



- **What are the conditions in which there will be production of anti-HLA antibodies?**
 - **Rejection** (this occurs when transplantation is done but the HLA of the donor and the recipient are not matching).
 - **A multiparous female** (having borne more than one child): there will be anti-HLA antibodies to part of the fetus because 50% of his HLA reading is inherited from his father while the other 50% is inherited from the mother.
- **Why do we need to do HLA typing (also known as tissue typing):**
 - It is done when **transplantation** is needed to check if the donor is matching with the recipient so rejection doesn't occur.
 - It is used to check for **paternity** (الأبوة والأصل).
 - There are some **HLA-associated diseases**:
 - ✓ The most important is ankylosing spondylitis in which the relative risk (RR) is increased.
 - ✓ Other diseases include: type-I diabetes (DR3 & DR4), Systemic Lupus Erythematosus (SLE) and rheumatoid arthritis.
- **The MHC molecule is expressed on chromosome 6 and there are two main classes:**

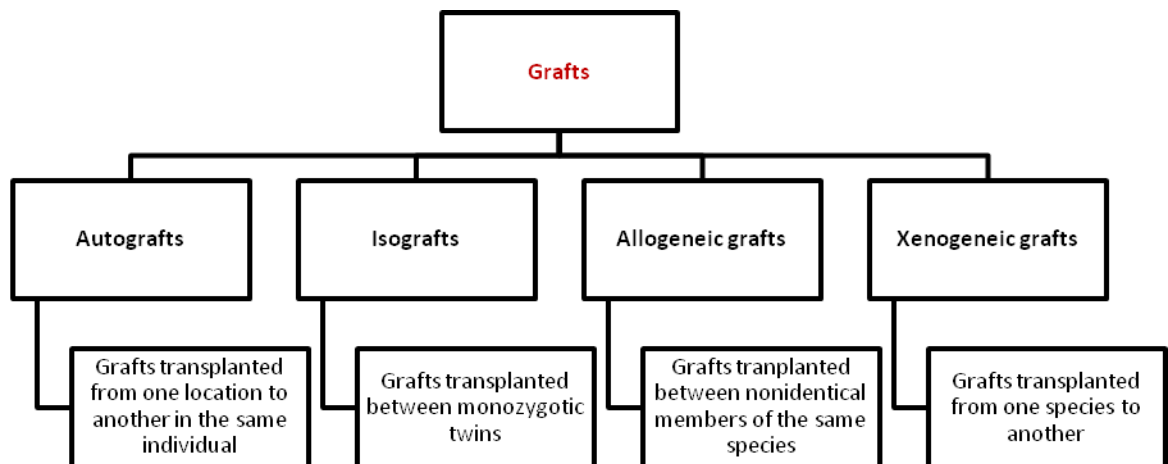
| | MHC-I | MHC-II |
|------------------------------------|---|---|
| Gene products | HLA-A, HLA-B (complex) & HLA-C (antigenically not strong & will not evoke rejection in the process of transplantation) | HLA-DP, HLA-DQ, HLA-DR |
| Tissue distribution | In all nucleated cells + platelets | On antigen presenting cells (APC): macrophages, B-lymphocytes and dendritic cells |
| Recognized by | Cytotoxic T cells (CD8+) | Helper T cells (CD4+) |
| Peptides bound | Endogenously synthesized | Exogenously synthesized |
| Function | Elimination of infected host cells by cytotoxic T cells | Presentation of foreign antigens to helper T cells |
| Presence of invariant chain | No | Yes |
| Structure | α heavy chain with 3 extracellular domains & an intracytoplasmic carboxy-terminus + light chain (β ₂ -microglobulin) | Two chain structures of similar length called α and β |
| Expression | Codominantly expressed: which means that each cell expresses two A, two B and two C products (one from each parent) | Codominantly expressed: same concept |

- **HLA-restriction:**
 - **MHC-I → interacts with CD8+ cytotoxic T-cells.**
Where intracellular viral proteins will be converted to peptides by proteosomes present in the cytosol of the cell → these peptides will be transported to the rough endoplasmic reticulum via TAP-complex → where these peptides will be loaded in MHC class I molecules and then expressed on the cell surface to be recognized by CD8+ cytotoxic T-cells.
 - **MHC-II → interacts with CD4+ helper T-cells.**
Where exogenous antigens will be taken by the cell and surrounded by a vesicle which will fuse with another vesicle that is containing the MHC class II molecule with the invariant chain → as these vesicles fuse, the invariant chain is degraded and peptides are loaded into the MHC-II → the complex is then transported to the cell surface where it will be accessible for interaction with helper T-cells (CD4+).



- **Transplantation immunology:**

- **We need an identical donor:**
 - ✓ *Mother & father:* they are haploidentical to their children because each one of them transmit 50% of their HLA reading to their children.
 - ✓ *Siblings:* they are preferred as donors with 25% chance of being different than his/her brother or sister, 50% of being haploidentical and 25% of being identical.
- **Methods of HLA typing (tissue typing):**
 - ✓ Complement-dependent lymphocytotoxicity.
 - ✓ Molecular methods: including probes (SSO) or primers (SSP).
- **Tissue compatibility testing involves:**
 - ✓ ABO blood typing.
 - ✓ Cross-matching.
 - ✓ The mixed lymphocyte reaction (for class II compatibility).
 - ✓ Microcytotoxicity test (for class I compatibility).
- **Types of grafts:**



- During graft rejection, MHC-I allele products are recognized as foreign by cytotoxic t-cells (CD8+) and the graft is destroyed.
- **Graft-versus-host disease:** occurs when mature T-cells inside bone marrow transplants become activated against the MHC-II products of the graft recipient.
Note: immunosuppression is required to ensure the survival of all grafts (except autografts because they are from the same person).