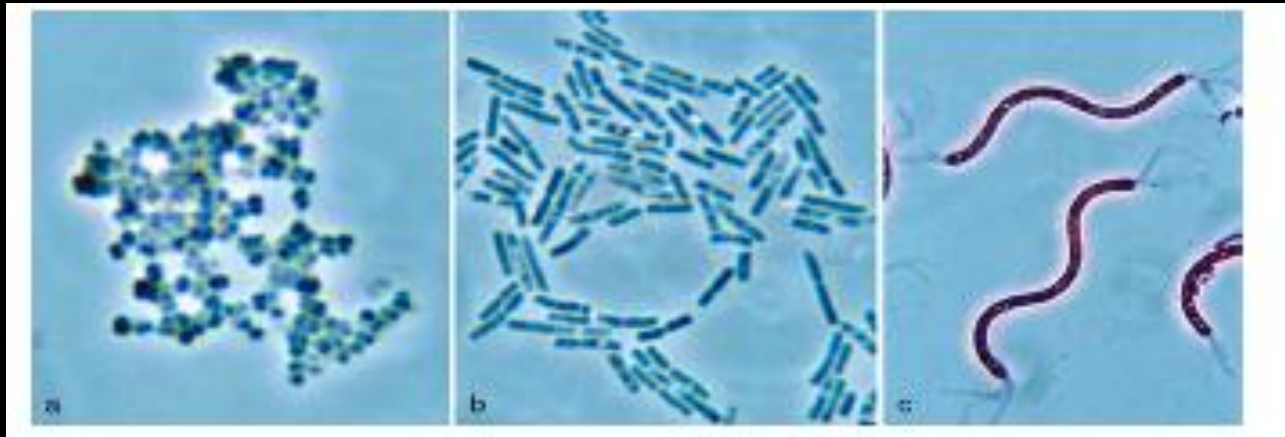


Bacteria are small and simple

Come in a variety of shapes.....



cocci

bacilli

spiral



Bacteria are small and simple

Come in a variety of shapes.....
and sizes

Red blood cells 8 μm

 *Mycoplasma genitalium* 0.4 μm

 *Haemophilus influenzae* 1.0 μm

 *Staphylococcus aureus* 0.9 μm

 *Escherichia coli* 1.5 μm

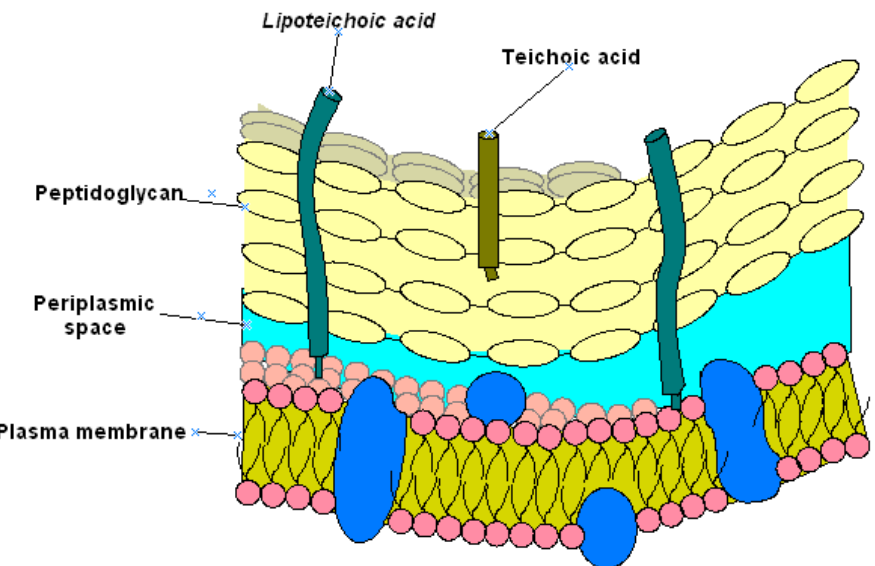
 *Bacillus megaterium* 4 μm



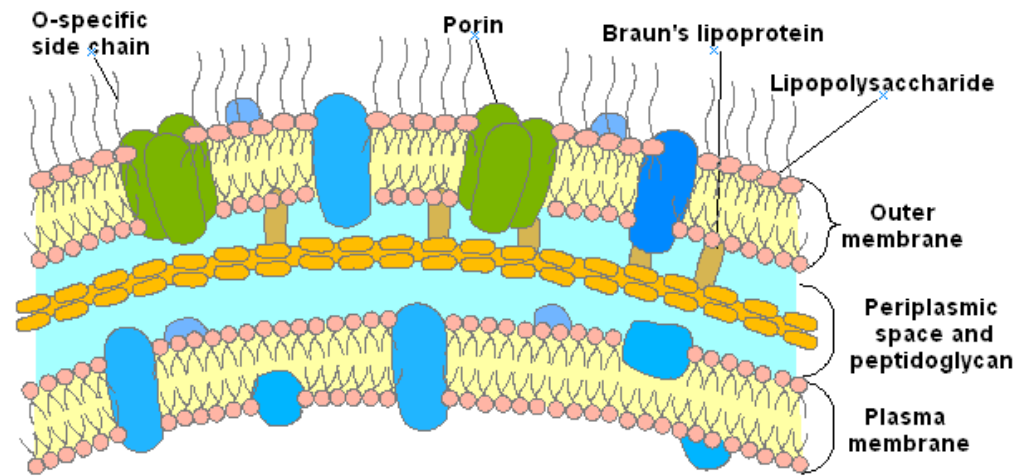
Bacteria are small and simple

Come in a variety of shapes.....
and sizes
and are Gram positive or negative

Gram-Positive Envelope



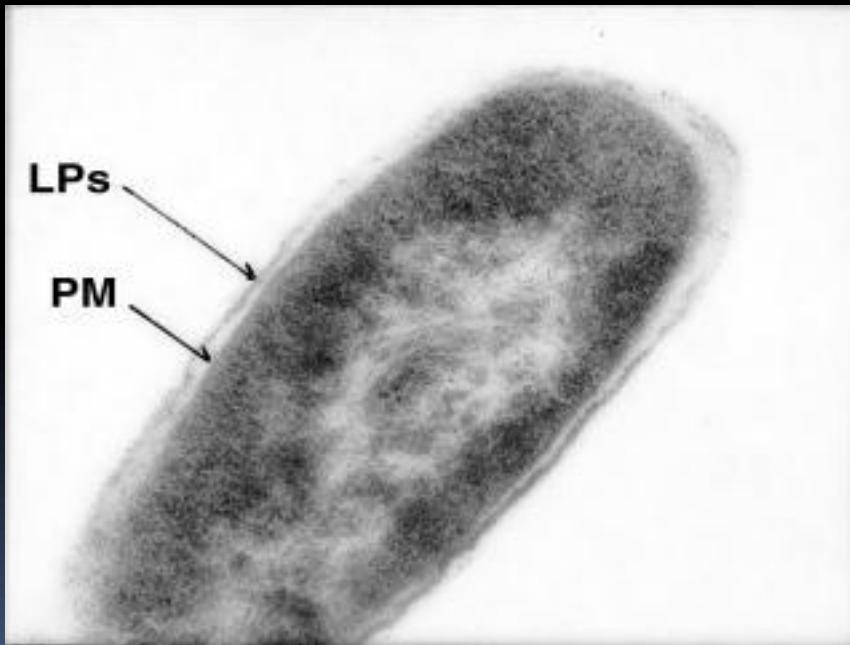
Gram-Negative Envelope



Bacteria are small and simple

Come in a variety of shapes.....
and sizes
and are Gram positive or negative

Escherichia coli

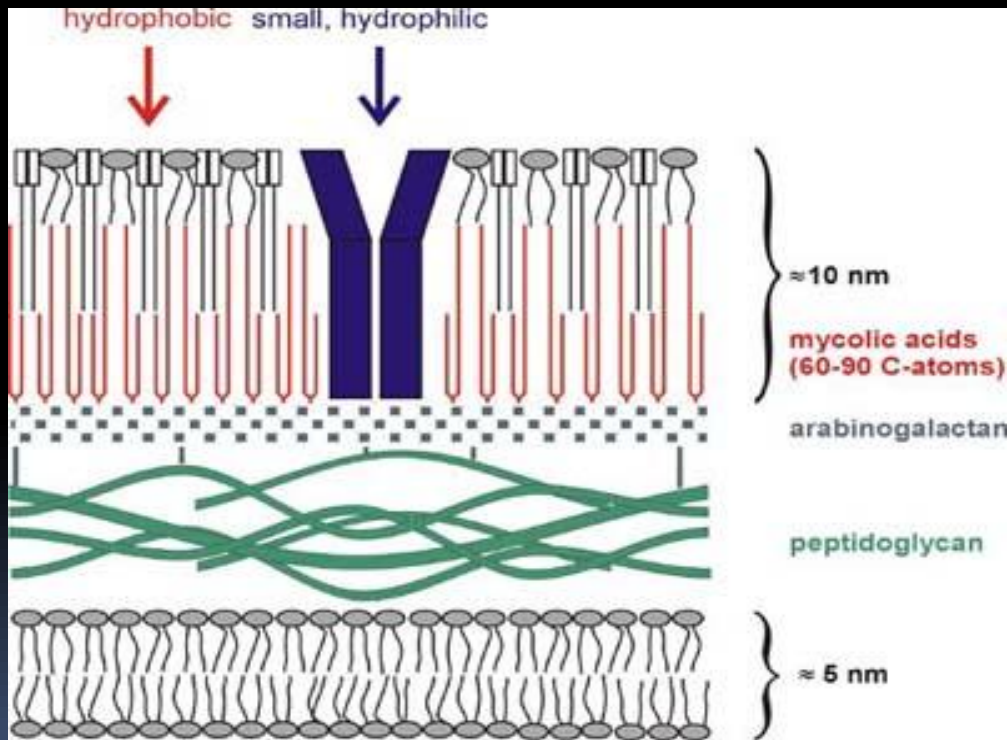


Streptococcus pyogenes



Bacteria are small and simple

Come in a variety of shapes.....
and sizes
and are Gram positive or negative OR Acid fast



Complex lipids, sugars,
Mycolic acid

Mycobacterium spp.

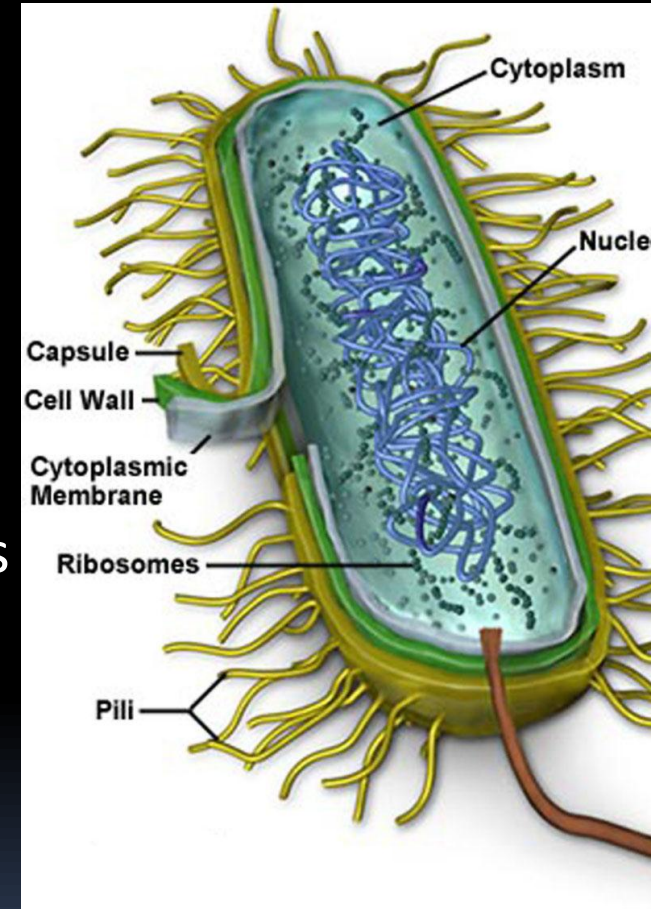


Bacterial structures

- contain complex nanomachines
- diagnostic
- epidemiologic
- key roles in pathogenesis

Targets

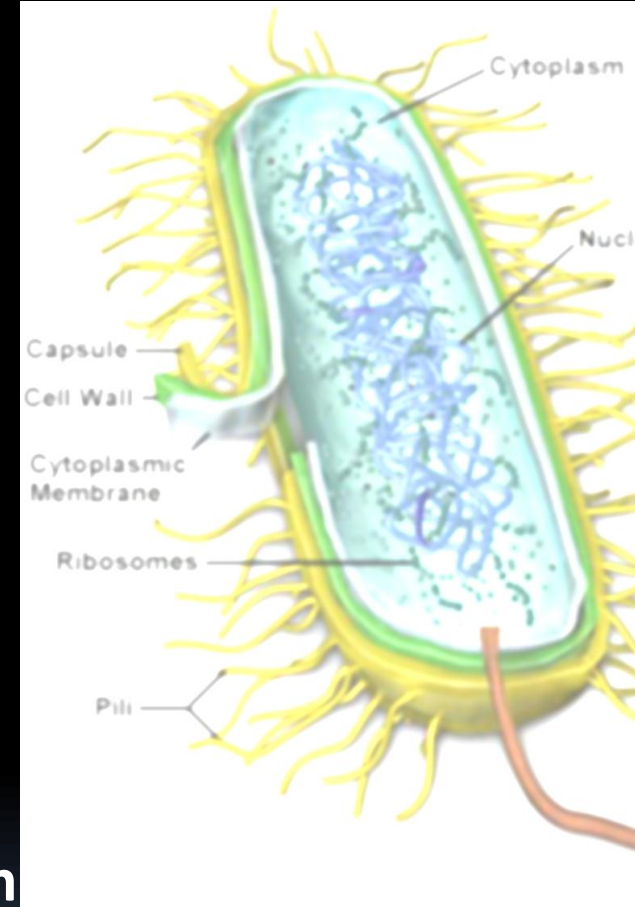
- for interventions
- for the immune system



Learning objectives

1) Describe important bacterial structures

- cell wall
- cell membrane
- capsule
- pili/fimbriae
- lipo-polysaccharide
- secretion systems
- spores



2) Biosynthesis of one of these

3) Recognition of these structures by the immune system

- examples

4) Role in pathogenesis/lifecycle

- for interventions

5) Examples : *Escherichia coli*

- for the immune system

The basic building blocks -cell wall

Bacterial cell walls (always) contain **murein**, which is a polymer of **peptidoglycan**

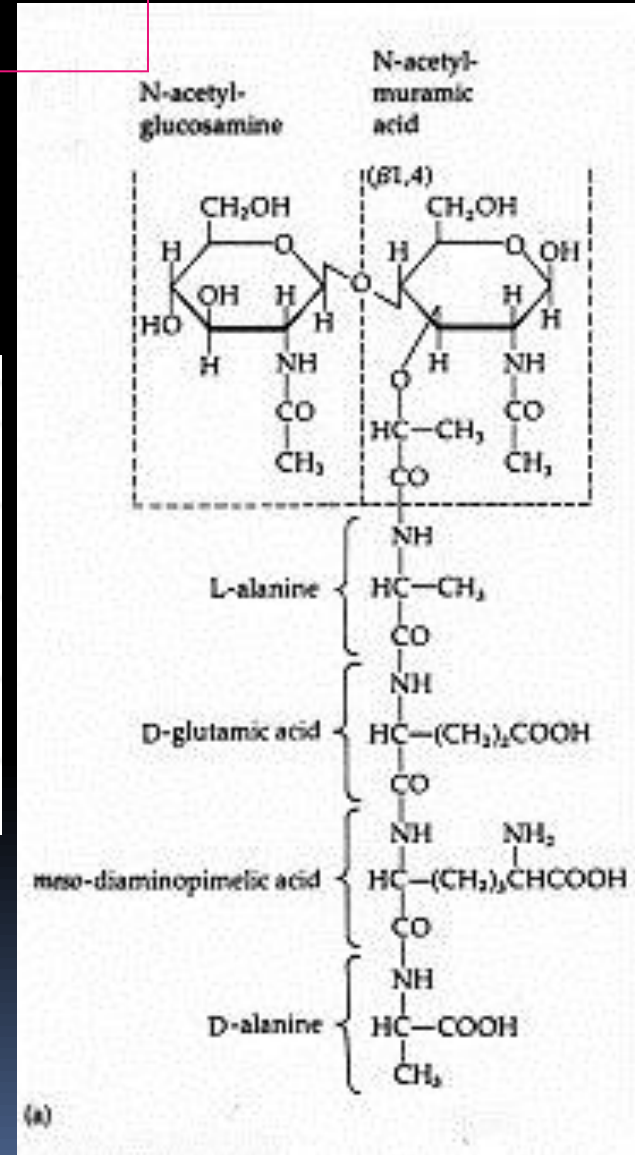
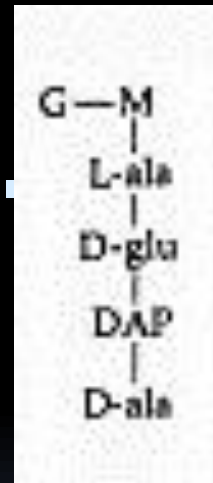
Chemical nature of murein accounts for the function of the cell wall

Murein is only found in bacterial cells

■

■

■



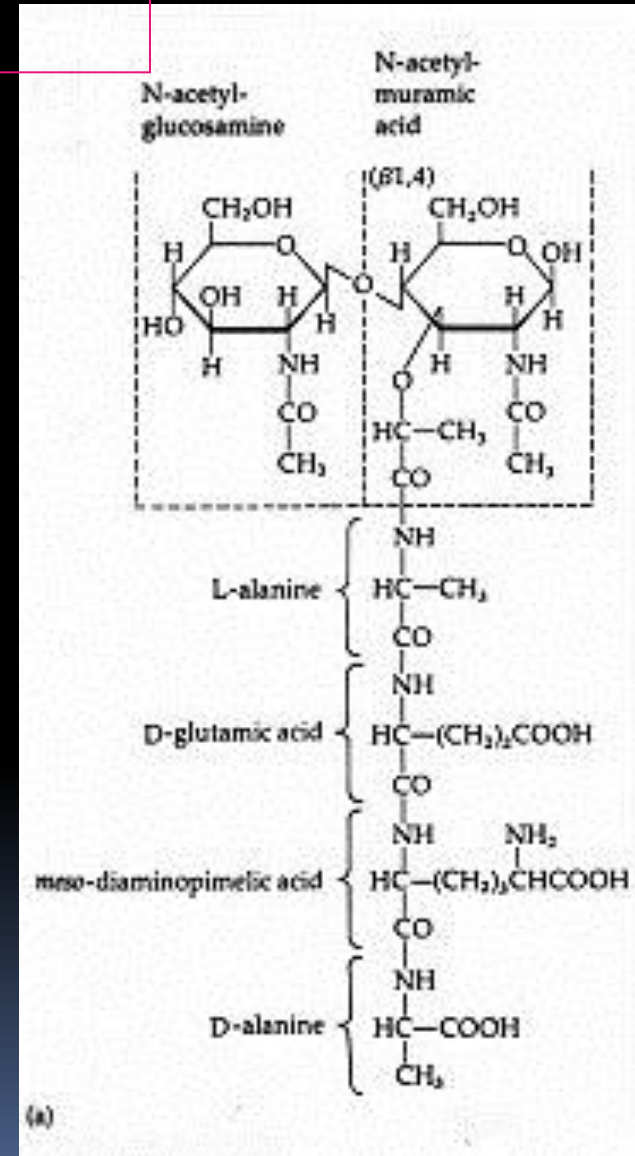
E. coli peptidoglycan

The basic building blocks -cell wall

Peptidoglycan is made up of

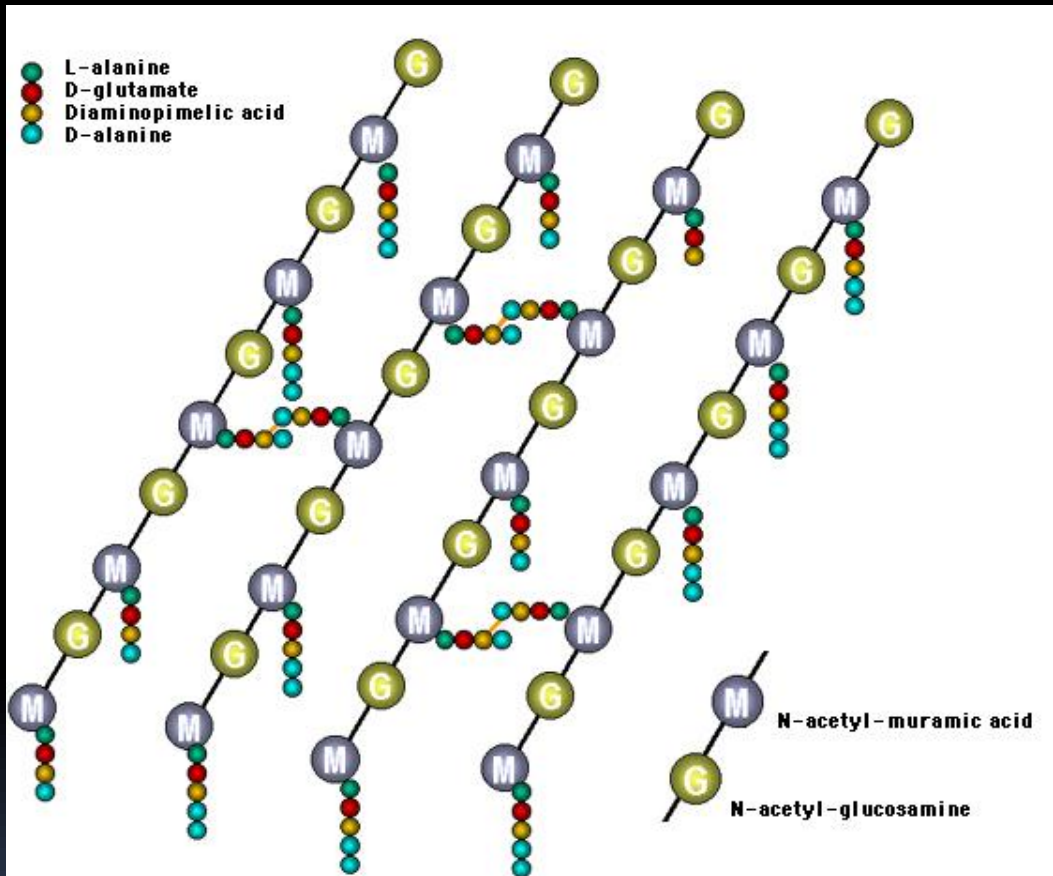
2 amino sugars ■
 = G N-acetyl glucosamine
 = M N- acetyl muramic acid

4 amino acids ■
 L-ala L-alanine
 D-glu D-glutamic acid
 DAP diaminopimelic acid
 D-ala D-alanine



E. coli peptidoglycan

The basic building blocks -cell wall



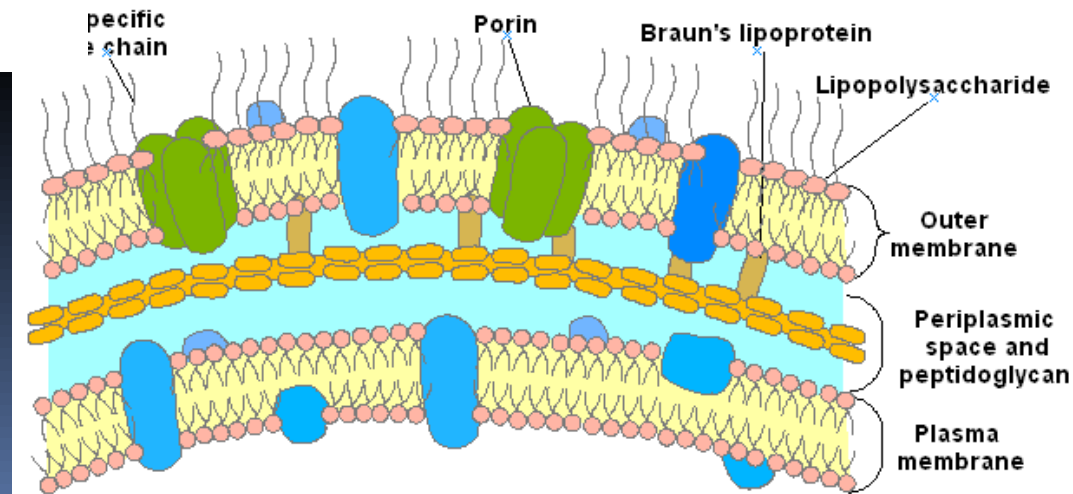
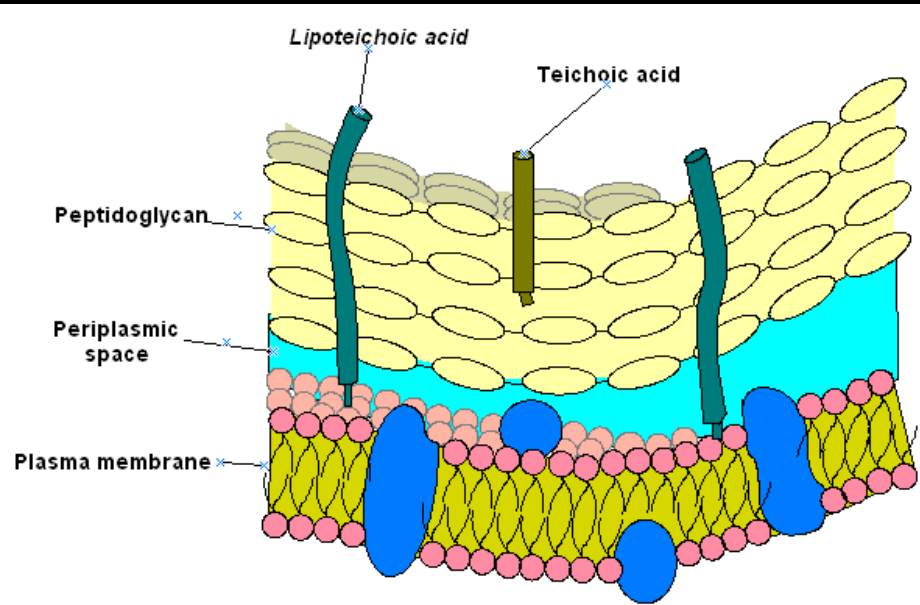
Murein is a polymer of the peptidoglycan subunit. The sugars form the glycan backbone (G-M-G-M-etc.) and the amino acids comprise the peptide side chains of the molecule.

The basic building blocks -cell wall

Peptidoglycan

Different locations in Gram positive and negative bacteria

Different extent in Gram positive and negative bacteria



The basic building blocks -cell membrane

The cell membrane (often called the plasma membrane) is composed of 2 layers of phospholipids.

Phospholipids have polar heads and non-polar tails.

“Polar” implies that the heads are hydrophilic: they like to stay in an aqueous environment: facing the outside world and the inside of the cell.

“non-polar” means that the tails are hydrophobic: they orientate away from water, The tails are in the central portion of the membrane

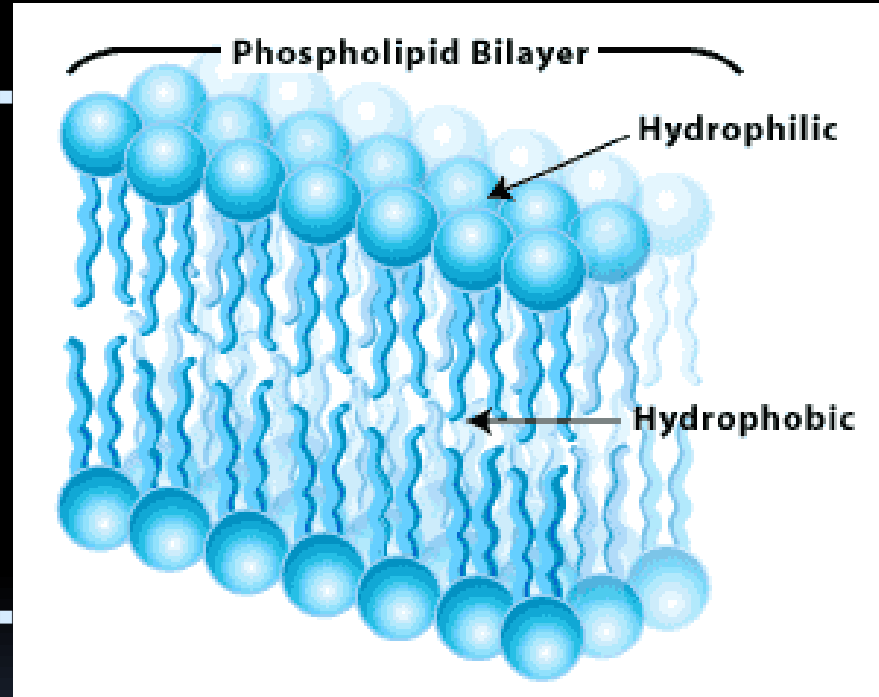
A pure phospholipid membrane only allows water, gases, and a few small molecules to move freely through it.

■

■

■

■

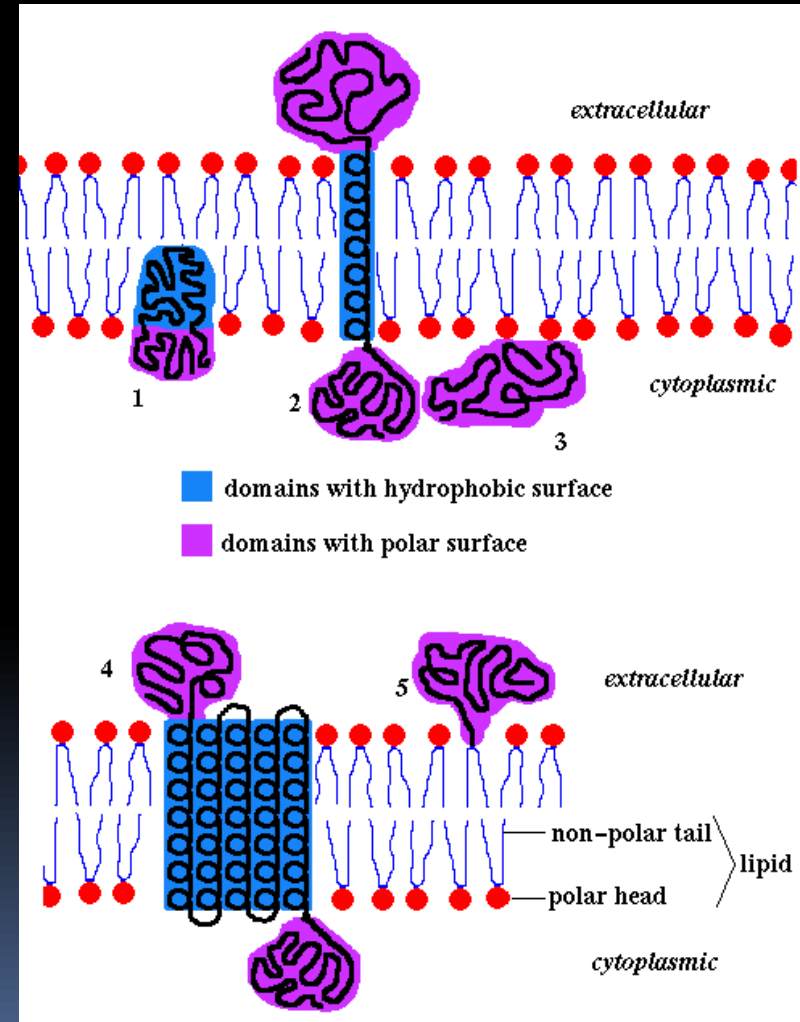


The basic building blocks -cell membrane proteins

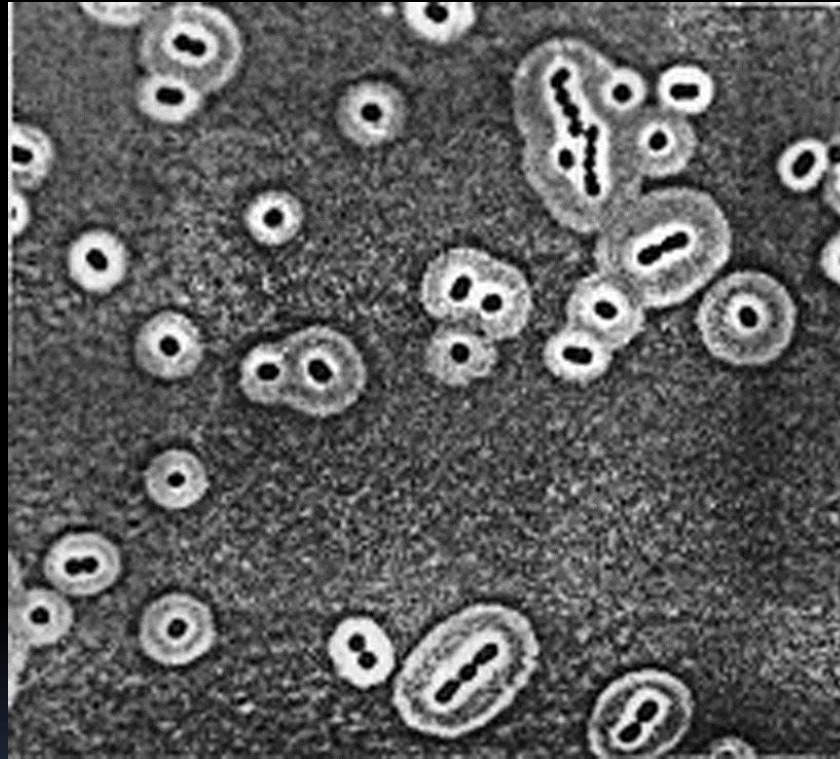
Peripheral membrane proteins

- some attached to the cell membrane by a fatty acid covalently attached to one of the protein's amino acids i.e. lipoproteins
- or attached by stretches of hydrophobic amino acids of the protein's surface

Integral membrane proteins are embedded in the membrane by one or more stretches of hydrophobic amino acids. Many of these proteins transport molecules in and out of the cell. The transport proteins are selective: each type of molecule needs its own transporter.

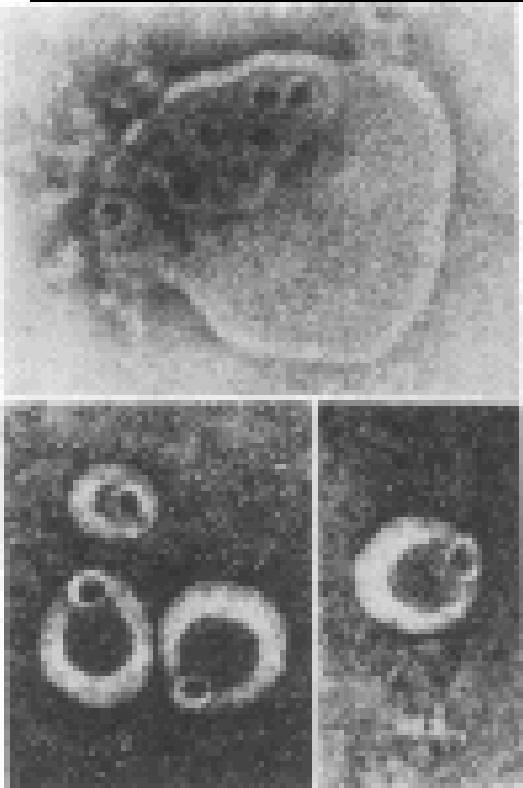


Decoration of bacteria -polysaccharide capsules

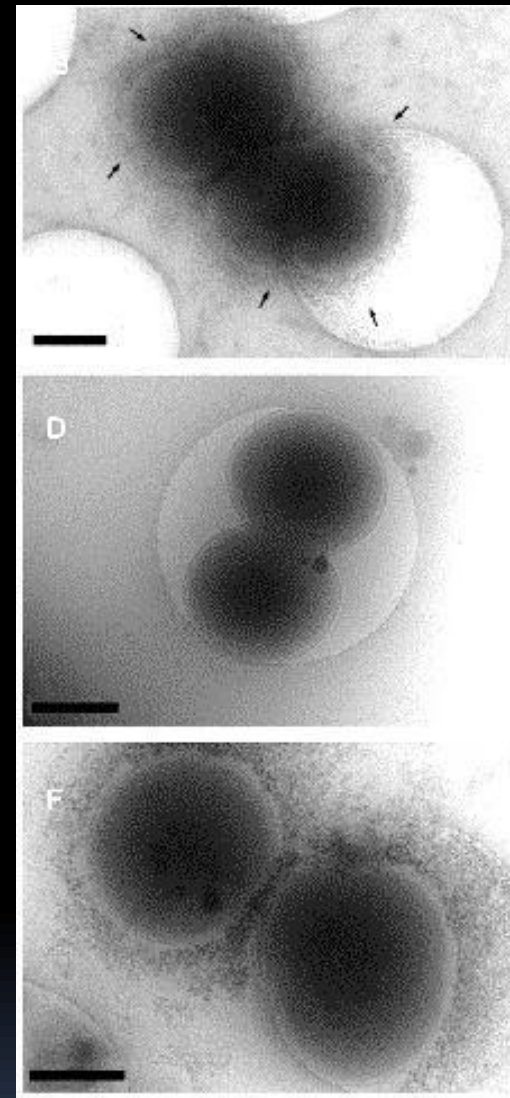


Capsular polysaccharides are water soluble and have high molecular weights (100-1,000 kDa). They are linear and consist of regularly repeating subunits of simple sugars.

Decoration of bacteria -polysaccharide capsules



Müller-Eberhard



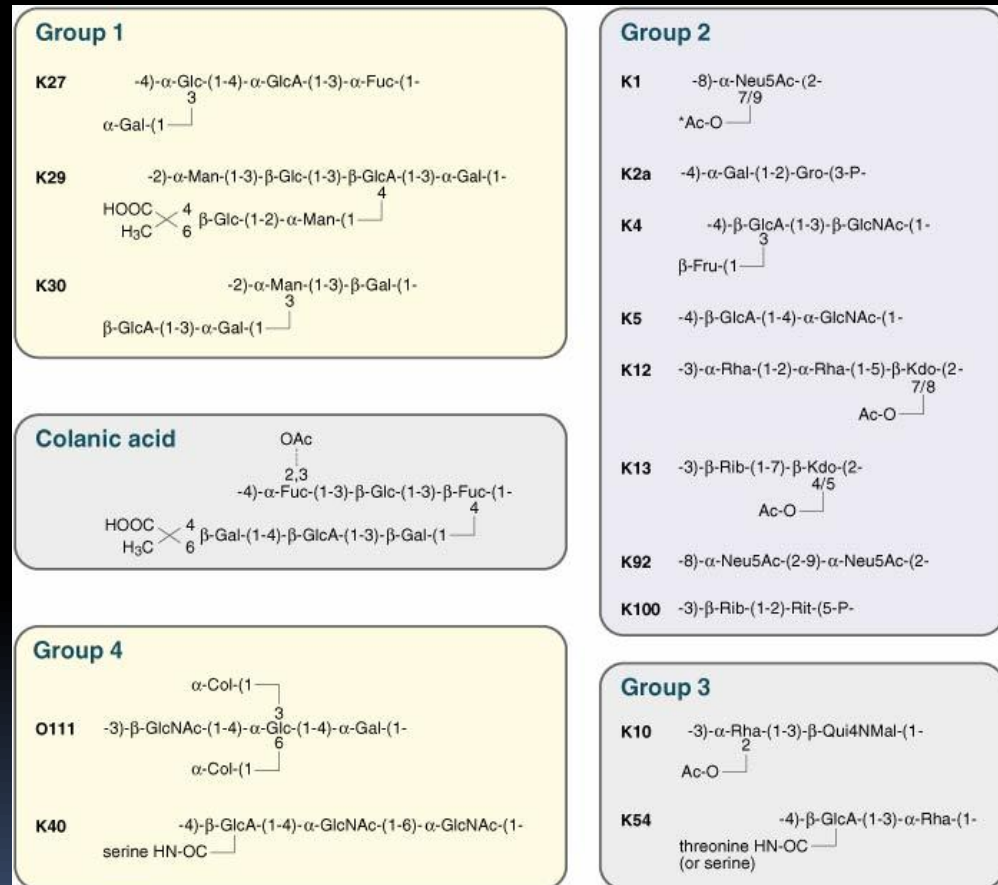
- Protects bacteria from phagocytosis and attack by antimicrobial agents,
- Interferes with the complement system,

Decoration of bacteria -polysaccharide capsules

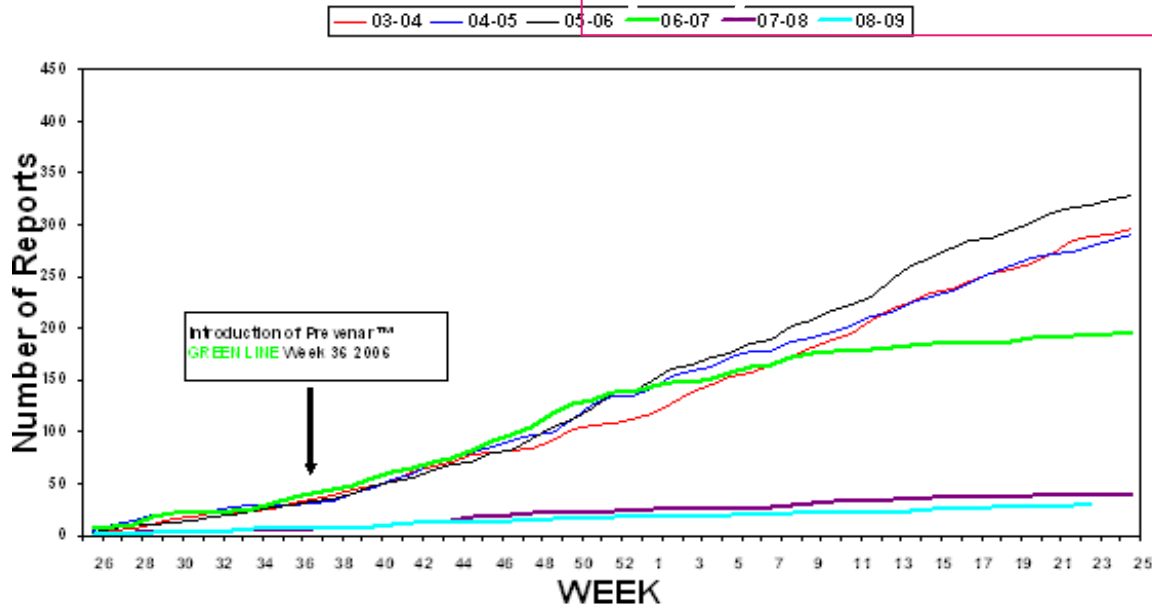
There is an enormous structural diversity; nearly 80 capsular serotypes are produced by *E. coli* alone...

The capsular polysaccharide is the basis of--

K typing of *E. coli*
90 serotypes of *S. pneumoniae*
12 serogroups of *N. meningitidis*



Decoration of bacteria -polysaccharide capsules

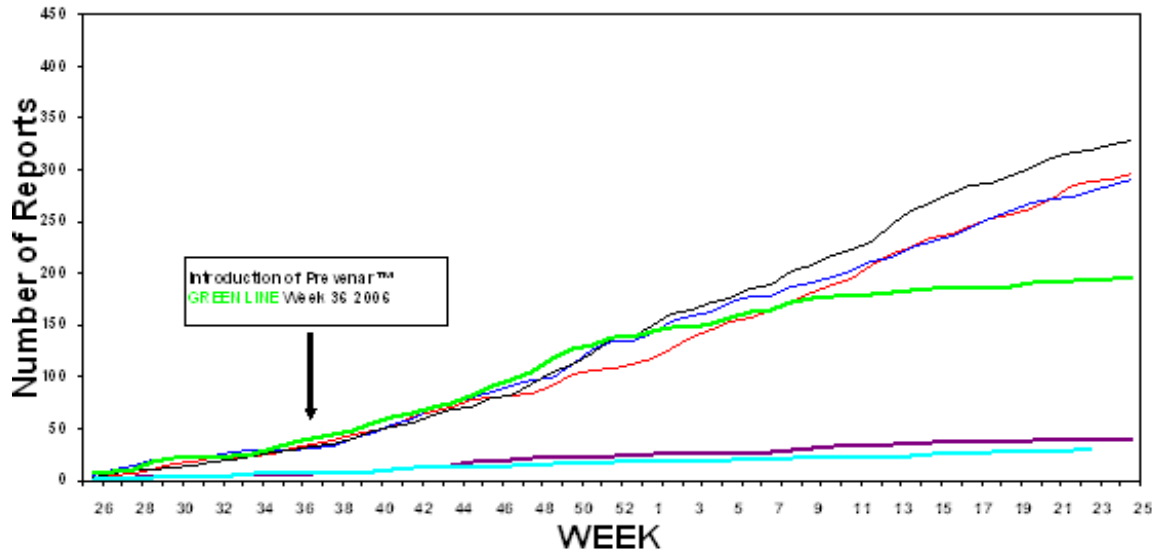


Invasive Pneumococcal Disease
due to any of the serotypes
NOT in Prevenar™

**REDUCTION IN DISEASE
DUE TO VACCINE STRAINS**

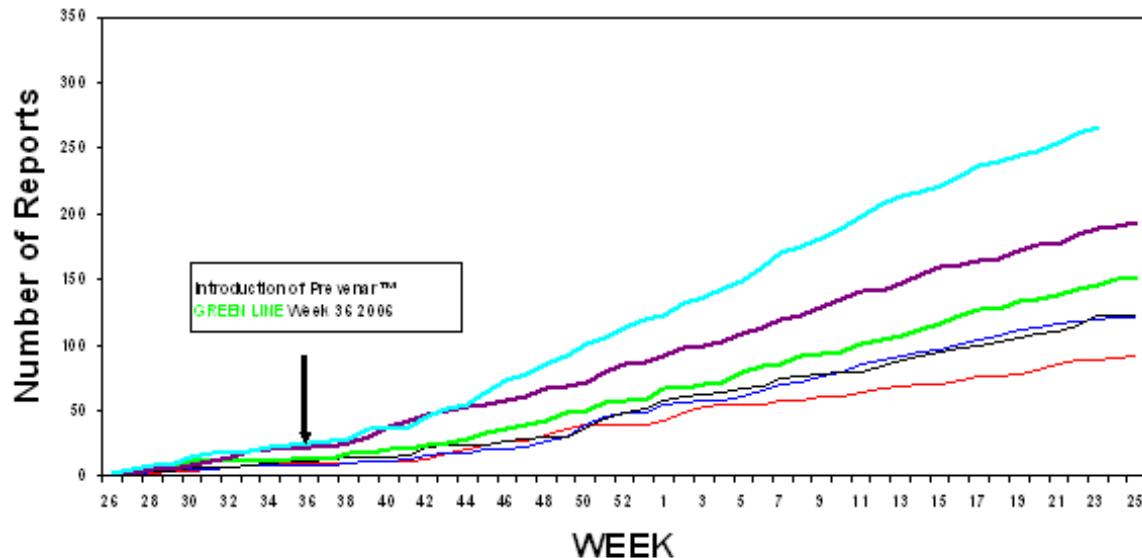
Decoration of bacteria -polysaccharide capsules

03-04 04-05 05-06 06-07 07-08 08-09



Invasive Pneumococcal Disease
due to any of the serotypes
NOT in Prevenar™

**REDUCTION IN DISEASE
DUE TO VACCINE STRAINS**



Invasive Pneumococcal Disease
due to any of the serotypes
NOT in Prevenar™ :

**INCREASE IN DISEASE
DUE TO NON-VACCINE
STRAINS**

Decoration of bacteria -flagella and pili

SINGULAR - flagellum and pilus

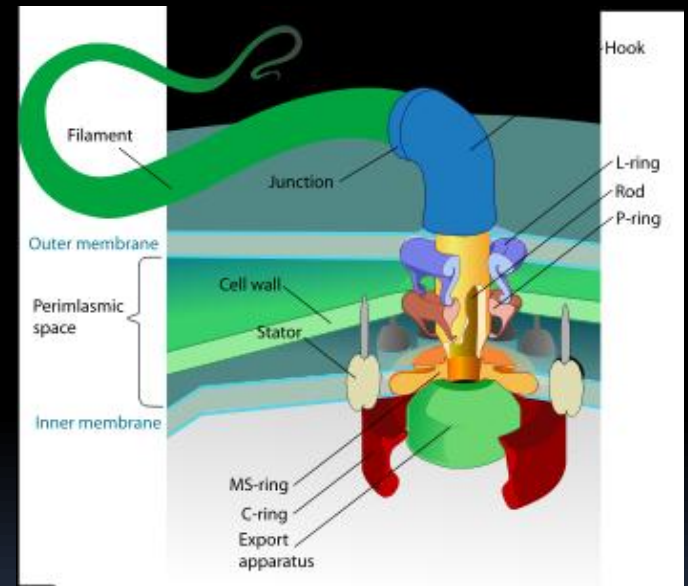
Long **protein** appendages or organelles...

Decoration of bacteria -flagella

Flagella are long hairs used to propel the cells. They are composed of flagellin protein.

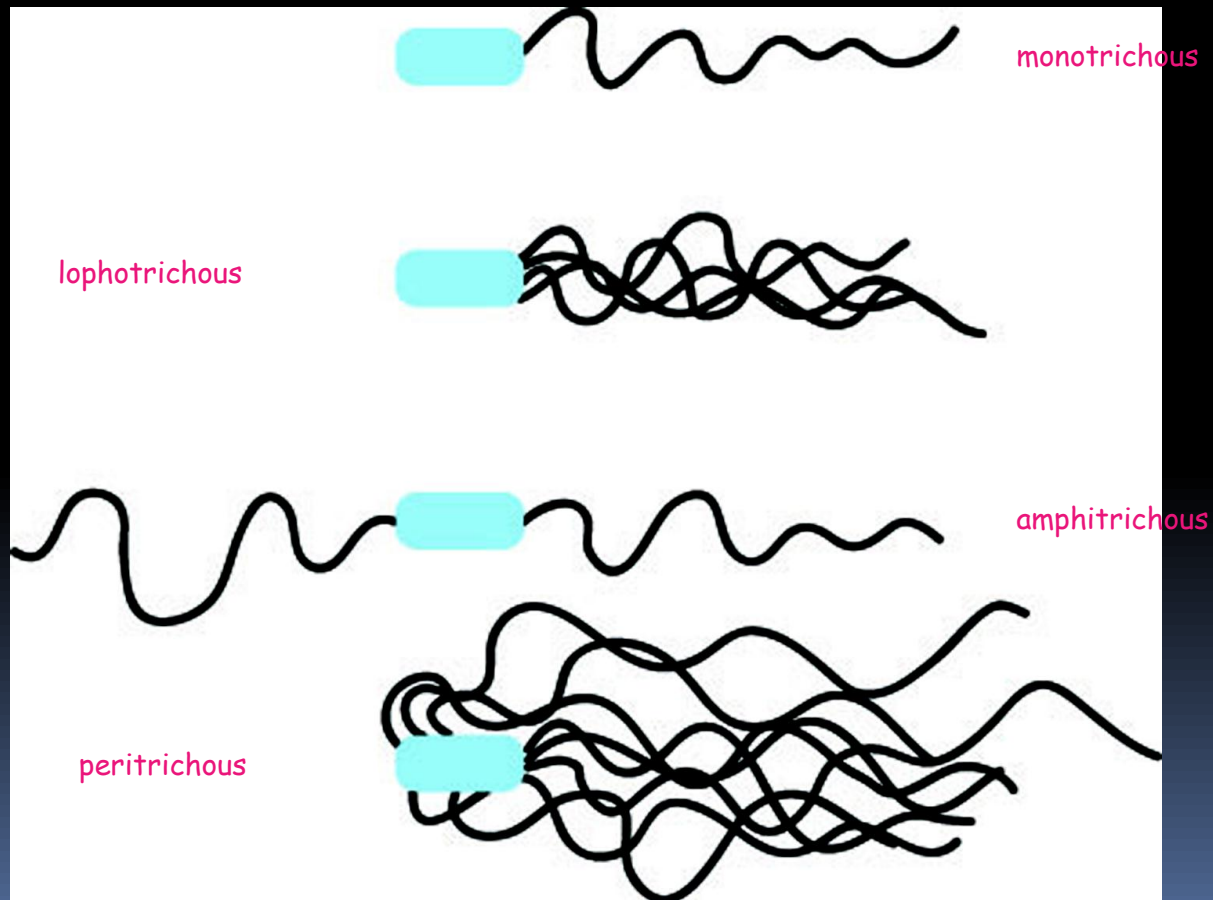
At the base of each flagellum is a motor embedded in the membrane and cell wall. It turns in a rotary motion, driven by proton-motive force (the flow of protons i.e. H^+ ions across the cell membrane).

Spins at 13,000 rpm



Decoration of bacteria -flagella

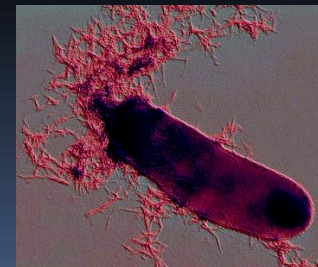
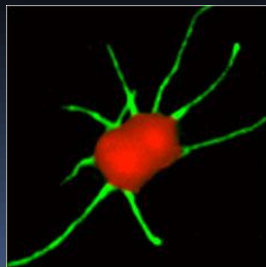
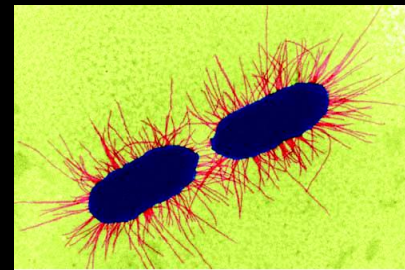
A flagellum can extend up to 10 μm from the bacterial body.
Can have several cellular distributions



Decoration of bacteria

- pili

A pilus (plural pili) is a hairlike long filament, thinner than flagella, made up primarily of pilin extending up to several μm from the bacterial body.



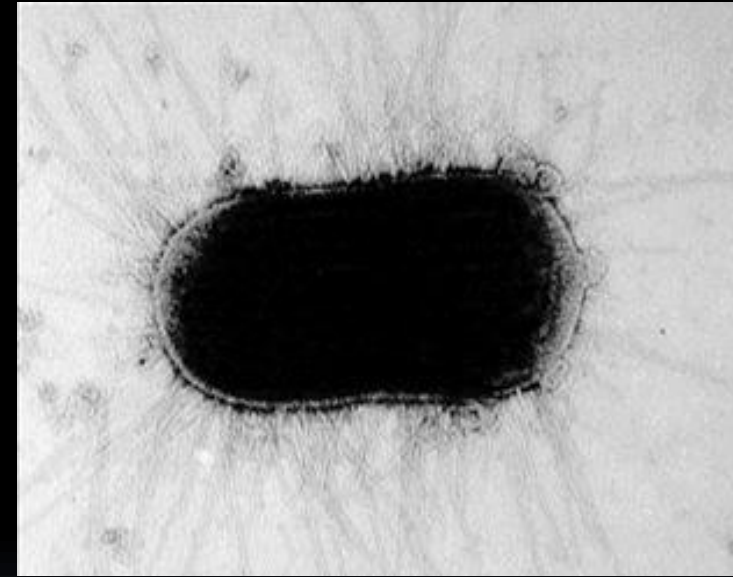
Decoration of bacteria

- pili

Pili are hairs projecting from the surface. They are composed of pilin protein. There are several types.

DNA can be transferred between bacteria when sex pili on the donor cell attach to and draw in the recipient cell.

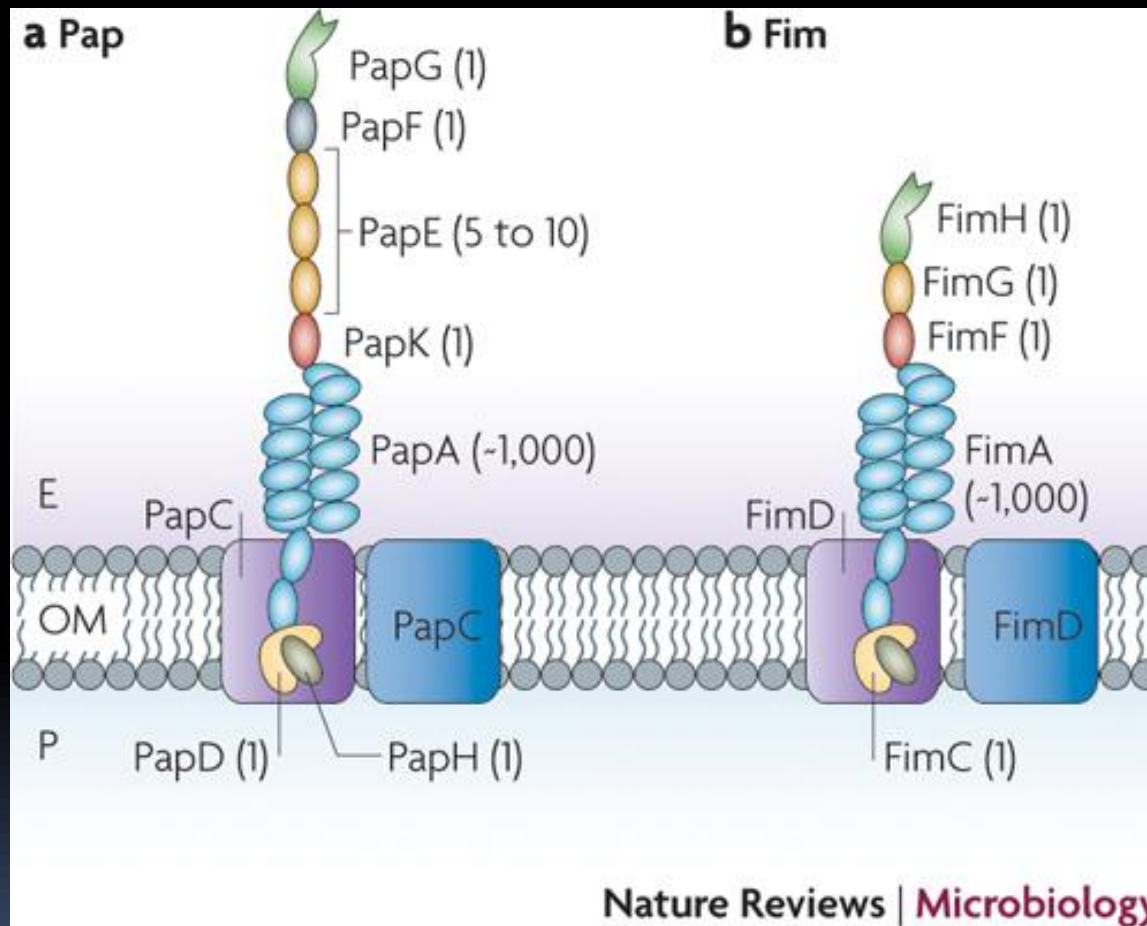
Fimbriae are pili used to attach the bacteria to target cells (in infection) or to abiotic surfaces,



Type IV pili of *N. meningitidis*

Decoration of bacteria - pili

Escherichia coli



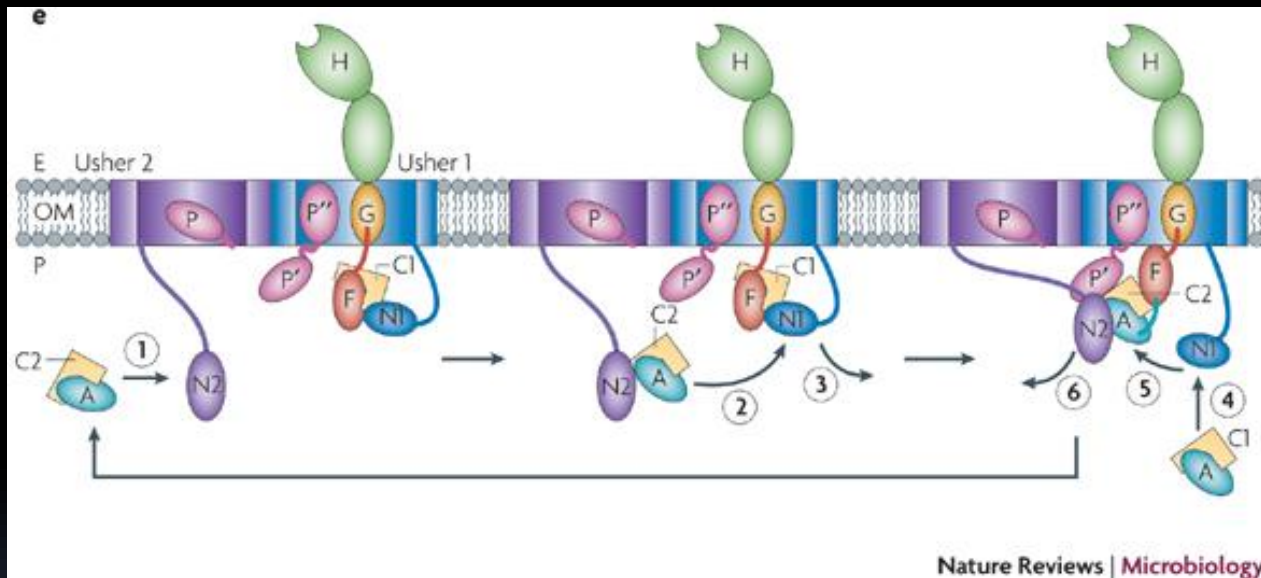
P or PAP pili

Type 1 fimbriae

Decoration of bacteria - pili

Escherichia coli

Chaperone-usher pathway



- pilus sub-units and chaperones cross the inner membrane by the Sec system
- the dimer is transferred to one outer membrane usher protein, then passed to another usher and incorporated into the growing pilus

Decoration of bacteria - pili

Gram-positive pili

Until their recent characterization in *Corynebacterium diphtheriae* (2003), it was widely believed that pili were not present in Gram-positive species.

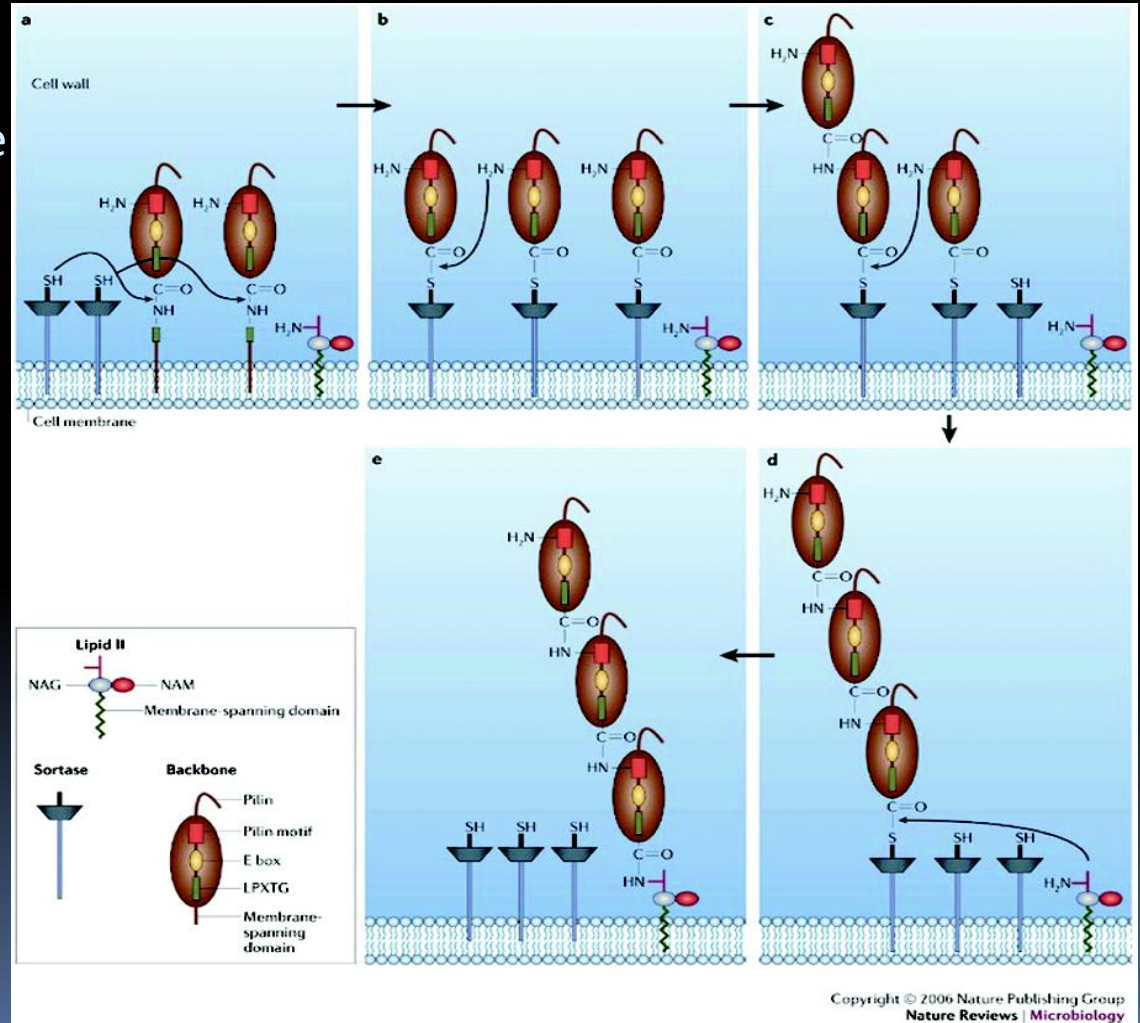


Since then pili have been found in many Gram-positives, most notably streptococci and even mycobacteria, and they have been shown to be important virulence factors.

Decoration of bacteria - pili

Gram-positive pili

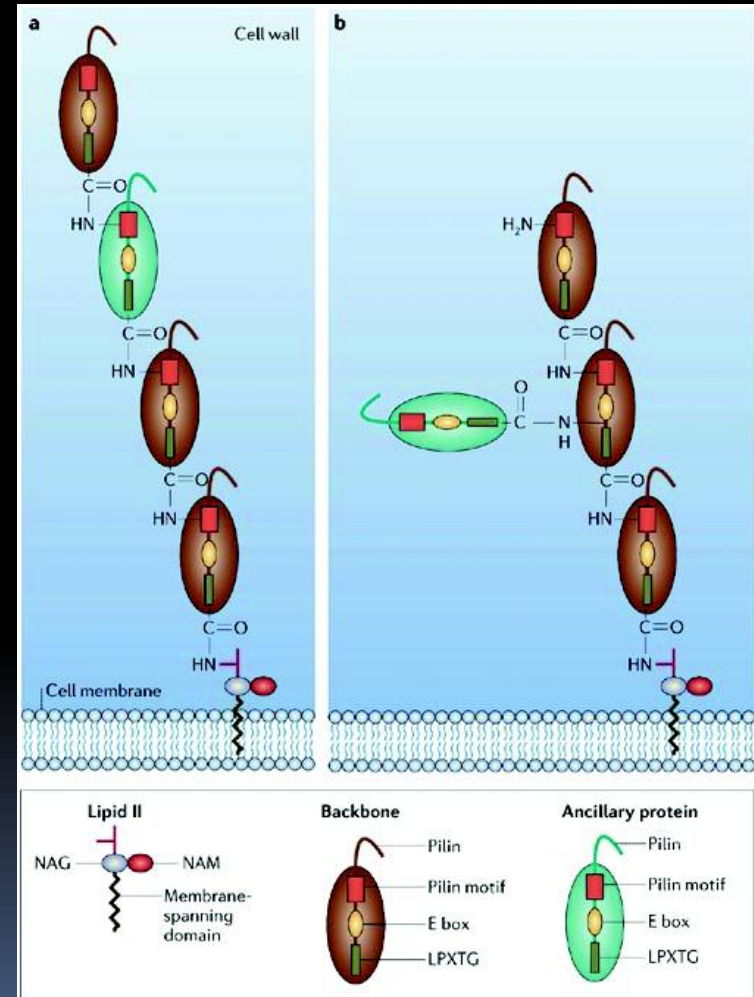
Assembly occurs on the surface and the pilus subunits are covalently linked.



Decoration of bacteria - pili

Gram-positive pili

Minor pilus components are either incorporated into the pilus backbone by the same process as the main pilus subunit or form 'branches' in the pilus shaft and might be more accessible for interaction with host-cell molecules.

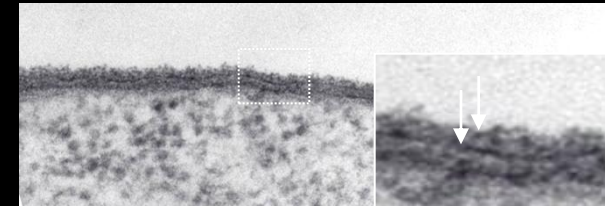


Decoration of bacteria - lipopolysaccharide

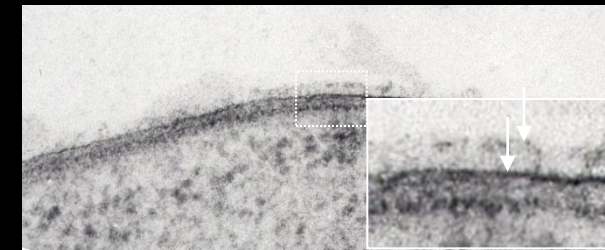
predicted conformation of the O antigen

Detection of the O antigen

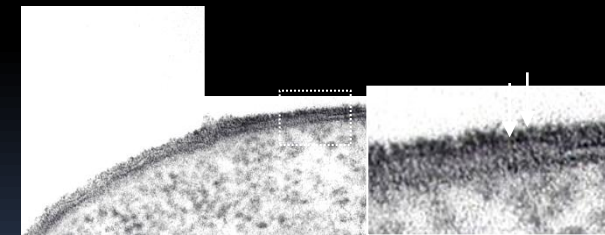
M90T



M90T Δ *gtr*



M90T Δ *gtrp5a*



Shigella

Decoration of bacteria - lipopolysaccharide

O104:H4
(2011)

Adults>children
Women>adults
Haemolytic uraemic syndrome c 25%

> 3,000 cases, 50 deaths

Enterohaemorrhagic *E. coli*

O157:H7

O111

Children>adults

Haemolytic uraemic syndrome c 5%



Specialised structures of bacteria - spores

Medically-important Endospore-forming Bacteria

- *Bacillus anthracis* causes anthrax
- *Bacillus cereus* causes food poisoning
- *Clostridium tetani* causes tetanus
- *Clostridium botulinum* causes botulism
- *Clostridium perfringens* causes food poisoning and gas gangrene
- *Clostridium difficile* causes antibiotic-induced diarrhea and pseudomembranous colitis

Induction of spores

Small colony variants

Specialised structures of bacteria

- spores

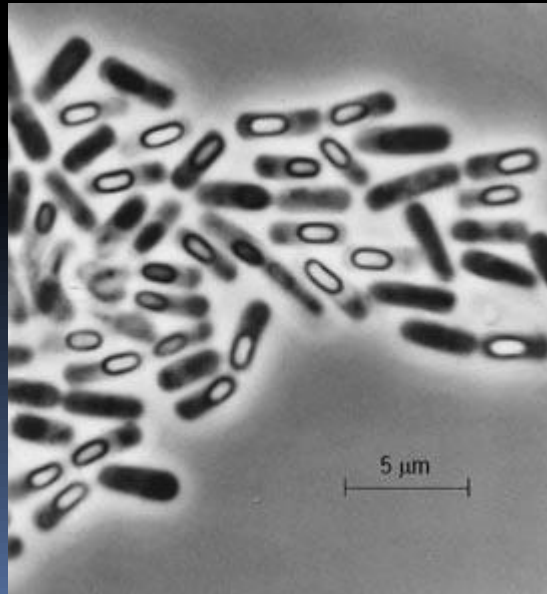


C. tetani
-terminal spore



C. difficile
-sub-terminal spore

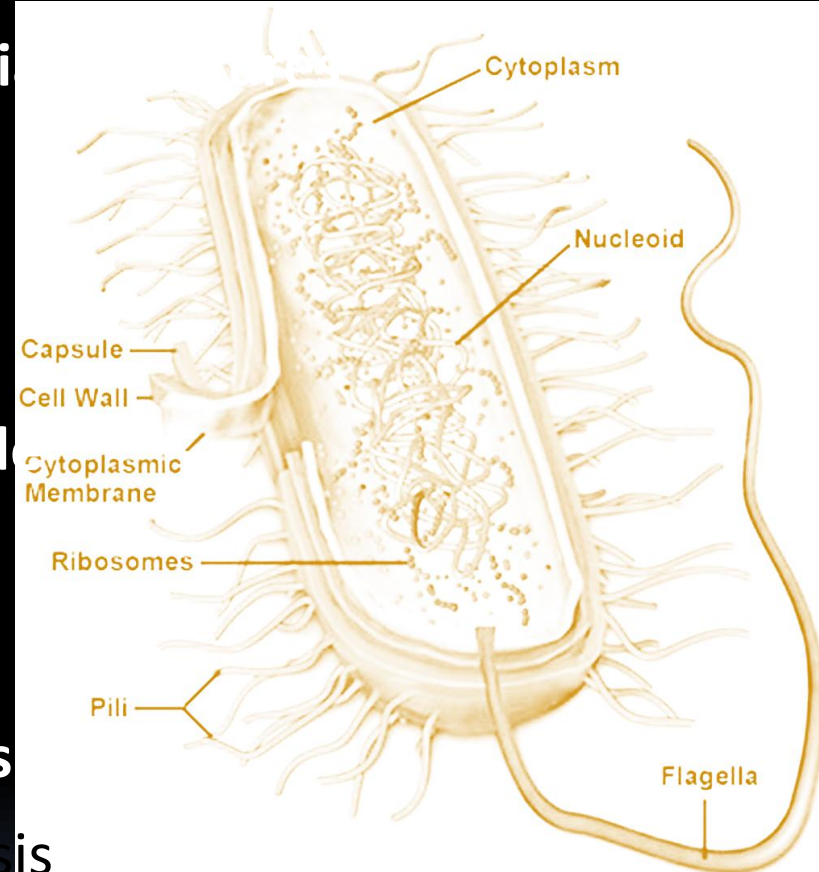
Bacillus cereus
-endospore



Learning objectives

1) Describe important bacteri

- cell wall
- cell membrane
- capsule
- pili/fimbriae
- lipo-polysaccharid
- secretion systems
- spores



2) Biosynthesis of one of these

- key roles in pathogenesis

3) Recognition of these structures by the immune system

- examples

Targets

4) Role in pathogenesis/lifecycle

- for interventions

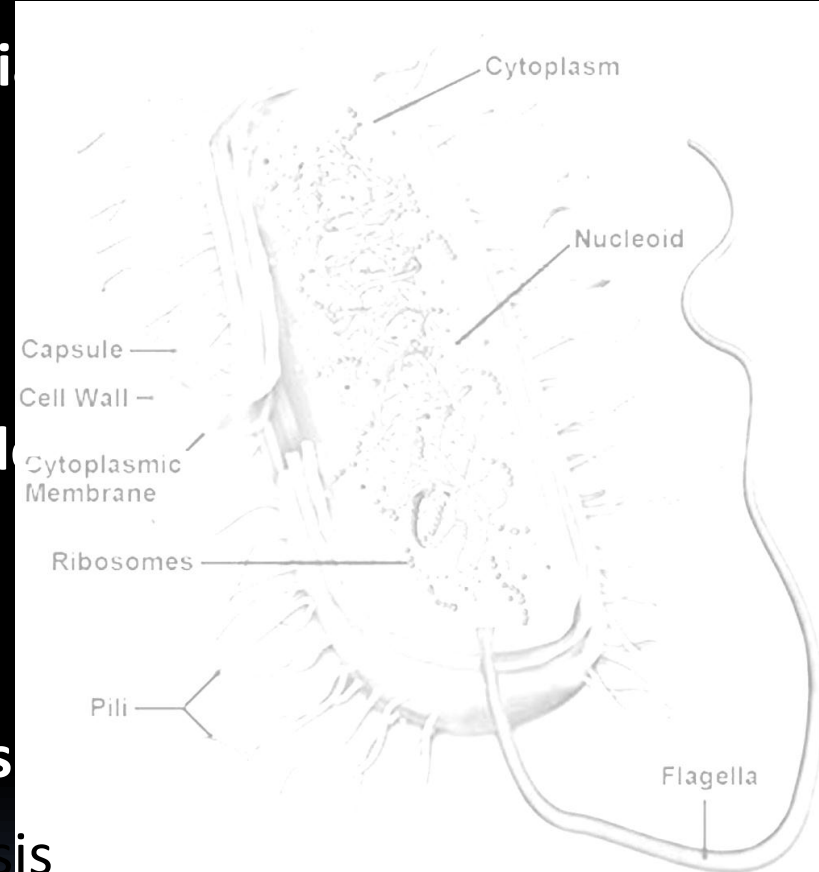
- for the immune system

5) Examples : *Escherichia coli*

Learning objectives

1) Describe important bacterium

- cell wall
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- for the immune system

5) Examples : *Escherichia coli*

Role in pathogenesis

Uropathogenic E. coli

- primary causative agent of Urinary Tract Infections (UTIs)
- Bladder is primary site of infection in 95% of all UTIs
- Infection of the kidney can also occur (pyelonephritis)
 - back pain, fever, vomiting and may lead to septicaemia
- UPEC expresses (at least) two types of pili:
 - P pili - adhesion to renal tissue (pyelonephritis)
 - Type I pili - adhesion to uro-epithelium (bladder infection)

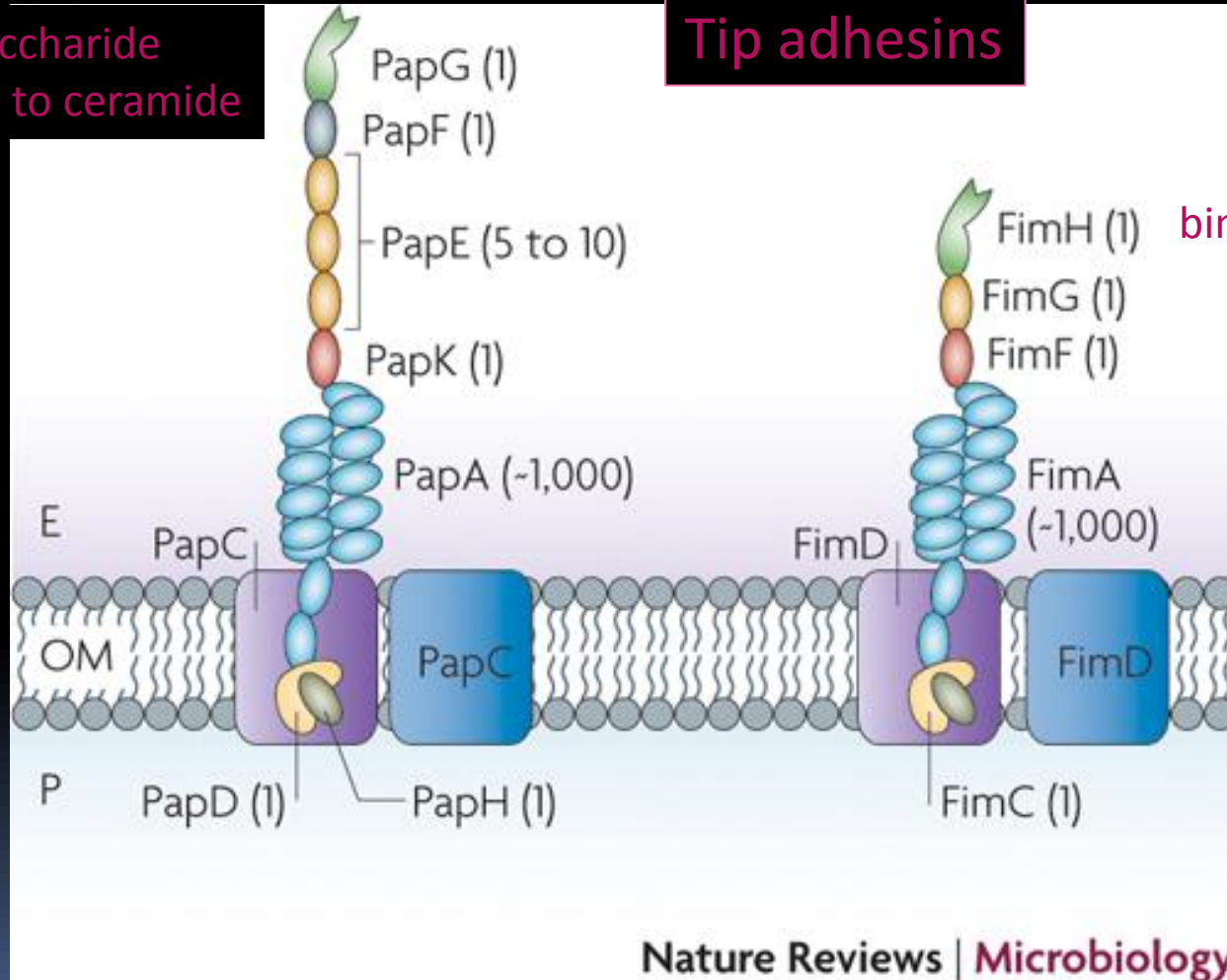
Decoration of bacteria - pili

Escherichia coli

binds di-saccharide
(globiose) linked to ceramide

Tip adhesins

binds mannose



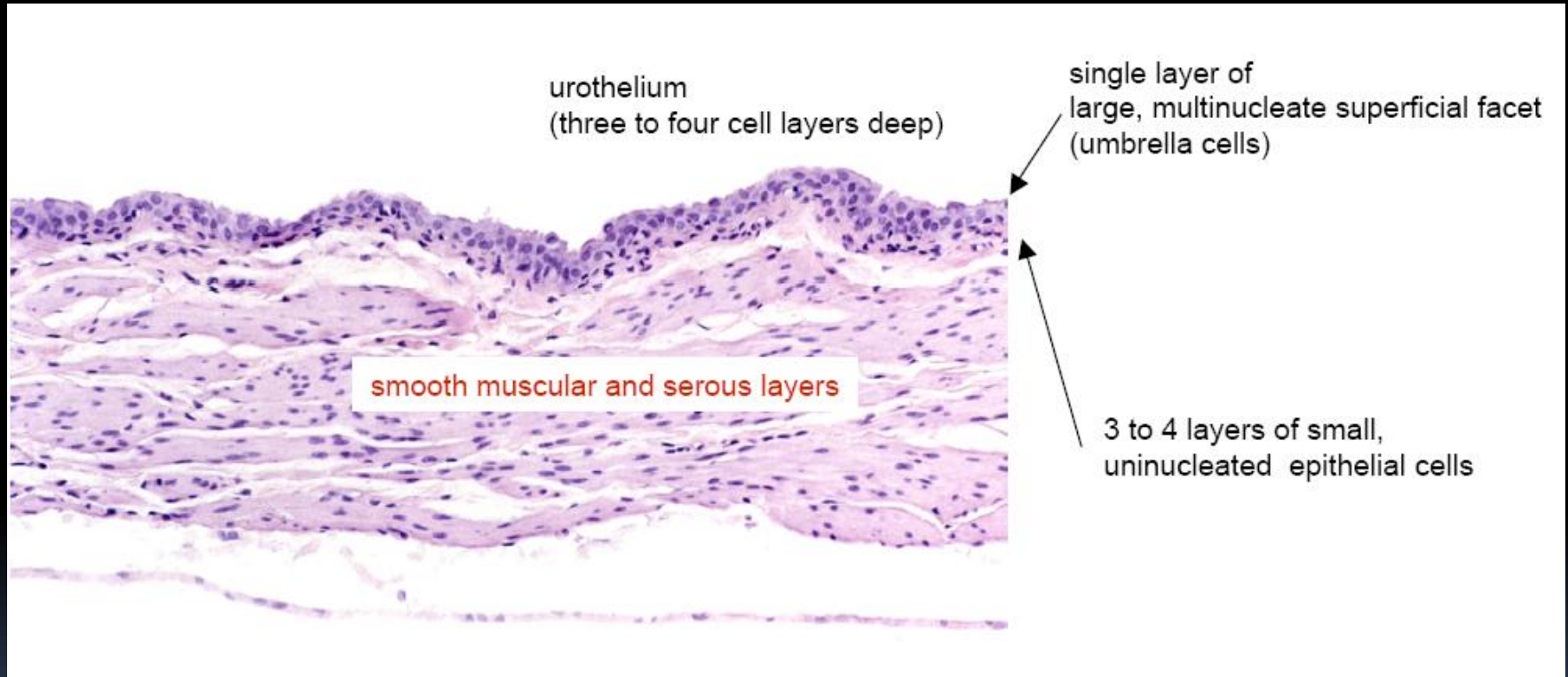
Nature Reviews | Microbiology

P or PAP pili

Type 1 fimbriae

Role in pathogenesis

Type 1 pili are required for bladder infections

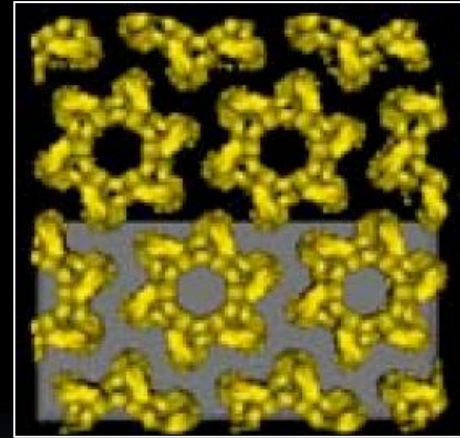
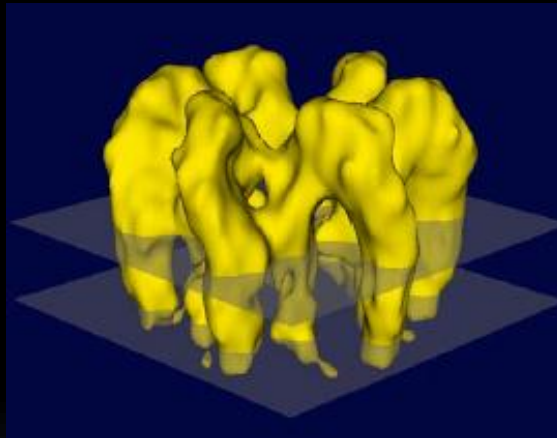


- Umbrella cells deposit complexes of **uropilin** on their apical surface

Role in pathogenesis

Type 1 pili are required for bladder infections

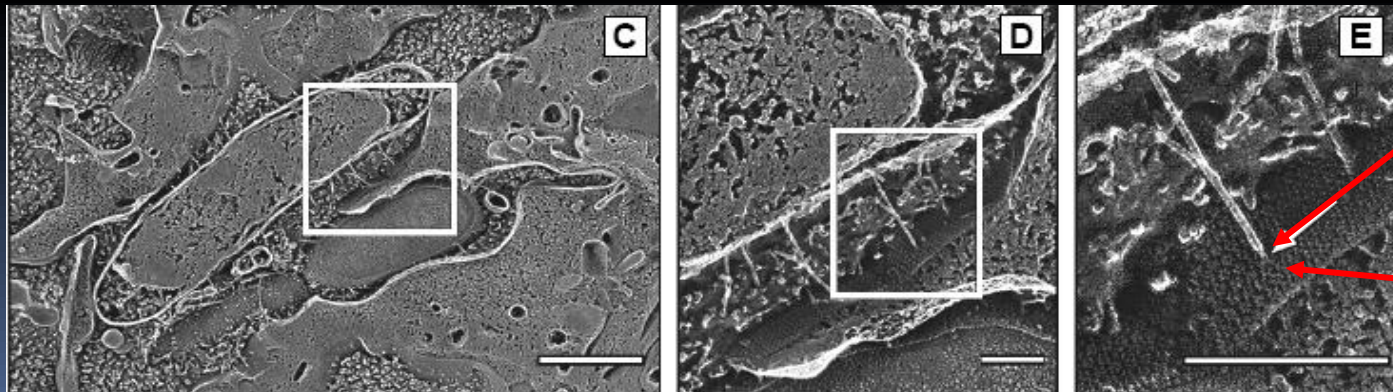
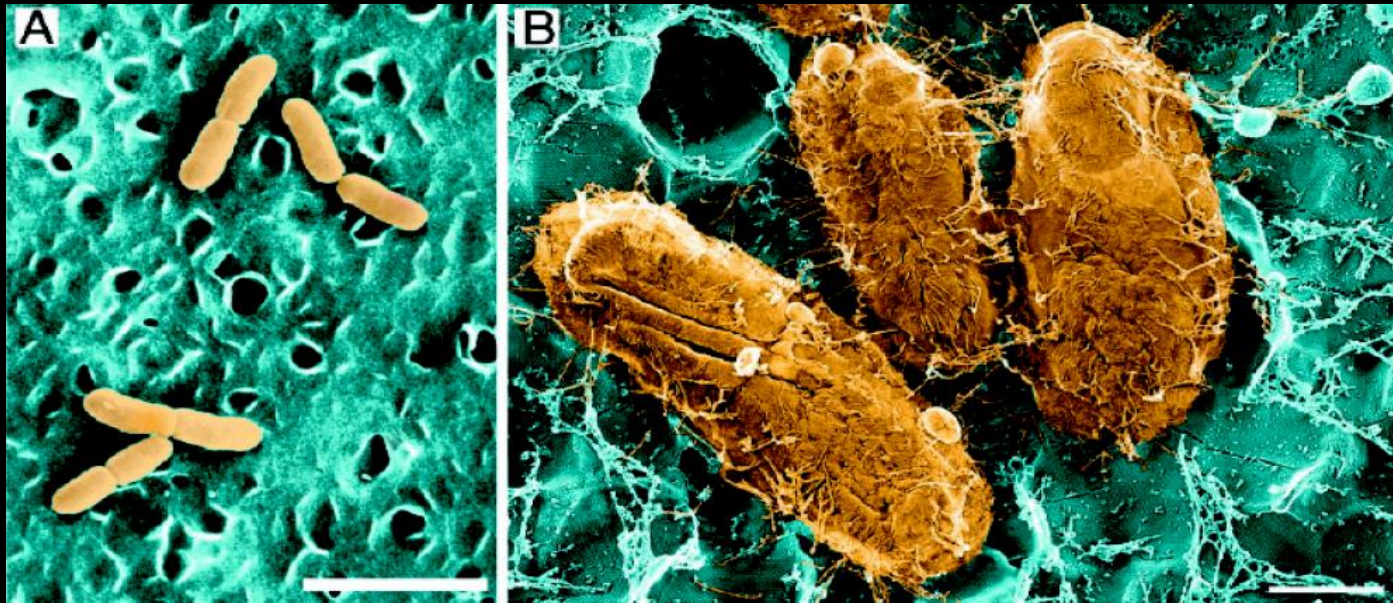
Uroplakins are the target of type I pili



- uroplakins are integral membrane glycoproteins
- four uroplakins form hexagonal complex
- these complexes are organized into plaques
- FimH (type I pilus adhesin) binds to uroplakin

Role in pathogenesis

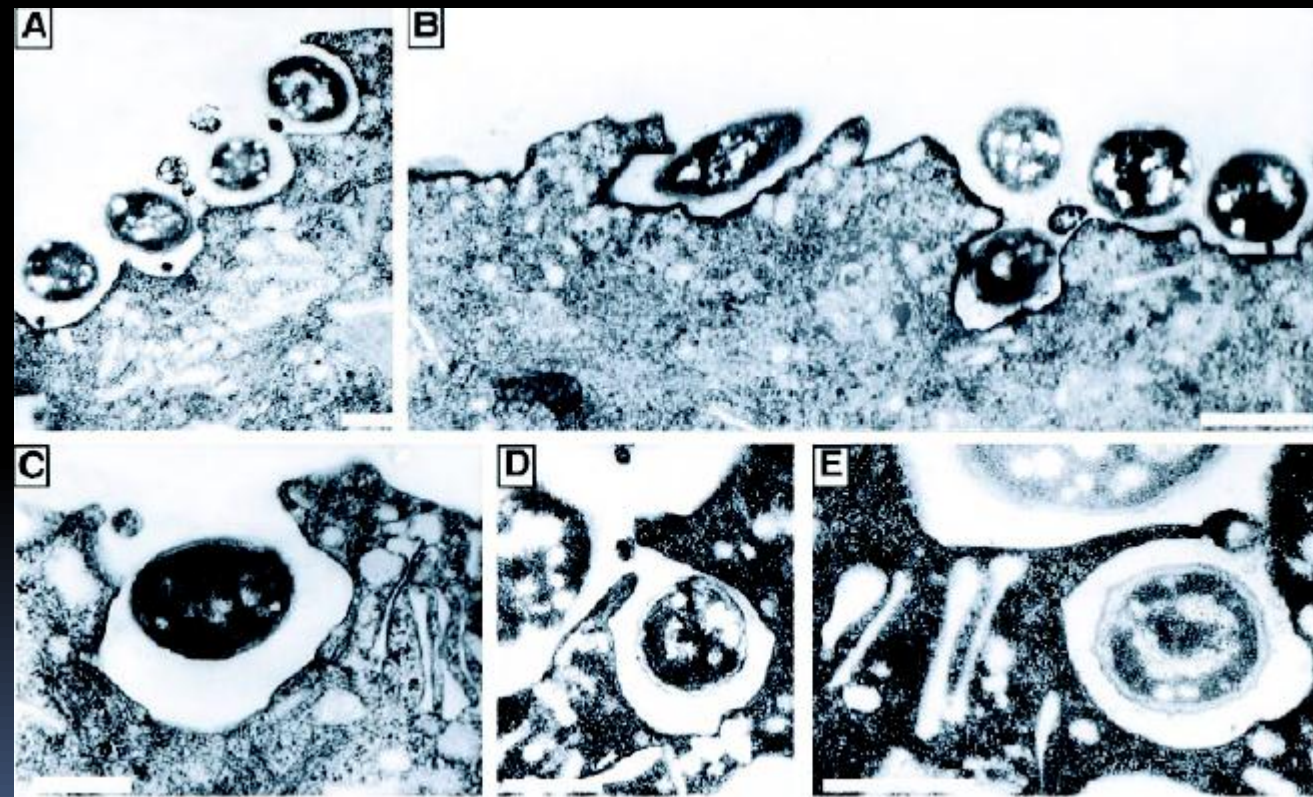
Type 1 pili are required for bladder infections



Type 1
pilus
uroplakin

Role in pathogenesis

Type 1 pili are required for bladder infections



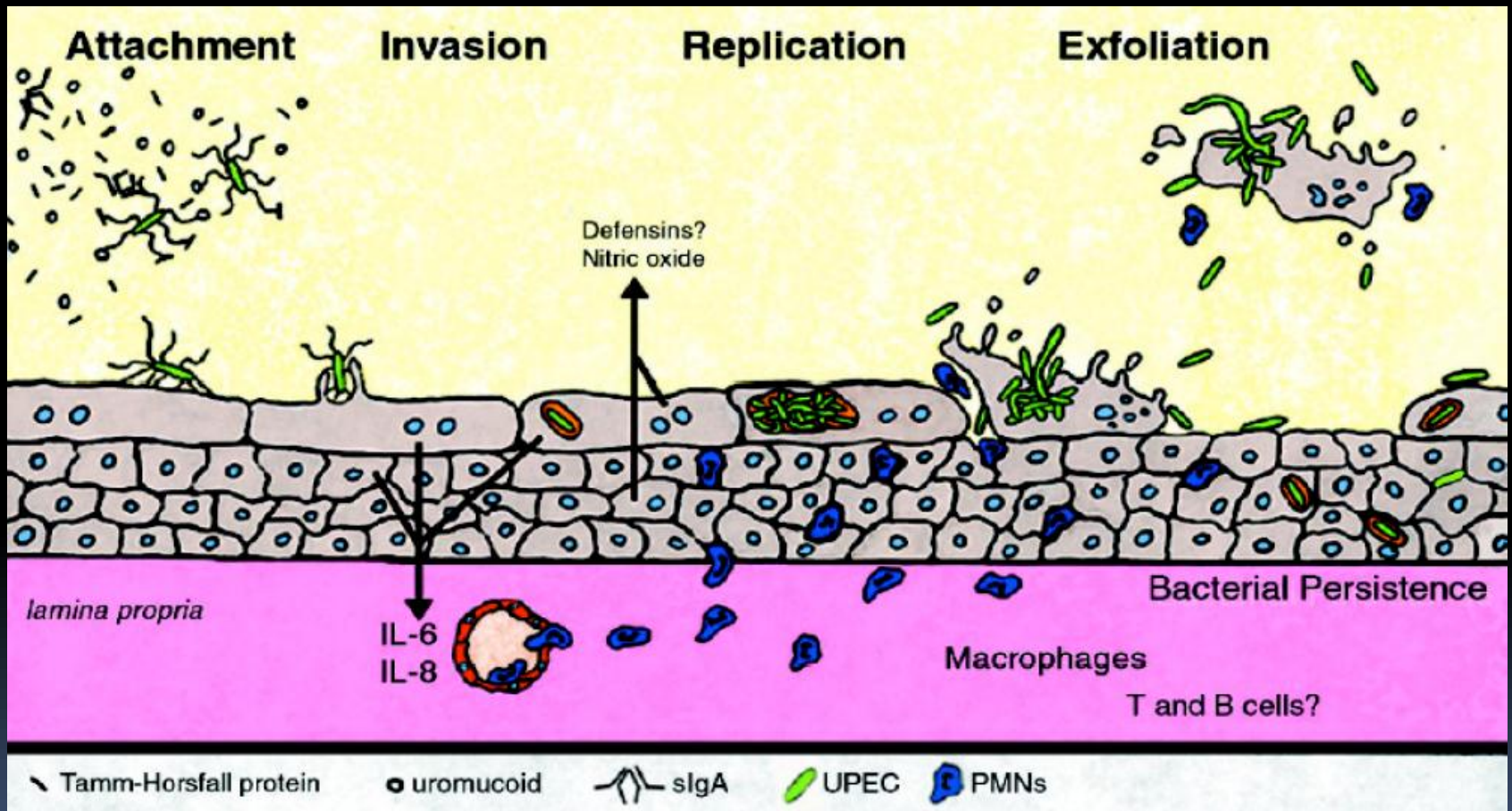
Internalization of UPECs by mouse bladder epithelial cells



Formation of intracellular pods

Role in pathogenesis

Type 1 pili are required for bladder infections



Learning objectives

1) Describe important bacteri

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- capsule
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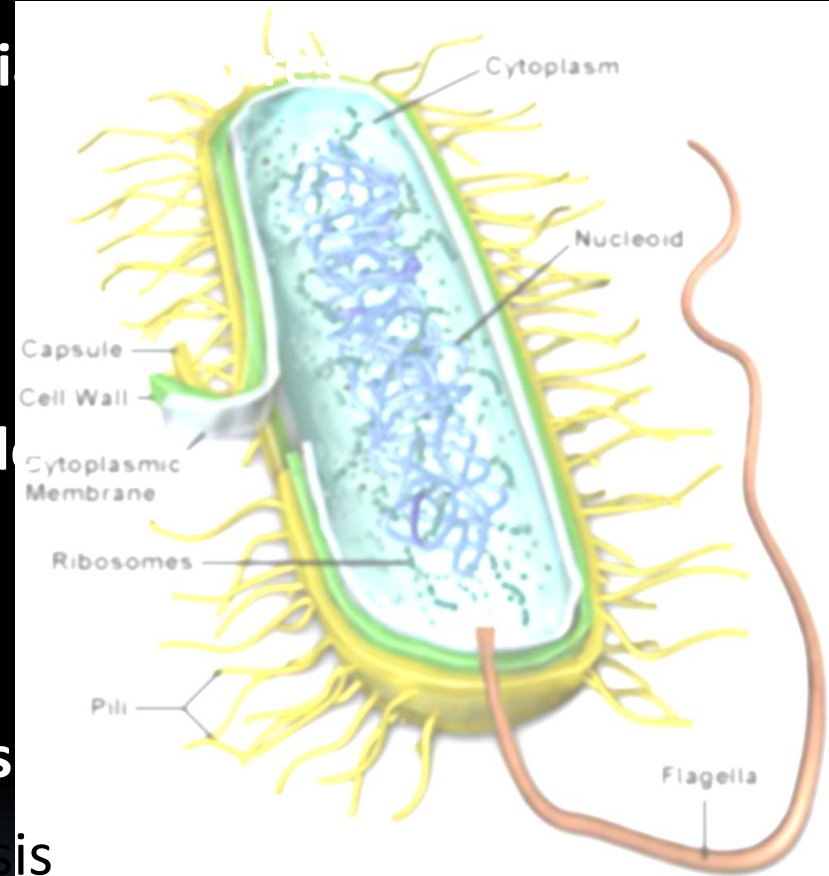
Targets

4) Role in pathogenesis/lifecycle

- for interventions

- for the immune system

5) Examples : *Escherichia coli*



Learning objectives

Cell surface is special

Enables homeostasis

Uptake

Export

Locomotion

Adhesion

Site of respiration

Sensing of environment

Protection

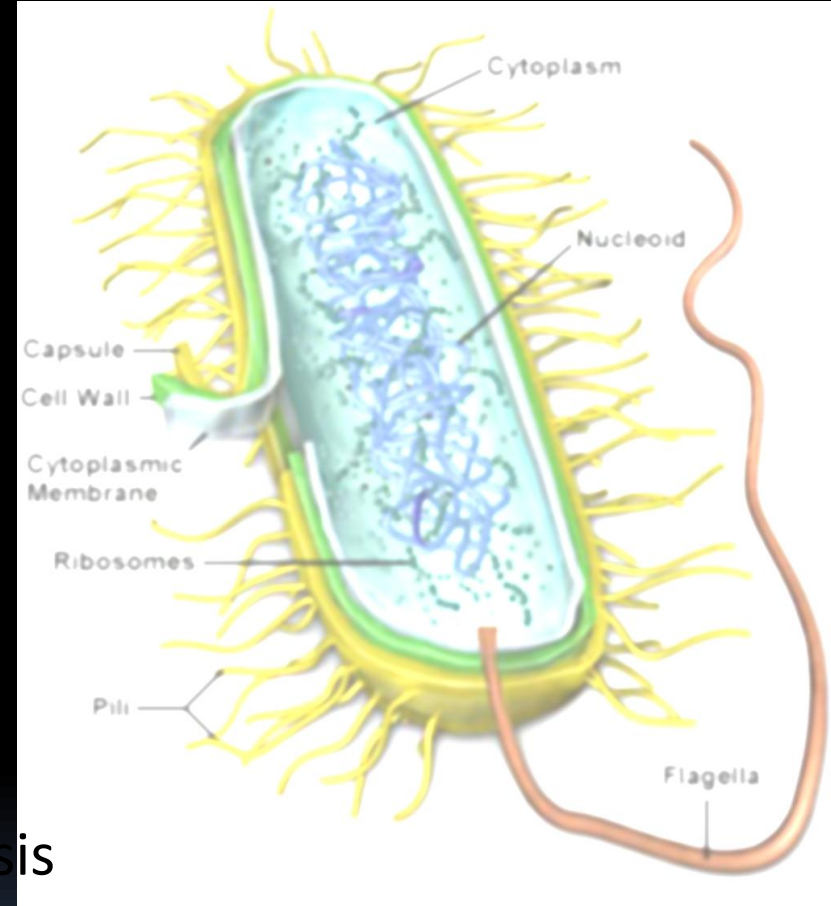
- key roles in pathogenesis

- examples

Targets

- for interventions

- for the immune system



Learning objectives

Cell surface is special

Enables homeostasis

Uptake

Export

Locomotion

Adhesion

Site of respiration

Sensing of environment

Protection



Cell surface functions as

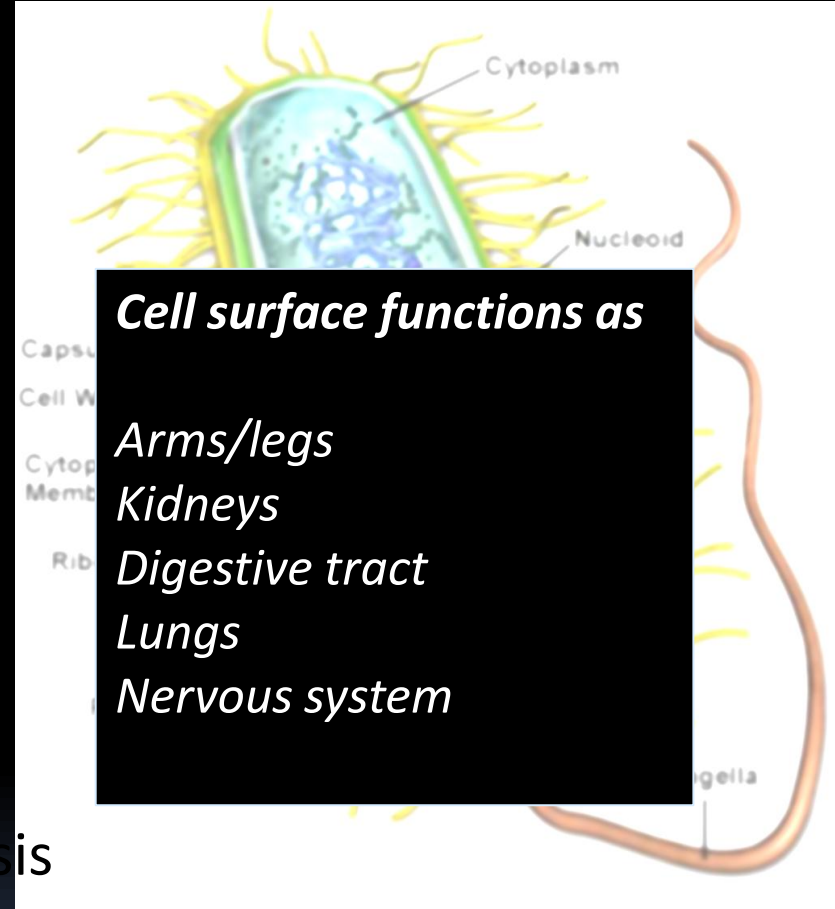
Arms/legs

Kidneys

Digestive tract

Lungs

Nervous system



- key roles in pathogenesis
- examples

Targets

- for interventions
- for the immune system