Transplantation

- Rejection of foreign tissue grafts is due to immune responses to alloantigens on the graft
  - Blood group antigens
  - Polymorphic MHC antigens
  - Minor histocompatibility antigens

Slide 16-1: Graft rejection is an immune response

From Abbas, Lichtman, & Pober: Cellular and Molecular Immunology. W.B. Saunders, 1999. Fig. 16-1
Alloantigen Presentation

- **Direct recognition**
  - MHC-peptide complexes on Donor APC are recognized directly by recipient T cells without processing by recipient APC

- **Indirect recognition**
  - Foreign MHC and other alloantigens are processed by recipient APC and presented to recipient T cells
Slide 16-3

Direct and indirect presentation of alloantigens

(A) Direct alloantigen presentation
- Allogeneic MHC
- Alloreactive T cell specific for intact allogeneic MHC molecule

Direct presentation of allogeneic MHC molecule by APC in graft

(B) Indirect alloantigen presentation
- Professional APC in recipient
- Uptake and processing of allogeneic MHC molecules by recipient APC

T cell specific for polymorphic peptide from allogeneic MHC molecule

Peptide containing polymorphic sequence of allogeneic MHC molecule

Presentation of processed peptide of allogeneic MHC molecule bound to self-MHC molecule

From Abbas, Lichtman, & Pober: Cellular and Molecular Immunology. W.B. Saunders, 1999, Fig. 16-3

Slide 16-4

Molecular basis of direct allogenic MHC recognition

(A) Normal
- T cell contact residues of peptide
- Polymorphic residues of MHC
- Self MHC

(B) Allorecognition
- T cell receptor
- Polymorphic residues of allogenic MHC

The self MHC–restricted T cell recognizes the allogeneic MHC molecule whose structure resembles the self MHC–foreign peptide complex

(C) Allorecognition
- T cell receptor
- Polymorphic residues of allogenic MHC

The self MHC–restricted T cell recognizes a structure formed by both the allogeneic MHC molecule and the bound peptide

From Abbas, Lichtman, & Pober: Cellular and Molecular Immunology. W.B. Saunders, 1999, Fig. 16-4
Transplantation

- Rejection is mediated primarily by T cells but antibodies are also important
- Rejection occurs with the same timing as other immune responses
  - Hyperacute rejection
  - Acute Rejection: First-set rejection & Second set rejection
  - Chronic rejection

From Abbas, Lichtman, & Pober: Cellular and Molecular Immunology. W.B. Saunders, 1999, Fig. 16-7a
Immune mechanisms of graft rejection (b)

Acute rejection

Endothelial cell
Alloreactive antibody

Alloantigen-specific CD8+ T cell
Parenchymal cells

Endothelialitis, parenchymal cell damage, interstitial inflammation

From Abbas, Lichtman, & Pober: Cellular and Molecular Immunology. W.B. Saunders, 1999, Fig. 16-7b

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Immune mechanisms of graft rejection (c)

Chronic rejection

Vascular smooth muscle cell
Cytokines

Alloantigen-specific CD4+ T cell

Macrophage

Chronic DTH reaction in vessel wall, intimal smooth muscle cell proliferation, vessel occlusion

From Abbas, Lichtman, & Pober: Cellular and Molecular Immunology. W.B. Saunders, 1999, Fig. 16-7c
Graft vs. Host disease

- When immunocompetent T cells are transplanted into a tissue incompatible immunodeficient recipient the donor T cells recognize and reject the recipient
  - This is more of a problem in bone marrow transplantation but can occur in any grafting procedure