

Transplantation barriers

• Structures recognized and significance according to type of transplantation

	blood transfusion	organ transplantation	HSC transplantation
Blood groups	+++	+++	(-)
Major histocompatible antigens	(+)	++	+++
Minor histocompatible antigens	-	(+)	++

- **Major histocompatibility complex** (human MHC = HLA):

Genetic region (> 200 genes on chromosome 6)

three classes of genes:

HLA class I (A, B and C genes) --> class I MHC molecule

HLA class II (DP, DQ and DR genes) --> class II MHC molecule

HLA class III --> proteins of complement system

very high polymorphism of MHC molecules in human populations

Function of MHC molecules: antigen presentation to T cells

- **Minor histocompatibility antigens:**

mHC are polymorphic (different between donor and recipient) self proteins

Recognized on tissues of MHC-matched individuals

- weaker transplantation antigens, and less important when major histocompatibility antigens are mismatched

- **Blood groups:**

Not relevant in HSC transplantation, HSC do not express ABO antigens

Important transplantation barriers when blood is transfused because incompatible ABO blood group antigens are recognized by natural antibodies. Important in organ transplantation because ABO blood group antigens are also expressed on vascular endothelial cells of the organs.

• **Allorecognition**

Designates the response to histoincompatible tissue (by alloantibodies or by alloreactive T cells)

Histoincompatible antigens may be recognized by alloreactive T cells in two ways:

- **directly** on the foreign antigen presenting cell

- **indirectly** after processing and presentation by the antigen presenting cell

Alloreactions against allogeneic MHC are very strong because:

MHC shaped to be recognized by T cells, (self) peptides presented by an incompatible MHC molecule represent numerous foreign epitopes, very high polymorphism --> 2 unrelated individuals virtually always express different MHC. Transplantation results are always better when the recipient and the donor are HLA-matched.

Recipient & Transplantation

- Hematopoiesis
- Type of transplant
- Indications
- Decision to treat
- Conditioning
- Transplantation

Donor & Compatibility

- Criteria
 - HLA typing
- Search
- Stem cell source

Immunosuppression

- Immunosuppressive drugs
- T cell depletion

Complications

- Graft rejection
- GVHD
 - Infections
 - Side effects
 - Relapse

Reconstitution

- Engraftment
- Myeloid cells
- T cells
- B cells
- Chimerism

LERANING OBJECTIVES

- T and B responses against allo-antigens
- Direct and indirect recognition
- Transplantation barriers: blood groups, major histocompatibility antigens, minor histocompatibility antigens