RESPIRATORY BLOCK

# Biochemistry Team ~ 430

## 4th Lecture
## Phospatidylinositol and Phospholipases


**Done By :**

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- **Phospholipids :**

**A. Glycerophospholipids**

**Glycerol-containing phospholipids**

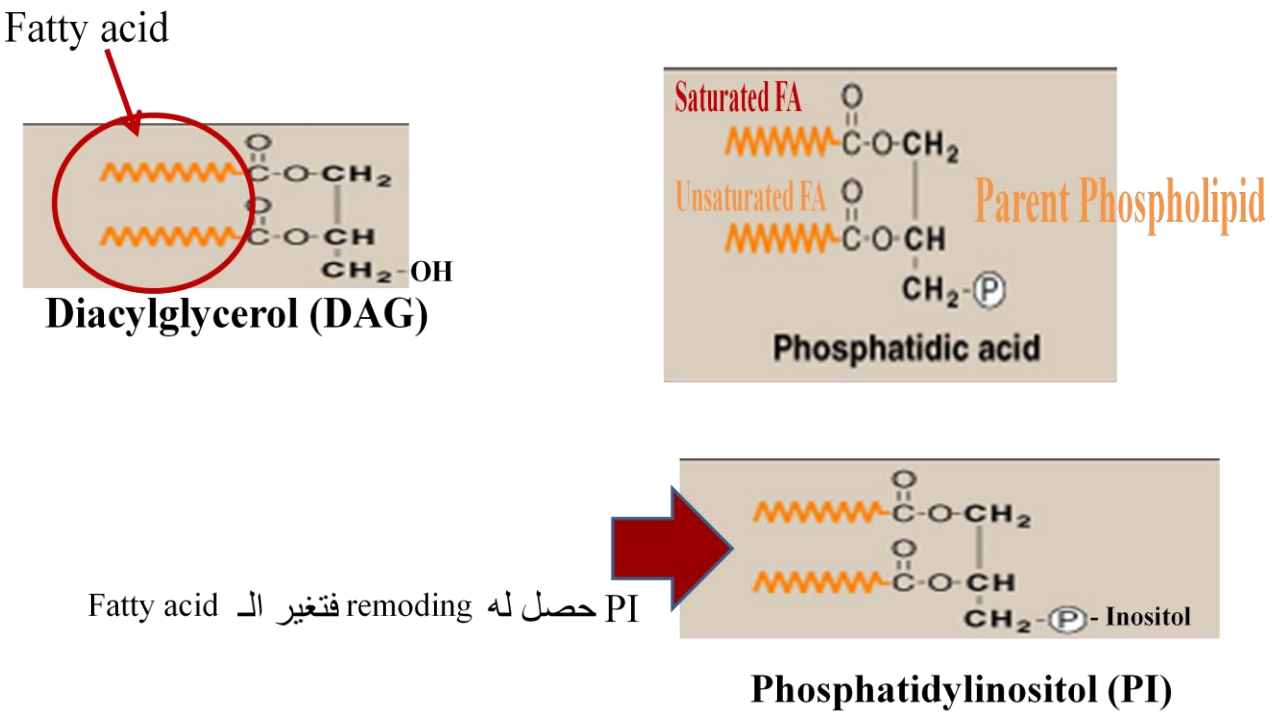
**e.g., Phosphatidylinositol**

**B. Sphingo-phospholipids:**

**Sphingosine-containing phospholipids**

**e.g., Sphingolmyelin**

- **Phosphatidylinositol (PI) :**



- **Functions :**

**1. Protein anchoring to plasma membranes**

يعني يربط البروتين بالغلاف حق الخلية

**2. Reservoir of arachidonic acid in membranes Arachidonic acid is the precursor of prostaglandins**

يرتبط به الاراكودينك اسيد في الغلاف الخلوي، لذلك يمنعه من الخروج

لكن Phosoholipase A2 يأتي ويفكه منه ..

**3. Signal transmission across membranes via production of second messengers:**

يأتي معه كاليسوم ويضعه في منتصف الـ PI فيقسمه لـ :

Inositol trisphosphate (IP3)

Diacylglycerol (DAG)

**PI- Protein Anchoring**

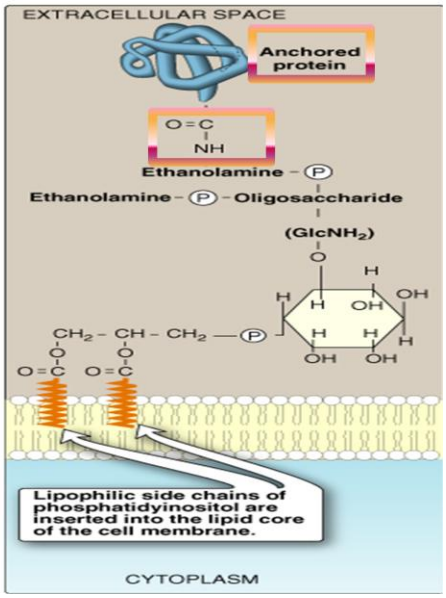
سلايد أخذناها في محاضرة سابقة

**Anchoring of proteins to membranes via Carbohydrate-Phosphatidylinositol Bridge**

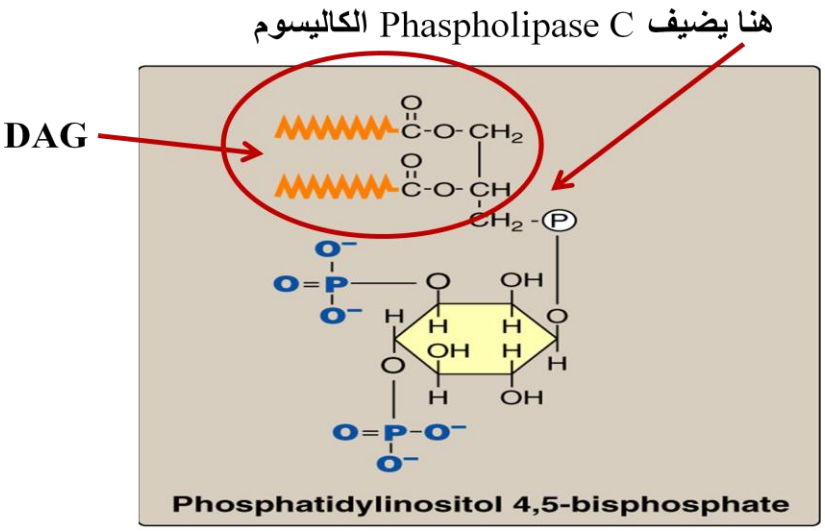
**Examples of anchored proteins:**

1. **Alkaline phosphatase**
   (to the surface of small intestine)
2. **Acetylcholine esterase**
   (to postsynaptic membrane)

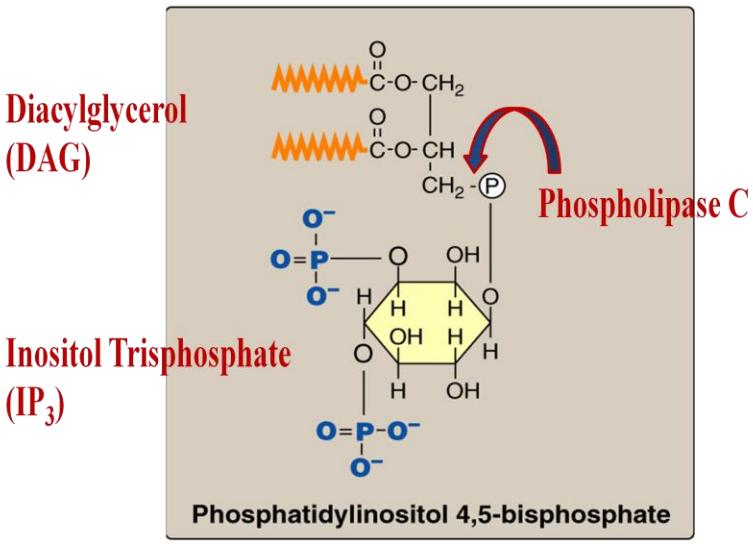
These proteins can be cleaved from their attachment to the membranes by **phospholipase C**



- **Phosphatidylinositol 4,5 bisphosphate :**

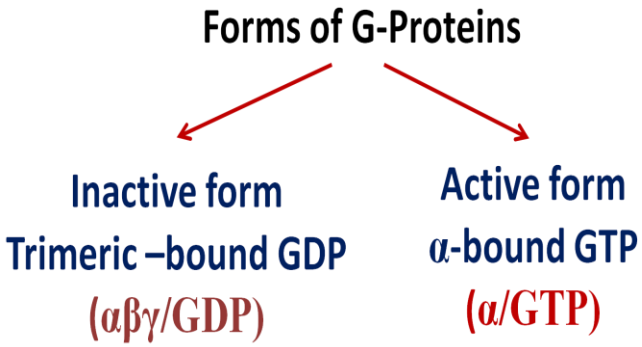



- **Calcium/Phosphatidylinositol System :**



- **GTP-Dependant Regulatory Proteins (G-Proteins:**

**-- Gq -Proteins:** **Trimeric membrane proteins (αβγ)**
**Binds to GTP/GDP**




- **The α-subunit has intrinsic GTPase activity, resulting in:**

**-- Hydrolysis of GTP into GDP and Inactivation of G-proteins**

**The α-subunit has intrinsic GTPase activity ::**

**يعني بهذه العبارة أن الالفا تقدر تخلص نفسها من حبة فوسفات**
**عشان ترتبط مع البيتا والقاما ، بعد ما تنشط**

- **So we can understand the second messenger we have to first revise the mechanism of G- protein**
- **Activation of G-protein receptor**
- **Disassociation of the alpha subunit from beta and gamma to attach to GTP**
- **In activation of G-protein receptor**
- **The alpha subunit also has an intrinsic GTP-ase activity which means the hydrolysis of the GTP into GDP which leads to the inactivation of G-protein and the alpha subunit reattaches its self to the beta and gamma**

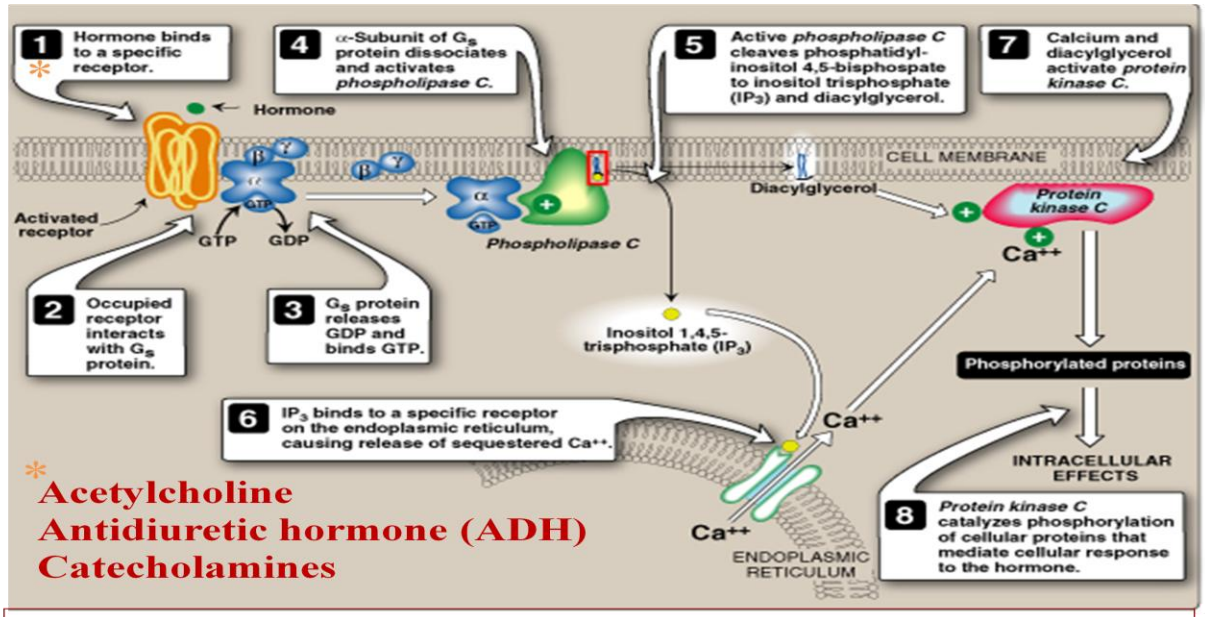
- **Phosphatidylinositol System :**

**Signal:** **Hormones or neurotransmitters**
**e.g., Acetylcholine, antidiuretic hormone (V1-receptor) and catecholamines (α1 actions)**

**Receptor:** **G-protein coupled receptor**

**Effects:** **Activation of phospholipase C**
**Hydrolysis of phosphatidylinositol 4,5-bisphosphate**
**Production of IP3 ( Ca2+) and DAG**
**Activation of protein kinase C**

**Response:** **Phosphorylation of cellular proteins and responses to hormones**




**Intracellular Signaling by Inositol trisphosphate**

**1- the initial or beginning signal starts with a hormone that bind to the receptor**

**2- Stimulation and activation of the Gq protien receptor**

**3- After stimulation the Receptor Releases GDP and gets attached To GTP**

**4- alpha Subunit of Gq protein dissociate (break off) and activate Phospholipase C**

**5- active phospholipase C breaks down PIP2 to give us IP3 and Diacyigycerol**

**6- the IP3 can goes intracellularly to anysote of calcuime inside the cell ( e.g.endoplasmic retculum ) and gets attach to the IP3 receptor leading to the release of Ca+ leading to the cytoplasmic Ca+ concentration will increase**

**7- the Ca+ with DAG (that remained in the membrane) with stimulate the Protein Kinase C (Kinase means Addition of Phospate to a protein) to do its job**

**So finally the whole Idea is that the first messenger which is the HORMONE cant do its job without the second messenger which is IP3**

- **Phospholipases :**

**(1) For glycerophospholipids:**

**Phospholipases A1, A2, C and D < it is found in plants only**

**They are found in all tissues**
**However they are more abundant in pancreatic juice (why? Because they break the dietry phospholipds) ,snake venoms and bacterial toxins ( why? Because it needs to break the phospholipds in the cell membrane to get access inside your cells and kill you ☺ ,,, Jk hehe)**

**(2) For sphingophospholipids:**

**Lysosomal phospholipase (which are present in the lysosoms) and example of it is Sphingomyelinase ( breaks down sphingomylein)**

Phospholipase breaks down phospholipds
And there is two typer of phospholipds
So obvioulsy there is going to be different types of
Phospholopase for each one

- **Functions of Phospholipases :**

**(1) Degradation of phospholipids**

**-- Production of second messengers**

**-- Digestion of phospholipids by pancreatic juice**

**-- Pathogenic bacteria degrade phospholipids of membranes and causing spread of infection**

**(2) Remodeling of phospholipids:**

**-- Specific phospholipase removes fatty acid from phospholipid**

**لاحظ .. الفوسفولايبيز فقط يشيل الفاتي اسيد**

**Replacement of fatty acid by alternative fatty acid**

**using fatty acyl CoA transferase**

**e.g., Binding of 2 palmitic acids in:**

**Dipalmitoylphosphatidylcholine (DPPC)**

**Binding of arachidonic to carbon 2 of PI or PC**

-- We talked previously about :

- IP3 functions :
  1- anchoring
  2- being a reservoir of archidonic acid
  3- signaling

…….

-- Now Phospholipases :

- functions :

1- degredation

(when do you want to degrade phospholipids? When you want to do second messenger correct? <<if you don't remember go back to the explination the G-protein mechanism )

2- remodeling :

- Specific phospholipase REMOVES a fatty acid from phopholipid
- fatty acyl CoA Transferase REPLACES the removed fatty acid in the phospholipid

**-- Explanation of the first example :**

**- Phospholipd doesn't have 2 palmitic acid**

**- Phosphotaidylcholine in our body and the lungs want to make surfactint**

**- So then one of the specific phospholipase takes a non palmatic acid away from the phosphatifylchonline to make room for the palmitic acid we need**

**- And who carrys the palmitic acid? It's the fatty acid acyl transferase and attaches it to make**

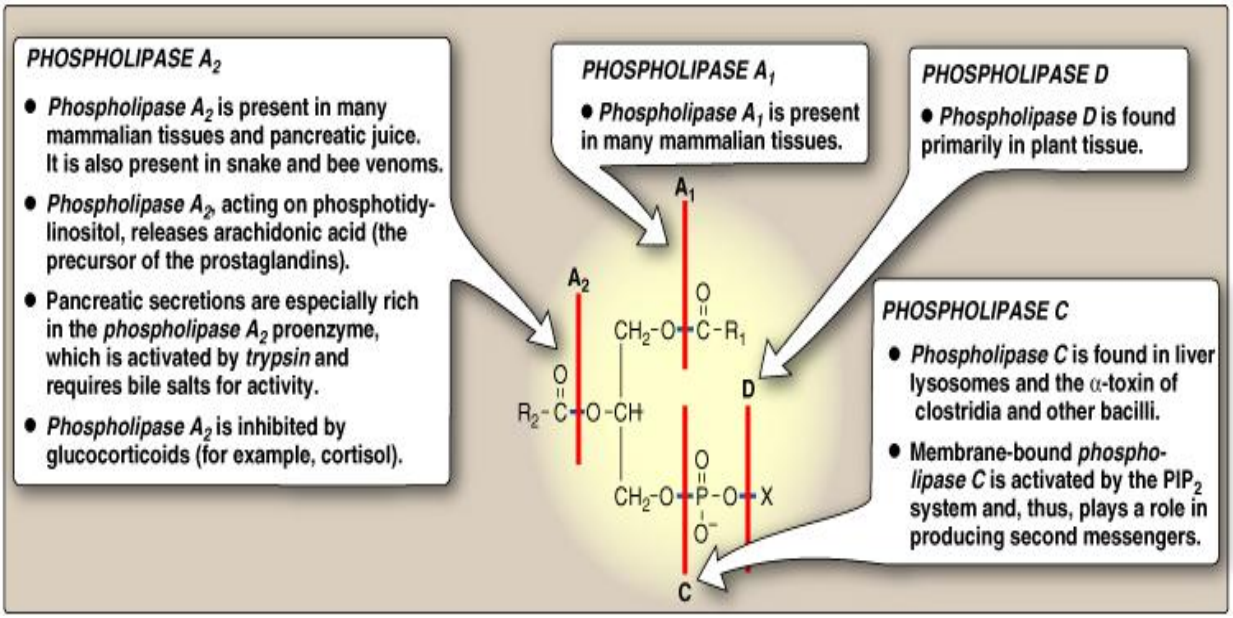
**- Dipalmitoylphosphatidylchholine**

**- Explination of the Second example :-**

**- To store active form of arachidonic acid in the cell ,,, it is**

**- Attachment of arachidonic acid in the second position (second carbon) of PI (phosphoinsitol ) , so it can be stored in the cell and used when needed (making of postagalndins)**

- **(1) Glycero-phospholipases :**




■ **What do you see in the picture?**

**Okay, this is an example of any phosphlipd ( because there is X)**

■ **Main structure of the phospholipd**

**R1 , R2 fatty acids**

**Glycerol**

**Phospahte group**

**X= could be anything e.g choline or inisitol**

■ **Okay now for example if you wanted to make surfactant ,, you would need 2 palmitic acids**

**Correct?**

**So instead of R1 and R2 we replace them with palmitic acid**

- **What happens is that the phospholipase A1 carries or breaks the fatty acid = R1 fatty acid and then fatty acyle CoA transferase puts palmatic acid**

- **Then phospholipase A2 would break = R2 fatty acid and then again the fatty acyle Co A transferase replaces it with palamtic acid**

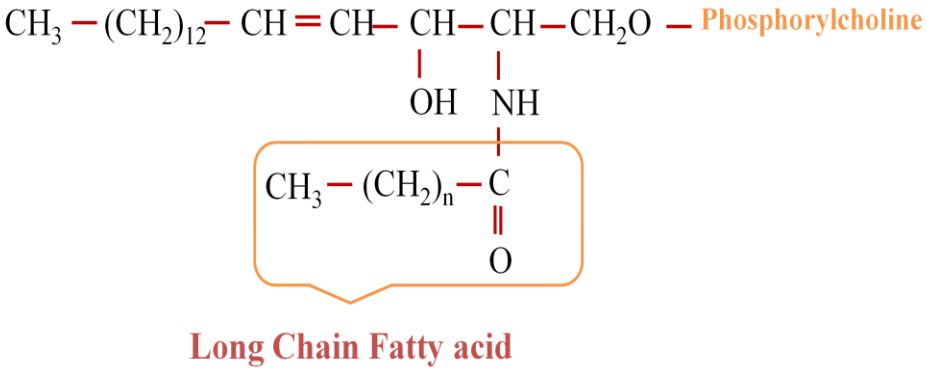
- **further explination of the previouse example**

**So mainly in this picture**

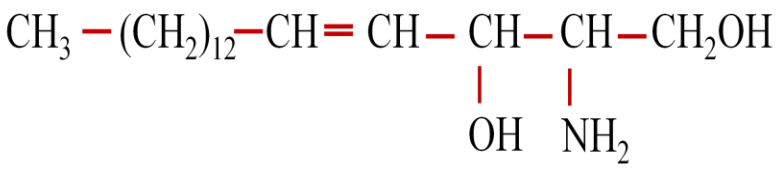
**You could see that every position has its own phosplipase to break it**

| *A1* | *A2* | *C 2* |
|---|---|---|
| *In all tissues* | *In all tissues* | *Membrane bound* |
| *remodeling* | *remodeling* | *NO* |
| -------- | *In venom* | *In toxin* |
| -------- | *In pancreatic juice to inhibit trypsin* | *In liver lysosomes* |
| -------- | *Ihibited by glucostroids* | *Produce second messenger* |

- **Sphingosine-containing phospholipids: Sphingomyelin :**



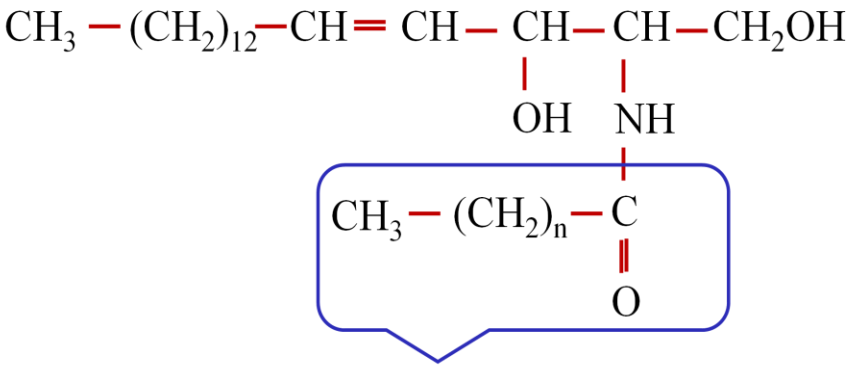
- **Sphingosine :**



Long chain, unsaturated amino alcohol

- **Ceramide: Parent Sphingolipid Compound :**

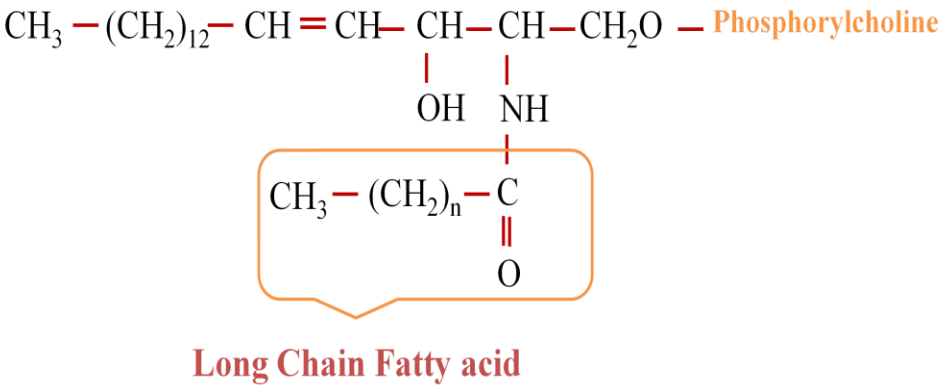
**Ceramide = Sphingosine + Fatty acid**



Long Chain Fatty acid

- **Sphingomyelin :**

**Sphingomyelin = Ceramide + phosphorylcholine**

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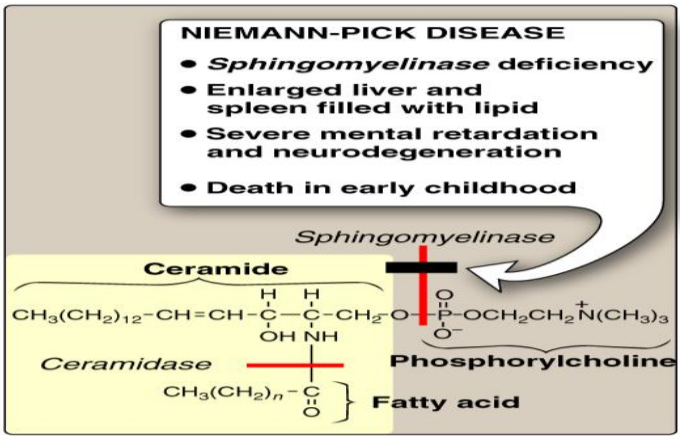
## (2) Lysosomal Phospholipase: Sphingomyelinase

**Degradation of sphingomyelin**

**by sphingomyelinase and ceramidase**

**produce intracellular messengers:**

**Ceramide and sphingosine**



# Take Home Message

- **Phosphatidylinositol (PI) is present in membranes**
- **Functions of PI:**
  - **Anchoring for proteins to membrane**
  - **Production of second messengers**
  - **Reservoir of arachidonic acid, a PG precursor**

- **Phospholipases:**
  - **Phospholipases A1, A2, C and D**
  - **Lysosomal Phospholipase: Sphingomyelinase**

- **Function of phospholipases:**

**Degradation of phospholipids**

**e.g., production of second messengers**

**Remodeling of phospholipids**

**e.g., production of DPPC (lung surfactant)**

THANK YOU