

12) MHC Molecules and Transplantation

I. The Major Histocompatibility Complex (MHC)

The MHC is a large cluster of genes that encode glycoproteins essential for the immune system to distinguish self from non-self. In humans, these are called **Human Leukocyte Antigens (HLA)**.

Genetics and Expression

- **Polymorphism:** MHC genes are the **most polymorphic genes** in the human genome.
- **Haplotype:** The set of alleles present on a single chromosome is termed the **MHC haplotype**.
- **Codominance:** MHC alleles are **expressed codominantly**, meaning products from both parents are expressed equally on cells.
- **Locus:** The MHC is located on **Chromosome 6**.

MHC Restriction

- T-cell receptors (TCRs) do not recognize isolated antigens; they recognize a **unique combination of a peptide and a specific MHC molecule**.
- **CD8+ T cells** are restricted to **MHC Class I**, while **CD4+ T cells** are restricted to **MHC Class II**.

II. Transplantation Immunology

Transplantation is the process of replacing damaged organs or tissues with healthy ones from a donor.

Types of Grafts

- **Autograft:** Tissue moved within the **same individual**.
- **Isograft:** Tissue moved between **genetically identical** individuals (identical twins).
- **Allograft:** Tissue moved between **non-genetically identical members of the same species** (the most common type).
- **Xenograft:** Tissue moved **between different species** (e.g., pig valves).

Alloantigen Recognition

Recipient T cells recognize donor (allogeneic) MHC molecules in two ways:

1. **Direct Recognition:** T cells bind directly to **intact allogeneic MHC** on donor antigen-presenting cells (APCs).
2. **Indirect Recognition:** Recipient APCs process donor MHC molecules into **peptides** and present them on **self-MHC**.

III. Graft Rejection Stages

Rejection is the immune system's destruction of a transplant identified as foreign.

- **Hyperacute Rejection:** Occurs within **minutes or hours**; caused by **preexisting antibodies** in the recipient. It leads to thrombosis and immediate graft failure.
- **Acute Rejection:** Occurs within **days to weeks** (usually within 6 months). It is mediated by **T cells and antibodies** causing damage to graft parenchyma and blood vessels.
- **Chronic Rejection:** Occurs over **months to years**. It is characterized by **vascular occlusion** (arterial narrowing) due to smooth muscle proliferation and scarring.

IV. Clinical Management

- **Matching:** Success depends on matching **ABO blood groups** and **HLA antigens** (specifically **HLA-A, HLA-B, and HLA-DR**).
- **Cross-matching:** Donor cells are mixed with recipient serum to check for pre-formed antibodies; a **positive cross-match** indicates a high risk of hyperacute rejection.
- **Immunosuppression:** Drugs like **cyclosporine, tacrolimus, and steroids** are used to dampen the immune response.
- **Graft vs. Host Disease (GVHD):** Occurs in bone marrow transplants when **donor T cells** attack the **recipient's tissues**.

V. Summary Table of MHC Classes

Feature	MHC Class I	MHC Class II	MHC Class III / Cytokines
Gene Products	HLA-A, HLA-B, HLA-C	HLA-DP, HLA-DQ, HLA-DR	Complement (C2, C4, B), TNF-\alpha, TNF-\beta
Tissue Distribution	All nucleated cells	B cells, APCs (macrophages, DCs)	Plasma proteins
Function	Destroys infected cells via CD8+ CTLs	Antigen ID via CD4+ Helper T cells	Defense, growth, and inflammation
Peptide Length	8–10 amino acids	13–17 amino acids	N/A
Groove Shape	Deep, closed ends	Shallow, open ends	N/A