

Metabolism of Sphingolipids

Sphingophospholipids

Glycosphingolipids

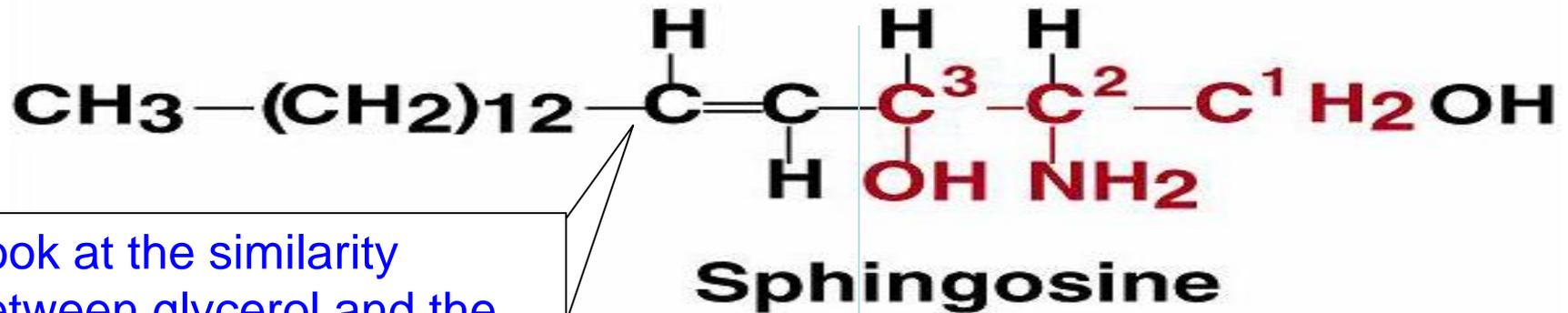
This class of lipids is named according to the name of alcohol that form the backbone which is **sphingosine** instead of glycerol.

It includes

Sphingophospholipids: sphingosine is joined to **phosphate**

Glycosphingolipids: sphingosine joined to **carbohydrate**

Sphingosine; Amino Alcohol



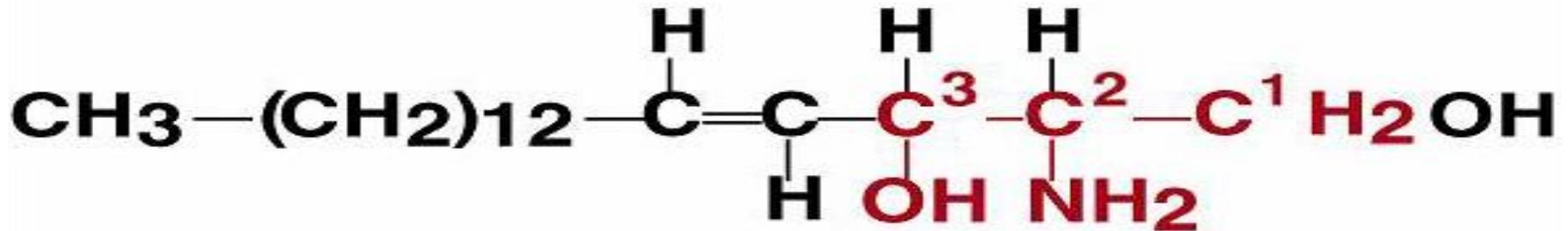
Look at the similarity between glycerol and the first three atoms of sphingosine.

This is **sphingosine**. It is a long chain amino alcohol (the suffix -ine). Describe its structure! How many carbon atoms? What are the functional groups?

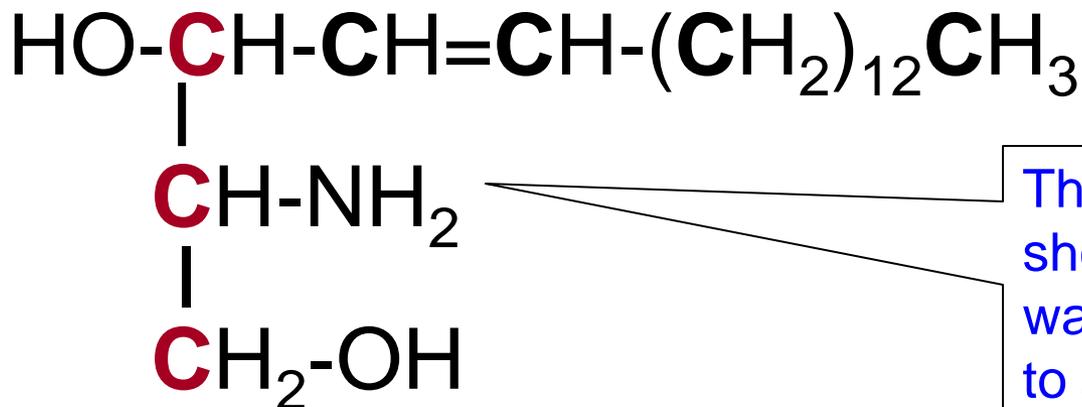
branched
ups
to hydroxyl
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n 4 and 5



Sphingosine; Amino Alcohol

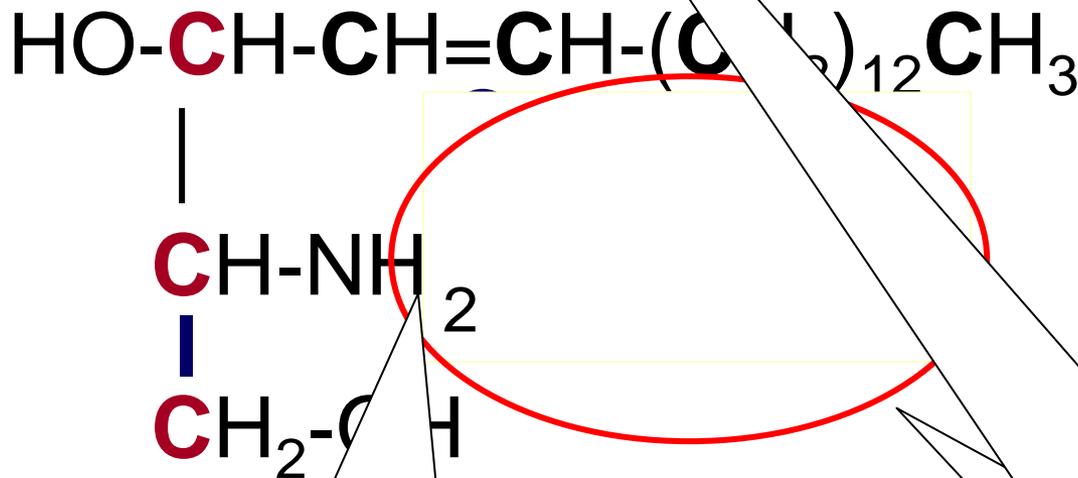


Sphingosine



This is **sphingosine** again shown in a different way. In this way it looks like glycerol joined to a long hydrocarbon chain. Similar to monoacylglycerol

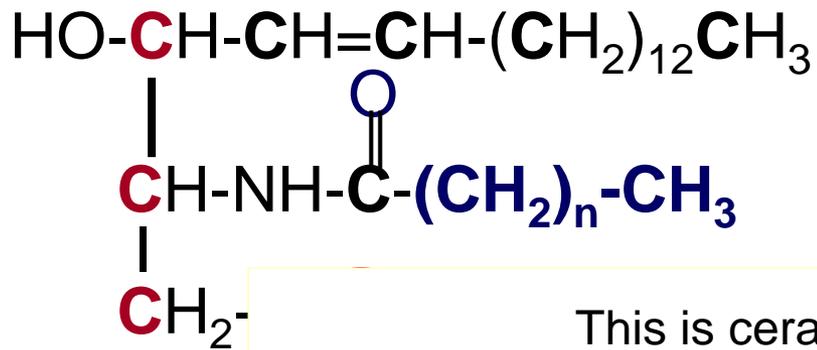
Ceramide: Fatty Acid joined to Sphingosine



What do we call the bond that is formed between an amino group and a carboxyl group?

It is called amide bond. So the name Ceramide suggests that it contains amide bond

Sphingomyelin is Phosphocholine Ester of Ceramide

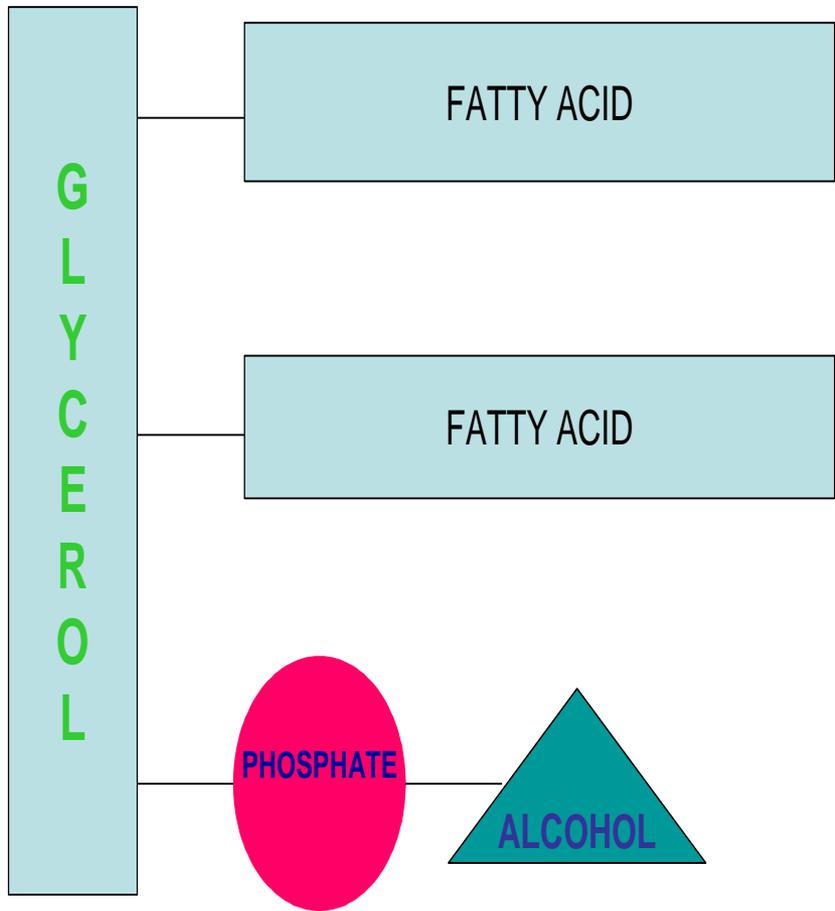


This is ceramide,
It is similar to diacylglycerol

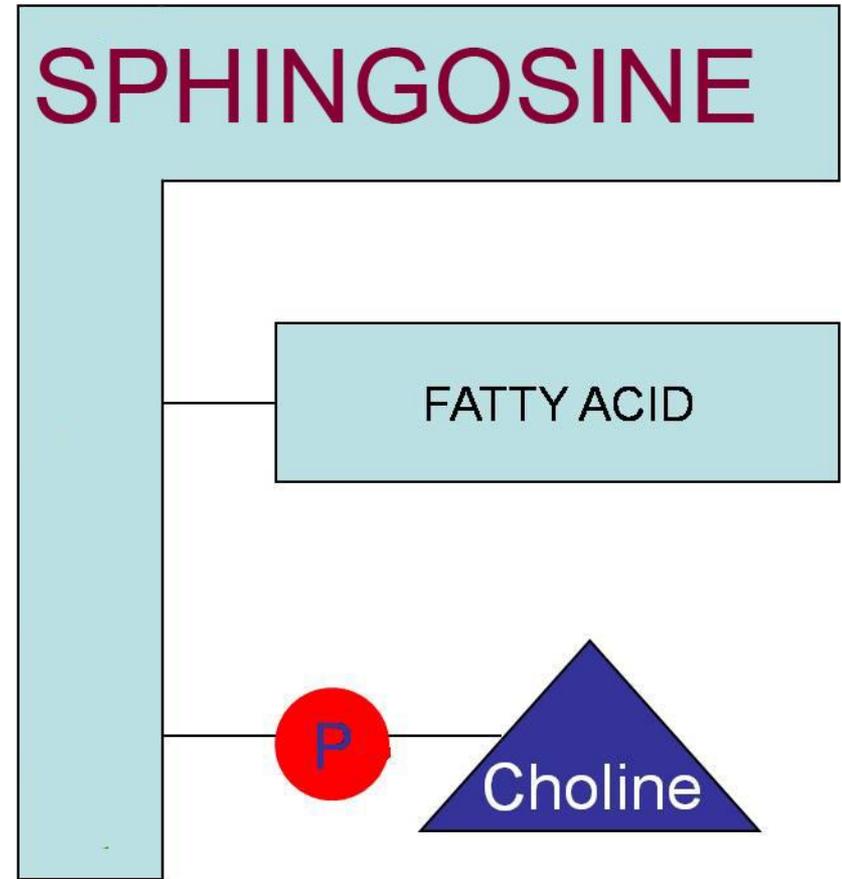
Therefore sphingomyelin is similar to
phosphatidylcholine

Adding phosphocholine to
Ceramide produces
sphingomyelin

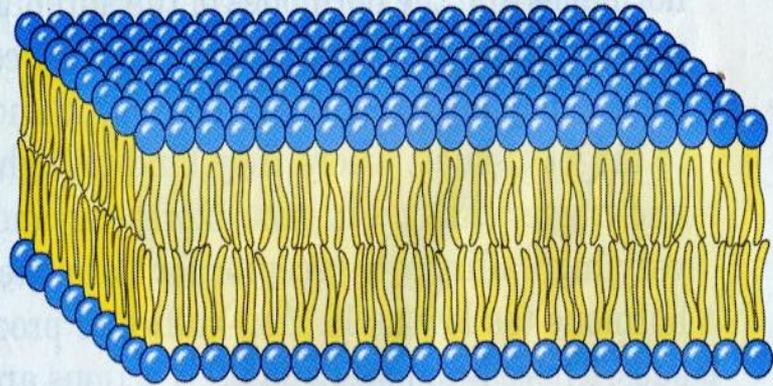
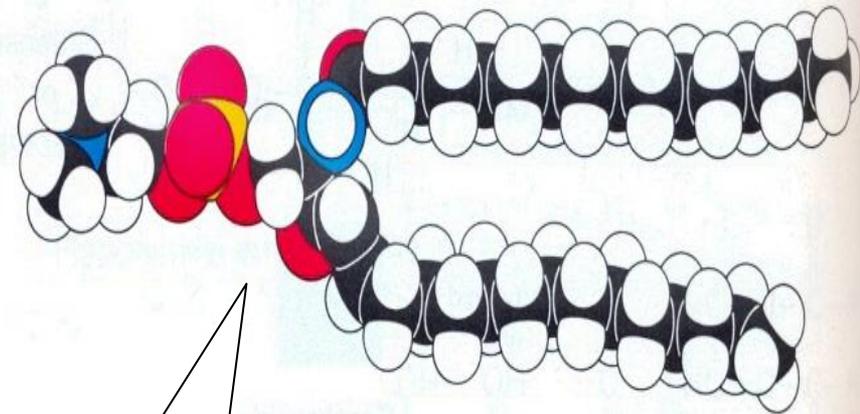
This is to compare the components of glycerophospholipids and sphingophospholipids



PHOSPHOACYLGLYCEROL

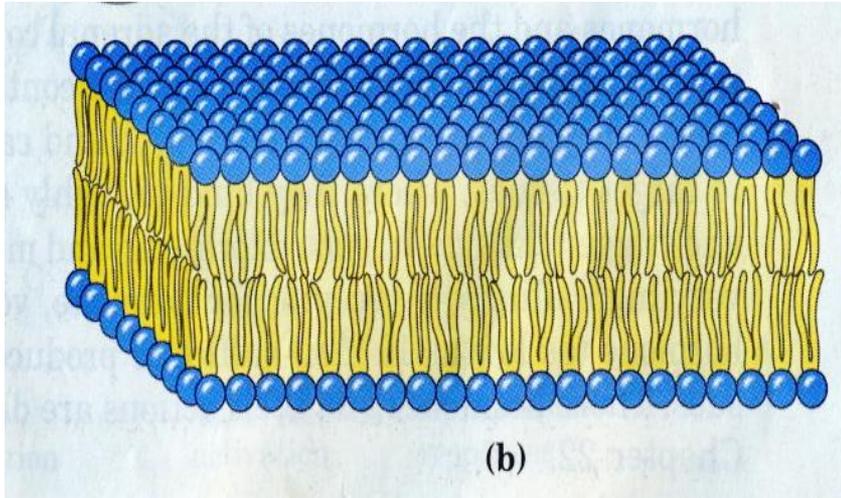


Sphingophospholipids

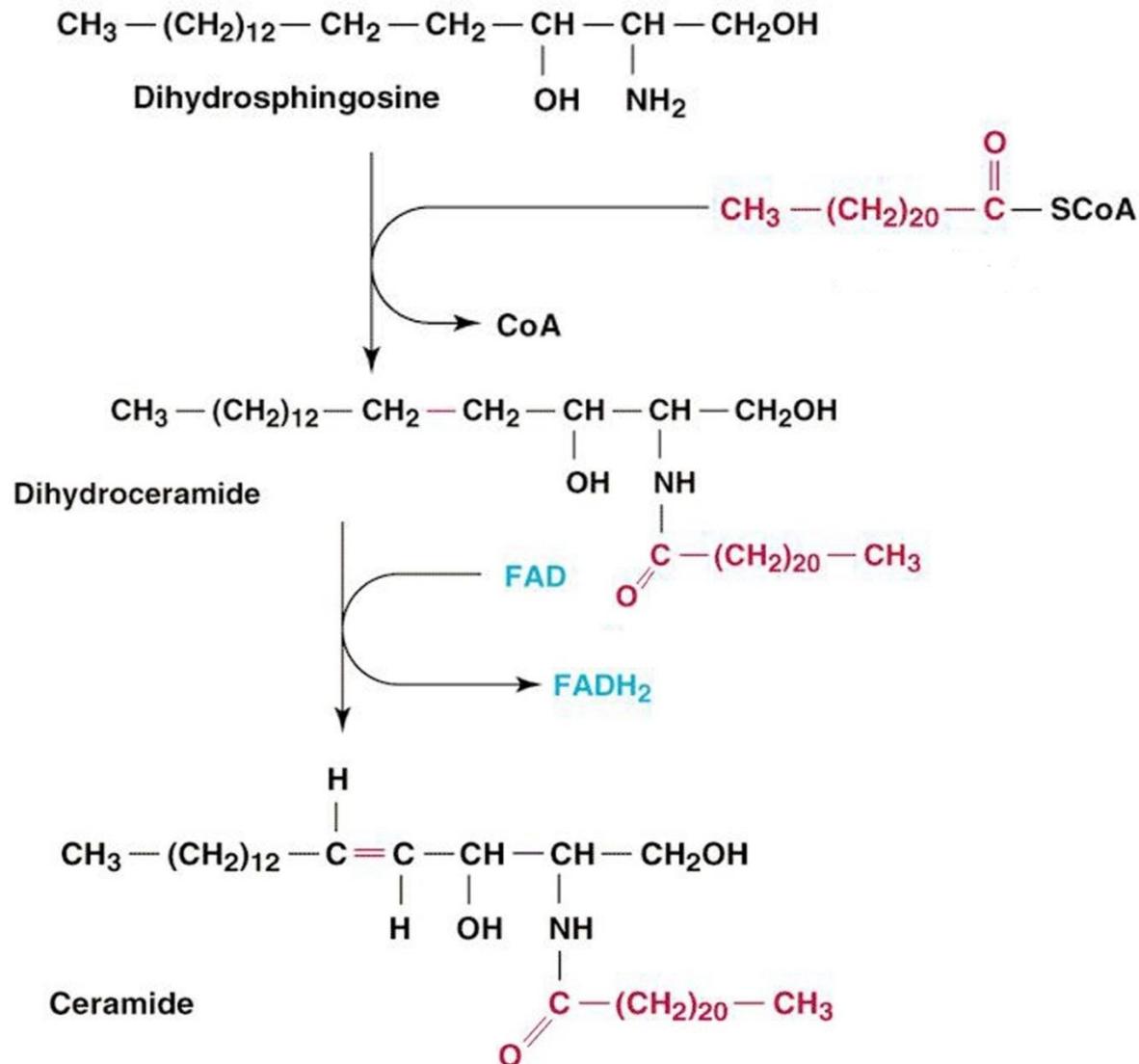


(b)

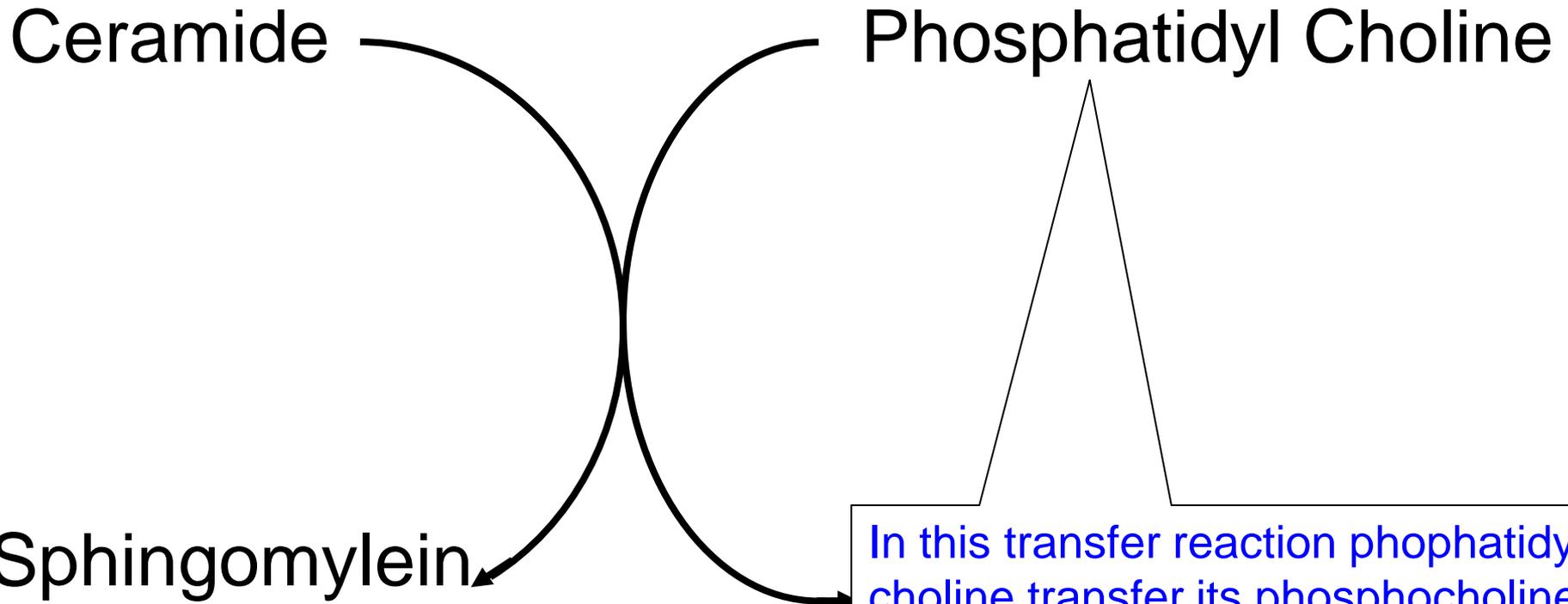
So sphingomyelin is an amphipathic molecule, it can form lipid bilayer, it is found in plasma membrane



Ceramide is formed then by transfer of fatty acid followed by introduction of double bond



Transfer Of Phosphocholine to Ceramide Produces **Sphingomyelin**



In this transfer reaction phosphatidyl choline transfer its phosphocholine group to Ceramide. What is the molecule that remains after giving phosphocholine

Glycolipids are Formed by Linking one or More Sugars to Ceramide

Ceramide +

-Glucose or Galactose →

Sugars or modified sugars are joined to ceramide to give different classes of glycolipids.

Notice that glycolipids contain **NO** Phosphate.

-Oligosaccharide →

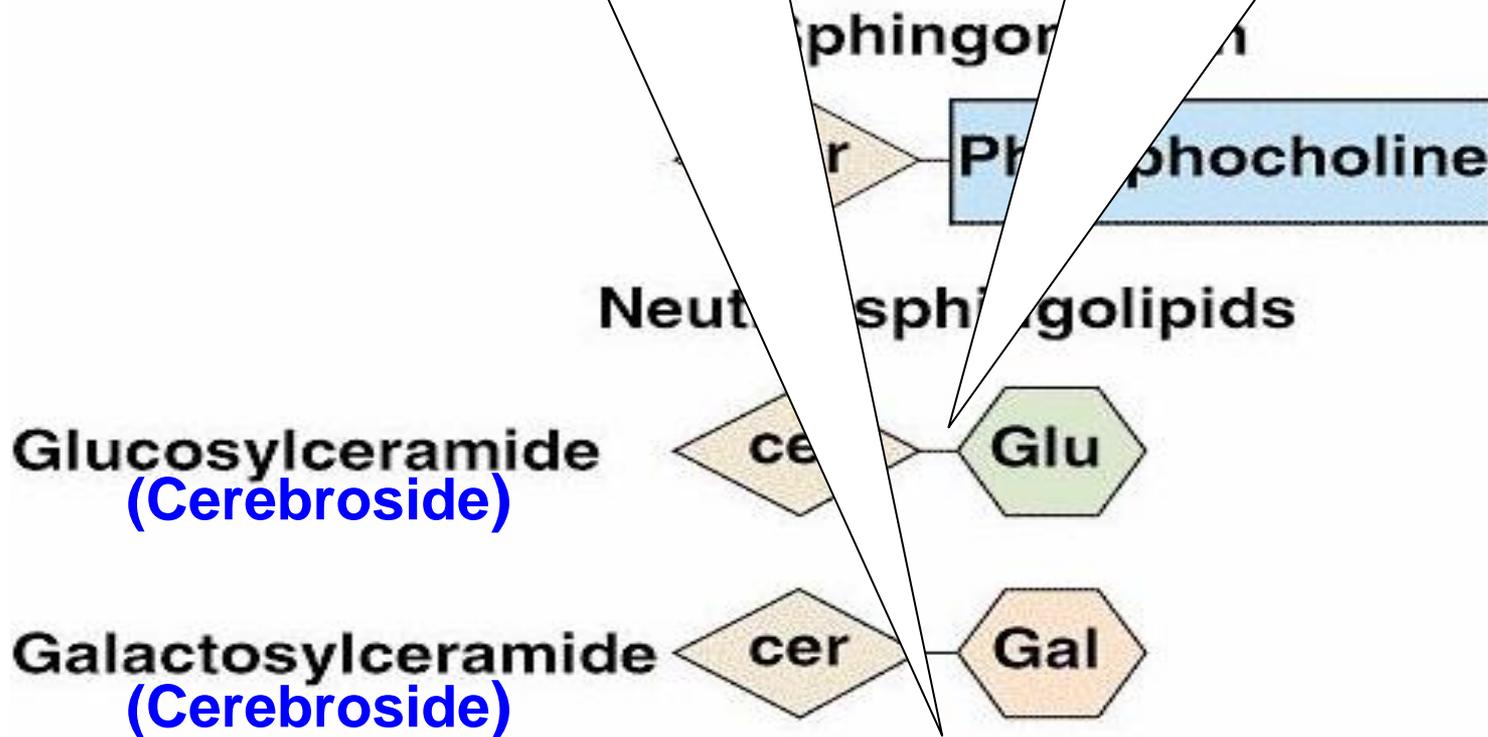
Globoside

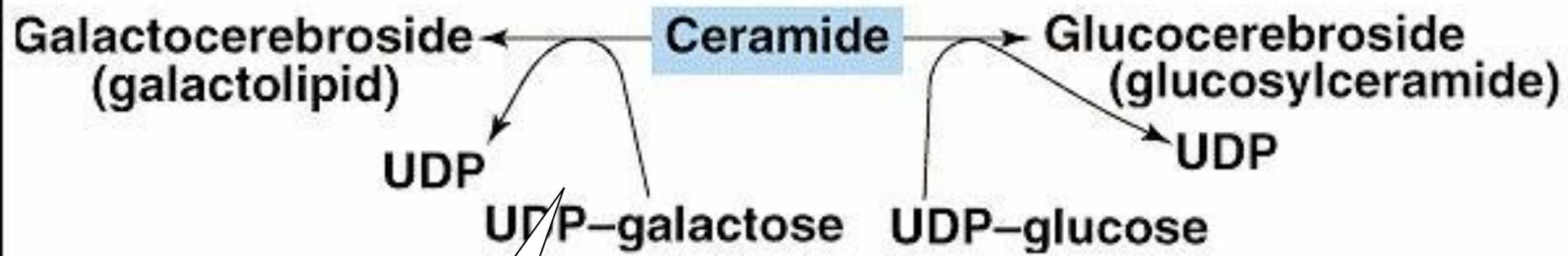
-Oligosaccharide with silalic acid → **Gangliosides**

-Sulfated Galactose → **Sulfoglycosphingolipids**

Sugars are added one at a time. In a specific order. By specific enzymes

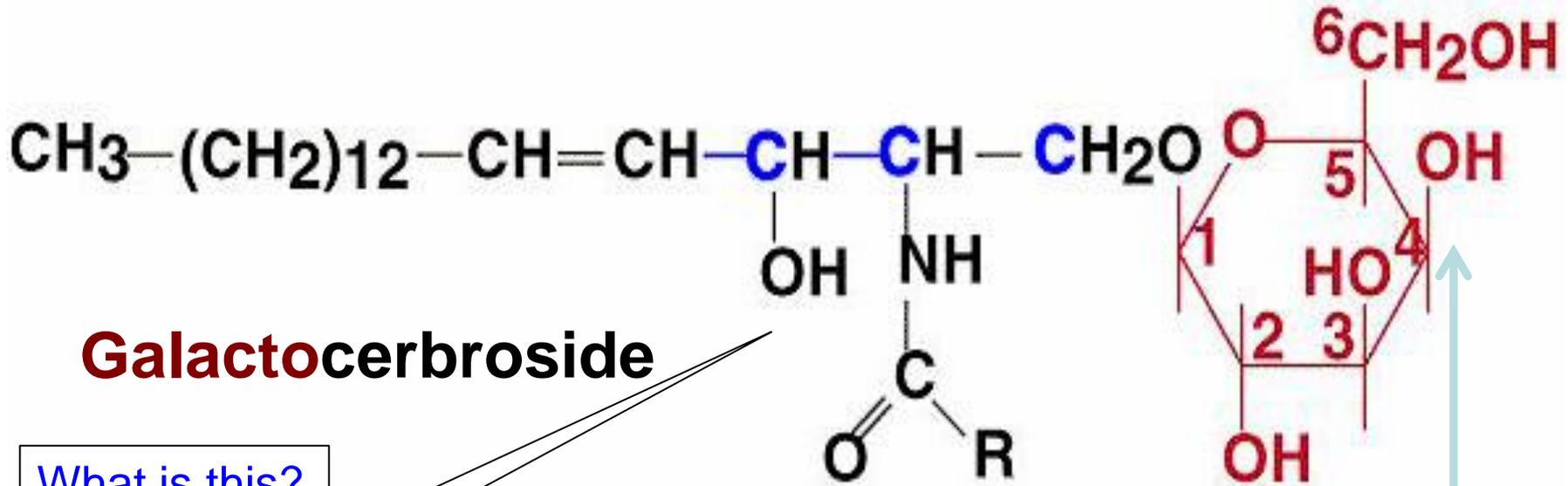
UDP glucose or UDP galactose donate the sugar to ceramide
The type of sugar is determined by the specificity of the enzyme





Addition of galactose to ceramide

Or glucose



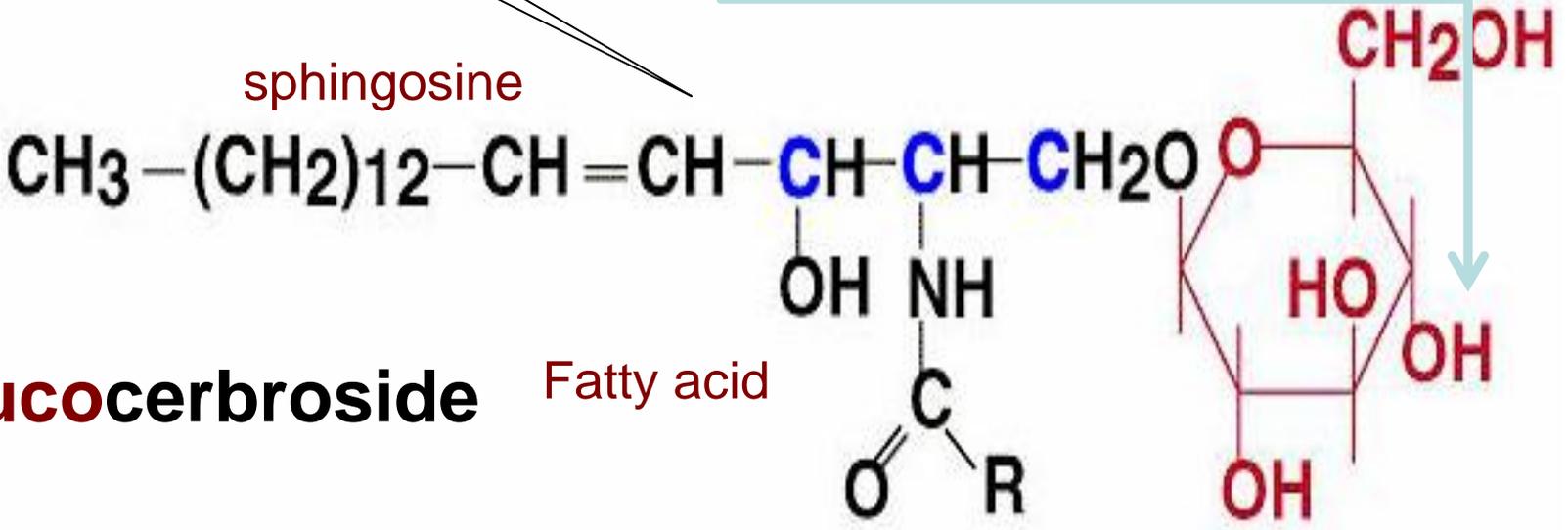
Galactocerebroside

What is this?

What is this?

Notice that the difference is minor. Yet each sugar is added by a different enzyme

sphingosine



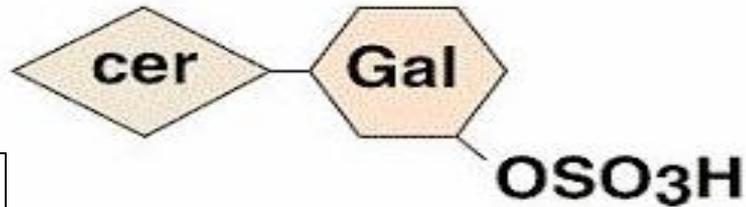
Glucocerebroside

Fatty acid

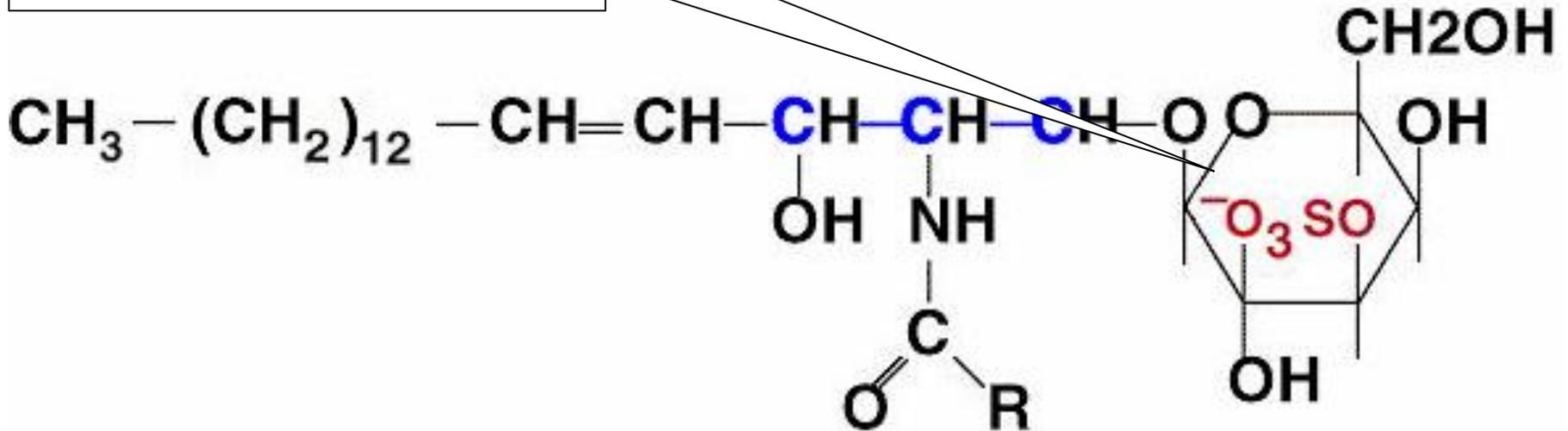
Transfer of Sulfate Group to Galactocerebroside Produces **Sulfogalactocerebroside** (Sulfatide)

Acid sphingolipids

Sulfatide



Notice that sulfate is acidic group, therefore it carries a negative charge?



Transfer of sialic acid (**N-Acetyl Neuraminic Acid (NANA)**) produces Gangliosides

N-Acetylneuraminic Acid is 9 carbon acidic sugar

The active donor is **CMP- N-Acetylneuraminic Acid**

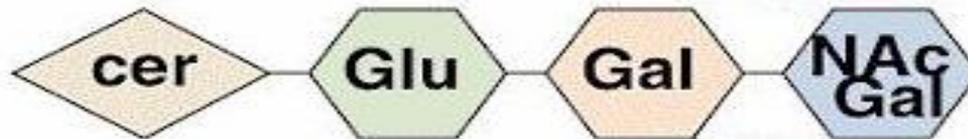
Gangliosides

GM3



NANA

GM2



NANA

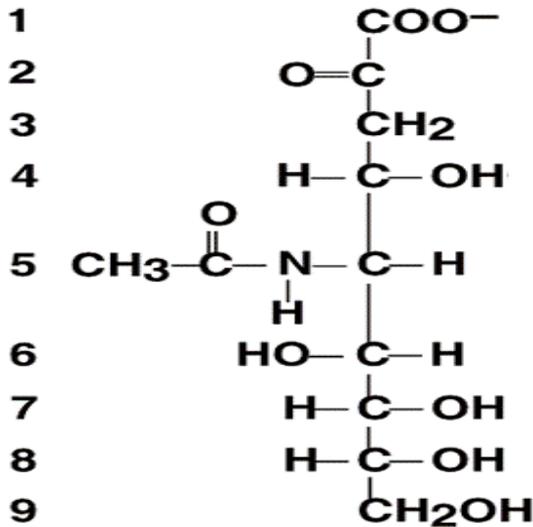
GM1



NANA

N-Acetylneuraminic Acid (NANA)

Carbon atom



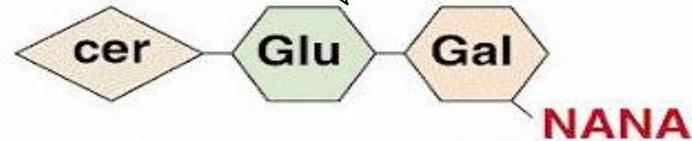
Open-chain form

Gangliosides are commonly identified by symbols like GM1, GM2....

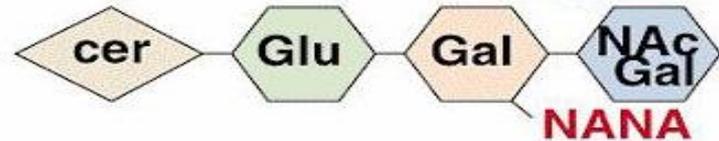
G stands for Gangliosides
M = Mono (number of sialic acid). D=Di
1,2 or 3 Refer to the specific sequence of oligosaccharide. Example 3= Glu-Gal

Gangliosides

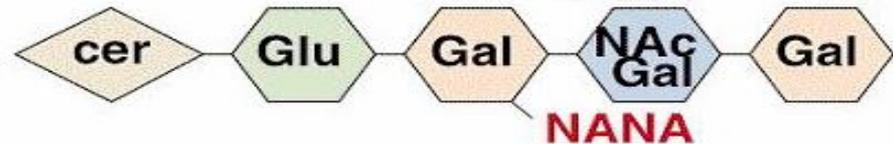
GM3



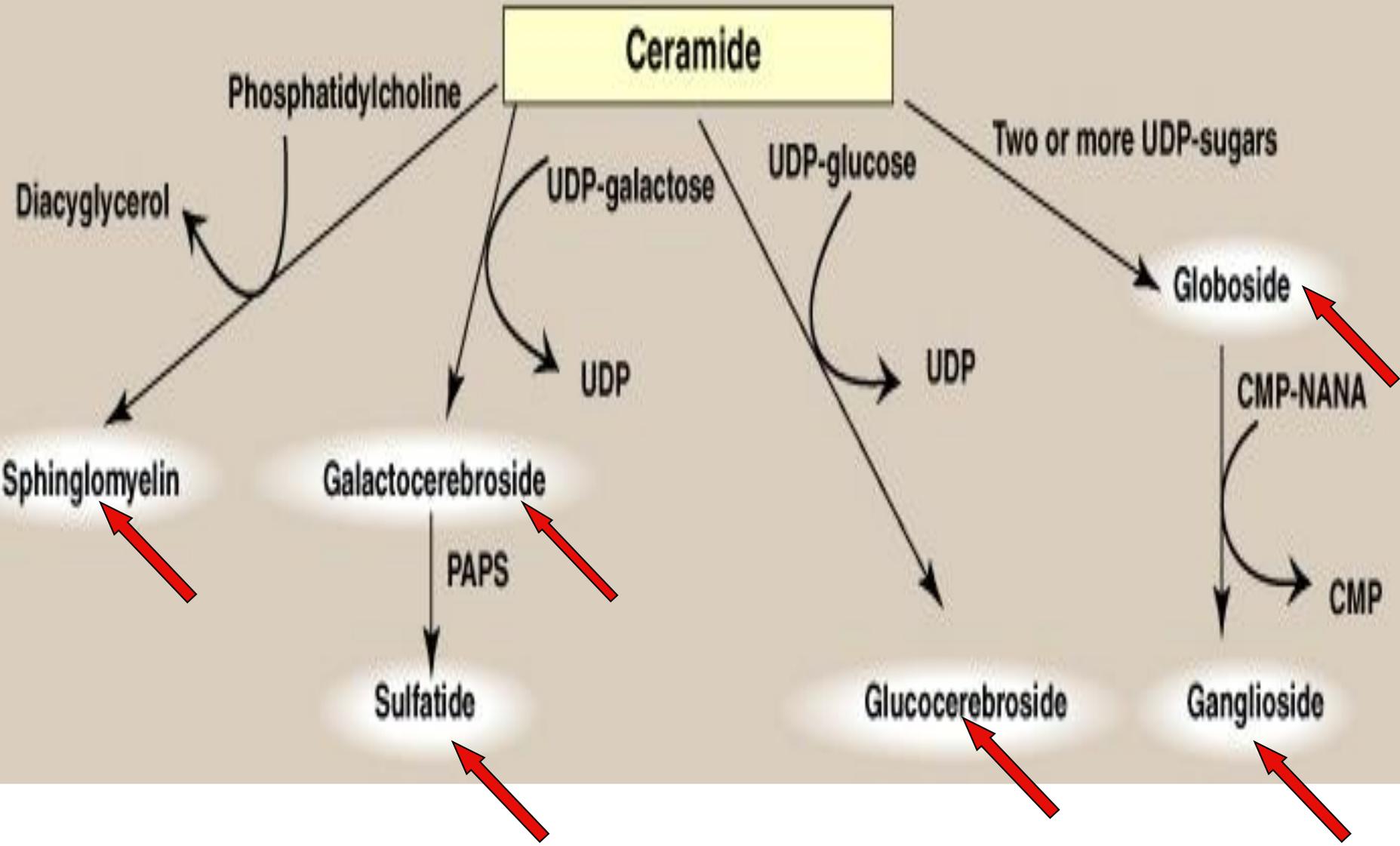
GM2



GM1



Summary of the synthesis of various glycolipids



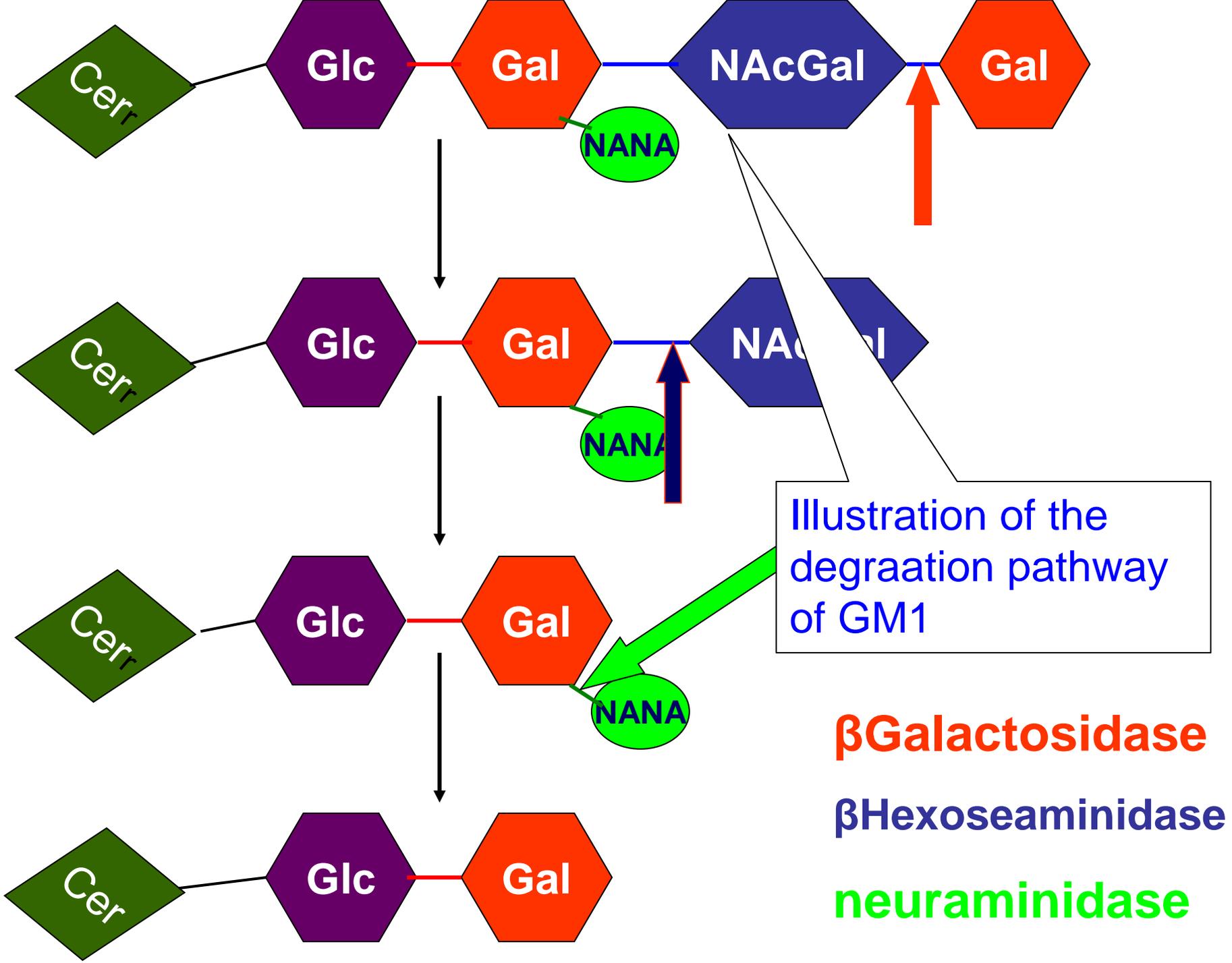
Degradation of Sphingolipids

- Hydrolytic Enzymes, Specific for the Sugar

- - α Galactosidase
 - β Galactosidase
 - neuraminidase
 - Hexoaminidase

Glycolipids are membrane components. They undergo slow turnover. They are synthesized and degraded at a slow rate by a group of enzymes

- In Lysosomes
- Enzymes are firmly Bound to Lysosomal Membrane.
- The pH Optimum 3.5-5.5
- Stepwise Sequential Process
- “Last on, First off”



Sphingolipidoses

- **Lipid Storage Diseases**
- **Defect in one of the Enzyme**
- **Accumulation of Specific Lipid**

Substrate of the Defective Enzyme

Inherited as Autosomal Recessive Disease

- **Brain is Mostly Affected.**
- **Extent of Enzyme deficiency is the same in Different Tissues.**

Degradation of Sphingomyelin

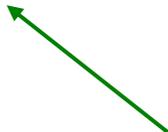
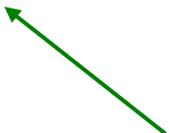
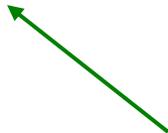
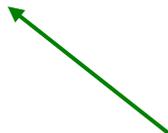
Sphingomyelin



Ceramide

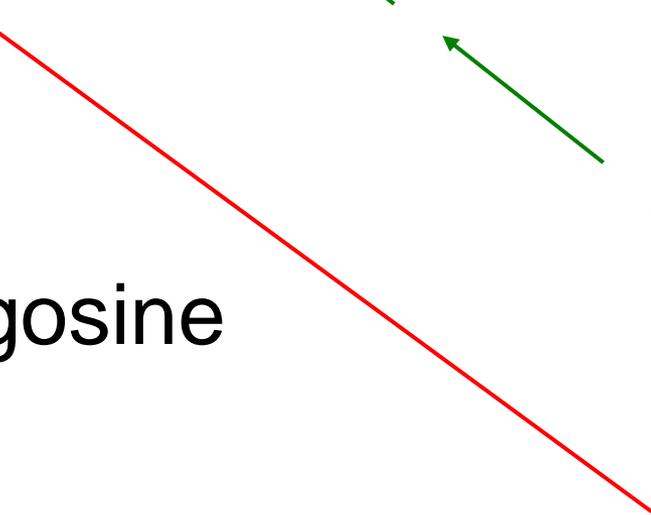


Sphingosine



Sphingomyelinase

Ceramidase



TAY-SACHS DISEASE

- Accumulation of gangliosides (GM₂)
- Rapid and progressive neurodegeneration
- Blindness
- Cherry-red macula
- Muscular weakness
- Seizures

GAUCHER DISEASE

- Accumulation of glucocerebrosides
- Most common lysosomal storage disease
- Hepatosplenomegaly
- Osteoporosis of long bones
- CNS involvement in rare infantile and juvenile forms

METACHROMATIC LEUKODYSTROPHY

- Accumulation of sulfatides
- Cognitive deterioration
- Demyelination
- Progressive paralysis
- Dementia in adult form
- Nerves stain yellowish-brown with cresyl violet (metachromasia)

KRABBE DISEASE (GLOBOID CELL LEUKODYSTROPHY)

- Accumulation of galactocerebrosides
- Mental and motor deterioration
- Blindness and deafness
- Near-total loss of myelin
- Globoid bodies (glycolipid-laden macrophages) in white matter of brain

GM₁ GANGLIOSIDOSIS

- Accumulation of gangliosides (GM₁) and keratan sulfate
- Neurologic deterioration
- Hepatosplenomegaly
- Skeletal deformities
- Cherry-red macula

FABRY DISEASE

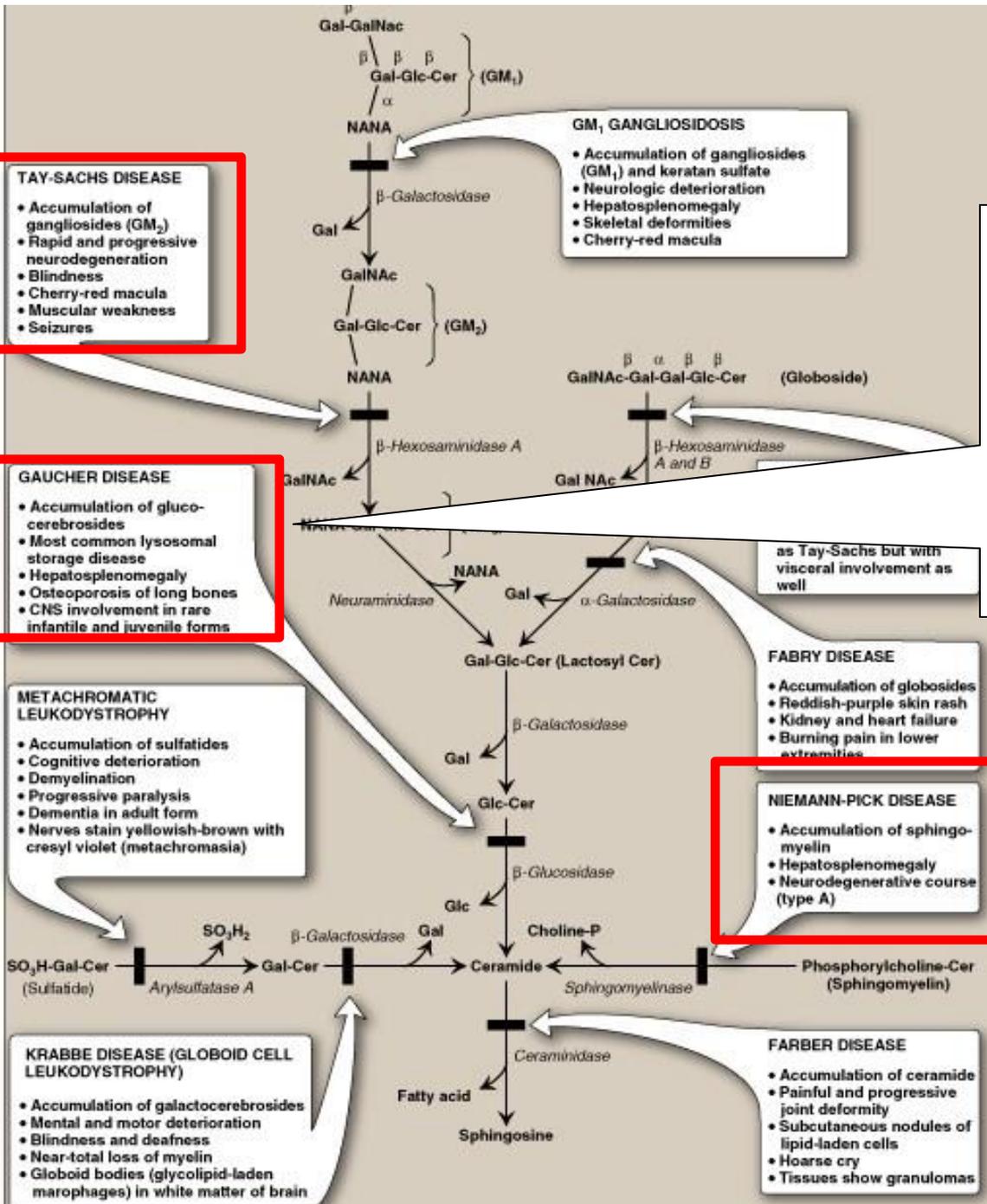
- Accumulation of globosides
- Reddish-purple skin rash
- Kidney and heart failure
- Burning pain in lower extremities

NIEMANN-PICK DISEASE

- Accumulation of sphingomyelin
- Hepatosplenomegaly
- Neurodegenerative course (type A)

FARBER DISEASE

- Accumulation of ceramide
- Painful and progressive joint deformity
- Subcutaneous nodules of lipid-laden cells
- Hoarse cry
- Tissues show granulomas



These are some of the lipidoses
 You are expected to know just these 3 names in the red squares without the details