Transplantation Immunology
Grafts

**Autologous** (autograft): from one individual to the same individual

**Syngenic**: between two genetically identical or syngeneic individuals

**Allogenetic** (allograft): between two genetically different individuals of the same species

**Xenogenic** (xenograft): between two genetically different individuals of different species
Genetics of graft rejection

Rejection is caused by MHC antigens
First-set and second-set rejection

Rejection is mediated by lymphocytes
Rejection of skin grafts

1. Skin graft with Langerhans cells
2. Langerhans cells migrate to local lymph node, where they activate effector cells
3. Effector cells migrate to graft via blood
4. Graft destroyed by effector cells
Direct and indirect presentation of MHC alloantigens

A. Direct alloantigen recognition
- Allogeneic antigen-presenting cell in graft
- Allogeneic MHC
- Alloreactive T cell
- T cell recognizes unprocessed allogeneic MHC molecule on graft APC

B. Indirect alloantigen recognition
- Allogeneic MHC
- Professional APC in recipient
- Self MHC
- Uptake and processing of allogeneic MHC molecules by recipient APC
- Alloreactive T cell
- Peptide derived from allogeneic MHC molecule
- Presentation of processed peptide of allogeneic MHC molecule bound to self MHC molecule
Direct alloantigen recognition

Positive selection in the thymus allows all T lymphocytes that recognize MHC molecules to survive. Negative selection eliminates T lymphocytes with strong affinity for self-MHC molecules, but T lymphocytes with strong affinity for non-self (allo) MHC molecules survive.

High frequency of allo-reactive T lymphocytes (~2%)

Each allogenic cell can activate many T lymphocyte clones

Density of alloantigens is higher than self-MHC/antigens
Mixed leucocyte reaction

- Mix blood mononuclear cells from two donors in tissue culture
- Primary MLR
  - Responder T cell recognition of allogeneic MHC molecules
  - Clonal expansion and functional differentiation of responder T cells
  - Effector functions of T cells
  - Lysis of target cell
  - Cytokine secretion

- Donor X CD8⁺ T lymphocyte (Responder cell)
- Donor Y APC (Stimulator cell)
- Donor X CD4⁺ helper T cells
- Donor Y class I MHC⁺ target cell
- Donor Y class II MHC⁺ stimulator cell
Hyperacute and acute rejection

(A) Hyperacute rejection
- Endothelial cell
- Blood vessel
- Alloantigen (e.g., blood group antigen)
- Circulating alloantigen-specific antibody
- Complement activation, endothelial damage, inflammation and thrombosis

(B) Acute rejection
- Parenchymal cells
- Alloreactive antibody
- Endothelial cell
- Parenchymal cell damage, interstitial inflammation
- Endothelialitis

(C) Microscopic images
Chronic rejection

Chronic DTH reaction in vessel wall, intimal smooth muscle cell proliferation, vessel occlusion
Minor Histocompatibility Antigens (H)

Polymorphic self proteins that differ in amino acid sequence between individuals give rise to minor H antigen differences between donor and recipient.
Graft-versus-host-disease (GVDH)

Caused by the donor T lymphocytes after bone-marrow transplantation, but also after transplantation of organs that contain T lymphocytes

Acute GVHD: skin, liver, gastrointestinal tract (rash, jaundice, diarrhea)

Chronic GVDH: organ fibrosis and dysfunction