The Major Histocompatibility Complex

What it is

What it does
- Required for antigen recognition by T lymphocytes

Differences in antigen recognition by B and T lymphocytes

B cell antigen receptor
- Immunoglobulin (Ig)
- B cells
  Transmembrane protein
- Secreted by effector cells (Plasma cell)

T cell antigen receptor
- T cell receptor (TCR)
- T cells
  Transmembrane protein
- Transmembrane protein on effector cells
- CD4 Helper T Cells
- CD8 Cytotoxic T Cells
Review of Differences in T and B Cells

• B cells
  - Recognize native protein antigens in solution or on cell surfaces
  - Secreted antibody is effector molecule
  - Antibodies can operate at a distance

Antigen-antibody Interaction

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Review of Differences in T and B Cells

• **B cells**
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• **T cells**
  - Recognize peptides from degraded antigens
  - Peptides are displayed on cell surfaces in association with specialized proteins (MHC)

Lysozyme
T cells recognize processed (degraded) protein antigens

Review of Differences in T and B Cells

- **B cells**
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  - Secreted antibody is effector molecule
  - Antibodies can operate at a distance

- **T cells**
  - Recognize peptides from degraded antigens
  - Peptides are displayed on cell surfaces in association with specialized proteins (MHC)
  - Antigen-specific T cell functions require direct cell-cell interactions
**Major Histocompatibility Complex**

- Discovered using inbred strains of mice and examining tumor immunity
- Were really studying transplantation immunology - histocompatibility antigens
- MHC is the major histocompatibility antigen that needs to be matched for organ transplantation
- A complex of linked genes encodes the MHC proteins
- Normal function of MHC is to display peptide antigens (self AND non-self) to T cells

**MHC**

- **MHC I and MHC II**
  - Genes
  - Structure
  - Polymorphisms
- **MHC and T cell responses**
MHC Class I

- Expressed by all nucleated cells
- Presents peptide to CD8 T cells
  - Cytotoxic “killer” cells
  - Kill virus infected cells

MHC Class II

- Expressed by specialized antigen presenting cells (APC)
  - Dendritic cells
  - B cells
  - Macrophages
- Presents peptide to CD4 T cells
- “Helper” T cells
  - Help B cells proliferate, differentiate, isotype switch
  - Help activate macrophages to kill intracellular pathogens
Class I and Class II MHC Molecules

- Membrane bound glycoproteins
- Structurally very similar
- Both have 4 domains
  - 2 membrane proximal domains
  - 2 membrane distal domains that form a peptide binding cleft

3-D Structure of Human Class I HLA Molecule
Peptides in the MHC groove
Class I
Class II
BCR

B Cell
- Self peptide
- Foreign peptide

Help!

TCR

B Cell
- Class I
- Class II
- Self peptide
- Foreign peptide
MHC Polymorphisms

- Allelic variations in MHC genes
- Concentrated in the peptide binding regions of Class I and Class II
MHC Polymorphisms

The human MHC gene complex
HLA - human leukocyte antigen
MHC Polymorphisms

• Allelic variations in MHC genes
• Concentrated in the peptide binding regions of Class I and Class II
• Population level
• Individual will inherit 9 maternal and 9 paternal MHC genes
• All are expressed

Consequences of MHC Polymorphism

• Organ and tissue transplants are difficult
• Polymorphic residues change the peptide binding specificity of the MHC
• If all MHC were identical, pathogens might avoid immune detection by mutation to prevent MHC binding
Why have two antigen recognition systems?