Virulence factors

Slides made by Special Consultant Henrik Hasman, Statens Serum Institut
Entry into the human body

The most frequent **portals of entry**
- Mucus
- Skin

**Routes:**
Ingestion, inhalation, trauma, needles, catheters, arthropod bite, sexual transmission
Bacterial pathogenicity and virulence

The virulence of pathogenic microorganisms is associated with:

- adherence
- invasiveness
- capsule production
- toxin production
- aggressiveness
- and other factors

Virulence factors:

- "Anchor"
- "Ropes"
- "Camouflage"
- "Poison"
- "Weapons"
- "Costume, Hide, dig-in…ect"
The capsule
Virulence factors

The adherence
<table>
<thead>
<tr>
<th><strong>Adherence factor</strong></th>
<th><strong>Description</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Filamentous hemagglutinin</td>
<td>Causes adherence to erythrocytes</td>
</tr>
<tr>
<td>Fimbriae</td>
<td>Help attach to bacteria to solid surfaces</td>
</tr>
<tr>
<td>Glycocalyx or capsule</td>
<td>Inhibits phagocytosis and aids in adherence</td>
</tr>
<tr>
<td>Pili</td>
<td>Bind bacteria together for transfer of genetic material</td>
</tr>
<tr>
<td>Slime</td>
<td>Tenacious bacterial film that is less compact than a capsule</td>
</tr>
<tr>
<td>Teichoic and lipoteichoic acid</td>
<td>Cell wall components in Gram positive bacteria that aid in adhesion</td>
</tr>
</tbody>
</table>
Virulence factors

Adherence bacteria to cell surfaces
Some virulent microbes are characterized by the ability to penetrate tissues of the infected organism (invasive properties).

- Immunoglobulin A protease
- Leukocidins
- Collagenase and hyaluronidase
- Protein A
**Virulence factors**

Immunoglobulin A protease degrades IgA, allowing the organism to adhere to mucous membranes, and is produced chiefly by *N. gonorrhoeae, Haemophilus influenzae, and S. pneumoniae*.

Leukocidins can destroy both neutrophilic leukocytes and macrophages. Leukocidins are often associated with *S. aureus*; see later.
Virulence factors

Collagenase and hyaluronidase degrade collagen and hyaluronic acid, respectively, thereby allowing the bacteria to spread through subcutaneous tissue (Streptococci, Staphylococci, Clostridium).
Virulence factors

Collagenase and hyaluronidase degrade collagen and hyaluronic acid, respectively, thereby allowing the bacteria to spread through subcutaneous tissue (Streptococci, Staphylococci, Clostridium).

(a) Extracellular enzymes
Virulence factors

Protein A of *S. aureus* binds to IgG and prevents the activation of complement.
According to their nature of production, microbial toxins are subdivided into **exotoxins and endotoxins**.
Exotoxins easily diffuse from the cell into the surrounding nutrient medium.

They are characterized by a markedly distinct toxicity, and act on the susceptible organism in very small doses.

Exotoxins have the properties of enzymes hydrolysing vitally important components of the cells of tissues and organs.
Virulence factors

**Exotoxins** exert their effects in a variety of ways:

- by inhibition of protein synthesis
- inhibition of nerve synapse function
- disruption of membrane transport
- damage to plasma membranes.
AB toxins

A subunit: Activity
B subunit: Binding
**AB$_5$ toxins**

Colera toxin  
Heat lable toxin I  
Heat lable toxin IIb  
Shiga toxin
Virulence factors

Action of the hemolysin on red blood cells
### Virulence factors

<table>
<thead>
<tr>
<th>MICROORGANISM</th>
<th>TOXIN</th>
<th>DISEASE</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clostridium botulinum</td>
<td>Several neurotoxins</td>
<td>Botulism</td>
<td>Paralysis; blocks neural transmission</td>
</tr>
<tr>
<td>Clostridium tetani</td>
<td>Neurotoxin</td>
<td>Tetanus</td>
<td>Spastic paralysis; interferes with motor neurons</td>
</tr>
<tr>
<td>Corynebacterium diphtheriae</td>
<td>Cytotoxin</td>
<td>Diphtheria</td>
<td>Blocks protein synthesis</td>
</tr>
<tr>
<td>Bordetella pertussis</td>
<td>Pertussis toxin</td>
<td>Whooping cough</td>
<td>Blocks G proteins that are involved in regulation</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>Hemolysin</td>
<td>Scarlet fever Food</td>
<td>Lysis of blood cells</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Enterotoxin</td>
<td>Poisoning</td>
<td>Intestinal inflammation</td>
</tr>
<tr>
<td>Aspergillus flavus</td>
<td>Cytotoxin</td>
<td>Aflatoxicosis</td>
<td>Blocks transcription of DNA → stopping protein synthesis</td>
</tr>
<tr>
<td>Amanita phalloides</td>
<td>Cytotoxin</td>
<td>Mushroom food poisoning</td>
<td>Blocks transcription of DNA → stopping protein synthesis</td>
</tr>
</tbody>
</table>
Endotoxins

- are associated with Gram negative bacteria only
- are more firmly bound with the body of the bacterial cell
- are less toxic and act on the organism in large doses
- their latent period is usually estimated in hours
Virulence factors
Endotoxins

- According to chemical structure, endotoxins are related to glucoside-lipid and polysaccharide compounds or phospholipid-protein complexes.

- They are thermostable. Some endotoxins withstand boiling and autoclaving at 120°C for 30 minutes.
Virulence factors
Virulence factors

Action of the endotoxin

Endotoxin in the bloodstream

- Fever
- Blood clotting
- Internal hemorrhaging
- Inflammation
- Hypotension
## Virulence factors

### Differences between exotoxins and endotoxins

<table>
<thead>
<tr>
<th>exotoxins</th>
<th>endotoxins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteins</td>
<td>Lipopolysaccharides</td>
</tr>
<tr>
<td>Heat labile</td>
<td>Heat stable</td>
</tr>
<tr>
<td>Action often enzymatic</td>
<td>No enzymatic action</td>
</tr>
<tr>
<td>Specific pharmacological effect for each exotoxin</td>
<td>Non-specific action of all endotoxins</td>
</tr>
</tbody>
</table>
Bacterial pathogenicity and virulence

The virulence of pathogenic microorganisms is associated with:

- adherence
- invasiveness
- capsule production
- toxin production
- aggressiveness
- interference with the immune system
VirulenceFinder 1.5

View the version history of this server.

Select species
- Listeria
- S. aureus
- Escherichia coli
- Enterococcus

Select threshold for %ID
- 90%

Select minimum length
- 60%

Select type of your reads
- Assembled Genome/Contigs*

Isolate File

<table>
<thead>
<tr>
<th>Name</th>
<th>Size</th>
<th>Progress</th>
<th>Status</th>
</tr>
</thead>
</table>

Upload | Remove
Virulence Finder – How does it work

Unknown seq

BLAST

Resistant genes

VirulenceFinder

Resistant profile
## VirulenceFinder-1.5 Server - Results

**SETTINGS:**
Selected %ID threshold: **90.00**

<table>
<thead>
<tr>
<th>Virulence factor</th>
<th>%Identity</th>
<th>Query/HSP length</th>
<th>Contig</th>
<th>Position in contig</th>
<th>Protein function</th>
<th>Accession number</th>
</tr>
</thead>
<tbody>
<tr>
<td>agg3B</td>
<td>100.00</td>
<td>441 / 441</td>
<td>Supercontig_1.9</td>
<td>12444..12884</td>
<td>AAF/III minor adhesin. Enterobacteria AfaD invasin protein</td>
<td>AF411067</td>
</tr>
<tr>
<td>iha</td>
<td>100.00</td>
<td>2091 / 2091</td>
<td>Supercontig_1.1</td>
<td>12778..14868</td>
<td>Adherence protein</td>
<td>CP003289</td>
</tr>
<tr>
<td>agg3A</td>
<td>100.00</td>
<td>501 / 501</td>
<td>Supercontig_1.9</td>
<td>13059..13559</td>
<td>AAF/III major fimbrial subunit</td>
<td>HE603111</td>
</tr>
<tr>
<td>sigA</td>
<td>100.00</td>
<td>3858 / 3858</td>
<td>Supercontig_1.2</td>
<td>13971..17828</td>
<td>Shigella IgA-like protease homologue</td>
<td>AE005674</td>
</tr>
<tr>
<td>astA</td>
<td>100.00</td>
<td>117 / 117</td>
<td>Supercontig_1.9</td>
<td>14203..14319</td>
<td>EAST-1 heat-stable toxin</td>
<td>AF411067</td>
</tr>
<tr>
<td>stx2A</td>
<td>100.00</td>
<td>960 / 960</td>
<td>Supercontig_1.2</td>
<td>1501200..1502159</td>
<td>Shiga toxin 2, subunit A, variant a</td>
<td>AY143336</td>
</tr>
<tr>
<td>stx2B</td>
<td>100.00</td>
<td>270 / 270</td>
<td>Supercontig_1.2</td>
<td>1502171..1502440</td>
<td>Shiga toxin 2, subunit B, variant a</td>
<td>AE005174</td>
</tr>
<tr>
<td>ORF3</td>
<td>100.00</td>
<td>1029 / 1029</td>
<td>Supercontig_1.9</td>
<td>15211..16239</td>
<td>Isoprenoid Biosynthesis</td>
<td>CU928159</td>
</tr>
<tr>
<td>ORF4</td>
<td>99.81</td>
<td>540 / 540</td>
<td>Supercontig_1.9</td>
<td>16243..16782</td>
<td>Putative isopentenyl-diphosphate delta-isomerase</td>
<td>AFRH01000026</td>
</tr>
<tr>
<td>aggR</td>
<td>100.00</td>
<td>798 / 798</td>
<td>Supercontig_1.9</td>
<td>19214..20011</td>
<td>AraC transcriptional activator</td>
<td>55989</td>
</tr>
<tr>
<td>capU</td>
<td>100.00</td>
<td>1089 / 1089</td>
<td>Supercontig_1.2</td>
<td>201326..202414</td>
<td>Hexosyltransferase homolog</td>
<td>CU928145</td>
</tr>
<tr>
<td>gad</td>
<td>100.00</td>
<td>1401 / 1401</td>
<td>Supercontig_1.2</td>
<td>2050426..2051826</td>
<td>Glutamate decarboxylase</td>
<td>CP003297</td>
</tr>
<tr>
<td>aap</td>
<td>100.00</td>
<td>351 / 351</td>
<td>Supercontig_1.9</td>
<td>20851..21201</td>
<td>Dispersin, antiaggregation protein</td>
<td>Z32523</td>
</tr>
<tr>
<td>aar</td>
<td>100.00</td>
<td>201 / 201</td>
<td>Supercontig_1.9</td>
<td>21932..22132</td>
<td>AggR-activated regulator</td>
<td>SSI_AA784</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Microcin H47 part of colicin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>98.14</td>
<td>324 / 324</td>
<td>Supercontig_1.9</td>
<td>21932..22132</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Questions?