

Major Histocompatibility Complex (MHC)

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- * The MHC is a **closely linked complex of genes** that **govern** production of the **major histocompatibility**
- * In humans, **MHC resides** on the **short arm** of chromosome 6
- * **Three genes** (HLA-A, HLA-B, HLA-C) **code** for the **class I MHC** proteins
- * Several **HLA-D loci** determine the **class II MHC** proteins i.e. DP, DQ and DR
- * **HLA genes** are very **diverse** (polymorphic) i.e. there are many alleles of the class I and II genes

Major Histocompatibility Complex (MHC)

- * Between the **class I and class II gene loci**, there is a third locus (**Class III**)
- * This locus contains genes **encoding tumor necrosis factor, lymphotoxin and two complement components (C2 and C4)**
- * **Class III** antigens **do not participate** in MHC restriction or graft rejection

MHC Class I Antigens

- * **Class I MHC antigens** are : HLA-A, HLA-B and HLA-C
- * These antigens are glycoproteins found on **surfaces of all nucleotide human cells and on platelets**
- * **HLA-A** contains **24 different antigenic specificities**, **HLA-B** contains **52** and **HLA-C** contains **11**
- * **Class I MHC antigens** are **involved** of **MHC restriction** of cell mediated cytotoxicity

MHC Restriction

- * **Endogenously processed** cytosolic **peptides** in virus infected cells or tumor cells are **transported** to the surface of the cells
- * They **bind** to **MHC I molecules** to be **recognized** by cytotoxic T-cells which then **kill** these cells
- * In other words;
T-cells are only **activated** when they **recognize** both **antigen and class I MHC molecules in association**

MHC Class II Antigens

Class II antigens are: HLA-DP, HLA-DQ, HLA-DR antigens

These antigens are glycoproteins found on the surface of macrophages, B-cells, Dendritic cells, Langerhans cells of skin and activated T cells

HLA-DP contain 6 different antigenic specificities, HLA-DQ contains 9 and HLA-DR contains 20

MHC Class II Antigens

- * **Helper T-cells recognize** antigens on antigen-presenting cells **only** when the antigens are **presented** on the surface of cells in **association** with class II MHC
- * **Class II antigens react** with the **CD4** molecule on the **helper T-cells** which **secrete cytokines**

Class I MHC and Class II MHC

	MHC Class I	MHC Class II
Nomenclature	HLA-A, HLA-B, HLA-C	HLA-DP, HLA-DQ, HLA-DR
Found on	All nucleated somatic cells	Macrophages, B-cells, Dendritic cells, Langerhans cells of skin and activated T cells
Recognized by	CD8 TC cells	CD4 TH cells
Functions	Presentation of Ag to TC cells leading to elimination of tumor or infected host cell	Presentation of Ag to TH cells which secrete cytokines

Transplantation and Graft Rejection

Types of grafts

1) Autografts :

The transfer of an individual's own tissues from place to place

e.g. Skin grafts (regularly accepted)

2) Isografts :

Transfer of tissues between genetically identical persons

e.g. Identical twins (accepted permanently)

Types of grafts

3) Allografts (homograft):

- Transfer of a graft between genetically different members of same species
e.g from one human to another
- Rejection occur if donor and recipient are not matched

4) Xenograft (heterograft):

- Transfer of tissues between different species
- Always rejected

Mechanism Of Graft Rejection

1) Both TH and TC are activated

- **TC cells** destroy graft cells by direct contact
TH cells secrete cytokines that attract and activate macrophages, NK cells and polymorphs leading to cellular infiltration and destruction of graft (**Type IV**)
- **B cells** recognize foreign antigens on the graft and produce antibodies which bind to graft cells and
 - . Activate complement causing cell lysis
 - . Enhance phagocytosis, i.e. opsonization
 - . Lead to ADCC by macrophages, NK, PML(**Type II**)
- **Immune complex deposition** on the vessel walls induce platelets aggregation and microthrombi leading to ischemia and necrosis of graft (**Type II**)

Types Of Graft Rejection

1) Hyperacute rejection:

- It occurs **hours** after transplantation
- In individual with preformed antibodies either due to
- blood groups incompatibility or previous sensitization by blood transfusion, previous transplantation

2) Acute Rejection:

- It occurs **10 to 30 days** after transplantation
- It is mainly T-cell mediated

3) Chronic or late rejection:

- It occurs over a period of **months or years**
- It may be cell mediated, antibody mediated or both

Graft Versus Host (GVH) Reaction

- * An immunologically competent graft is transplanted into an immunologically suppressed recipient (host)
- * The grafted cells survive and react against the host cells i.e instead of reaction of host against the graft, the reverse occurs
- * GVH reaction is characterized by fever, pancytopenia, weight loss, rash, diarrhea, hepatosplenomegaly and death