Transplantation barriers

- **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)
  Histoimmune 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.

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<thead>
<tr>
<th>Blood transfusion</th>
<th>Organ transplantation</th>
<th>HSC transplantation</th>
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<tbody>
<tr>
<td>Blood groups</td>
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<td>Major histocompatible antigens</td>
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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**

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