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 - ✓ Unit 3
 - ✓ Unit 4
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- ✓ Unit 1
 - ✓ Unit 2
 - ✓ Unit 3
 - ✓ Unit 4
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- ✓ Unit 1
 - ✓ Unit 2
 - ✓ Unit 3
 - ✓ Unit 4
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- ✓ Unit 1
 - ✓ Unit 2
 - ✓ Unit 3
 - ✓ Unit 4
 - ✓ Unit 5
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- ✓ Unit 1
 - ✓ Unit 2
 - ✓ Unit 3
 - ✓ Unit 4
 - ✓ Unit 5
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PHARMACEUTICAL BIOTECHNOLOGY

UNIT 3

TOPIC :

- b) Structure and Function of MHC



Major Histocompatibility Complex (MHC)

- Major Histocompatibility Complex (MHC) is a group of genes that code for cell-surface glycoproteins called MHC molecules.
- In humans, MHC is known as the Human Leukocyte Antigen (HLA) System.

Functions of MHC

- Distinguishes self from non-self.
- Presents antigenic peptides to T-cells.
- Essential for activation of adaptive immunity.
- Plays an important role in organ transplantation and graft rejection.

Important Point

- **B-cells** can recognize free antigens directly.
- **T-cells** cannot recognize free antigens and require MHC molecules for antigen recognition.

Location of MHC Genes

In humans, MHC genes are located on: Chromosome 6 (Short arm, 6p21)

Classification of MHC

MHC is divided into three classes:

1. MHC Class I
2. MHC Class II
3. MHC Class III

MCH Class I

MHC Class I molecules are glycoproteins present on the surface of almost all nucleated cells of the body.

Distribution

Present on:

- All nucleated cells

Absent on:

- Red Blood Cells (RBCs)

Genes Encoding MHC-I

MHC-I molecules are encoded by:

- HLA-A
- HLA-B
- HLA-C

Function

MHC-I presents endogenous antigens (antigens produced inside the cell).

Examples

- Viral proteins
- Tumor proteins
- Intracellular pathogen proteins

Structure of MHC-I

MHC-I consists of:

1. Heavy α Chain

Contains three domains:

- α_1
- α_2
- α_3

2. β_2 -Microglobulin

- Small non-covalently attached protein
- Stabilizes MHC-I structure

Antigen Presentation Pathway of MHC-I

Step 1

- Intracellular proteins are degraded into peptides by proteasomes.

Step 2

- Peptides enter the Endoplasmic Reticulum (ER).

Step 3

- Peptides bind to MHC-I molecules.

Step 4

- MHC-I-peptide complex moves to the cell surface.

Step 5

- CD8⁺ Cytotoxic T-cells recognize the complex.

Step 6

- Activated CD8⁺ T-cells destroy infected or abnormal cells.

Key Features of MHC-I

Feature	MHC-I
Present On	All nucleated cells
Genes	HLA-A, HLA-B, HLA-C
Antigen Type	Endogenous
Recognized By	CD8 ⁺ T-cells
Function	Killing infected cells

MHC Class II

- MHC Class II molecules are glycoproteins found only on professional Antigen Presenting Cells (APCs).

Distribution

Present on:

- Dendritic Cells
- Macrophages
- B-Lymphocytes

Genes Encoding MHC-II

MHC-II molecules are encoded by:

- HLA-DP
- HLA-DQ
- HLA-DR

Function

MHC-II presents exogenous antigens (antigens originating outside the cell).

Examples

- Bacteria
- Toxins, Fungi
- Extracellular pathogens

Structure of MHC-II

MHC-II consists of two polypeptide chains:

 α Chain

Contains:

- $\alpha 1$
- $\alpha 2$ domains

 β Chain

Contains:

- $\beta 1, \beta 2$ domains

Antigen Presentation Pathway of MHC-II**Step 1**

- APCs engulf pathogens through phagocytosis or endocytosis.

Step 2

- Pathogens are degraded into peptide fragments inside lysosomes.

Step 3

- Peptides bind to MHC-II molecules.

Step 4

- MHC-II-peptide complex moves to the cell surface.

Step 5

- CD_4^+ Helper T-cells recognize the complex.

Step 6

- Helper T-cells become activated and initiate immune responses.

Key Features of MHC-II

Feature	MHC-II
Present On	APCs only
Genes	HLA-DP, HLA-DQ, HLA-DR
Antigen Type	Exogenous
Recognized By	CD_4^+ T-cells
Function	Immune activation

MHC Class III

- MHC Class III genes do not participate in antigen presentation.
- Instead, they encode several important proteins involved in immunity and inflammation.

Functions of MHC-III

Produces:

Complement Proteins

- C₂
- C₄
- Factor B

Cytokines

- Tumor Necrosis Factor (TNF- α)
- TNF- β

Role of MHC-III

- Enhances immune responses
- Participates in inflammation
- Supports complement activation
- Helps regulate immune functions