Lipooligosaccharide

Lipooligosaccharide (LOS):

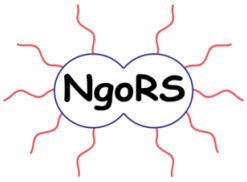
- Amphipathic glycolipid that constitutes a major component of the outer membrane.
- Gonococcal LOS lacks the repeating polysaccharide O-antigen, which is characteristic of LPS; thereby, LOS is considered a more appropriate term.
- Oligosaccharide substitutions exhibit inter- and intrastrain variability. Interconversion (phase and antigenic variability) of LOS oligosaccharides occurs spontaneously and is dependent upon the presence or absence of available substrates for, and enzymes involved in, LOS biosynthesis.
- LOS (and LPS) is also called "endotoxin", which refers to the toxicity associated with lipid A, a constituent of the LOS core structure.

Molecular Mimicry:

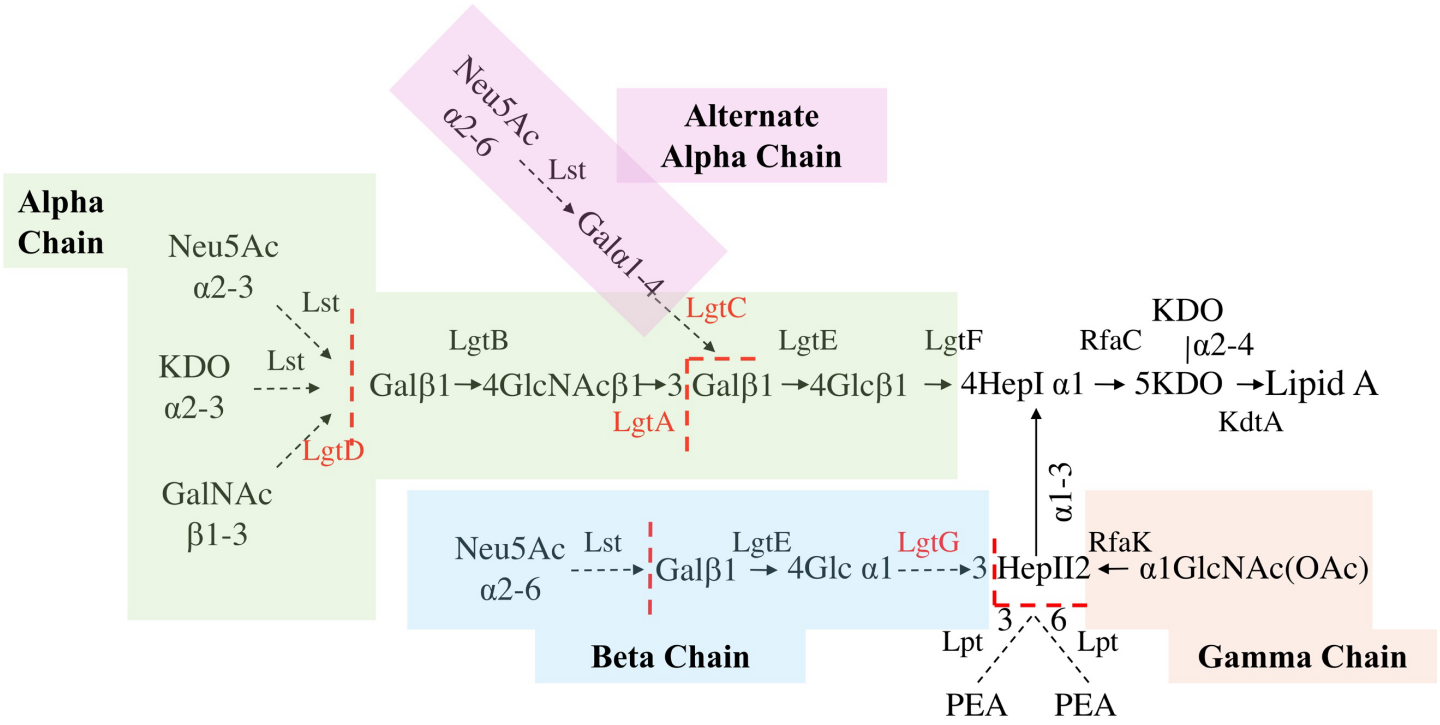
- LOS oligosaccharide side chains terminate in epitopes that mimic oligosaccharide moieties of host glycosphingolipids.

Oligosaccharide Branch Structure	Antigen Mimicked
Galβ1 - 4Glcβ1	Lactosyl
Galα1 - 4Galβ1 - 4Glcβ1	P^k antigen
Galβ1 - 4GlcNAcβ1 - 3Galβ1 - 4Glcβ1	Lacto-*N*-neotetraose (LnNT)* (paragloboside)
Neu5Acα2 - 3Galβ1 - 4GlcNAcβ1 - 3Galβ1 - 4Glcβ1	Sialyllactosamine (i antigen)
Neu5Acα2-	Sialic Acid

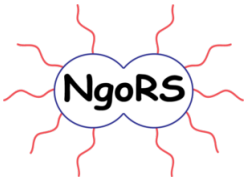
* Greater than 95% of gonococci express a terminal lacto-*N*-neotetraose
Gal – Galactose; Glc – Glucose; GlcNAc – N-acetylglucosamine; Neu5Ac – sialic acid (5-N-acetylneuraminic acid)



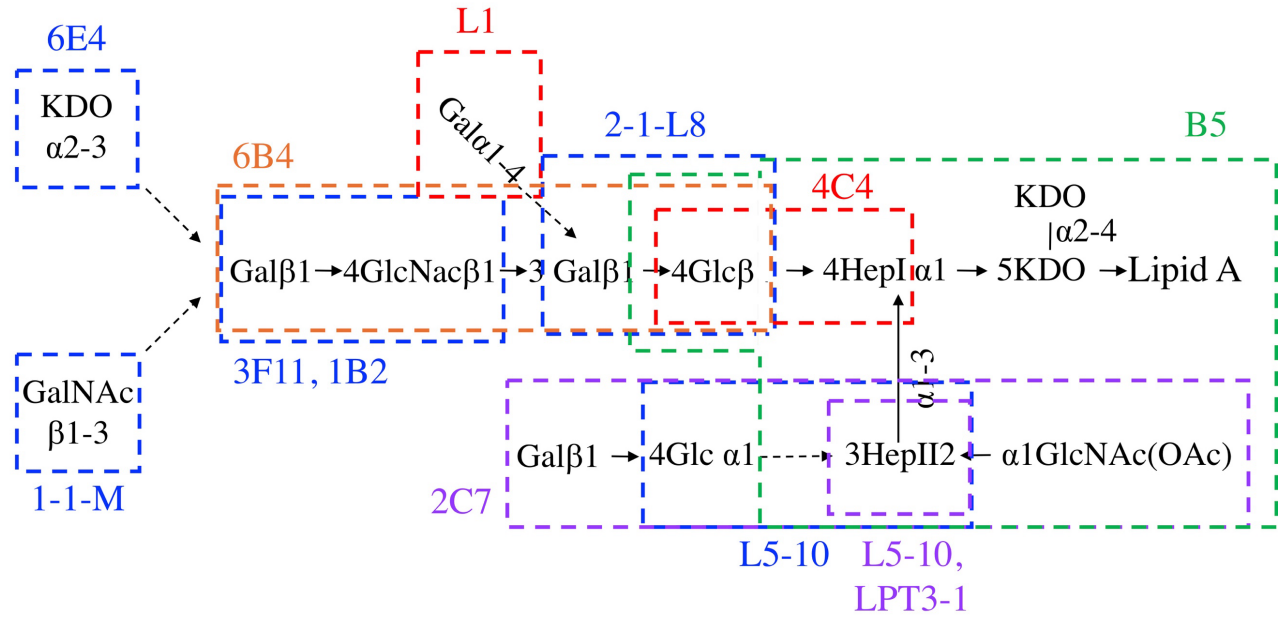
LOS Structural Variation:

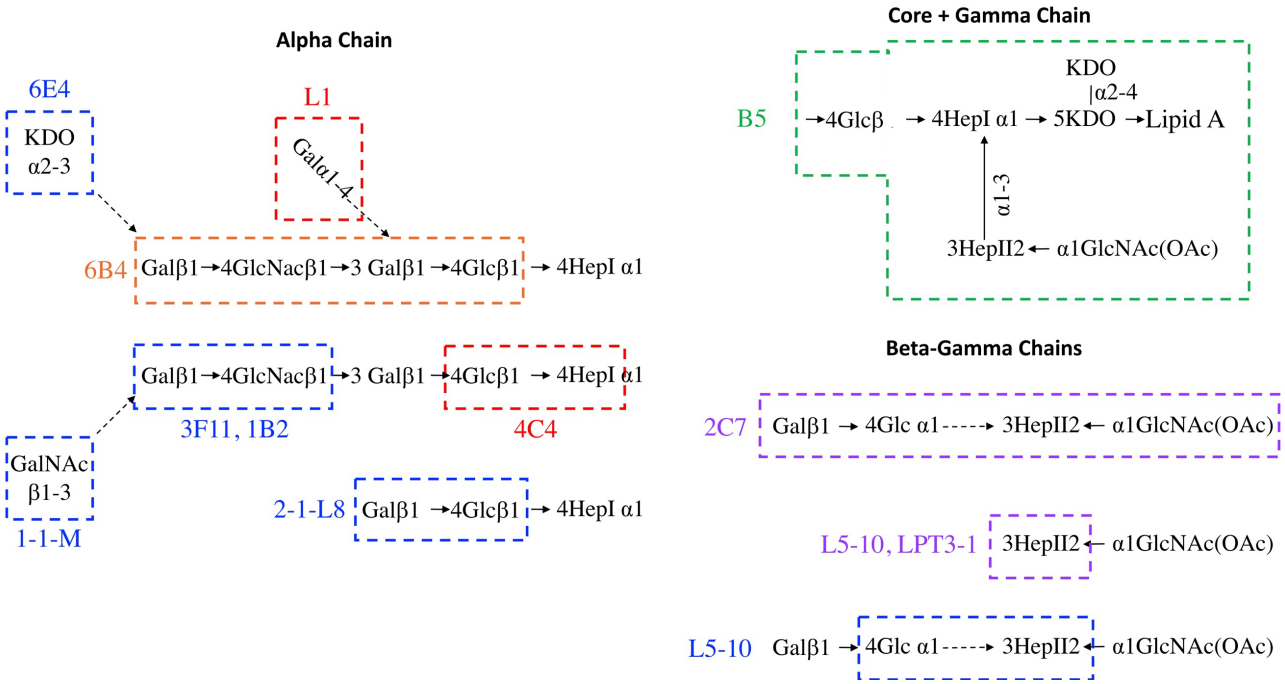


Possible LOS Structures. LOS general structure showing the alpha (green), alternative alpha (pink), beta (blue), and gamma (orange) chains comprising the LOS molecule. Glycosyltransferases mediating each addition to the lipid A-KDO-heptose core region are noted. Phase variable proteins/genes are shown in red text and lead to alternative LOS structures – points of potential variation are noted as (red) dotted lines. Lst, N-acetyllactosaminide alpha-2,3-sialytransferase; LgtA-G, glycosyltransferases; KdtA, 3-deoxy-d-manno-2-octulosonic acid (KDO) transferase; RfaK, alpha-1,2-N-acetylglucosamine (GlcNAc) transferase; Lpt3/6, lipopolysaccharide transport protein; Hep, heptose; PEA, phosphoethanolamine.

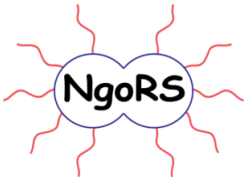


Anti-LOS Antibodies:





Anti-LOS antibody recognition sites: Specific sites within the LOS molecule that are recognized by available monoclonal antibodies are noted (top panel). Epitopes recognized are outlined with dotted lines. Antibodies recognizing each site are noted adjacent to the appropriate epitope and are color coded (top and bottom panels).

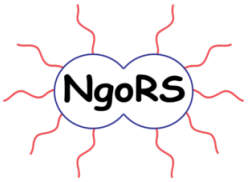


Gonococcal LOS Structures Described to Date

Table derived from Tzeng *et al. Front. Immunol.* https://doi.org/10.3389/fimmun.2024.1350344

Strain	α-chain (HepI)	β-chain (HepII)		L type[1]
		3-	6-	
1291	*Gal – GlcNAc – Gal - Glc-	PEA	H	L3
FA1090[2]	GalNAc – Gal – GlcNAc – Gal - Glc-	*Gal – Glc –	PEA	
	*Gal – GlcNAc – Gal - Glc-	*Gal – Glc –	PEA	L2
	*Gal - Glc-	*Gal – Glc -	PEA	
MS11	*Gal – GlcNAc – Gal – GlcNAc – Gal - Glc-	*Gal – Glc -	$PEA_{(0-1)}$	
	*Gal – GlcNAc – Gal – GlcNAc – Gal - Glc-	PEA[3]	$PEA_{(0-1)}$	
	GalNAc – Gal – GlcNAc – Gal - Glc-	PEA	$PEA_{(0-1)}$	
	*Gal – GlcNAc – Gal -Glc-	PEA	$PEA_{(0-1)}$	L3
	GlcNAc – Gal -Glc-	PEA	$PEA_{(0-1)}$	L6
	*Gal – Gal -Glc-	PEA	$PEA_{(0-1)}$	L1
FA19	*Gal – GlcNAc – Gal - Glc-	PEA[3]	PEA	L3
	*Gal - Glc-	PEA	PEA	L8
	*Gal – Gal - Glc-	PEA	PEA	L1
F62	GalNAc – Gal – GlcNAc – Gal - Glc-	PEA[3]	ND	
	*Gal – GlcNAc – Gal - Glc-	PEA	ND	L3

1 – L immunotypes are more commonly used when referring to *N. meningitidis*; therefore, L types noted are based on similarity to oligosaccharides found within meningococcal LOS.
2 - FA1090 structure predicted by mAb reactivities.
3 - F62, MS11, and FA19 are reported to be positive for mAb B5, which recognizes 3-PEA-HepII.
ND, Not defined
* Potential Neu5Ac sialylation site



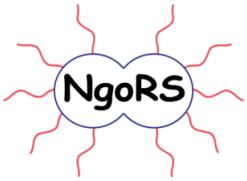
Nomenclature of Select Surface Antigens

Look for future protocols focused on some of the proteins and antigens noted below.

Historical designations of select proteins and antigens:

Protein or Antigen	Designation	Prior Designation(s)
Porin	PorB[1] PorB1.A and PorB1.B isotypes Various serovars/classes	Protein I (P.I, PI) Major Protein[2] Major outer membrane protein (MOMP) Principal outer membrane protein (POMP)
Opacity-associated outer membrane protein (Opa)	Opa OpaA-I(J) serotypes	Protein II (P.II, PII, PII*) Protein 2 (P.2, P2, P2*) Minor protein (mP) Heat-modifiable proteins (hmP) Opacity-associated protein (OAP) Leukocyte-associated protein
Reduction-modifiable Protein (Rmp)	Rmp	Protein III (P.III, PIII) Protein 3 (P3) Protein 3,3* (P3,3*)
Lipooligosaccharide (LOS)	LOS	Lipopolysaccharide (LPS) Endotoxin
Pilin[3]	Pilin (Pil) *pilE* gene	NA
H.8 antigen[4]	H.8 antigen	NA[5]

1 - Gonococcal nomenclature regarding porin is based on its homology to meningococcal PorB.
2 - Porin accounts for greater than 60% of the total weight of proteins present in the outer membrane of the gonococcus
3 – Pilin refers to each individual pilin subunit, which polymerize to form a pilus fiber.
4 – The H.8 antigen comprises an AAEAP pentameric repeat found in the Lip (lipoprotein) and Laz (lipid-modified azurin) proteins.



5 – The H.8 epitope is named after the first monoclonal antibody hybridoma shown to recognize this surface epitope in pathogenic *Neisseria*

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