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Antigen Processing and Presentation: MHC Structure, Function and Ligands

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Abstract

Antigen processing and presentation are crucial steps in the immune response, enabling the immune system to recognize and respond to foreign substances, such as pathogens or abnormal cells. These processes involve the presentation of antigens, which are small parts of foreign proteins, to immune cells called T lymphocytes (T cells). Antigens can enter the body through various routes, such as ingestion, inhalation, or through wounds. Antigen-presenting cells (APCs), primarily dendritic cells, macrophages and B cells, are responsible for capturing antigens. They have specialized receptors, such as Pattern Recognition Receptors (PRRs), which can recognize pathogen-associated molecular patterns (PAMPs) present on pathogens. Once captured, the antigens undergo processing within the APCs.

Keywords: Antigen processing • Immune cells • Intracellular bacteria

Introduction

There are two major pathways for antigen processing. This pathway is used for intracellular pathogens, such as viruses or intracellular bacteria. The antigens are broken down into smaller peptide fragments by proteasomes in the cytoplasm. These peptide fragments are then transported into the Endoplasmic Reticulum (ER), where they bind to Major Histocompatibility Complex Class I (MHC-I) molecules. This pathway is used for extracellular pathogens, such as bacteria or parasites. The antigens are taken up by the APCs through phagocytosis or endocytosis. Within the endosomes or phagosomes, the antigens are degraded by enzymes and the resulting peptide fragments bind to Major Histocompatibility Complex class II (MHC-II) molecules.

Peptide-MHC Complex Formation: Once the antigens are bound to MHC molecules, they form peptide-MHC complexes. In the MHC class I pathway, the peptide-MHC-I complex is then transported to the cell surface for presentation to cytotoxic CD8+ T cells. In the MHC class II pathway, the peptide-MHC-II complex is transported to the cell surface for presentation to helper CD4+ T cells. The presentation of the peptide-MHC complexes on the surface of APCs allows T cells to recognize them. CD8+ T cells recognize peptide-MHC-I complexes, while CD4+ T cells recognize peptide-MHC-II complexes. When a T cell encounters its specific peptide-MHC complex, it binds to it through its T cell receptor (TCR). This interaction, along with additional co-stimulatory signals, triggers the activation of the T cell.

Literature Review

Immune Response: Once activated, T cells initiate various immune responses. CD8+ T cells become cytotoxic T cells, which can directly kill infected or abnormal cells presenting the specific antigen. CD4+ T cells can differentiate into different subsets, such as helper T cells, which provide signals to other immune cells to enhance their effector functions. Antigen processing and presentation play a critical role in the adaptive immune response, allowing the immune system to identify and respond to specific antigens. This process helps coordinate the immune response, leading to the elimination of pathogens and infected cells and ultimately protecting the body from disease. Major Histocompatibility Complex (MHC) molecules play a crucial role in the immune system by presenting antigens to T cells. They are involved in both innate and adaptive immune responses. MHC molecules are highly polymorphic and are encoded by a set of genes known as the Human Leukocyte Antigen (HLA) genes in humans. MHC molecules are membrane-bound glycoproteins that are expressed on the surface of nearly all nucleated cells in the body. There are two main classes of MHC molecules: MHC class I and MHC class II. These are expressed on the surface of almost all nucleated cells [1].

They consist of a heavy chain (alpha chain) encoded by the HLA-A, -B, or -C genes and a small protein called beta-2 micro globulin. The heavy chain has three extracellular domains: alpha-1, alpha-2 and alpha-3. The alpha-1 and alpha-2 domains form a peptide-binding cleft where antigens are bound. MHC Class II molecules: These are primarily expressed on antigen-presenting cells such as dendritic cells, macrophages and B cells. They consist of two chains: An alpha chain (encoded by the HLA-DP, -DQ, or -DR genes) and a beta chain. Both chains have two extracellular domains: alpha-1, alpha-2, beta-1 and beta-2. The peptide-binding cleft is formed by the interaction of the alpha-1 and beta-1 domains. The main function of MHC molecules is to present antigens to T cells, which are key players in adaptive immune responses. MHC class I molecules present antigens derived from intracellular pathogens, such as viruses and intracellular bacteria, to CD8+ cytotoxic T cells. This process helps activate the cytotoxic T cells to destroy infected cells [2].

Discussion

MHC class II molecules present antigens derived from extracellular pathogens, such as bacteria and parasites, to CD4+ helper T cells. This interaction helps activate the helper T cells, which can then coordinate immune responses by providing signals to other immune cells. The antigens that bind to MHC molecules and are presented to T cells are called ligands. MHC class I molecules present peptides derived from endogenous proteins synthesized within the cell. These peptides are usually 8-10 amino acids in length and are derived from cytosolic proteins that have been degraded by the proteasome. MHC class II molecules present longer peptides, typically 13-25 amino acids, derived from exogenous antigens that have been taken up by antigen-presenting cells through phagocytosis or endocytosis. The process of antigen presentation involves the binding of antigens to the peptide-binding cleft of MHC molecules. The peptides that bind to MHC molecules are determined by the specific amino acid sequences of the MHC molecules and the antigen processing pathways within the cell [3].

MHC molecules play a critical role in the immune response by presenting

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antigens to T cells. MHC class I molecules present intracellular antigens to CD8+ cytotoxic T cells, while MHC class II molecules present extracellular antigens to CD4+ helper T cells. The peptides that bind to MHC molecules are determined by the specific amino acid sequences of the MHC molecules and the antigen processing pathways within the cell. Major Histocompatibility Complex (MHC) assembly and trafficking play crucial roles in the immune system's recognition and response to foreign antigens. MHC molecules are cell surface proteins that display peptide fragments derived from intracellular pathogens (such as viruses or bacteria) to T cells, which are key players in adaptive immune responses. MHC molecules can be divided into two main classes: MHC class I and MHC class II. MHC class I molecules are composed of a trans membrane heavy chain (encoded by the MHC class I gene) and a small peptide called β2-microglobulin. The heavy chain has three domains: α1, α2 and α3. Inside the cell, the MHC class I heavy chain is synthesized in the Endoplasmic Reticulum (ER) and associates with the β2-microglobulin. Peptide loading occurs in the ER [4].

In the ER, MHC class I molecules associate with a protein complex called the Peptide-Loading Complex (PLC). The PLC consists of several chaperone proteins, such as calnexin, calreticulin, tapasin and ERp57. These chaperones facilitate the binding of short peptide fragments derived from intracellular proteins to the MHC class I molecule. Proper peptide binding stabilizes the MHC class I molecule and allows it to exit the ER. Once the MHC class I molecule is loaded with a peptide, it is transported from the ER to the cell surface via the Golgi apparatus. This process involves vesicular transport and is mediated by various proteins, including Coat Protein Complex II (COPII) vesicles. At the cell surface, MHC class I molecules present the peptide fragments to CD8+ T cells, which recognize and respond to these peptides. MHC class II molecules are composed of two trans membrane chains, an α chain and a β chain. Both chains are encoded by genes within the MHC class II region. Inside the cell, the α and β chains are synthesized in the ER and associate with an invariant chain (Ii), which prevents premature peptide binding. In the ER, the invariant chain associates with the α and β chains of the MHC class II molecule. The invariant chain helps in the correct folding of the MHC class II molecule and targets it to specialized compartments called MHC Class II Compartments (MIICs). In MIICs, the invariant chain is progressively degraded, leaving a small fragment called the Class Ii-Associated Invariant Chain Peptide (CLIP) bound in the peptide-binding groove of the MHC class II molecule [5,6].

Conclusion

In MIICs, the MHC class II molecule encounters a separate set of proteins involved in peptide loading. These proteins include HLA-DM in humans or H-2M in mice. HLA-DM/H-2M facilitates the release of CLIP and the binding of antigenic peptides derived from extracellular proteins. Once the MHC class II molecule is loaded with an antigenic peptide, it is transported to the cell surface via vesicular trafficking pathways. MHC class II molecules are predominantly expressed on Antigen-Presenting Cells (APCs) such as dendritic cells, macrophages and B cells. At the cell surface, MHC class II molecules present antigenic peptides to CD4+ T cells, which recognize and respond to these peptides. In summary, MHC assembly and trafficking involve intricate processes that ensure the correct presentation of peptide antigens to T cells. MHC class I molecules present intracellular antigens.

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Conflict of Interest

The author shows no conflict of interest towards this article.

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