Study Of Compound Lipids

Compound Lipids

- Compound lipids are **class of Lipids**
- Chemically **Esters of Fatty acids with Alcohols attached with Additional groups.**

- **Additional Groups** in **Compound Lipids** may be either of these:
  - **Phosphoric acid**
  - **Nitrogenous Base**
  - **Carbohydrate moieties**
  - **Proteins**
  - **Sulfate groups**

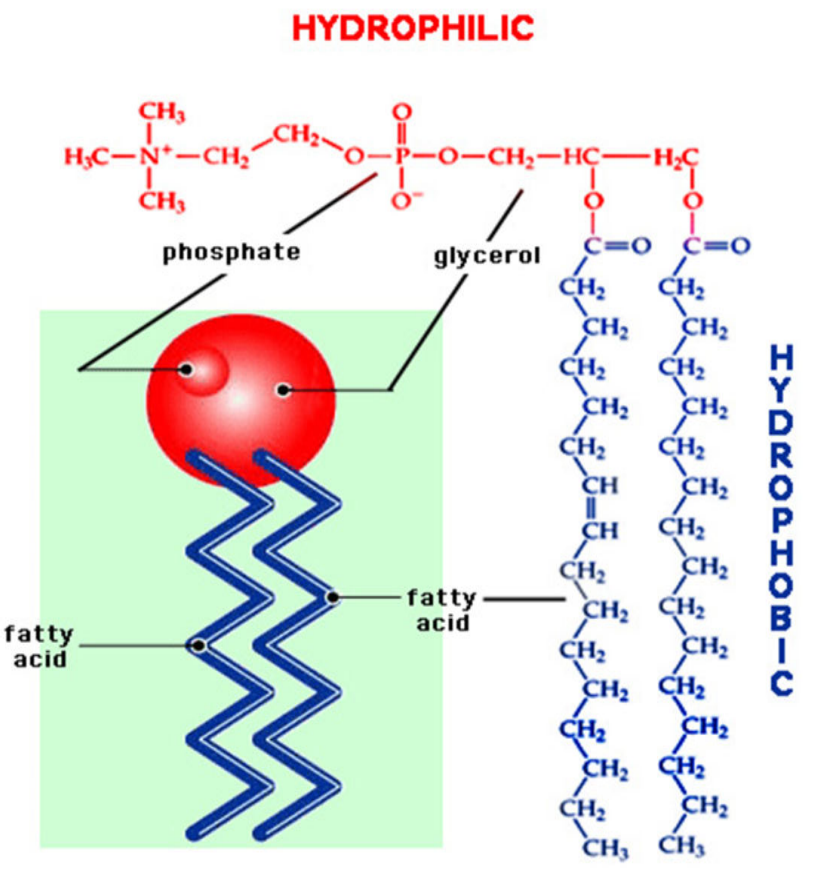
3 Main Compound Lipids

- **Phospholipids**
- **Glycolipids**
- **Lipoproteins**

Phospholipids

Phospholipids

- **Compound Lipids**



- **Components:**
  - **Alcohol**- Glycerol/Sphingol
  - **Fatty Acids-** PUFAs and SFAs
  - **Additional Group-** Phosphoric acid and Nitrogenous /Non Nitrogenous moiety

- **Nature**- Amphipathic

- **Phospholipids (PL) Chemically Possess:**

  – **Fatty acids** esterified to **Alcohol** and

  – **Phosphoric acid** attached with **Nitrogenous /non nitrogenous base.**

Types Of Phospholipds

Based upon Alcohol

Present in Phospholipid structure

- **Two Types of Phospholipids are :**

–Glycerophospholipids:

Glycerol containing Phospholipids

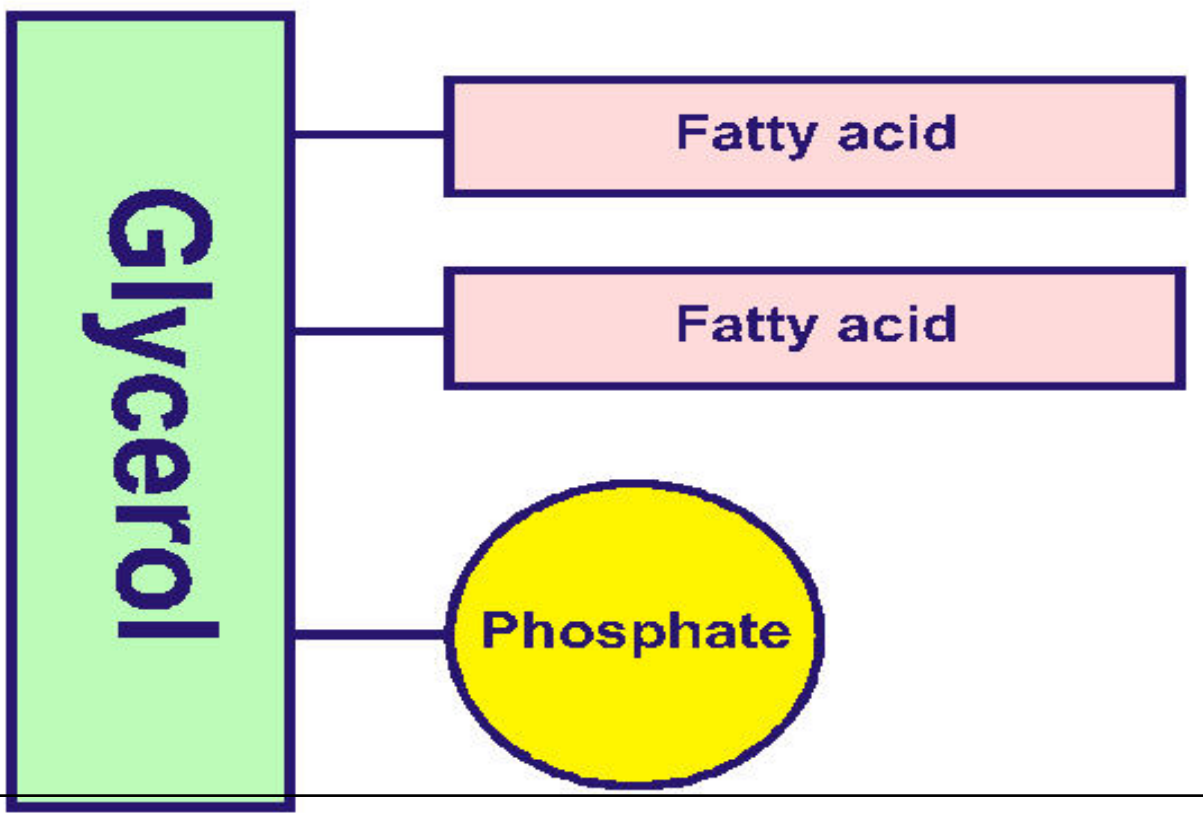
–Sphingophospholipids:

Sphingosine/ Sphingol containing Phospholipids.

Glycerophospholipids/ Glycerophosphatides

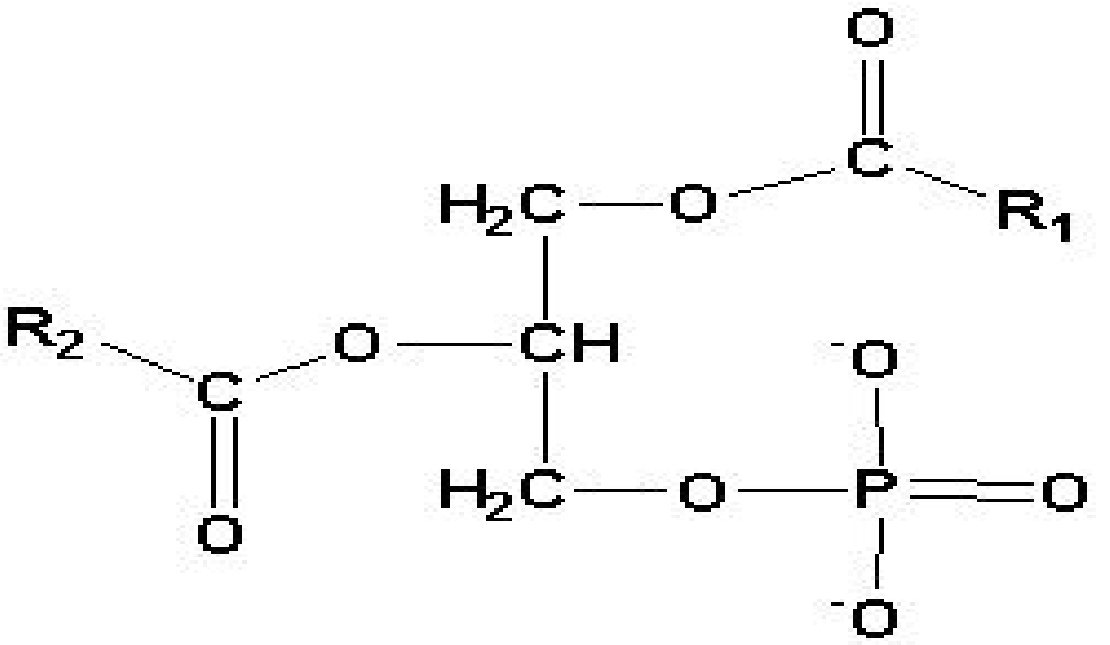
Names & Structures
OF
7 Glycerophospholipids

Simplest Glycerophospholipid
PHOSPHATIDIC ACID

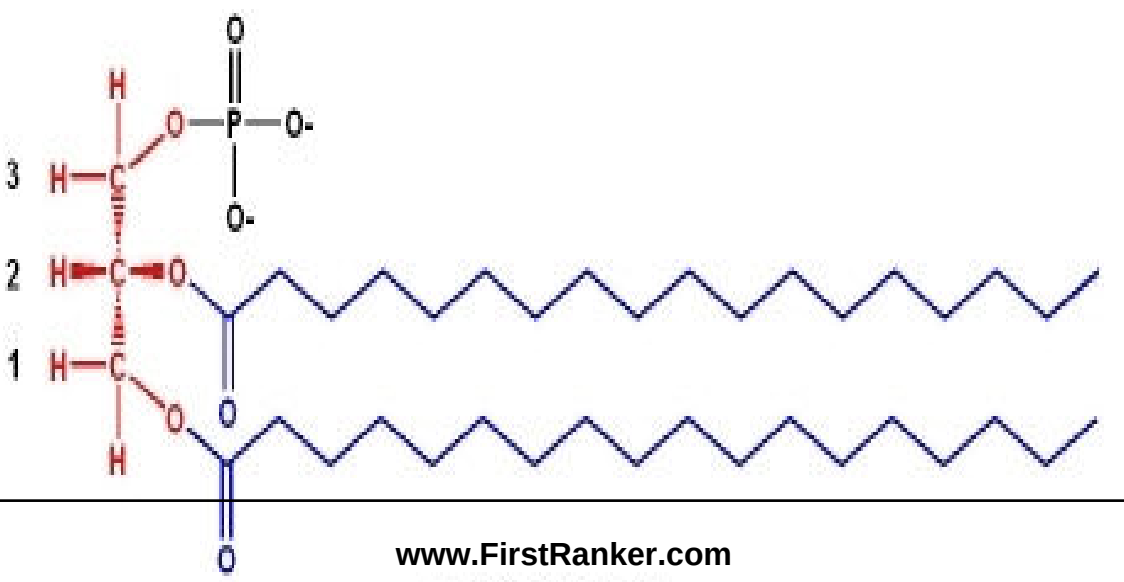


- **Depending upon Nitrogenous and Non Nitrogenous moiety attached.**

- **Examples of 7 Glycerophospholipids are:**
  1. **Phosphatidic Acid (Simplest PL)**
  2. **Phosphatidyl Choline (Lecithin)**
  3. **Phosphatidyl Ethanolamine (Cephalin)**
  4. **Phosphatidyl Serine (Cephalin)**
  5. **Phosphatidyl Inositol/ Lipositol**
  6. **Phospatidal Ethanolamine/ Plasmalogen**
  7. **DiPhosphatidyl Glycerol /Cardiolipin**



Phosphatidic Acid



Phosphatidic Acid

Phosphatidic Acid

- **Phosphatidic acid** is a **simplest Glycerophospholipid.**

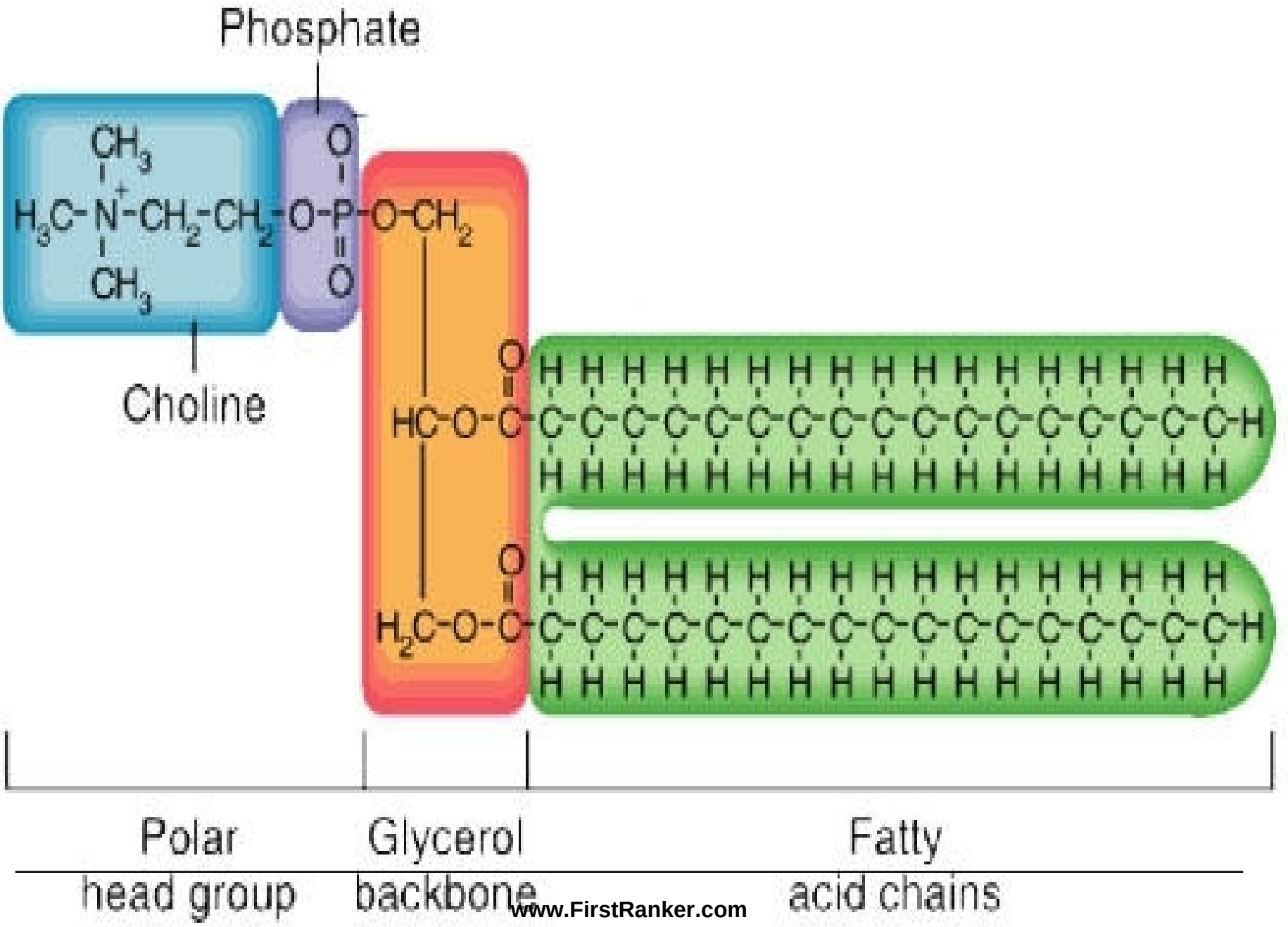
- Phosphatidic acid has Glycerol esterified with **two Fatty acids at C1 and C2 .**

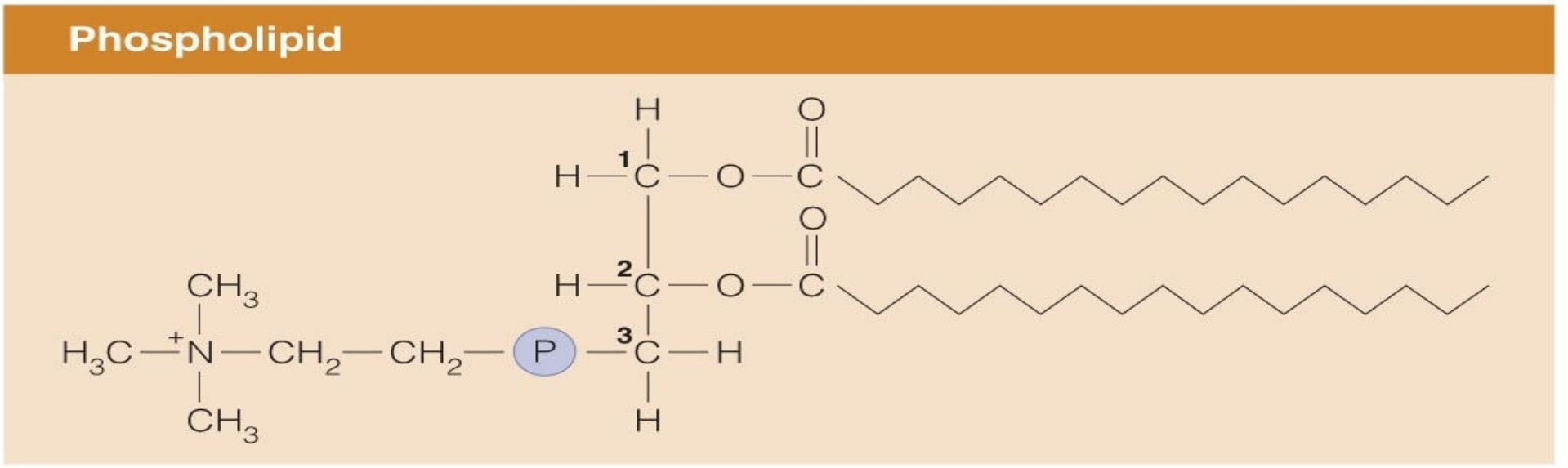
- C3 is esterified with **Phosphoric acid.**

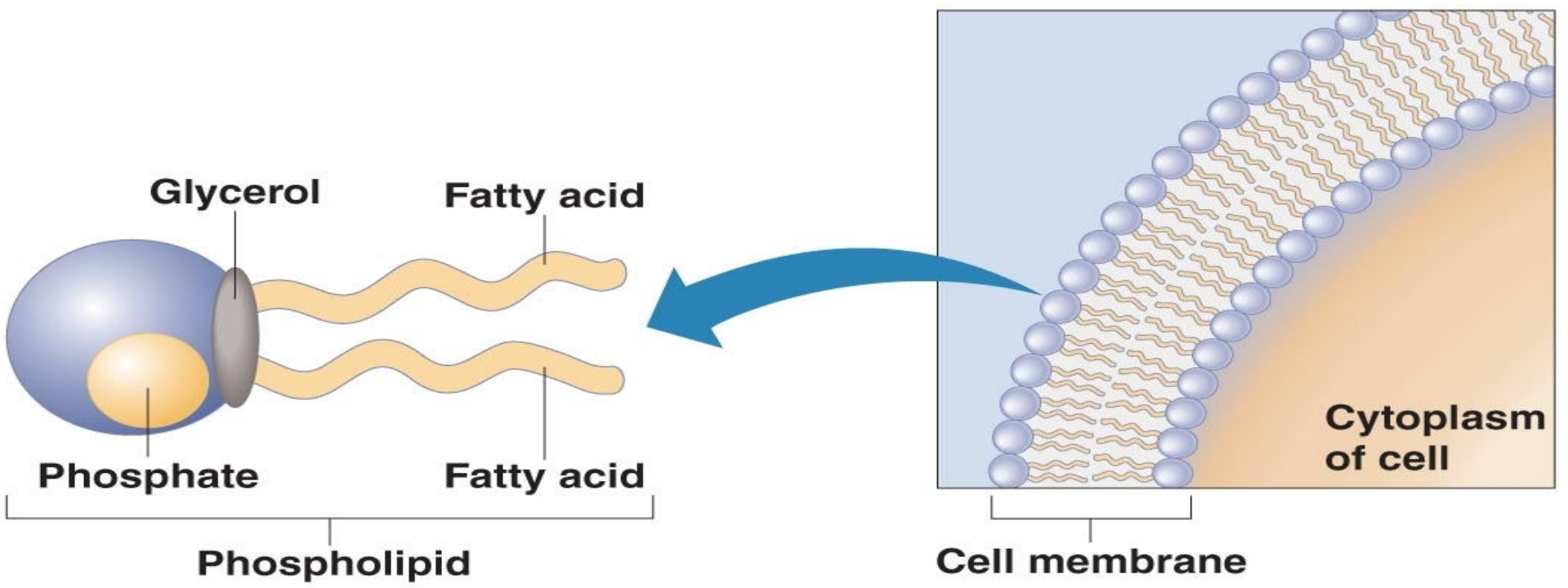
- **Phosphatidic acid serve as a precursor for biosynthesis of** other **Glycerophospholipids**

- Either by **linking of**
  - **Nitrogenous** or
  - **Non nitrogenous base**

Phosphatidyl Choline/Lecithin







- **Phosphatidyl Choline** (**Lecithin**) is most **commonest** and **abundant** **Glycerophospholipid** in body.

- Phosphatidyl Choline is commonly called as **Lecithin.**

- Derived from word '**Lecithos' meaning Egg Yolk.**

- **Phosphatidic acid** is linked to a Nitrogenous base Choline to form **Phosphatidyl Choline.**

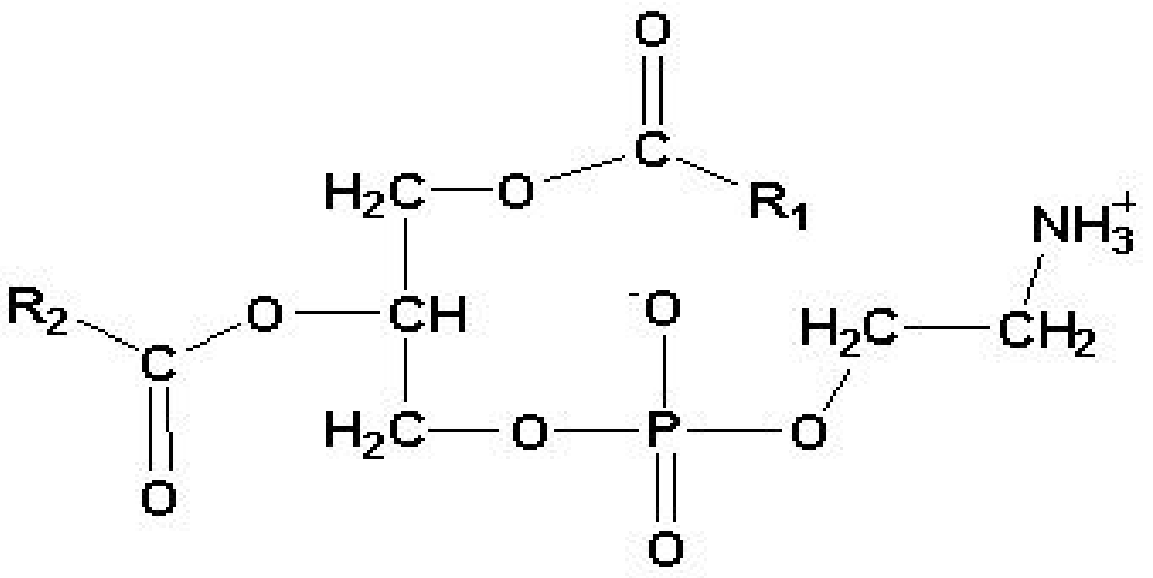
Cephalins

–Type of Glycerophospholipids

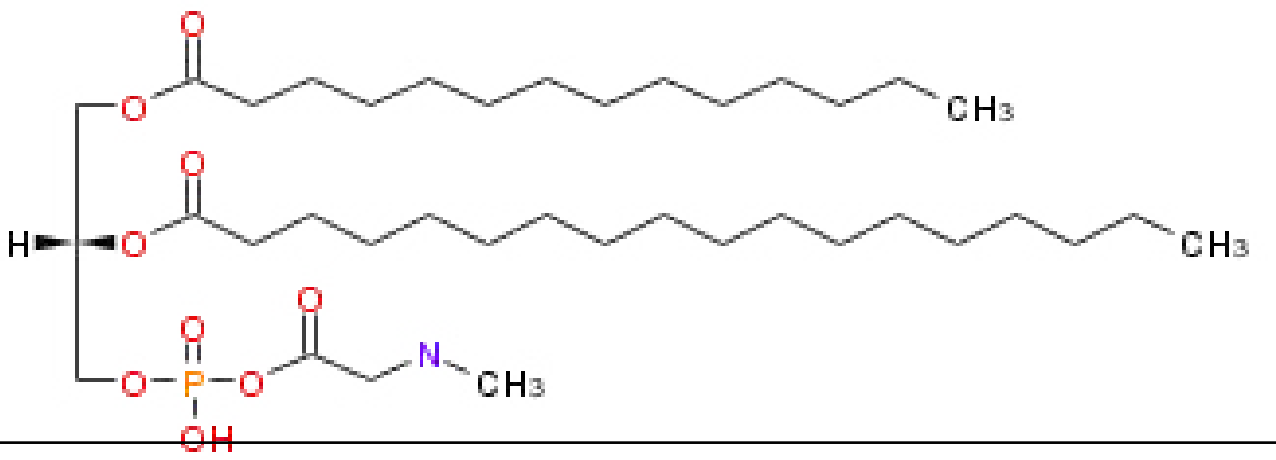
–Nitrogen base is **Ethanolamine or Serine.**

–Phosphatidylethanolamine and Phosphatidylserine are **Cephalins**.

Phosphatidyl Ethanolamine



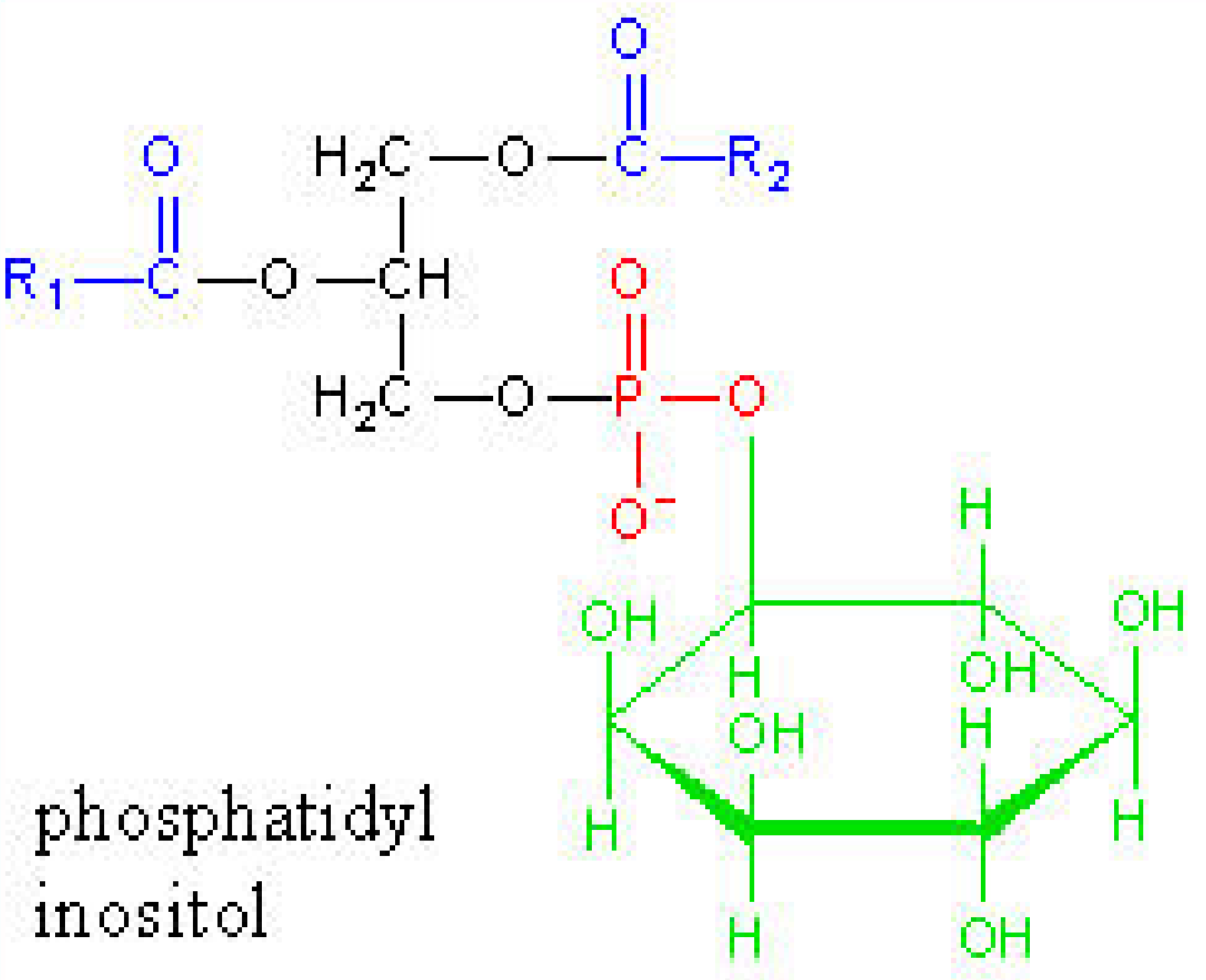
Phosphatidylethanolamine



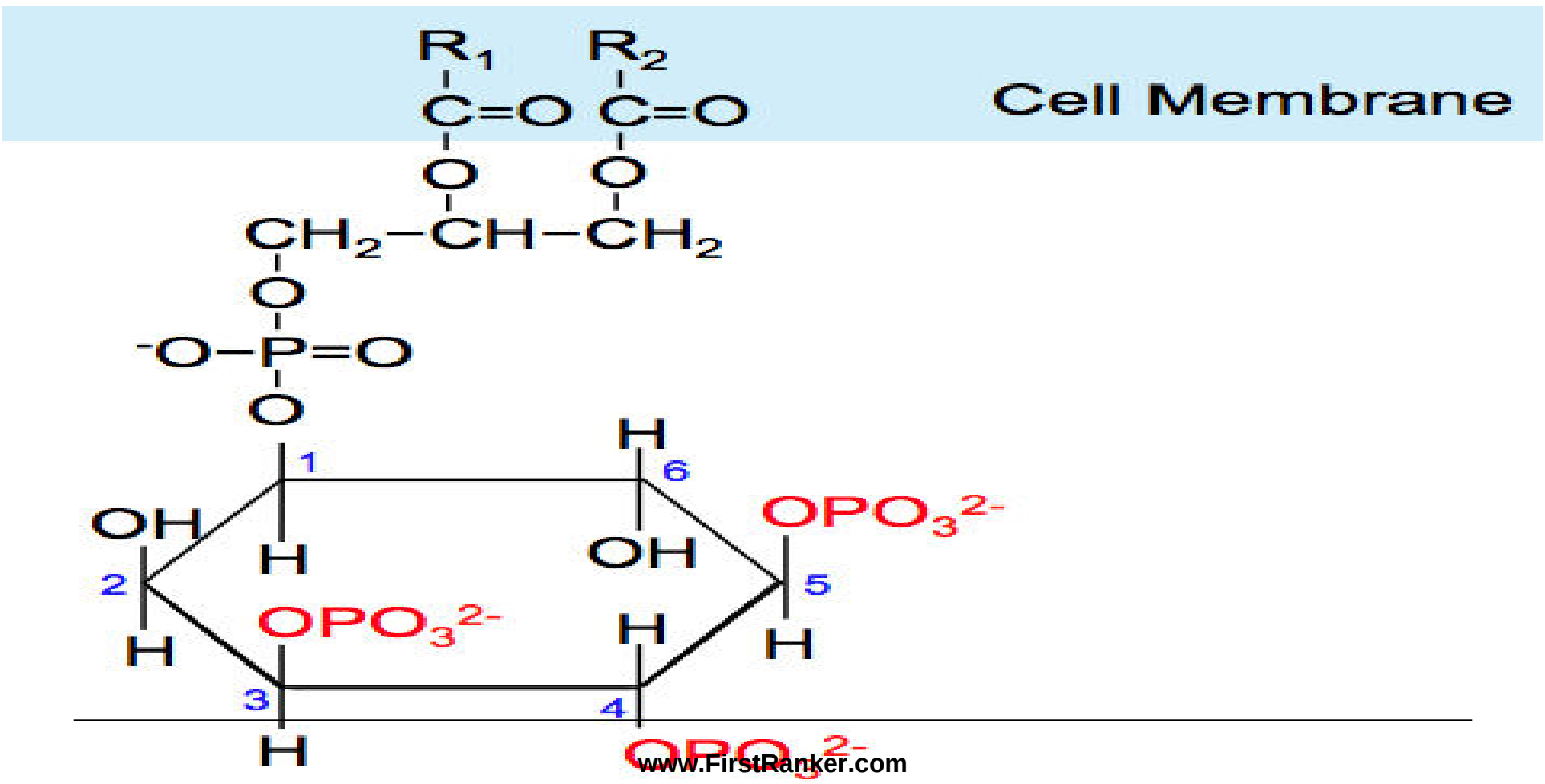
Phosphatidyl Serine

- An Amino acid **Serine** linked to **Phosphatidic acid** forms **Phosphatidyl Serine.**

Phosphatidyl Inositol/ Lipositol



Phosphatidyl Inositol Tri Phosphate (PIP3)

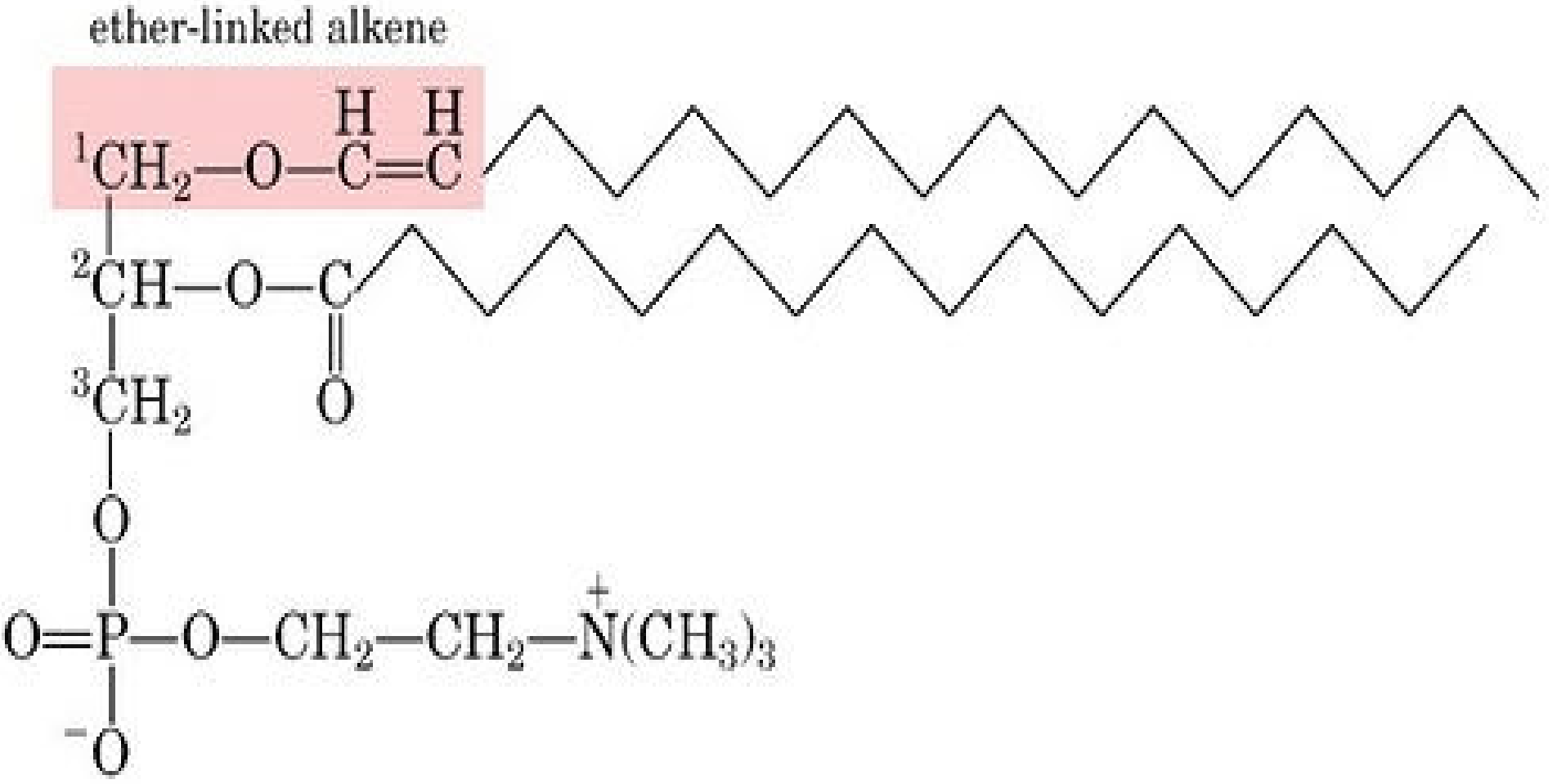


- **Inositol/Myo Inositol** a **Polyol derived from Glucose**
- **Non Nitrogenous , Carbohydrate Derivative.**
- Inositol linked to Phosphatidic acid forms **Phosphatidylinositol.**

- **Phospahatidyl Inositol 3,4,5 Tri Phosphate** (PIP3) in presence of enzyme **Phospholipase C**

- Generates **Diacyl Glycerol** and **Inositol Tri Phosphate.**

Phosphatidalethanolamine/ Plasmalogen

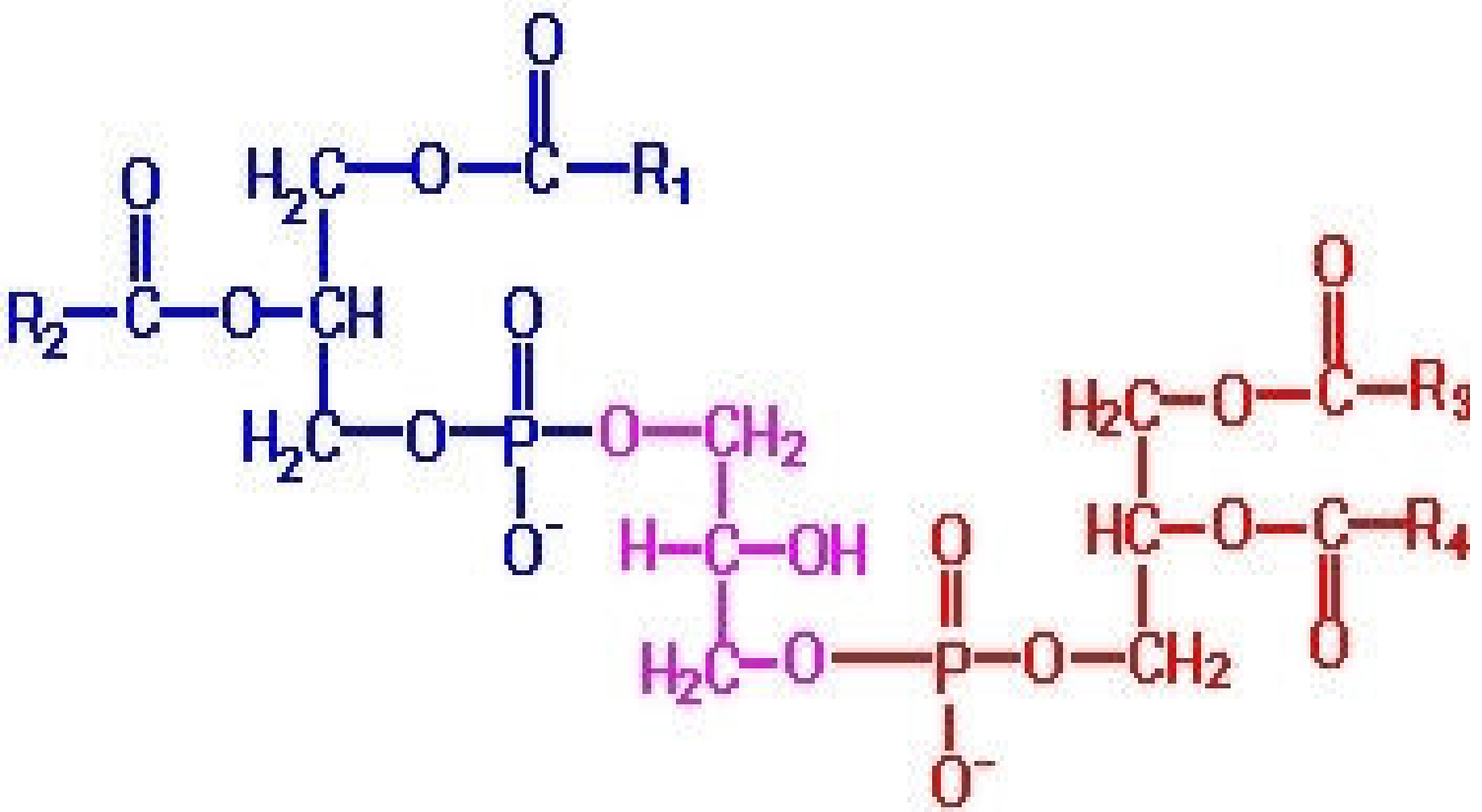


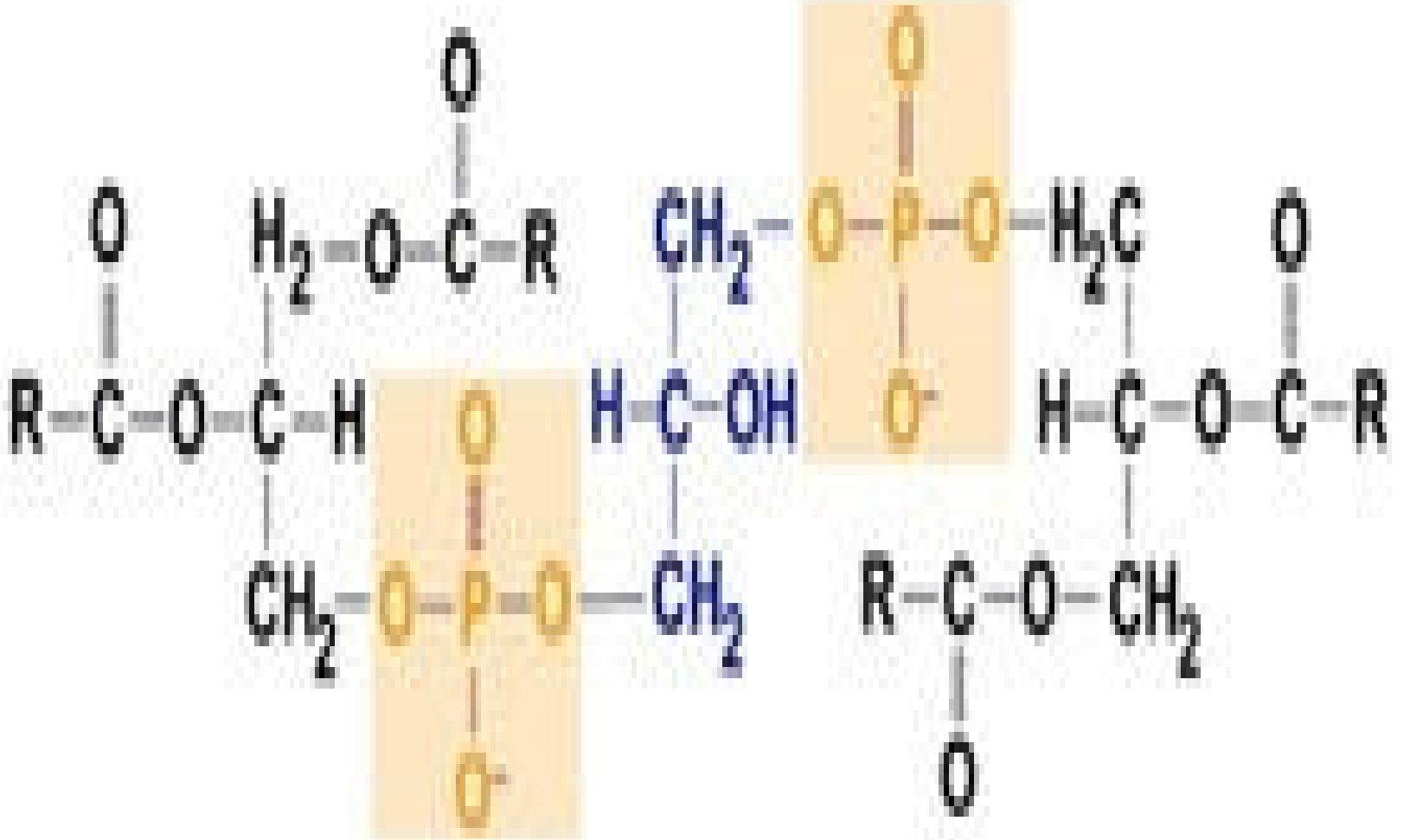
Plasmalogen

- **Plasmalogen** possess an **Ether linkage at C1.**
- **Fatty acid** is linked to **C1 of Glycerol**, by an **Vinyl(CH=CH2) Ether (C-O-C)linkage instead of usual Ester bond.**
- Nitrogen base linked are **Ethanolamine/Choline.**

Diphosphatidylglycerol/ Cardiolipin

Di Phosphatidyl Glycerol





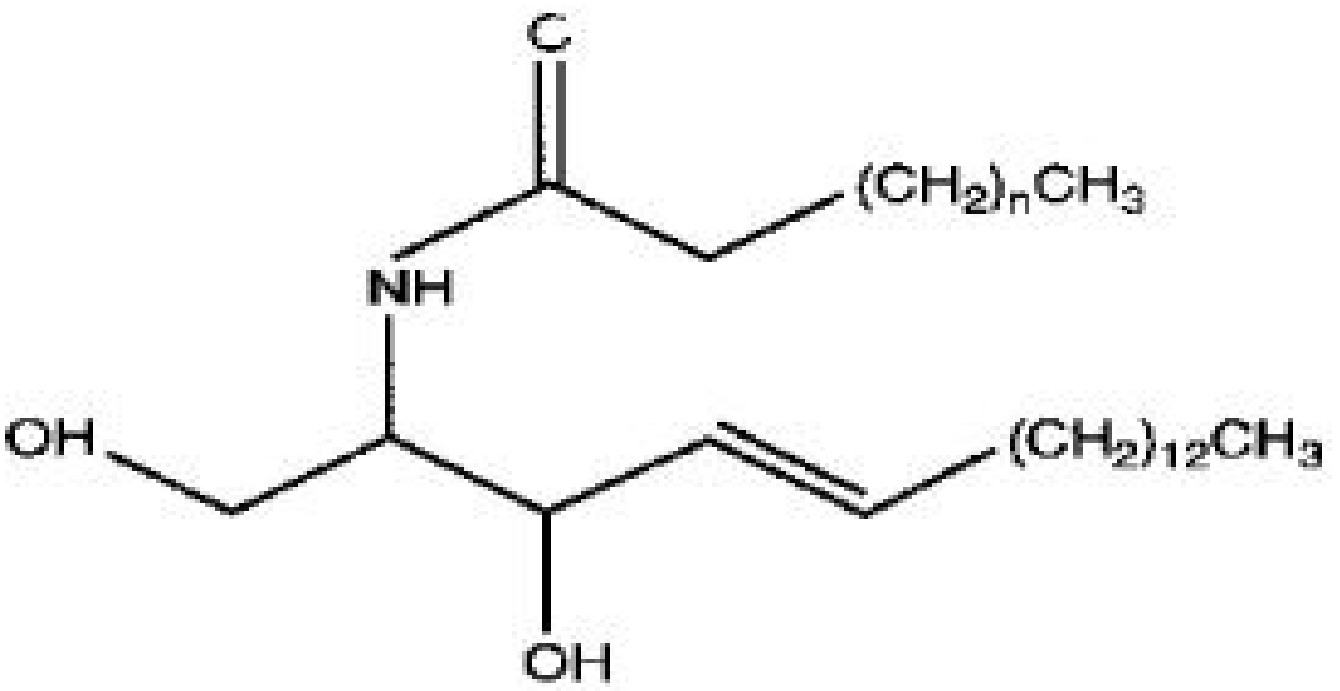
- **Cardiolipin** was first isolated from **Cardiac Muscles of Calf** and hence the name derived.

- Diphosphatidylglycerol/Cardiolipin is chemically composed of

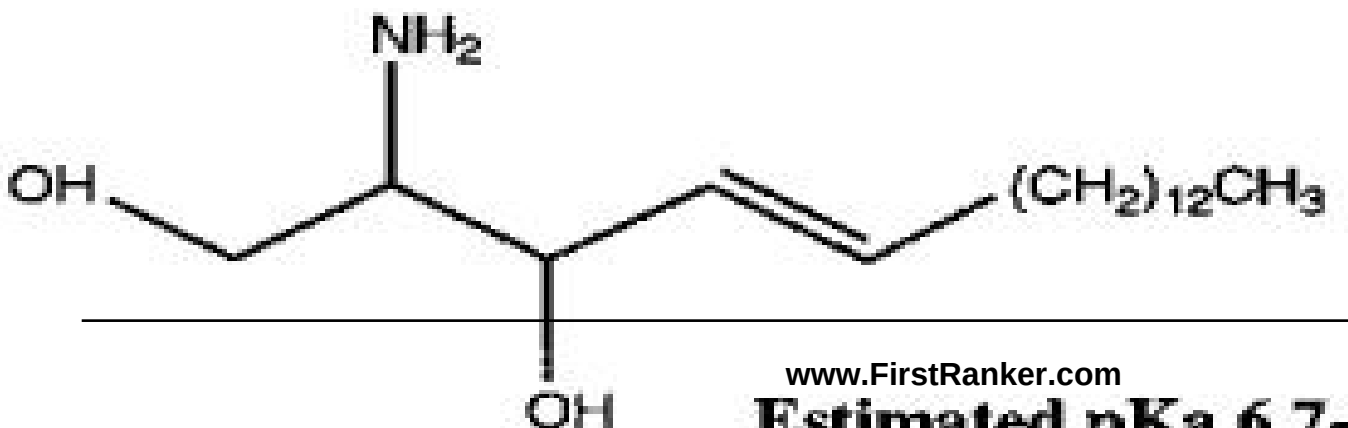
- **Two molecules of Phosphatidic acid linked to one Glycerol .**

Figure 3 Different classes of glycerophospholipids according to their polar head group.

SphingoPhospholipids/ Sphingophosphatides



Ceramide

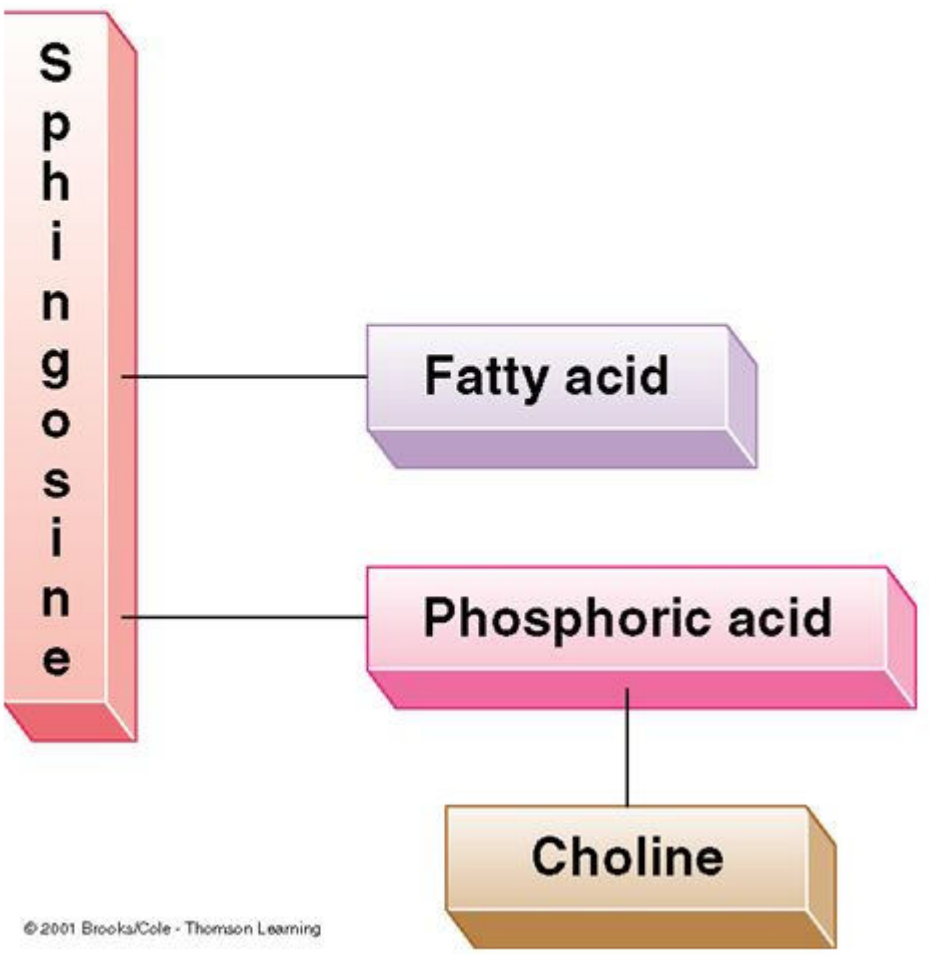


Sphingosine

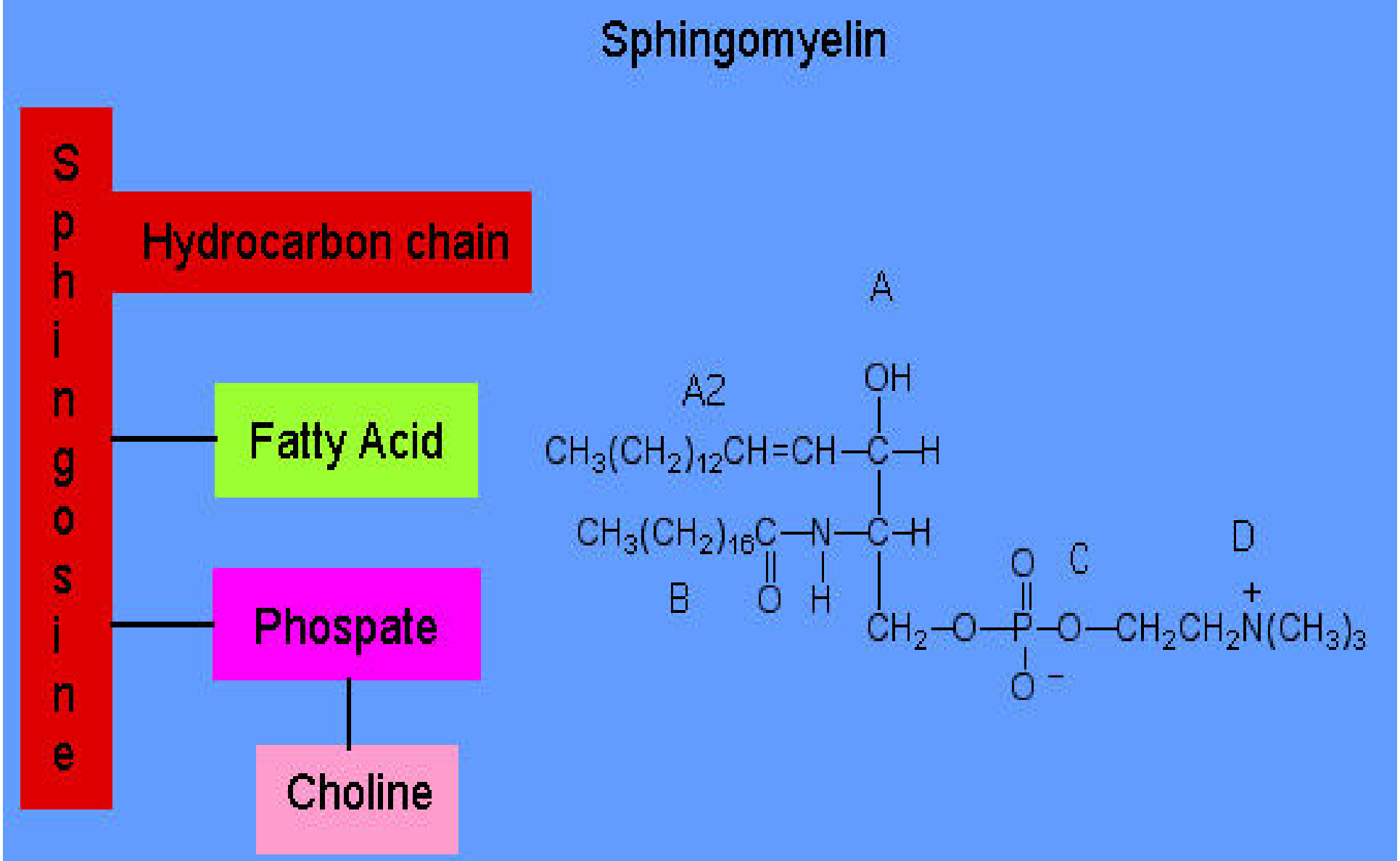
Estimated pKa 6.7-8.4

Sphingomyelin: sphingosine, fatty acid, phosphate and choline

A sphingomyelin.



Sphingomyelins found in myelin sheath around neurons



- **Sphingomyelin** is an example of **Sphingophospholipid**.

- **Sphingophospholipid** is **Sphingosine based Lipid**

- Which has **Sphingosine linked with Fatty acid-Phosphate and Choline**.

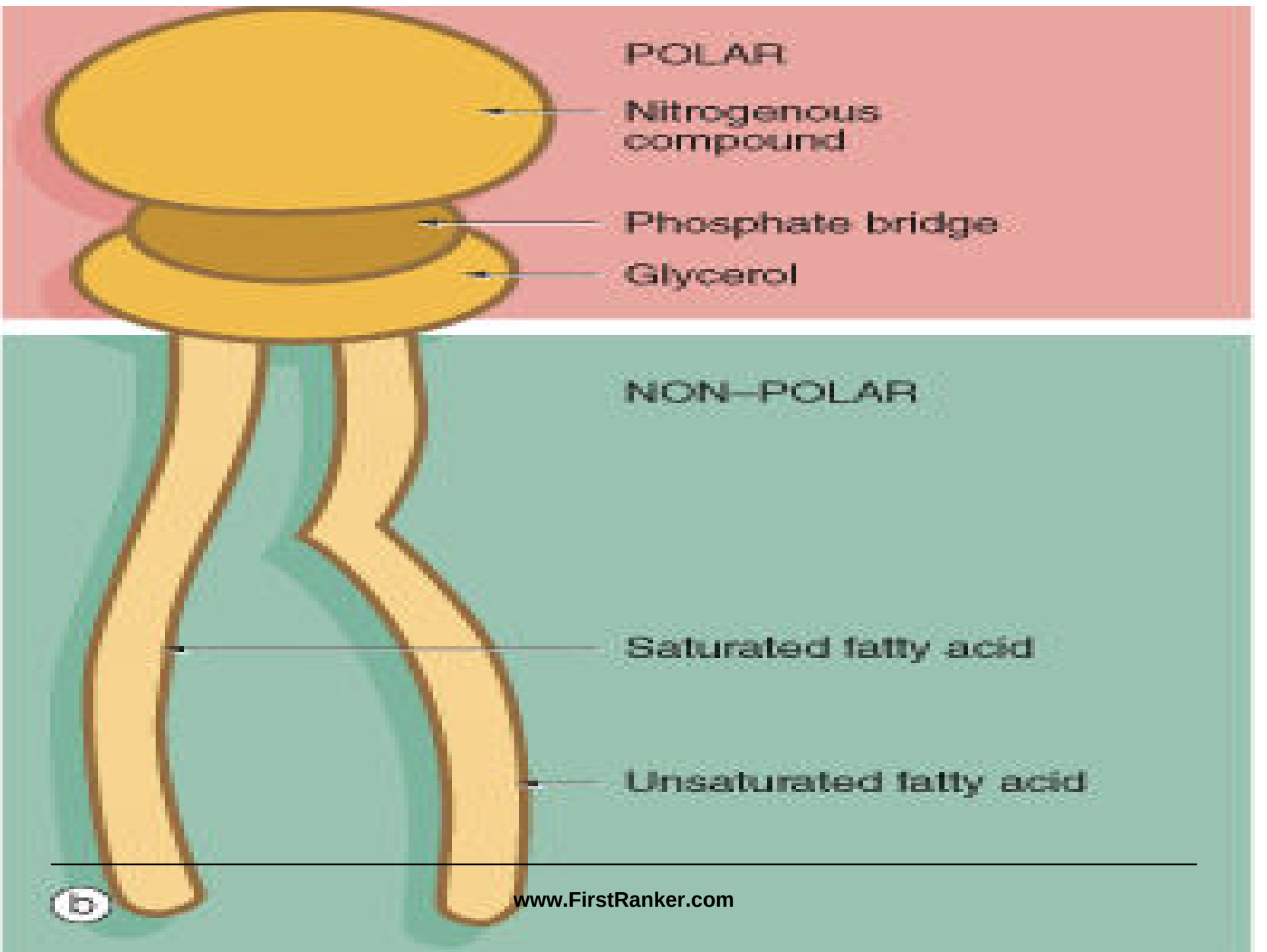
- **Sphingosine** is linked with a Fatty acid by an **amide linkage** to form **Ceramide.**
- **Ceramide is then** linked to **Phosphoric acid and Choline to form Sphingomyelin.**

Properties Of Phospholipids

Amphipathic Nature Of PL

- **Phospholipds** are **Amphipathic/ Amphiphillic** in nature.

- Since the structure of PL possess **both polar** and **nonpolar groups.**



- **Hydrophilic/Polar groups of Phospholipids:**
  - **–Phosphoric acid**
  - **–Nitrogenous groups**
- **Hydrophobic/non polar groups of Phospholipids :**
  - **–Fatty acid/Acyl chains**

Exogenous And Endogenous Sources Of Phospholipids

Phospholipids in Foods

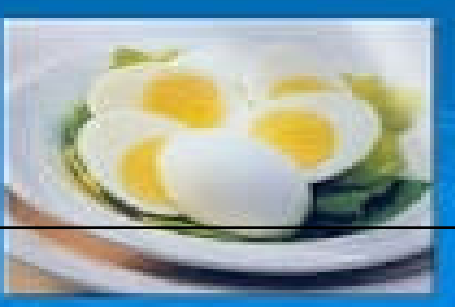
Lecithin (phosphatidylcholine)

- Major phospholipid

Found in:

- Liver
- Eggs
- Soybeans
- Peanuts
- Wheat germ

Liver produces lecithin as well.

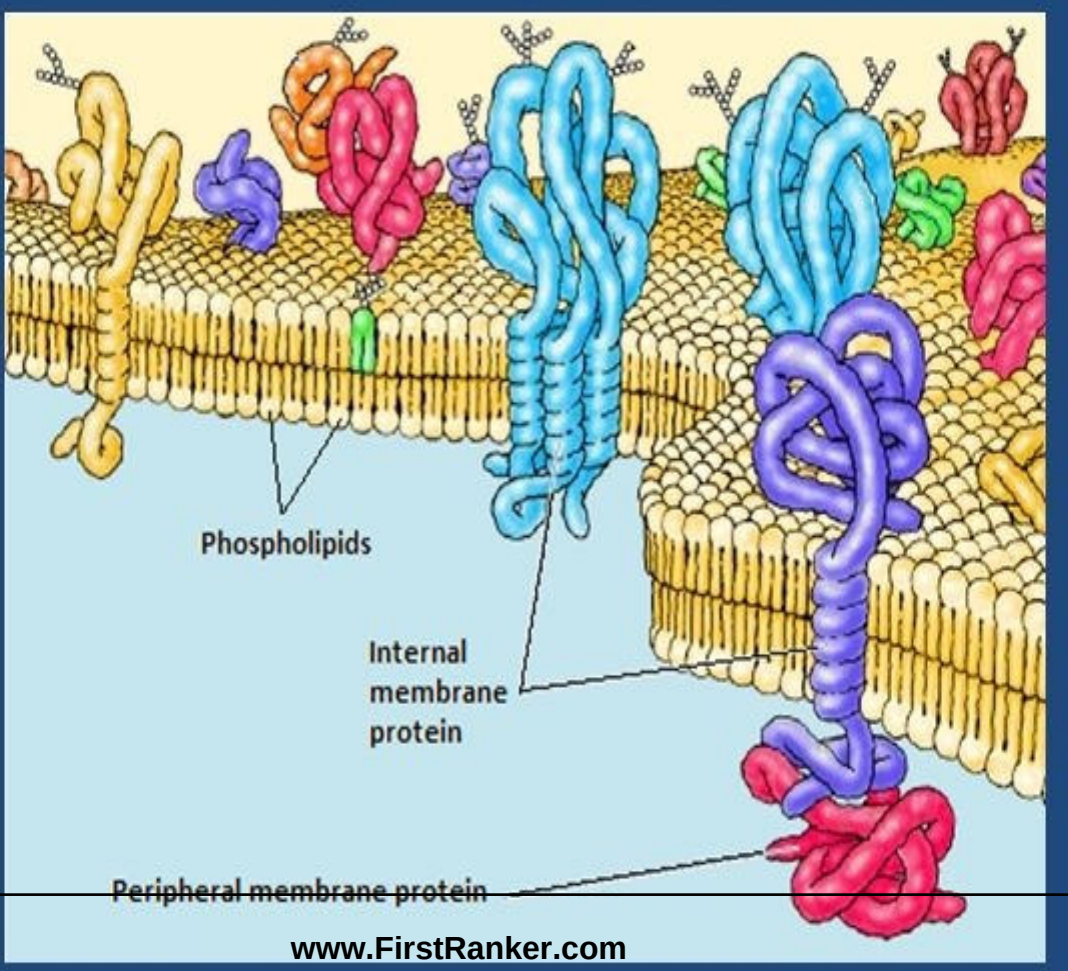


Occurrence And Distribution Of Phospholipids

- Various types of Phospholipids **Associated to all over body cells**.
- Most predominantly associated to **Biomembranes**
- **Myelin Sheath**
- **Alveoli in Lungs**

13. Where are phospholipids found in the body?

Phospholipids are found in cellular membranes, of which they are a major component.



Functions Of Phospholipids (PL)

1. Biomembrane Components
2. Lung Surfactant
3. Lipid Digestion and Absorption
4. LCAT activity for Cholesterol Esterification and Excretion
5. Lipotropic Factor
6. Clotting Mechanism
7. Cardiolipin role
8. Coenzyme Role
9. Choline from Lecithin Methyl Donor
10. Detoxification role of Lecithin
11. Eicosanoids biosynthesis
12. Nerve Impulse Conduction
13. Second Messenger of Hormone Regulation

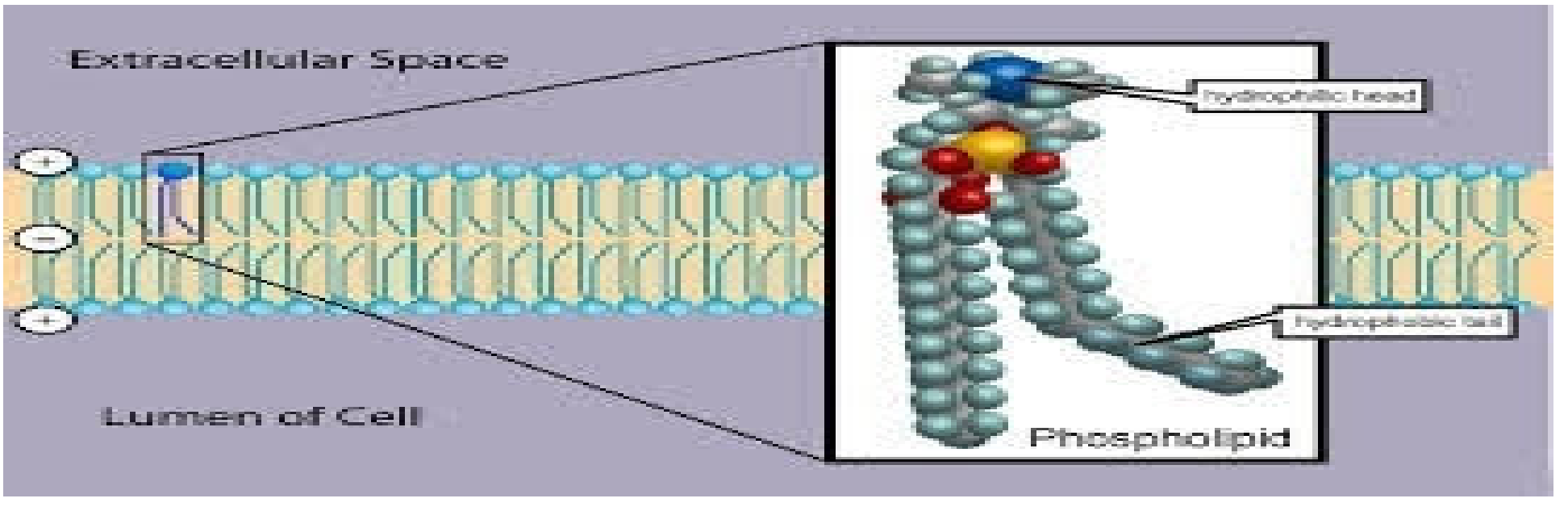
Functions of Phospholipids

- Components of cell membrane, mitochondrial membrane and lipoproteins
- Participate in lipid absorption and transportation from intestine
- Play important role in blood coagulation
- Required for enzyme action- especially in mitochondrial electron transport chain
- Choline acts as a lipotropic agent
- Membrane phospholipids acts as source of Arachidonic acid
- Act as reservoir of second messenger- Phosphatidyl Inositol
- Act as cofactor for the activity of Lipoprotein lipase
- Phospholipids of myelin sheath provide insulation around the nerve fibers
- Dipalmitoyl lecithin acts as a surfactant

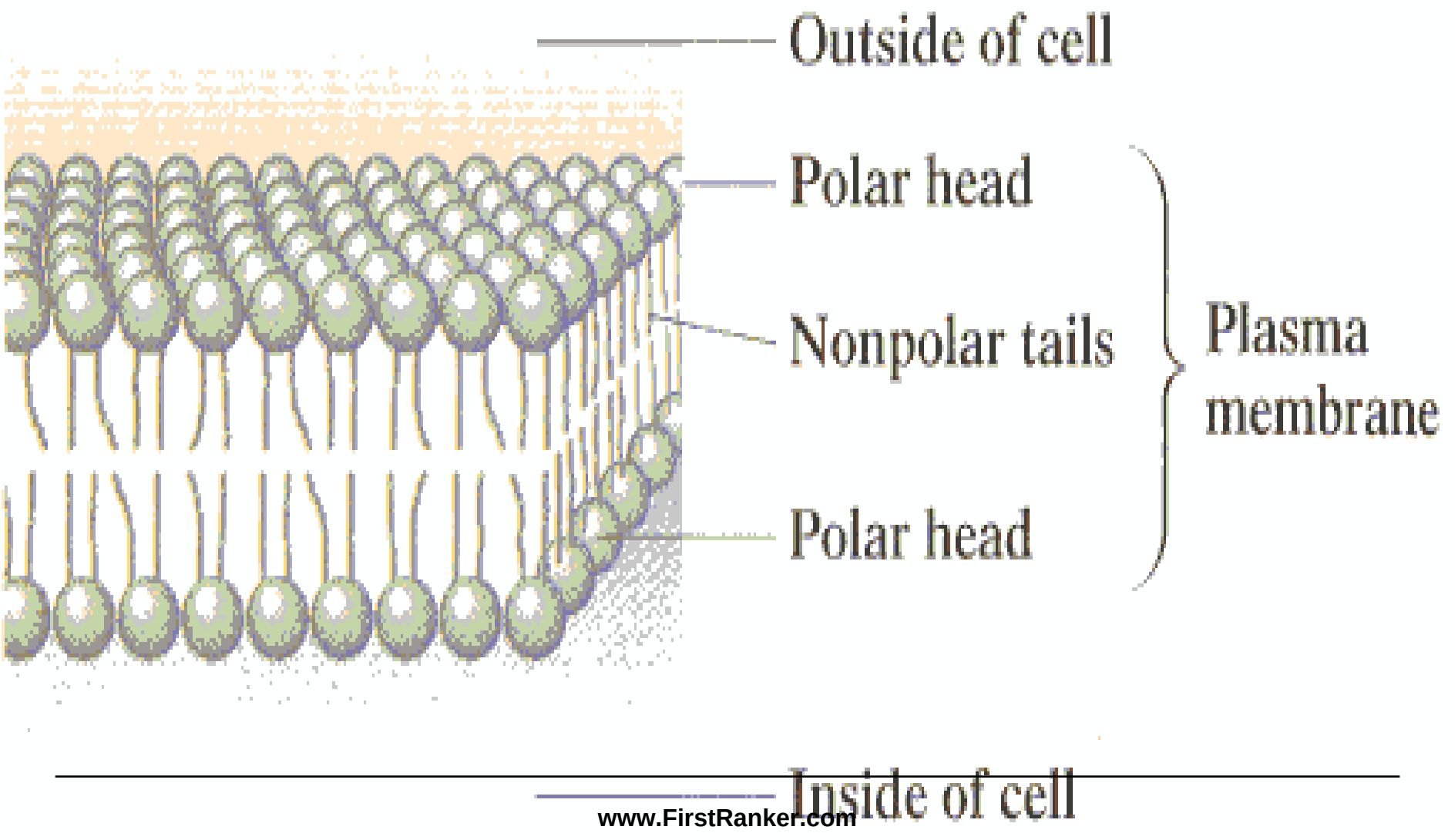
Glycerophospholipid Functions

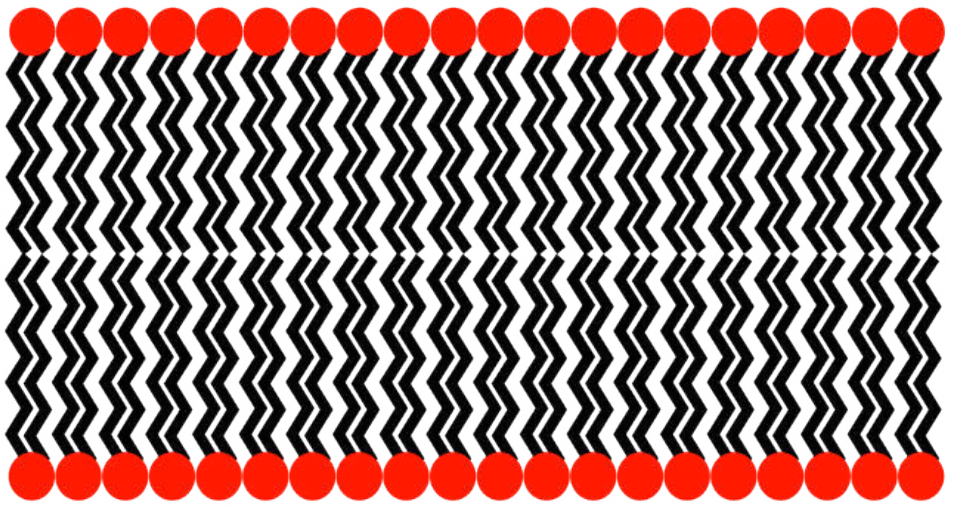
Lecithin Is Most Functional Phospholipid

1. Phospholipids Components Of Biomembranes



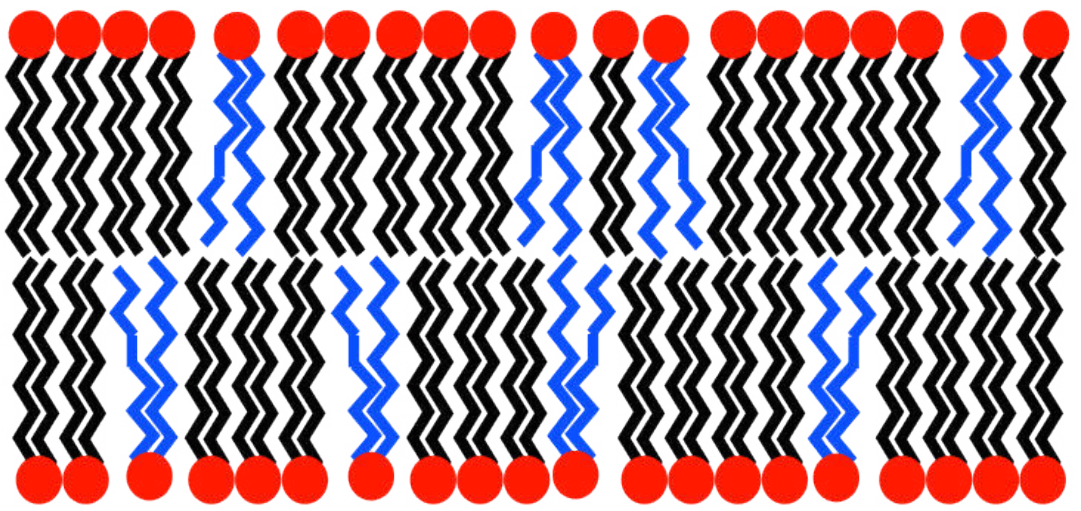
Phospholipid Bilayer of Plasma membrane



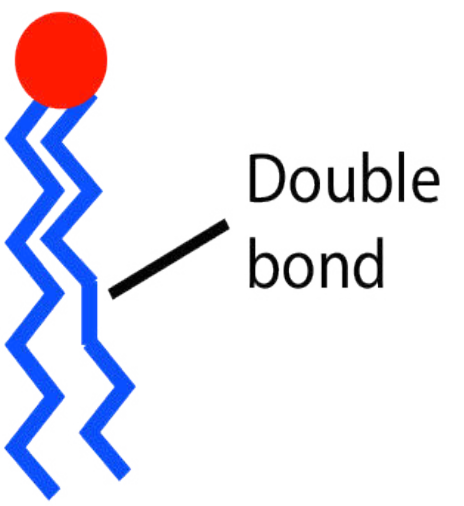


Saturated lipids only

Saturated



Mixed saturated and unsaturated

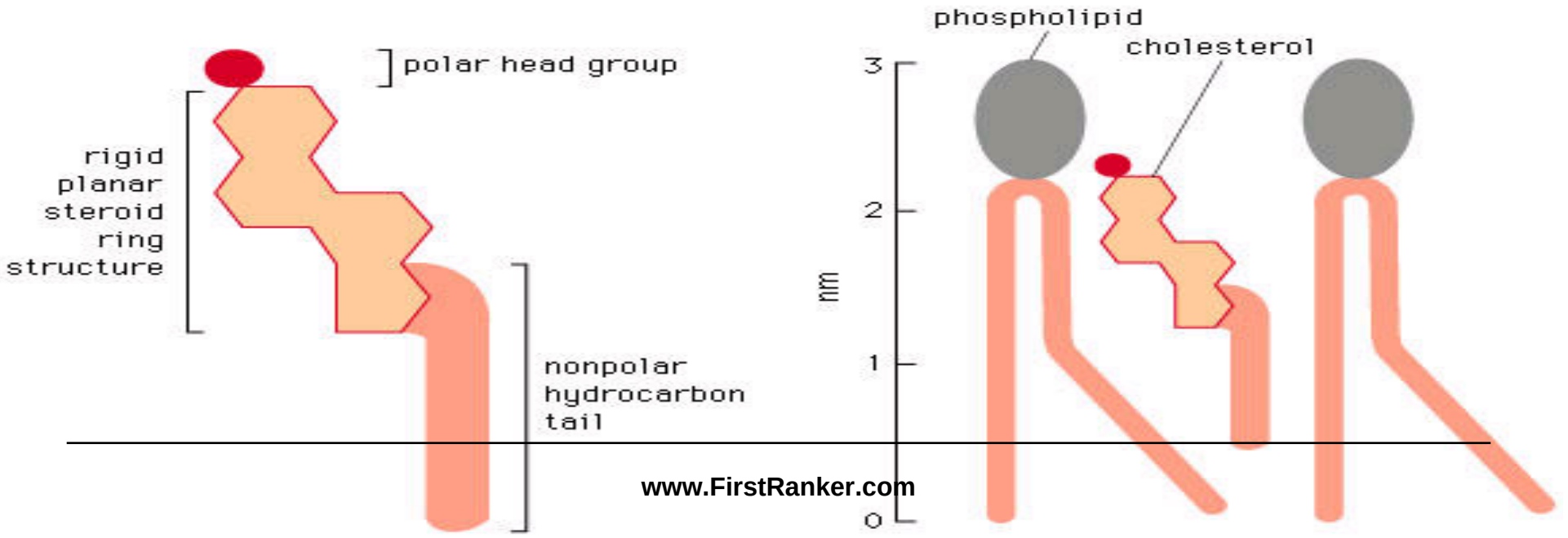


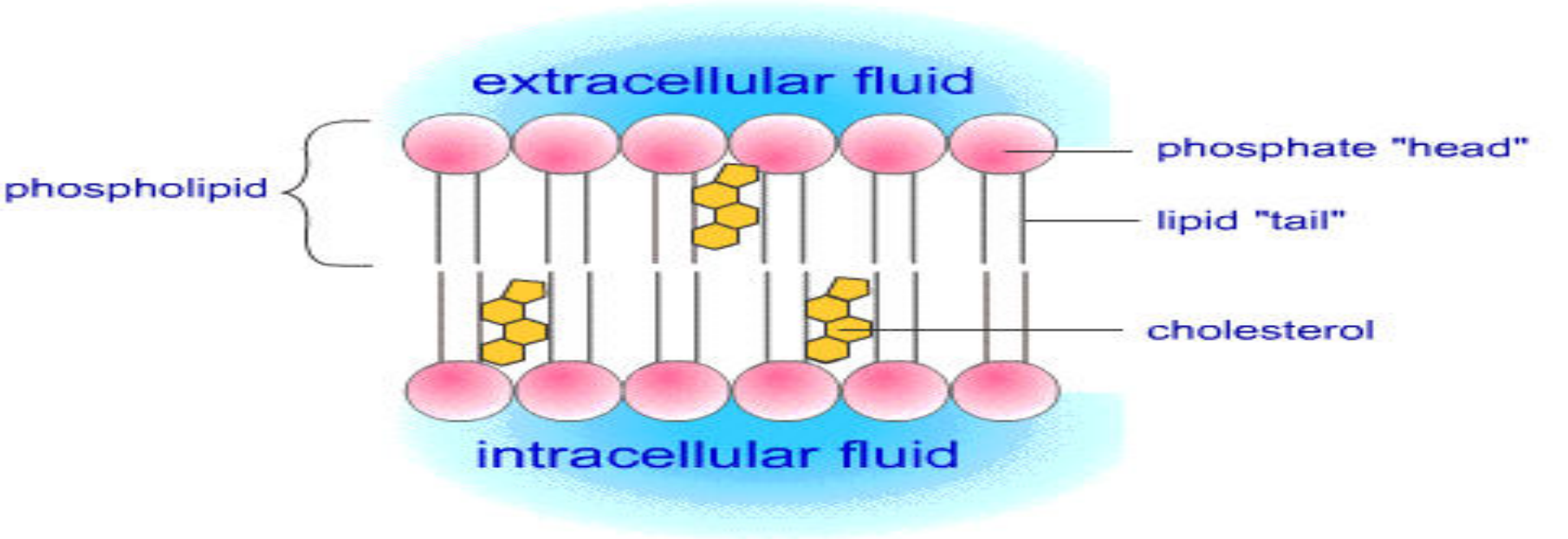
Monounsaturated

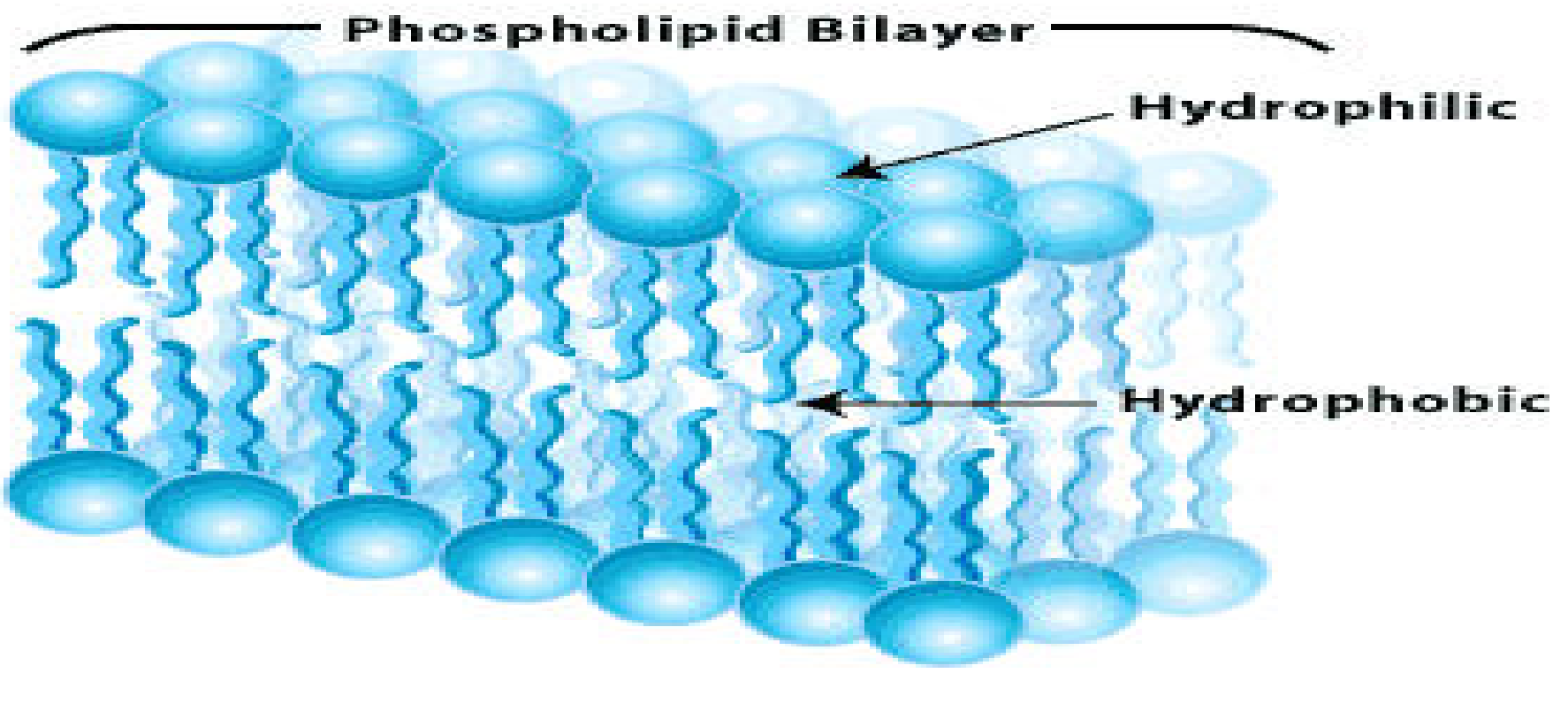
Cholesterol intercalates among Phospholipids.

Cholesterol fills in the spaces left by the kinks of PUFAs .

Cholesterol stiffens the bilayer and makes membrane **less fluid and less permeable**.







- **Role Of Lecithin**

- The **Glycerophospholipid Lecithin** is the major **structural components of biomembranes**.

- An **Amphipathic phospholipid bilayer** has polar head groups of PL directed outwards.

- **Membrane Phospholipid bilayer ,constituent of cell membranes imparts:**

  - **Membrane Structural Integrity**
  - **Membrane Fluidity**
  - **Membrane Flexibility**
  - **Selective Permeability**

- **Phospholipids** may have fatty acids which are **saturated or unsaturated**.
- This affects the properties of the resulting bilayer/cell membrane:

– Most membranes have phospholipids derived from **unsaturated** fatty acids.

– **Unsaturated fatty acids** add **fluidity to a bilayer** since **'kinked' tails do not pack tightly together.**

– Phospholipids (PL) derived from unsaturated phospholipids **allow faster transport of nonpolar substances across the bilayer**.

– **Polar substances are restricted** to cross the membrane .

– **PL bilayer in membranes protect the cell from an entry of polar reactive and interfering substances and serve as security guards of cells.**

- **Membranes of Nerve cells,** which are **stiffer** contain a much higher percentage of **phospholipids derived** from **saturated fatty acids**.

- They also contain **high levels of Cholesterol** which **stiffens membrane** structure.

2.Phospholipid As Lung Surfactant

Pulmonary surfactant composition

80% phospholipids

- Dipalmitoylphosphatidylcholine DPPC (60%)
- Phosphatidyl glycerol / ethanolamine / inositol (20%)

10% neutral lipids

- Mostly cholesterol

10% Surfactant proteins

- SP-A, SP-D: hydrophilic
- SP-B, SP-C: hydrophobic

- **DiPalmitoyl Phosphatidyl Choline** serve as an **Lung surfactant.**

- It **Lowers surface tension** and keeps **Alveoli of lungs blown. (prevent adherence of alveoli)**

- **Enables effective exchange of gases** (Oxygen) in Lungs.

- After expiration of air the alveoli gets deflated.

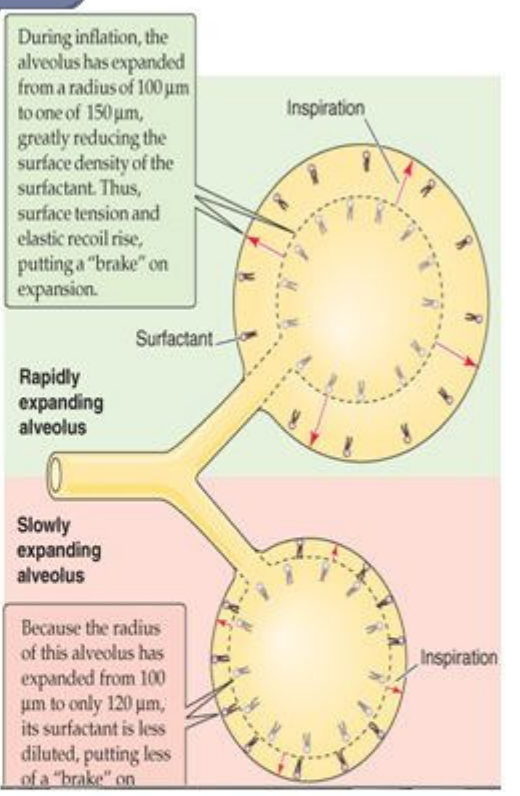
- The **lung surfactant** reduces the surface tension and allow the **alveolar walls to reinflate**.

Pulmonary Surfactant

- **Surfactant** contains phospholipids, proteins and glycosaminoglycans, reduces the surface tension and prevents collapse of the alveolus during expiration.
- The reduced surface tension in the alveoli decreases the force that is needed to inflate alveoli during inspiration.
- Therefore surfactant stabilizes the alveolar diameters, facilitates their expansion and prevents their collapse by minimizing the collapsing forces.
- Surfactant also has bactericidal properties

Functions of Surfactant

1. **Lowers surface tension of alveoli & lung**
   1. Increases compliance of lung
   2. Reduces work of breathing
2. **Promotes stability of alveoli**
   1. 300 million tiny alveoli have tendency to collapse
   2. Surfactant reduces forces causing atelectasis
   3. Assists lung parenchyma 'interdependant' support
3. **Prevents transudation of fluid into alveoli**
   1. Reduces surface hydrostatic pressure effects
   2. Prevents surface tension forces from drawing fluid into alveoli from capillary; LaPlace
4. **Expansion of lungs at birth**



- **Phospholipid as Lung surfactant**
- Prevent body to suffer from **Respiratory Distress Syndrome (RDS).**

3.Phospholipids

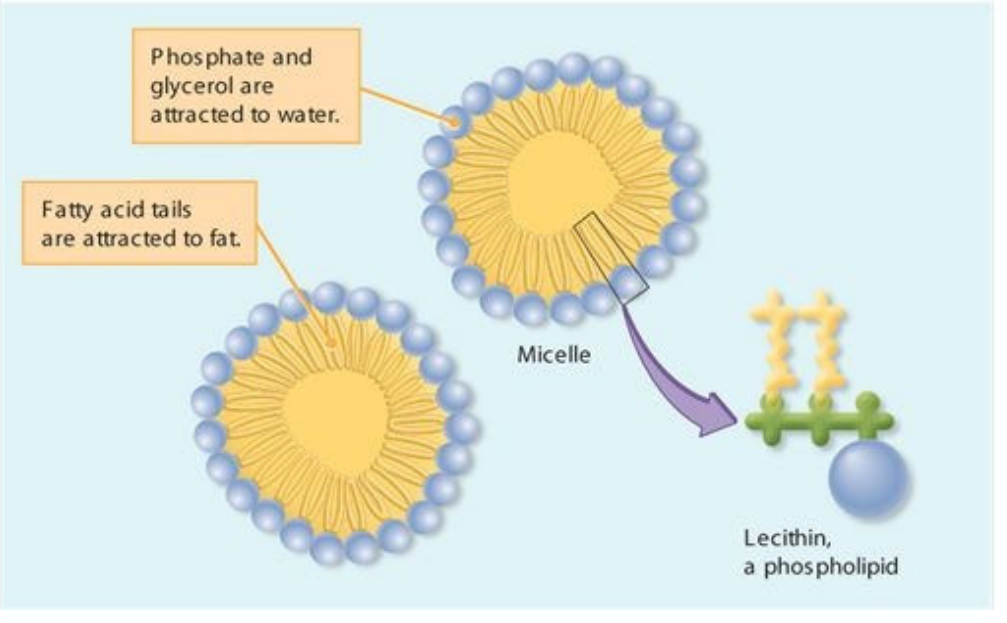
Help In Digestion And Absorption Of Dietary Lipids

- **Phospholipids being amphipathic** in nature act as good **emulsifying agents.**

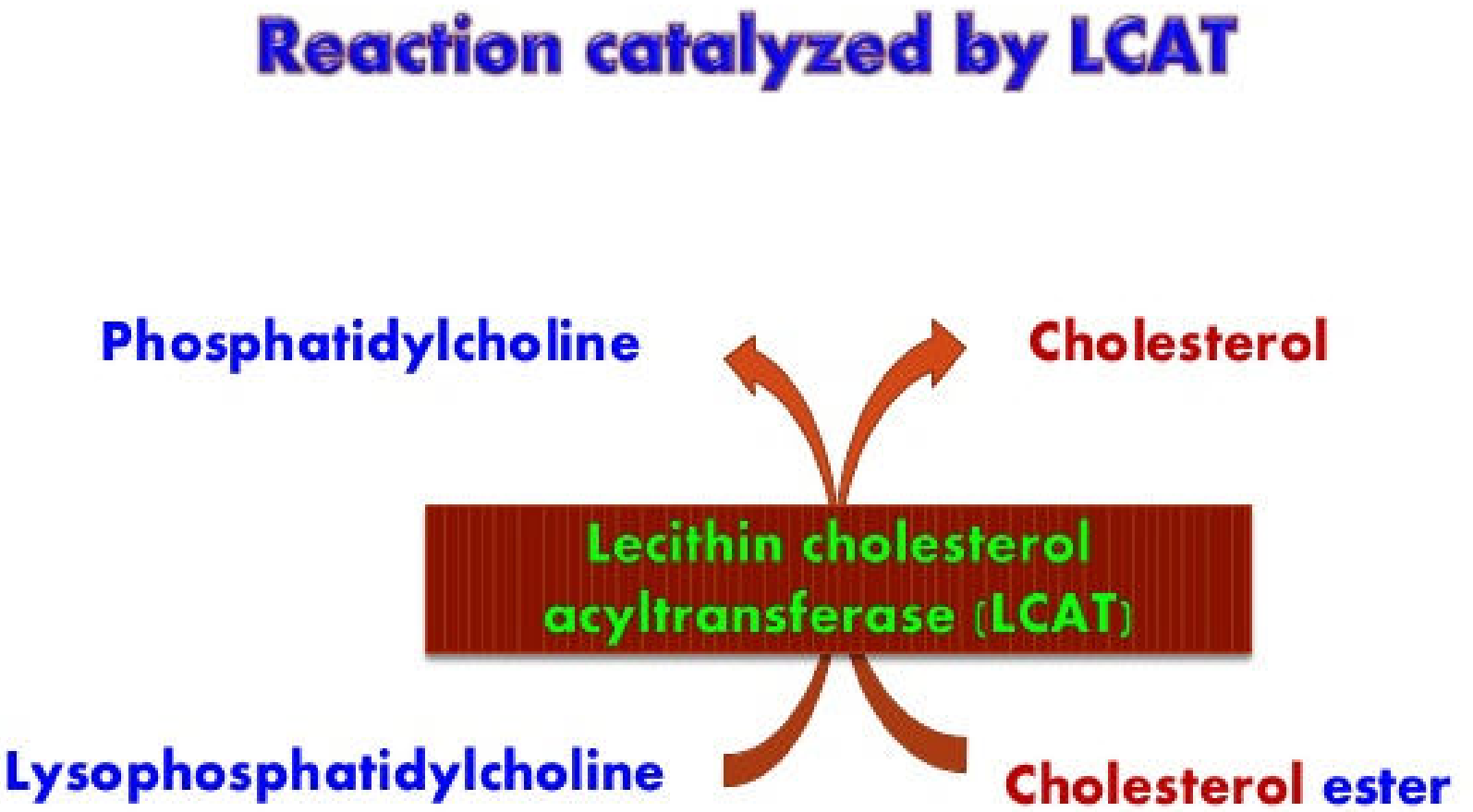
- **Along with Bile Salts** they help in **digestion and absorption** of non polar **dietary Lipids.**

Phospholipids

- Emulsifiers (**Lecithin**)
  - In body
    - Phospholipid with **choline →** phosphotidylcholine
  - In food
    - Blend of phospholipids with different nitrogen-containing components
    - Used as emulsifiers (e.g. salad dressing, chili, sloppy-joe mixes, and chewing gum).



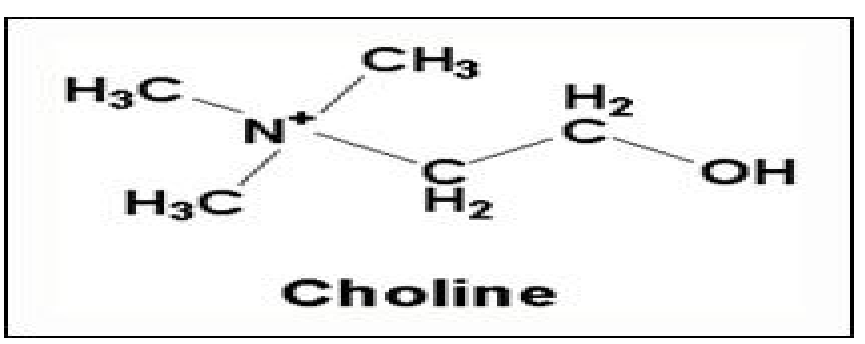
4.Phospholipid Lecithin Helps In Cholesterol Excretion



- **Lecithin** helps in **Cholesterol Esterification by LCAT activity.**

- **Cholesterol Ester is later** dissolved in Bile and further **excreted it out**.

- **Lecithin** serve as a **storage depot of Choline.**
- **Choline** is a store of **labile Methyl groups**
- Hence **Choline** participate in **Transmethylation reactions .**



Choline

- **Choline** is used for generation of neurotransmitter **'Acetyl Choline"** which helps **in nerve impulse transmission.**
- **Choline** serve as **Lipotropic factor** hence helps in Lipoprotein formation in Liver to mobilize out Lipids and **prevent from Fatty Liver.**

6. Phospholipids Releases Arachidonic Acid For Eicosanoid Biosynthesis

- **Lecithin** at 2nd carbon has **Arachidonic acid (PUFA).**

- **It donates Arachidonic acid** which is a precursor for **Eicosanoid biosynthesis.**

- Phosphatidyl Inositol **also provides Arachidonic acid** for Eicosanoids biosynthesis.

- Lecithin helps CYT450 system for **drug detoxification**.

8. Phospholipids Has Role In Blood Coagulation

- **Role Of Cephalin**

- Phosphatidyl Ethanolamine has **role in blood coagulation.**

- It converts clotting factor **Prothrombin to Thrombin by factor X.**

- Phosphatidyl Serine has **role in Apoptosis** (Programmed Cell death).

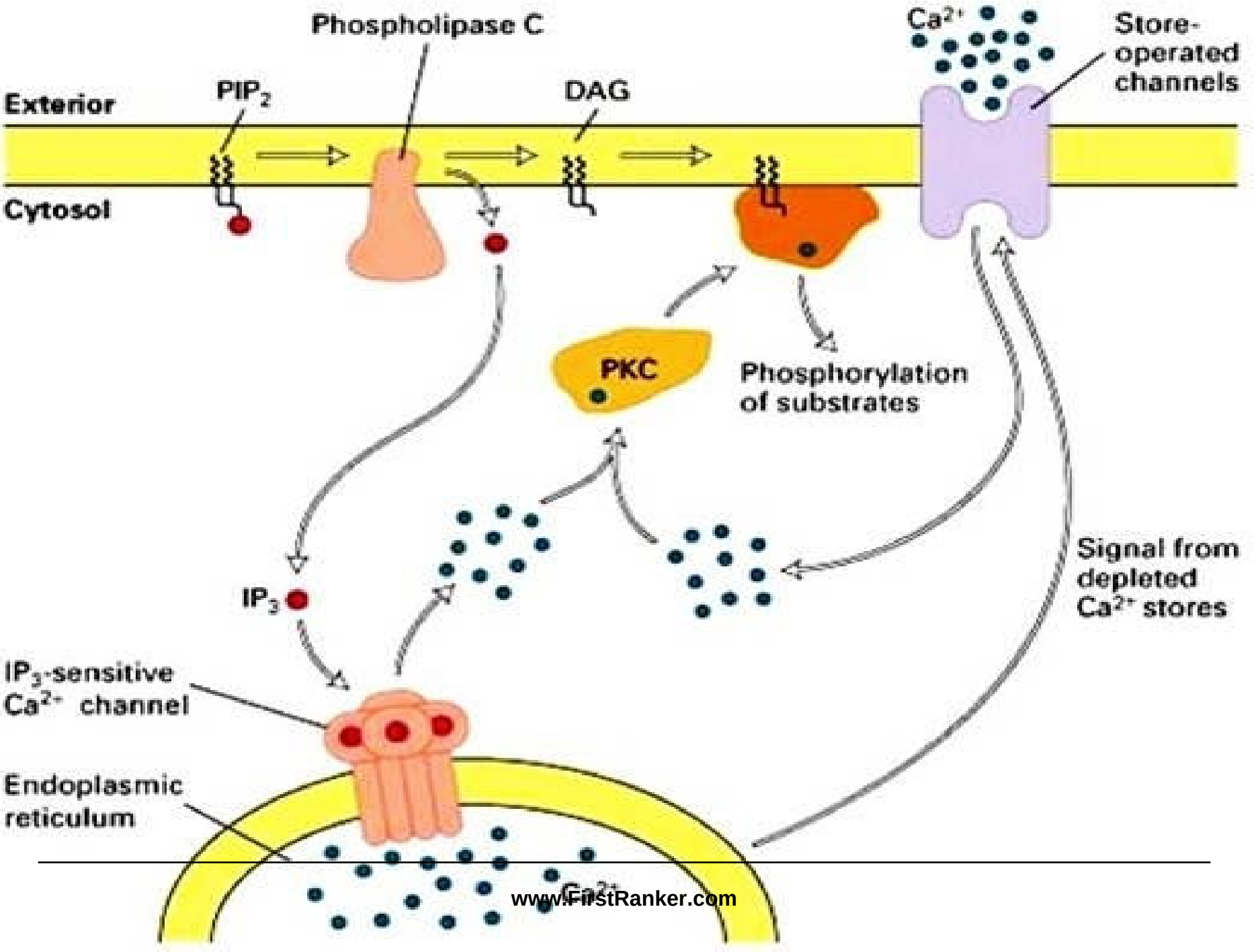
10.Role Of Phospholipids In Hormonal Action

Mediates Cell Signal Transduction

- **Role Of Phosphatidylinositol**

- **Phosphatidyl Inositol Triphosphate (PIP3)** is a constituent of **cell membrane**

- **It mediate hormone action /cell signal transduction** and **maintain intracellular Calcium.**



- **Inositol tri phosphate** and **Diacylglcerol** are released from **PIP3** by membrane bound **Phospholipase C**

- **The Inositol triphosphate and DAG** serve as **second messenger** to **hormones Oxytocin and Vasopressin.**

- **Plasmalogen** associated to **brain and muscles** helps in Neural functions.

• Role Of Cardiolipin

- **Cardiolipin** is rich in **inner mitochondrial membrane** and supports **Electron Transport Chain and cellular respiration.**

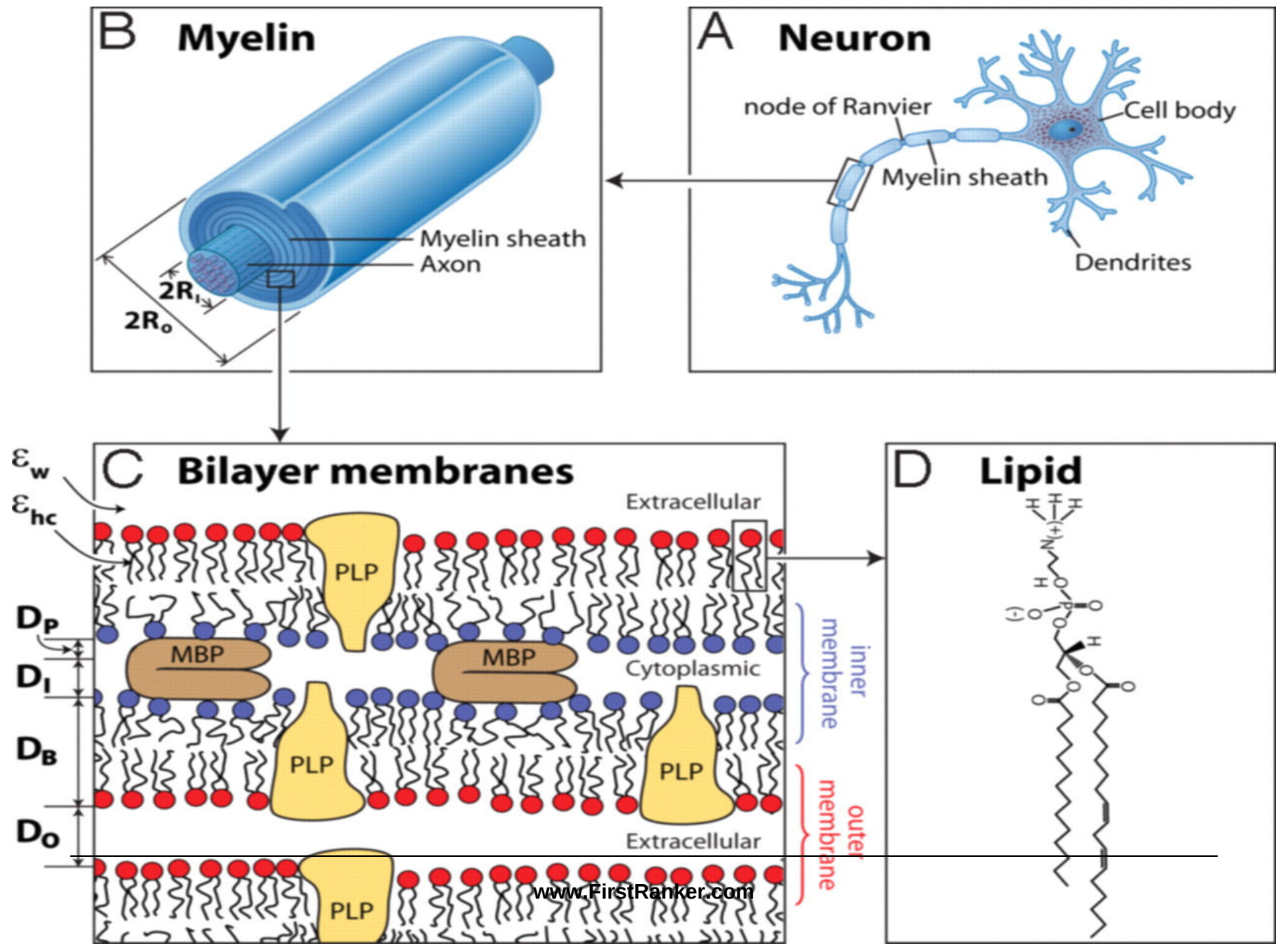
- **Cardiolipin** exhibits antigenic properties and used in **VDRL serological tests** for diagnosis **Syphilis**.

- Phospholipid serve as **Coenzyme for certain Enzymes** :
  - **–Lipoprotein Lipase**
  - **–Cytochrome Oxidase**

Functions OF Sphingophospholipids

- **Sphingomyelins** are rich in **Myelin sheaths** which surrounds and **insulate the axons of neurons.**

- Sphingomyelin helps in **nerve impulse transmission.**

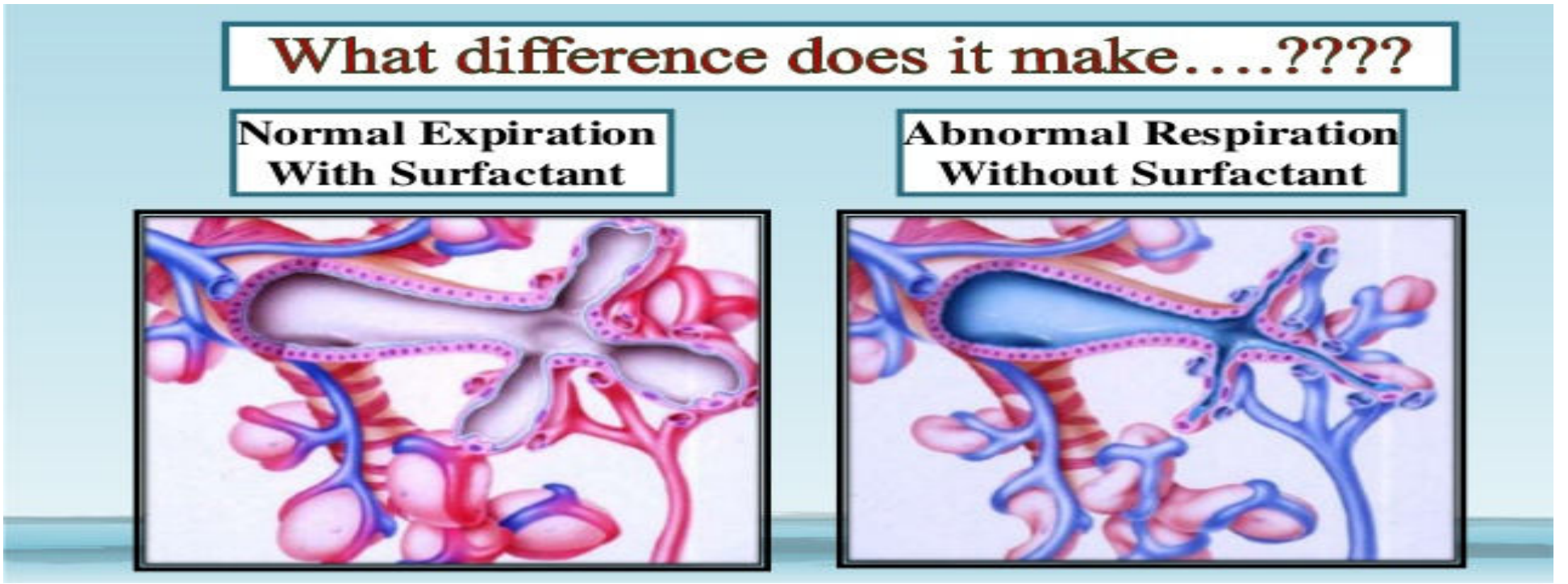


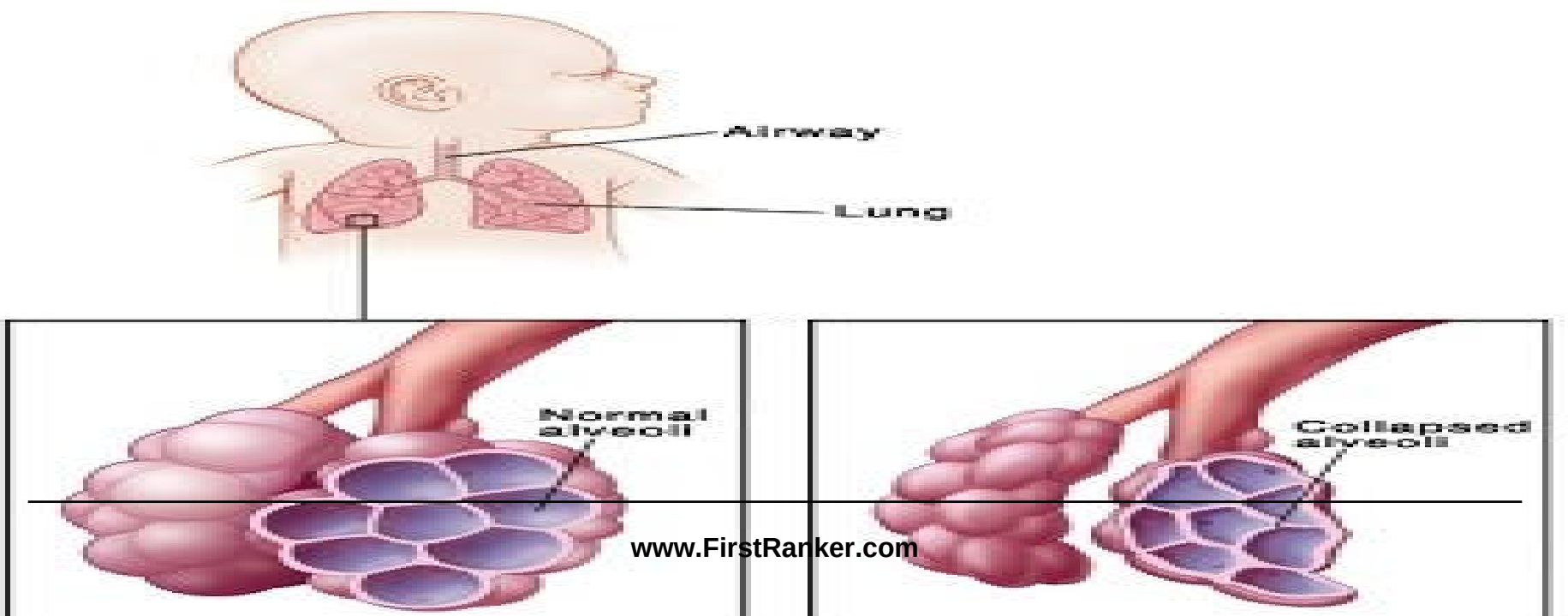
Disorders Related To Phospholipids

- **Respiratory Distress Syndrome (RDS)**

- Suffered by **premature born infants**.
- Caused due to **deficiency** of **Lung surfactant DiPalmitoyl Phosphatidyl Choline.**

- Since **Lung** is **last organ to mature**.
- **Premature babies** has **insufficient lung surfactant** lining in the alveoli walls.
- Which supports **no normal respiration.**
- Has respiration difficulties due to **alveolar collapse.**





- **Signs And Symptoms Of RDS**

- Low ATP production
- Weakness ,Lethargy
- Low Cellular Functions
- Poor Coordination

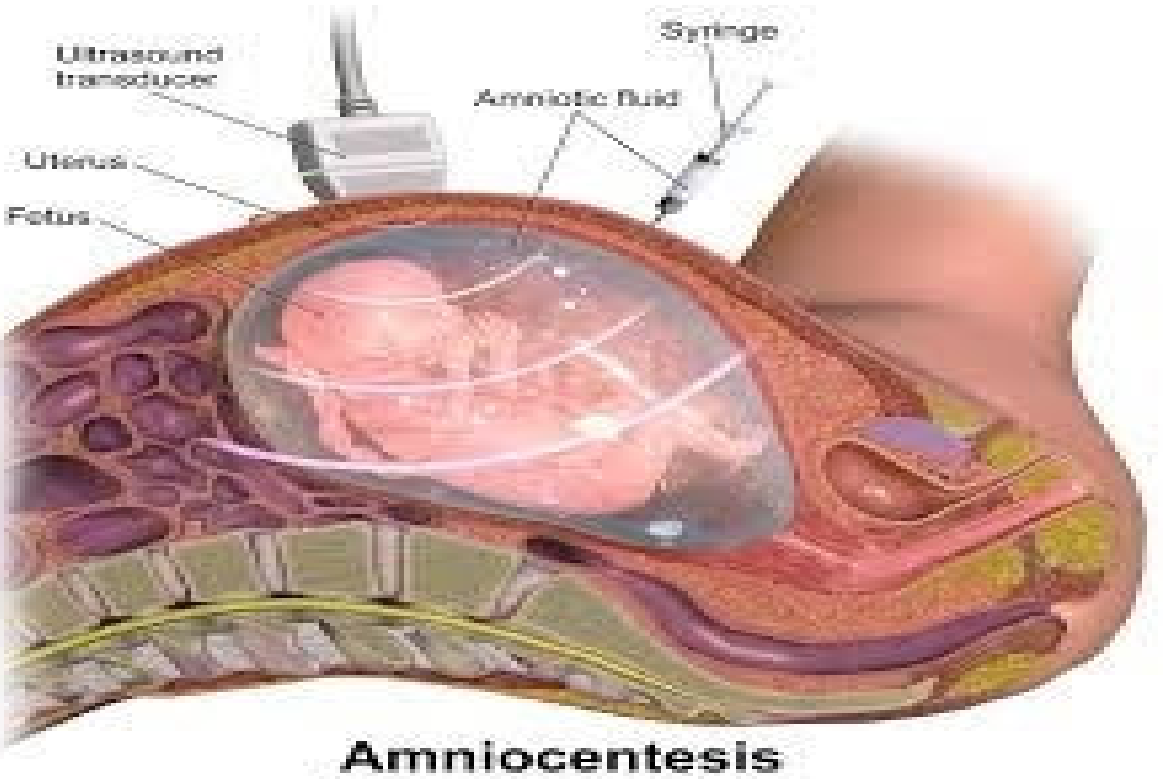
Lecithin/Sphingomyelin (L/S) Ratio of Amniotic Fluid

Assessment Of Fetal Lung Maturity

And

Diagnostic Criteria For RDS

- Lecithin /Sphingomyelin (L/S) ratio of **amniotic fluid, collected by Amniocentesis** is a good indicator to evaluate **fetal lung maturity.**



Amniocentesis

- **Prior to 34 weeks** of gestation the concentration of **Lecithin and Sphingomyelin** in amniotic fluid **is equal.**

- **In Later weeks of gestation the Lecithin levels are markedly increased.**

- **At full term** L/S ratio is **> 2/>5**

- **In pre term infants L/S ratio is 1.5 or < 1 results to suffer from RDS.**

OTHER RDS Sufferers

Individual with Lung Damage and Dysfunctions

- Old aged Persons
- Smokers
- Severely Infected Lungs
- Lungs toxicated and damaged by chemicals

- **Old** age **persons** and **Adults** with Lung damage

  (Due to Smoking/ Infections)

- Who **unable to biosynthesize the lung surfactant** may also **exhibit RDS.**

Lecithin-Sphingomyelin (L/S) Ratio

- Considered the reference method
- Lecithin is the primary component of the lung surfactants; increased production occurs after the 35th week
- Sphingomyelin is produced at a constant rate after the 26th week and serves as a control for the rise in lecithin
- L/S ratio is 1.6 prior to week 35 and rises to 2.0 or greater for alveolar stability after week 35
- Therefore, preterm delivery is considered safe with an L/S ratio of 2.0 or higher
- Test is performed using thin-layer chromatography
- Many laboratories have replaced the L/S ratio with the quantitative phosphatidyl glycerol immunoassays and lamellar body density procedures

Management of RDS:

A) General:

* Basic support including thermal regulation and parentral nutrition and medications (antibiotics).
* Oxygen administration, preferably heated and humidified

B) *Specific:*

Surfactant replacement therapy through ET tube.

Prevent And Manage RDS

- Pregnant Women **Diet** for biosynthesis of L and S
- Pregnant Women **Activities** and Positions
- Prevent Damaging **Environment** Exposures

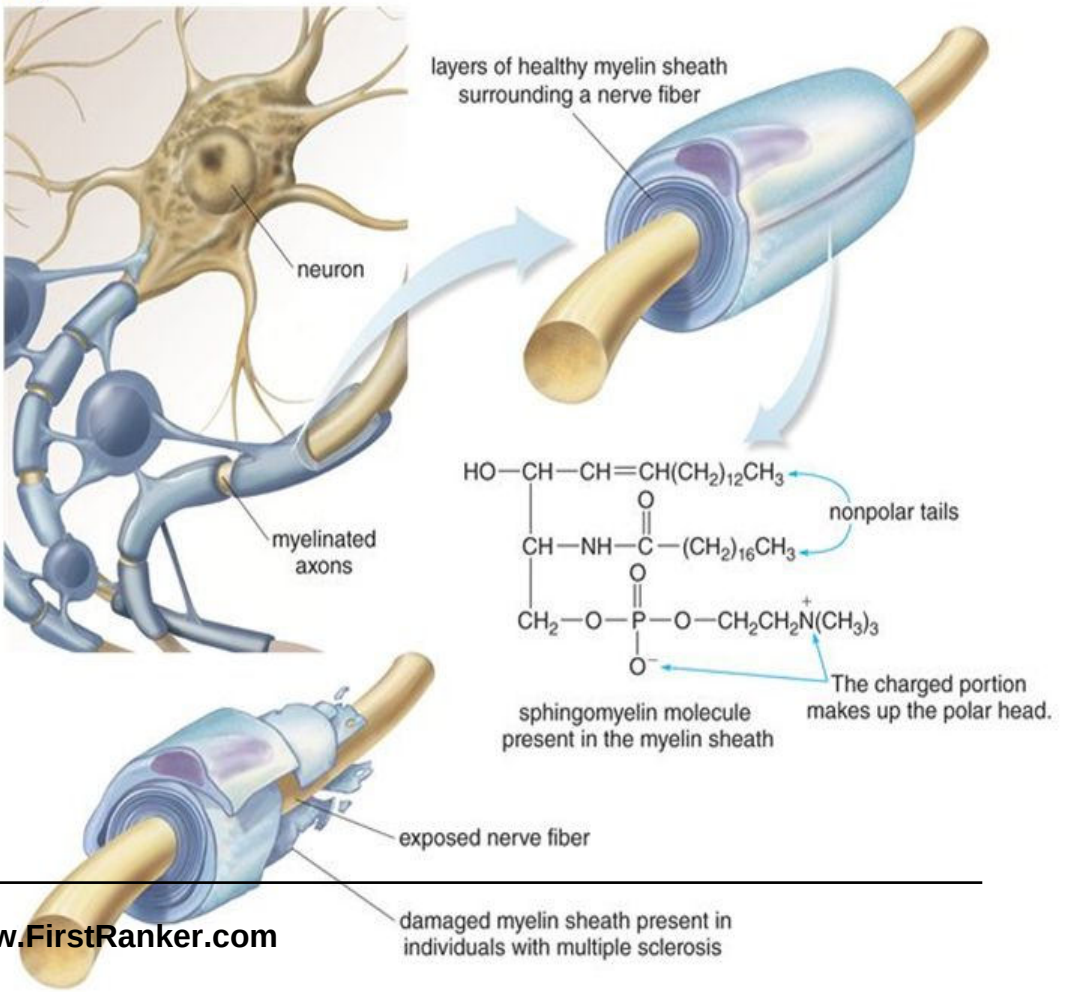
Membrane Related Disorders Due To Defective Phospholipds

Multiple Sclerosis Due to Defect In Sphingomyelins and Myelin Sheaths

Further modifications to the hydroxyl group, leads to a variety of other sphingolipids. One important example is sphingomyelin.

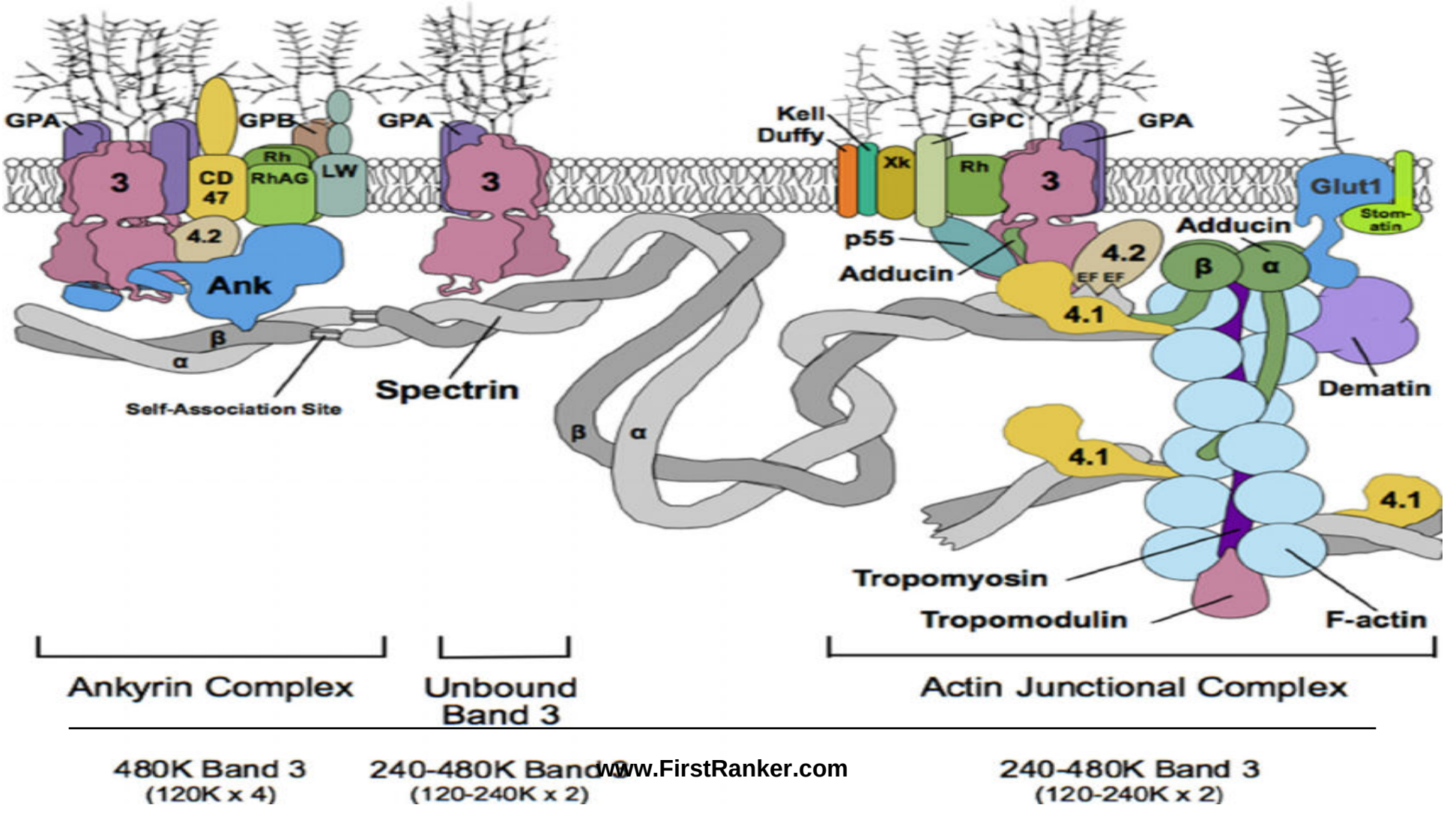
The coating that surrounds and insulates nerve cells, the **myelin sheath**, is particularly rich in sphingomyelins, and is vital for proper nerve function. Deterioration of the myelin sheath, as seen in multiple sclerosis, leads to disabling neurological disorders.

Multiple sclerosis (MS) is a degenerative disease characterized by scarring of the myelin sheath, the insulating layer that surrounds a nerve fiber. Without the protective myelin sheath, normal nerve transmission is disrupted and a variety of effects—numbness, blindness, speech disorders, and tremors—can result.

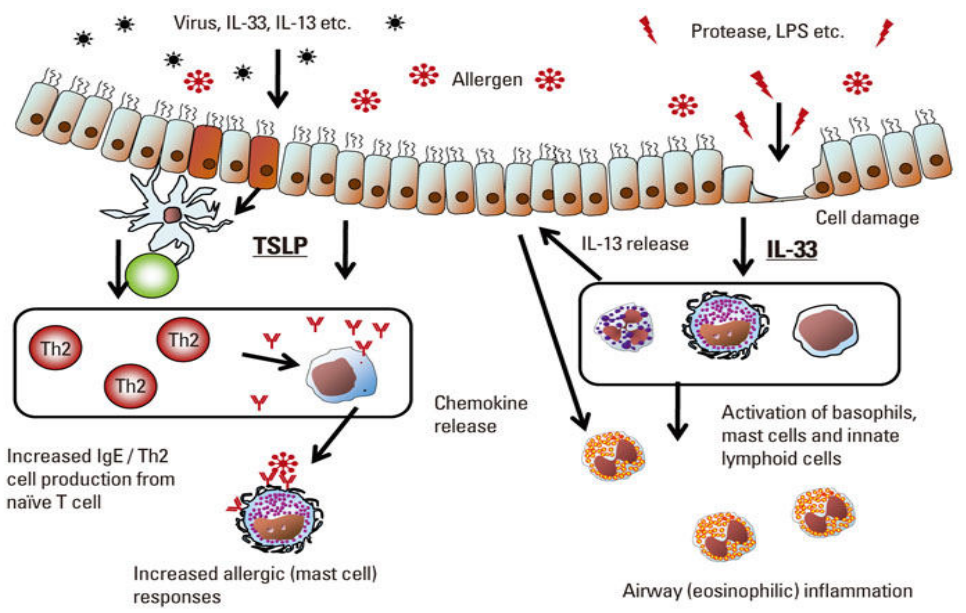


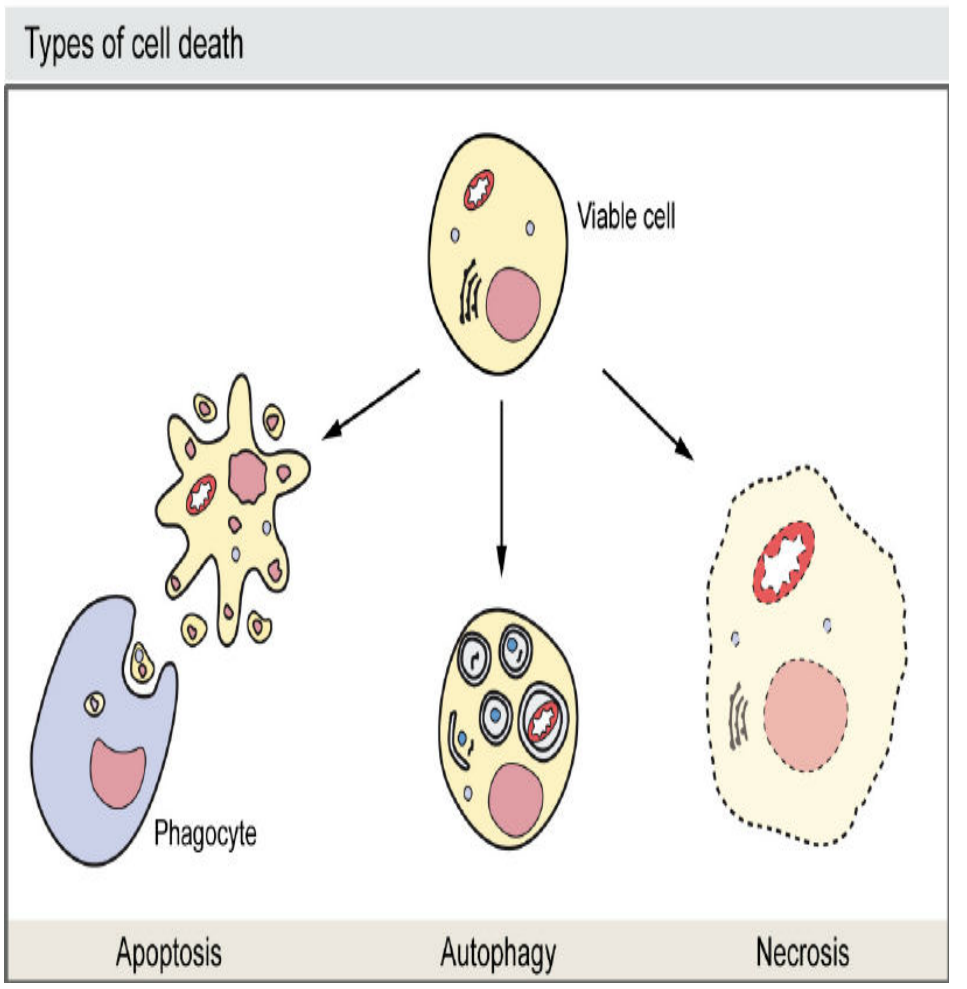
Defect In Sphingomyelins May Affect Nerve Impulse Conduction

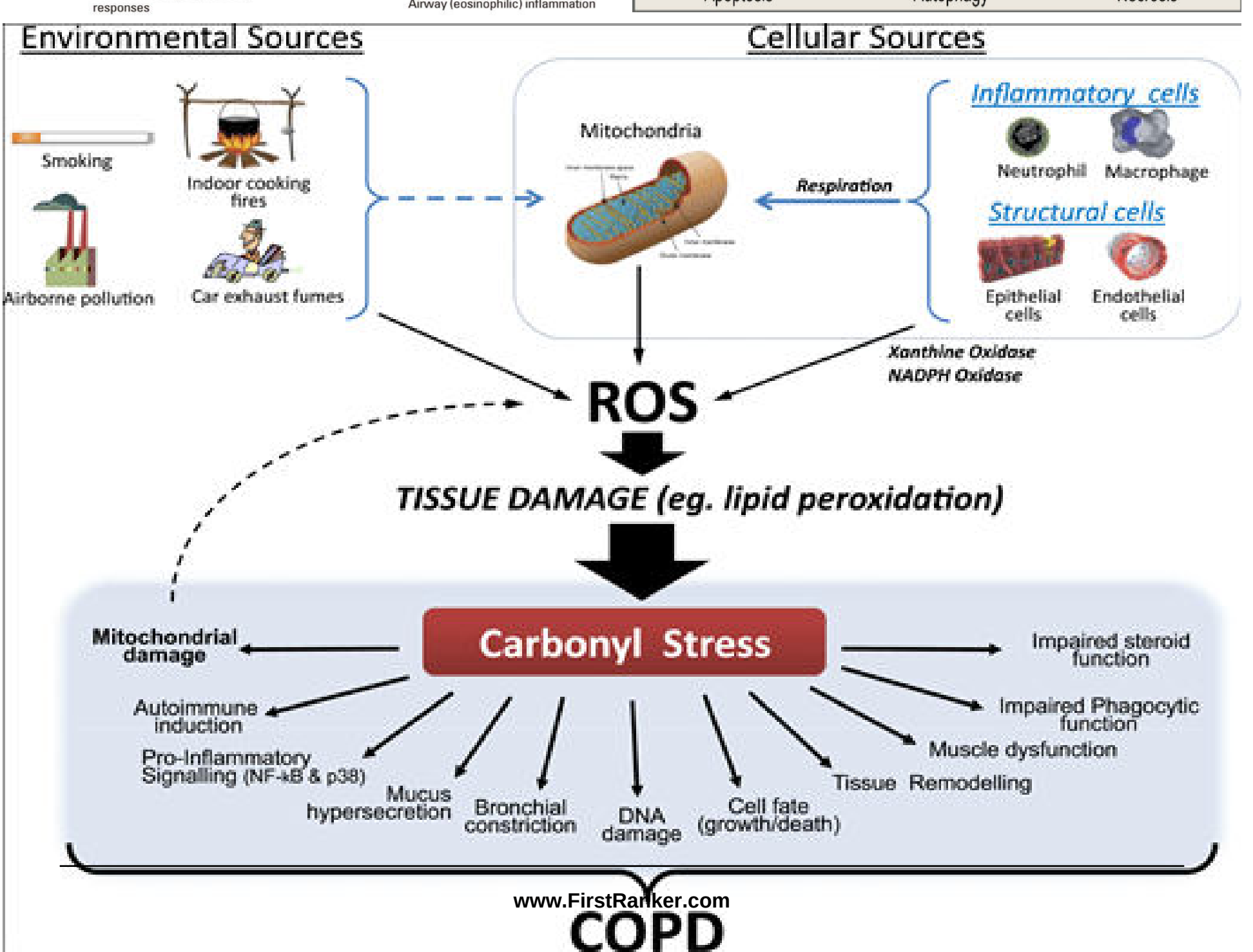
Membrane Carbs,Lipids and Proteins Structurally Important For Functional Role



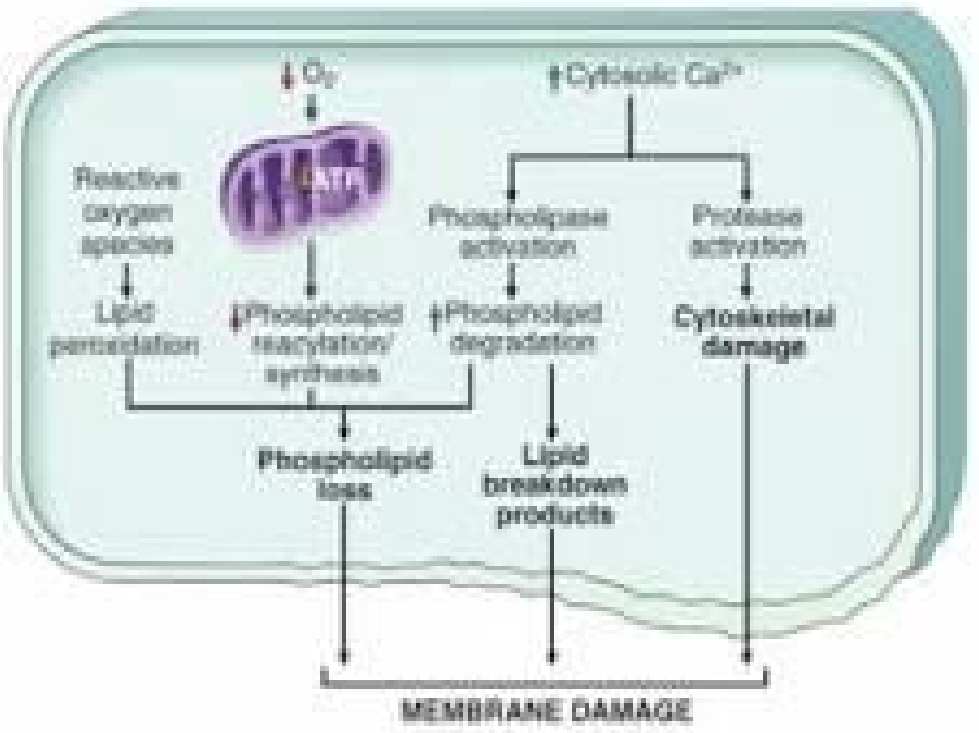
- Deranged Cellular Environment
- Cell membrane Damage
- Tissue Necrosis
- Cell Death







5. Defects in Membrane Permeability

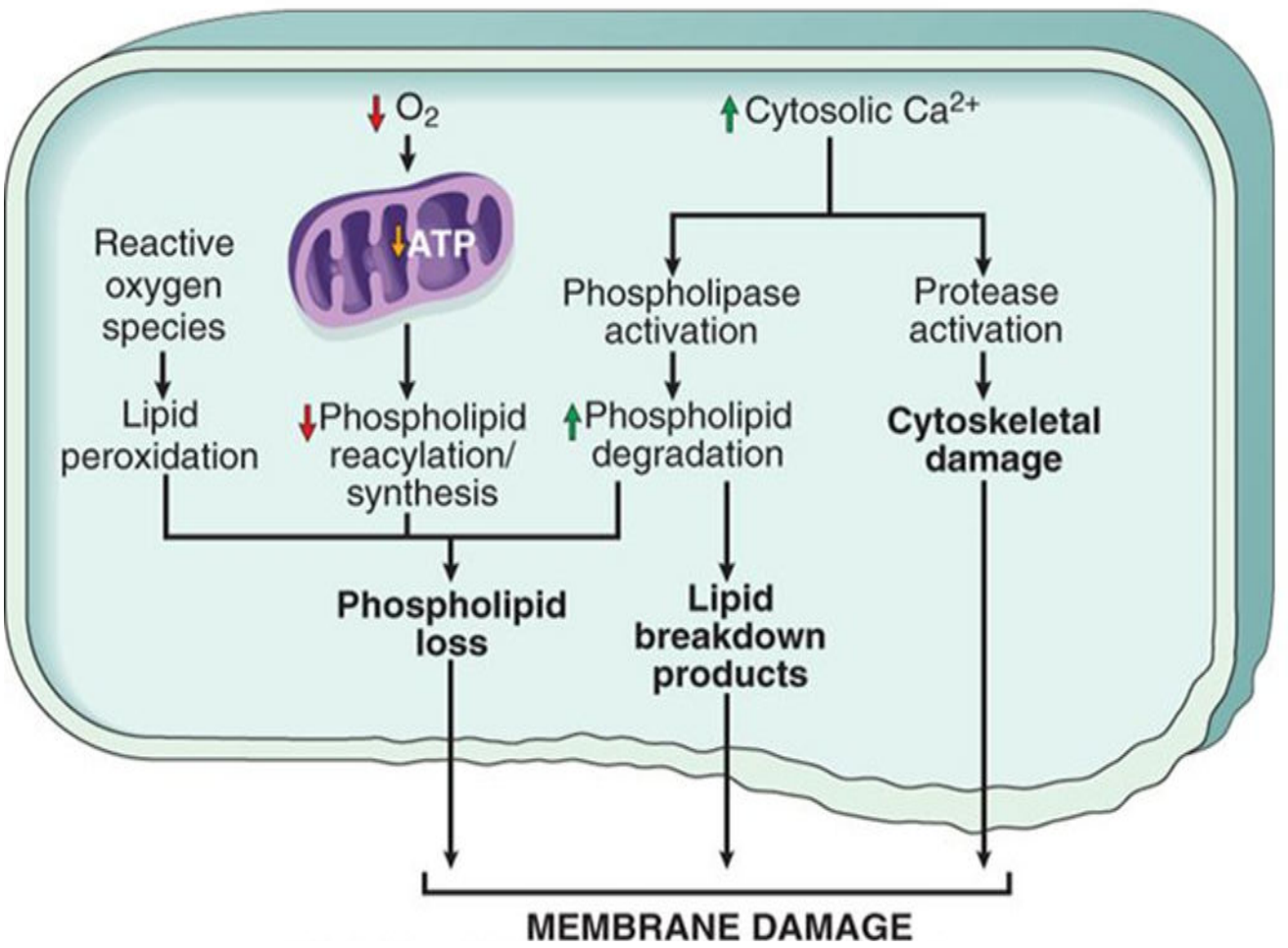


- The plasma membrane can be damaged by:
  - ischemia,
  - various microbial toxins,
  - lytic complement components,
  - physical and chemical agents.
- The most important sites of membrane damage during cell injury are:
  - *Mitochondrial membrane damage*
  - *Plasma membrane damage*
    - leads to loss of osmotic balance and influx of fluids and ions, as well as loss of cellular contents.
  - *Injury to lysosomal membranes*
    - leads to leakage of their enzymes into the cytoplasm and enzymatic digestion of cell components, necrosis

Mitochondrial Electron Transport Chain Defects
Due to Phospholipid Deficits

Membrane Damage

- ROS → lipid peroxidation
- ↓ phospholipid synthesis
- ↑ phospholipid degradation (Ca influx activates phospholipases)
- Cytoskeletal damage (Ca influx also activates proteases)

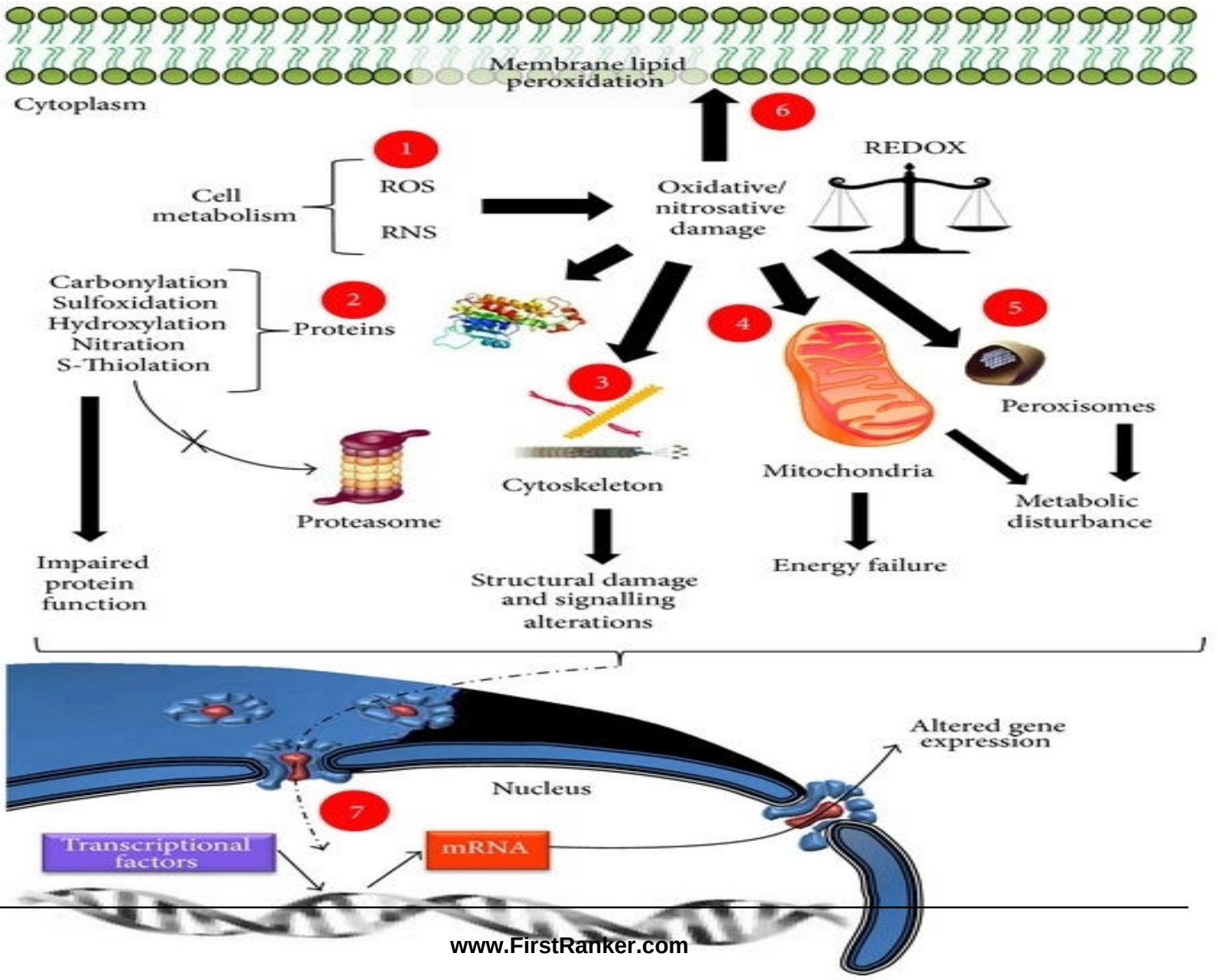


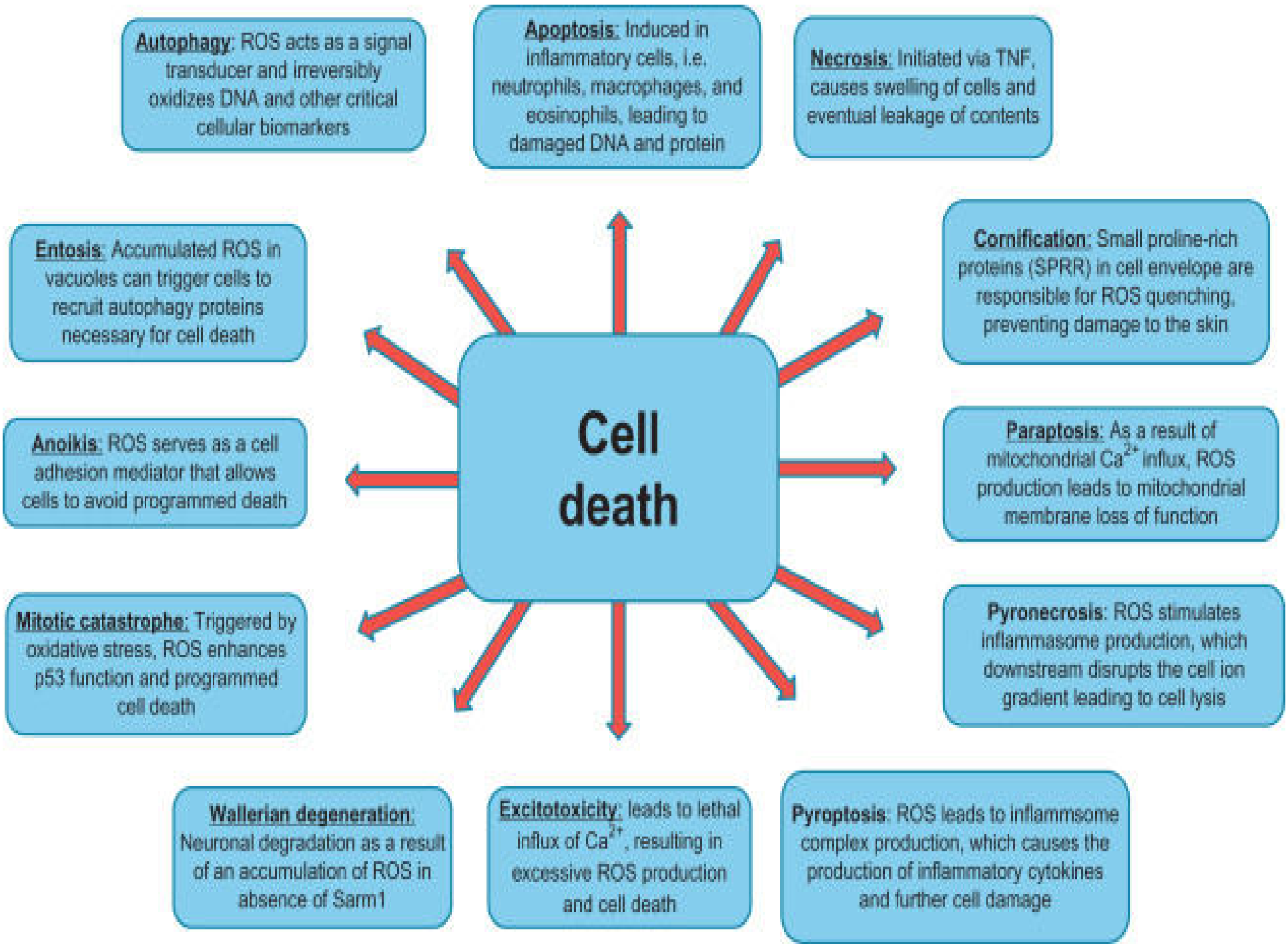
EFFECTS:

Mitochondrial membrane damage causes increased cytosolic Ca^{++}, oxidative stress, lipid peroxidation, phospholipase activity, loss of membrane potential, leakage of Cytochrome c

Plasma membrane damage causes loss of osmotic balance, loss of proteins, enzymes and nucleic acids.

Injury to lysosome membranes causes leakage of enzymes with destruction of cellular components.





Fatty Liver
Due to Phospholipid Defects