Biochemistry of myelin

Sphingolipids properties	1-Cell transformation 2-Abundant in nervous tissue 3-Also exist in Extra-nervous tissue (e.g.: They are used as cell surface receptors for cholera and Diphtheria toxins as well as for certain viruses). 4- Very antigenic (They're also the source of blood group antigens, various embryonic antigens and some tumor antigens.) 5-Play role in Regulation of growth & development 6-Essential component of membranes
Sphingolipids chain	- are based on the unsaturated long chain amino alcohol called sphingosine CH3 – (CH2)12 – CH = CH – CH – CH –CH2OH | | OH NH2 - When a long fatty acid chain is attached to the amino group of sphingosine, it will produce Ceramide, which is the parent compound of the most of sphingolipids.

Ceramide

What is it?

- It's the precursor of sphingomyelin – and the other sphingolipids -.

How is it produced?

- By attaching of a long fatty acid chain to the amino group of sphingosine.

Ceramide = Sphingosine + fatty acid.

Sphingomyelin

What is it?

- It's the major structural lipid in the membranes of nerve tissue.

Sphingomyelin = Ceramide + Phosphorylcholine.

How is it produced?

- By reaction of ceramide and phosphatidylcholine. It'll result in separation of phosphatidylcholine to diacylglycerol and phosphorylcholine (phosphate + choline) . Phosphorylcholine will then bind to ceramide to make sphingomyelin

Cerebrosides

What are they?

Cerebrosides = Ceramide + Monosaccharides

How is it produced?

By reaction of ceramide with UDP-Galactose or UDP-Glucose (UDP is a carrier for sugar), then UDP will leave the sugar with ceramide resulting in Gluco/Glactocerebroside

Glactocerebroside

Glactocerebroside may react with PAPS (which is a sulfate carrier) and take Sulfate from it to make Sulfatide, which is an important lipid compenent in the brain.

This is Glactocerebroside (Galactose + ceramide)

Gangliosides

What are they?

Gangliosides = Ceramide oligosaccharides + NANA

-oligosaccharide: is a saccharide polymer containing a small number of monosaccharides (from 3 to 10)

How is it produced?

By reaction of ceramide with two or more UDP-sugars to produce Globoside, which will react with CMP-NANA (CMP is a carrier for NANA) and CMP will leave resulting in the synthesis of a ganglioside

Myelin Structure & Function	**What is it?** Myelin is a specialized cell membrane that ensheathes an axon to form a myelinated nerve fiber. **It's function:** Myelin sheath insulates the nerve axon to: 1- avoid signal leakage. 2- greatly speeds up the transmission of impulses along axons.
Myelin is produced by	**1-Schwann cells** **(Exist in Peripheral nerves)** **2-Oligodendrocytes** **(Exist in CNS)** **Fatty acid of myelin sheath**: Very long chain fatty acids, it's either Lignoceric **(24:0)** or Nervonic **(24:1)**
Myelin composition	**1-Lipids (80%)** **A- Main component: Cerebrosides** **B- Other component: Sphingomyelin** **2-Proteins (20%)** **e.g., Myelin basic protein (MBP)**

Multiple sclerosis

What is it?

A Neuro-degenerative, auto-immune disease.

How does it happen?

By the breakdown of myelin sheath (demyelination), which leads to a defective transmission of nerve impulses.

Sphingolipidosis

What is it?

An abnormal condition where the Synthesis of sphingolipids is normal; but the Degradation is defective, which will result in Substrate accumulates in organs.

Sphingolipidosis characteristics:	1-Autosomal recessive (mostly) 2-it's Progressive and may cause early death 3- Phenotypic and genotypic variability 4-it's rare,Except in Ashkenazi Jewish
Sphingolipidosis Diagnosis	1-Measure enzyme activity 2-Histologic examination 3-DNA analysis
Treatment	1-Replacement Therapy: Recombinant human enzyme. 2-Bone marrow transplantation: For Gaucher disease.

Disease	Tay-sachs	Gaucher	Niemann-pick (A+B)	
Deficient Enzyme	β-Hexosaminidase A (α subunit)	β-glucosidase (glucocerebrosidase)	Sphingomyelinase	
Lipid Accumulated	Gangliosides (Gm2)	glucocerebrosides	Sphingomyelin	
Clinical Features	-Blindness. -Cherry-red macula. * -muscular weakness and seizures. -Deficiency of activator protein (Gm2 Activator)	-The most common one. -Hepatosplenomegaly -Osteoporosis of long bones. -CNS involvement in rare infantile (in infants) and juvenile (in children) forms. -Enzyme Replacement therapy is usually successful for this disease.	**Type A:** -Enzyme Activity is reduced to 1% and less than normal. -Fatal Disease	**Type B:** - Little enzyme act - Chronic Disease.
			-More severe. -Death in early childhood. -Hepatosplenomegaly -Neurodegenerative course. -*Cherry red macula	-Less severe form type A -Later onset - Little enzyme act -Hepatosplenomegaly -*Cherry red macula

*Cherry-red macula is: There is an area in the retina that is called macula, it acts as a natural sun-block (it blocks ultraviolet rays that enter and harm the eye), usually it's yellow in color but when it's affected it becomes red under the light.