Metabolism of Sphingolipids

Sphingophospholipids

Glycosphingolipids

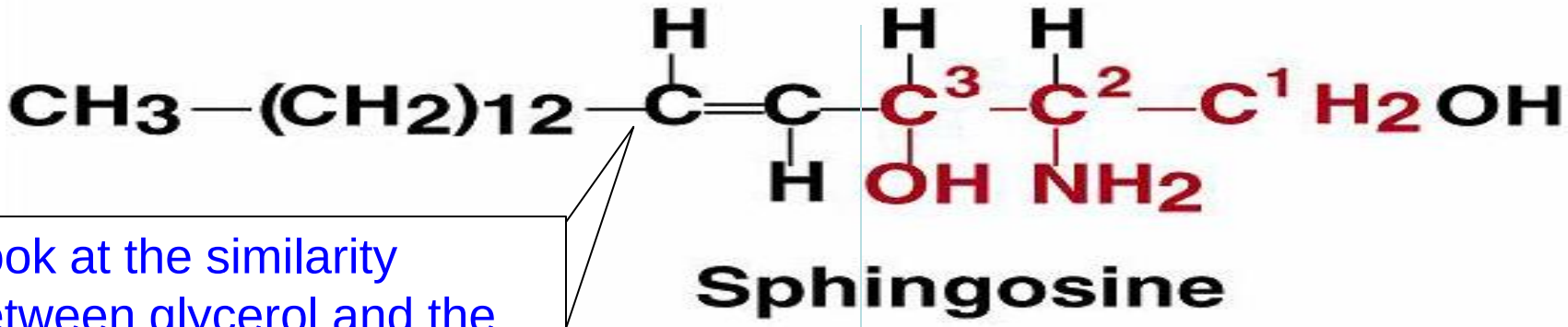
This class of lipids is named according to the name of alcohol that form the backbone which is **sphingosine** instead of glycerol.

It includes

Sphingophospholipids: sphingosine is joined to phosphate

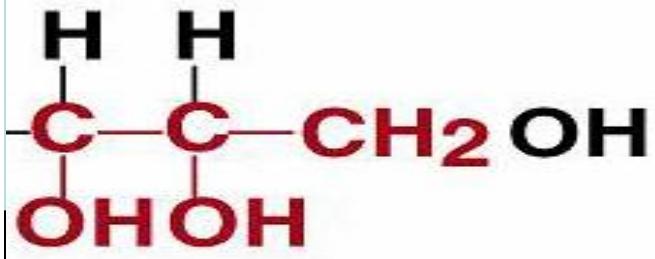
Glycosphingolipids: sphingosinjoined to carbohydrate

Sphingosine; Amino Alchol



Sphingosine

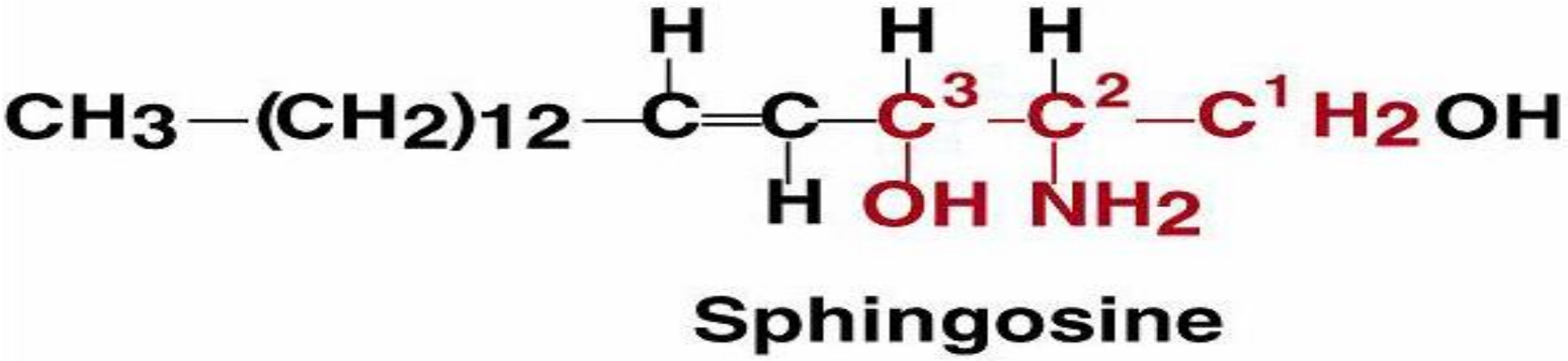
Look at the similarity between glycerol and the first three atoms of sphingosine.



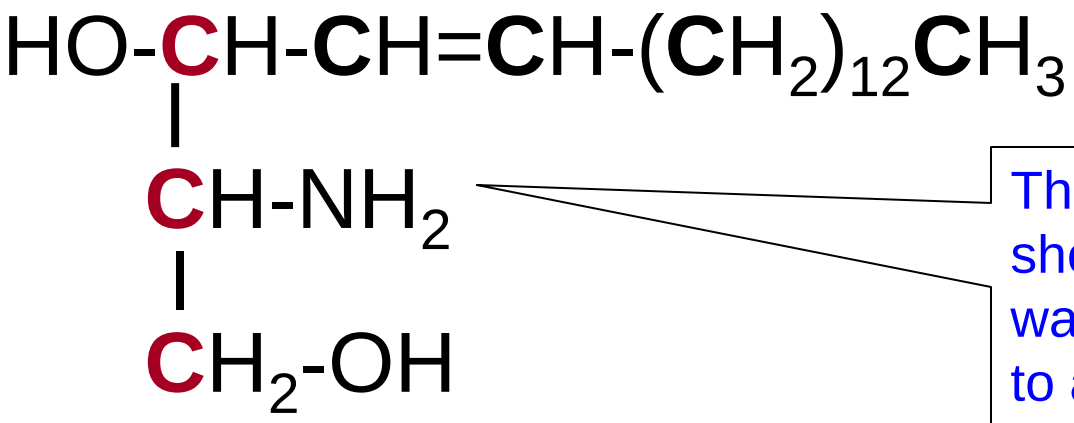
Glycerol

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?

Sphingosine; Amino Alchol

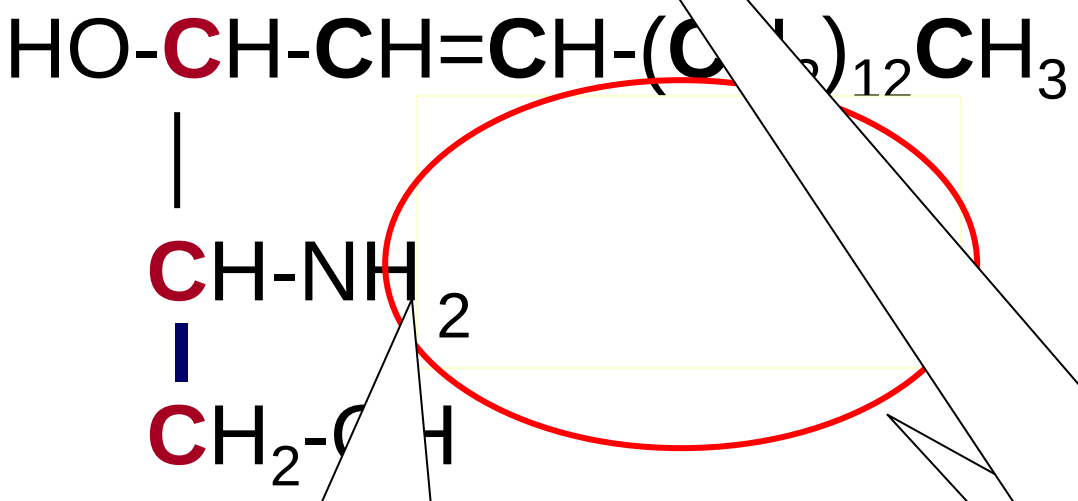


Sphingosine



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

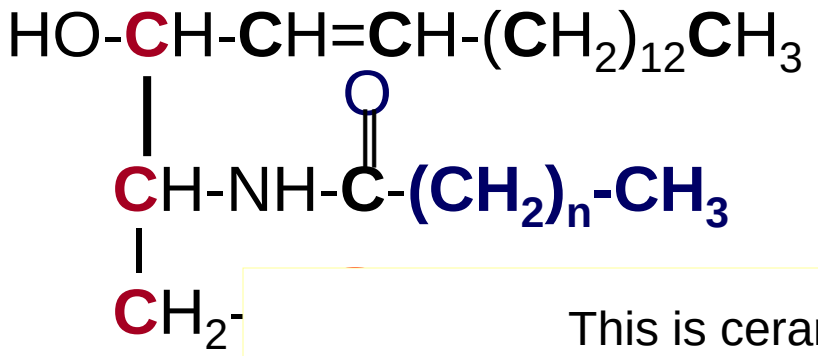
Ceramide: Fatty Acid joined to Sphingosine



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

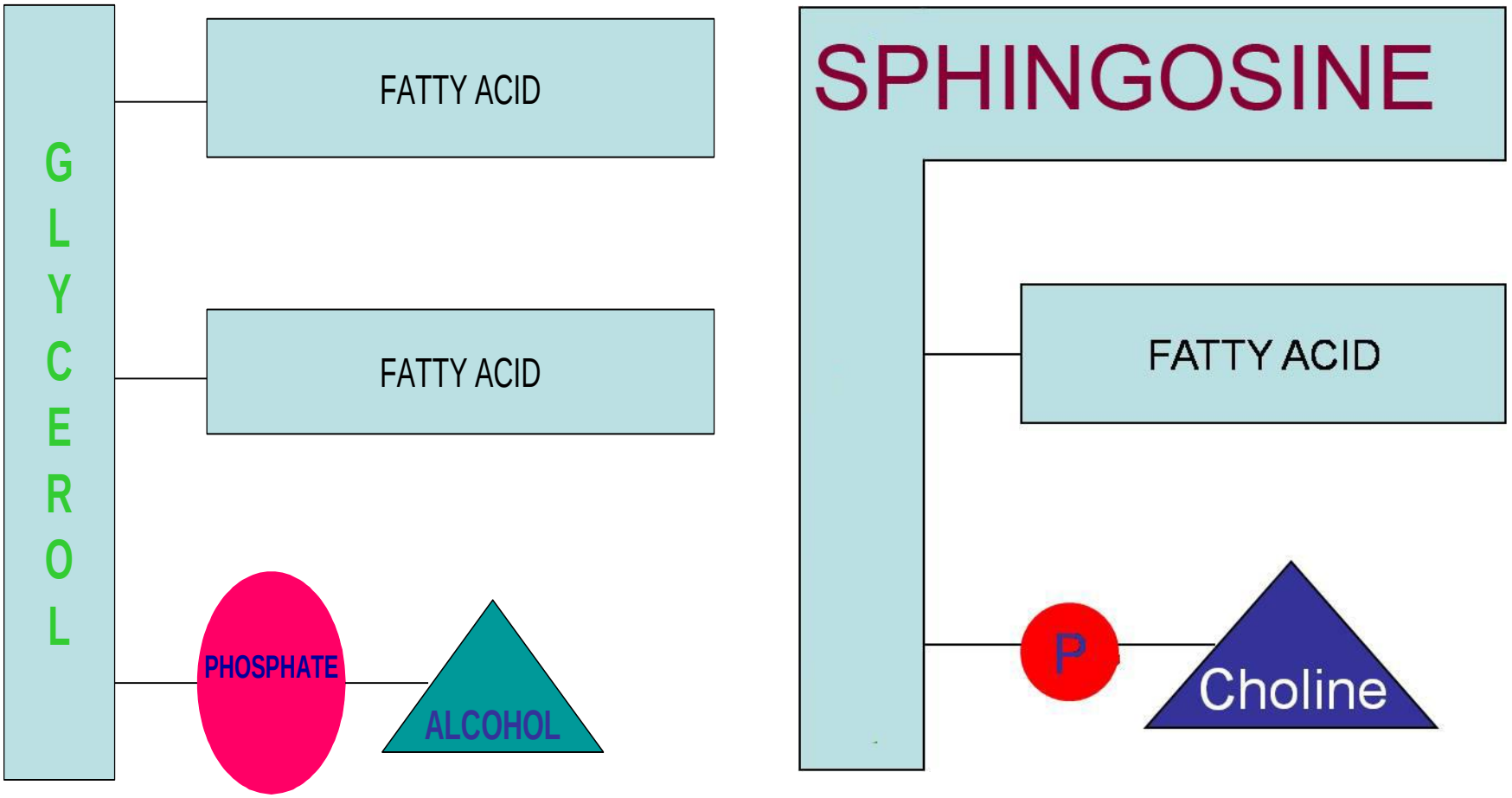


This is ceramide,
It is similar to diacylglycerol

Therefore sphingomylin is similar to phosphatidylcholine

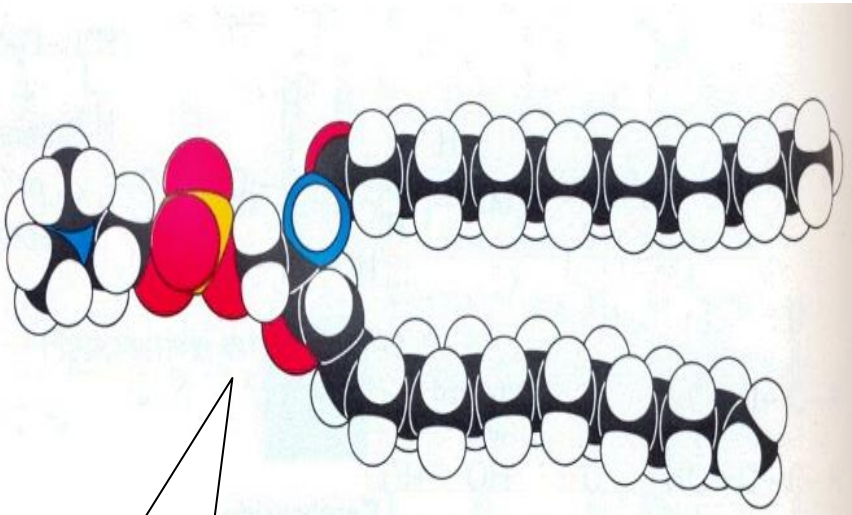
Adding phosphocholine to Ceramide produces sphingomyeline

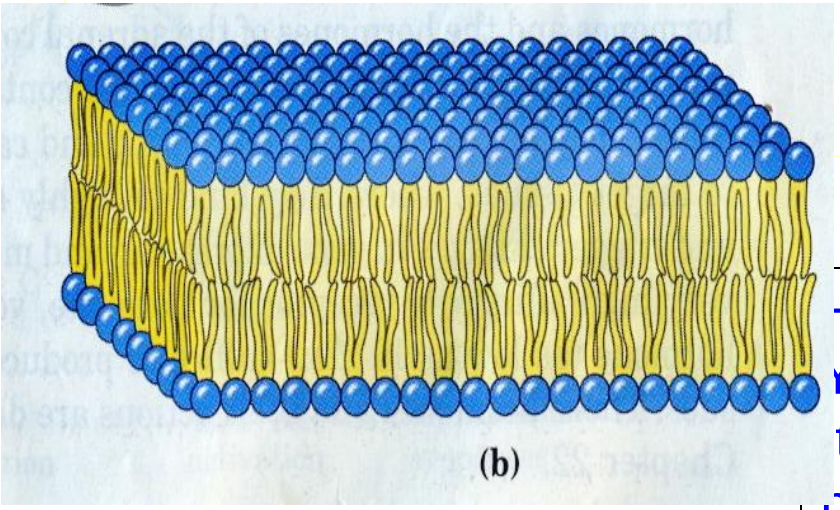
This is to compare the components of gycerophospholipids and sphingophospholipids



PHOSPHOACYLGLYCEROL

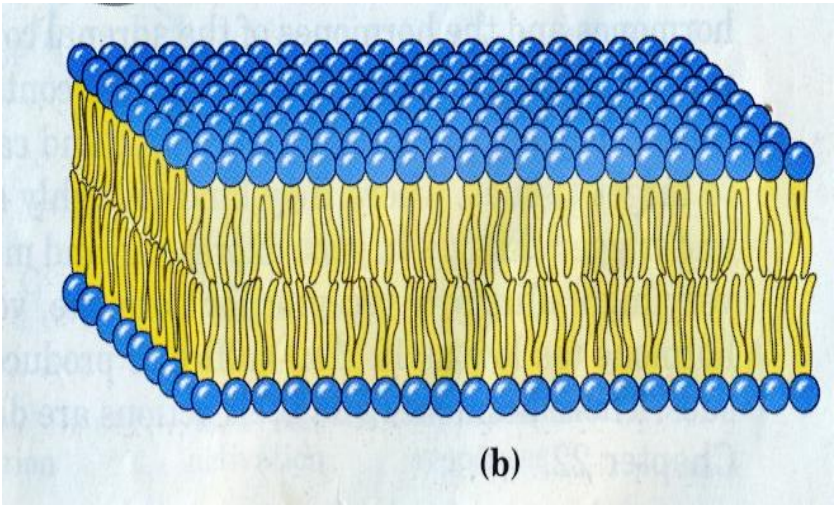
Sphingophospholipids





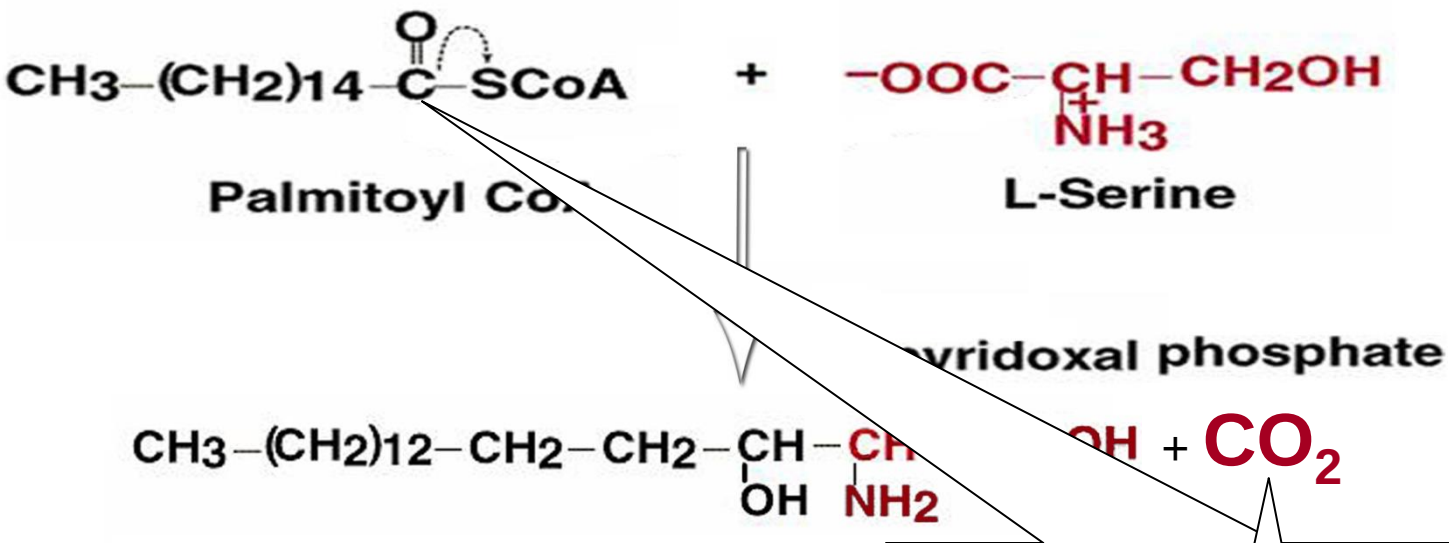
Have yo
You may thi
t is a space
phosphatidth

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



(b)

Biosynthesis of Ceramide



The first step i condensation between seri nd palmitoyl CoA with release e carboxyl group of serine

The product vdrosphingosine

What drives action?

Cleavage of the thioester bond in acyl CoA and release of CO_2

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

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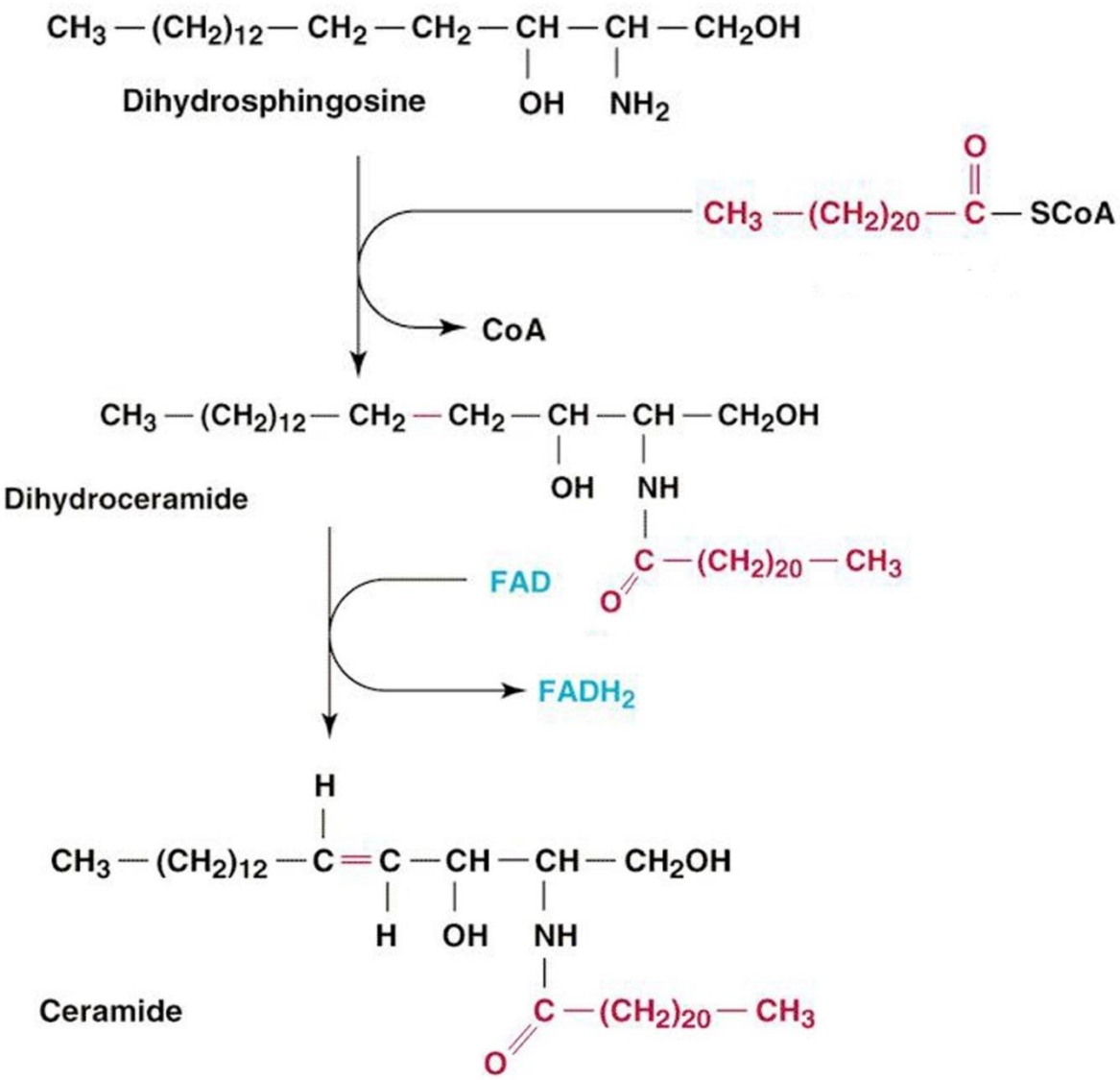
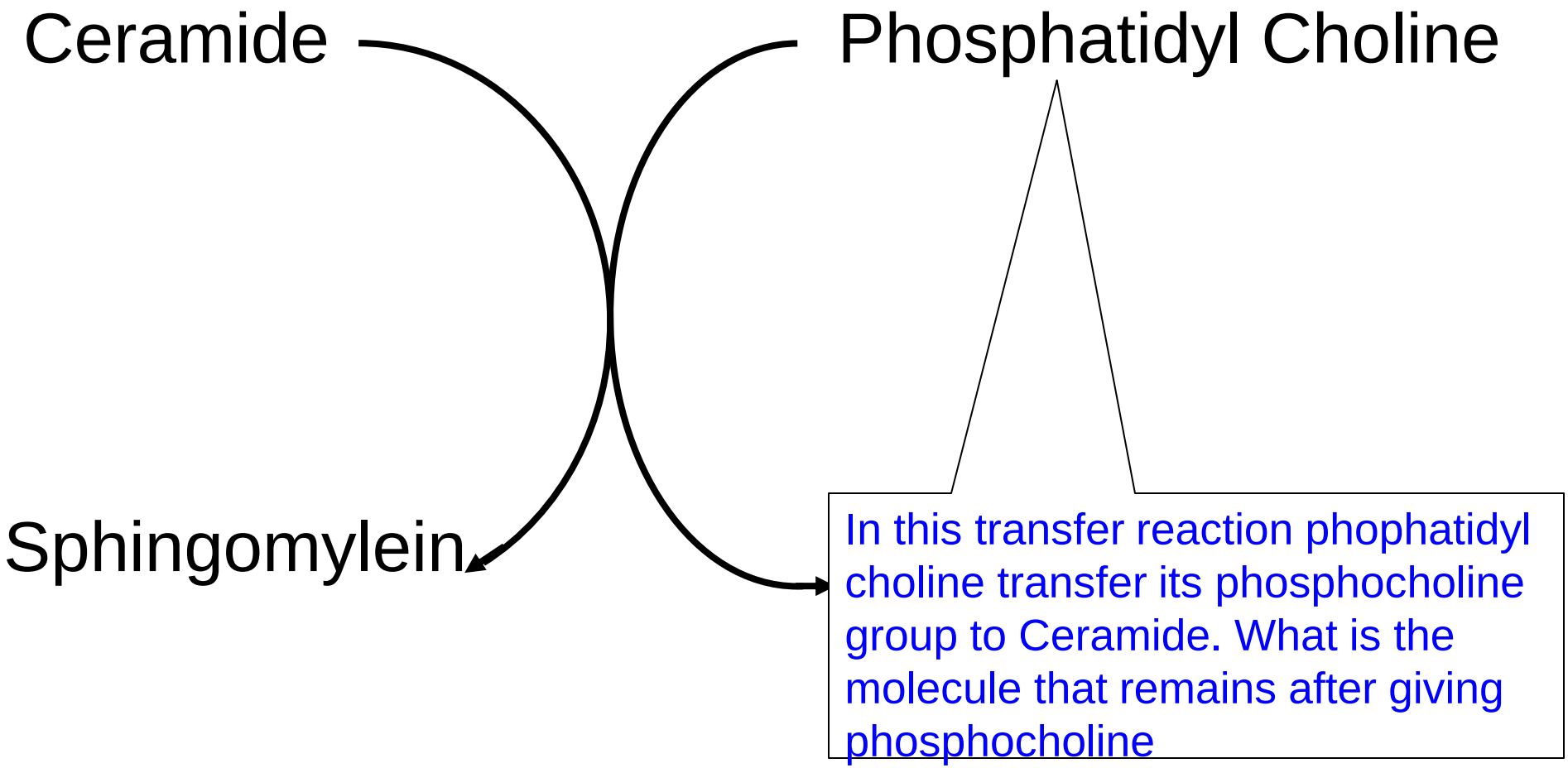


Transfer Of Phosphocholine to Ceramide Produces Sphingomylein



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.

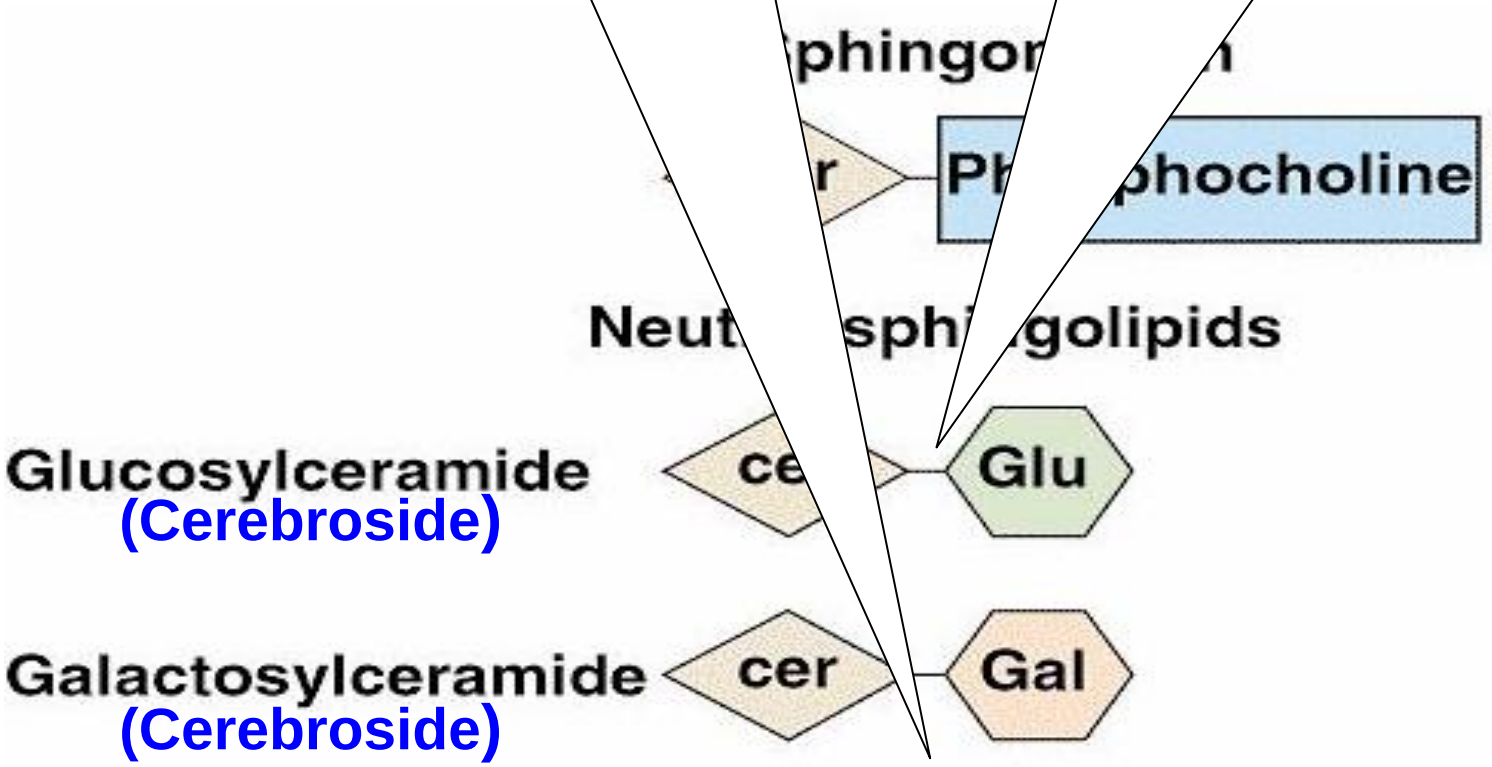
-Oligosaccharide ➔ Globoside

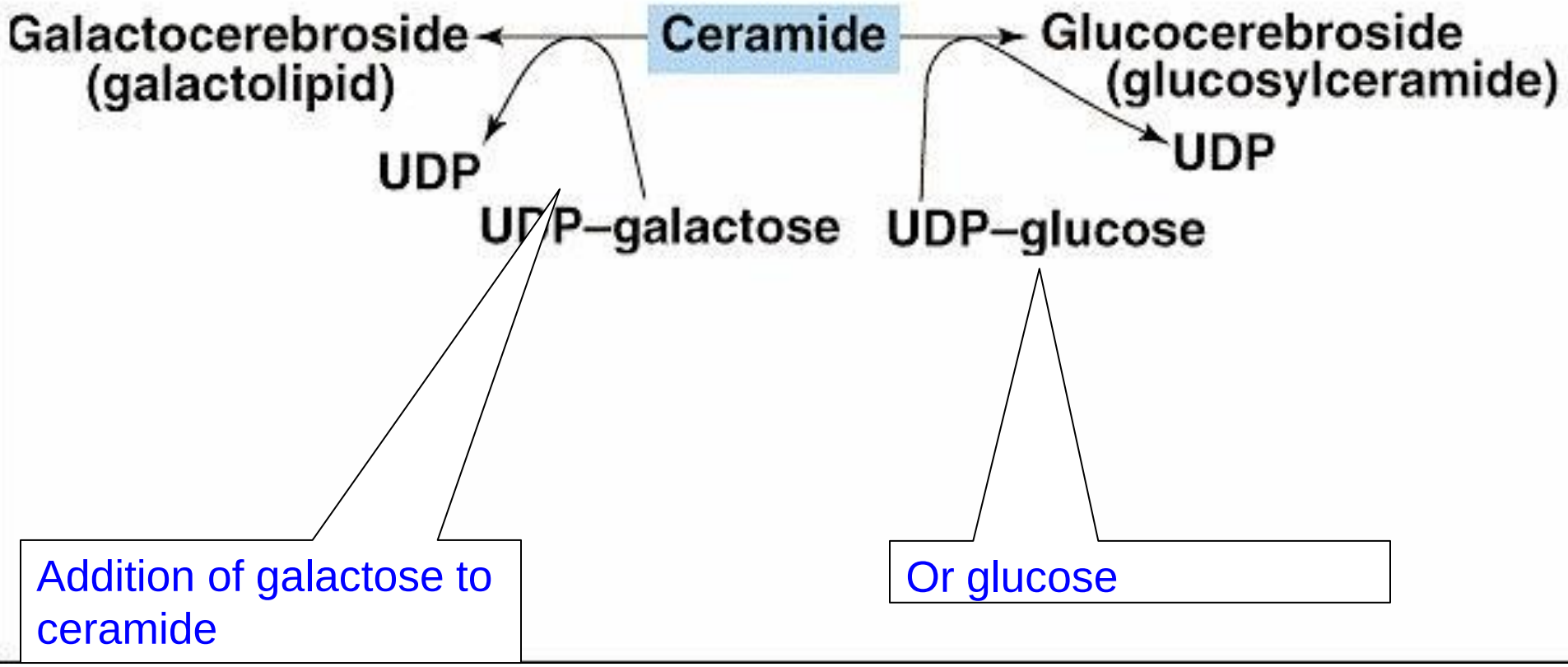
-Oligosaccharide with silalic acid ➔ Gangliosides

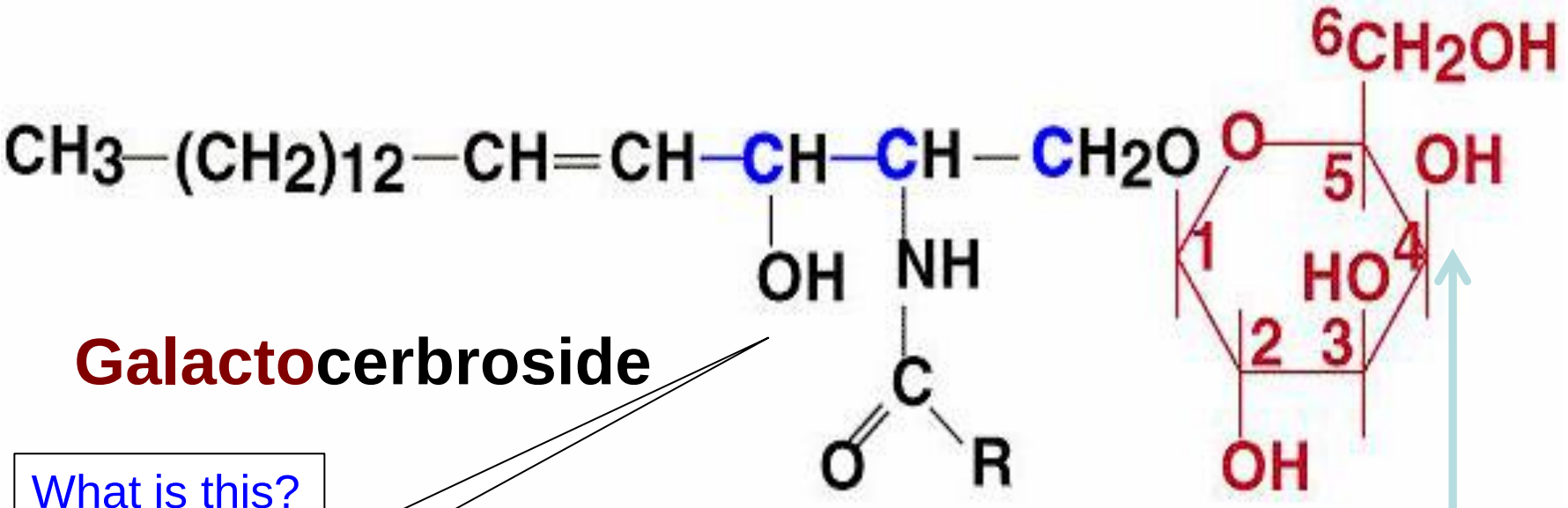
-Sulfated Galactose ➔ Sulfoglycosphingolipids

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




Galactocerebroside
(galactolipid)
Ceramide
Glucocerebroside
(glucosylceramide)
UDP
UDP
UDP–galactose
UDP–glucose
Addition of galactose to ceramide
Or glucose



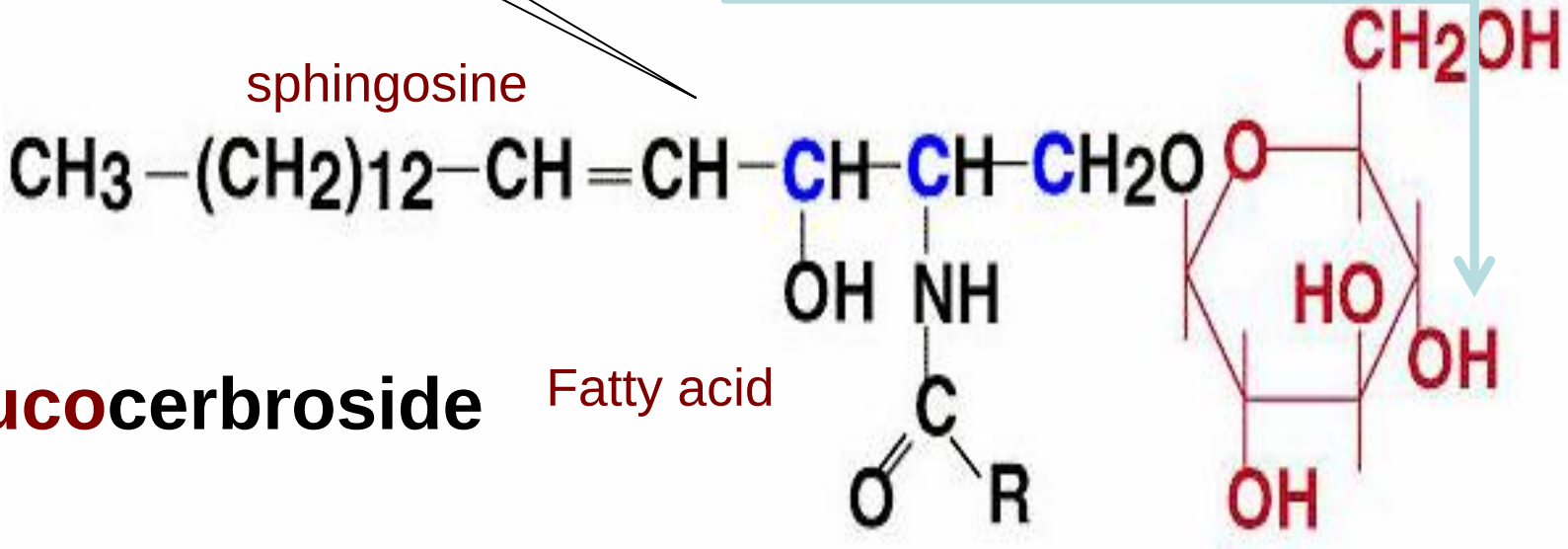
Galactocerbroside

What is this?

What is this?

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

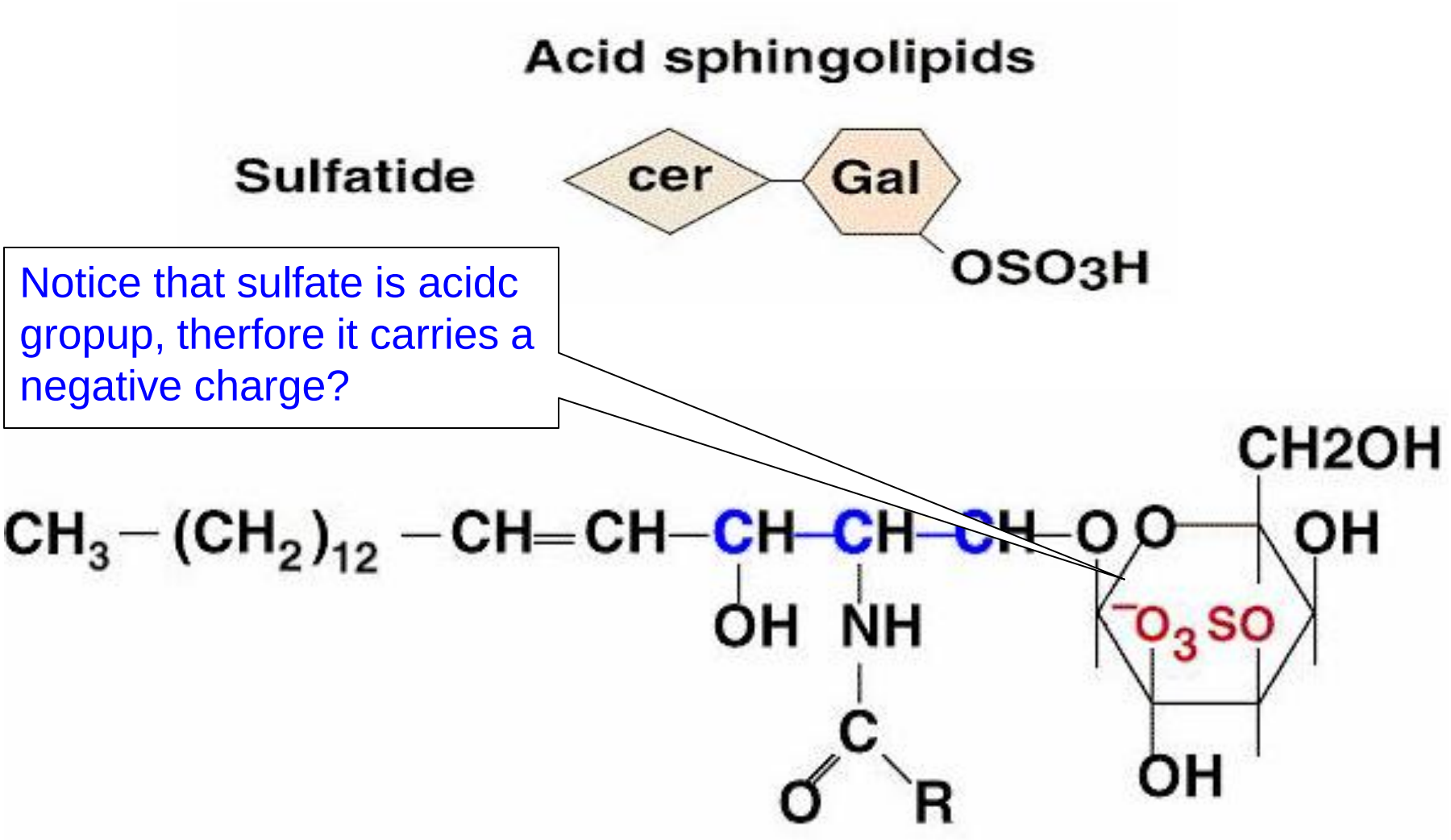
sphingosine



Glucocerbroside

Fatty acid

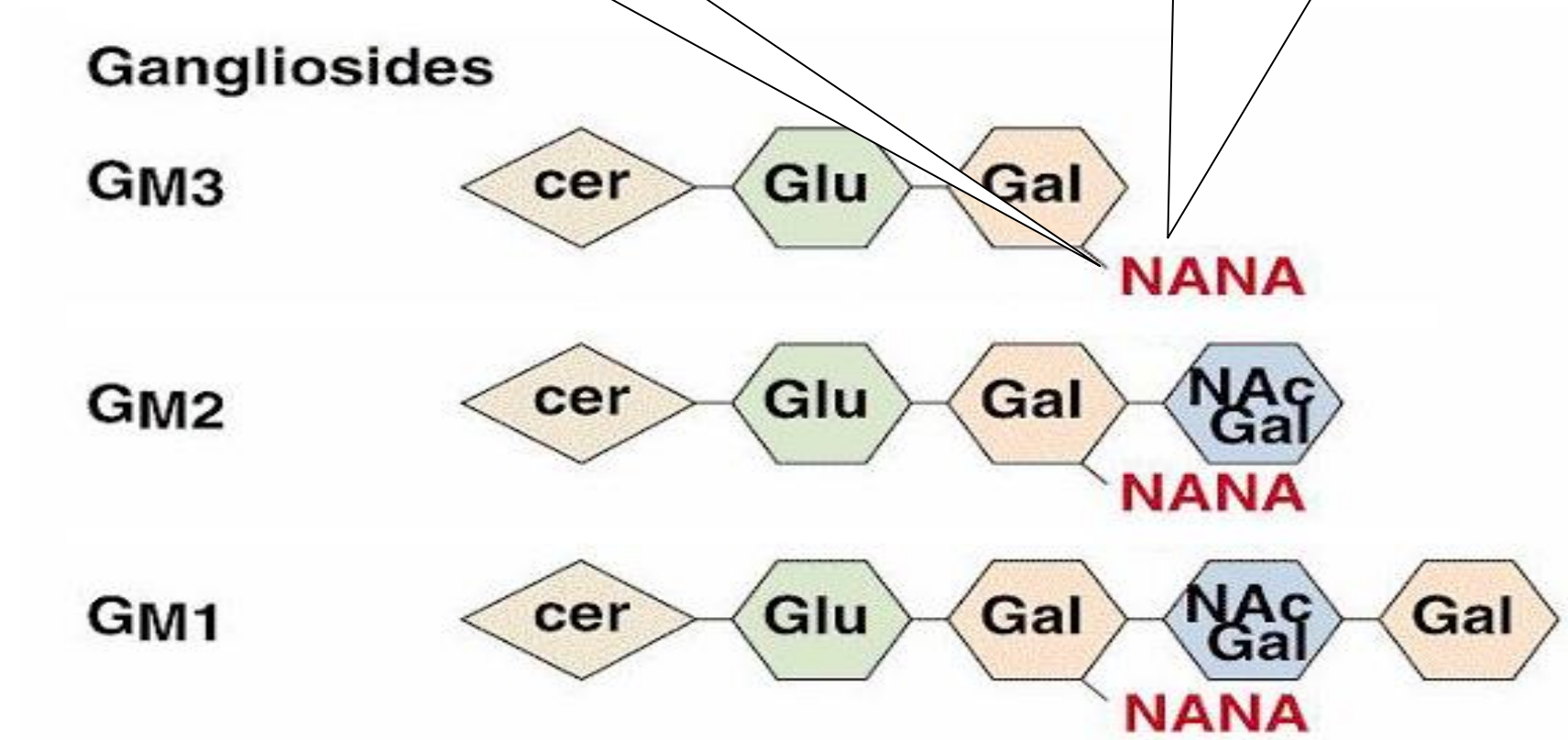
Transfer of Sulfate Group to Galactocerbroside Produces **Sulfogalatocerbroside** (Sulfatide)



Transfer of sialic acid (**N**-**A**cetyl **N**euraminic **A**cid (**NANA**)) produces Gangliosides

N-Acetylneuraminic Acid is 9 carbon acidic sugar

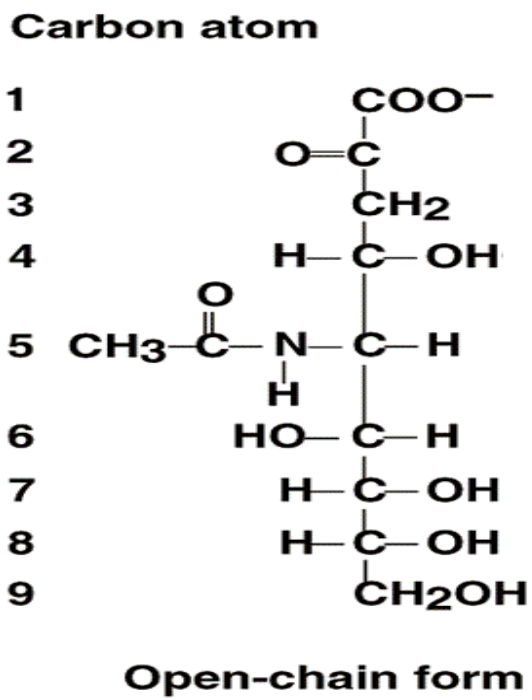
The active donaor is **CMP-** N-Acetylneuraminic Acid

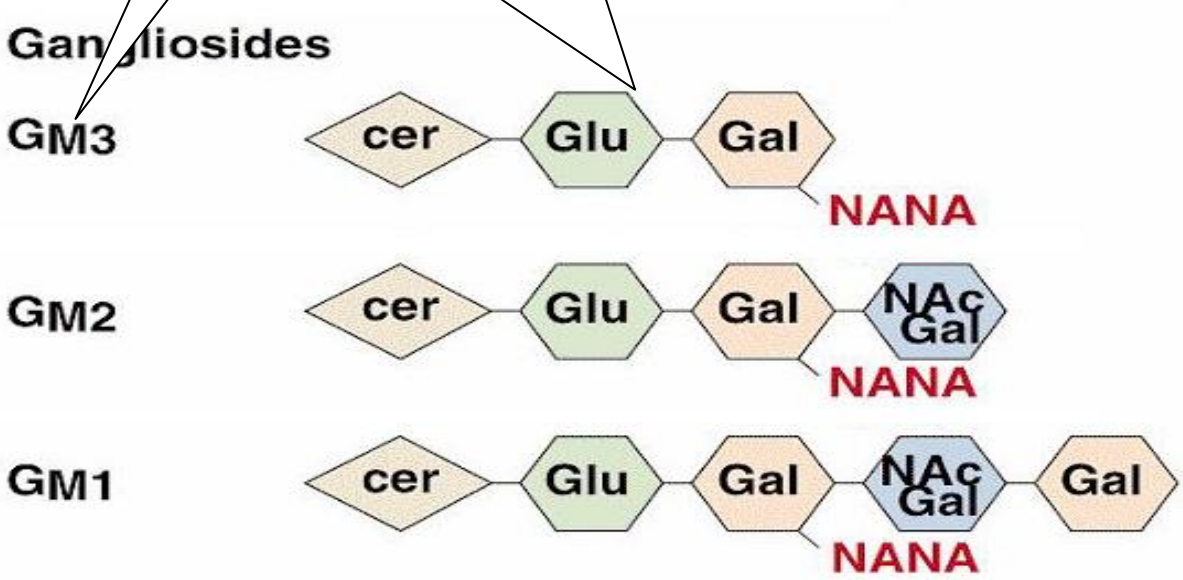


Gangliosides are commonly identified by symbols like GM1, GM2….

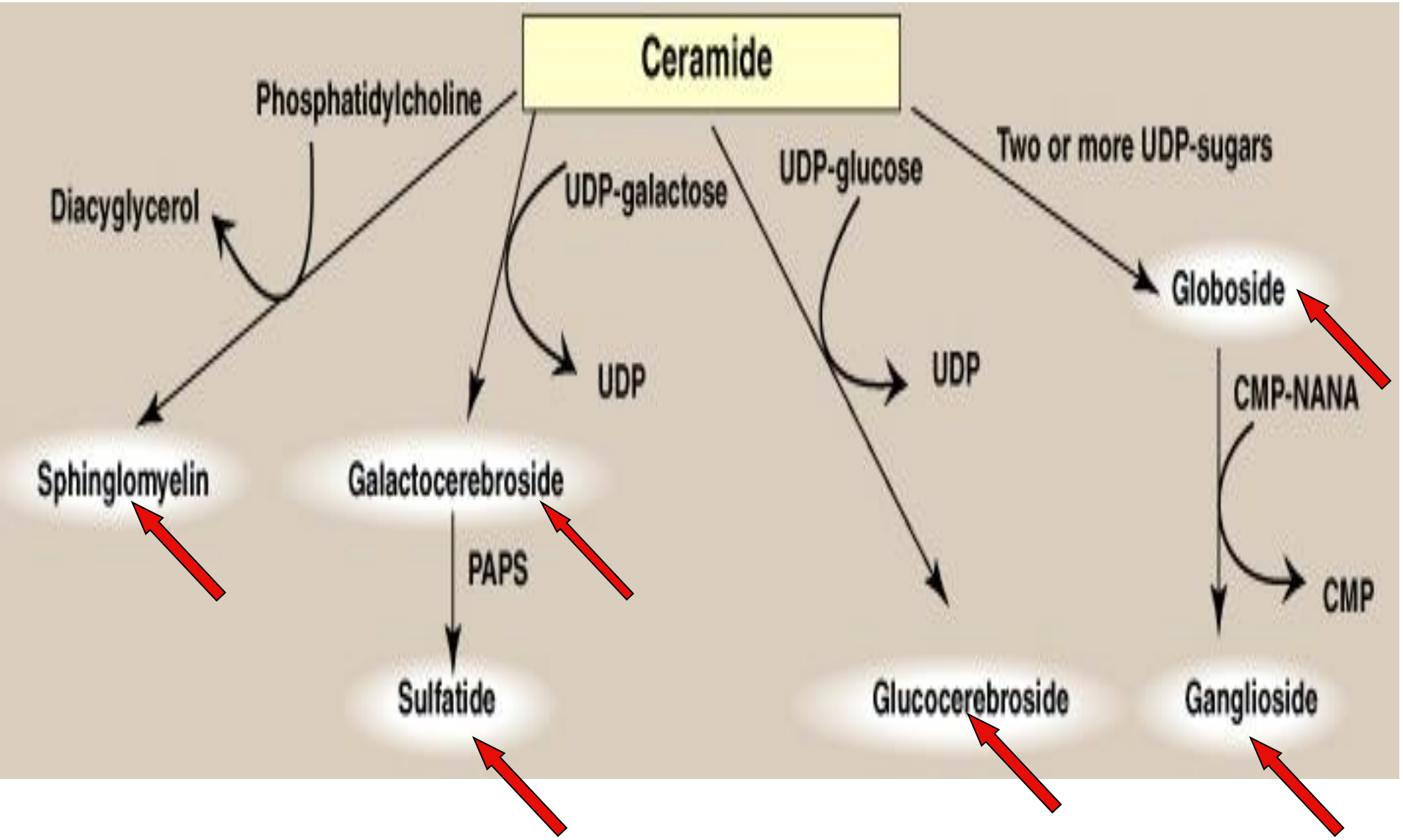
G stands for Gangliosides
M = Mono (number of sialic acid). D=Di
1,2 or 3 Refer to the specific sequence of oligosaccharide. Example 3= Glu-Gal

N-AcetylNeuraminic Acid (NANA)





Summary of the synthesis of various glycolipids

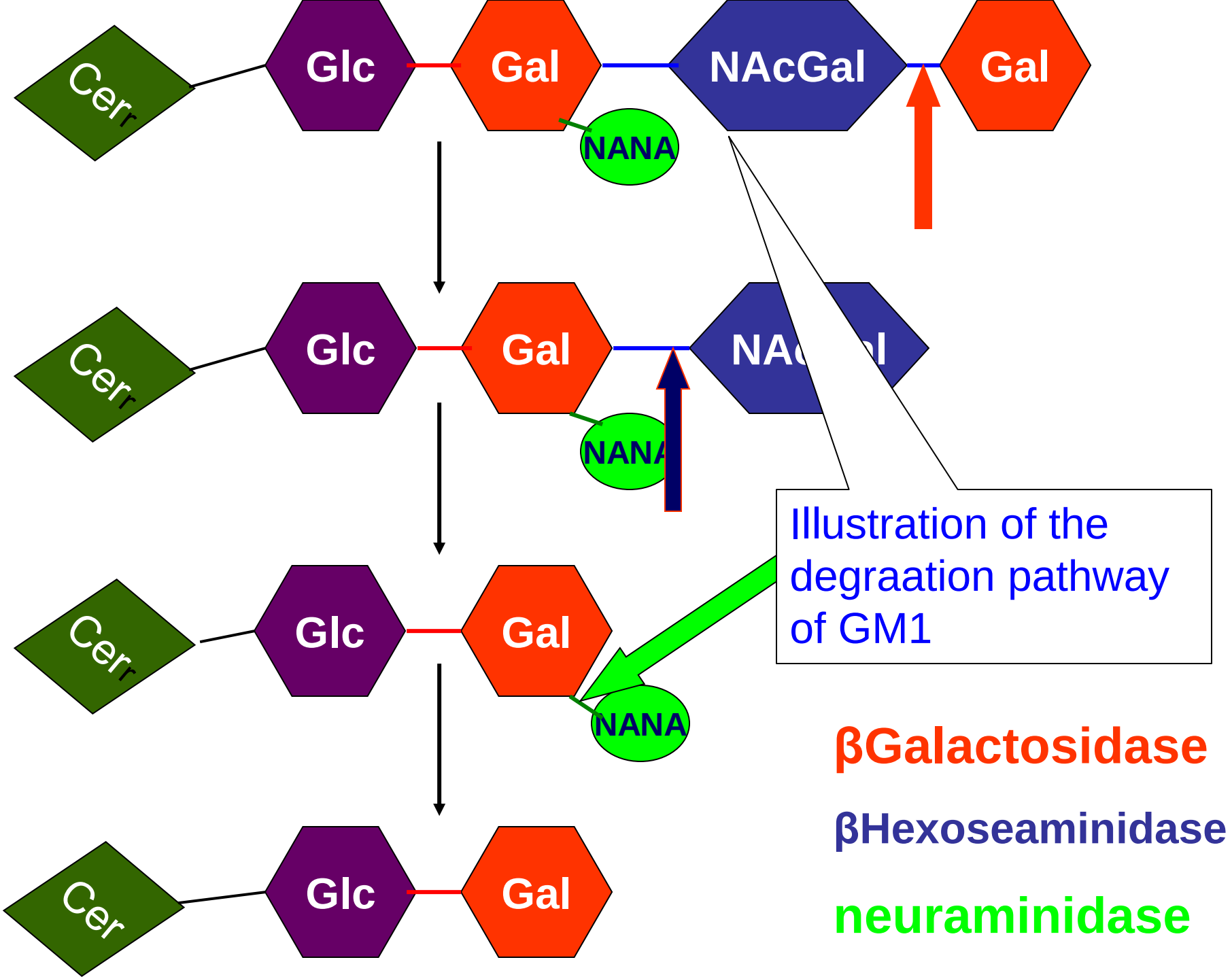


Degradation of Sphingolipids

- Hydrolytic Enzymes, Specific for the Sugar
- - α **Galactosidase**
  - β **Galactosidase**
  - **neuraminidase**
  - **Hexoaminidase**

Glycolipids are membrane components. They undergo slow turnover .the 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”


Cer
Glc
Gal
NAcGal
Gal
NANA
Cer
Glc
Gal
NANA
Cer
Glc
Gal
NANA
Cer
Glc
Gal
Illustration of the degraation pathway of GM1
βGalactosidase
βHexoseaminidase
neuraminidase

Sphingolipidoses

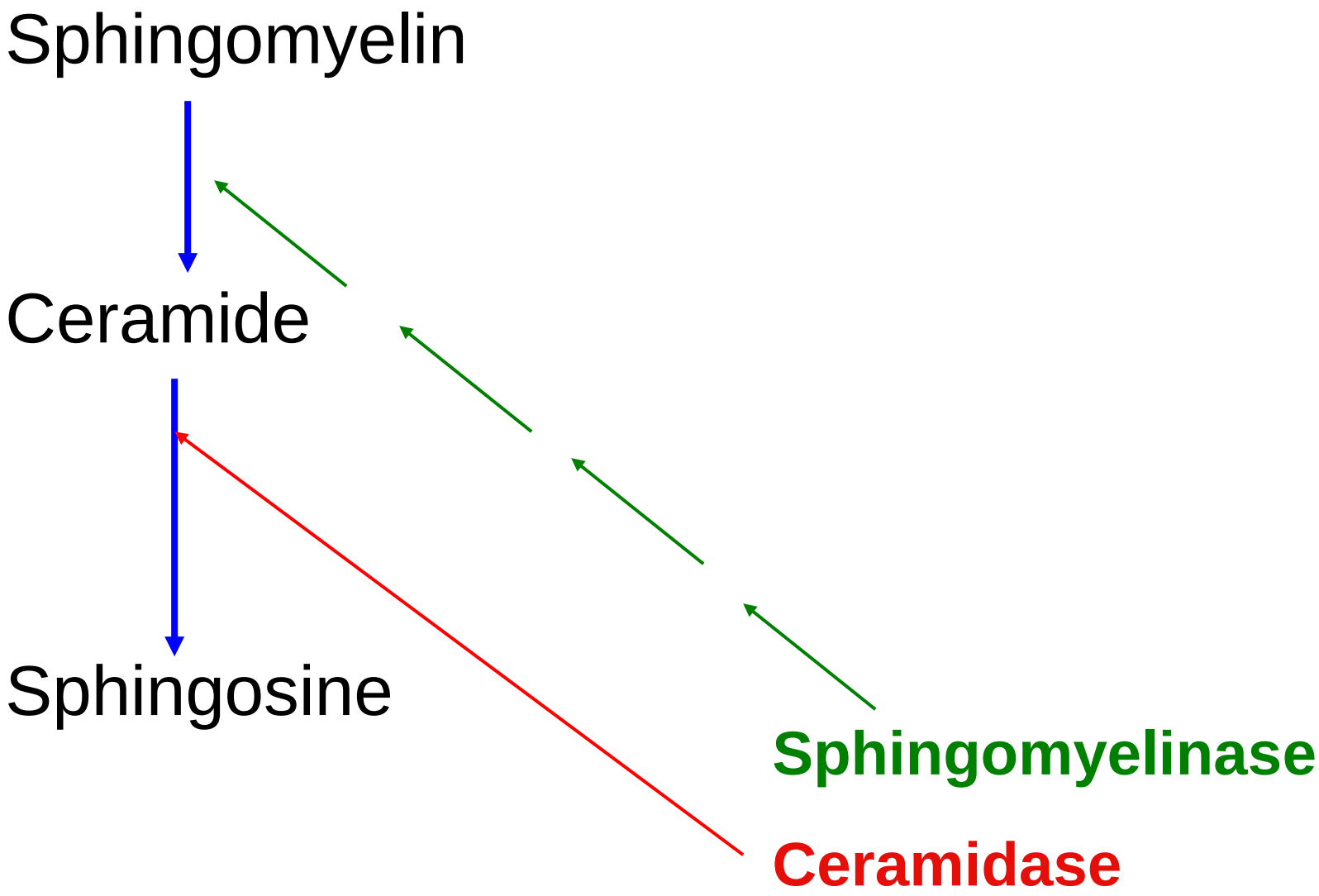
- **Lipid Storage Diseases**
- **Defect in one of the Enzyme**
- **Accumalation of Specific Lipid**

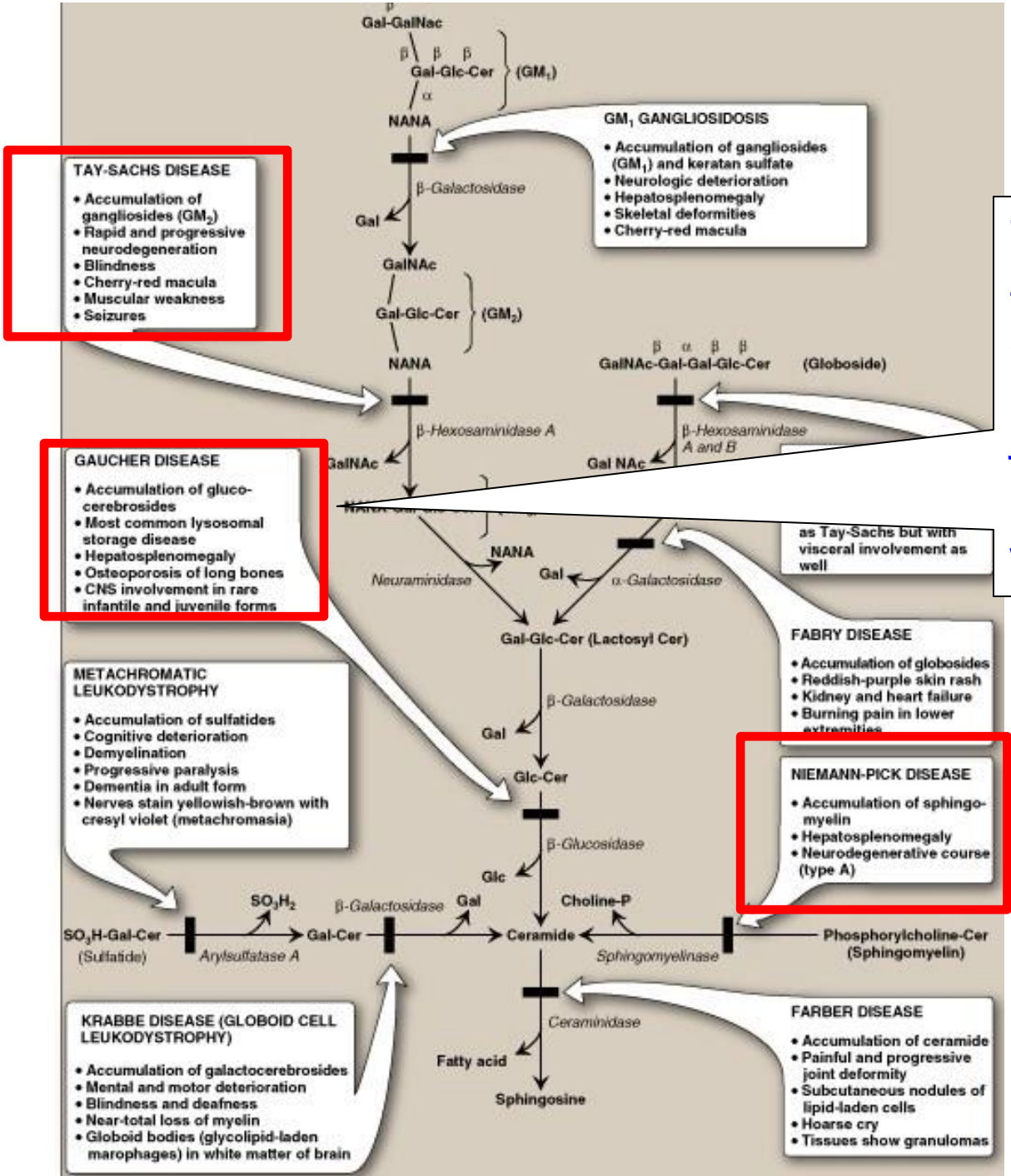
Substrate of the Defective Enzyme

Inherited as Autosomal RecessiveDisease

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

Degradation of Sphingomyelin





These are some o
the lipidoses
You are expected
just these 3 name
in the red squares
without the details