Welcome to BC2 lesson 7

Chimie Biologique II

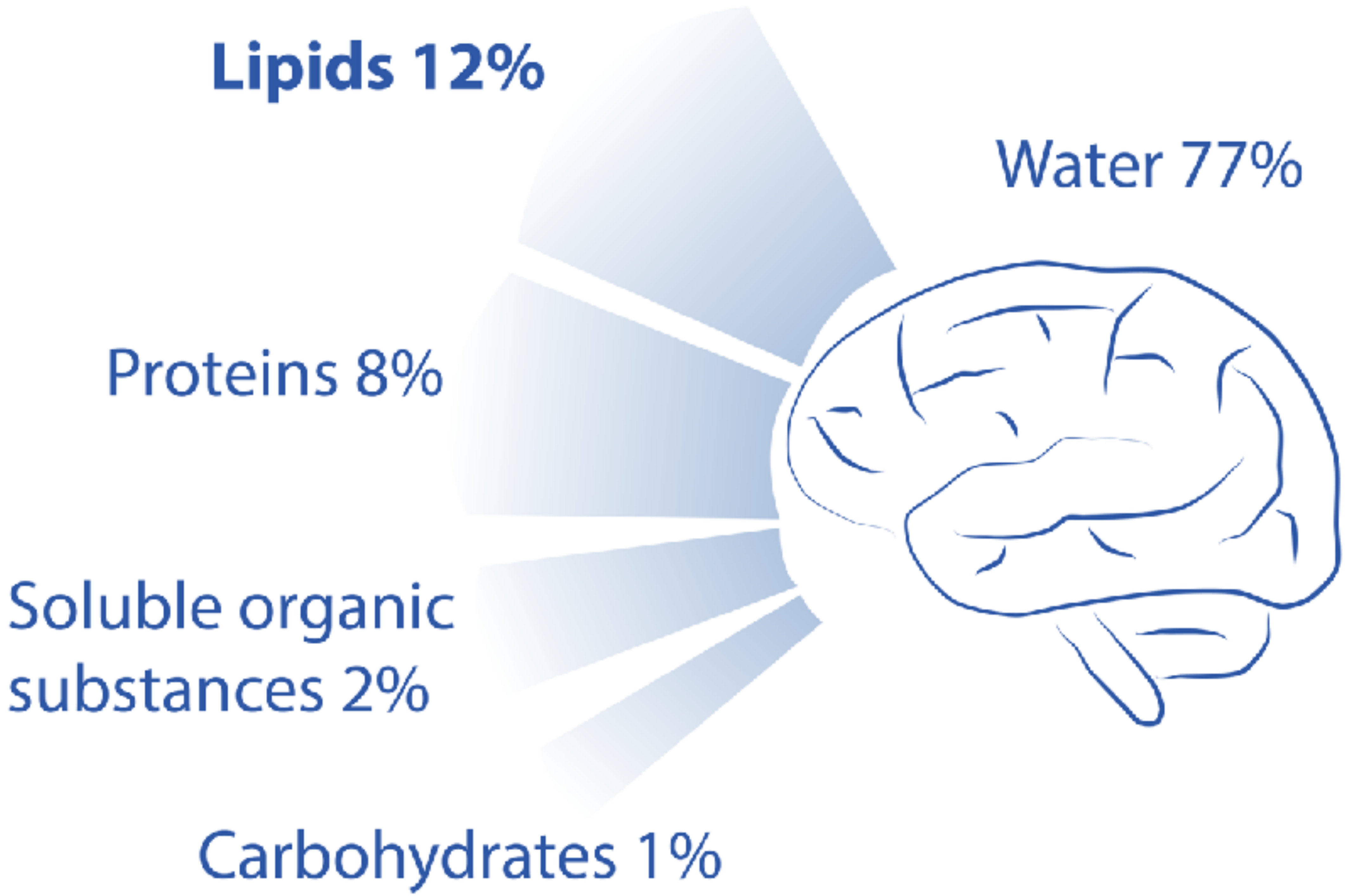
Biological Chemistry II

BIO-213

Teacher

Giovanni D’Angelo, IBI

LIPIDS



H McIlwain & H S Bachelard, Churchill Livingstone (1985), ISBN: 0-443-01961-4

What is a lipid?

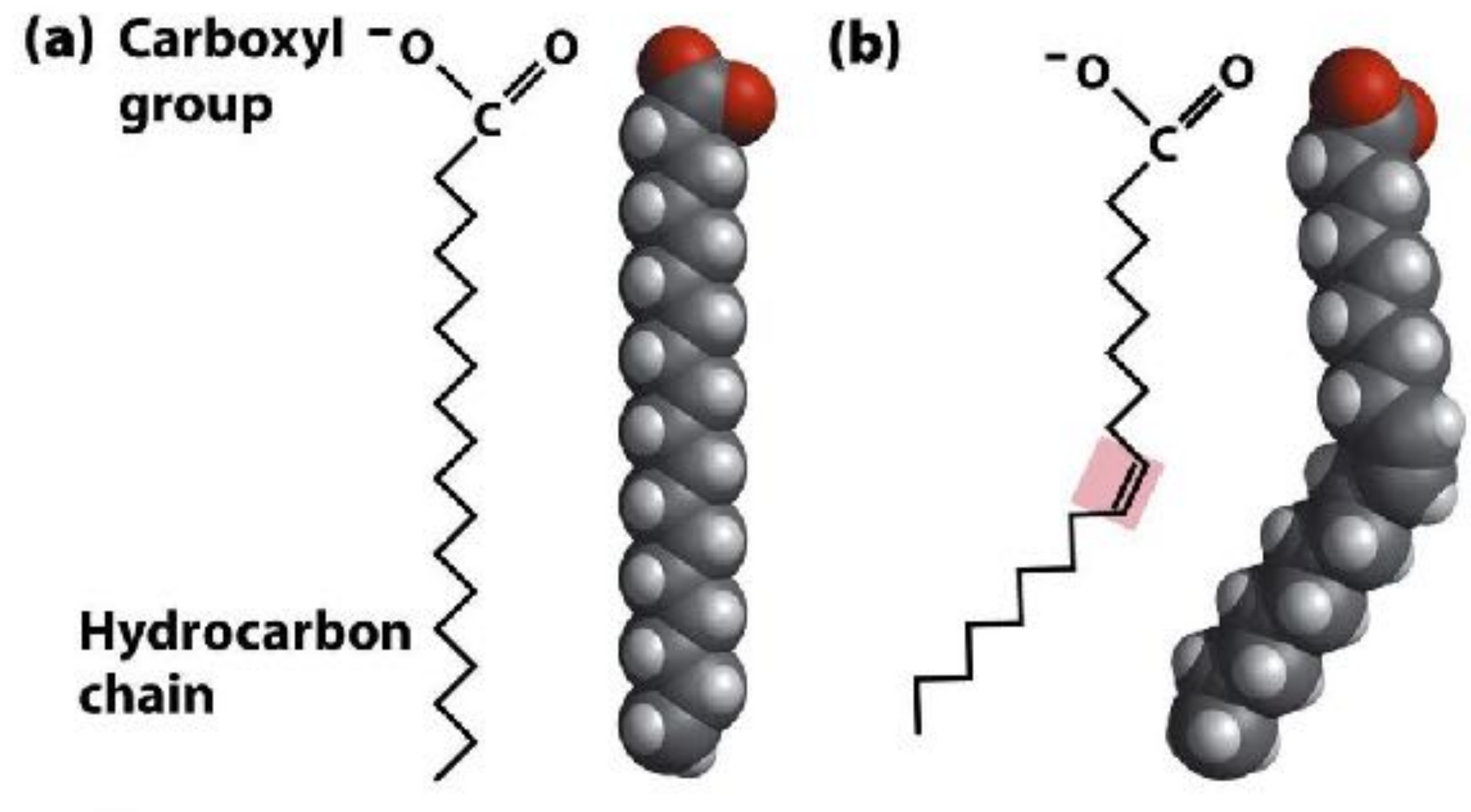
In biology and biochemistry, a **lipid** is a biomolecule that is soluble in non-polar solvents and does not readily dissolve in water.

Three Classes of Lipids Based on Their Functions:

- **Storage lipids:** Used for bioenergetic purposes and thermal insulation.
- **Structural lipids:** Used to make membranes.
- **Bioactive lipids:** Used as hormones and second messengers in signal transduction.

FATTY ACIDS

Naturally occurring monocarboxylic acids



Components of all lipids except sterols

"**Saturated** -> no double bonds."
"**Unsaturated** -> one double bond."
"**Polyunsaturated** (PUFAs) -> more double bonds."

FATTY ACIDS

TABLE 10–1 Some Naturally Occurring Fatty Acids: Structure, Properties, and Nomenclature

Carbon skeleton	Structure*	Systematic name†	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (mg/g solvent)	
					Water	Benzene
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus*, "laurel plant")	44.2	0.063	2,600
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica*, nutmeg genus)	53.9	0.024	874
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma*, "palm tree")	63.1	0.0083	348
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, "hard fat")	69.6	0.0034	124
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis*, legume genus)	76.5		
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum*, "wood" + *cera*, "wax")	86.0		

*All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

†The prefix *n*- indicates the "normal" unbranched structure. For instance, "dodecanoic" simply indicates 12 carbon atoms, which could be arranged in a variety of branched forms; "*n*-dodecanoic" specifies the linear, unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated; in biological fatty acids the configuration is almost always cis.

FATTY ACIDS

TABLE 10–1 Some Naturally Occurring Fatty Acids: Structure, Properties, and Nomenclature

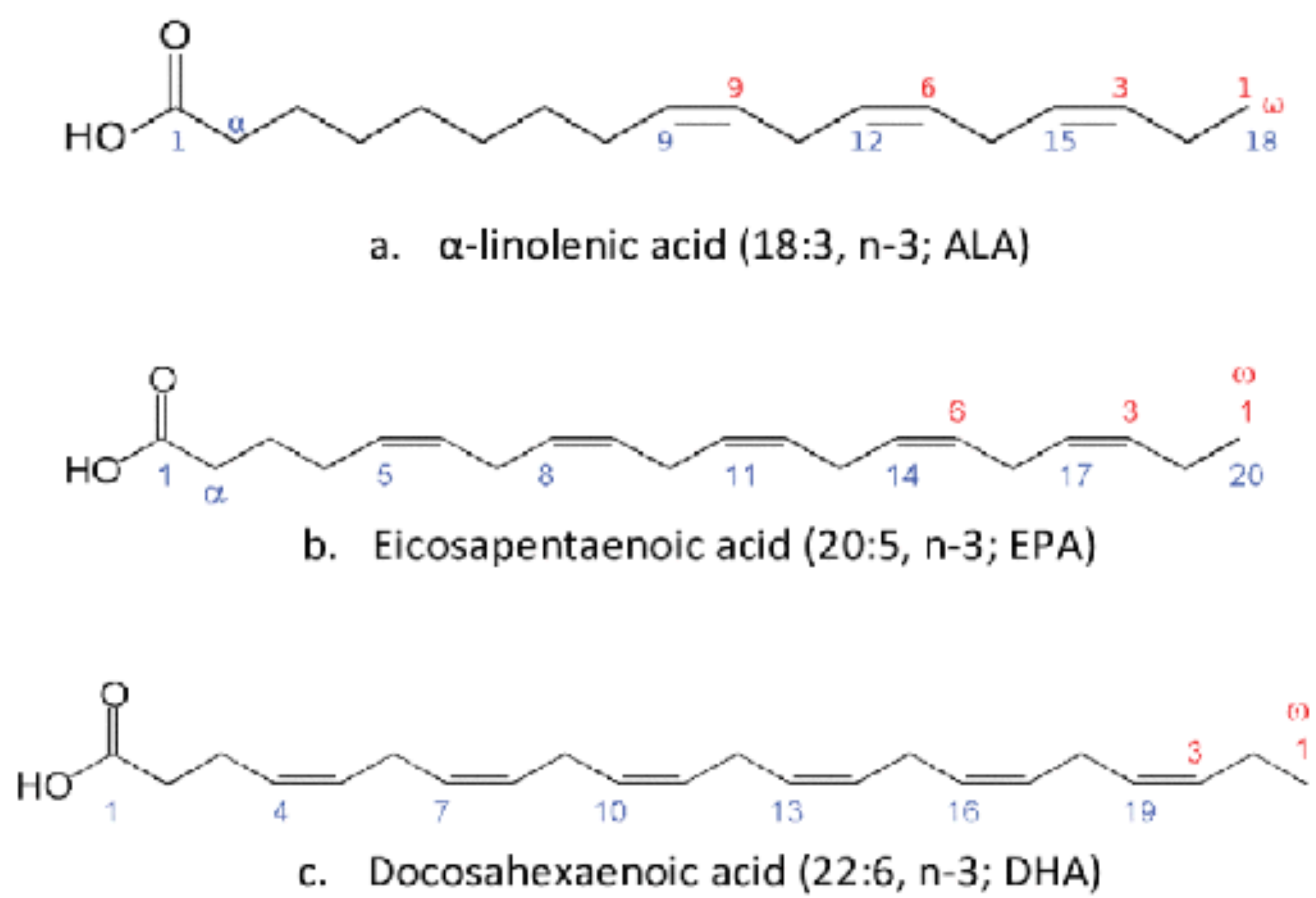
Carbon skeleton	Structure*	Systematic name†	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (mg/g solvent)	
					Water	Benzene
16:1(Δ^9)	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid	1 to –0.5		
18:1(Δ^9)	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum*, "oil")	13.4		
18:2($\Delta^{9,12}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon*, "flax")	1–5		
18:3($\Delta^{9,12,15}$)	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid	–11		
20:4($\Delta^{5,8,11,14}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid	–49.5		

*All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

†The prefix *n*- indicates the "normal" unbranched structure. For instance, "dodecanoic" simply indicates 12 carbon atoms, which could be arranged in a variety of branched forms; "*n*-dodecanoic" specifies the linear, unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated; in biological fatty acids the configuration is almost always cis.

FATTY ACIDS

Alpha-linolenic acid is the precursor of the Ω-3 fatty acids eicosapentaenoic acid (EPA; 20:5($\Delta^{5,8,11,14,17}$)) and docosahexaenoic acid (DHA; 22:6($\Delta^{4,7,10,13,16,19}$)), which are important fatty acids found in membranes of the retina, for example. Ω-3 fatty acids are important components of a heart-healthy diet.



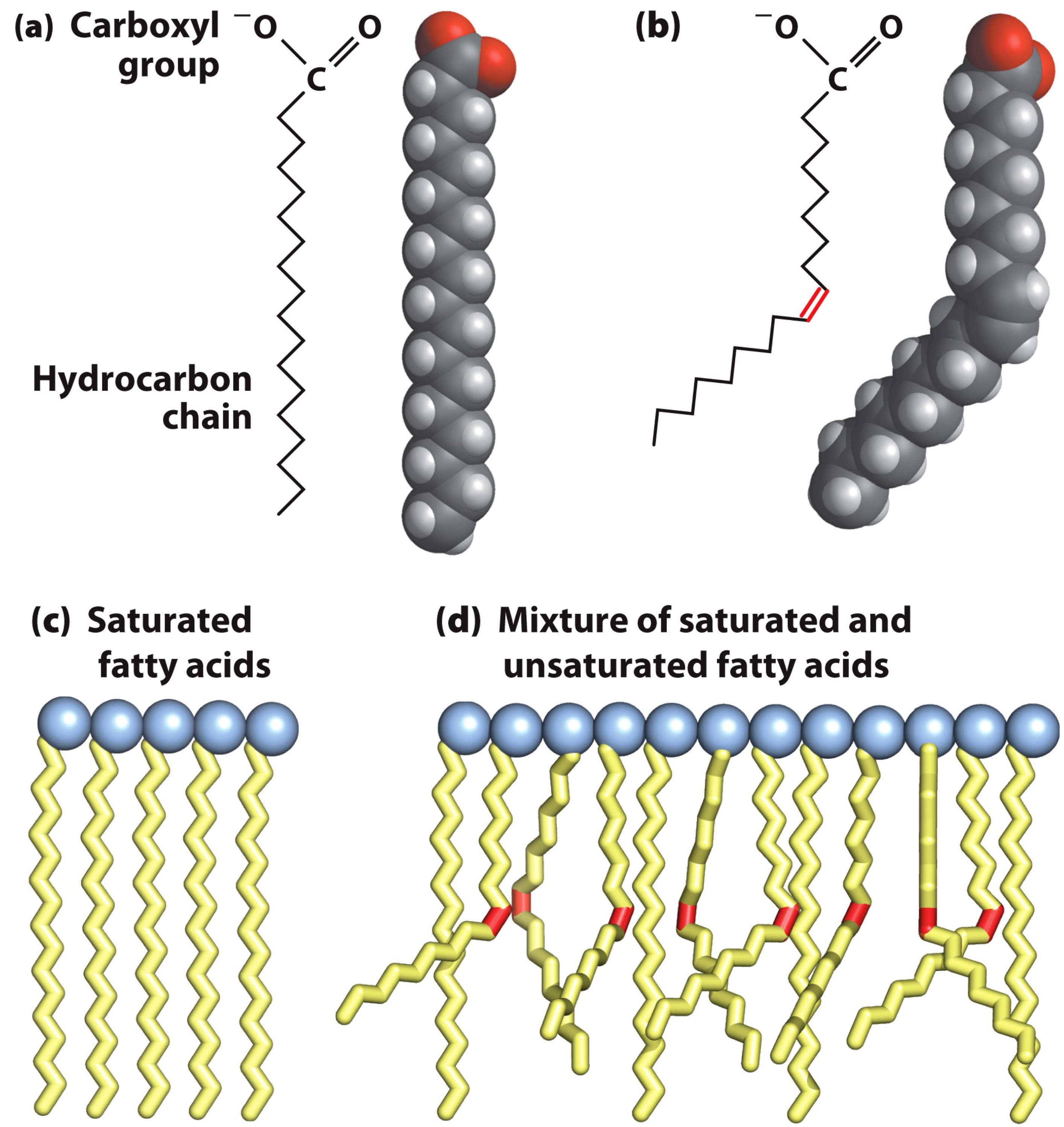
Δ and Ω nomenclatures

FATTY ACIDS

The hydrocarbon chain accounts for the poor solubility of fatty acids in water. Solubility **decreases** as the **fatty acid chain lengthens** and the number of **double bonds decreases**.

Lauric acid (12:0) [Mw = 200] has a solubility of 0.063 mg/g in water. In contrast, glucose [Mw = 180] is much more water-soluble, with a solubility of 1100 mg/g in water (approximately 17,000 times more water-soluble).

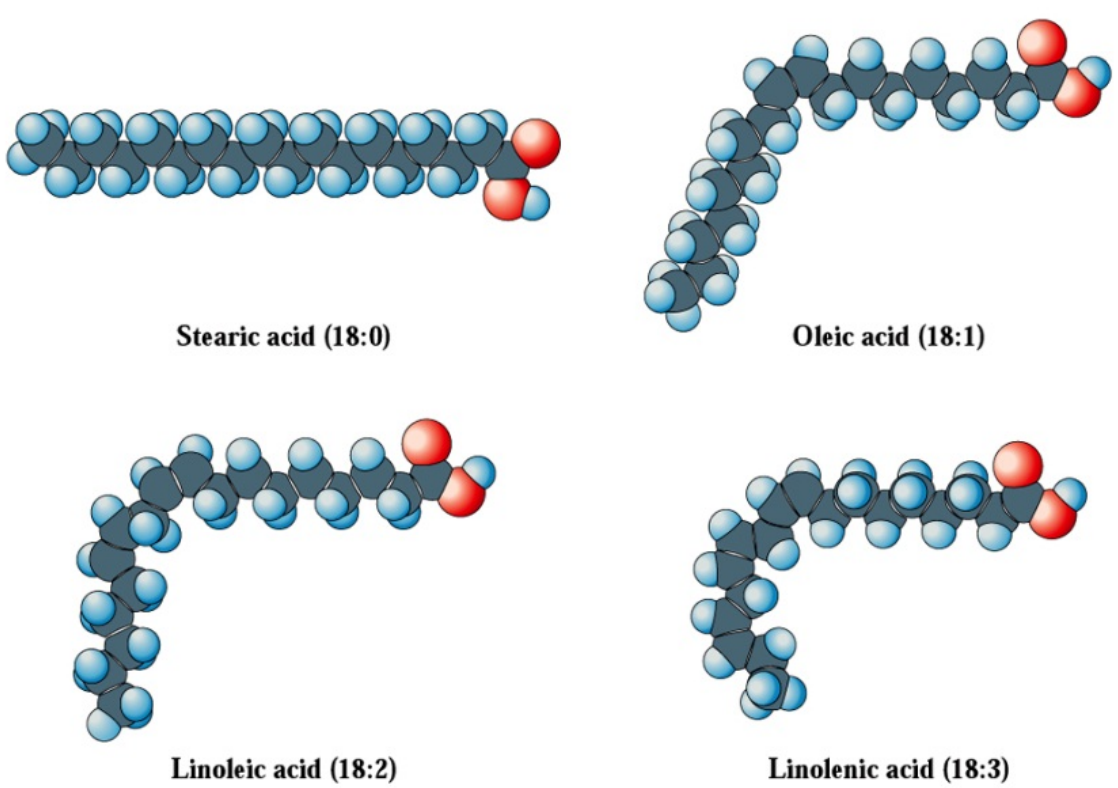
Albumin in blood binds and transports FAs

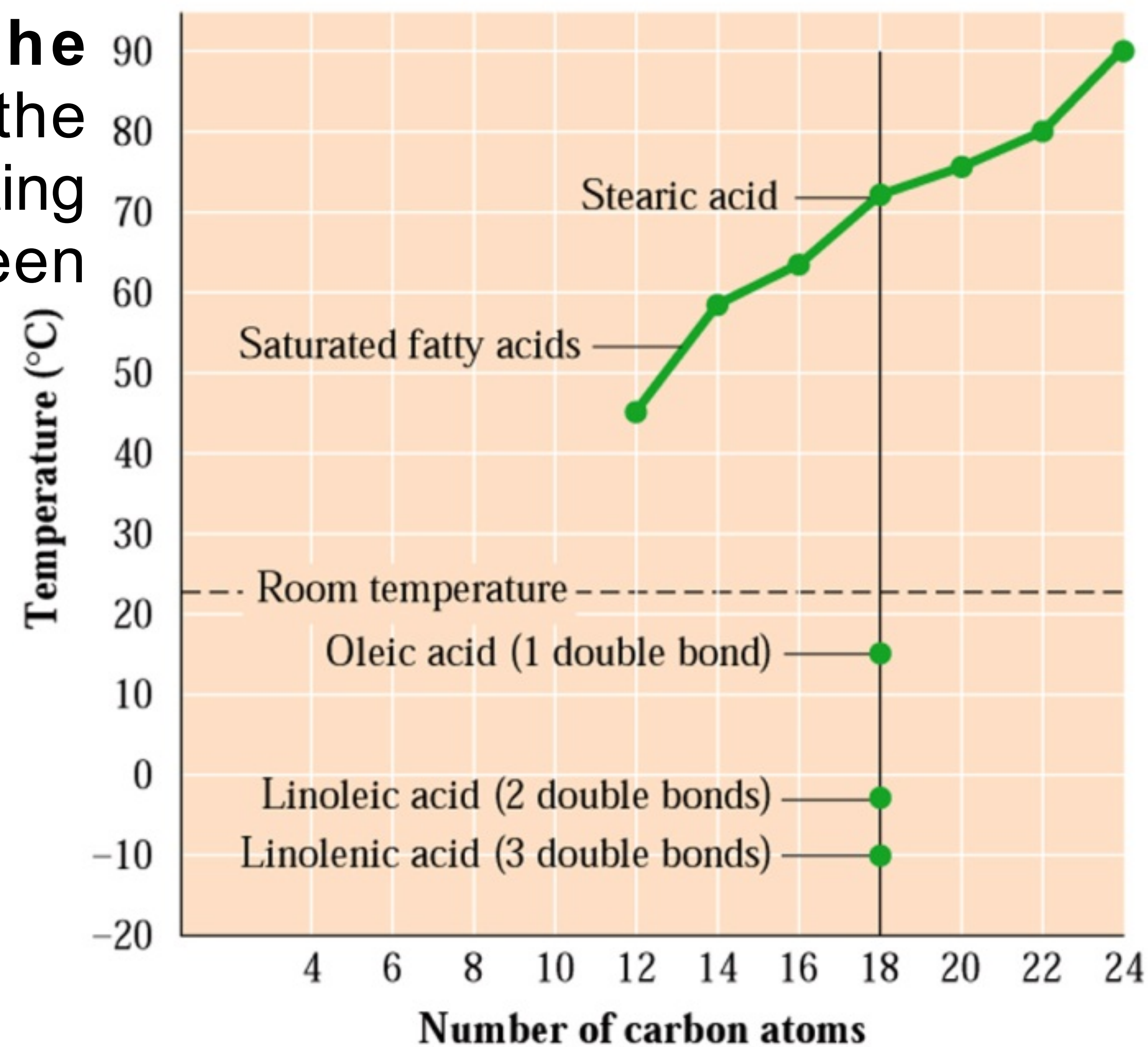


FATTY ACIDS

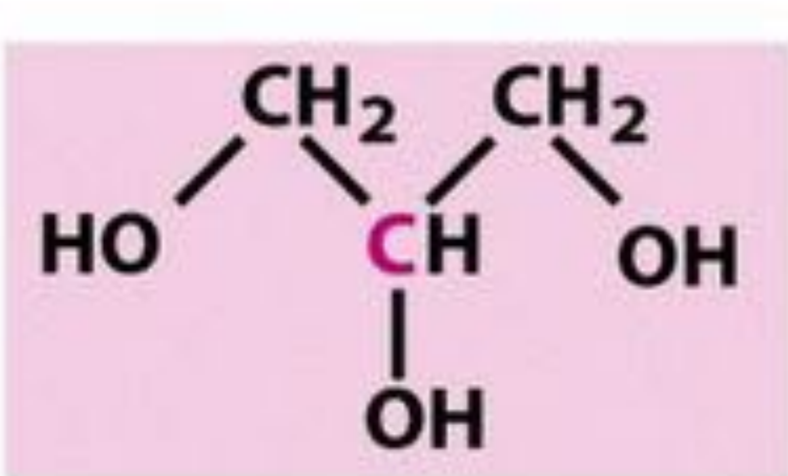
Melting points **increase with increasing molar mass** (due to London forces), meaning that the longer the carbon chain in a fatty acid, the higher its melting point.

Cis-double bonds **lower the melting point** by causing the molecule to become bent, resulting in reduced attractions between chains.

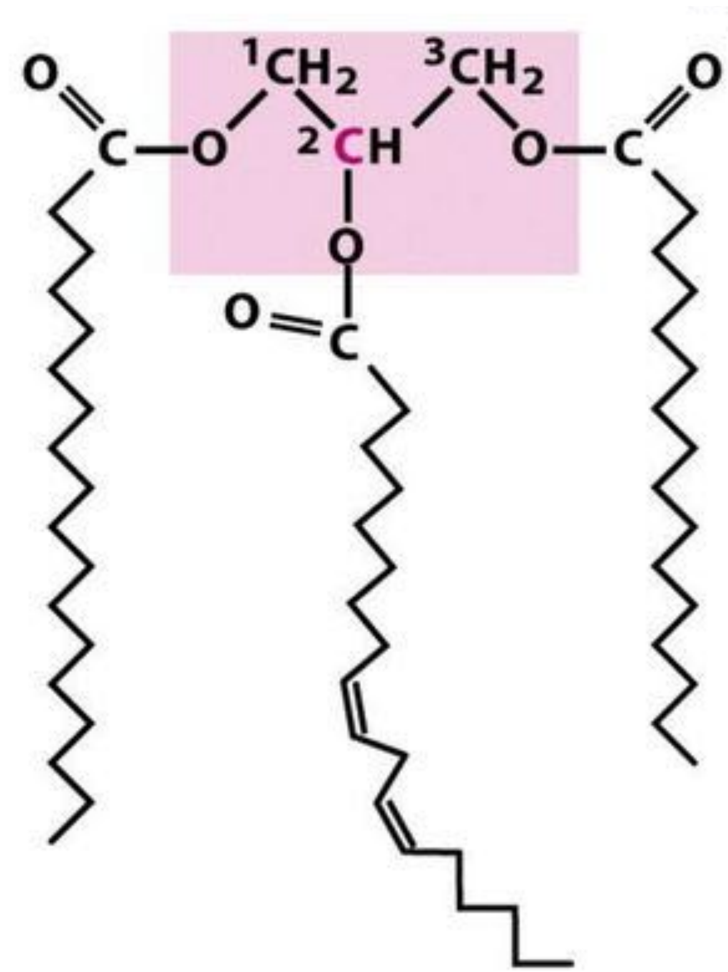




Storage Lipids- Triacylglycerols



Glycerol

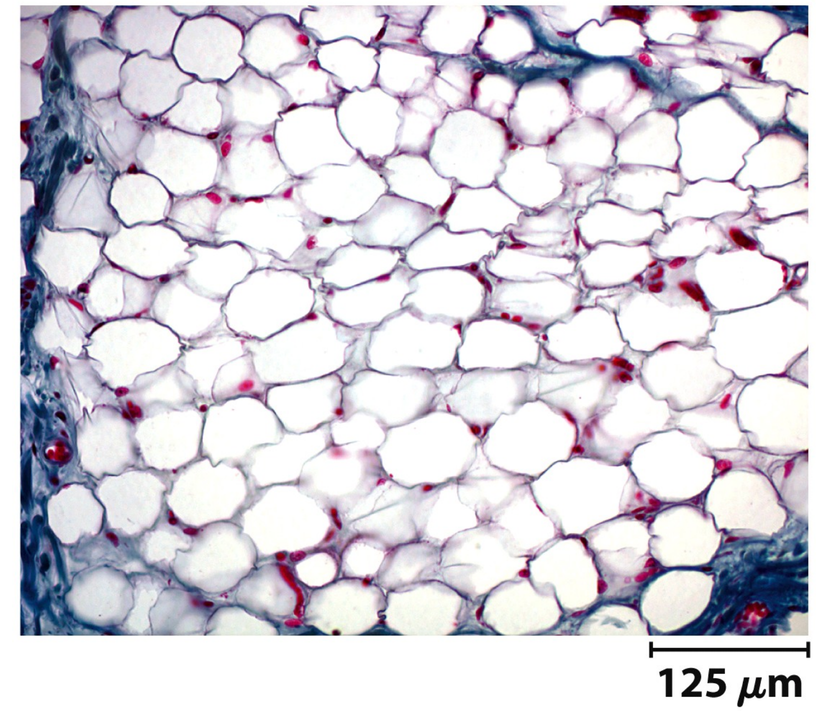


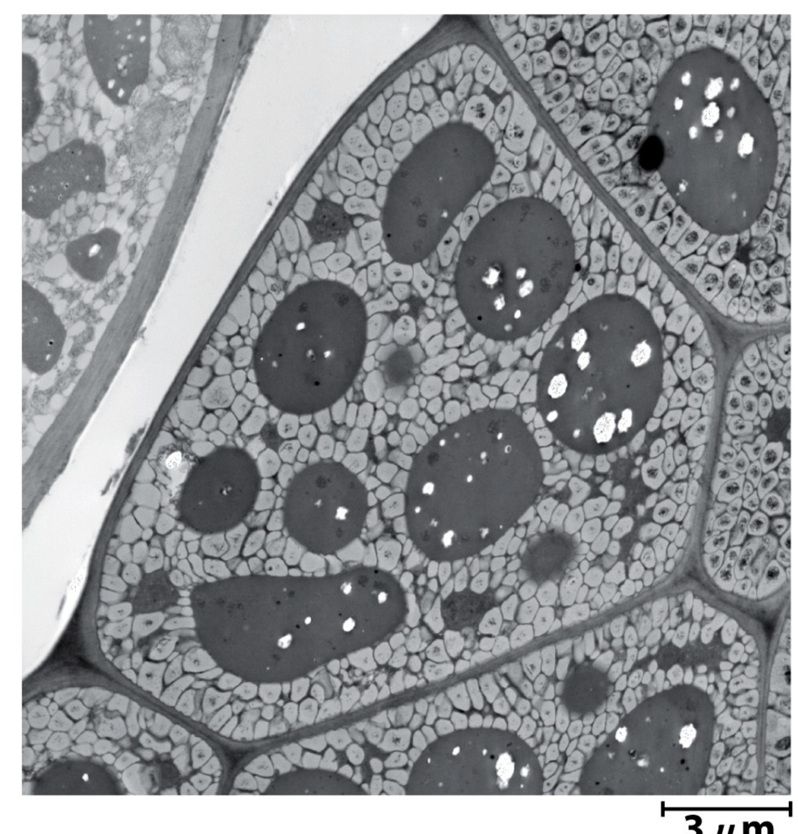
Triacylglycerols are composed of **three fatty acids** each in **ester** linkage with **a single glycerol molecule**. Those containing the same kind of fatty acid in all three positions are called **simple triacylglycerols** and are named after the fatty acid they contain. Simple triacylglycerols of 16:0, 18:0, and 18:1(Δ^9) are called tripalmitin, tristearin, and triolein, respectively. Most naturally occurring triacylglycerols are **mixed** and contain two or more different fatty acids.

Storage Lipids- Triacylglycerols

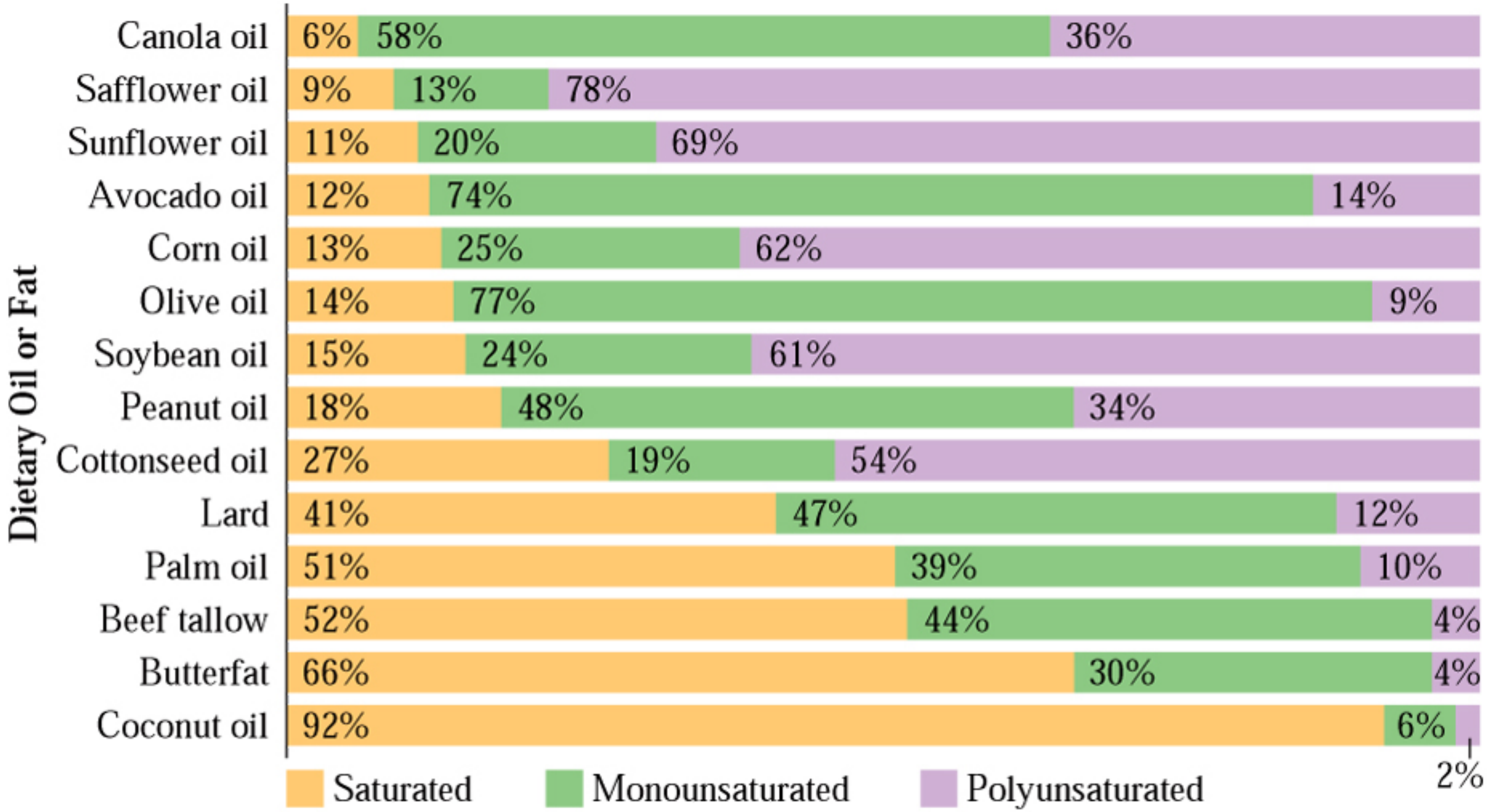
In most eukaryotic cells, triacylglycerols form microscopic, oily droplets in the aqueous cytosol, serving as **metabolic fuel**. In vertebrates, specialized cells called adipocytes or fat cells, store large amounts of triacylglycerols as fat droplets that nearly fill the cell.

Triacylglycerols contain **more energy per gram than do polysaccharides**. In addition, they are unhydrated, and the organism does not have to carry extra weight in the form of water as with stored polysaccharides. In some animals, like seals, penguins, and bears, fat stores under the skin also serve as **insulation against cold temperatures**.

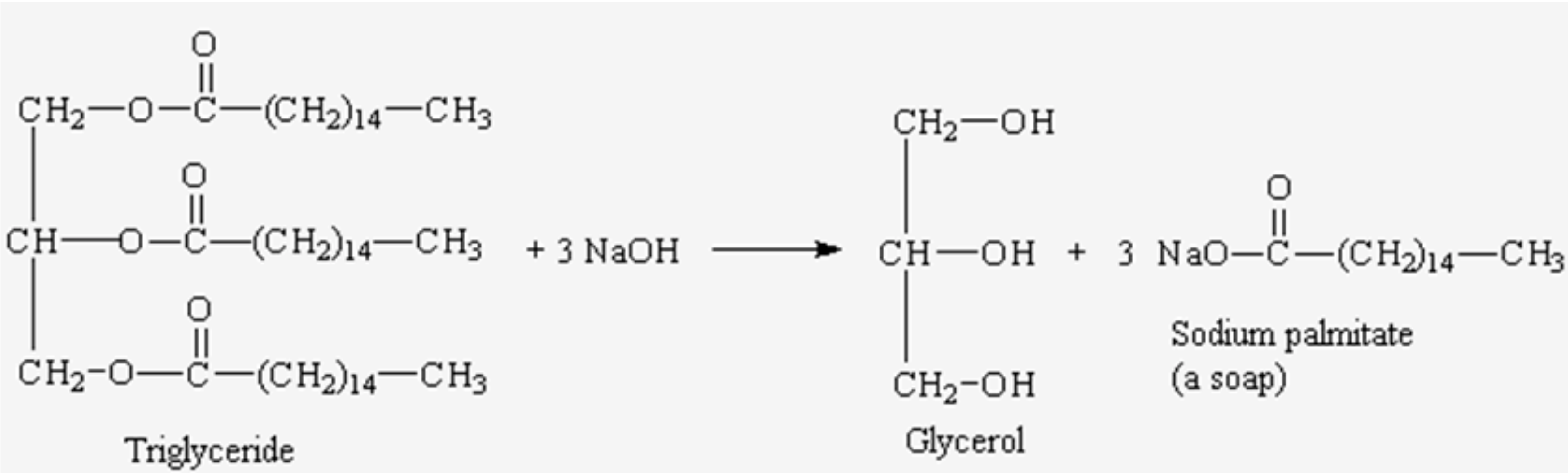




Storage Lipids- Triacylglycerols

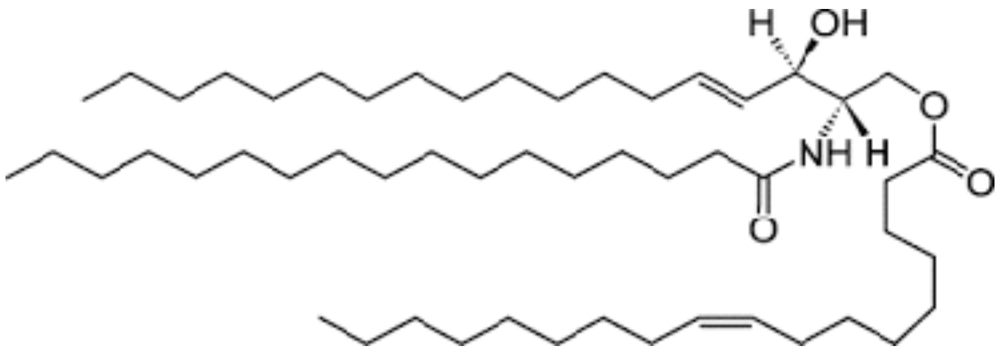


Storage Lipids- Triacylglycerols hydrolysis

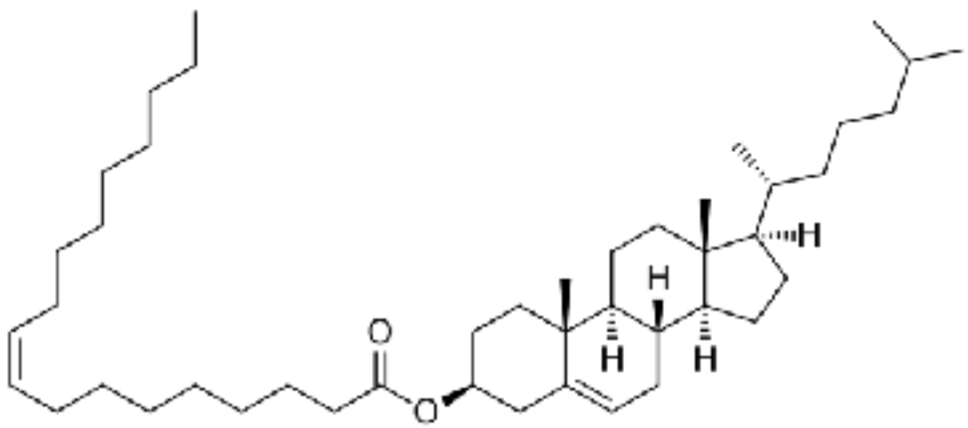


Saponification is a process that involves the conversion of fats, oils, or lipids into soap and alcohol through the application of heat in the presence of an aqueous alkali, such as NaOH. Soaps are the salts of fatty acids, which are monomers with long carbon chains.

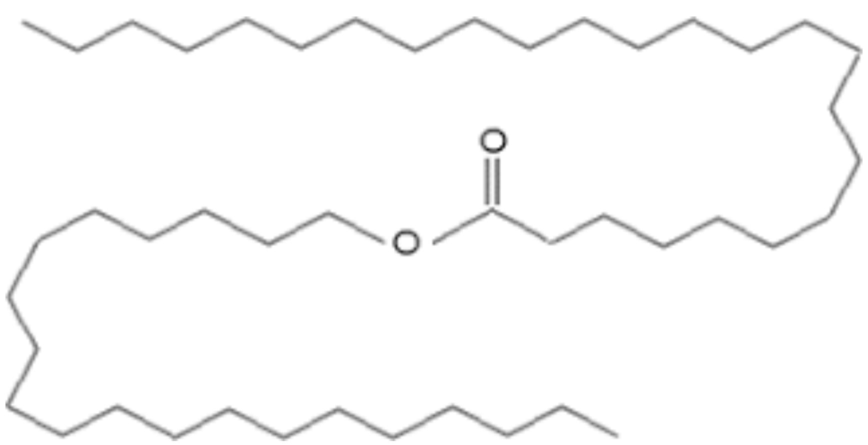
Other Storage Lipids



Acylceramides -> ceramide can be metabolised into acylceramide and stored in lipid droplets



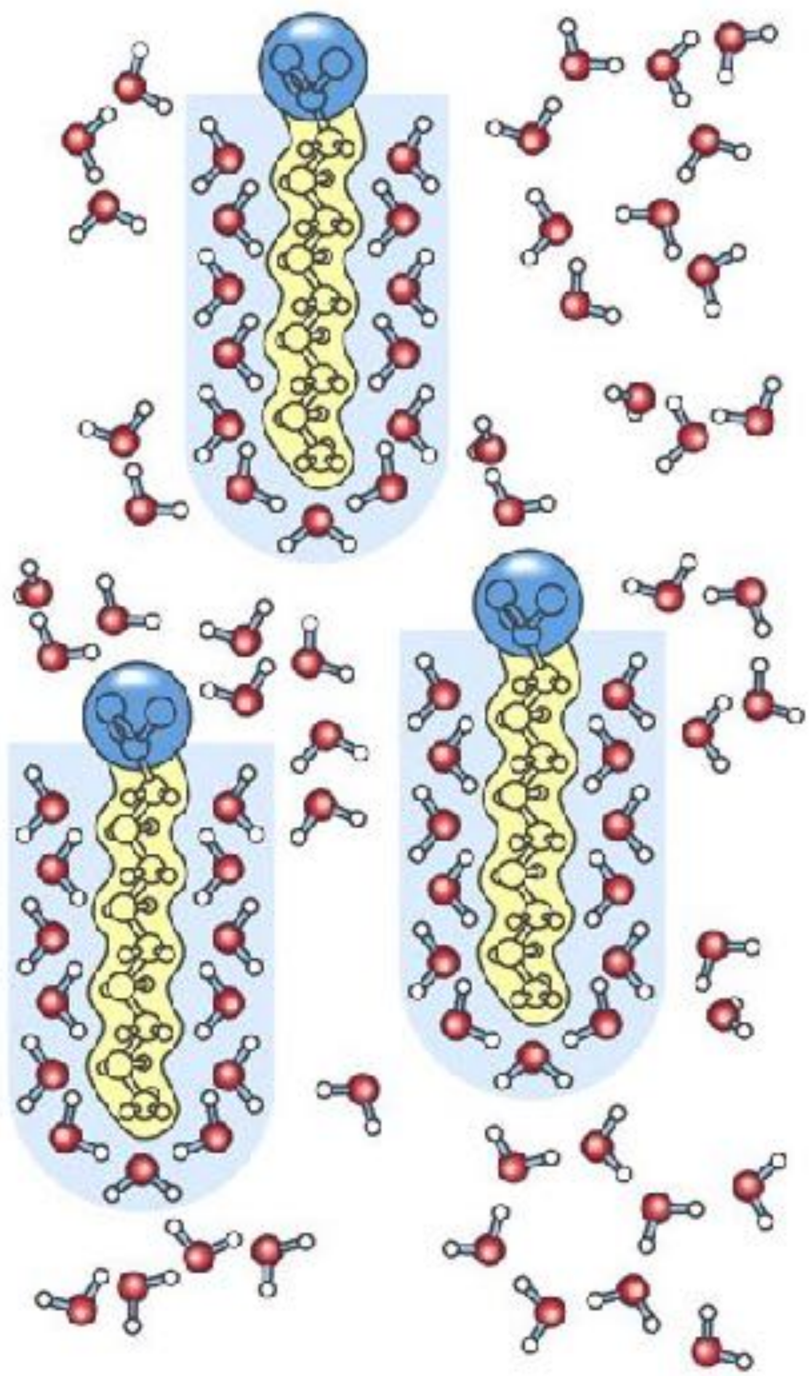
Cholesteryl esters -> A cholesteryl ester is formed through the bonding of the carboxylate group of a fatty acid with the hydroxyl group of cholesterol.

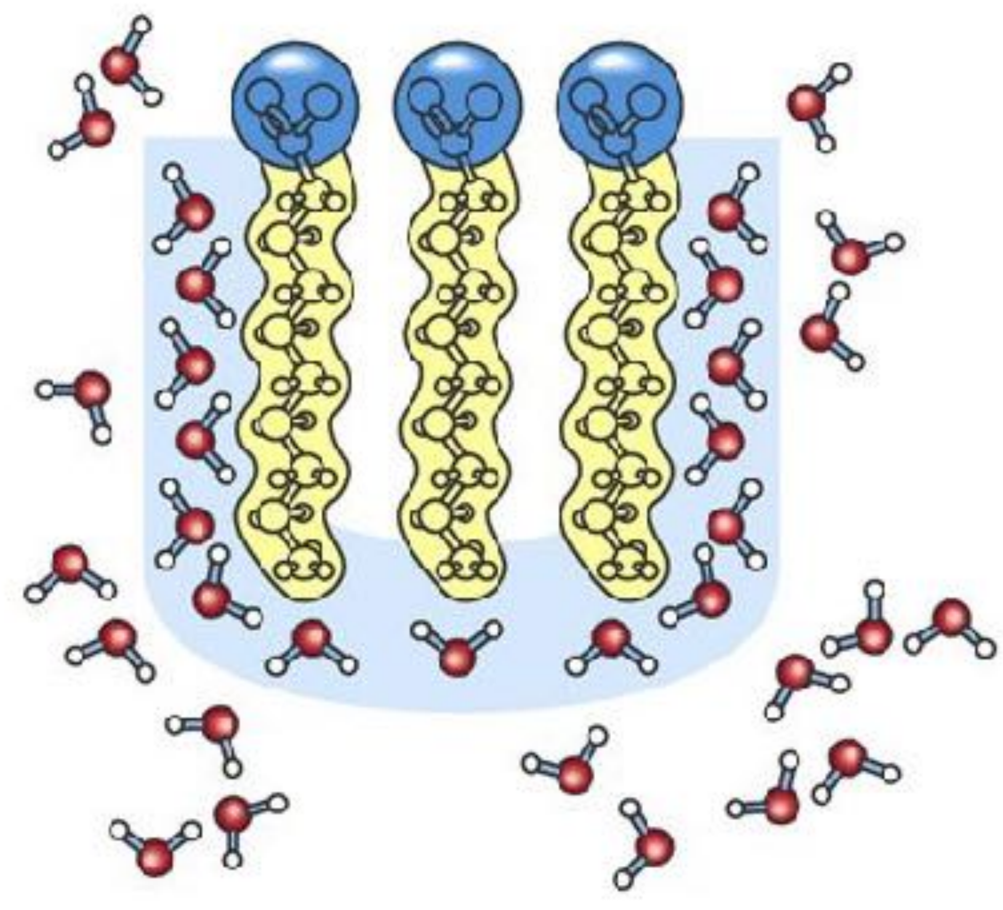


Waxes -> waxes are esters formed by long-chain (C14 to C36) saturated and unsaturated fatty acids with long-chain (C16 to C30) alcohols.

Membrane Lipids

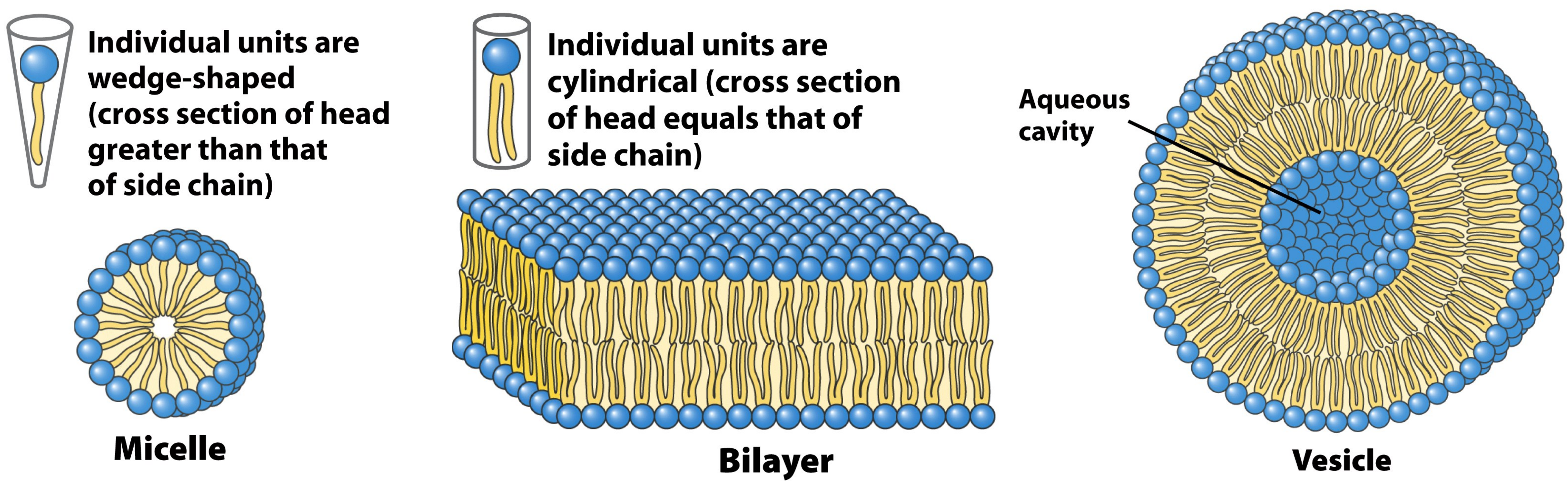
Membrane lipids are **amphipathic**: one end of the molecule is hydrophobic, the other hydrophilic.





Membrane Lipids

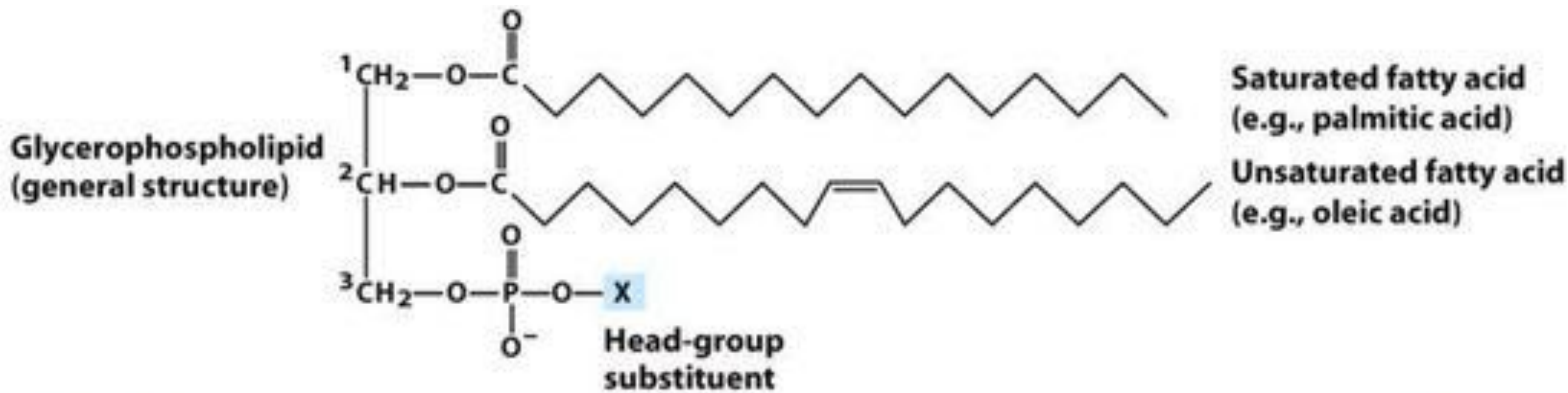
The hydrophobic interactions between **membrane lipids** and their hydrophilic interactions with water guide their arrangement into sheets known as membrane bilayers.



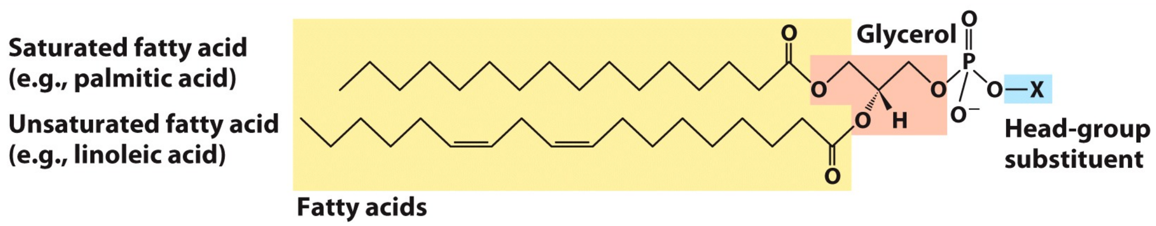
Cell Membranes are the **barrier** and the **interface** between the cell and the environment. Membranes also define sub-cellular compartments.

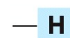
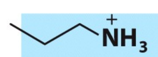
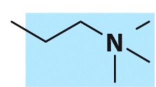
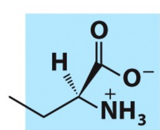
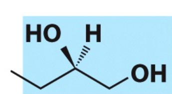
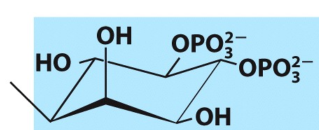
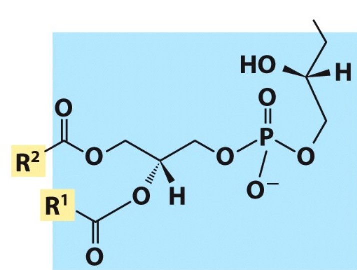
Glycerophospholipids

These lipids consist of **two fatty acids** attached via **ester linkage** to the **first and second carbons of glycerol**, with a **highly polar or charged group** attached through a phosphodiester linkage to the **third carbon**.



Glycerophospholipids



Name of glycerophospholipid	Name of X—O	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—		−2
Phosphatidylethanolamine	Ethanolamine		0
Phosphatidylcholine	Choline		0
Phosphatidylserine	Serine		−1
Phosphatidylglycerol	Glycerol		−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4*
Cardiolipin	Phosphatidyl-glycerol		−2

Glycerophospholipids are named based on **the polar alcohol within their head group**.

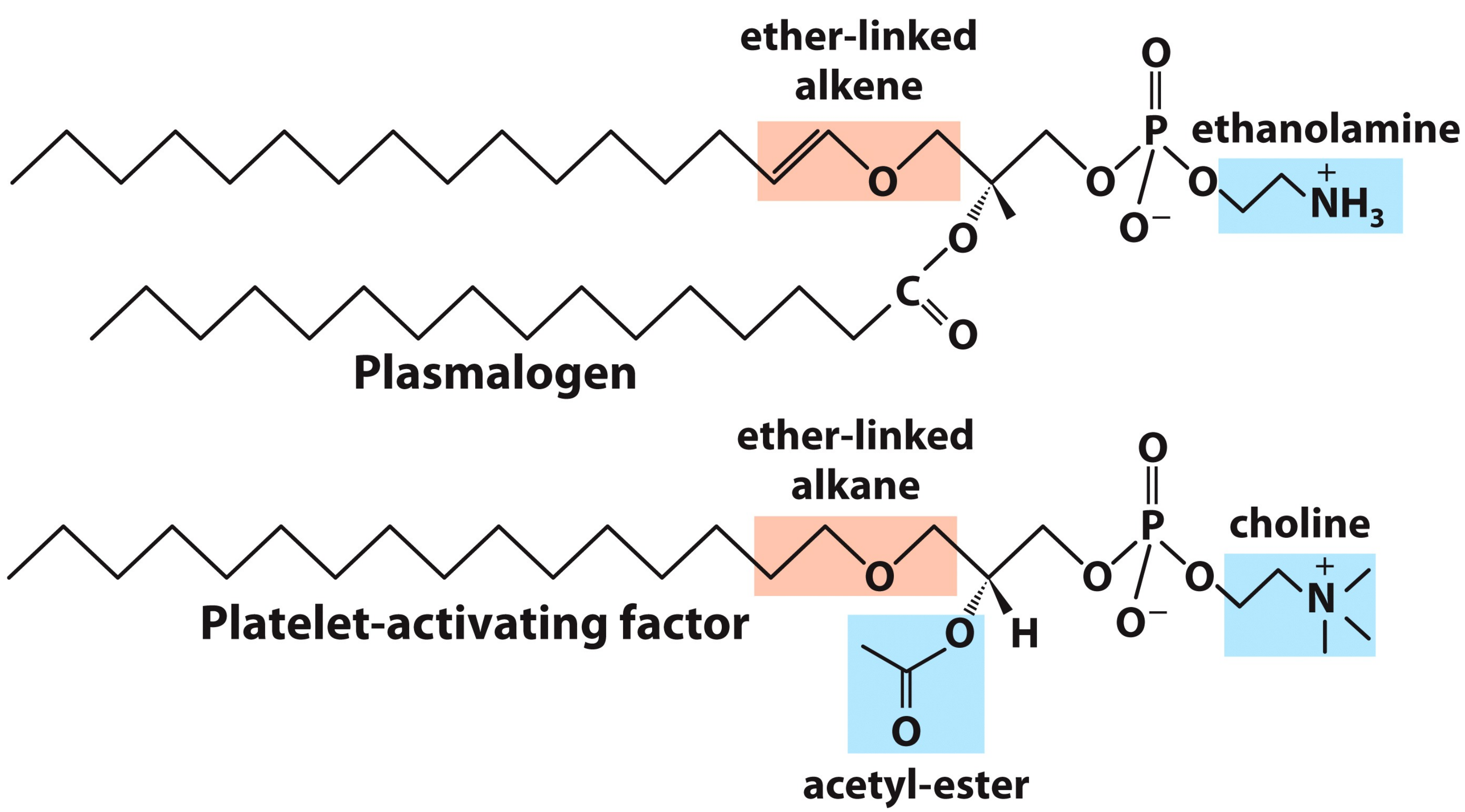
The polar alcohol can be negatively or positively **charged**.

The charges of these head groups play a significant role in determining the **surface properties of membranes**.

Glycerophospholipids account for the **bulk** of eukaryotic membranes

Ether Lipids

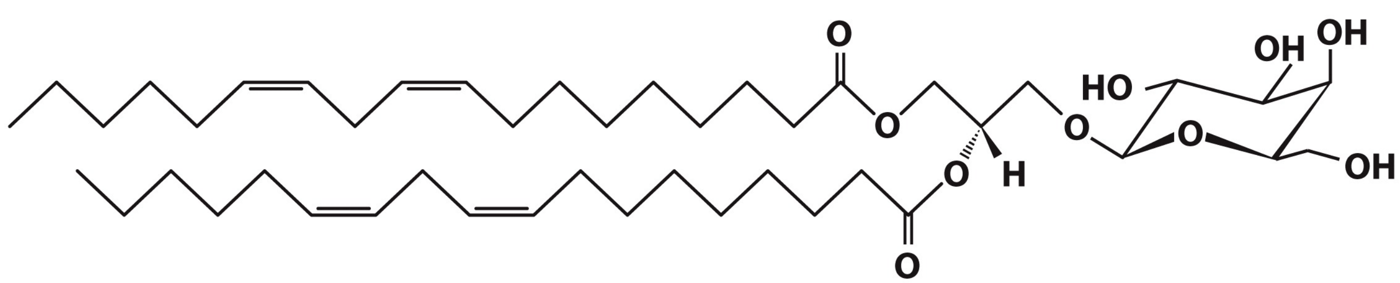
Lipids, in which one of the two hydrocarbon chains is attached to glycerol **in ether**, rather than ester, linkage. The ether-linked chain may be saturated, as in the alkyl ether lipids, or may contain a double bond between C-1 and C-2, as in plasmalogens



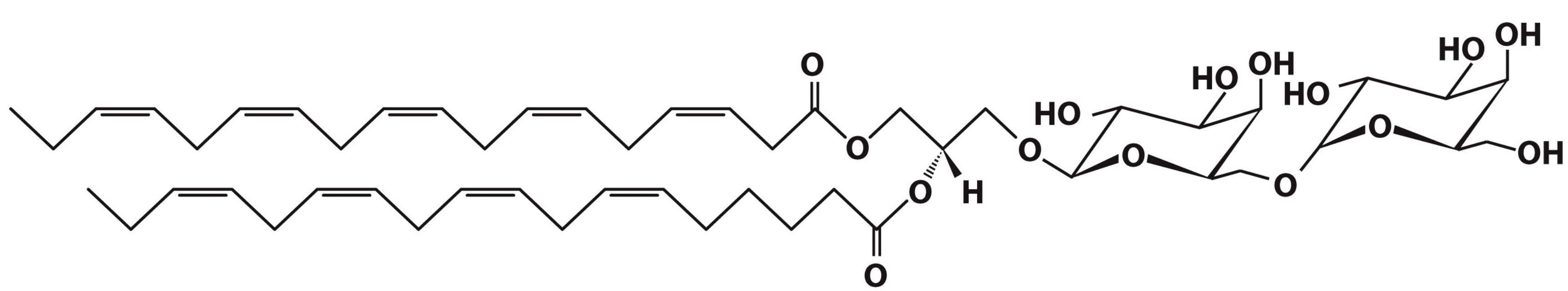
The vertebrate heart tissue is enriched in ether lipids, as are the halophilic bacteria, ciliated protists, and certain invertebrates. Notably, platelet-activating factor (PAF) is released from basophils and plays a role in stimulating platelet aggregation.

Galactolipids

Galactolipids contain one or two **galactose** residues connected via an α-glycosidic bond to the **C-3 position of a 1,2-diacylglycerol**. These lipids are particularly abundant in plant cells, primarily localized to the thylakoid membranes (internal membranes) of chloroplasts. They constitute 70% to 80% of the total membrane lipids in vascular plants, making them among **the most abundant membrane lipids in the biosphere.**



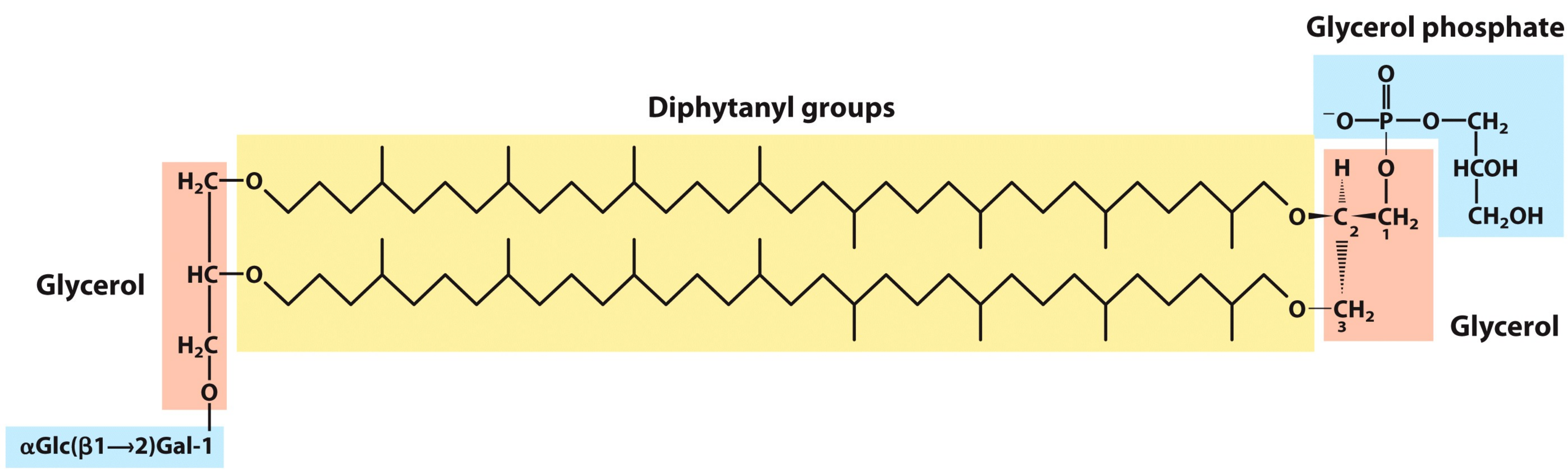
Monogalactosyldiacylglycerol (MGDG)



Digalactosyldiacylglycerol (DGDG)

Archean Membrane Lipids

Some **archaea** that thrive in **extreme conditions**, such as high temperatures (boiling water), low pH, and high ionic strength, have membrane lipids containing long-chain (32 carbons) branched hydrocarbons (**phytanol groups**) linked at **both ends** to glycerol. These lipids are based on five-carbon isoprene groups condensed end-to-end, making them **approximately twice the length of a 16-carbon fatty acid**. Consequently, **a single one of these lipids spans the entire membrane bilayer**.

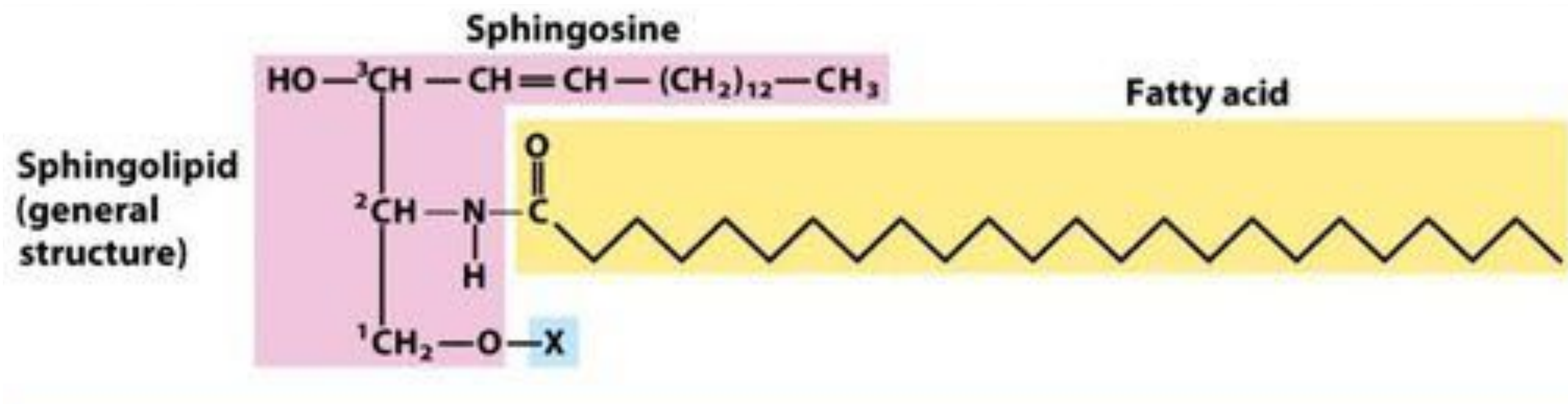


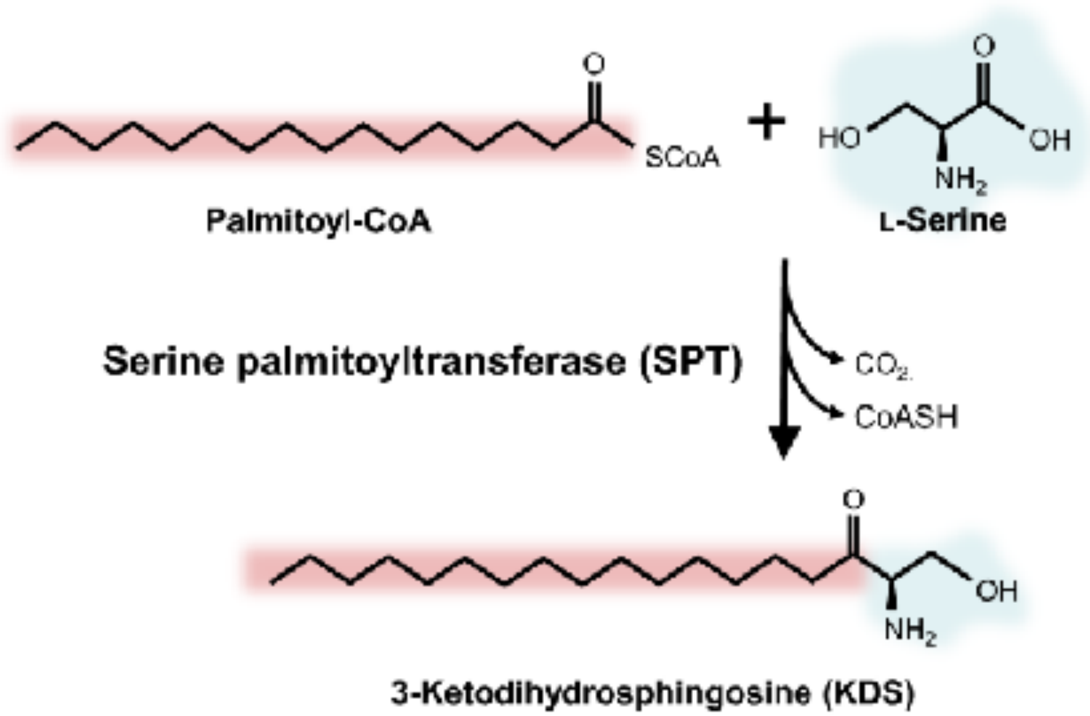
Welcome to BC1 lesson 6

15’ Break

Sphingolipids

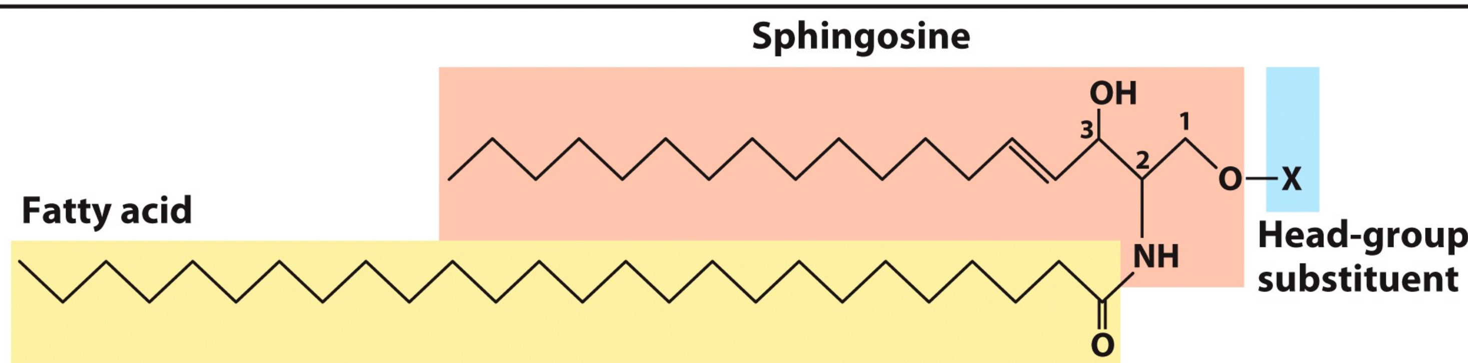
Unlike glycerophospholipids, **sphingolipids** contain **no glycerol**. Instead, sphingolipids are composed of one molecule of the **long-chain base** (here sphingosine).

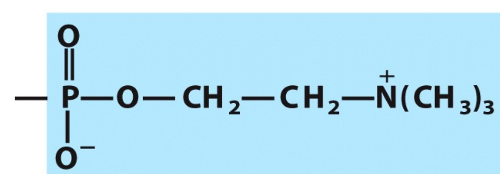
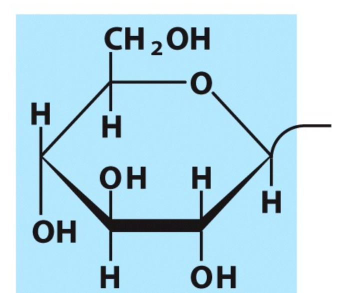
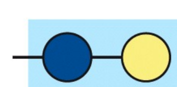
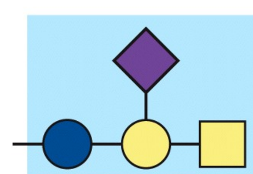




The long-chain base is formed through the condensation of the amino acid serine with an (activated) fatty acid.

Sphingolipids

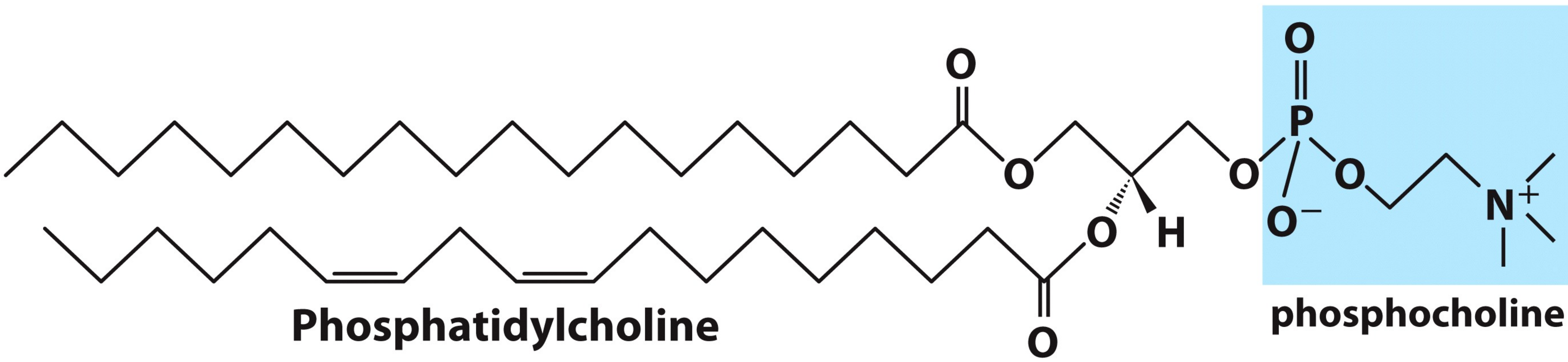


Name of sphingolipid	Name of X—O	Formula of X
Ceramide	—	—H
Sphingomyelin	Phosphocholine	
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

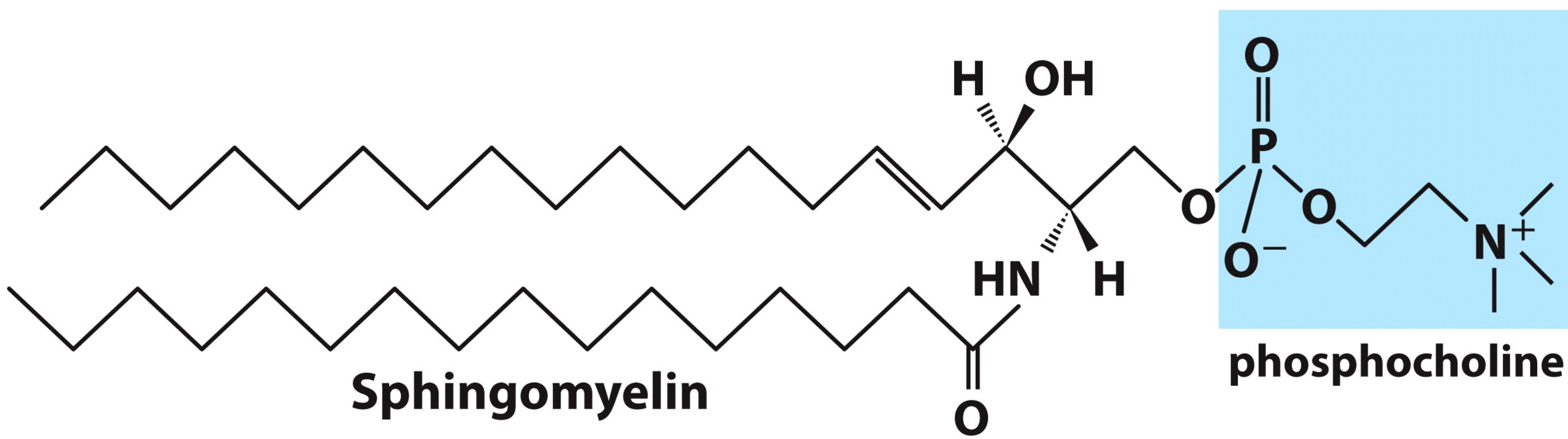
There are three subclasses of sphingolipids, which are all derivatives of ceramide, but differ in their head groups. These are the **sphingomyelins**, **neutral glycosphingolipids**, and **gangliosides.**

Sphingomyelins are found in the plasma membranes of animal cells and are particularly **abundant in myelin**, a membranous sheath that surrounds and insulates the axons of certain neurons—hence the name 'sphingomyelins.'

Sphingolipids *vs* Glycerophospholipids

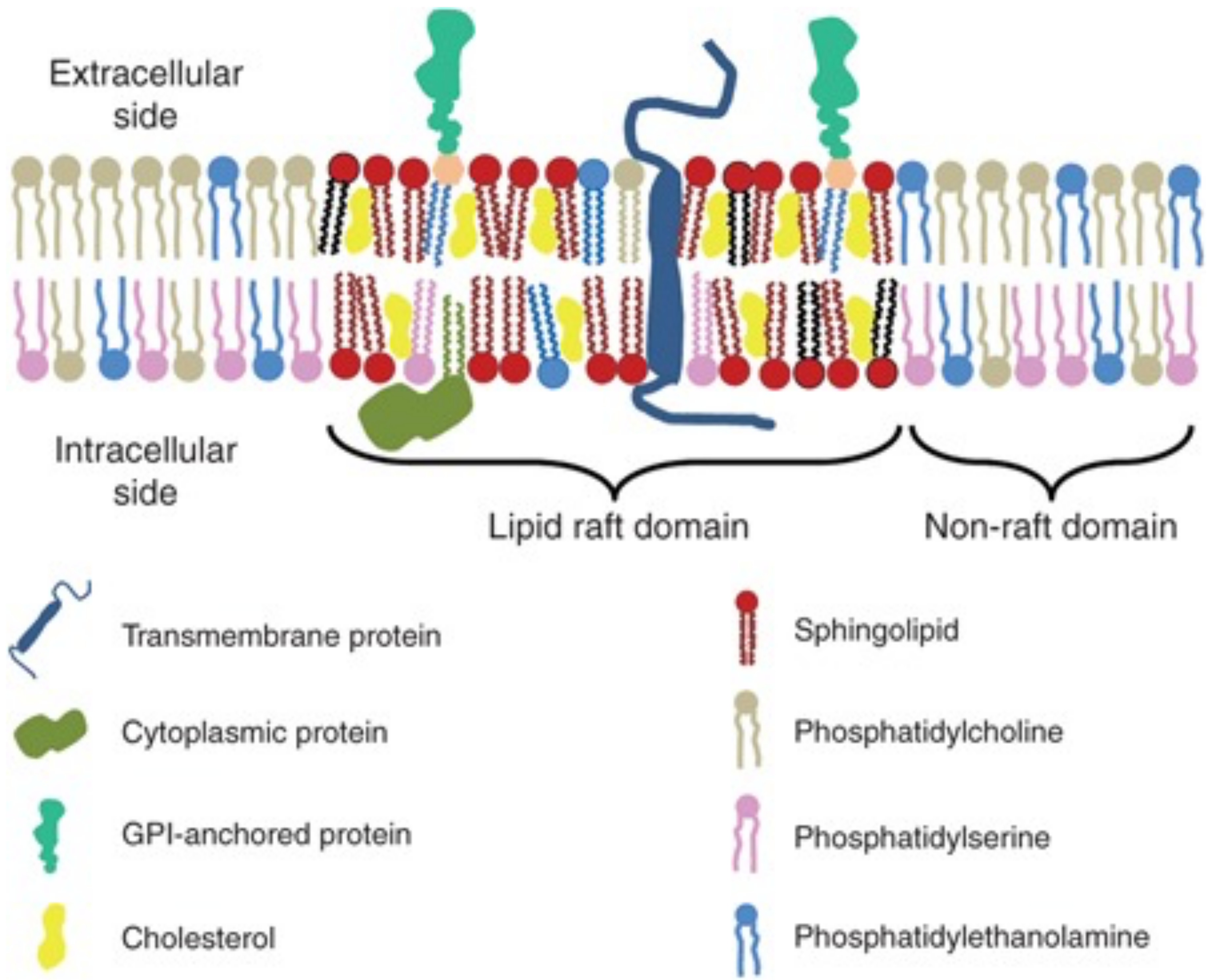


Phosphatidylcholine

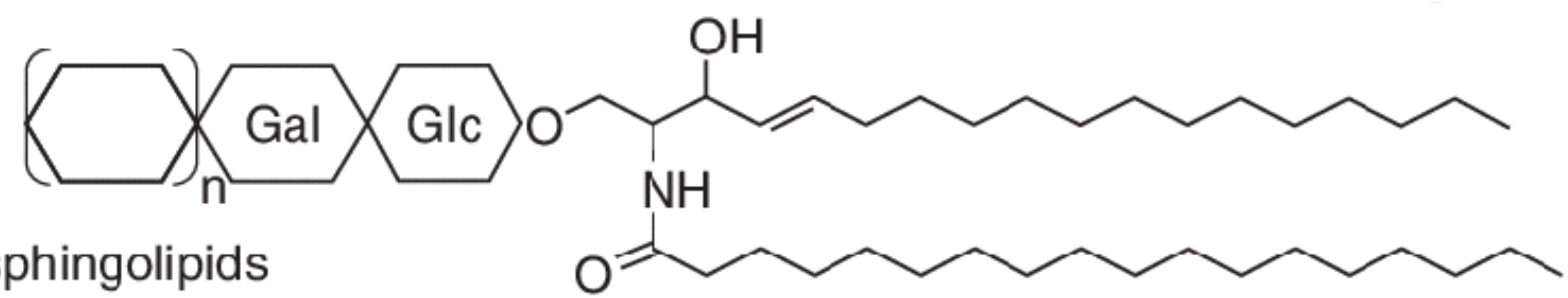


Sphingomyelin

Membrane domains

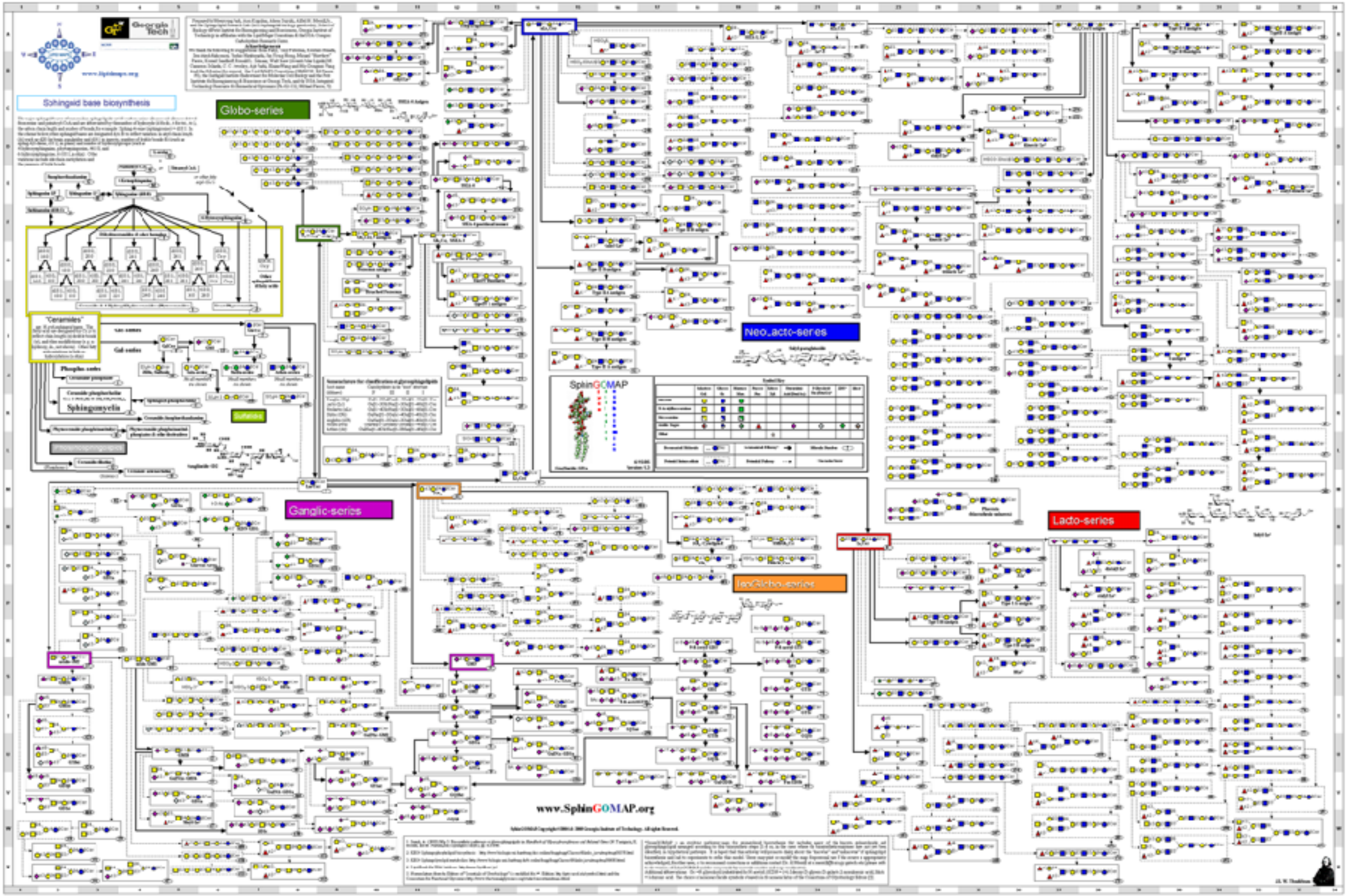


Glycosphingolipids

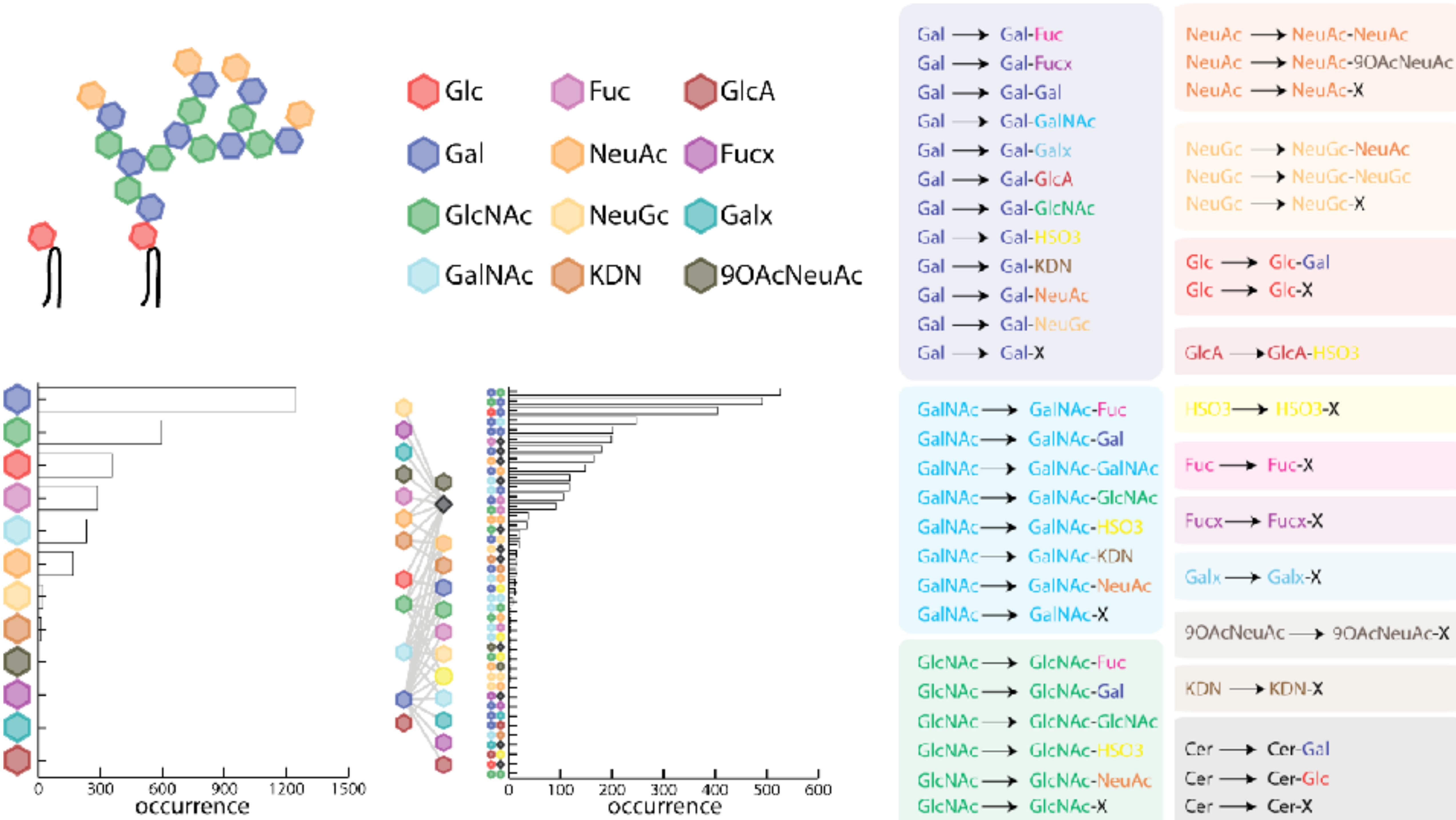


Glycosphingolipids
(GSLs)

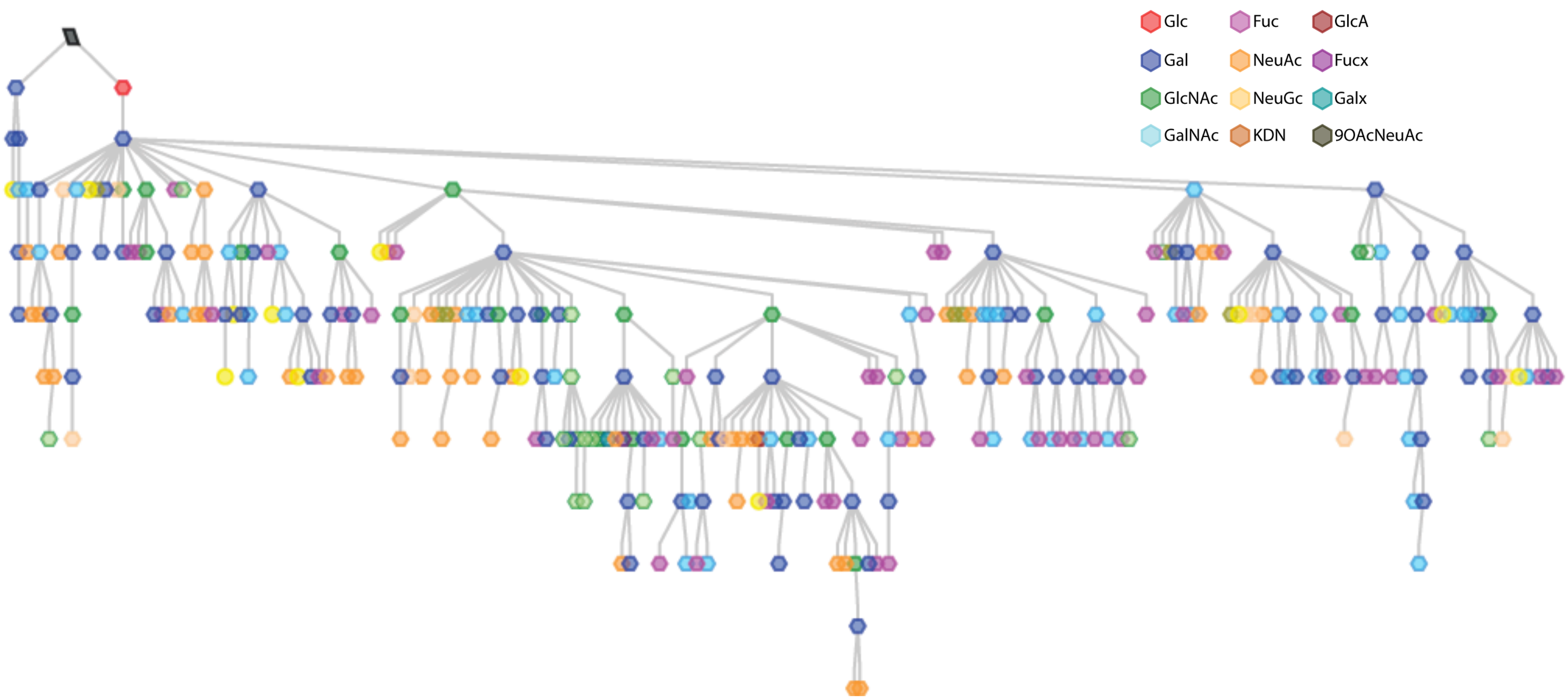
Glycosphingolipids

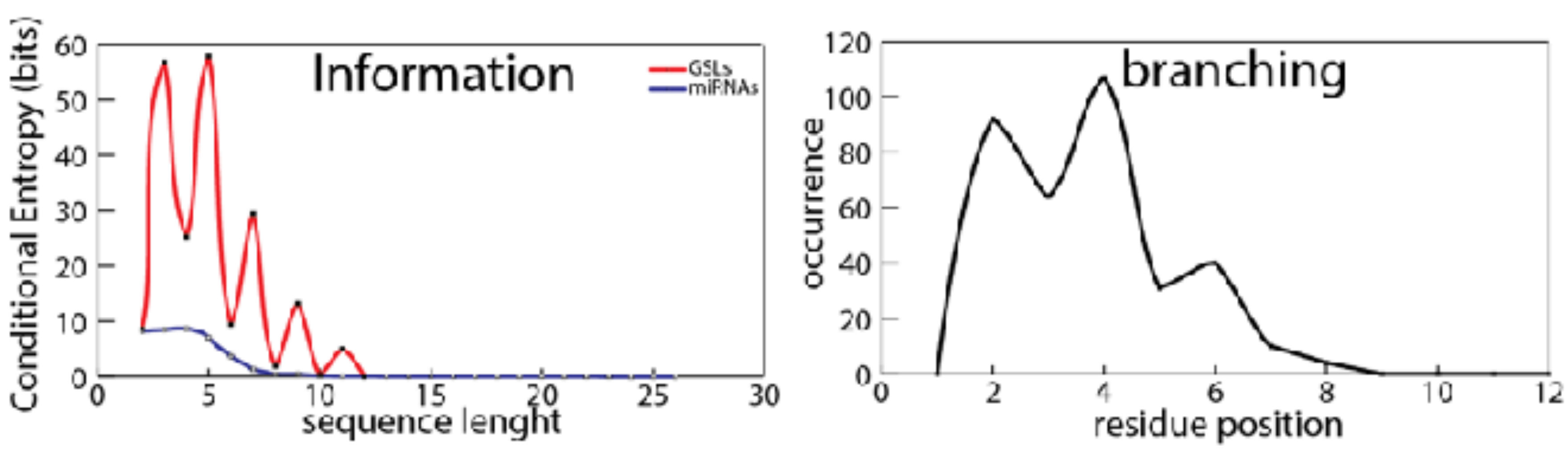


Glycosphingolipids

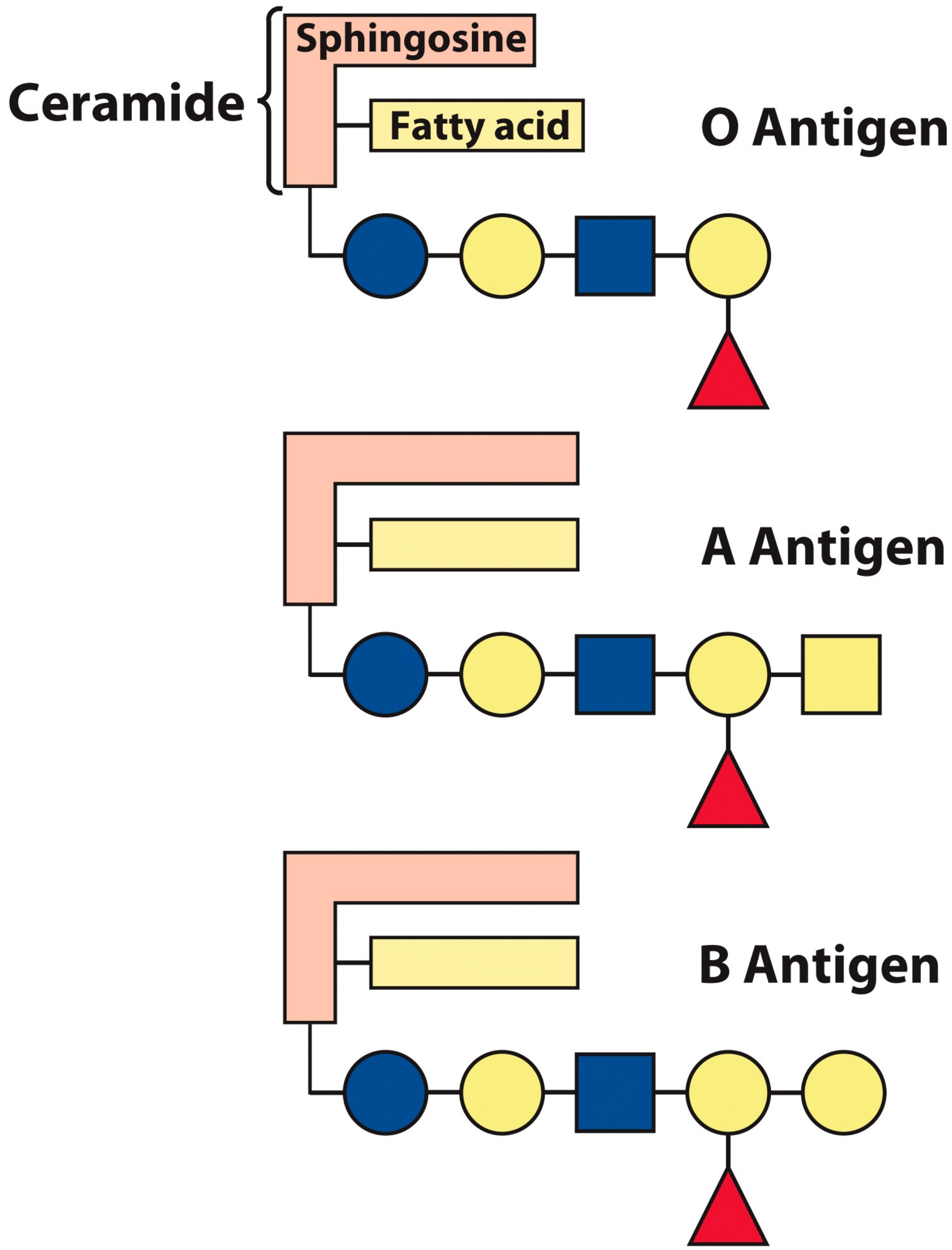


Glycosphingolipids





Blood Group Antigens



The human blood groups (ABO) are determined by the **oligosaccharide head groups of glycosphingolipids present in the outer leaflet of the red blood cell membrane**.

All three blood group antigens contain the same core of five sugars, but A and B antigens also contain an additional terminal N-acetylgalactosamine (yellow square) or galactose (yellow circle) residue, respectively.

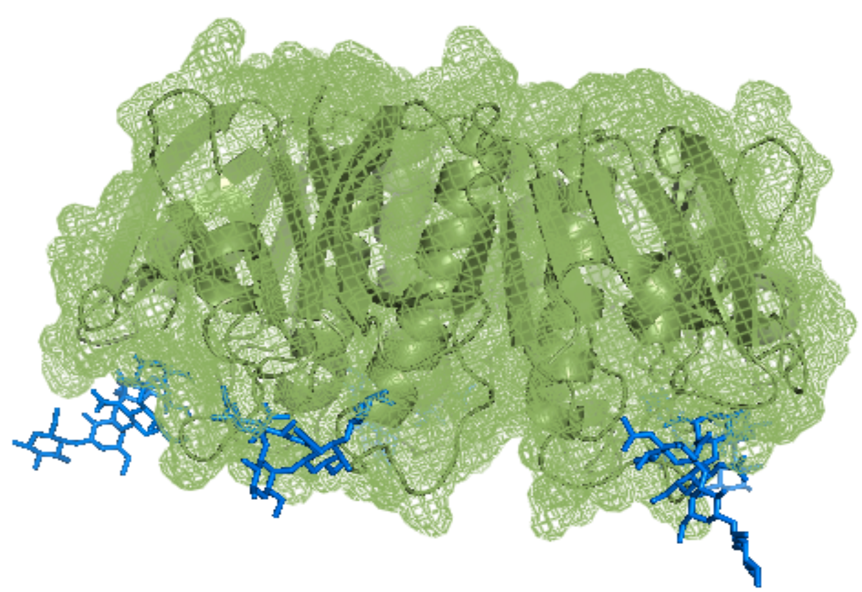
Glycosphingolipids

Virus	Glycosphingolipid Receptors
Picornaviridae	
Porcine sapelovirus (PSV)	GD1a
Caliciviridae	
Human Norovirus (HuNoV)	Type 1, 2, 3 HBGA
Human Norovirus (HuNoV), GII.4 strain	H, B, and A type 1 Lewis b
Murine Norovirus (MNV): MNV-1 and CR3 strains	GD1a; GT1b
Bovine Norovirus (BoNoV)	HBGA
Rabbit Hemorrhagic Disease Virus (RHDV)	A and H Type 2 HBGA
Adenoviridae	
Adenovirus type 37 (Ad37)	GD1a
Reoviridae	
Reovirus serotype 1 (T1)	GM2
Porcine Rotavirus: OSU strain	GM3
Porcine Rotavirus: CRW-8 strain	GD1a
Porcine Rotavirus: TFR-41 strain	Unknown ganglioside
Simian Rotavirus: SA11 strain	NeuGcGM3, IV^{3}NeuAcLc4, GM2, GD1a
Simian Rhesus Rotavirus: RRV strain	Unknown ganglioside
Bovine Rotavirus: NCVD strain	NeuGcGM3, IV^{3}NeuAcLc4, GM2, GD1a
Bovine Rotavirus: UK strain	NeuGcGM3, GM1, GD1a, GM2, IV^{3}NeuAcLc4
Human Rotavirus: KU, MO, DS-1 and Wa strains	GM3, GM1
Polyomaviridae	
Trichodysplasia spinulosa-associated Polyomavirus (TSPyV)	GM1
Murine Polyomavirus (MPyV)	GD1a, GT1b
Simian Virus 40 (SV40)	GM1
BK Virus (BKV)	GD1b, GT1b
JC Virus (JCV)	GT1b
Merkel Cell Polyomavirus (MCPyV)	GT1b
Parvoviridae	
Human Parvovirus B19	Gb4, SSEA-3, SSEA-4, nLc4
Simian Parvovirus	Gb4; Forssmann antigen
Bovine Adeno-associated Virus (BAAV)	Unknown ganglioside
Retroviridae	
Human Immunodeficiency Virus (HIV)	Gb3, GM3, GalCer, GD3, SM4 sulfatide
Flaviviridae	
Dengue virus (DENV) type 2	GM3, nLc4
Orthomyxoviridae	
Influenza A virus, subtype H3N2: A/Victoria/3/75 strain	Ganglioside with Neu5Acα2-3Galβ1-4 (Fucα1-3) GlcNAc epitope: nLc8, nLc10 and nLc12
Influenza A virus, subtype H3N2: A/Hiroshima/52/2005 strain	
Poxviridae	
Vaccinia virus (VACV): Western-Reserve strain	SM4 sulfatide
Paramyxoviridae	
ParamyxoVirus 1 (Newcastle Disease)	GM3, GM2, GM1, GD1a
Sendai virus (SV) (murine parainfluenza virus type 1)	GD1a, GQ1b, IV^{3}NeuAcLc4, nLC4
Human parainfluenza virus types 1 (Hpiv-1)	IV3NeuAcLc4, Nlc4
Human parainfluenza virus types 3 (hPIV-3)	

Bacterial Toxin	Glycosphingolipid Receptors
Cholera toxin *Vibrio cholera*	GM1
Heat labile toxin 1 Escherichia coli	GM1
Shiga Toxin Shighella dysenteriae	Gb3
Shiga like toxins (SLT1 and SLT 2) *Escherichia coli* (*Verotoxins*)	Gb4
Tetanus neurotoxin (TeNT) *Clostridium tetani*	GT1b, GD1b
Botulinium toxin BoNT *Clostridium botulinum*	GT1b, GD1a
Heat labile toxin IIB *Escherichia coli*	GD1a

Glycosphingolipids play important **recognition roles** in the outer leaflets of cell membranes. In the nervous system, gangliosides are believed to play a role in the **wiring of neurons** during development. In various epithelia, glycosphingolipids act as **receptors** through which toxins and viruses can enter cells.

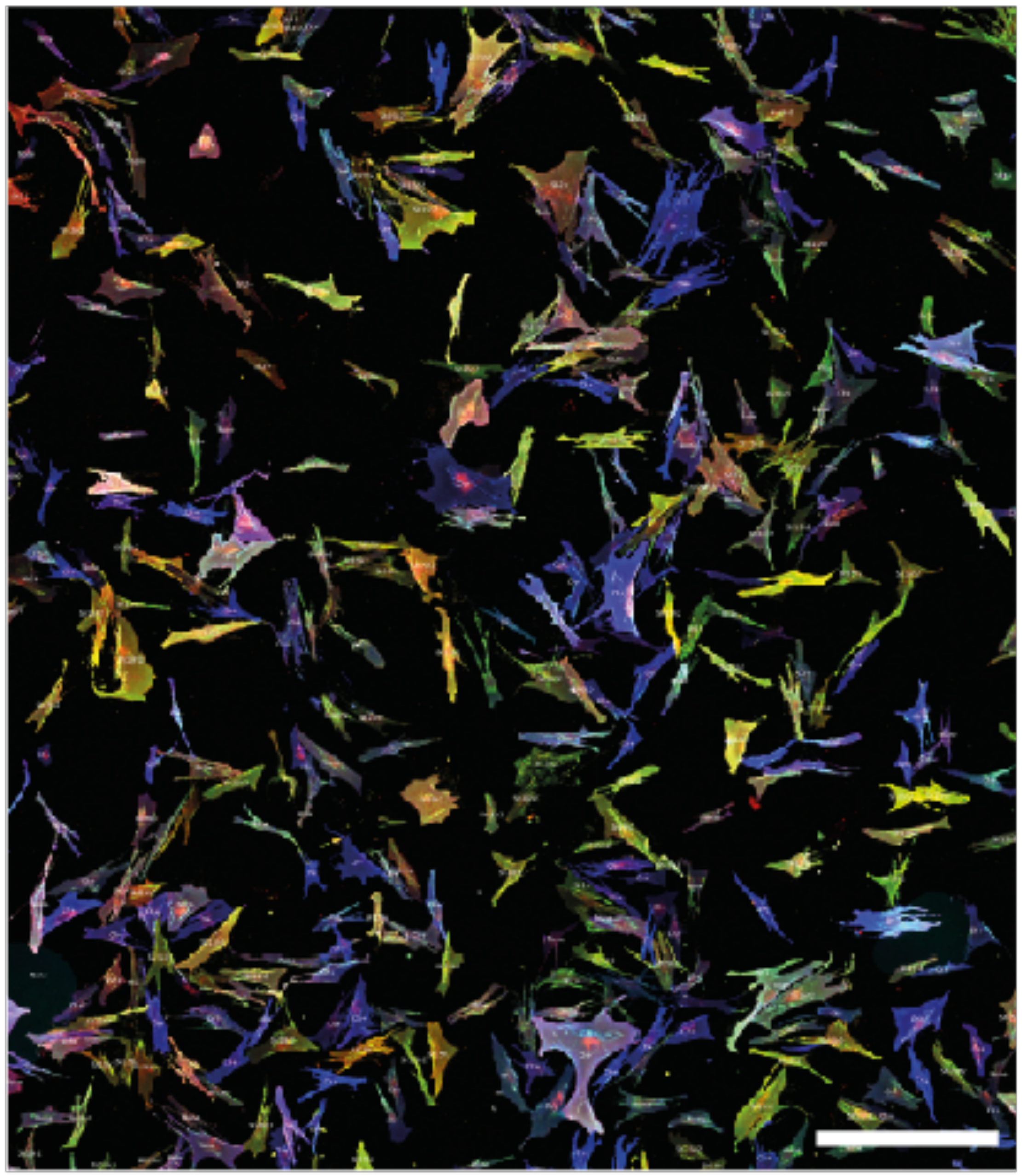
ChTxB



Glycosphingolipids

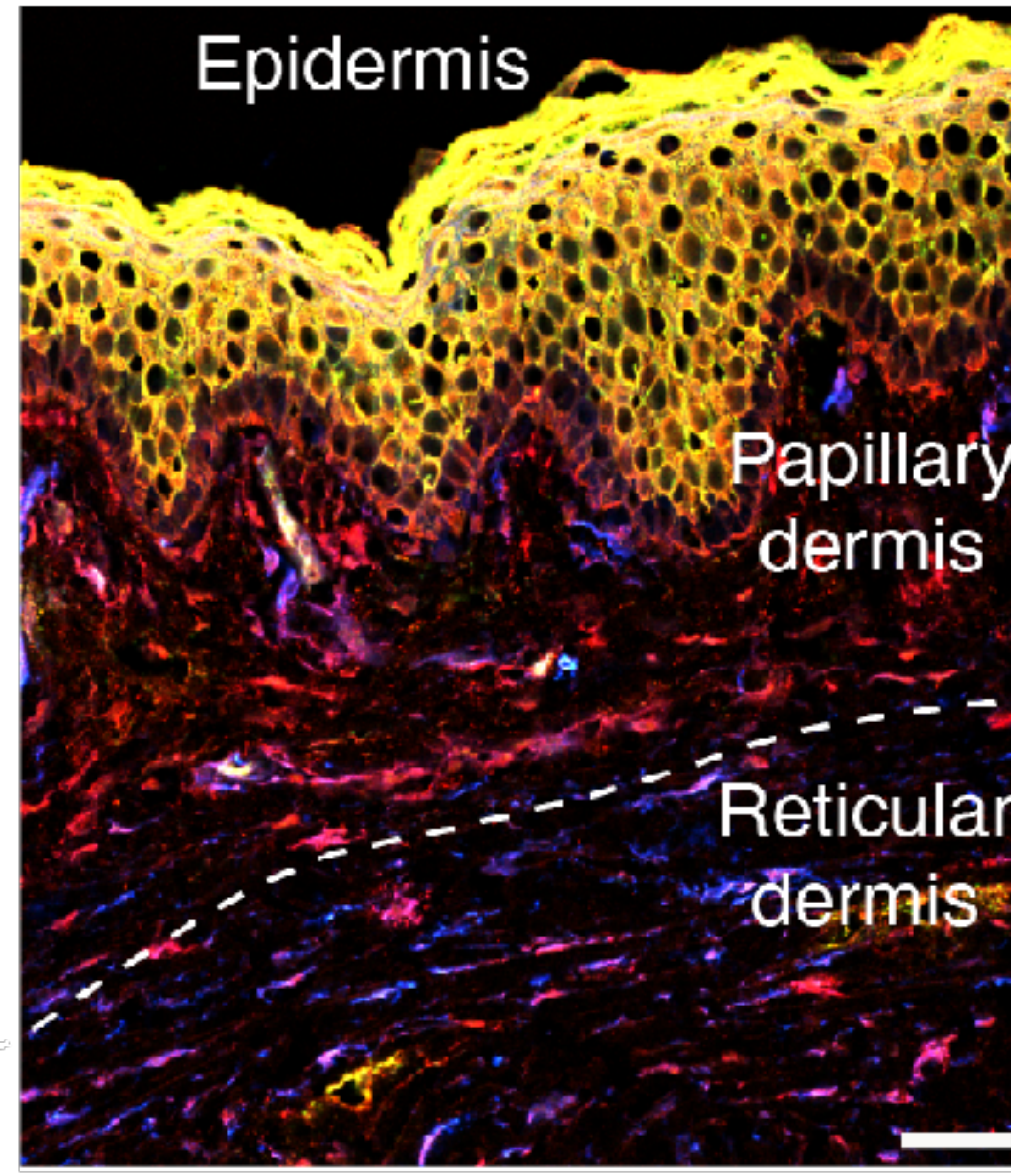
in vitro

ChTxB ShTxB1a ShTxB2e

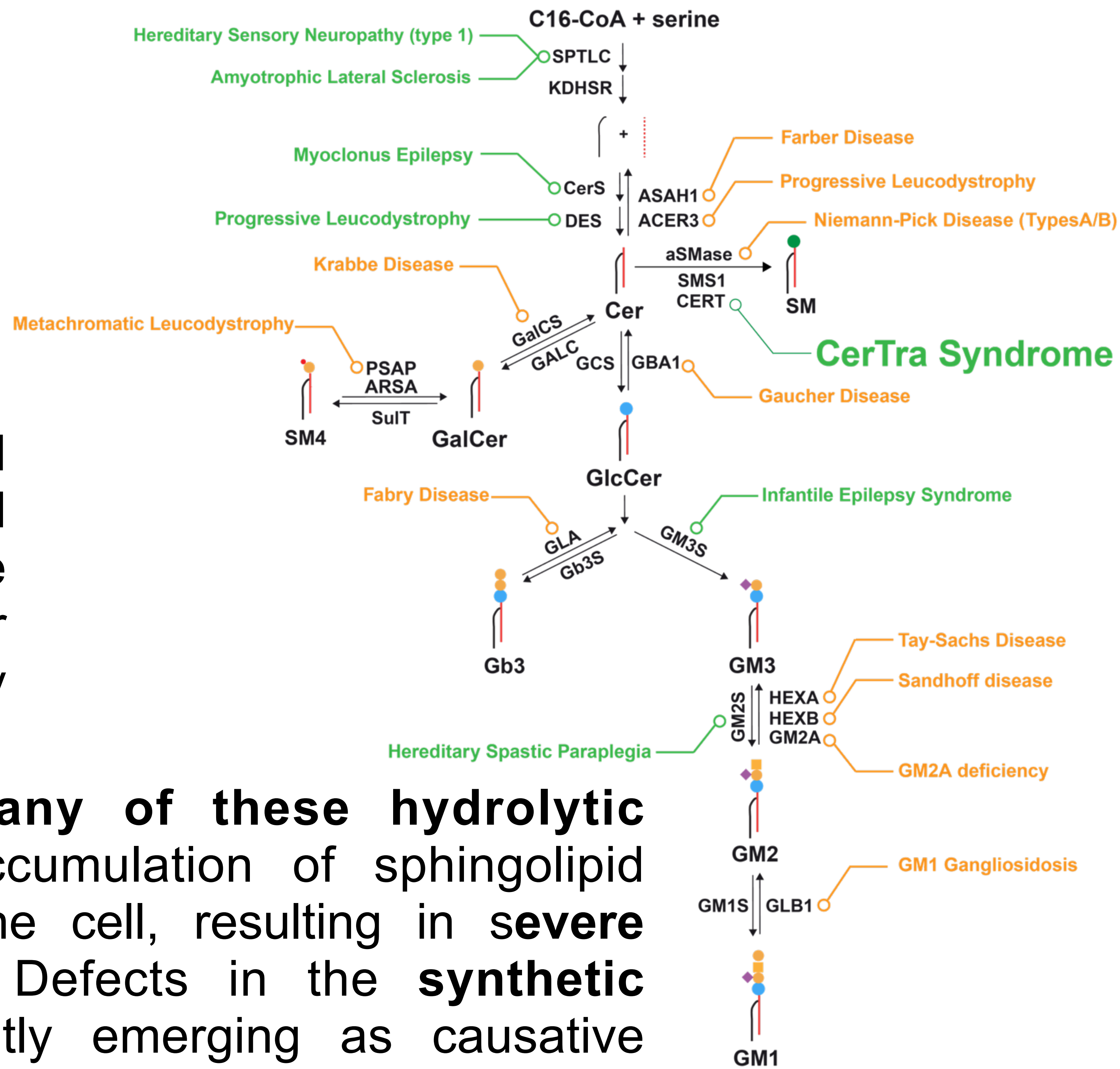


in vivo

ChTxB ShTxB1a ShTxB2e



Inborn errors of sphingolipid metabolism

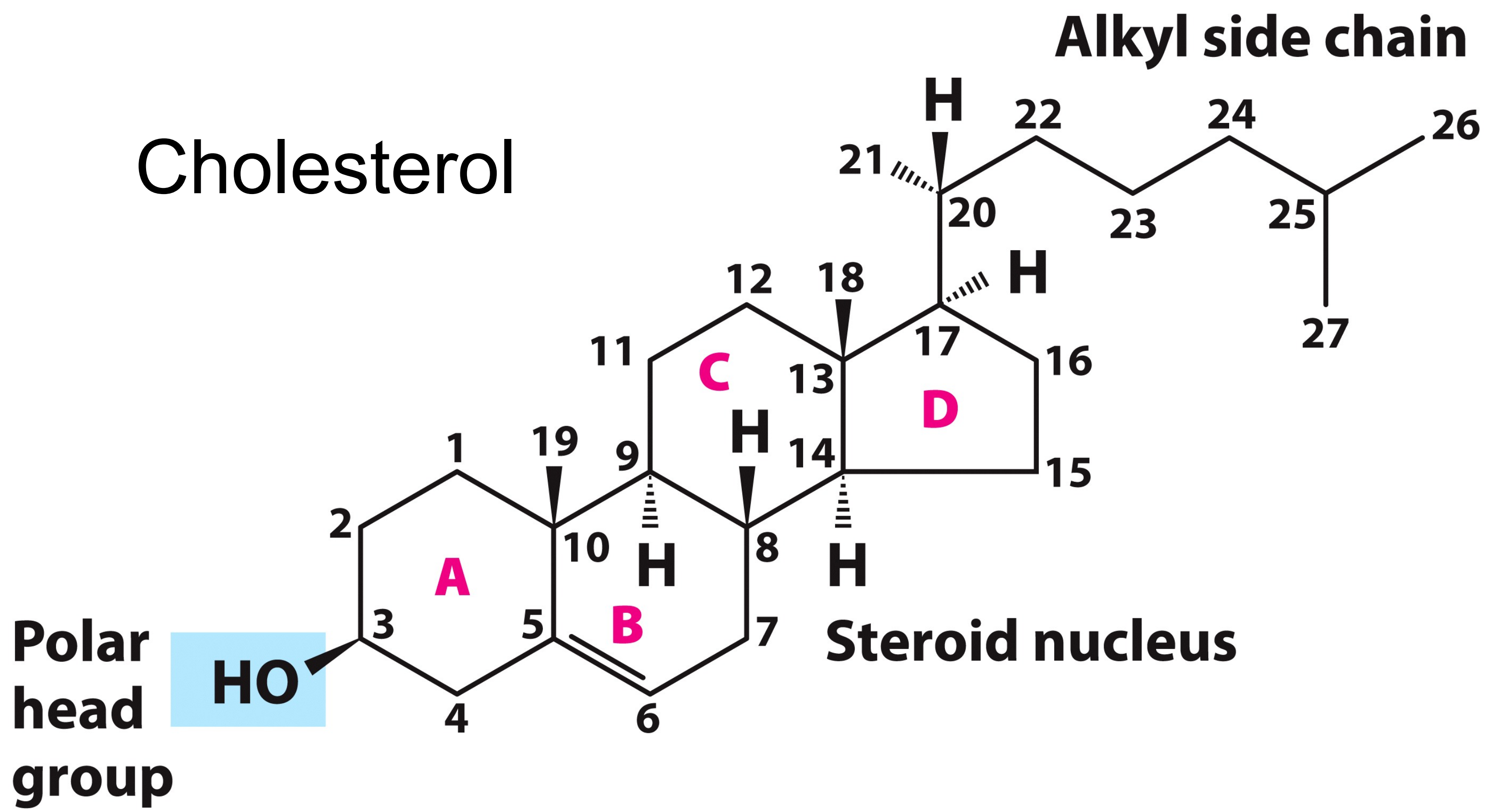


Sphingolipids are degraded by a set of lysosomal enzymes that catalyze the stepwise dismantling of their head groups, ultimately yielding sphingoid bases.

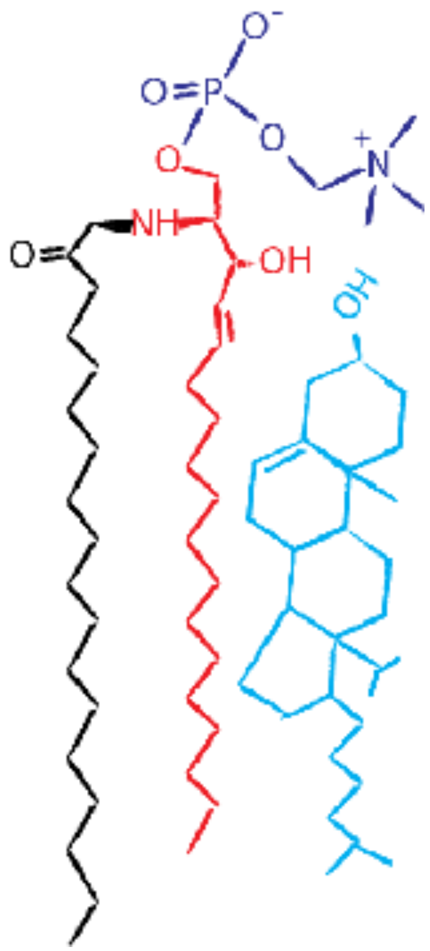
Inherited defects in many of these hydrolytic enzymes lead to the accumulation of sphingolipid degradation products in the cell, resulting in **severe medical consequences**. Defects in the **synthetic pathway** are more recently emerging as causative factors in **neurodevelopmental** disorders.

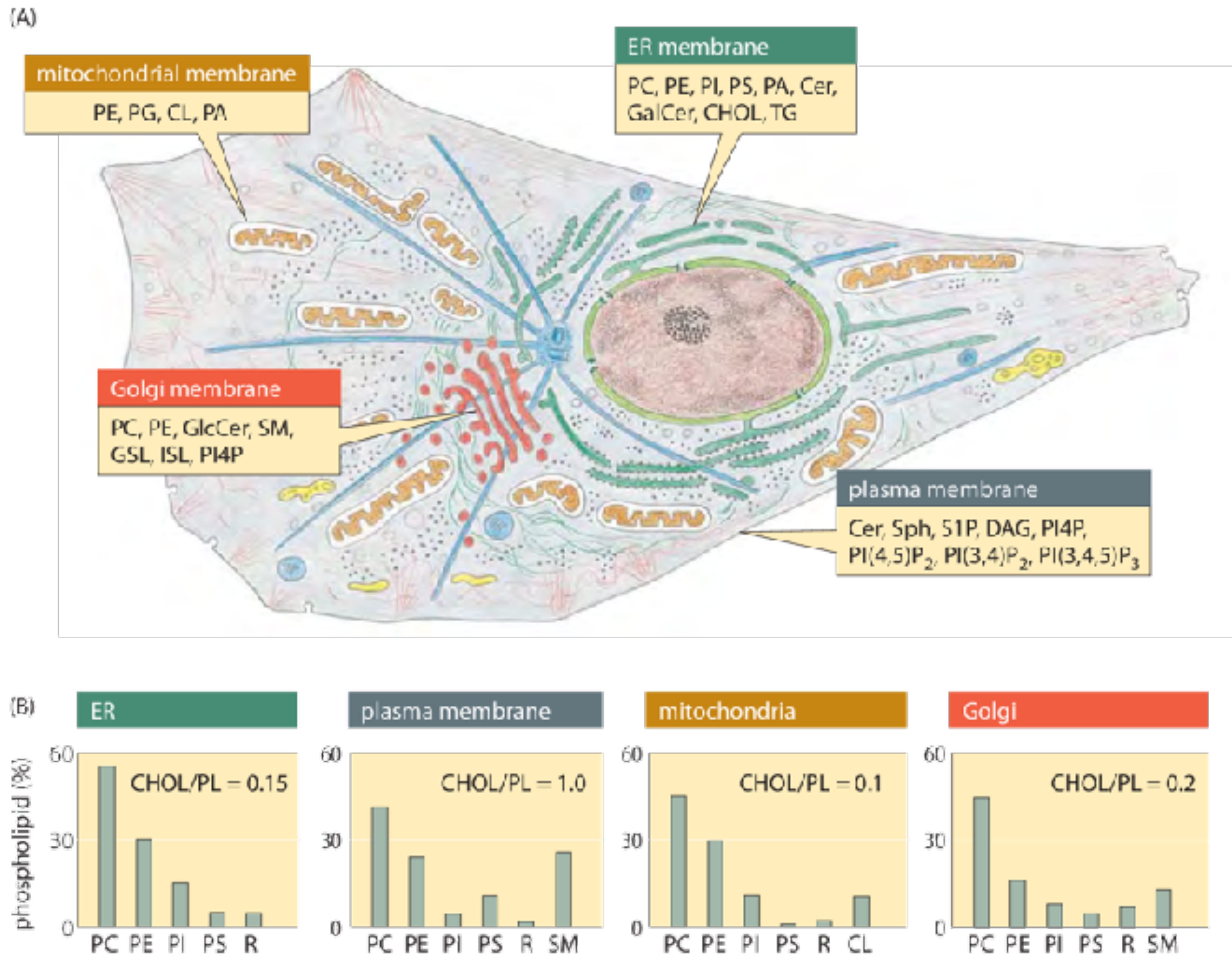
Sterols

Sterols are present in the membranes of most eukaryotic cells. They consist of a **rigid steroid nucleus containing four fused rings**, an alkyl side chain of 8 carbons, and a single hydrophilic hydroxyl group attached to C-3 of ring A. The steroid nucleus is nearly planar, and the molecule efficiently **packs with the acyl chains of membrane glycerophospholipids and sphingolipids**. The overall length of the molecule is similar to that of a 16-carbon fatty acid in its extended form.



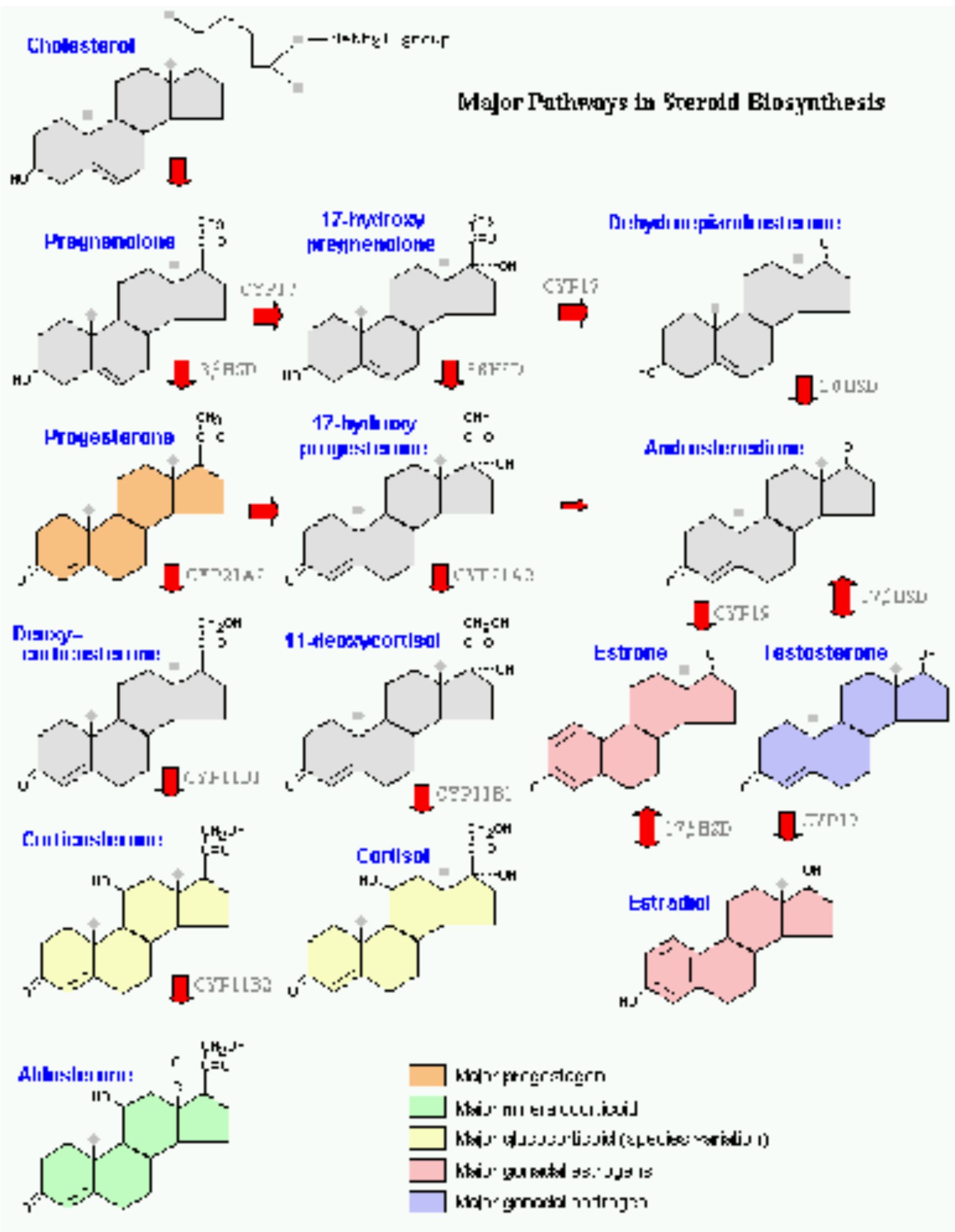
Cholesterol gradient

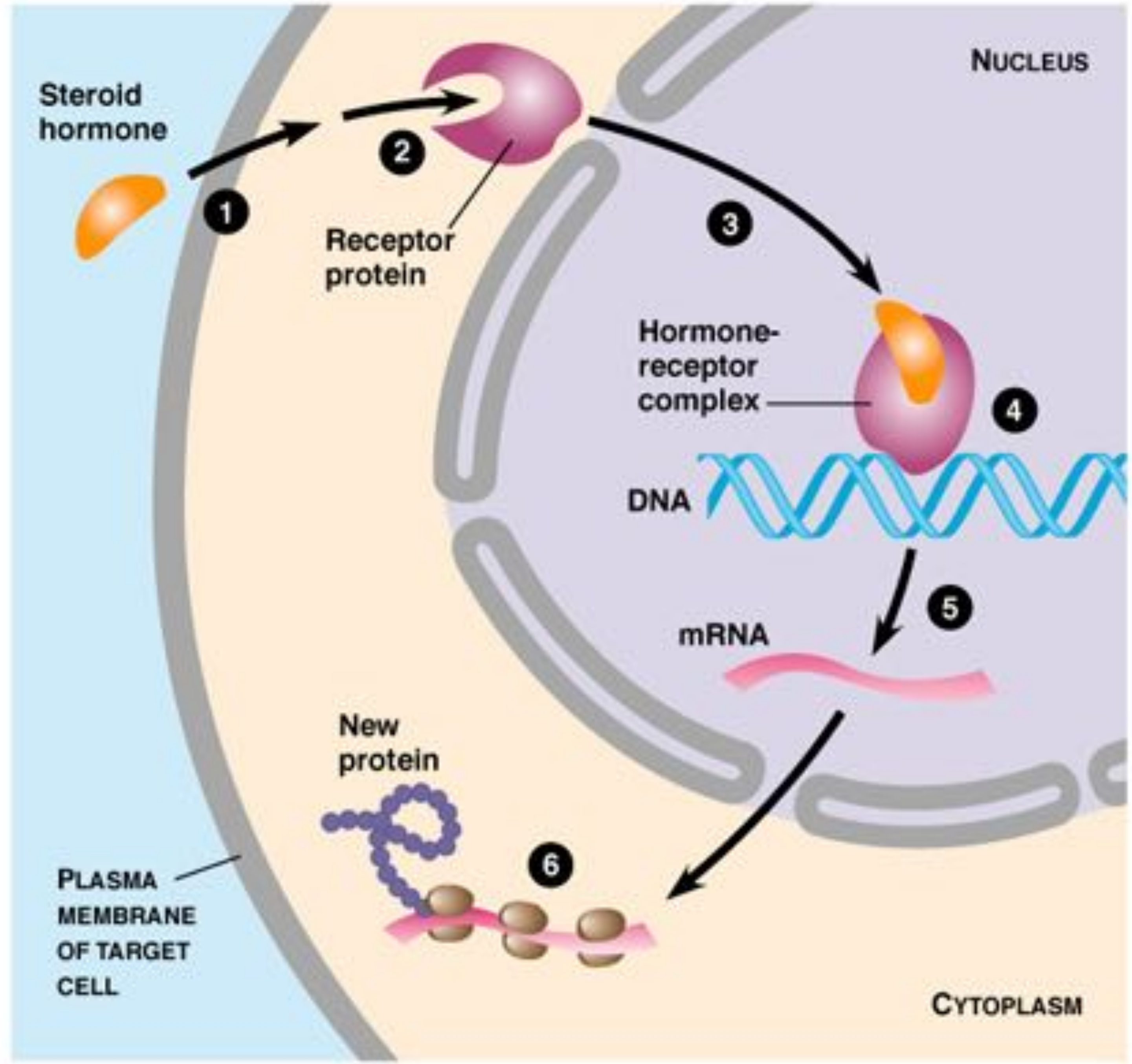




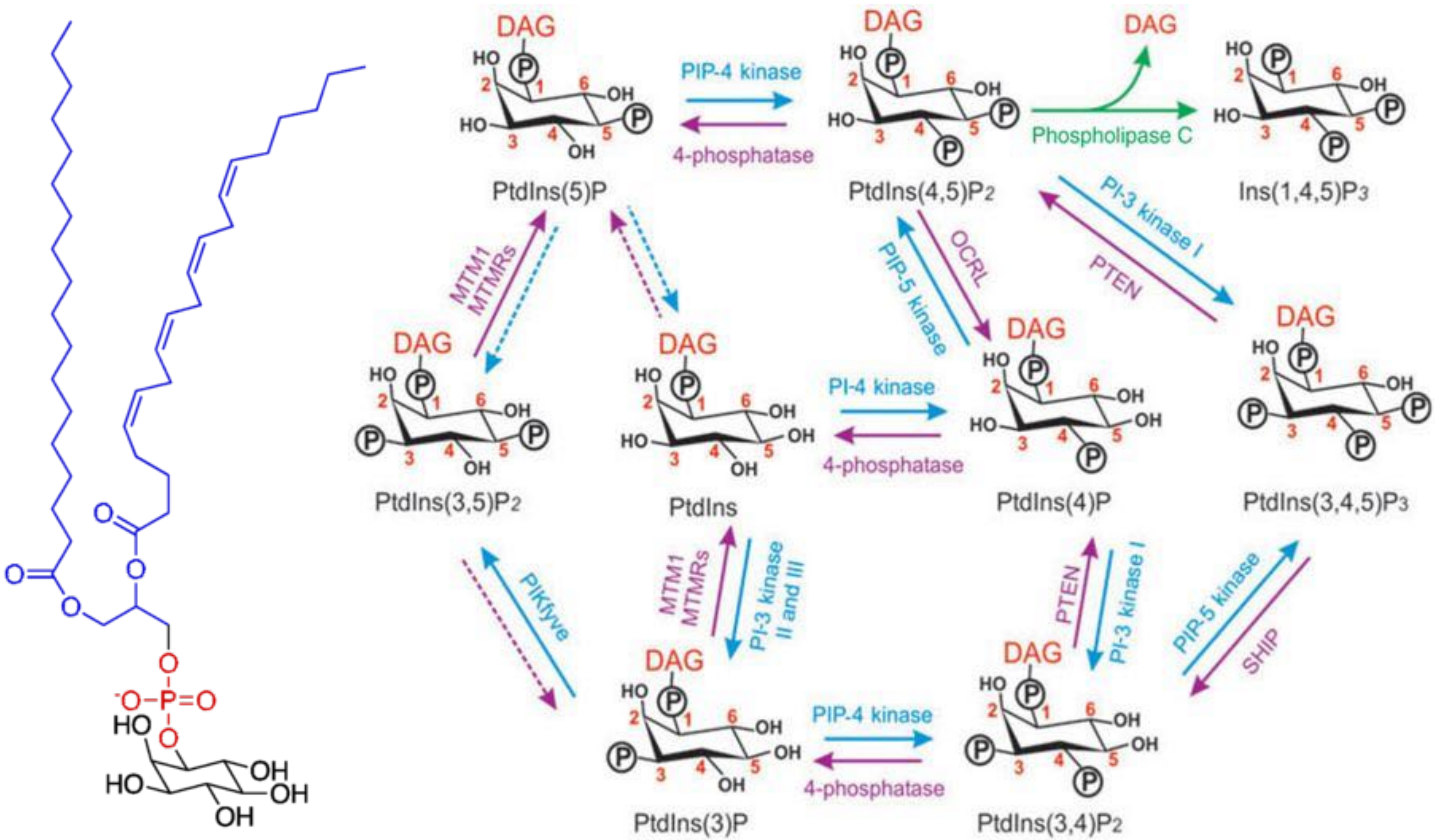
Sphingolipids organise intrabilayer interactions with cholesterol.

Bioactive Lipids - Steroid hormones

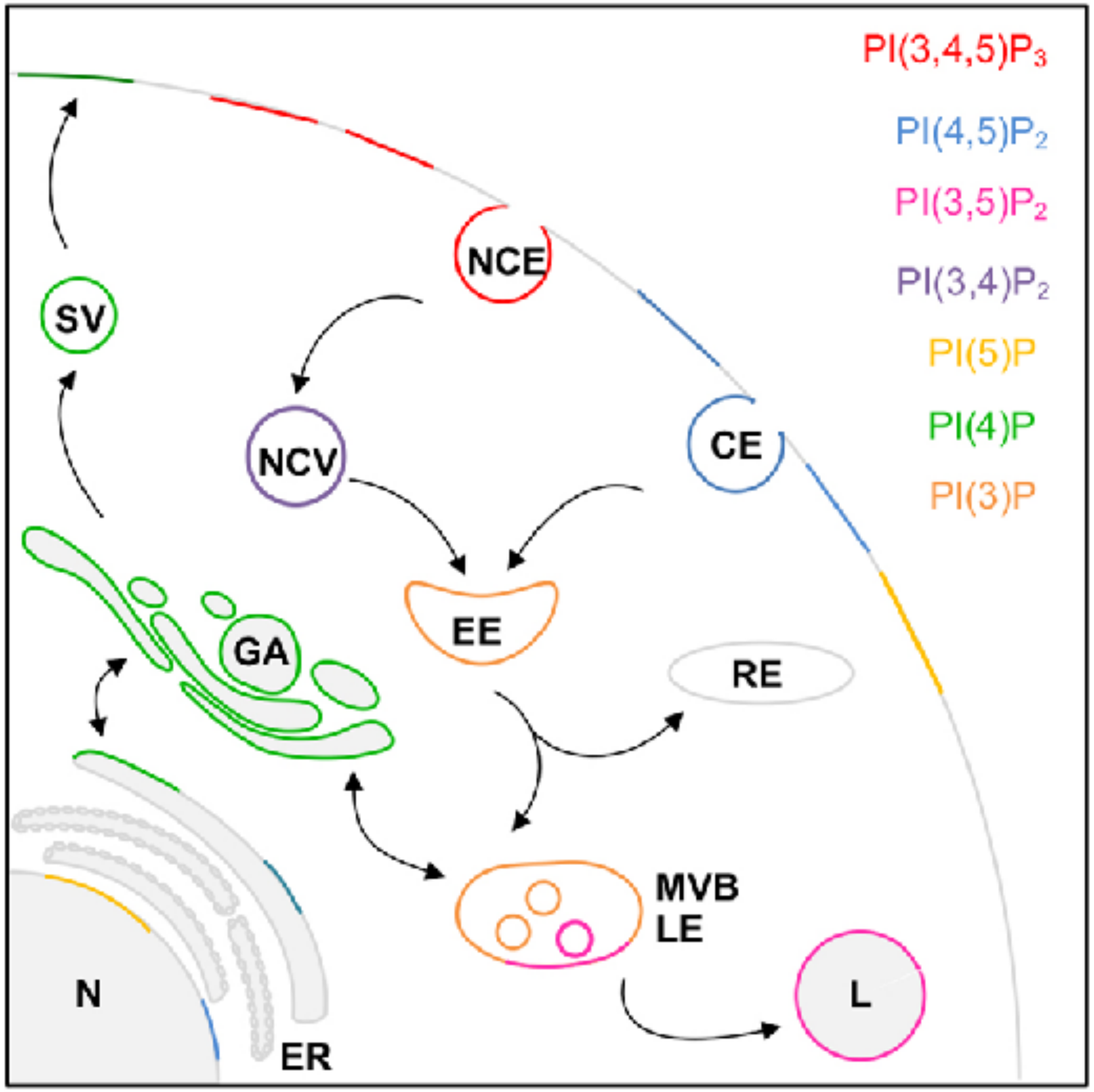




Bioactive Lipids - Phosphoinositides



Bioactive Lipids - Phosphoinositides

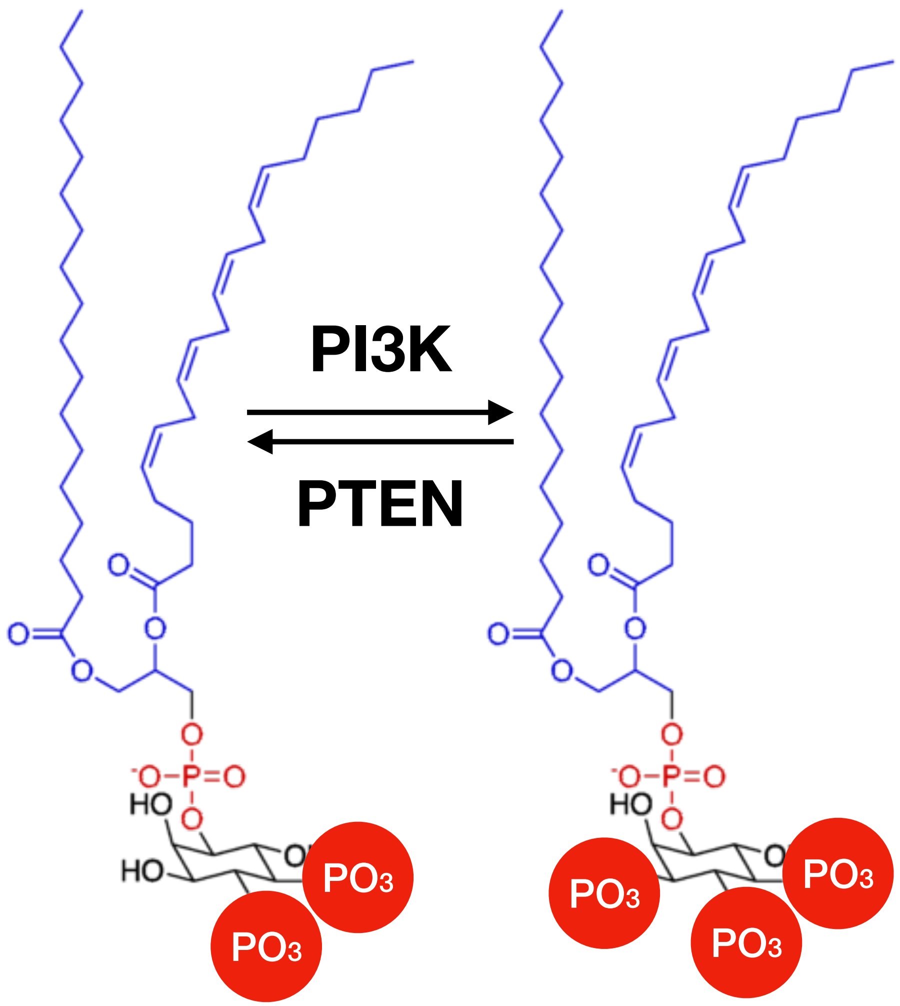


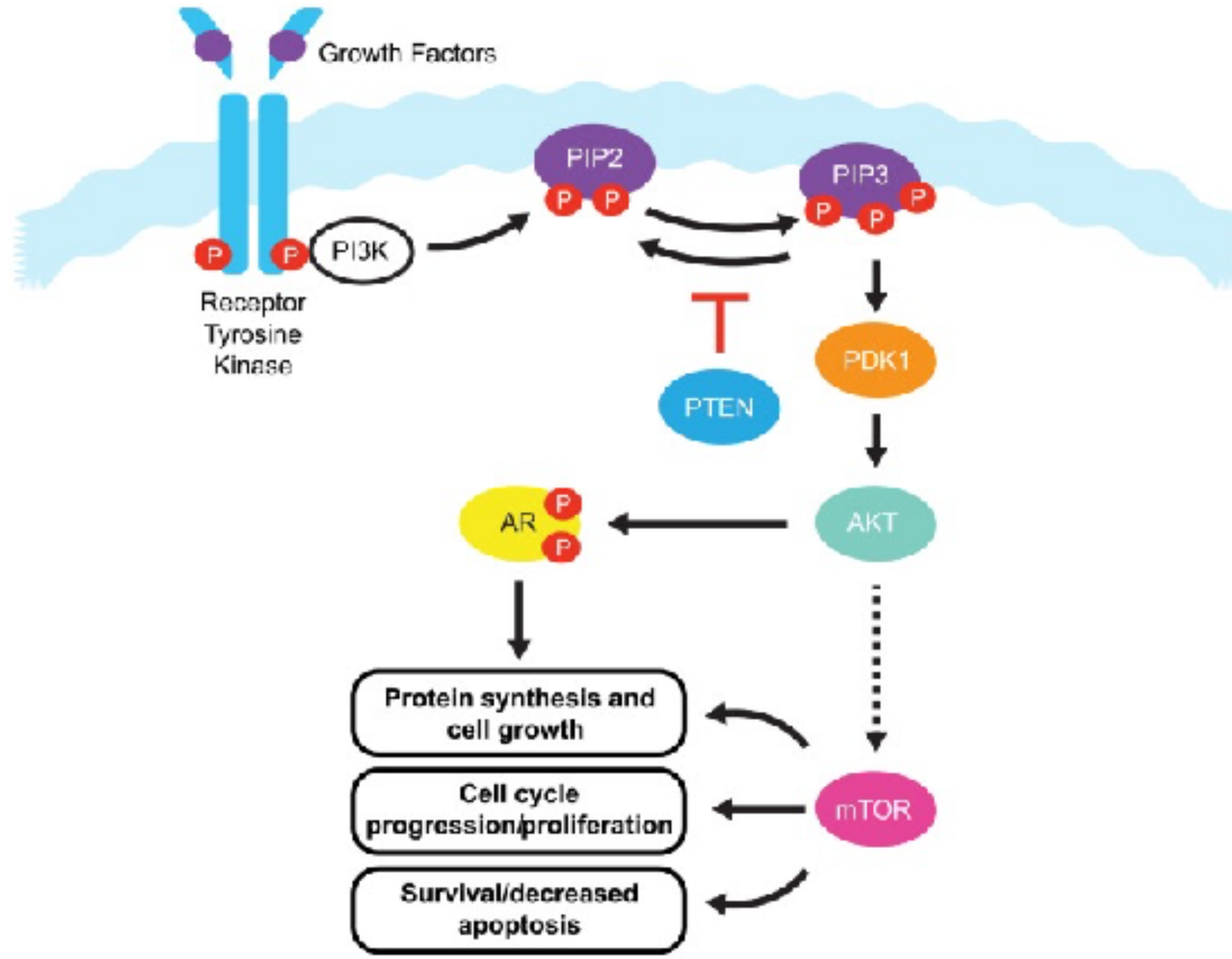
Different phosphoinositides populate the membranes of **specific intracellular organelles**.

Different phosphoinositides are recognised by **specific protein domains** that drive the recruitment of cytosolic proteins to the cytosolic membrane aspects where a given phosphoinositide is enriched.

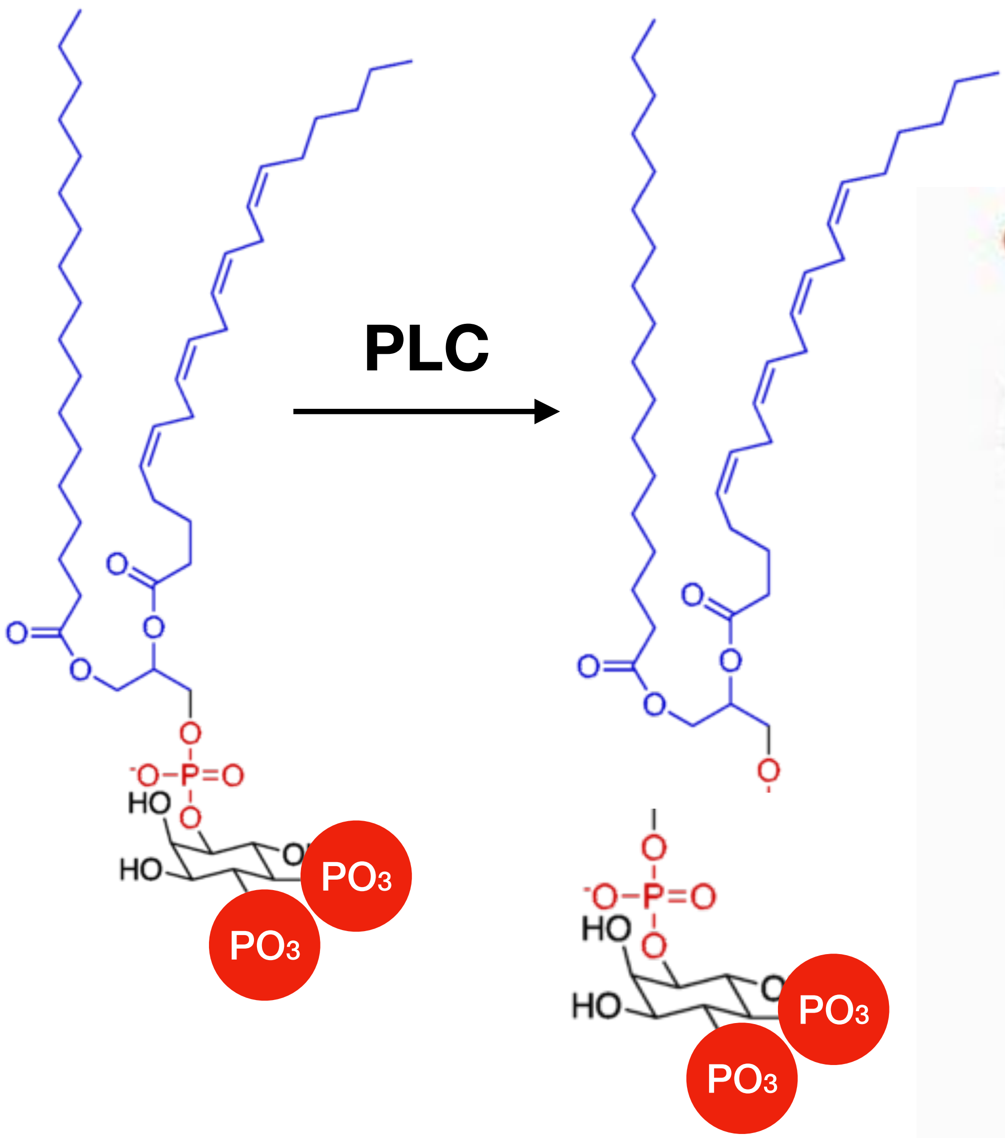
By this virtue phosphoinositides dictate **the identity of intracellular compartments**.

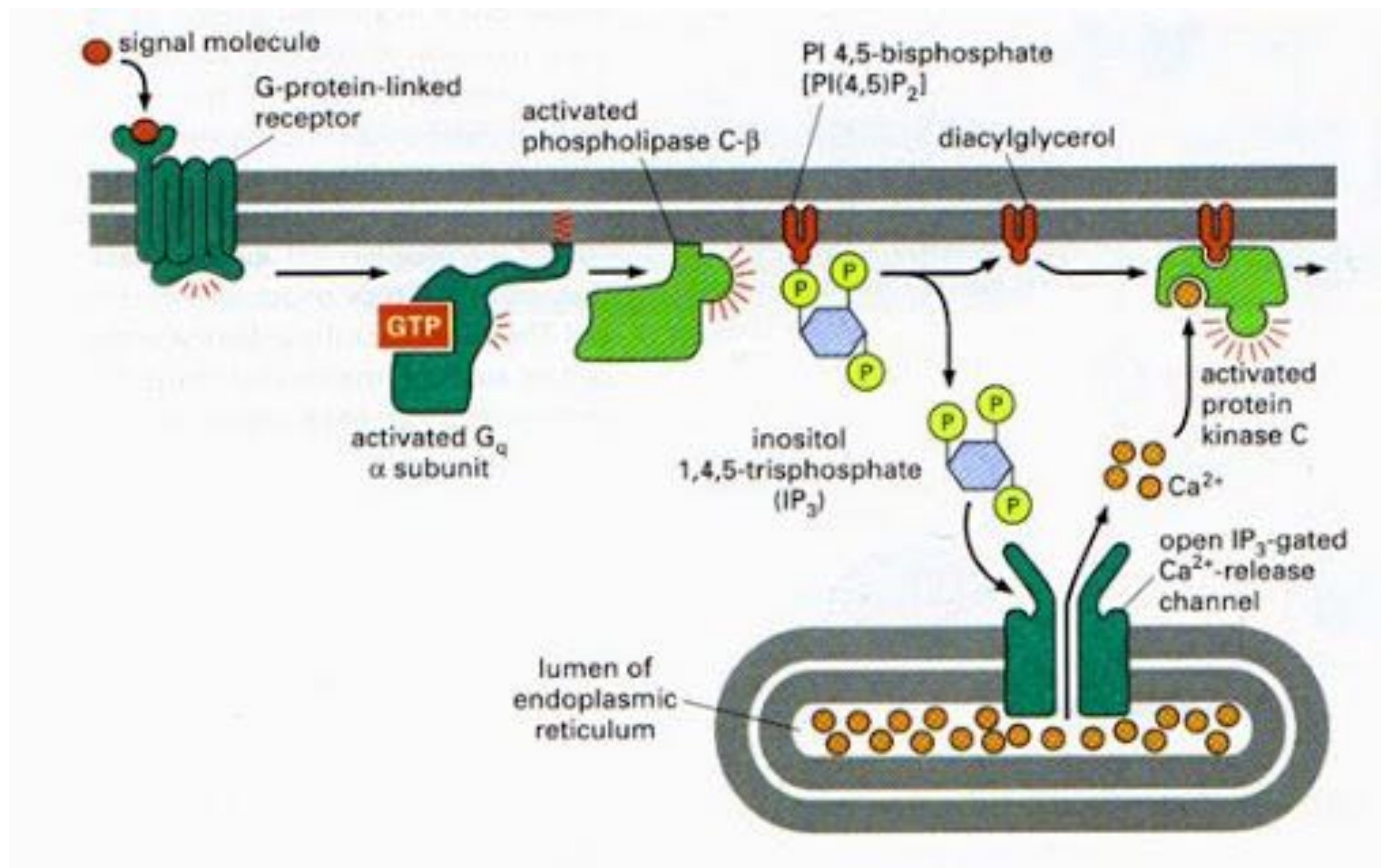
Bioactive Lipids - PtdIns3,4,5,P3



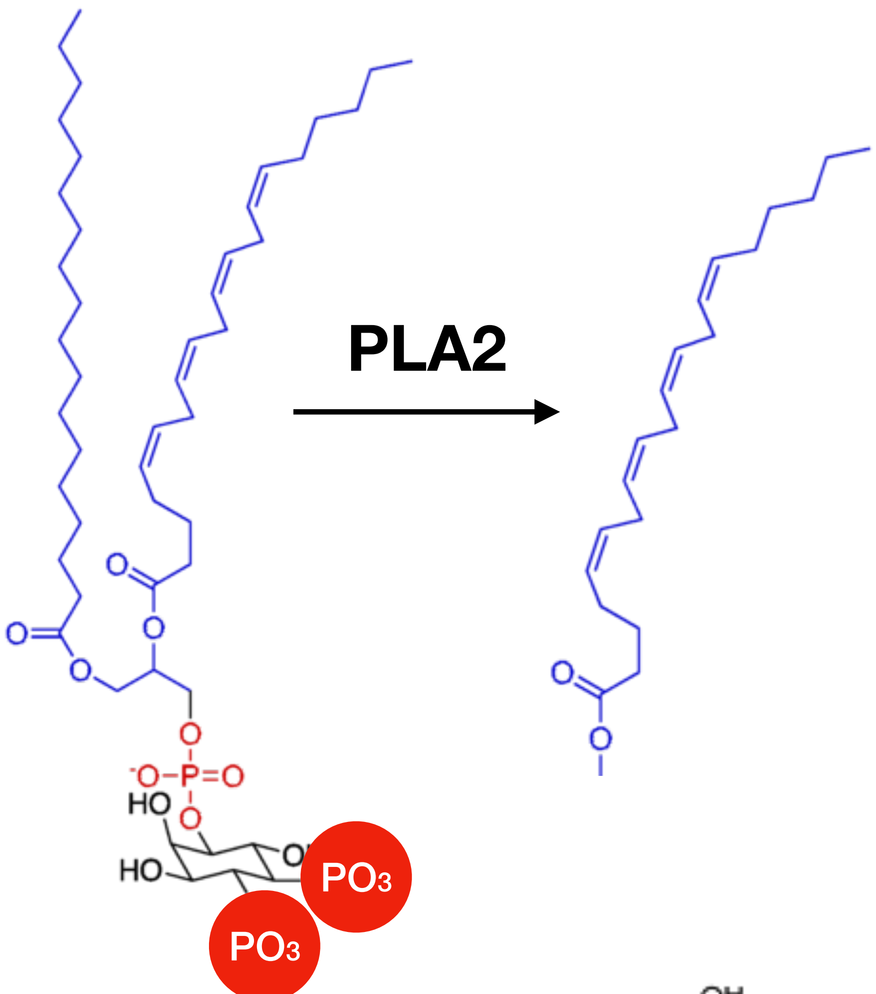


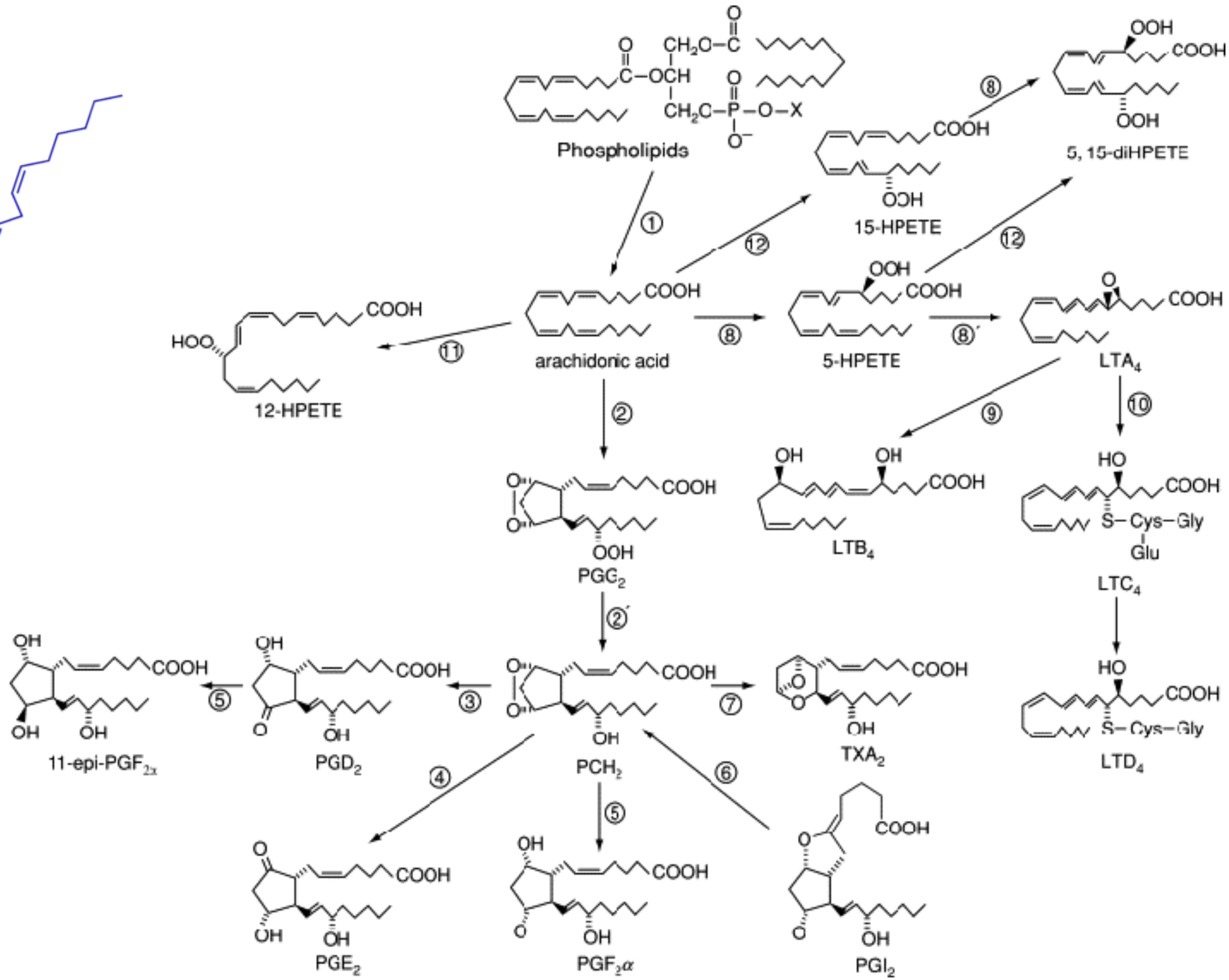
Bioactive Lipids - PLC



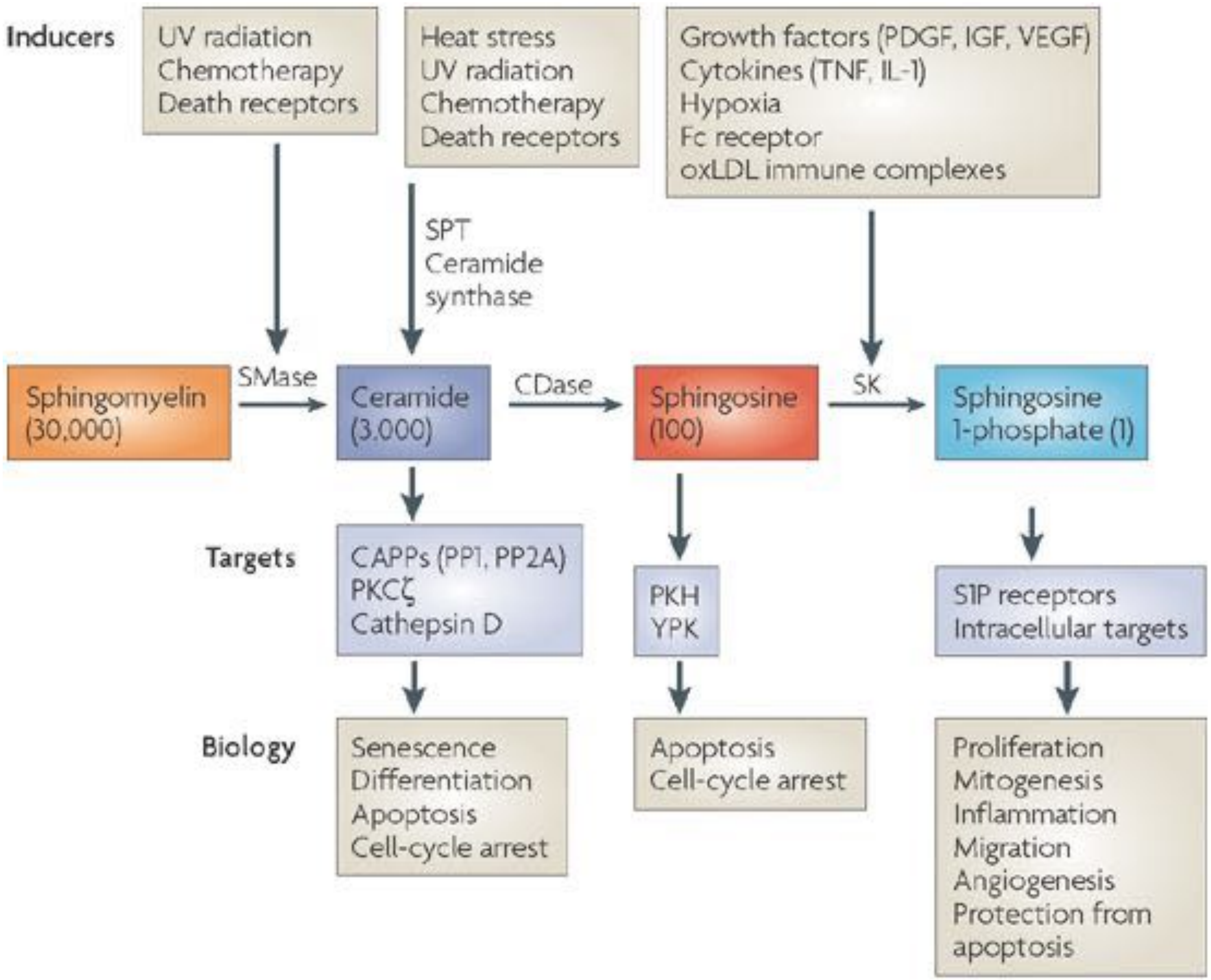


Bioactive Lipids - PLA2

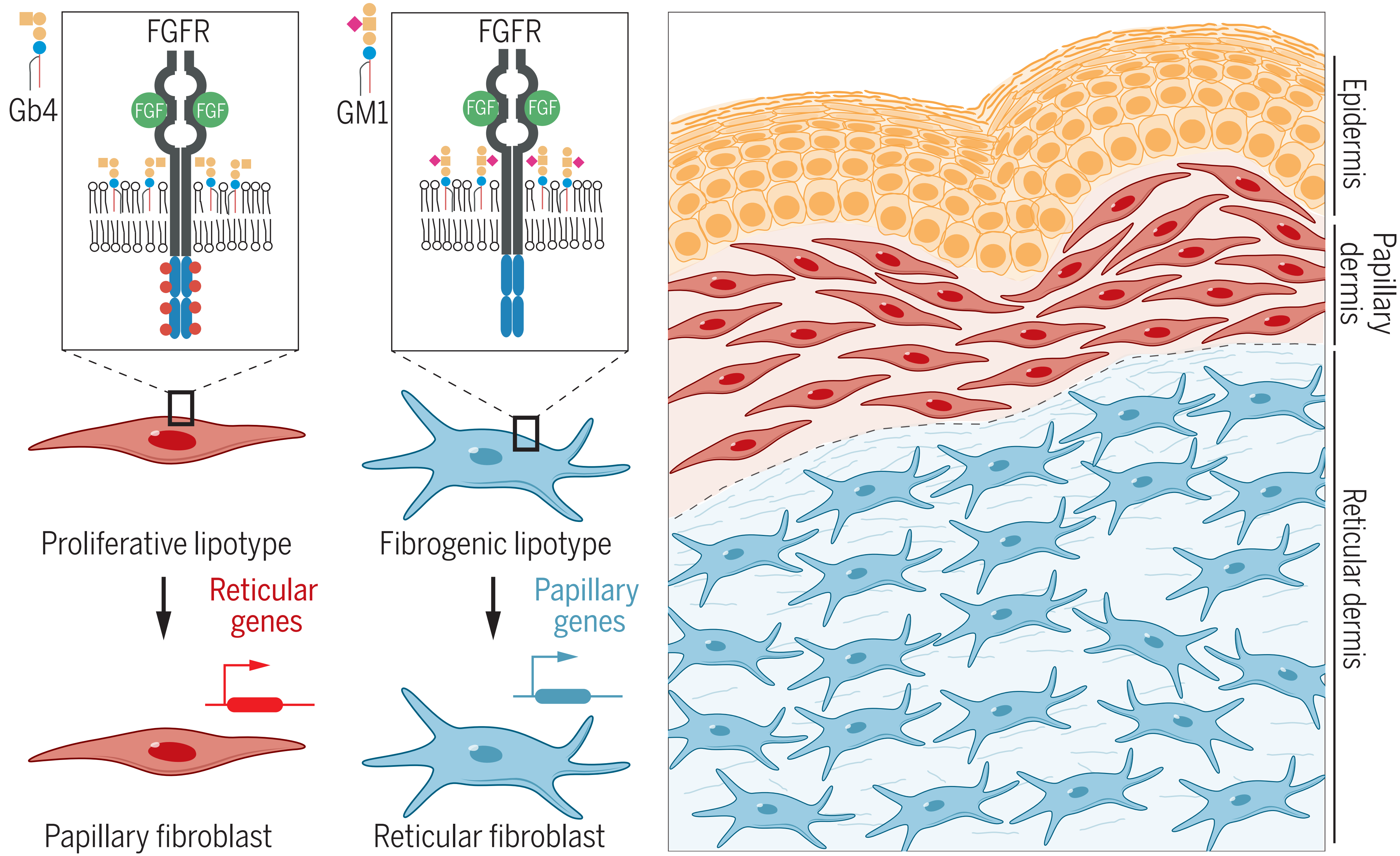




Bioactive Lipids - Sphingolipids



Bioactive Lipids - Sphingolipids



Lipids - Take Home Messages

- Lipids are non-water soluble constituents of living organisms
- Lipids may serve as energy stores and thermal insulators
- Lipids constitute the building blocks of biological membranes
- Lipids can serve as first and second messengers in signal transduction
- Lipids are structurally and functionally heterogeneous
- The three main classes of lipids in eukaryotes are glycerophospholipids, sphingolipids and sterols