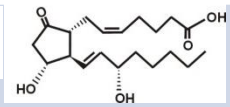
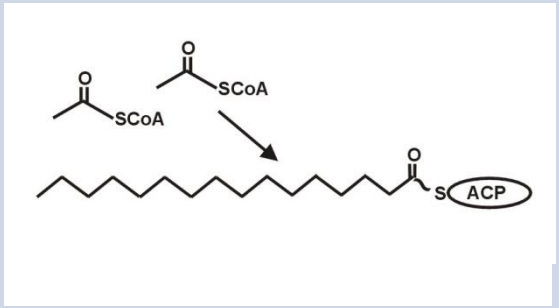
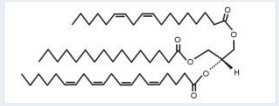
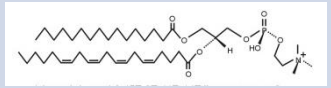
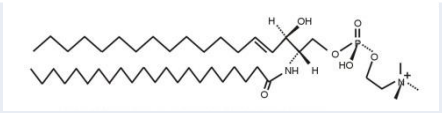
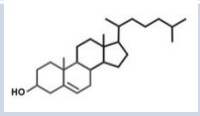
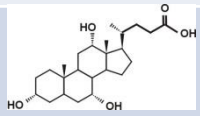
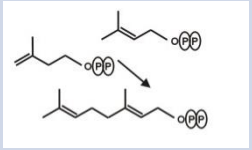
# LIPIDS

## Introduction
## - complex lipids

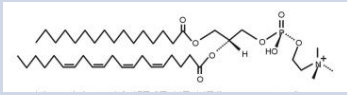
*Marek Vecka*

# CLASSIFICATION OF LIPIDS IV

## - biosynthetic route

| Lipid class | Biosynthetic route |
|---|---|
| Fatty acyls   | condensation of thioesters  |
| Glycerolipids  | |
| Glycerophospholipids  | |
| Sphingolipids  | |
| Sterol lipids   | condensation of activated isoprene units  |
| Prenol lipids  | |
| Other – saccharolipids, polyketides | other types |

# CLASSIFICATION OF LIPIDS

| Lipid class | Abbreviation |
|---|---|
| Fatty acyls | **FA** |
| Glycerolipids | **GL** |
| Glycerophospholipids  | **GP** |
| Sphingolipids | **SP** |
| Sterol lipids | **ST** |
| Prenol lipids | **PL** |
| Other – saccharolipids, polyketides | **SL, PK** |

# GLYCEROPHOSPHOLIPIDS

***esters of glycerol with fatty acids; 3C of glycerol – bound (P)***

**Glycerophospholipids = esters of glycerol with FA**
**+ 3rdC of glycerol has bound phosphoric acid residue**

Phosphoric acid residue
often esterified with groups with -OH

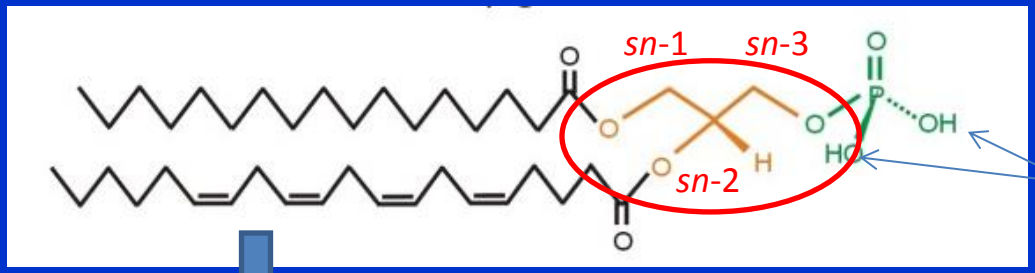
**1. Amphipathic**
**2. Complex = FA, glycerol, group with -OH**

# GLYCEROPHOSPHOLIPIDS

***esters of glycerol with fatty acids; 3C of glycerol – bound (P)***

**Glycerophospholipids are derived from Phosphatidic acid**

- FAs on *sn*-1,2 positions of glycerol backbone
- on *sn*-3 position is phosphoric acid




usually charged/polar

hydrophobic part of the molecule

hydrophilic part of the molecule

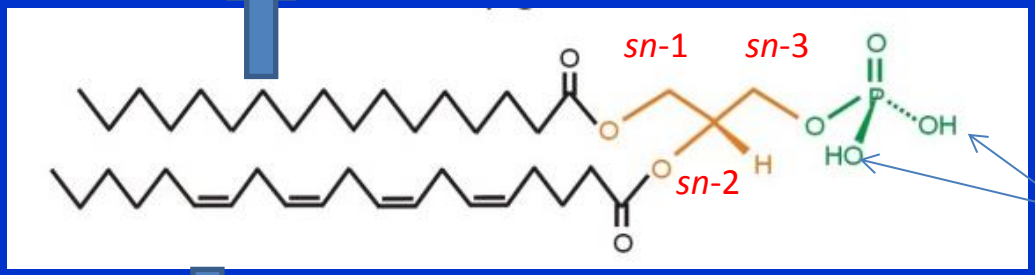
# GLYCEROPHOSPHOLIPIDS

***esters of glycerol with fatty acids; 3C of glycerol – bound P***

## Phosphatidic acid

- FAs on *sn*-1,2 positions of glycerol backbone
- on *sn*-3 position is phosphoric acid

usually saturated FA




usually unsaturated FA

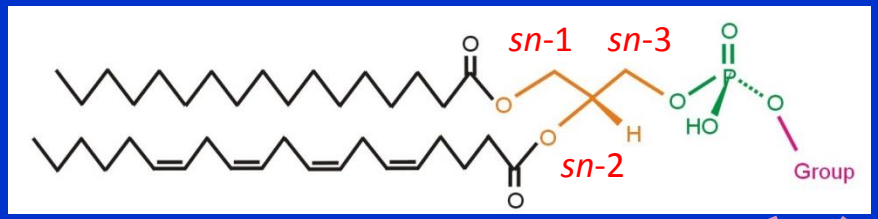
can be esterified with group cont. –OH group

**various classes of glycerophospholipids**

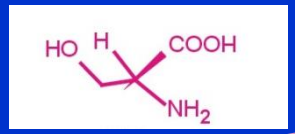
# GLYCEROPHOSPHOLIPIDS

***esters of glycerol with fatty acids; 3C of glycerol – bound P***

The type of Group determines PL class:

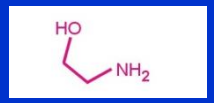



+ serine



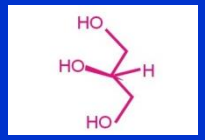

phosphatidylserines (PS)

+ ethanolamine



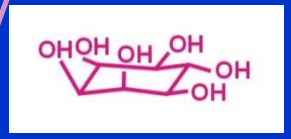

phosphatidylethanolamines (PE)

+ glycerol



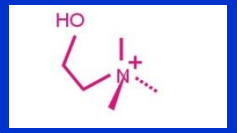

phosphatidylglycerols (PG)

+ inositol




phosphatidylinositols (PI)

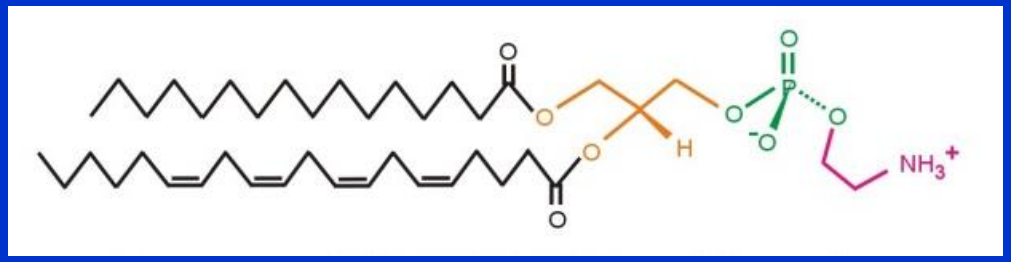
+ choline



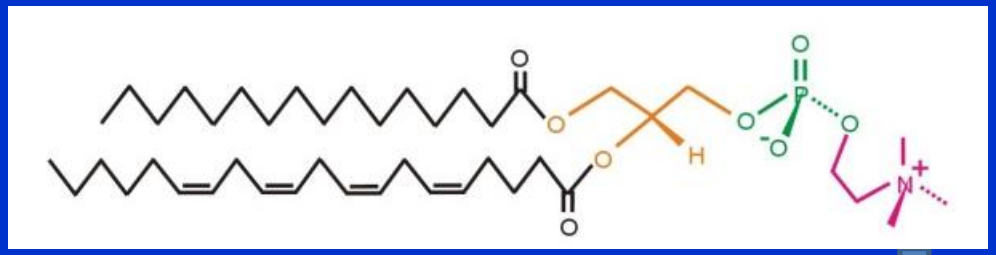

phosphatidylcholines (PE)

# GLYCEROPHOSPHOLIPIDS

***phosphatidylethanolamines and phosphatidylcholines***




**phosphatidylethanolamines (PE)**

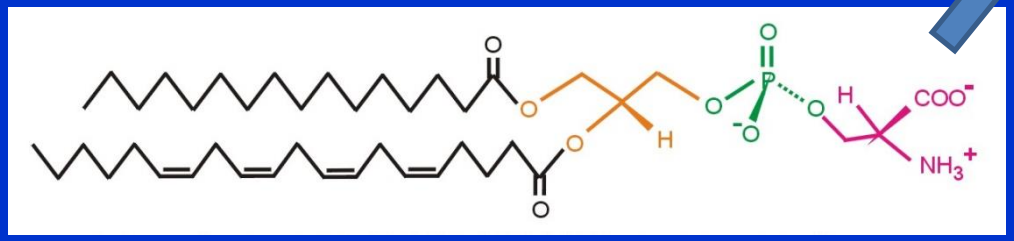


**phosphatidylcholines (PC)**

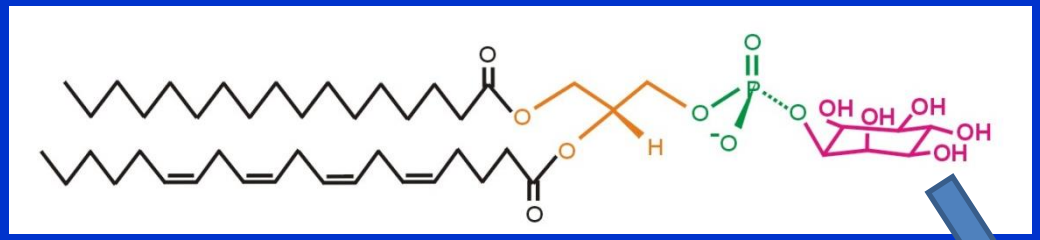
basic group

# GLYCEROPHOSPHOLIPIDS

acidic group

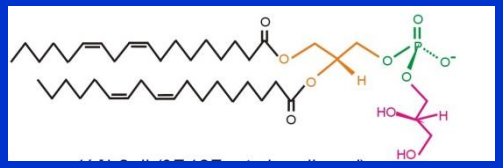



**phosphatidylserines (PS)**




**phosphatidylinositols (PI)**

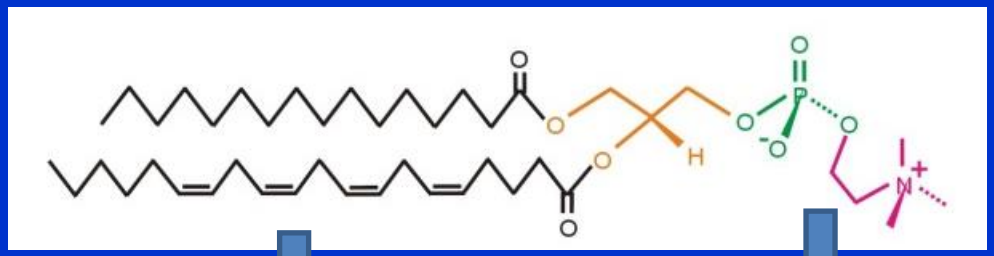
polarity group




**phosphatidylglycerols (PG)**

# GLYCEROPHOSPHOLIPIDS

***properties of GP***



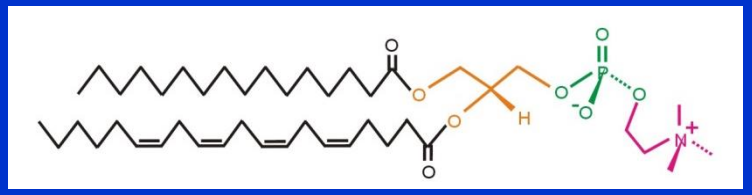
hydrophobic part of the molecule

hydrophilic part of the molecule

- amphipathic $\rightarrow$ used in membranes, as emulgators/tensids ( $\downarrow$surface tension)
- their components can take part in signalling cascades

# GLYCEROPHOSPHOLIPIDS

***phosphatidylcholines***



**Occurence**

- mainly in the outer leaflet of cell membranes
- in bile (emulgator), lipoproteins (stabilization of the structure)

choline can be used for acetylcholine synthesis
PC in signalization cascades

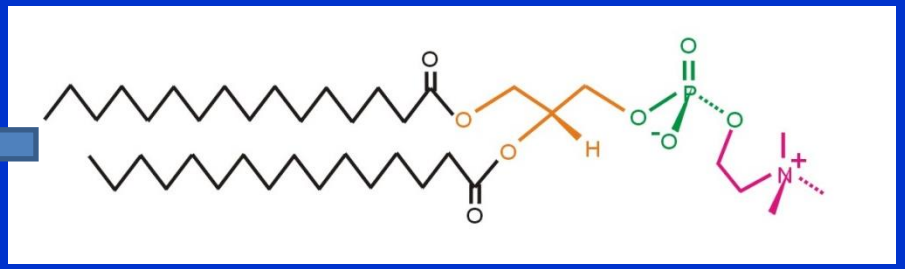
# GLYCEROPHOSPHOLIPIDS

***phosphatidylcholines of pulmonary surfactant***

**dipalmitoylPC**

- important part of pulmonary surfactant

both FA chains
are saturated



- the surfactant prevents the alveoli from collapsing (lowers surface tension)

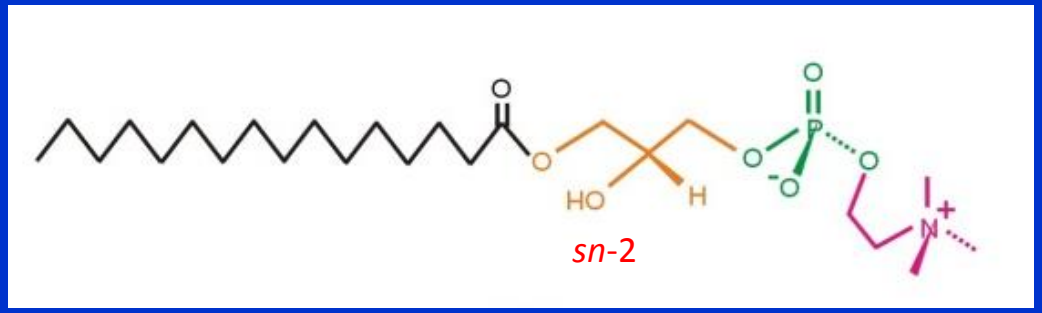
# GLYCEROPHOSPHOLIPIDS

## *lysophosphatidylcholines*

**Occurence**

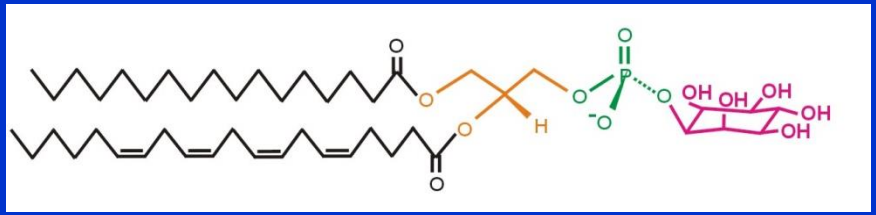
- products of hydrolysis of PC on sn-2 position (by LCAT, $PLA_2$)
- in snake venom

LPC also takes part in signalization cascades



# GLYCEROPHOSPHOLIPIDS

***phosphatidylinositols***



## Occurence

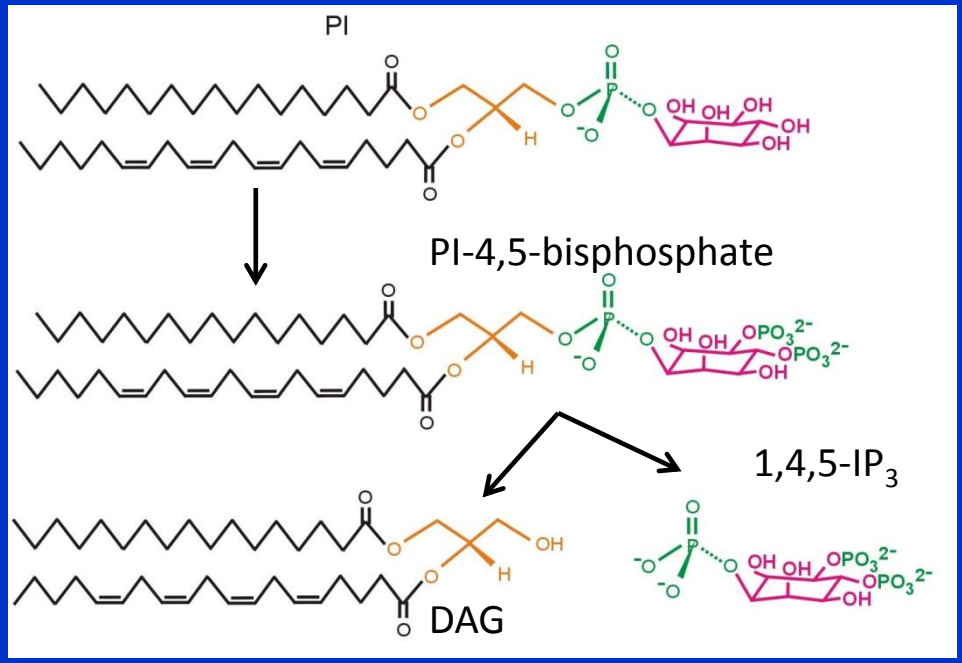
- mainly in the inner leaflet of cell membranes

## I. PI in signalization cascades

a) PI is doubly phosphorylated to form
PI-4,5-bisphosphate

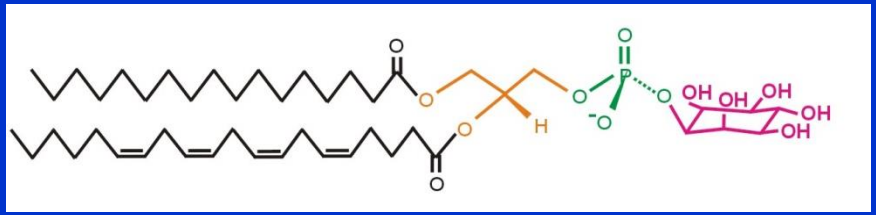
b) PI-4,5-bisphosphate is then hydrolyzed by phospholipase C to second messengers:

1. DAG
   **via PKC stimulates protein phosphorylation**
2. inositol-1,4,5-trisphosphate
   **releases $Ca^{2+}$ from intracelullar depots**



# GLYCEROPHOSPHOLIPIDS

***phosphatidylinositols***



**Occurence**

- mainly in the inner leaflet of cell membranes

**II. PI anchor**

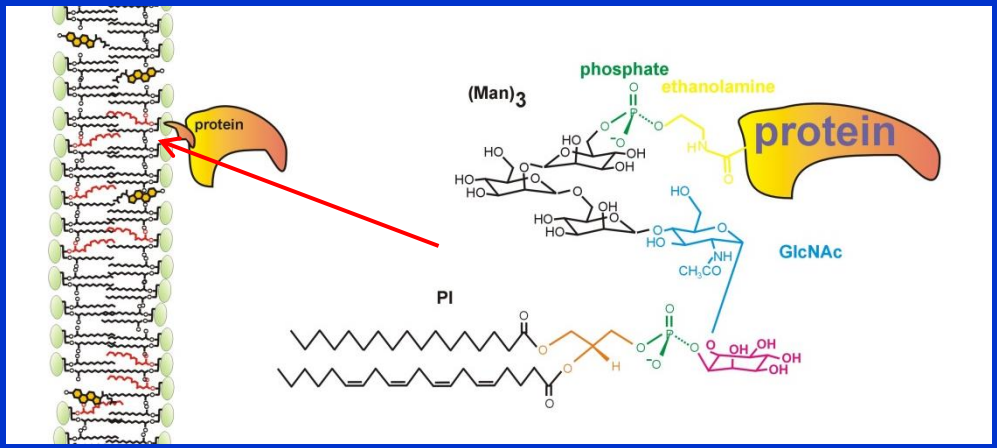
GPI-anchored proteins – on outer face;

bonded via short oligosaccharide to glycophosphatidylinositol (GPI)

various receptors

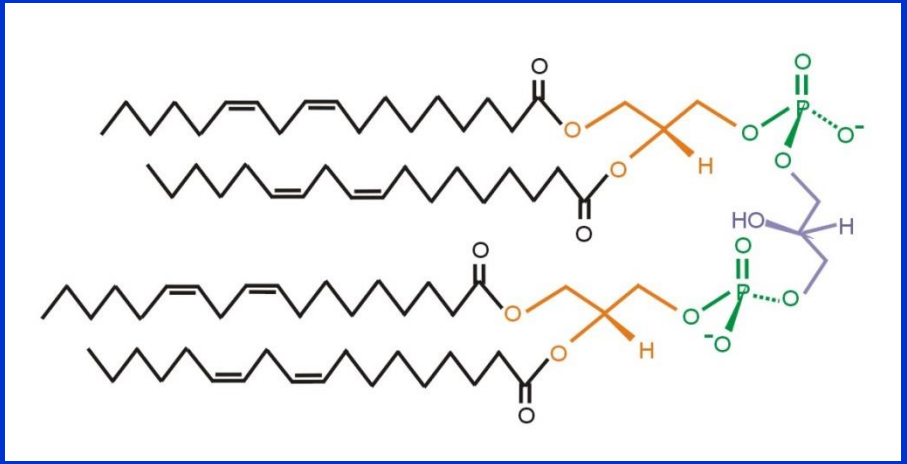
enzymes

adhesive proteins



# GLYCEROPHOSPHOLIPIDS

***Diphosphatidylglycerols (cardiolipins)***



**Occurence**

- mainly in the inner leaflet of mitochondrias

**Functions**

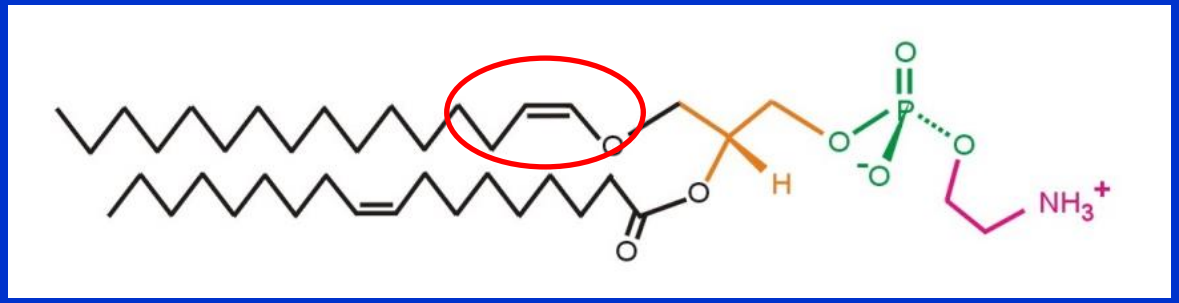
- in mitochondria, it can take part in $H^+$ transfer
- diagnostics of syphilis (in *Treponema pallidum* membranes)

Antiphospholipid syndrome

- Ab against DPG produced $\rightarrow$ recurrent thrombosis, recurrent abortions

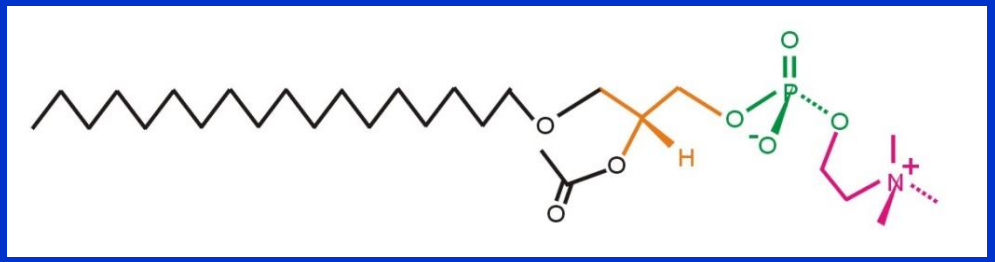
# GLYCEROPHOSPHOLIPIDS

***plasmalogens***




**Occurence**

- mainly in brain and heart
- up 10% of membrane PL

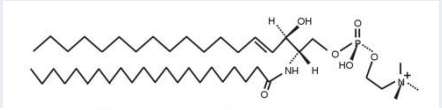



Platelet activating factor - PAF

= 1-alkyl-2-acetylphosphocholine

- activates polymorphonuclear leukocytes and thrombocytes

# CLASSIFICATION OF LIPIDS

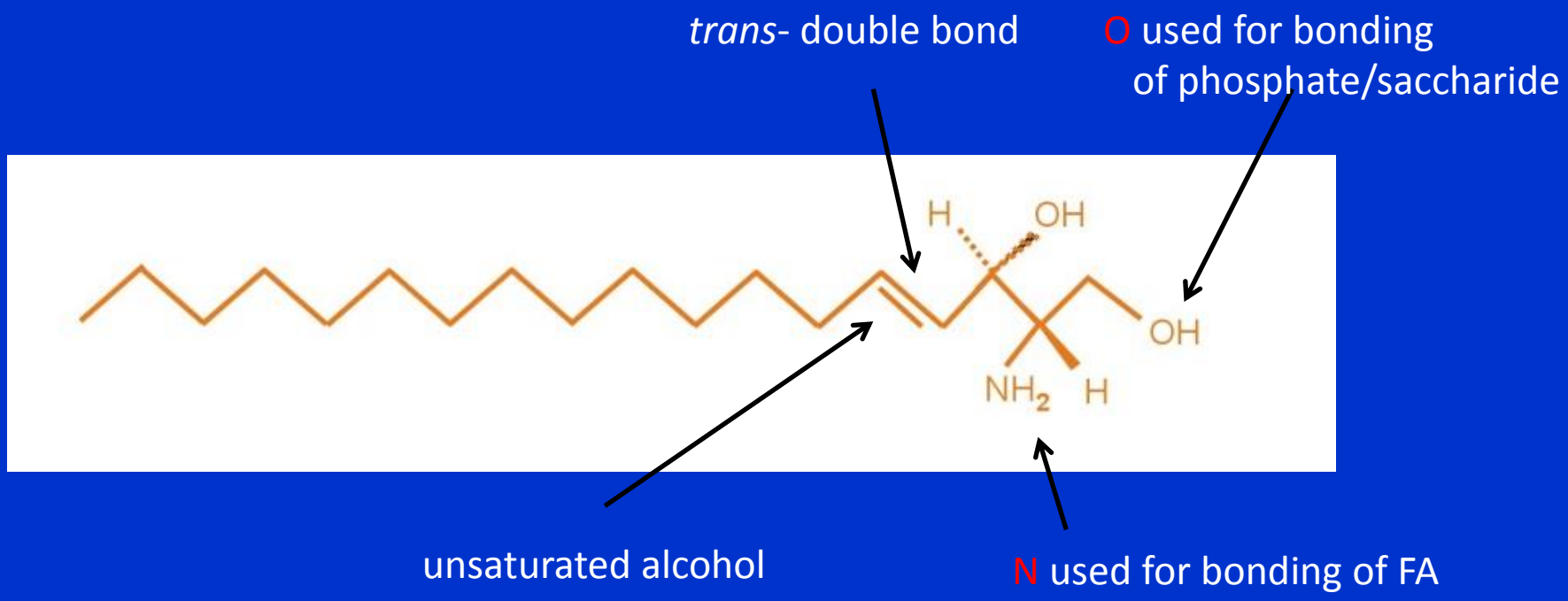
| Lipid class | Abbreviation |
|---|---|
| Fatty acyls | **FA** |
| Glycerolipids | **GL** |
| Glycerophospholipids | **GP** |
| Sphingolipids  | **SP** |
| Sterol lipids | **ST** |
| Prenol lipids | **PL** |
| Other – saccharolipids, polyketides | **SL, PK** |

# SPHINGOLIPIDS

***lipids with sphingosine backbone***

**sphingosine**

- (*E*)-2-aminooctadec-4-en-1,3-diol



# SPHINGOLIPIDS

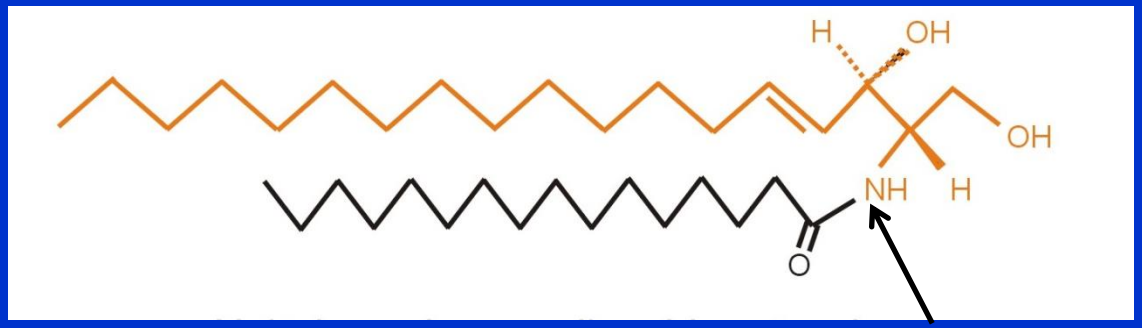
***ceramides***

**sphingosine**

- *N*-acylsphingosines (sphingenine + FA)
- intermediates in biosynthesis of sphingolipids

**biological function**

1. apoptosis (oxidative stress transducers)
2. stratum corneum in skin: prevent water losses and toxic compounds permeation




N used for bonding of FAs – VLCFA, hydroxyFA

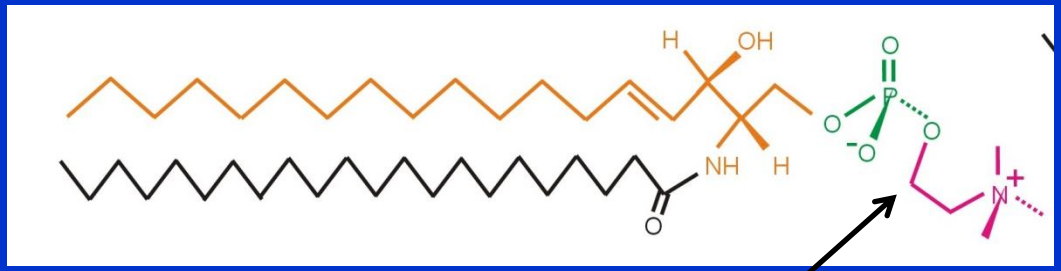
# SPHINGOLIPIDS

***sphingomyelines***

- *N*-(1-acyl)-sphing-4-enine-1-phosphocholines
  (ceramide + **phosphoric acid** + **choline**)
- intermediates in biosynthesis of sphingolipids

**biological function**

1. signalling cascades
2. components of plasma membranes: myeline sheaths




**phosphoric acid** and **choline**

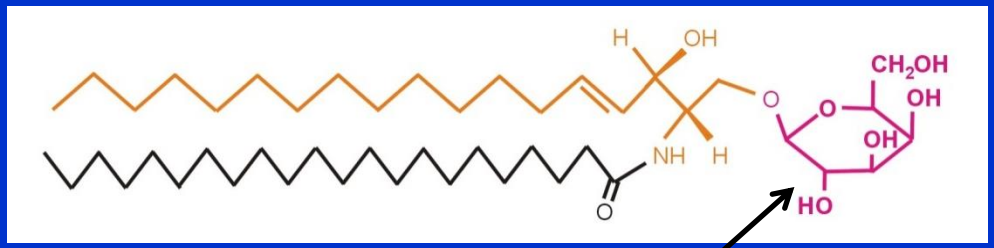
# SPHINGOLIPIDS

***glycosphingolipids***

- ceramide + **saccharide part** (no phosphoric acid)
- many types according to the saccharide:

**monosaccharide: glucose, galactose**
**oligosaccharides: lactose,**
**N-acetylated hexosamines**
**N-acetylneuraminic acid**

galacto cerebrosides




**saccharide moiety (e.g. galactose)**

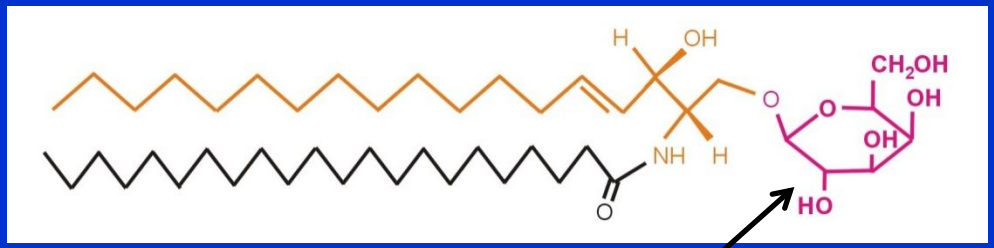
# SPHINGOLIPIDS

***glycosphingolipids***

**Cerebrosides**

- monosaccharide ceramides
- *O*-glycosidic bond
- mainly in brain (galactocerebrosides)

galactocerebrosides




**saccharide moiety (e.g. galactose)**

# SPHINGOLIPIDS

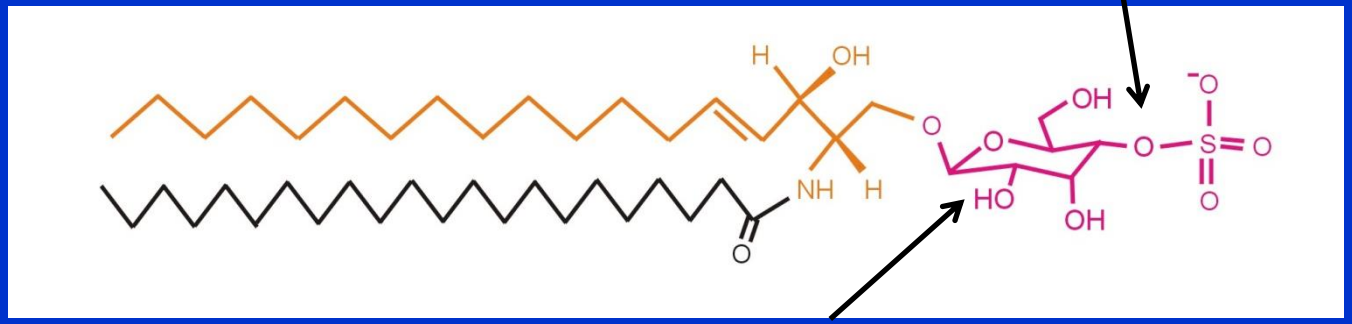
***glycosphingolipids***

**sulfatides**

- monosaccharide ceramides with sulfogroup (on C3 of the saccharide)
- *O*-glycosidic bond as in the cerebrosides

**sulphated saccharide**

sulfatide



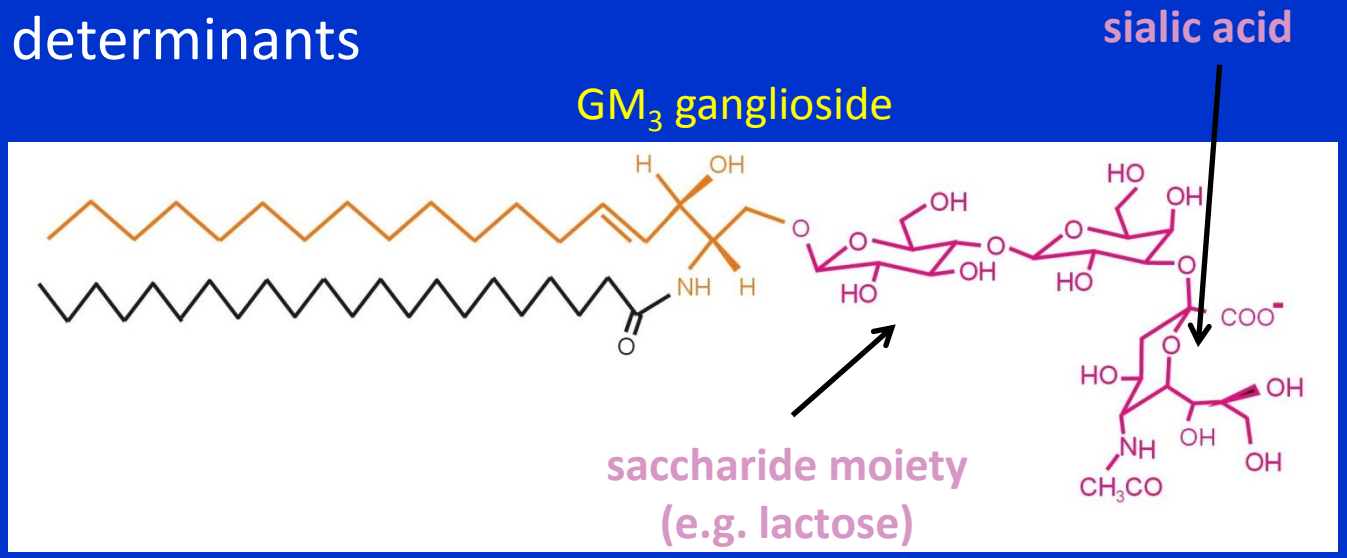

**saccharide moiety (e.g. galactose)**

# SPHINGOLIPIDS

***glycosphingolipids***

**gangliosides**

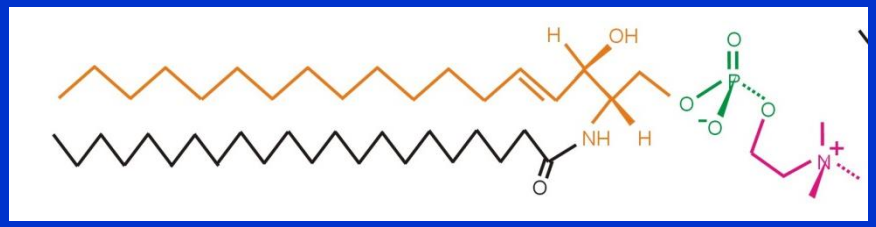
- contain apart from saccharides also the derivatives of sialic acid (*N*-acetylneuraminic acid)
- neuronal tissue rich in gangliosides, content is tissue specific
- responsible for blood group specificity in erythrocytes
- many antigenic determinants



# SPHINGOLIPIDS

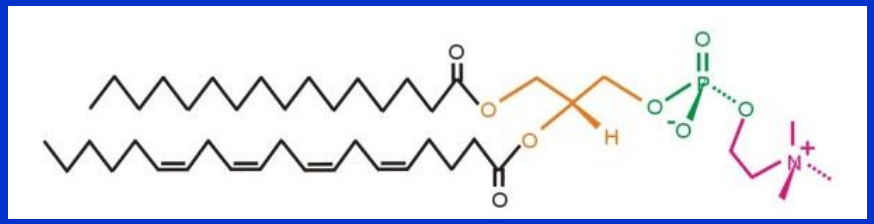
***similarity to glycophospholipids***

**sphingomyelines**

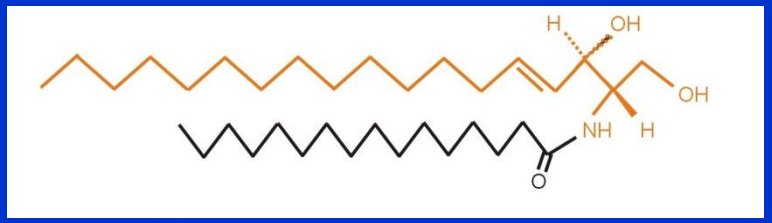



**vs.**

**phosphatidylcholines**

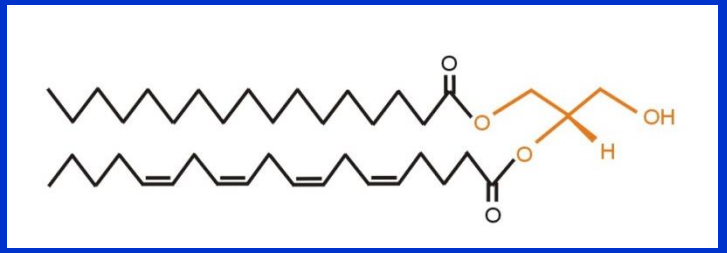



**ceramides**




**vs.**

**diacylglycerols**



## Further reading

### Textbooks, monographs

*Biochemistry of Lipids, Lipoproteins and Membranes (5th Ed)*; Vance DE, Vance Je (Eds.), Elsevier, Amsterodam (The Netherlands) 2008

*Lehninger Principles of Biochemistry (6th Ed);* Nelson DL, Cox MM (Eds.), Susan Winslow, New York (U.S.A.) 2013

*Harper´s Illustrated Biochemistry (28th Ed);* Murray RK, Bender DA, Botham KM, Kennely PJ, Rodwell VW, Weil PA (Eds.), McGraw-Hill, New York (U.S.A.) 2009

### Articles

Fahy E, Subramaniam S, Brown HA, Glass CK, Merrill Jr. AH, Murphy RC, Raetz CRH, Russell DW, Seyama Y, Shaw W, Shimizu T, Spener F, van Meer G,Van Nieuwenhze MS, White SH, Witztum JL, Dennis EA: A comprehensive classification system for lipids. *J Lipid Res* 2005; **46**: 839–861.

Fahy E, Subramaniam S, Murphy RC, Nishijima M, Raetz CHR, Shimizu T,Spener F, van Meer G, Wakelam MJO, Dennis EA: Update of the LIPID MAPS comprehensive classification system for lipids. *J Lipid Res* 2009; **50**: S9–S14.

### Web sources

http://www.cyberlipid.org
http://lipidlibrary.aocs.org
http://www.lipidmaps.org
http://www.chem.qmul.ac.uk/iupac - IUPAC Nomenclature page
http://themedicalbiochemistrypage.org - the Medical Biochemistry Page