CHAPTER III. STRUCTURE-FUNCTION RELATIONSHIP OF THE CELL

A. Biosynthesis of lipids, membrane proteins, and secretory proteins

I. The endoplasmic reticulum

The endoplasmic reticulum (ER) is a complex set of membranes delimiting closed cavities (cisternae). They have two sides:

- A hyaloplasmic side facing the cytosol;
- A luminal side facing the lumen of the cisternae.

The ER exists in two forms corresponding to two functional aspects.

- **Rough or granular endoplasmic reticulum** (RER or REG): this is very often perinuclear and contains ribosomes and polysomes.
- **Smooth endoplasmic reticulum** (SER): its membranes do not carry ribosomes. It may be continuous with the RER.

The distribution and abundance of ER varies depending on the cell type and physiological state of the cell.

- LRE: developed in cells that synthesize lipids (adipocytes).
- GRE: developed in cells that synthesize proteins (exocrine/endocrine pancreatic cells).

The membranes of the endoplasmic reticulum do not have the same composition as the plasma membrane, and are made up of:

- 70% proteins.
- 30% lipids.
- And a negligible amount of sugars.

Proteins are essentially:

- Enzymes necessary for protein synthesis, lipid metabolism, and detoxification processes.
- Enzymes involved in the transfer of sugars to proteins, glycosyl transferases.
- Enzymes involved in steroid synthesis and phospholipid biosynthesis.

Lipids: the high content of unsaturated fatty acids and low cholesterol content are responsible for increased membrane fluidity.

Roles of the endoplasmic reticulum

- Synthesis of proteins that will remain in the cell (ribosome proteins, membrane proteins, etc.) and those that will be exported (hormones, enzymes, etc.).
- Synthesis of lipids (phospholipids and cholesterol).
- Glycosylation: conversion of proteins and lipids into glycoproteins and glycolipids.
- Detoxification by converting toxic substances into non-toxic substances.

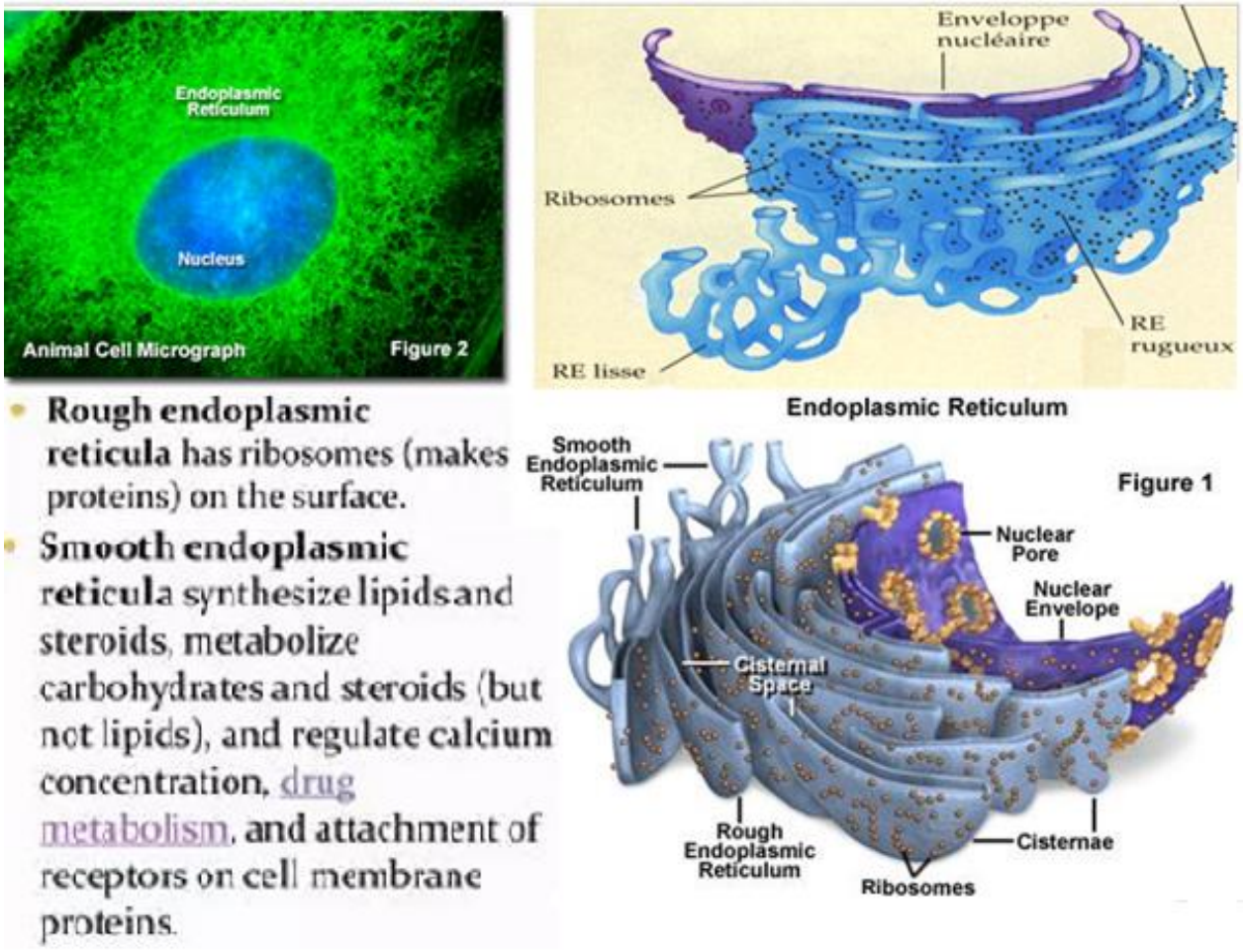


Figure III. 1. The endoplasmic reticulum **[22].**

II. Biosynthesis of membrane lipids

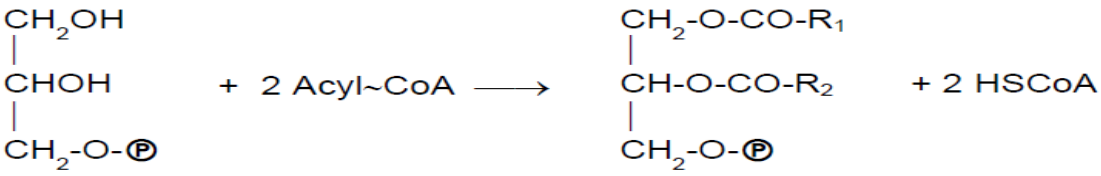
The basic metabolites required for the synthesis of membrane phospholipids are produced and stored in the cytosol. However, the enzymes that catalyze lipid biosynthesis reactions are embedded in the smooth endoplasmic reticulum membrane, with their active sites facing the cytosol.

II.1. Biosynthesis of triglycerides

This takes place in the endoplasmic reticulum. In higher plants and animals, lipids have two precursors: L-glycerol and acyl-CoA.

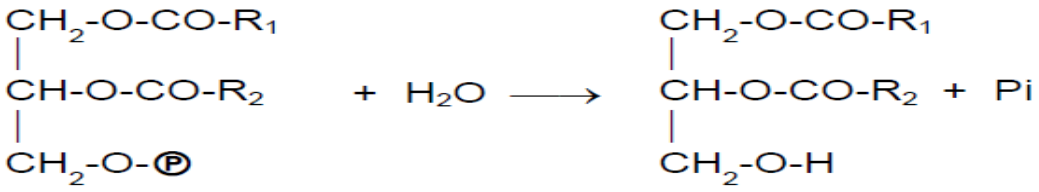
- **Formation of phosphatidic acid**

Two acyl-CoA molecules react with glycerol 3-P to produce phosphatidic acid. The primary and secondary alcohol functions of glycerol-P are esterified by the action of acyl transferase.



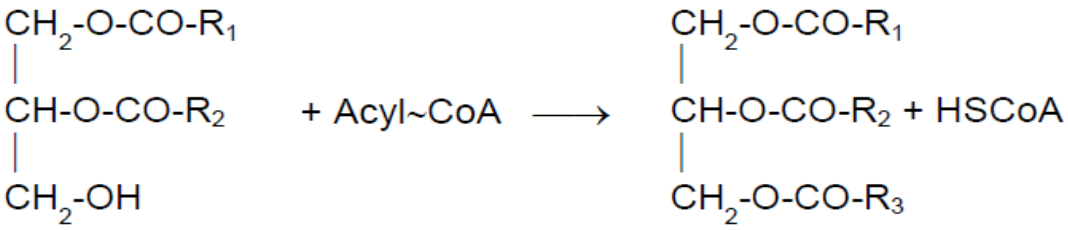
- **Formation of diacylglycerol or diglyceride**

This is the result of the departure of the phosphate group from phosphatidic acid. The reaction is catalyzed by a hydrolase called phosphatidate phosphatase.



- **Formation of triacylglycerol or triglyceride**

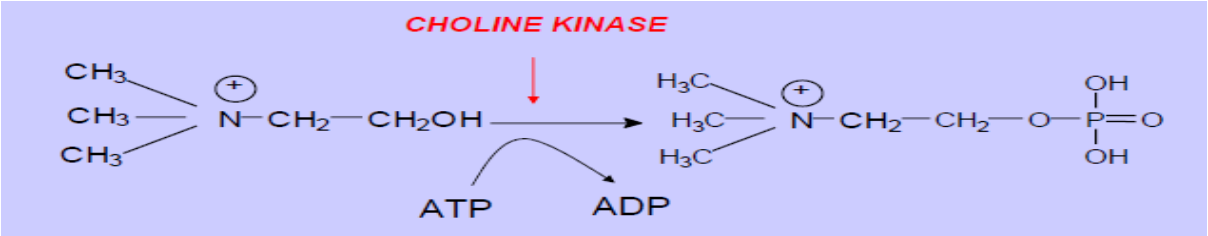
Diacylglycerol reacts with acyl-CoA to form triglyceride. All fatty acids can be different. An acyl-CoA transferase is involved.



II.2. Synthesis of phospholipids

With regard to phospholipids, specific reactions enable the binding of alcohol (choline, ethanolamine, inositol, etc.), which determines the nature of the phospholipid. Let us take the synthesis of phosphatidylcholine as an example. It is synthesized from diacylglycerol and choline in the endoplasmic reticulum. This pathway allows for the direct use of choline from either dietary intake or the breakdown of endogenous phospholipids.

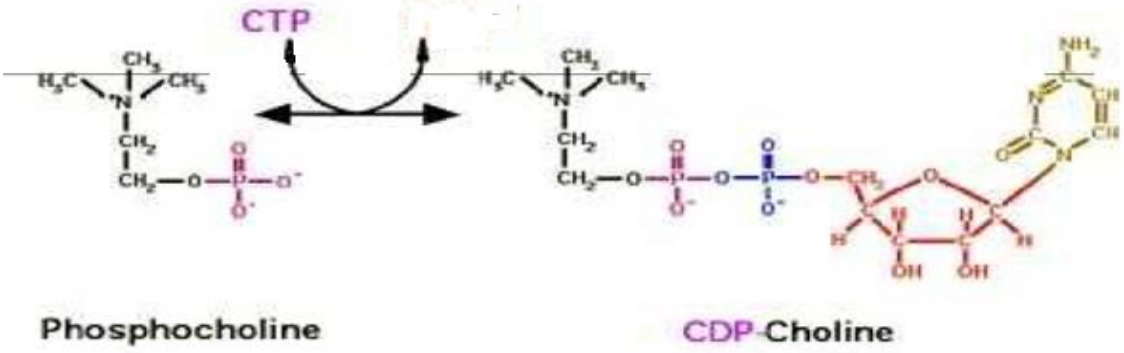
- **Choline phosphorylation:** The reaction is catalyzed by choline kinase.



- **Transfert of choline to CTP**

CTP + Choline phosphate ⟶ CDP-choline + PPi.

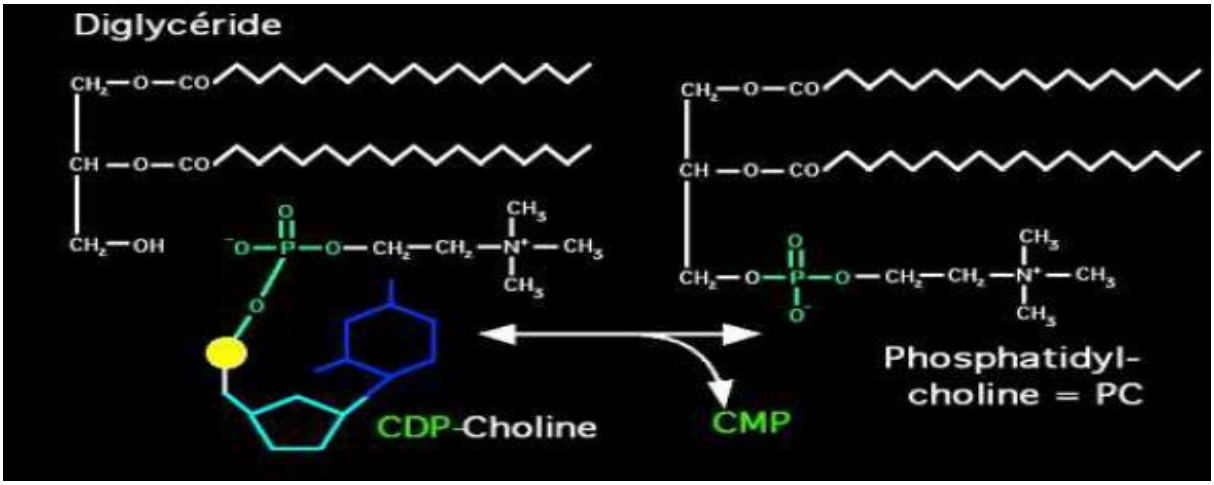
CDP-choline pyrophosphorylase



- **Synthesis of phosphatidylcholine**

The final step ensures the transfer of a phosphocholine to the diacylglycerol. The reaction is catalyzed by a phosphocholine transferase.

CDP-choline + 1,2-diacylglycérol ⟶ CMP + Phosphatidylcholine



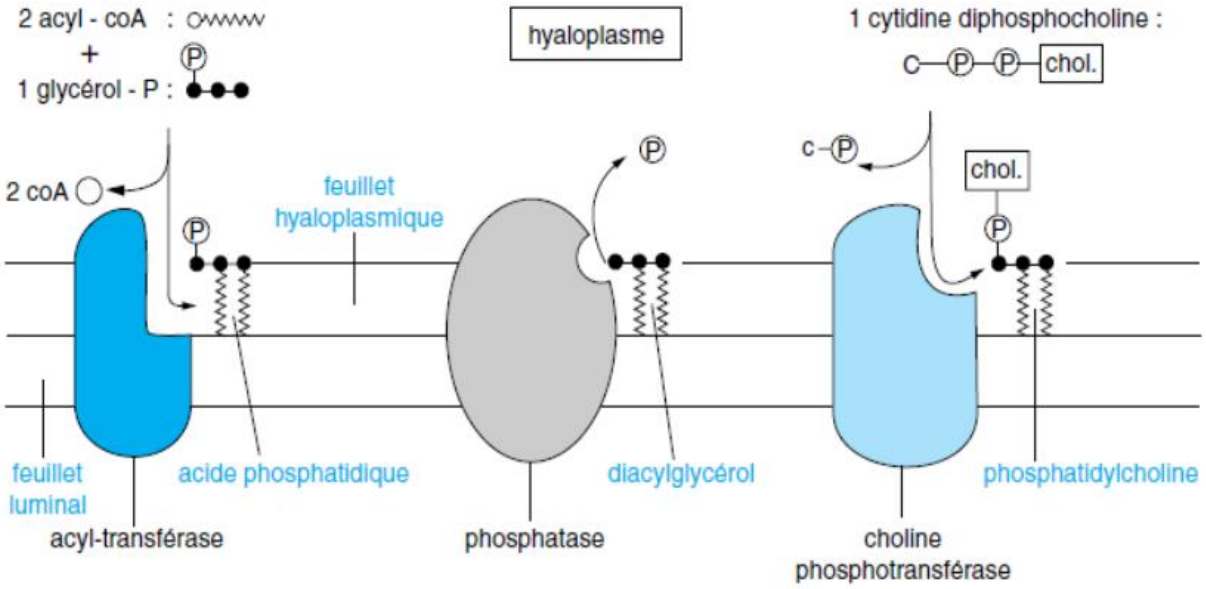
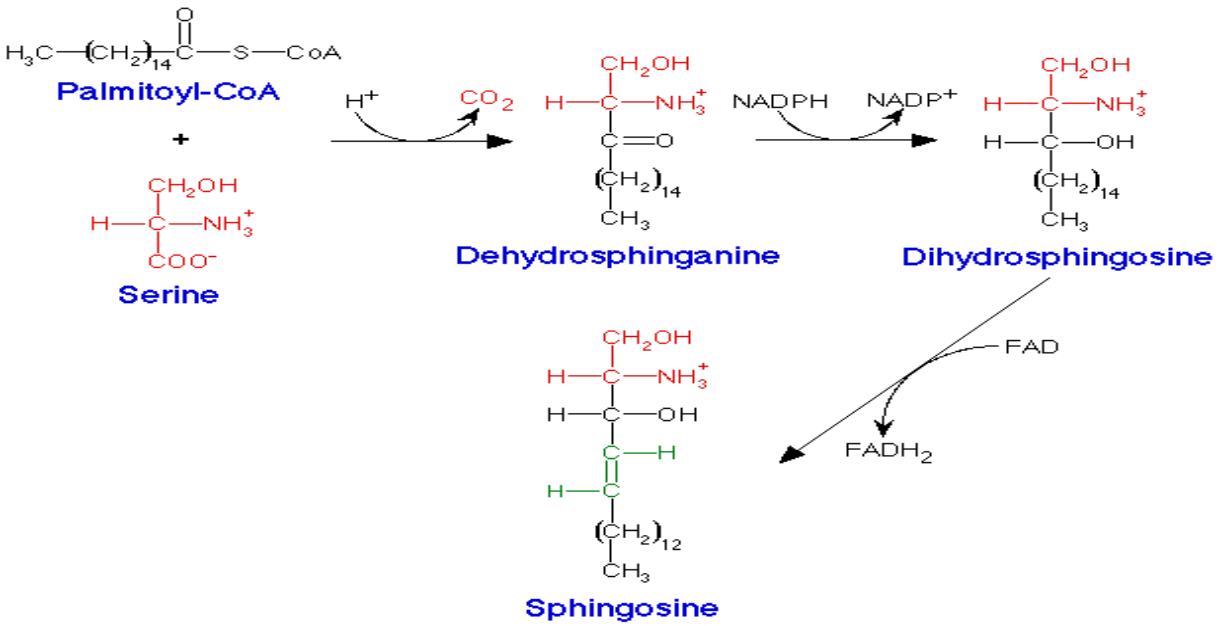


Figure III.2. Illustration of the steps involved in the synthesis of membrane phospholipids (phosphatidylcholine) **[22].**

II.3. Synthesis of sphingolipids

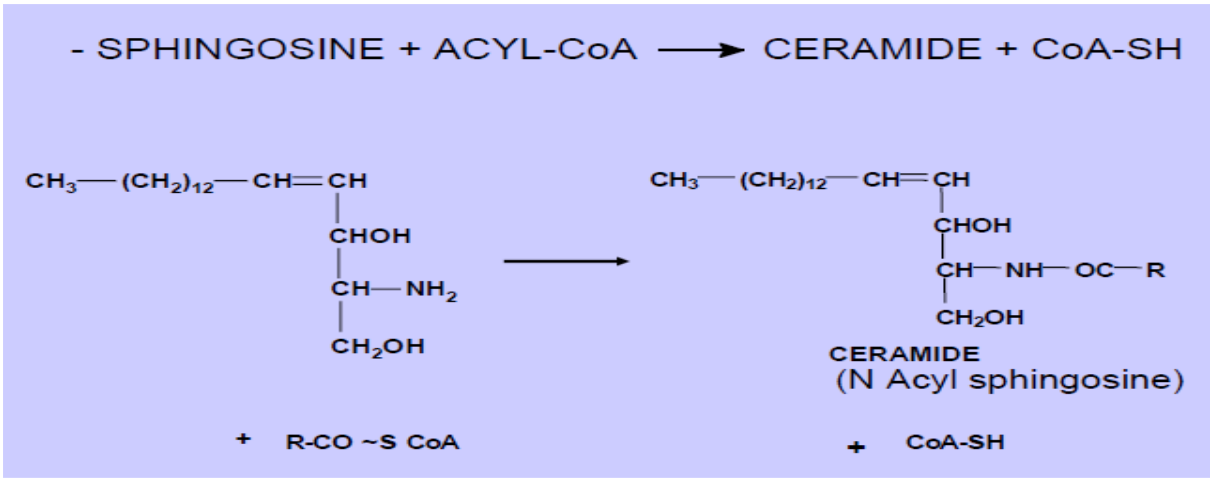
- **Sphingosine**

Sphinganine results from the condensation of the amino acid serine (3C) on palmitic acid (16C). Sphingosine and dehydrosphingosine are formed from palmitoyl-CoA :

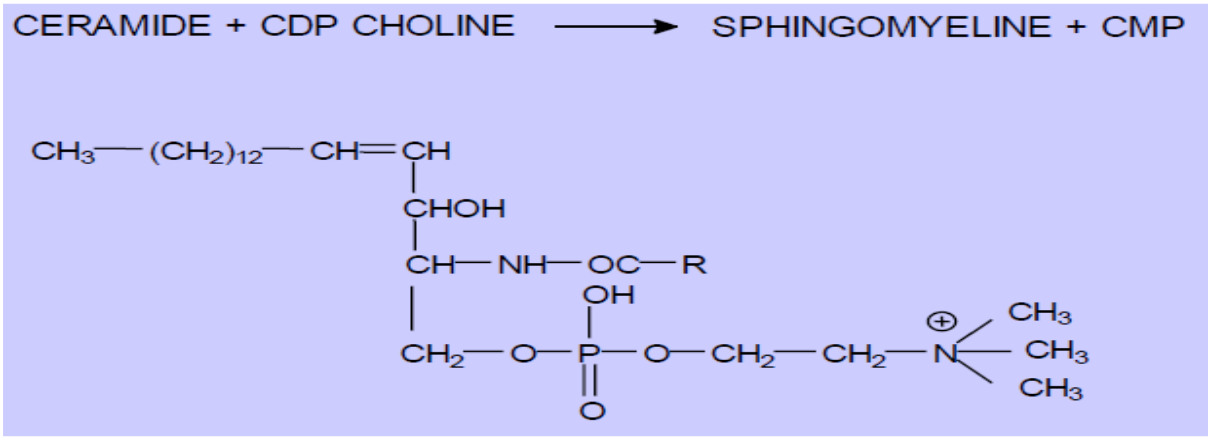


- **Ceramides**

Ceramide is the key intermediate in the synthesis of most sphingolipids.

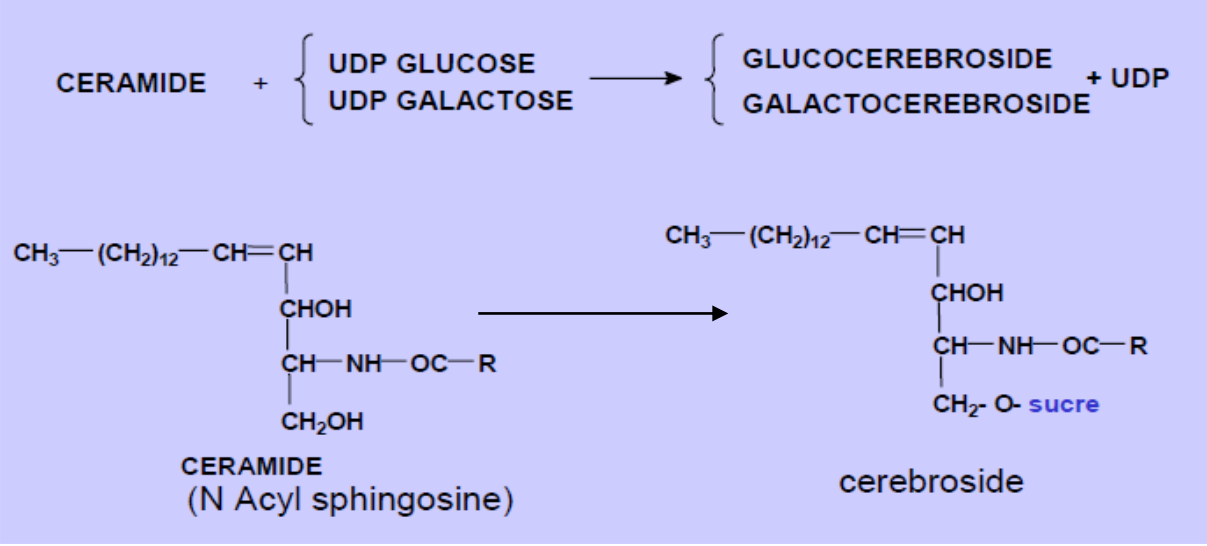


- **Biosynthesis of sphingomyelins**



- **Biosynthesis of glycolipids**

The primary alcohol function of ceramide binds a carbohydrate moiety via a glycosidic bond to the anomeric carbon of a sugar. The glycosidic moiety generally does not exceed ten units. They are classified according to the substituents carried by the carbohydrate portion.



After synthesis, lipids are transferred from the smooth ER to other membranes in various ways:

- Through direct communication with the RER, allowing lateral diffusion.
- Through vesicles that detach, move along the cytoskeleton, and fuse with thermo-membranous organelles.
- Through phospholipid transfer proteins.