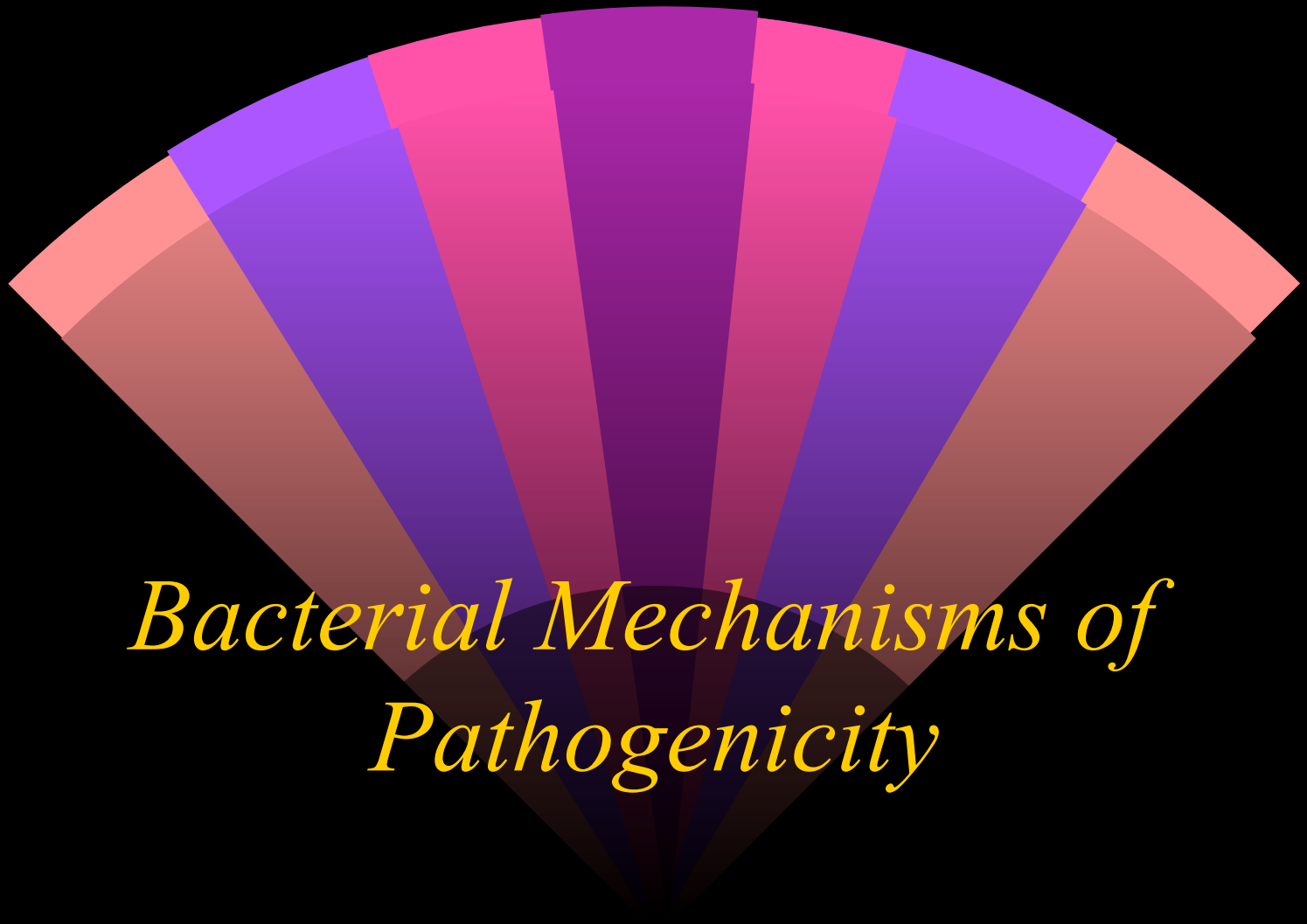


Bacterial Mechanisms of Pathogenicity

2nd Lecture

Preferred Portal of Entry

- Just because a pathogen enters your body it does not mean it's going to cause disease.

- pathogens - preferred portal of entry

Preferred Portal of Entry

- *Streptococcus pneumoniae*
  - if inhaled can cause pneumonia
  - if enters the G.I. Tract, no disease
- *Salmonella typhi*
  - if enters the G.I. Tract can cause Typhoid Fever
  - if on skin, no disease

Number of Invading Microbes

- LD_{50} - Lethal Dose of a microbes toxin that will kill 50% of experimentally inoculated test animal
- ID_{50} - infectious dose required to cause disease in 50% of inoculated test animals
  - Example: ID_{50} for *Vibrio cholerea* 10^8 cells (100,000,000 cells)
  - ID_{50} for Inhalation Anthrax - 5,000 to 10,000 spores ????

How do Bacterial Pathogens penetrate Host Defenses?

1. COLONIZATION

The first stage of microbial infection is colonization:

- the establishment of the pathogen at the appropriate portal of entry.
- Pathogens usually colonize host tissues that are in contact with the external environment. Sites of entry in human hosts include the urogenital tract, the digestive tract, the respiratory tract and the conjunctiva.
- Organisms that infect these regions have usually developed tissue adherence mechanisms and some ability to overcome or withstand the constant pressure of the host defenses at the surface.

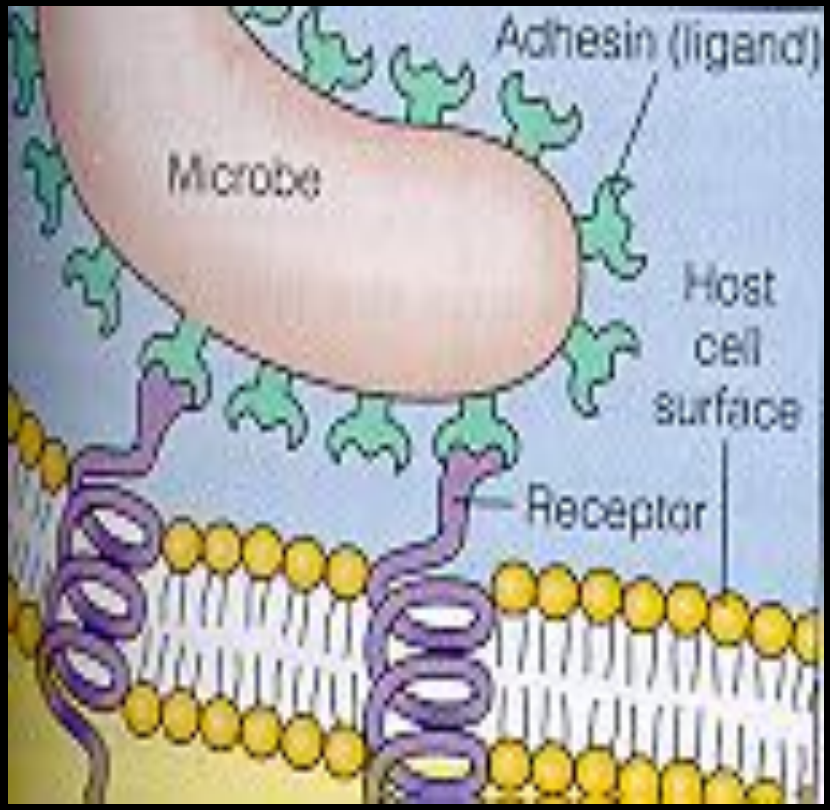
How do Bacterial Pathogens penetrate Host Defenses?

1. Adherence - almost all pathogens have a means to attach to host tissue

Binding Sites

adhesins

ligands



How do Bacterial Pathogens penetrate Host Defenses?

2. Bacterial Adherence to Mucosal Surfaces.

In its simplest form, bacterial adherence or attachment to a eucaryotic cell or tissue surface requires the participation of two factors: a receptor and an ligand.

- The receptors so far defined are usually specific carbohydrate or peptide residues on the eucaryotic cell surface.
- The bacterial ligand, called an adhesin, is typically a macromolecular component of the bacterial cell surface which interacts with the host cell receptor.
- Adhesins and receptors usually interact in a complementary and specific fashion.

TERMS USED TO DESCRIBE ADHERENCE FACTORS IN HOST-PARASITE INTERACTIONS

Table 1 is a list of medical terms microbiology to refer to microbial adherence to surfaces or tissues.

ADHERENCE FACTOR	DESCRIPTION
Adhesin	A surface structure or macromolecule that binds a bacterium to a specific surface
Receptor	A complementary macromolecular binding site on a (eucaryotic) surface that binds specific adhesins or ligands
Lectin	Any protein that binds to a carbohydrate
Ligand	A surface molecule that exhibits specific binding to a receptor molecule on another surface
Mucous	The mucopolysaccharide layer of glucosaminoglycans covering animal cell mucosal surfaces
Fimbriae	Filamentous proteins on the surface of bacterial cells that may behave as adhesins for specific adherence
Common pili	Same as fimbriae
Sex pilus	A specialized pilus that binds mating procaryotes together for the purpose of DNA transfer
Type 1 fimbriae	Fimbriae in *Enterobacteriaceae* which bind specifically to mannose terminated glycoproteins on eucaryotic cell surfaces
Type 4 pili	Pili in certain Gram-positive and Gram-negative bacteria. In *Pseudomonas*, thought to play a role in adherence and biofilm formation

TERMS USED TO DESCRIBE ADHERENCE FACTORS IN HOST-PARASITE INTERACTIONS

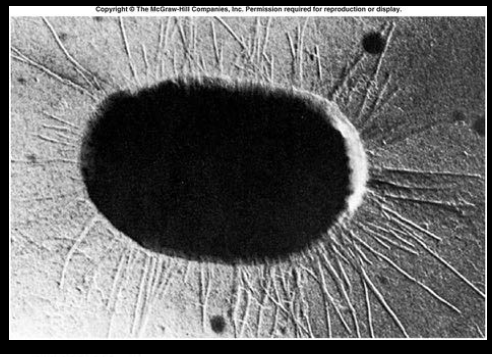
ADHERENCE FACTOR	DESCRIPTION
S-layer	Proteins that form the outermost cell envelope component of a broad spectrum of bacteria, enabling them to adhere to host cell membranes and environmental surfaces in order to colonize.
Glycocalyx	A layer of exopolysaccharide fibers on the surface of bacterial cells which may be involved in adherence to a surface. Sometimes a general term for a capsule.
Capsule	A detectable layer of polysaccharide (rarely polypeptide) on the surface of a bacterial cell which may mediate specific or nonspecific attachment
Lipopolysaccharide (LPS)	A distinct cell wall component of the outer membrane of Gram-negative bacteria with the potential structural diversity to mediate specific adherence. Probably functions as an adhesin
Teichoic acids and lipoteichoic acids (LTA)	Cell wall components of Gram-positive bacteria that may be involved in nonspecific or specific adherence

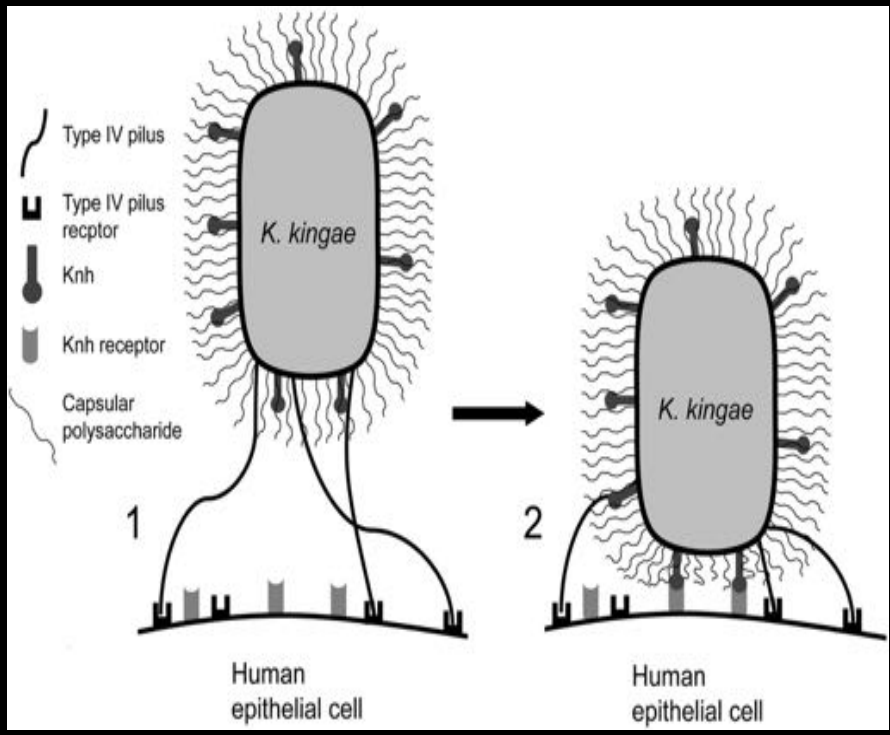
Some cells use fimbriae to adhere.

Fimbriae can play a role in tissue tropism

- is the cells and tissues of a host which support growth of a particular virus or bacteria. Some bacteria and viruses have a broad tissue tropism and can infect many types of cells and tissues. Other viruses may infect primarily a single tissue.

Example - attachment of Candida *to vaginal epithelial cells*



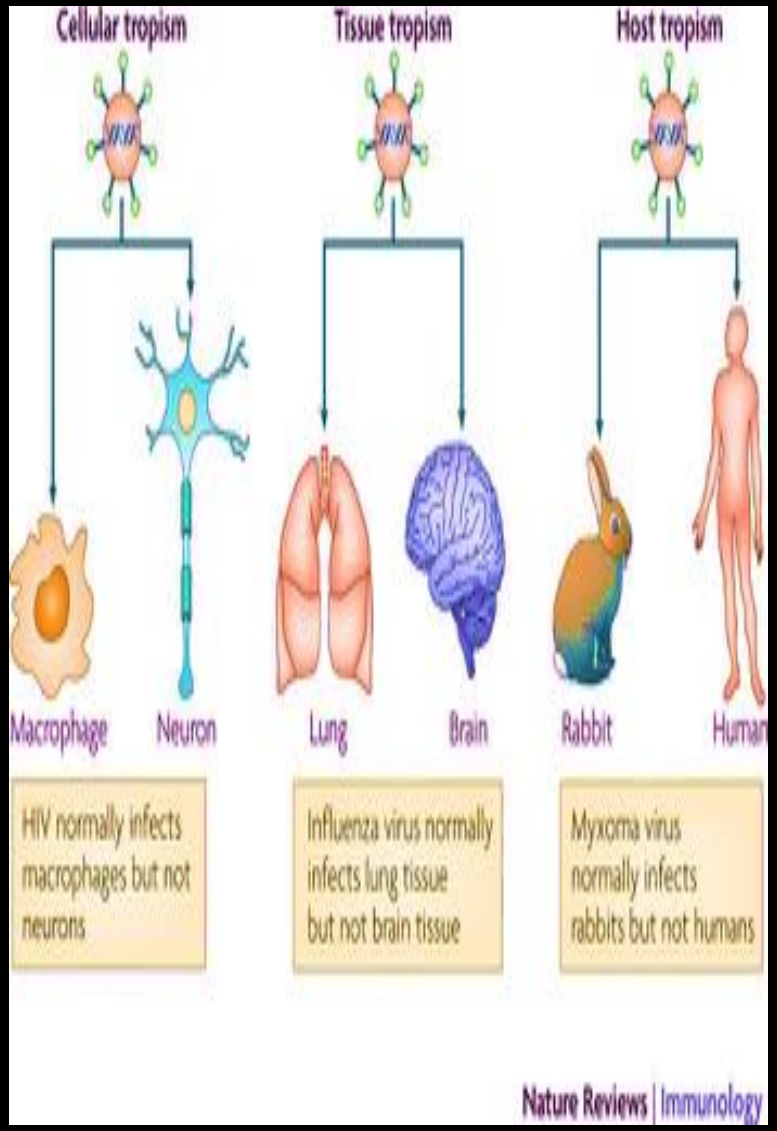


Tissue tropism

Specific Adherence of Bacteria to Cell and Tissue Surfaces

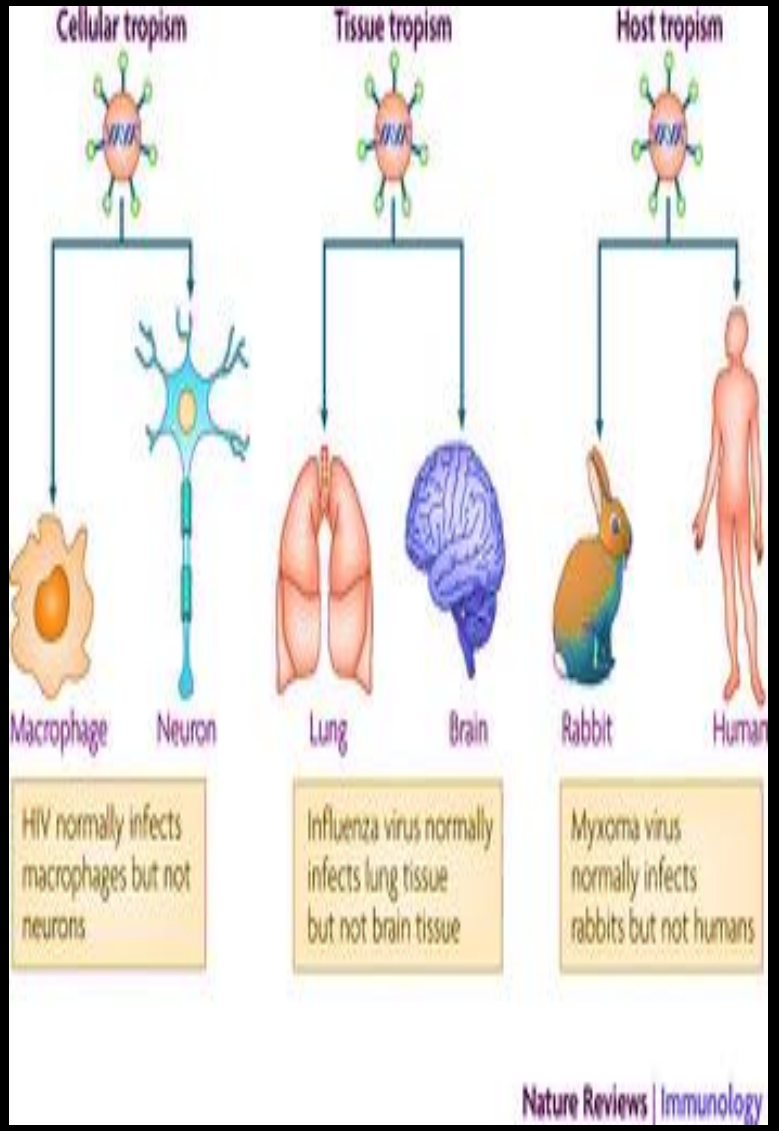
Several types of observations provide indirect evidence for specificity of adherence of bacteria to host cells or tissues:

1. **Tissue tropism:** particular bacteria are known to have an apparent preference for certain tissues over others, e.g. S. mutans is abundant in dental plaque but does not occur on epithelial surfaces of the tongue; the reverse is true for S. salivarius which is attached in high numbers to epithelial cells of the tongue but is absent in dental plaque.



Tissue tropism

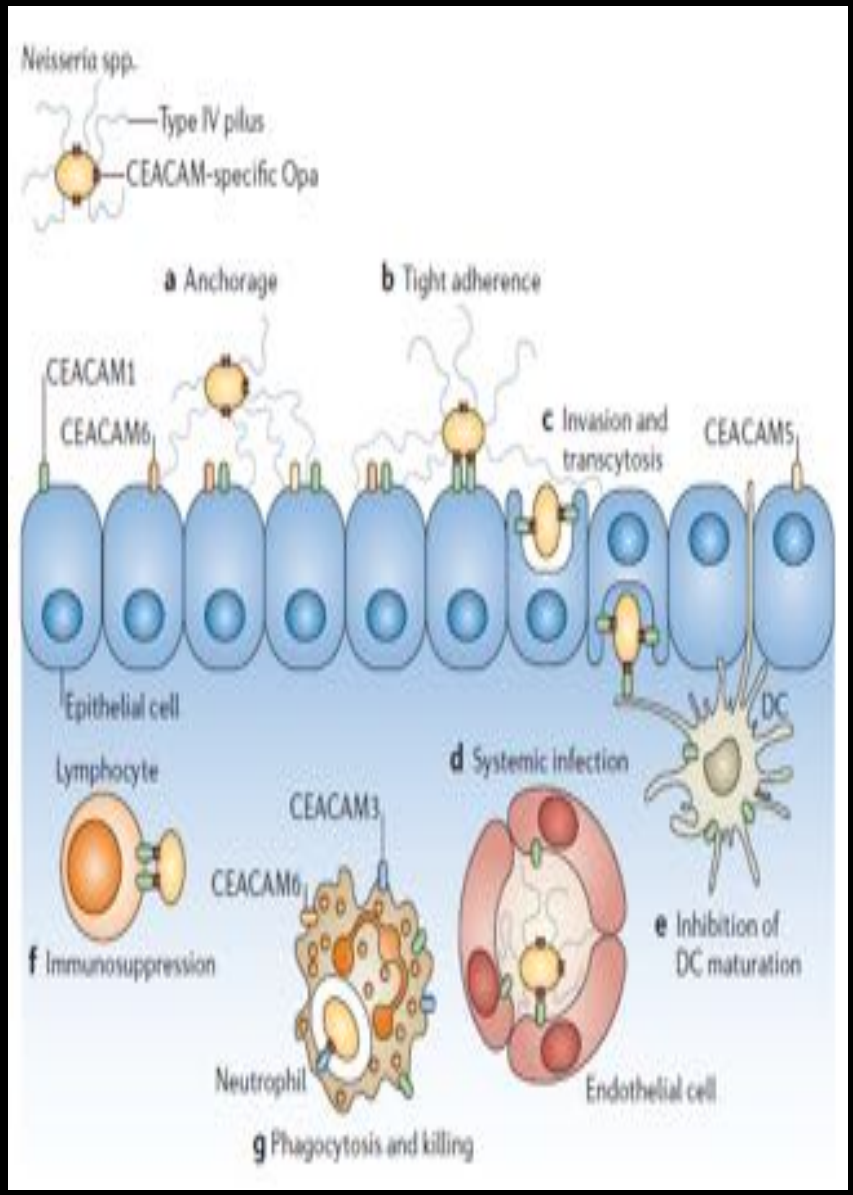
2. Species specificity: certain pathogenic bacteria infect only certain species of animals, e.g. N. gonorrhoeae infections are limited to humans; Enteropathogenic E. coli K-88 infections are limited to pigs; E. coli CFA I and CFA II infect humans; E. coli K-99 strain infects calves.; Group A streptococcal infections occur only in humans.



Tissue tropism

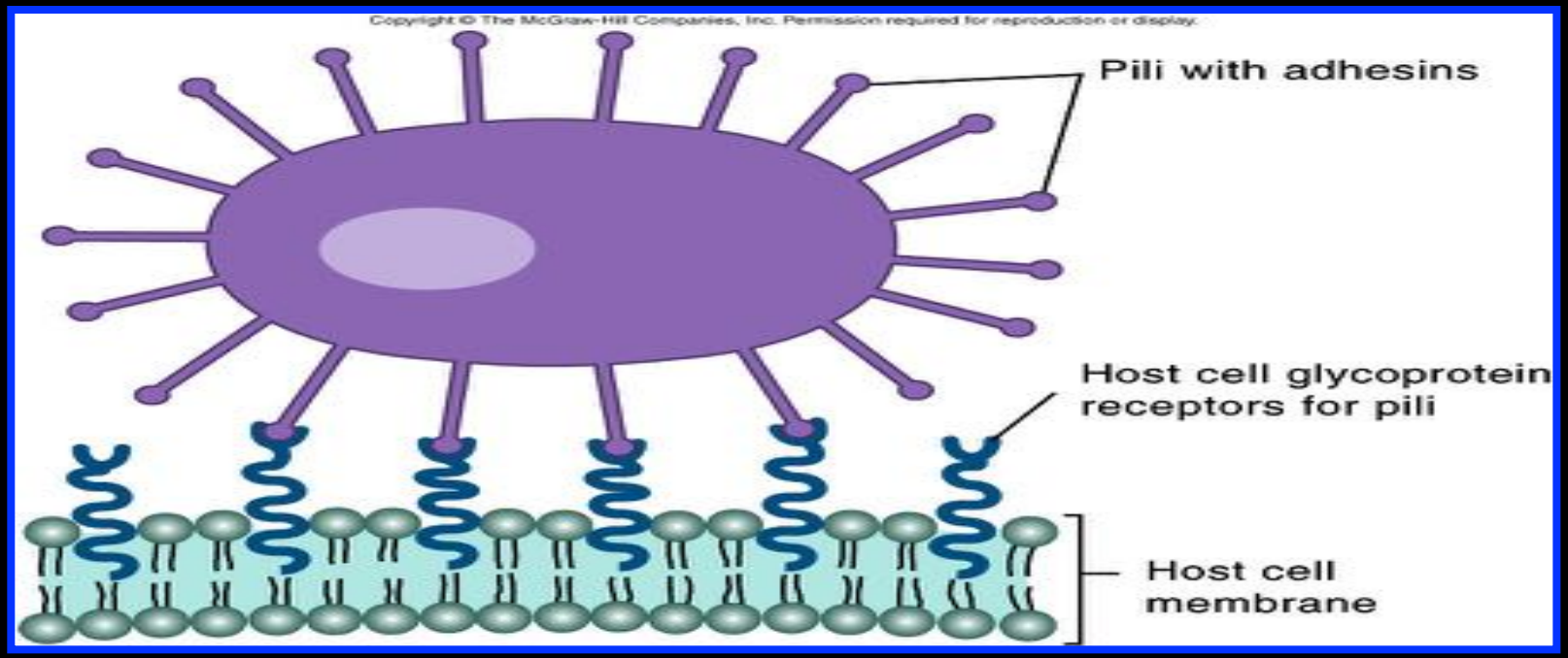
3. Genetic specificity within a species: certain strains or races within a species are genetically immune to a pathogen , e.g. Certain pigs are not susceptible to E. coli K-88 infections; Susceptibility to Plasmodium vivax infection (malaria) is dependent on the presence of the Duffy antigens on the host's red blood cells.

Although other explanations are possible, the above observations might be explained by the existence of specific interactions between microorganisms and eucaryotic tissue surfaces which allow microorganisms to become established on the surface.

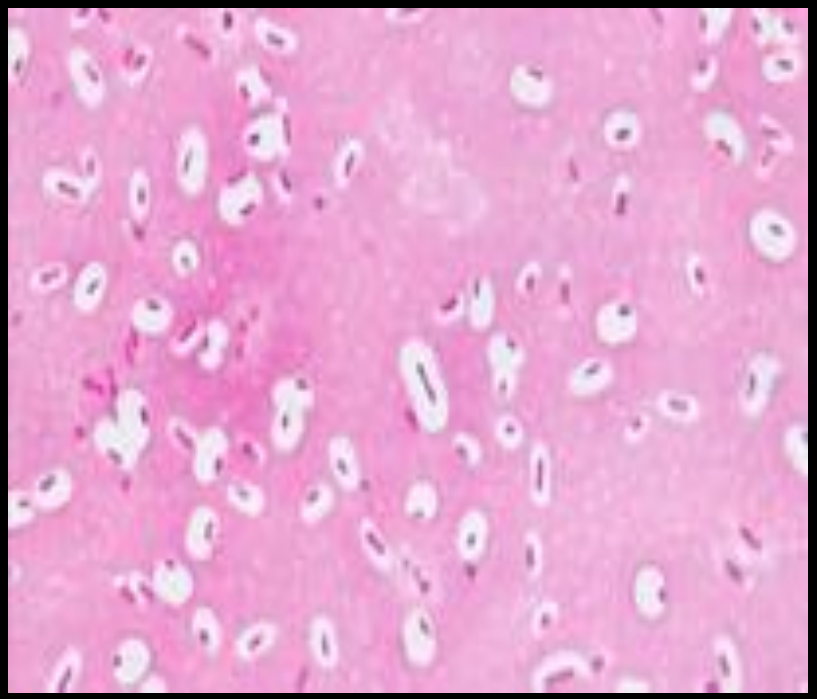


Bacteria typically employ proteins known as Adhesins to attach to host tissues, which usually are located on ends of fimbriae.

Alternatively, adhesins can consist of glycocalyx.



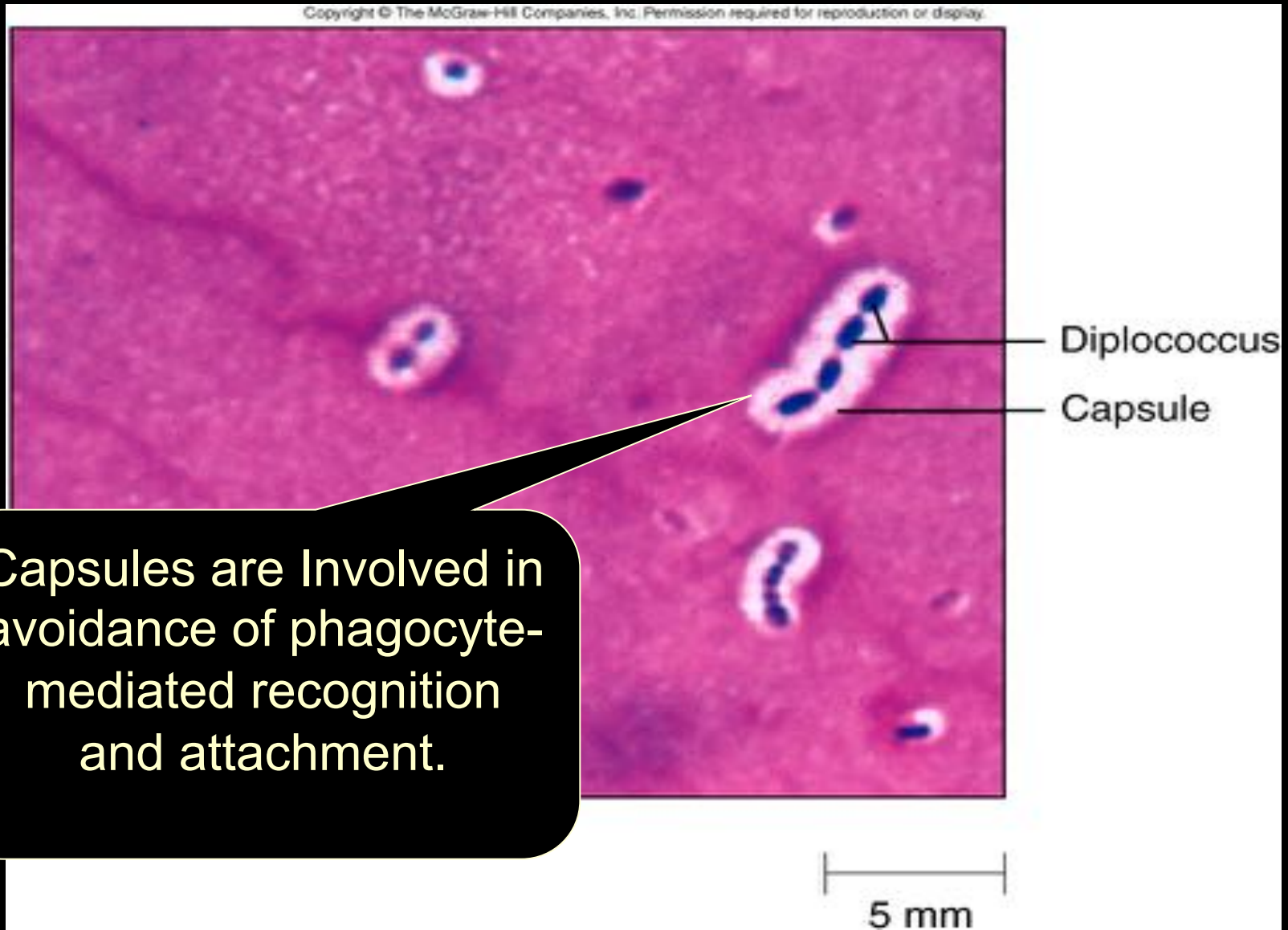
2. Capsules



K. pneumoniae

- Prevent phagocytosis
- attachment
- *Streptococcus pneumoniae*
- *Klebsiella pneumoniae*
- *Haemophilus influenzae*
- *Bacillus anthracis*
- *Streptococcus mutans*

Avoidance of Phagocytosis



Capsules are Involved in avoidance of phagocyte-mediated recognition and attachment.

Cell Wall Components

M protein: Found on cell surface and fimbriae of *Streptococcus pyogenes*. Mediates attachment and helps resist phagocytosis. M-protein is heat and acid resistant

Waxes [Mycolic Acid]: In cell wall of *Mycobacterium tuberculosis* helps resist digestion after phagocytosis and can multiply inside WBC.