Lecture one & two Dr. wurood &Dr. Zaid

Lec 1 :Complement System

1. Introduction

The complement system is a crucial part of the innate immune system and plays an important role in host defense against microorganisms. It consists of a group of plasma proteins that interact in a highly regulated cascade to eliminate pathogens, enhance inflammation, and support adaptive immunity. Although discovered as a heat-labile component that "complemented" antibodies, it is now known that the complement system can function independently of antibodies and serves as a bridge between innate and adaptive immune responses.

2. Definition

The complement system is composed of more than 30 soluble and membrane-bound proteins that made mainly in the liver and then secreted into the blood. They are numbered C1 to C9, and there are other supporting proteins that are also considered to be complement proteins (e.g. C1 inhibitor, properdin, factor B, factor D, factor H and factor I). Upon activation, these proteins undergo sequential proteolytic cleavage, resulting in a cascade that amplifies the immune response.

Or -a group of over 30 proteins made in the liver and then secreted into the blood and assist other cells of the immune system to fight infection and kill micro-organisms. Complement proteins also play an important role in inflammation

The main functions of the complement system include opsonization, direct cell lysis, promotion of inflammation, and clearance of immune complexes.

3. General Mechanism

Complement activation occurs through a cascade mechanism in which inactive precursor proteins are converted into active enzymes. All pathways converge at the activation of C3, producing C3a (inflammatory mediator) and C3b (opsonin). Further activation leads to formation of the membrane attack complex (MAC), which causes cell lysis.

4. Types of Complement Activation

Classical Pathway: Activated by antigen–antibody complexes (IgG or IgM).

Begins with **C1 (C1q, C1r, C1s)** binding to the Fc region of antibodies.

Leads to formation of **C4b2a (C3 convertase)**.

Lectin Pathway:

- Activated by **mannose residues** on microbial surfaces.
- Initiated by **mannose-binding lectin (MBL)** or ficolins.
- Uses MBL-associated serine proteases (MASPs).
- Forms the same C3 convertase as the classical pathway (**C4b2a**).

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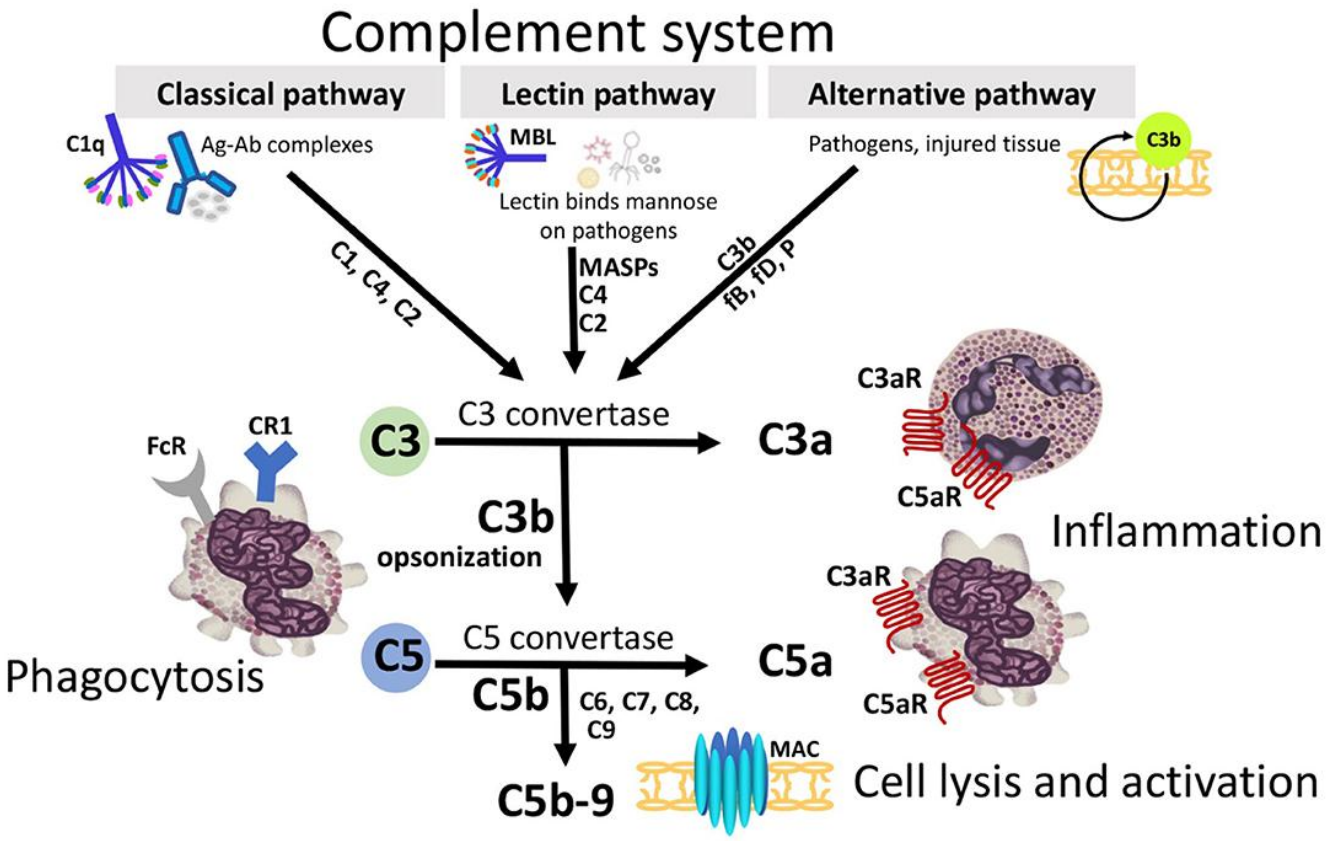
Alternative Pathway: Activated directly on microbial surfaces without antibodies and stabilized by properdin.

- Depends on spontaneous hydrolysis of C3.

- Uses **Factor B, Factor D, and Properdin**.
- Forms **C3bBb (C3 convertase)**



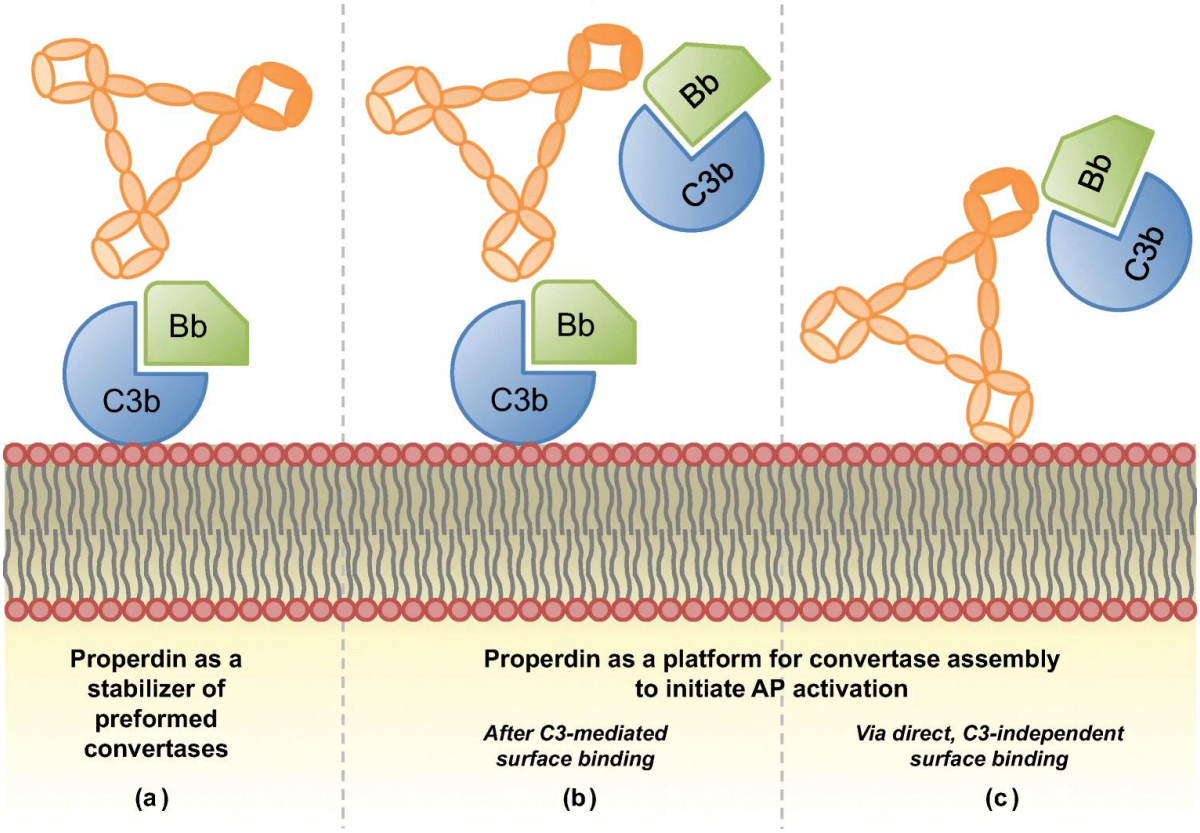
5. Complement Deficiencies

Complement deficiency results when any of the proteins are missing or do not work properly. Because each protein has a different role in the pathway, each complement deficiency has different symptoms and treatments. Complement deficiencies increase susceptibility to infections and autoimmune diseases. C3 deficiency causes severe infections, while C5–C9 deficiencies are associated with Neisseria infections. C1 esterase inhibitor deficiency causes hereditary angioedema.

Complement deficiency	Health complication
Deficiencies of early C components (C1, C2, C4)	Systemic lupus erythematosus (SLE), including the neonatal onset form in C1q deficiency Glomerulonephritis – inflammation of the kidney's blood vessels Polymyositis – inflammation of the muscles
C1 inhibitor	Hereditary angioedema
C3 and factor B	Severe bacterial infections
Factor I, C6 and C8	Severe neisserial infections

6. Properdin

Properdin is a positive regulator of the alternative pathway. It stabilizes C3 convertase and enhances pathogen clearance. Properdin deficiency is associated with severe meningococcal infections.



Lec 2 : Major Histocompatibility Complex (MHC)

Introduction

The Major Histocompatibility Complex (MHC) is a fundamental component of the immune system and plays a central role in antigen presentation and immune recognition. MHC molecules enable the immune system to distinguish between self and non-self by presenting antigenic peptides to T lymphocytes.

1. Definition

The Major Histocompatibility Complex (MHC) is a group of highly polymorphic genes that encode cell surface glycoproteins responsible for presenting peptide antigens to T cells. In humans, MHC genes are located on chromosome 6 and are collectively referred to as the Human Leukocyte Antigen (HLA) system.

MHC molecules bind peptide fragments derived from pathogens or self-proteins and display them on the cell surface for recognition by T-cell receptors (TCRs). This interaction is essential for the activation of adaptive immune responses.

2. Types of MHC Molecules

MHC molecules are divided into three main classes: MHC class I, MHC class II, and MHC class III. Each class has distinct structures, expression patterns, and immune functions.

2.1 MHC Class I

MHC class I molecules are expressed on almost all nucleated cells of the body. They present endogenous antigens, which are peptides derived from intracellular proteins such as viral or tumor antigens.

Structurally, MHC class I molecules consist of a heavy alpha (α) chain associated with β2-microglobulin. The peptide-binding groove is formed by the α1 and α2 domains.

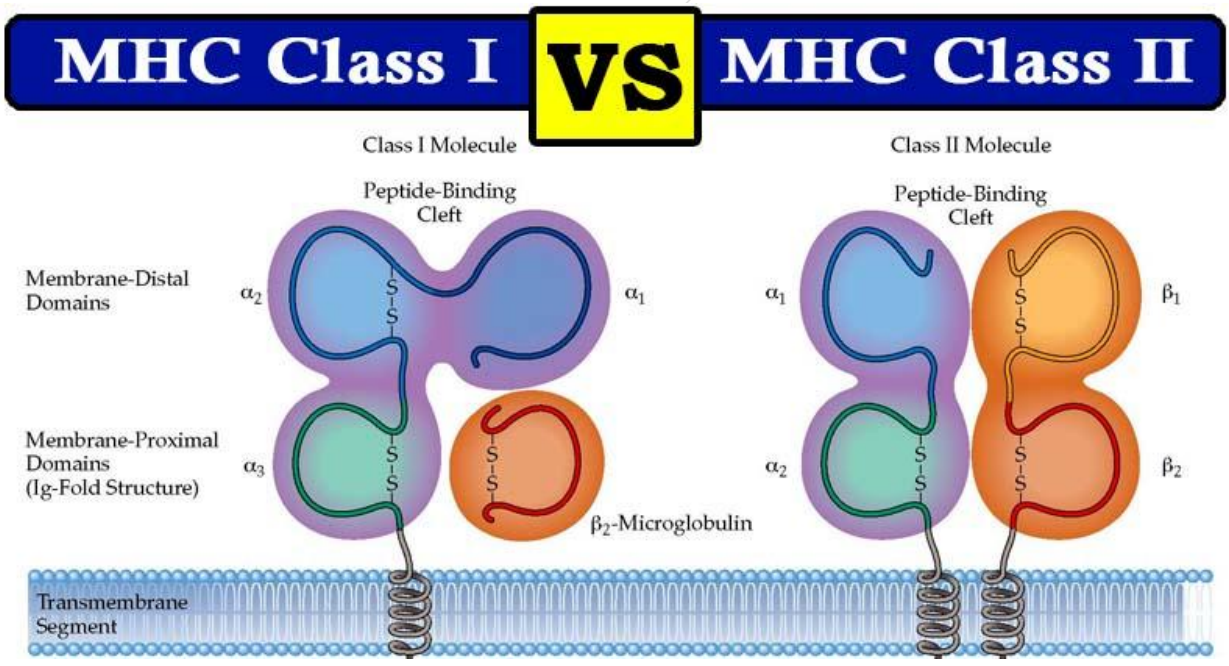
MHC class I molecules present antigens to CD8+ cytotoxic T lymphocytes (CTLs). Recognition of foreign peptides presented by MHC class I leads to activation of CTLs and destruction of infected or abnormal cells.

2.2 MHC Class II

MHC class II molecules are primarily expressed on professional antigen-presenting cells (APCs), including dendritic cells, macrophages, and B lymphocytes. They present exogenous antigens derived from extracellular pathogens.

MHC class II molecules are composed of two transmembrane chains, alpha (α) and beta (β), which together form the peptide-binding groove.

These molecules present antigens to CD4+ helper T cells, leading to activation of immune responses such as antibody production, macrophage activation, and cytokine secretion.



2.3 MHC Class III

MHC class III genes do not encode antigen-presenting molecules. Instead, they encode several immune-related proteins, including components of the complement system (such as C2, C4, and factor B) and certain cytokines like tumor necrosis factor (TNF).

Although MHC class III products are important in immune regulation and inflammation, they do not participate directly in antigen presentation.

3. Antigen Processing and Presentation

Antigen processing refers to the breakdown of protein antigens into peptide fragments, while antigen presentation involves displaying these peptides on MHC molecules for recognition by T cells. There are two major antigen processing pathways corresponding to MHC class I and class II molecules.

3.1 Endogenous Antigen Processing (MHC Class I Pathway)

Endogenous antigens originate from proteins synthesized within the cell, such as viral proteins in infected cells.

The processing steps include: 1. Degradation of intracellular proteins by the proteasome into peptide fragments 2. Transport of peptides into the endoplasmic reticulum (ER) by TAP (Transporter associated with Antigen Processing) 3. Binding of peptides to MHC class I molecules in the ER 4. Transport of peptide–MHC class I complexes to the cell surface

This pathway ensures immune surveillance by CD8+ T cells.

3.2 Exogenous Antigen Processing (MHC Class II Pathway)

Exogenous antigens originate from extracellular pathogens and are internalized by APCs through endocytosis or phagocytosis.

The processing steps include: 1. Uptake of antigen into endosomes 2. Degradation of antigen by lysosomal enzymes 3. Synthesis of MHC class II molecules in the ER, associated with invariant

chain (Ii) 4. Replacement of invariant chain fragment (CLIP) by antigenic peptides with the help of HLA-DM 5. Transport of peptide–MHC class II complexes to the cell surface

This pathway leads to activation of CD4+ helper T cells.