2.3A: The Gram-Positive Cell Wall

Skills to Develop

2. Describe the composition of a Gram-positive cell wall and indicate the possible beneficial functions to the bacterium of peptidoglycan, teichoic acids, and surface proteins.
3. Briefly describe how PAMPs of the Gram-positive cell wall can promote inflammation.
4. State the function of bacterial adhesins, secretion systems, and invasins.
5. Define antigen and epitope.

Highlighted Bacterium

1. Read the description of Enterococcus, and match the bacterium with the description of the organism and the infection it causes.

As mentioned in the previous section on peptidoglycan, Gram-positive bacteria are those that retain the initial dye crystal violet during the Gram stain procedure and appear purple when observed through the microscope. As we will learn in lab, this is a result of the structure and function of the Gram-positive cell wall.
Common Gram-positive bacteria of medical importance include *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis*, and *Clostridium* species.

**Structure and Composition of the Gram-Positive Cell Wall**

1. In electron micrographs, the Gram-positive cell wall appears as a broad, dense wall 20-80 nm thick and consisting of numerous interconnecting layers of peptidoglycan (see Figs. 1A and 1B). Chemically, 60 to 90% of the Gram-positive cell wall is peptidoglycan. In Gram-positive bacteria it is thought that the peptidoglycan is laid down in cables of several cross-linked glycan strands approximately 50 nm wide. These cables then themselves become cross-linked for further cell wall strength.

2. Interwoven in the cell wall of Gram-positive are teichoic acids and lipoteichoic acids. Teichoic acids extend through and beyond the rest of the cell wall and are polyalcohols composed of polymers of glycerol, phosphates, and the sugar alcohol ribitol and are covalently bound to the peptidoglycan. Teichoic acids covalently bound to cytoplasmic membrane...
lipids are called lipoteichoic acids (see Figure 1B).

3. The outer surface of the peptidoglycan is studded with surface proteins that differ with the strain and species of the bacterium (see Figure 1B).

4. The periplasm is the gelatinous material between the peptidoglycan and the cytoplasmic membrane.

For More Information: Peptidoglycan from Unit 1.

To view an electron micrograph of *Streptococcus* showing a Gram-positive cell wall, see the Rockefeller University web page.

Functions of the Gram-Positive Cell Wall Components

1. The peptidoglycan in the Gram-positive cell wall prevents osmotic lysis.

2. The teichoic acids probably help make the cell wall stronger (see Figure 1B).

3. The surface proteins (see Figure 1B) in the bacterial peptidoglycan, depending on the strain and species, carry out a variety of activities.

a. Some surface proteins function as enzymes.

b. Other proteins serve as adhesins. Adhesins enable the bacterium to adhere intimately to host cells and other surfaces in order to colonize those cells and resist flushing (See Figure 2).

Flash animation showing a bacterium using adhesins to adhere to a host cell.

html5 version of animation for iPad showing a bacterium using adhesins to adhere to a host cell.

c. Many bacteria involved in infection have the ability to co-opt the functions of host cells for the bacterium's own benefit. This is done by way of bacterial secretions systems that enable the bacterium to directly inject bacterial effector molecules into the cytoplasm of the host cell in order to alter its cellular machinery or cellular communication to the benefit of the bacteria. They do this by producing secretion systems such as the type 3 secretion system that produces hollow, needle-like tubes called injectisomes. Certain bacteria, for example, inject invasins into the cytoplasm of the host cell that enable the bacterium to enter that cell.

Flash animation showing bacteria secreting invasions into a non-immune host cell in order to enter that cell by phagocytosis.

html5 version of animation for iPad showing bacteria secreting invasions into a non-immune host cell in order to enter that cell by phagocytosis.
The role of these cell wall surface proteins will be discussed in greater detail later in Unit 3 under Bacterial Pathogenicity.

4. The periplasm contains enzymes for nutrient breakdown.

For More Information: The Ability to Adhere to Host Cells from Unit 3

For More Information: The Ability to Invade Host Cells from Unit 3

Concept map for the Gram-positive cell wall.

Significance of Gram-Positive Cell Wall Components to the Initiation of Body Defenses

The body has two immune systems: the innate immune system and the adaptive immune system.

1. Innate immunity is an antigen-nonspecific defense mechanisms that a host uses immediately or within several hours after exposure to almost any microbe. This is the immunity one is born with and is the initial response by the body to eliminate microbes and prevent infection.

2. Adaptive (acquired) immunity refers to antigen-specific defense mechanisms that take several days to become protective and are designed to react with and remove a specific antigen. This is the immunity one develops throughout life.

Initiation of Innate Immunity

In order to protect against infection, one of the things the body must initially do is detect the presence of microorganisms. The body does this by recognizing molecules unique to microorganisms that are not associated with human cells. These unique molecules are called pathogen-associated molecular patterns or PAMPs. (Because all microbes, not just pathogenic microbes, possess PAMPs, pathogen-associated molecular patterns are sometime referred to as microbe-associated molecular patterns or MAMPs.)

Fragments of peptidoglycan and teichoic acids are PAMPS associated with the cell wall of Gram-positive bacteria. In addition, bacteria and other microorganisms also possess mannose-rich glycans (short carbohydrate chains with the sugar mannose or fructose as the terminal sugar) that function as PAMPs. These mannose-rich glycans are common in microbial glycoproteins and glycolipids but rare in those of humans (see Figure 3).

These PAMPS bind to pattern-recognition receptors or PRRs on a variety of defense cells of the body and trigger such innate immune defenses as inflammation, fever, and phagocytosis.

For More Information: Pathogen-Associated Molecular Patterns (PAMPs) from Unit 5
Inflammation is the first response to infection and injury and is critical to body defense. Basically, the inflammatory response is an attempt by the body to restore and maintain homeostasis after injury. Most of the body defense elements are located in the blood, and inflammation is the means by which body defense cells and body defense chemicals leave the blood and enter the tissue around an injured or infected site.

Body defense cells such as macrophages, and dendritic cells have pattern recognition receptors such as toll-like receptors on their surface that are specific for the peptidoglycan fragments and lipoteichoic acids in the Gram-positive cell wall and/or to NODs in their cytoplasm that are specific for peptidoglycan fragments.

The binding of these cell wall components to their corresponding pattern recognition receptors triggers the macrophages to release various defense regulatory chemicals called cytokines, including IL-1, IL-6, IL-8, TNF-alpha, and PAF. The cytokines then bind to cytokine receptors on target cells and initiate inflammation and activate both the complement pathways and the coagulation pathway (see Figure 4).

The peptidoglycan and teichoic acids also activate the alternative complement pathway and the lectin pathway, innate immune defense pathways that play a variety of roles in body defense.

Initiation of Adaptive Immunity

Proteins and polysaccharides associated with the Gram-positive cell wall function as antigens and initiate adaptive immunity. An antigen is defined as a molecular shape that reacts with antibody molecules and with antigen receptors on lymphocytes. We recognize those molecular shapes as foreign or different from our body's molecular shapes because they fit specific antigen receptors on our B-lymphocytes and T-lymphocytes, the cells that carry out adaptive immunity.

The actual portions or fragments of an antigen that react with antibodies and with receptors on B-lymphocytes and T-lymphocytes are called epitopes. An epitope is typically a group of 5-15 amino acids with a unique shape that makes up a portion of a protein antigen, or 3-4 sugar residues branching off of a polysaccharide antigen. A single microorganism has many hundreds of different shaped epitopes that our lymphocytes can recognize as foreign and mount an adaptive immune response against.
The body recognizes an antigen as foreign when epitopes of that antigen bind to B-lymphocytes and T-lymphocytes by means of epitope-specific receptor molecules having a shape complementary to that of the epitope. The epitope receptor on the surface of a B-lymphocyte is called a B-cell receptor and is actually an antibody molecule. The receptor on a T-lymphocyte is called a T-cell receptor (TCR).

There are two major branches of the adaptive immune responses: humoral immunity and cell-mediated immunity.

1. Humoral immunity: Humoral immunity involves the production of antibody molecules in response to an antigen and is mediated by B-lymphocytes. Through a variety of mechanisms, these antibodies are able to remove or neutralize microorganisms and their toxins after binding to their epitopes. For example, antibodies made against cell wall antigens can stick bacteria to phagocytes, a process called opsonization. Antibodies made against cell wall adhesins can prevent bacteria from adhering to and colonizing host cells.

2. Cell-mediated immunity: Cell-mediated immunity involves the production of cytotoxic T-lymphocytes, activated macrophages, activated NK cells, and cytokines in response to an antigen and is mediated by T-lymphocytes. These defense cells help to remove infected cells and cancer cells displaying foreign epitopes.

Adaptive immunity will be discussed in greater detail in Unit 6.

Significance of Gram-Positive Cell Wall Components to Bacterial Pathogenicity

During severe systemic infections with large numbers of bacteria present, however, high levels of Gram-positive PAMPs are released resulting in excessive cytokine production by the macrophages and other cells and this, in turn, can harm the body (see Figure 5).

For More Information: Review of antigens and epitopes from Unit 6

For More Information: Inflammatory Gram-Positive Cell Wall Components from Unit 3

For More Information: Cytokines from Unit 5

For More Information: Inflammation from Unit 5

https://bio.libretexts.org/Bookshelves/Microbiology/Book%3A_Microbiology_(Kaiser)/Unit_1%3A_Introduction_to_Microbiology…

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Summary

1. Because of the nature of their cell wall, Gram-positive bacteria stain purple after Gram staining.
2. The Gram-positive cell wall consists of many interconnected layers of peptidoglycan and lacks an outer membrane.
3. Peptidoglycan prevents osmotic lysis in the hypotonic environment in which most bacteria live.
4. Teichoic acids and lipoteichoic acids are interwoven through the peptidoglycan layers.
5. Surface proteins embedded in the cell wall can function as adhesins, secretion systems, and enzymes.
6. The Gram-positive cell wall activates both the body's innate immune defenses and its adaptive immune defenses.
7. The body activates innate immunity by recognizing molecules unique to microorganisms that are not associated with human cells called pathogen-associated molecular patterns or PAMPs. PAMPs bind to Pattern-recognition receptors (PRRs) on defense cells to trigger the production of inflammatory cytokines.
8. Inflammation is the means by which the body delivers defense cells and defense molecules to an infection site, however, excessive inflammation can be harmful and even deadly to the body.
9. PAMPs associated with the Gram-positive cell wall include peptidoglycan monomers, teichoic acids, lipoteichoic acids, and mannose-rich sugar chains.
10. An antigen is a molecular shape that reacts with antigen receptors on lymphocytes to initiate an adaptive immune response.
11. Cell wall molecules can also trigger adaptive immunity such as the production of antibody molecules against bacterial cell wall antigens.

Questions

Study the material in this section and then write out the answers to these questions. Do not just click on the answers and write them out. This will not test your understanding of this tutorial.

1. State what color Gram-positive bacteria appear after the Gram stain procedure. (ans)
2. Describe the structure and appearance of a Gram-positive cell wall. (ans)
3. State the beneficial function to the bacterium of the following components of the gram-positive cell wall:
   a. peptidoglycan (ans)
b. teichoic acids \((ans)\)
c. adhesins \((ans)\)
d. invasins \((ans)\)

4. Briefly describe how PAMPs of the Gram-positive cell wall can promote inflammation. \((ans)\)

5. Define antigen. \((ans)\)

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**Contributors**

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