

**Bacterial Polysaccharide**  
**Function of Bacterial and Viral Polysaccharides**

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**Overview**

**General structure of bacterial cell walls**

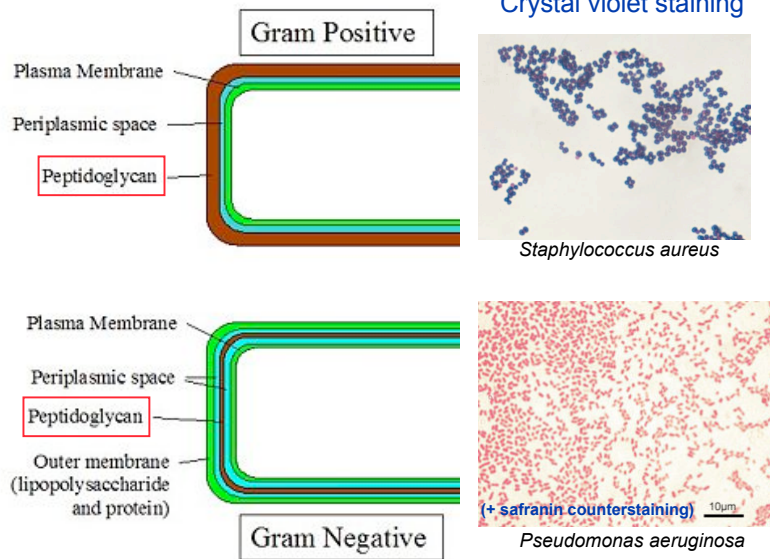
**Peptidoglycan (murein)**

**Periplasmic  $\beta$ -glucans (MDO)**

**Lipopolysaccharide (LPS)**

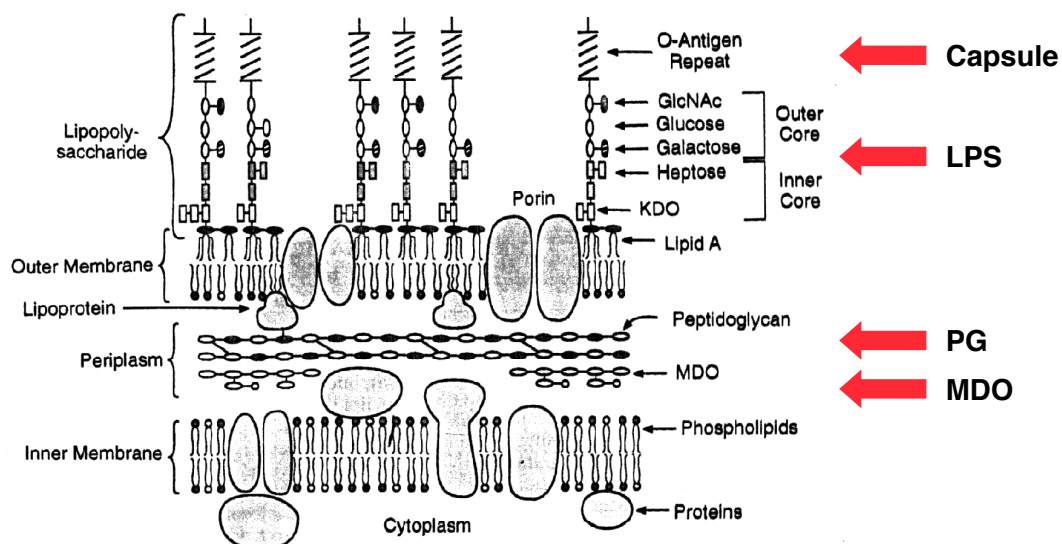
**Capsular polysaccharides**

## Gram-positive and Gram-negative bacteria



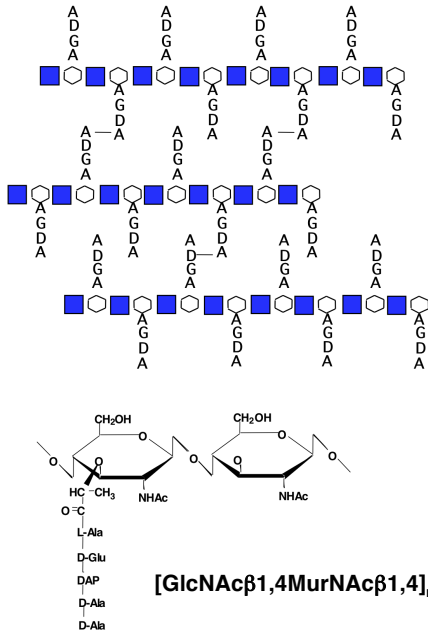
1. Based on retention of crystal violet dye (Gram staining)
2. The Gram staining classifying two distinct types of bacteria based on structural difference in their cell wall (Gram+ and Gram-)
3. The positive staining is caused by a high amount of peptidoglycan in the cell wall of Gram+ bacteria.
4. Gram+ bacteria lack outer membrane, and have a thicker peptidoglycan with teichoic acids
5. Many species of Gram-bacteria are pathogenic, causing disease in a host organism.
6. This pathogenic capability is usually associated with certain component of Gram- cell wall.

## Gram-negative bacteria cell wall



**Structure of the cell wall of E. coli.** The cell wall of gram-negative bacteria consists of several layers of various polysaccharides. The periplasm contains peptidoglycan, a copolymer of polysaccharide and short peptides, and a class of  $\beta$ -glucans known as MDOs. The outer leaflet of the outer membrane is rich in LPS. In mucoid strains, a capsular polysaccharide covers the entire cell.

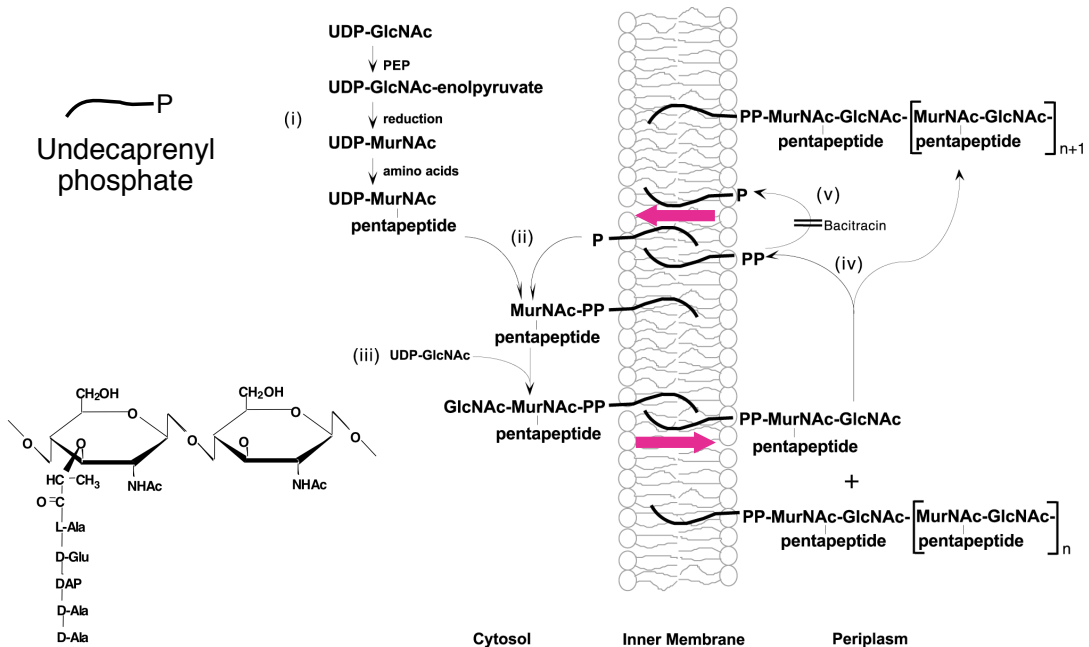
# Peptidoglycan



1. Consists of parallel strands of polysaccharide composed of GlcNAc and N-acetylmuramic acid (MurNAc) in  $\beta$ -1,4 linkages, cross-linked by covalently bound short peptides composed of L-Ala, unusual D-amino acids (D-Glu & D-Ala), and L-diaminopimelic acid (L-DAP).
2. 10% dry weight of cell wall, representing the major structural component of periplasm
3. Confers mechanical strength & Shape cell
4. Withstand internal osmotic pressure

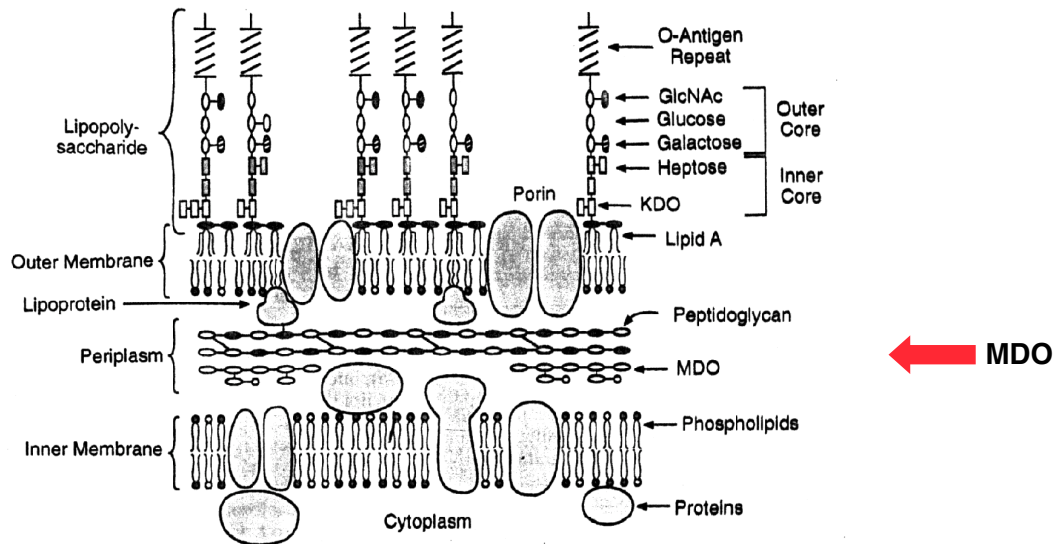
Heijenoort (2001) Glycobiology 11:25R

# Peptidoglycan Biosynthesis

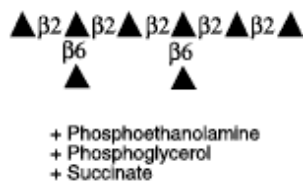




## Gram-negative Bacteria Cell Wall

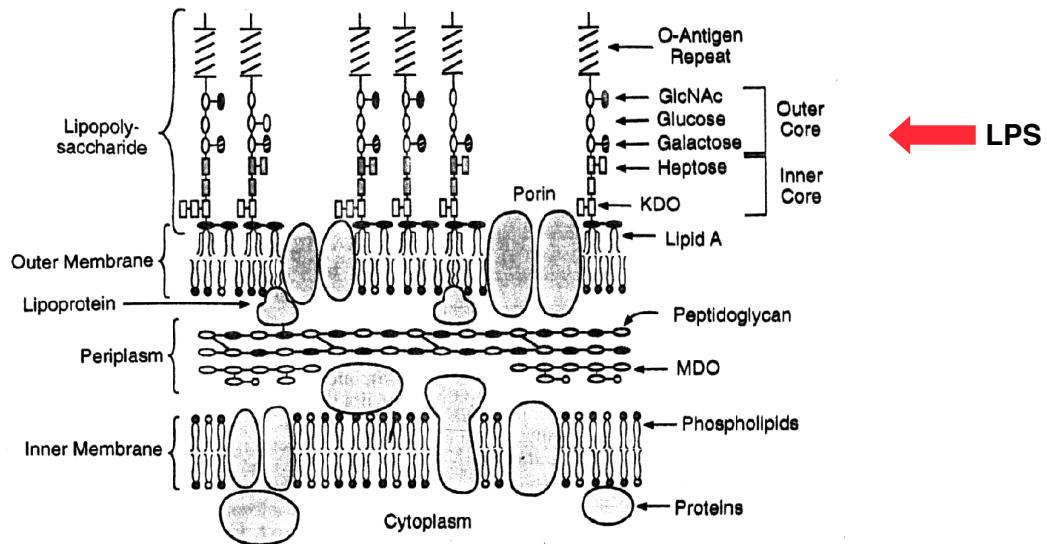


## Membrane Derived Oligosaccharides (MDO)

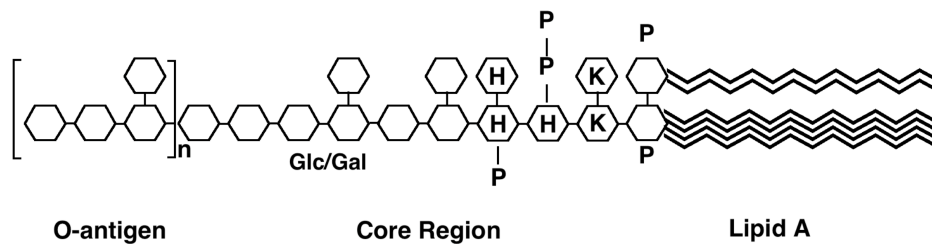


- Branched  $\beta$ -glucans
- Generally consists of 6–12 glucose units, mostly in  $\beta 1-2$  linkages with  $\beta 1-6$  branches
- Represent about 1-5% of dry weight
- Require UDP-Glc and undecaprenyl-PP-Glc as a primer and carrier for MDO assembly
- Charged substituents act as an osmolyte and protects the inner membrane against the large difference in osmolarity inside the cell compared to outside the cell

## Gram-negative Bacteria Cell Wall



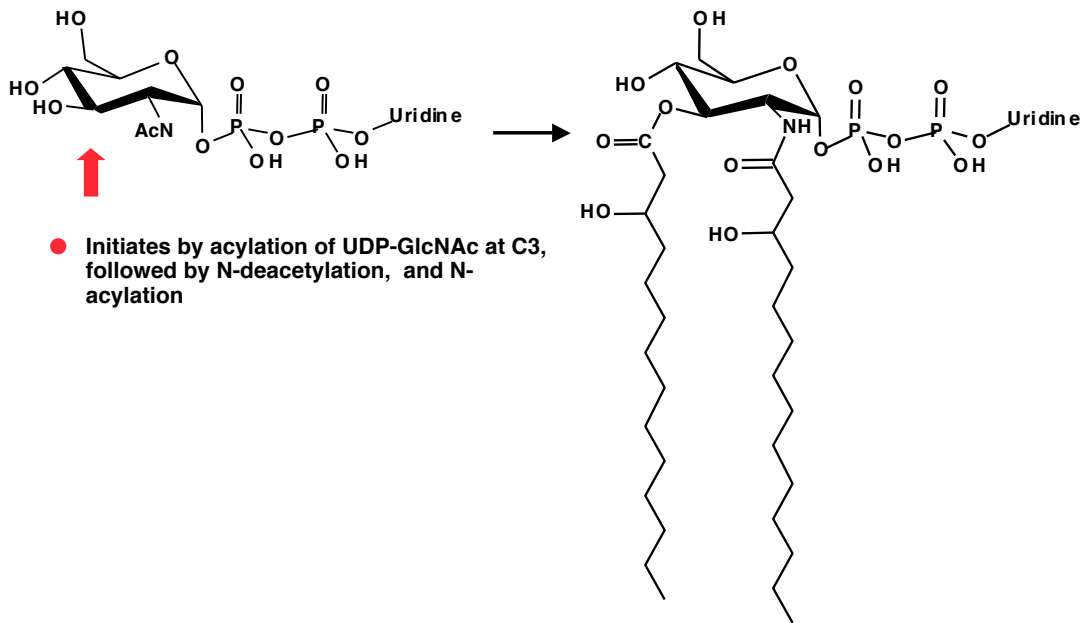
## Lipopolysaccharide (LPS)



LPS consists of three domains

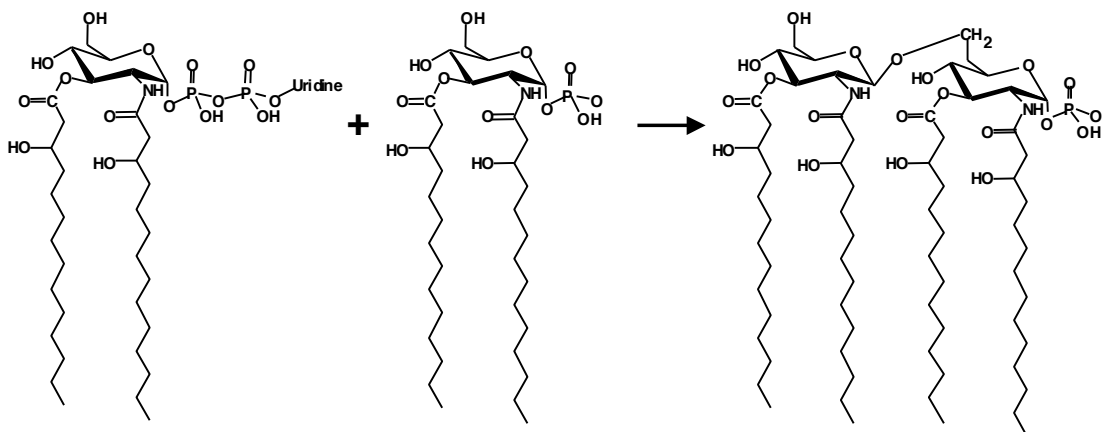
- Lipid A, also known as endotoxin
- Core region composed of KDO (K), heptoses (H), and hexoses (open hexagons)
- Highly variable outer O-antigen region

## Lipid A Assembly



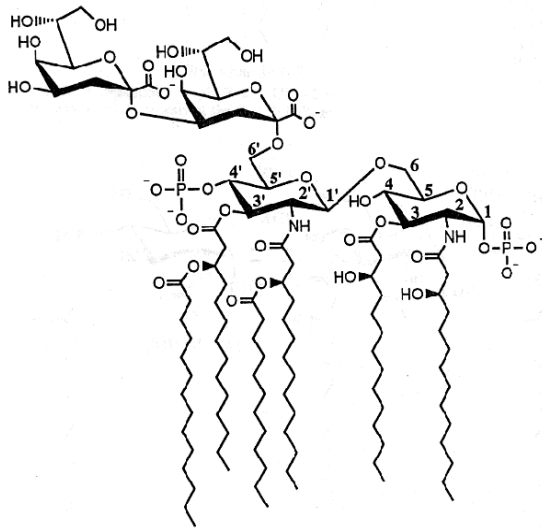
Wyckoff et al. (1998) Trends Microbiol. 6:154

## Lipid A Assembly



Diacylglucosamine-1-P condenses with another molecule of UDP-diacylglucosamine to form the tetraacyl disaccharide core

## Lipid A Assembly



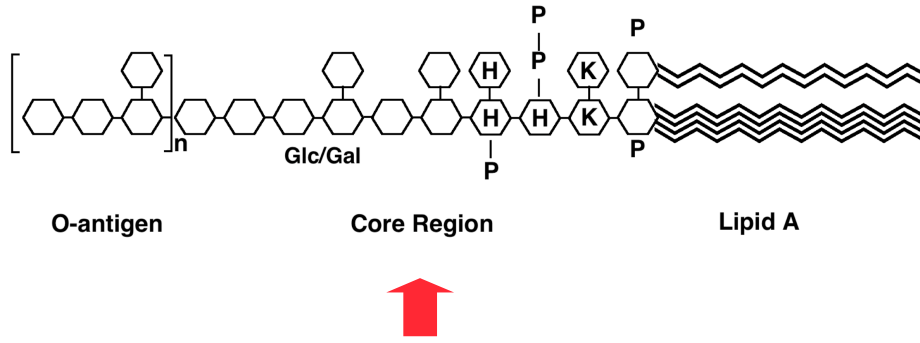
- KDO transferases initiate the formation of the core
- Additional C12 fatty acids added to  $\beta$ -hydroxy groups (wax)
- Lipid A translocates to the outer leaflet of the outer membrane by msbA (ABC transporter)

Doerrler et al. (2001) J Biol Chem. 276:11461

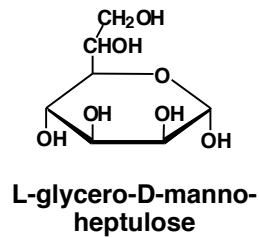
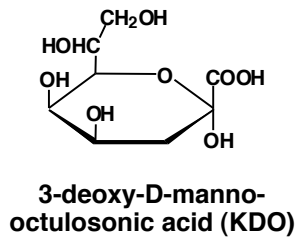
## Lipid A Biology

- Lipid A, the heat stable endotoxin of gram negatives
- Cause fever, septic shock, and a variety of deleterious physiological effects
- When released in blood circulation, LPS binds to CD14 on monocytes and macrophages, triggers cytokine secretion
- A significant target to treat bacterium-infection resulted human diseases

## LPS Structural and Functional Domains

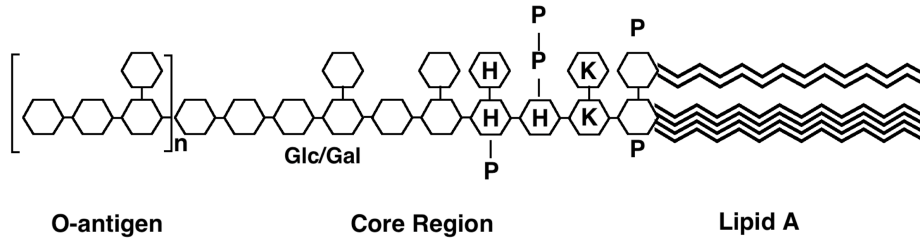


## Core region contains unusual sugars



- The inner core contains 1-4 KDO residues, which look like an analog of sialic acid
- The core also contains heptopyranoses, which can vary stereochemically
- The rest of the core consists of various combinations of Glc and Gal

# LPS Structural and Functional Domains

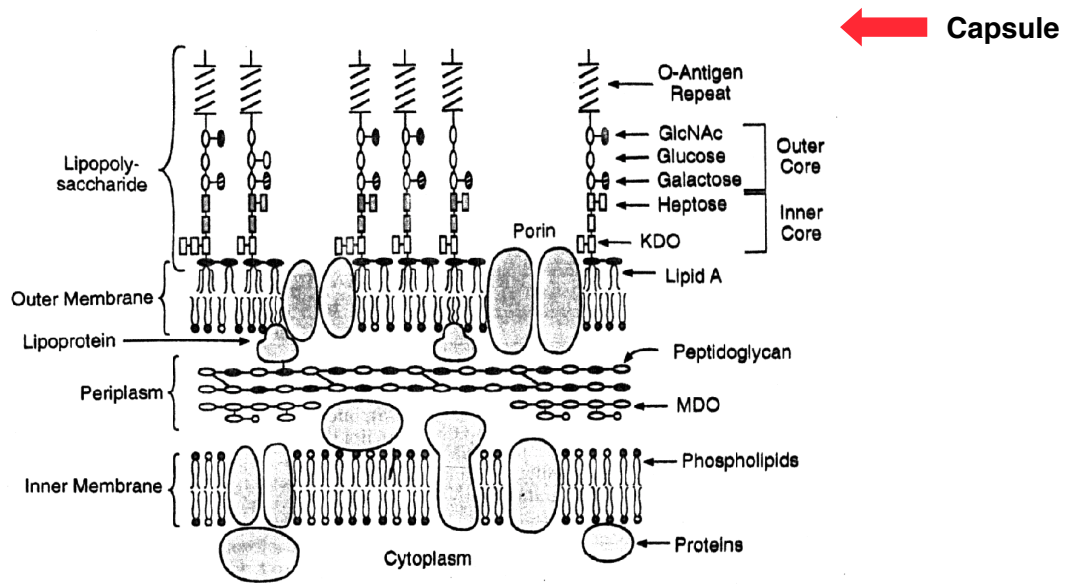


## O-antigens

O-antigen	Structure
O9	● <sub>α3</sub> ● <sub>α2</sub> ● <sub>α2</sub> ● <sub>α2</sub> ● <sub>α3</sub>
O6	■ <sub>α3</sub> ● <sub>β4</sub> ● <sub>β3</sub> ■ <sub>α4</sub> ● <sub>β2</sub>
O124	■ <sub>β3</sub> ● <sub>β6</sub> ● <sub>α3</sub> ● <sub>α4</sub> ● <sub>β6</sub> GlcLA

- O-antigens consist of 2-8 sugars, repeated ≤50 times
- O-antigens gives rise to different serotypes and some are correlated with disease

GlcLA = glucolactillic acid



**Gram-negative bacteria cell wall**

Capsule type	Structure
<b>K1, polysialic acid</b>	◆ $\alpha 8$ ◆ $\alpha 8$ ◆ $\alpha 8$ ◆ $\alpha 8$ ◆ $\alpha 8$ ◆
<b>K5, N-acetylheparosan</b>	■ $\alpha 4$ ◆ $\beta 4$ ■ $\alpha 4$ ◆ $\beta 4$ ■ $\alpha 4$ ◆
<b>Group A Streptococcus (hyaluronan)</b>	■ $\beta 4$ ◆ $\beta 3$ ■ $\beta 4$ ◆ $\beta 3$ ■ $\beta 4$ ◆

- Mucoid strains contain a polysaccharide capsule
- >80 different capsules types are known just in E. coli
- Extraordinary diversity of structure

## **Function of Capsule**

- **Adhesion receptor**
- **Deterrent to desiccation**
- **Resistance to phages and to complement in vertebrate host (virulence factor)**
- **Escape of host immunity (molecular mimicry)**

## **Carbohydrates of Bacterial Cell Wall**

**Peptidoglycan (murein)**

**Periplasmic  $\beta$ -glucans (MDO)**

**Lipopolysaccharide (LPS)**

**Capsular polysaccharides**

## **Function of Polysaccharides in Bacterial Cell Wall**

- **Have important structural and functional roles in the life of a bacterial cell**
- **The capsular polysaccharides and LPS represent the first line of defense against complement and bacteriophages**
- **Contain the major antigenic determinants that distinguish various serotypes of bacteria, which are sometimes correlated with diseases.**
- **Have compound effects on mammalian host. For example, Lipid A of LPS causes various secondary complications of infections, such as septic shock, multiple organ failure, and mortality.**
- **Considerable interest exists in developing anti-bacteria agents**