial membrane
- Function: maintenance of respiratory complexes of electron transport chain

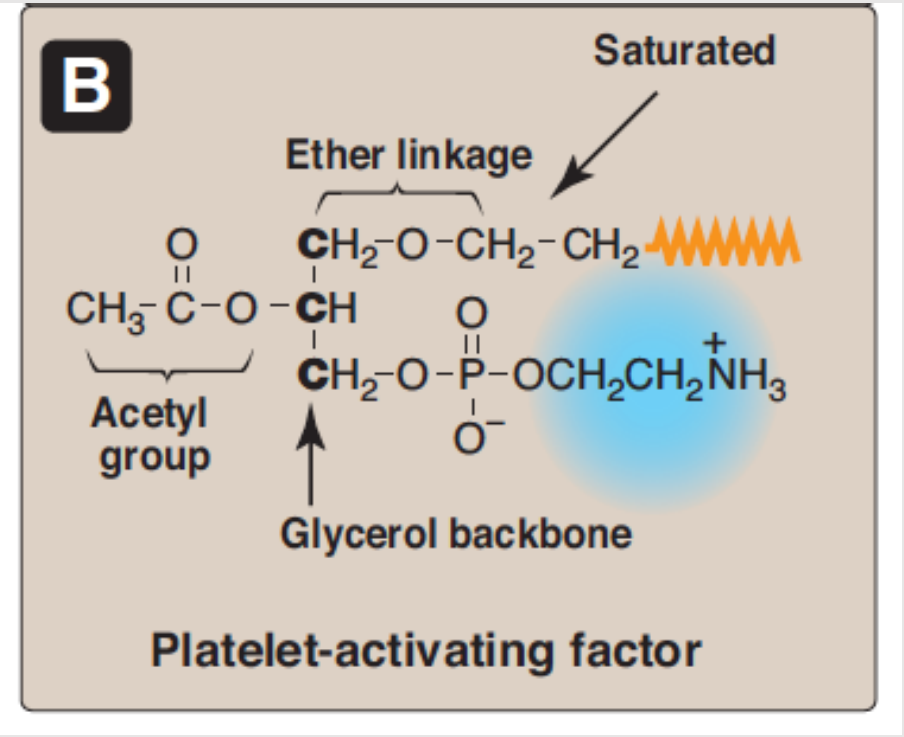


Triggers macrophages and neutrophils to release free radicals to kill bacteria

Some examples:

Platelet activating factor (PAF)

- Binds to cell surface receptors
- Triggers thrombotic and acute inflammatory reaction



PAF : triggers acute inflammatory reaction by activation of macrophages & neutrophils to produce free radical and cause tissue damage

Consist of: Ether linkage

Sphingophospholipids*

- Sphingophospholipids are a long-chain fatty acid attached to sphingosine.

Ex. Sphingomyelin. (the only significant sphingophospholipid in humans).

- Sphingomyelin is an important component of myelin sheath that protects and insulates nerve fibers.

And increase the velocity of transmission of the signal

* if the backbone is sphingosine we call it Sphingophospholipids

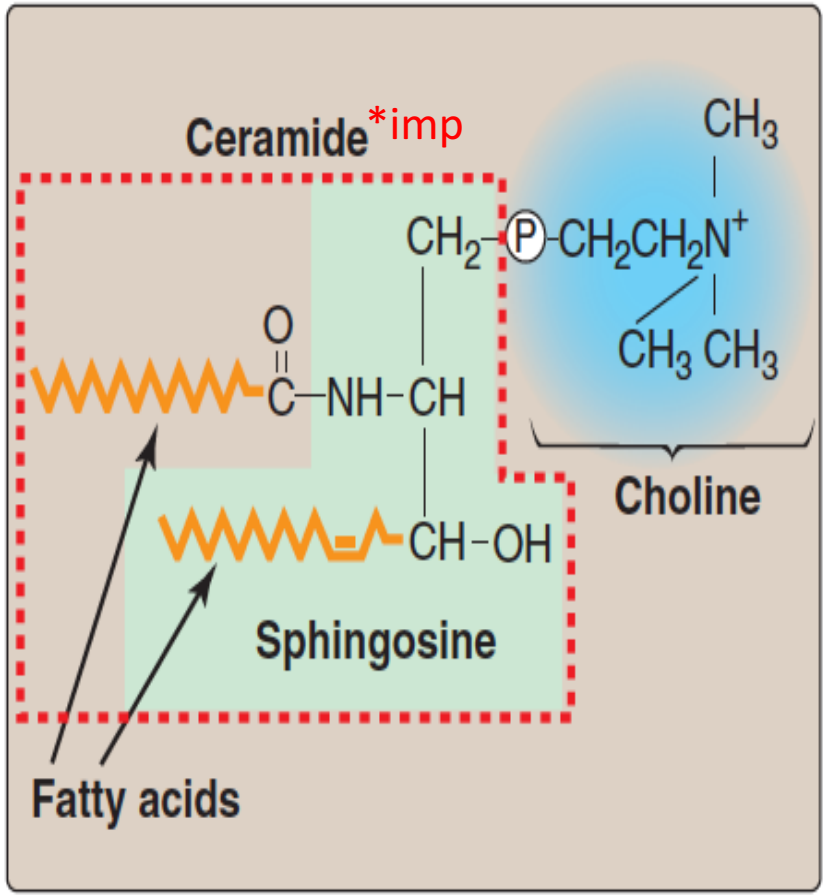


Figure 17.4
Structure of sphingomyelin, showing sphingosine (in green box) and ceramide components (in dashed box).

Phospholipids in lipoprotein* particles

Lipoproteins are composed of a neutral lipid core (containing triacylglycerol and cholesteryl esters) surrounded by a shell of amphipathic apolipoproteins, phospholipid, and unesterified (free)
cholesterol. They main function is to keep lipids soluble as they transport them between tissues.:

بحمد الله تم دخول الـLipid
للاسلام حيث غيرت اسمها الى ليبو بروتين ولبست العباءة المكونة من الفوسفوليبيد والكوليسترول لكي تمشي بدون جذب انتباه اقرانها المشابهين لها (الهيدروفوبيك)
شكر للولوة الشيحة *

- The outer core of lipoprotein particles is hydrophilic contains phospholipids and free cholesterol. This outer core allows transport of core lipids (hydrophobic) in aqueous plasma (hydrophilic).

*it has different types: Chylomicrons, high density lipoproteins (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL).

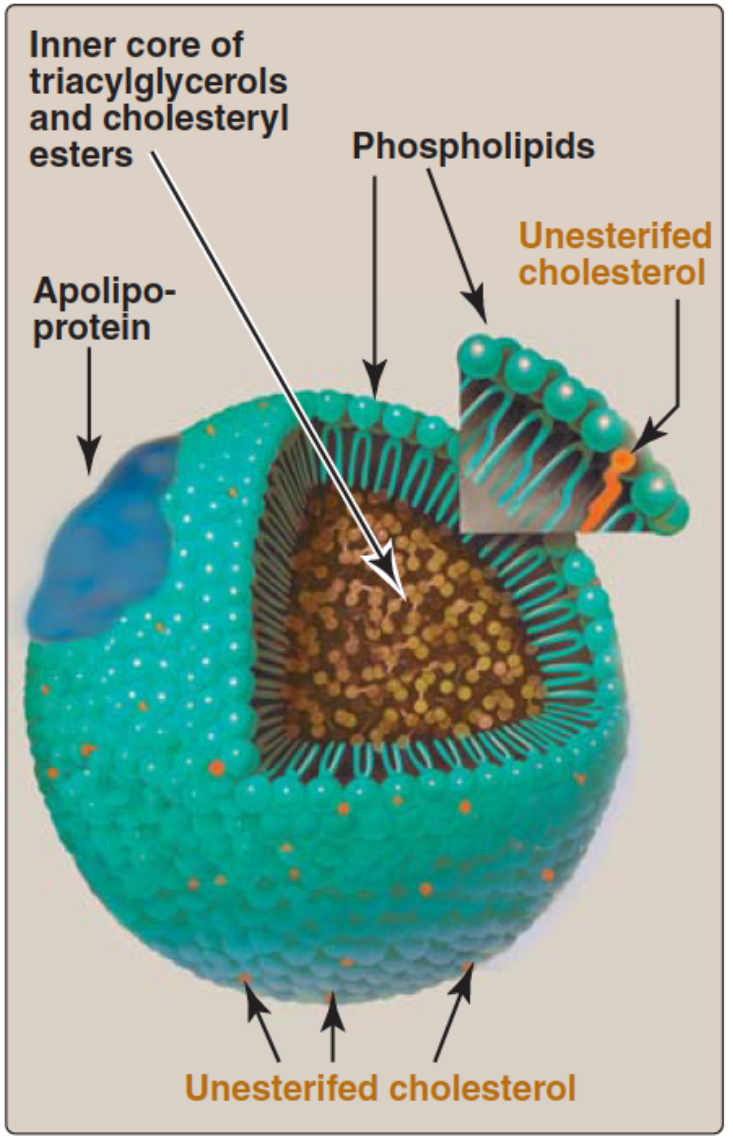


Figure 18.14
Structure of a typical lipoprotein particle.

When There is lipid being transported through blood as: triacylglycerol from diet, we use lipoprotein. The Inside (core) made up of lipids, the surface made up of phospholipid bi layer, The hydrophobic part interact with the lipid molecules and the hydrophilic part interact with aqueous environment. In addition to cholesterol and apolipoprotein.

Phospholipase

* what are they ? group of enzymes that catalyse the cleavage of phospholipid.

*Where there are found? in all tissues including pancreatic juice

.

***Glycerolphospholipids are degradated by** : phospholipase A1,A2,C,D

***sphingophospholipid are degraded by :**
Sphingomyelinase

Sphingomyelinase is type of phosphodiesterase a Type C and D phospholipase

Types of phospholipase :

1-phospholipase A2 : present pancreatic juice , activated by trypsin by acting as proenzyme.
Inhibited by glucocorticoids.
2-phospholipase A1: found in many mammalian tissue .
3-Phospholipase D: mostly found in planets tissue.
4-phospholipase C : responsible for producing second messengers.

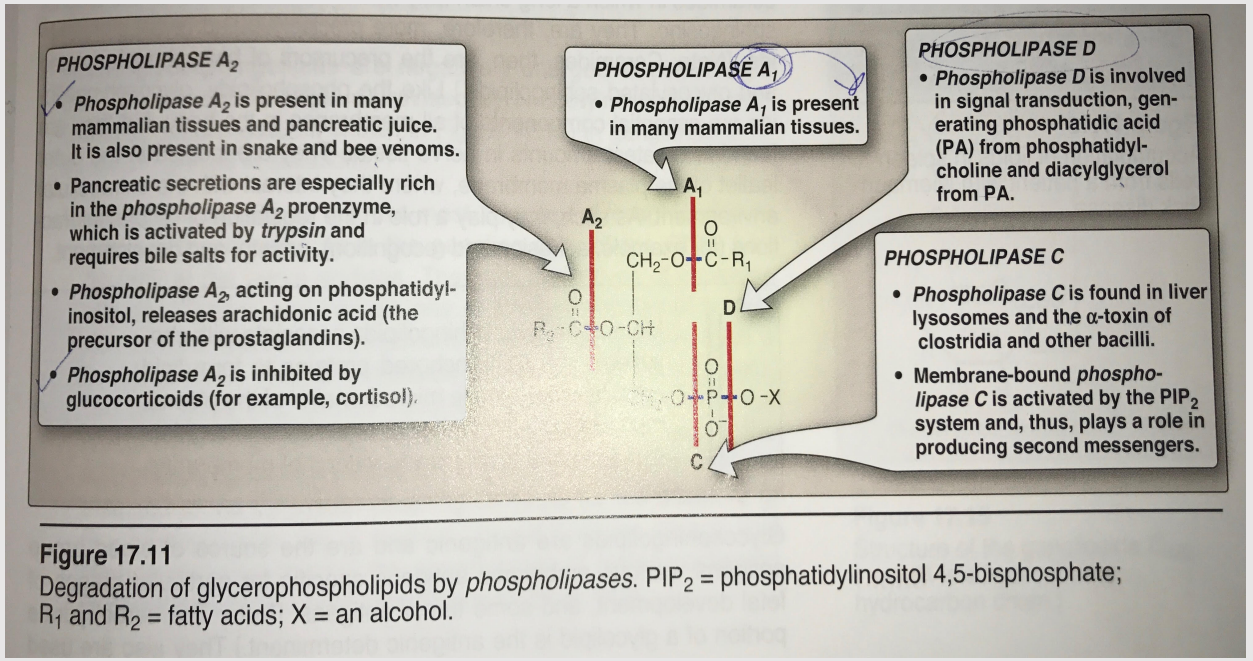


Figure 17.11
Degradation of glycerophospholipids by *phospholipases*. PIP_2 = phosphatidylinositol 4,5-bisphosphate; R_1 and R_2 = fatty acids; X = an alcohol.

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Functions of Phospholipase

digestion

- In pancreatic juice, it helps in digestion of phospholipids " by cleaving them".

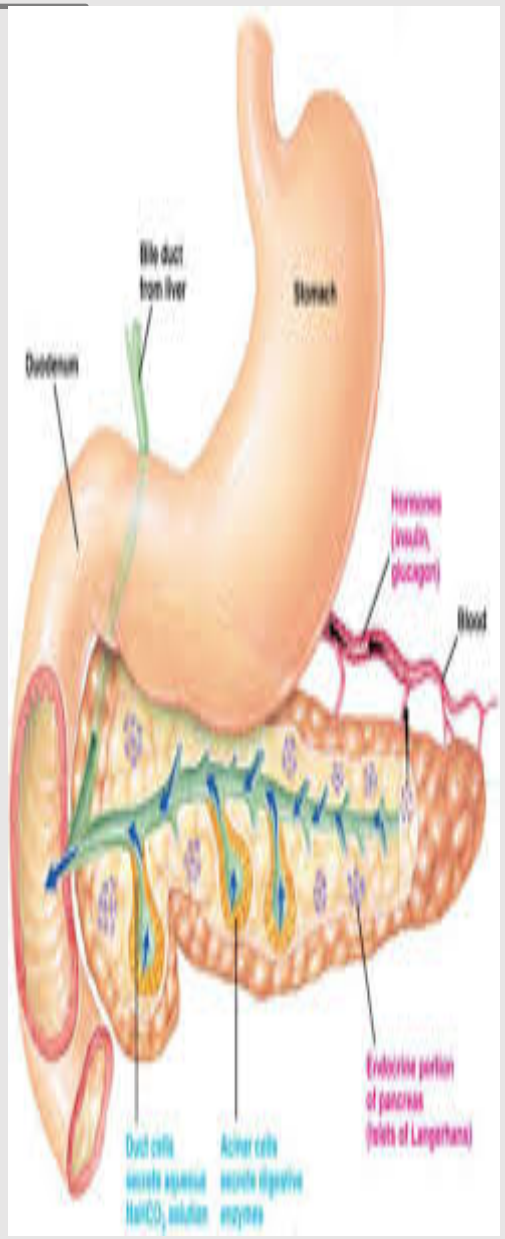
Remodeling

- Change in the composition of the phospholipid.
- Example: DDPC is produced remodeling.(consisting of two palmitic acids attached of a phosphatidylcholine head-group (Phospholipase cleaves the phosphatidylcholine ,and by the help of transferase enzyme it adds the palmitic acid)

Production of second messenger

Dissolving the cell membrane in infection

- Pathogenic bacteria produce phospholipases to dissolve cell membranes and spread infection.



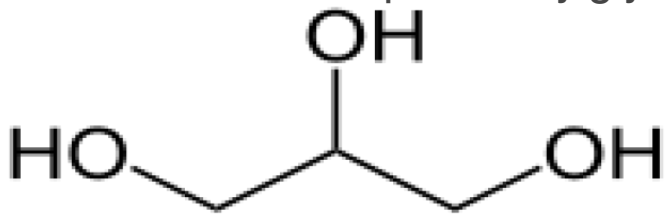
معلومات اثرائية:

- Essentially all cells except mature erythrocytes can synthesize phospholipids, whereas triacetyle glycerol synthesis occurs essentially only in liver, adipose tissue, lactating mammary glands, and intestinal mucosal cells.
- PC and PE are the most abundant phospholipids in most eukaryotic cells. The primary route of their synthesis uses choline and ethanolamine obtained either from the diet or from the turnover of the body's phospholipids.
- Sphingomylien, a sphingosine- based phospholipid is a major structural lipid in the membranes of nerve tissue.
- Cardiolipin is antigenic and is recognized by antibodies raised against Treponima palidum, the bacterium that causes syphillis

(المرض الي جاء جورج اومالي في جريز اناتومي)

There are two classes of phospholipids
The first class it's backbone is made up of diacylglycerol

Glycerol structure



Monoacylglycerol is made by removing one OH from glycerol and adding fatty acid chain.

Diacylglycerol is made by removing two OH from carbon No. 1 and carbon No. 2 and then adding two fatty acid chains at these two positions.

If the back bone is made of diacylglycerol, then the phospholipid going to be called: glycerophospholipid or phosphoglycerides

When adding a phosphate group on diacylglycerol it becomes phosphatidic acid, which is the simplest phospholipid (phosphatidic acid)

Diacylglycerol is lipid
The fatty acid chains are hydrophobic
The phosphate group is the hydrophilic polar head
Thus become parent phospholipid

Then adding an alcohol group like: Serine, choline, ethanolamine. Then they become different phospholipid

If you add choline group on phospholipid it becomes: phosphatidylcholine

The second class (spgingophospholipid):
Backbone: sphingosine. It's an amino alcohol

SUMMARY OF PHOSPHOLIPIDS:

- They have a hydrophobic tail and hydrophilic head.
- They are membrane bound or non membrane bound.
- Lipoproteins contain phospholipids to allow transport of core lipids in aqueous plasma.
- Phospholipase Functions:

1- Degrades phospholipids. (each type has a different enzyme)
2- Remodeling phospholipids.
3- Produce second messengers.
4- Bacteria produces phospholipase to dissolve cell membranes and spread infection.

Phospholipids on the cell membrane are two types:

1- Glycerophospholipids:

They all contain phosphatic acid (PA) which is the simplest phospholipid.
Many types of phospholipids are derived from PA:

1- Cardiolipin
2- Platelet activating factor (PAF)

And two important examples are
1- **Phosphatidylcholine (PC)(lecithin)** and its role in lung surfactant and RDS.
2- **Phosphatidylinositol (PI)** and its role in cell signaling and membrane protein anchoring.

2- Sphingophospholipids:

Like **sphingomyelin** and its role in protecting nerve fibers

Quiz

SAQ

https://www.onlineexambuilder.com/phospholipid-compounds-saq/exam-130261

MCQ's

https://www.onlineexambuilder.com/phospholipid-compounds/exam-130242

https://www.onlineexambuilder.com/phospholipids/exam-130270 **

Helpful video

Respiratory distress syndrome

https://www.youtube.com/watch?v=vO63j9m5grE

https://m.youtube.com/watch?v=cn6mMlKedwU

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THANK YOU

PLEASE CONTACT US IF YOU HAVE ANY ISSUE

- Review the notes

https://m.youtube.com/watch?v=cn6mMlKedwU

- Lippincott's Illustrated Reviews: Biochemistry, 6th E

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