

# The Major Histocompatibility Complex

Peter Burrows  
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4-6529  
peterb@uab.edu

- What it is
- What it does
  - Required for antigen recognition by T lymphocytes

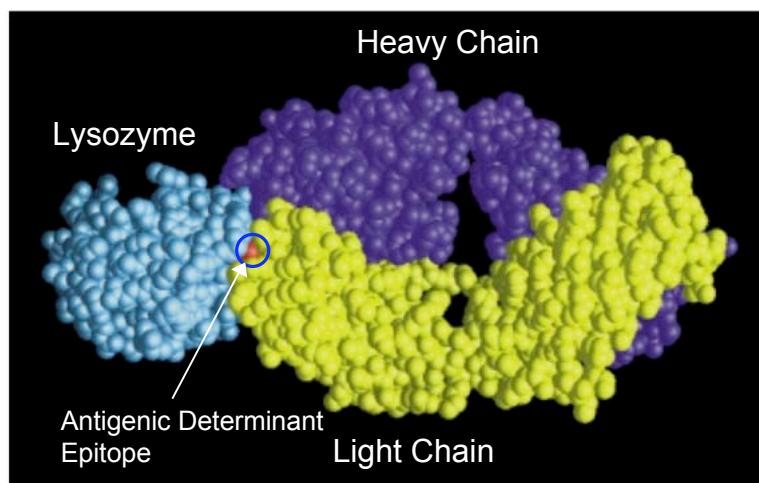
## Differences in antigen recognition by B and T lymphocytes

- |  |   |
|--|---|
| • <u>B cell antigen receptor</u>           | • <u>T cell antigen receptor</u>          |
| - Immunoglobulin (Ig)                      | - T cell receptor (TCR)                   |
| - B cells                                  | - T cells                                 |
| Transmembrane protein                      | Transmembrane protein                     |
| - Secreted by effector cells (Plasma cell) | - 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

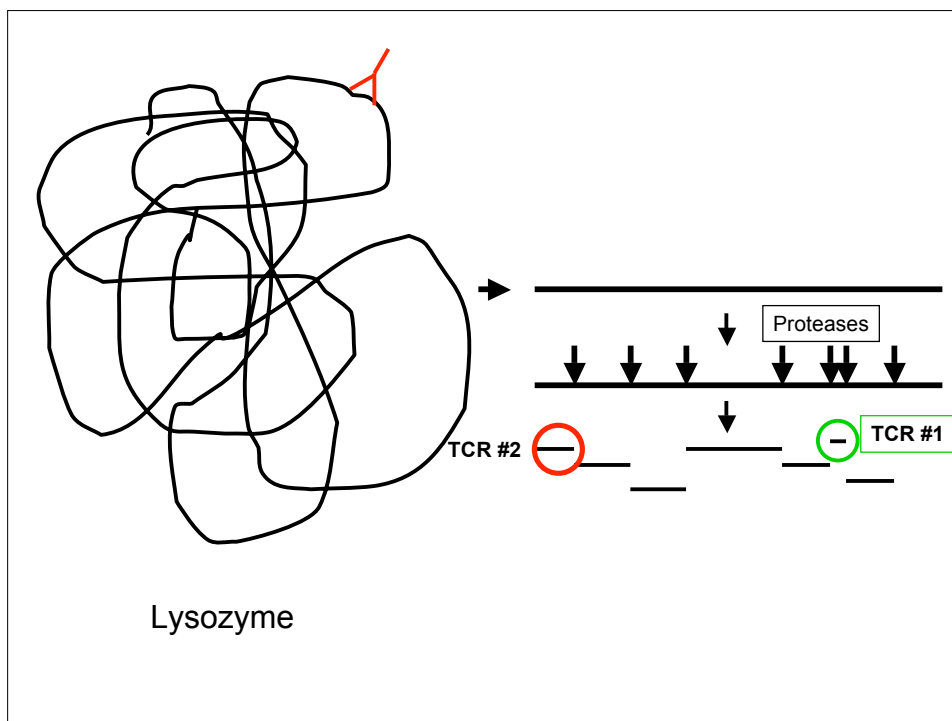
## Antigen-antibody Interaction



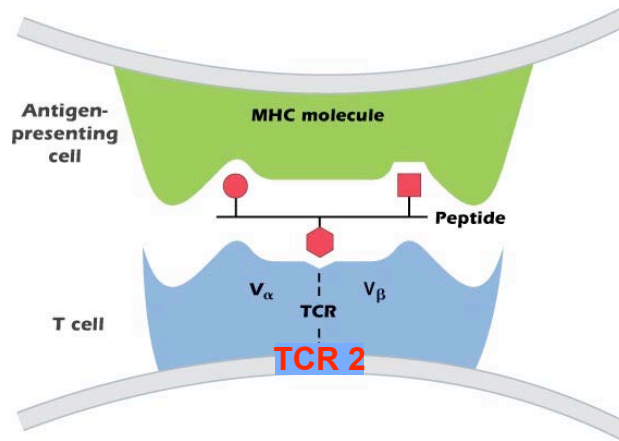
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# Review of Differences in T and B Cells

- B cells
  - Recognize native protein antigens in solution or on cell surfaces
  - Secreted antibody is effector molecule
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- T cells
  - Recognize peptides from degraded antigens
  - Peptides are displayed on cell surfaces in association with specialized proteins (MHC)



## 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

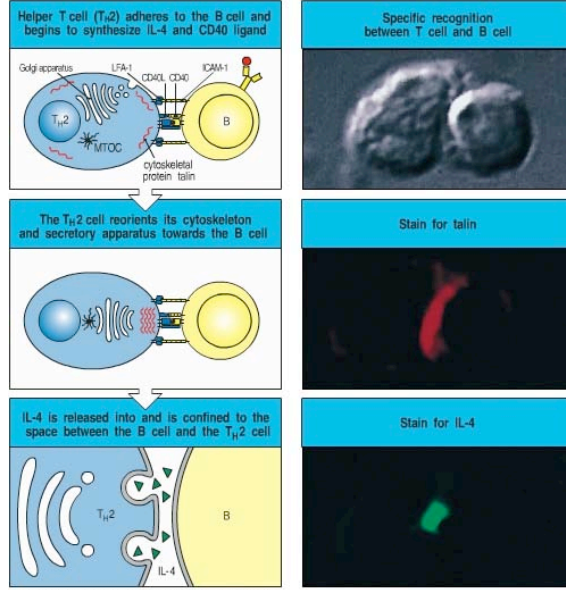


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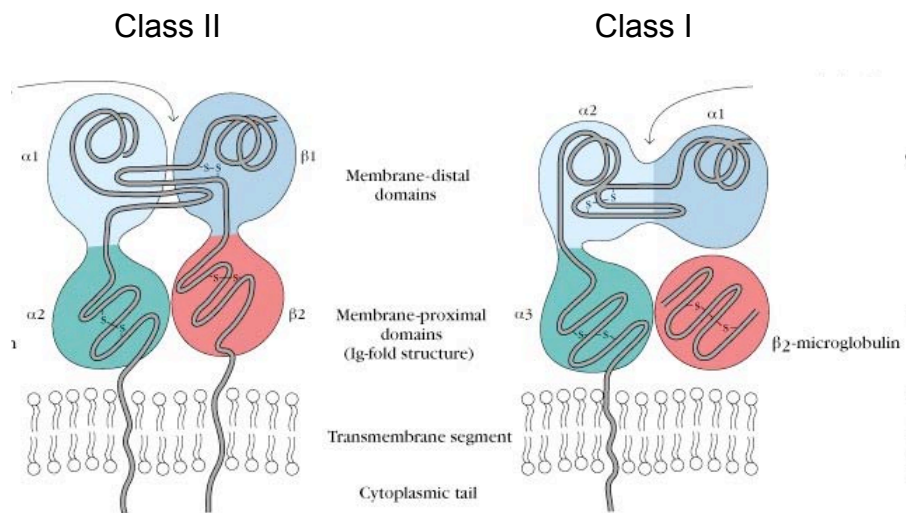
## MHC Class II

- 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

# Helper CD4 T cells



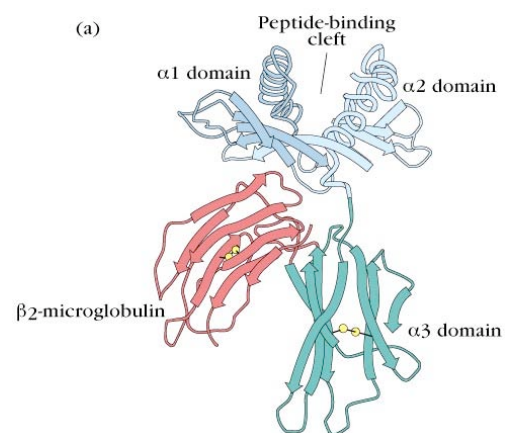
# MHC



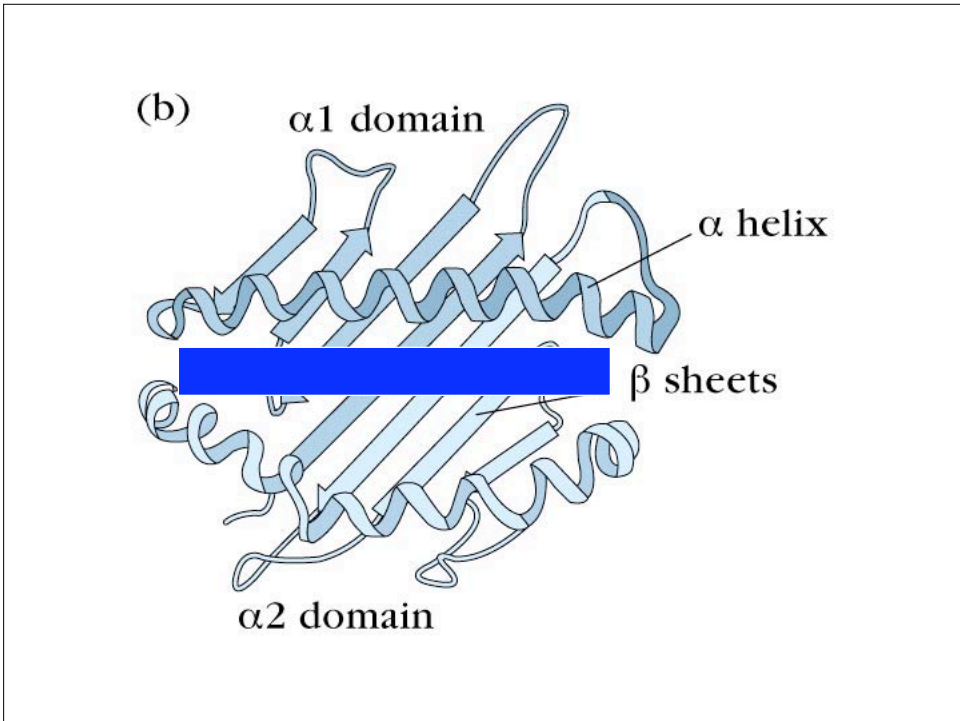
## Class I and Class II MHC Molecules

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

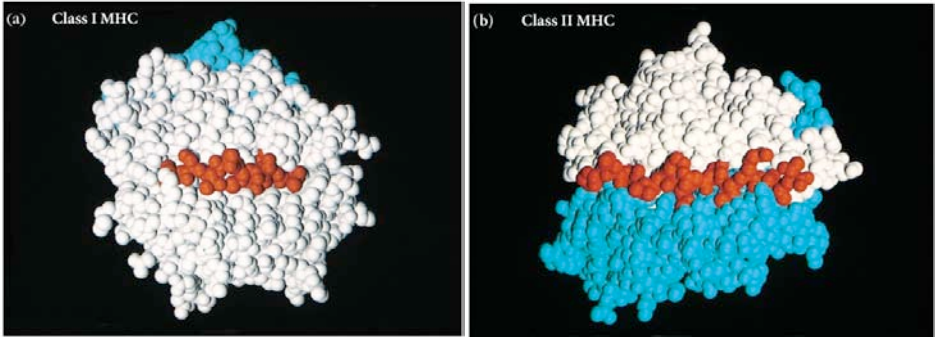
## 3-D Structure of Human Class I HLA Molecule

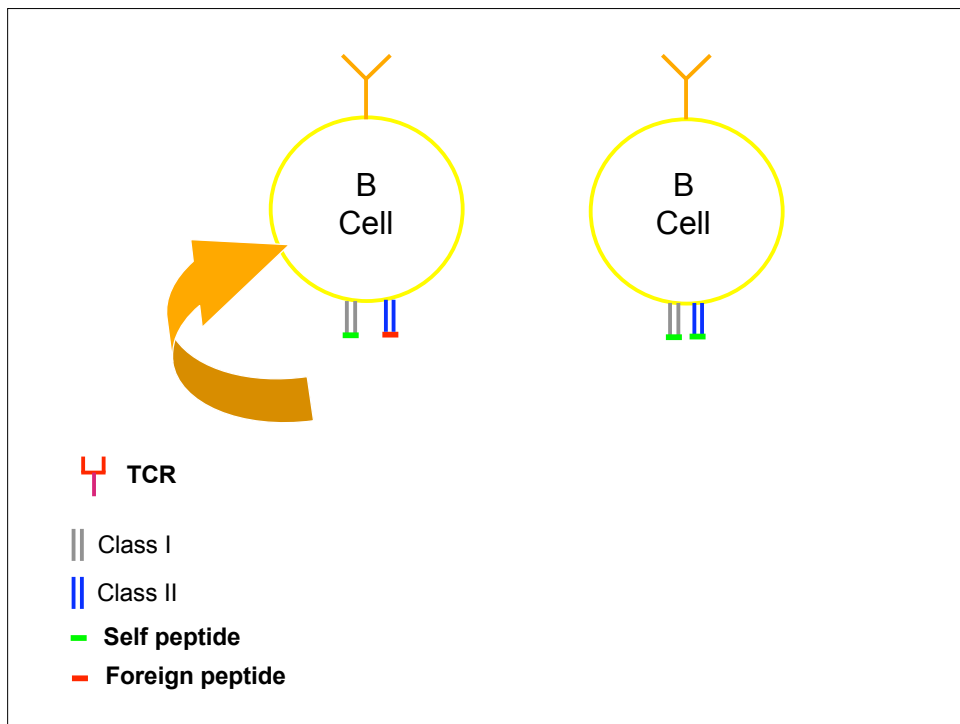
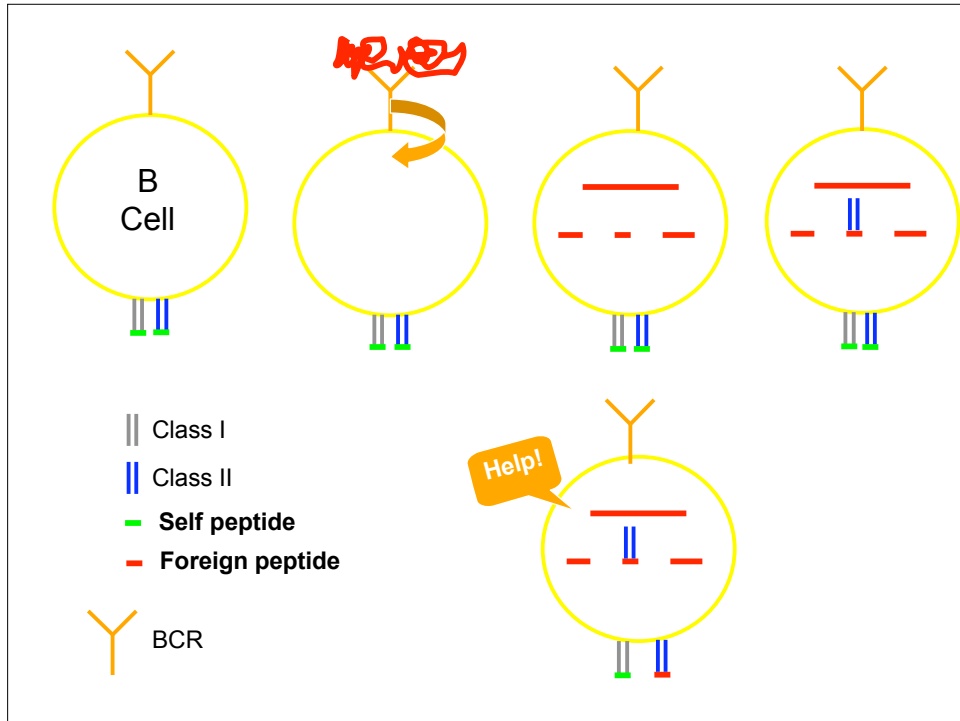


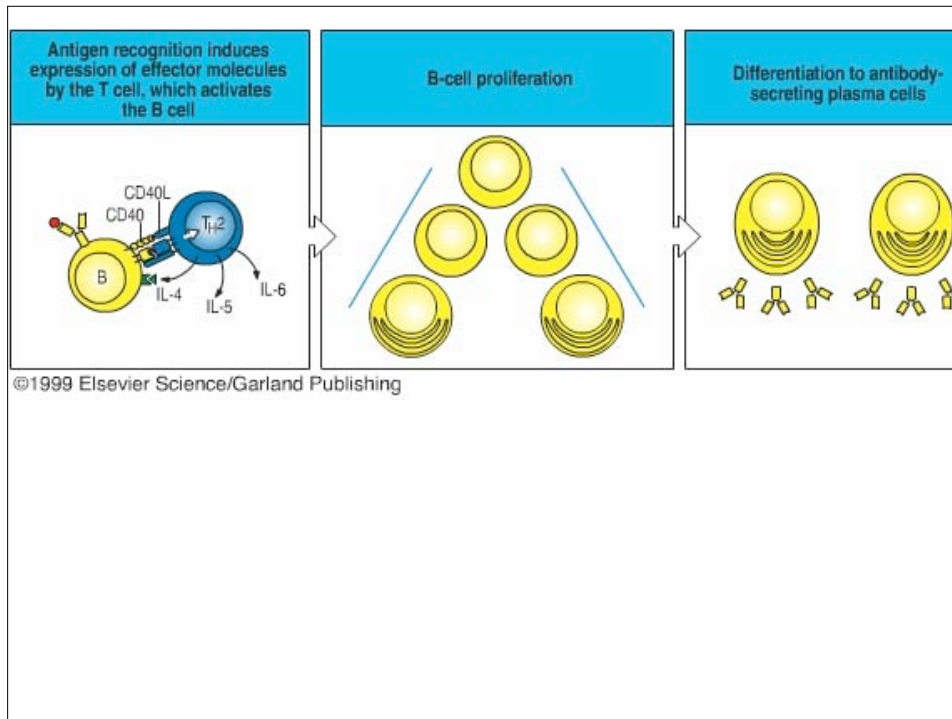




# Peptides in the MHC groove



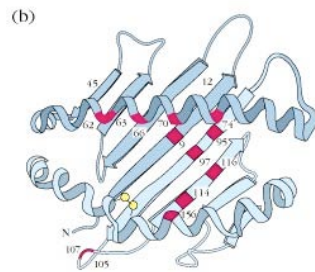
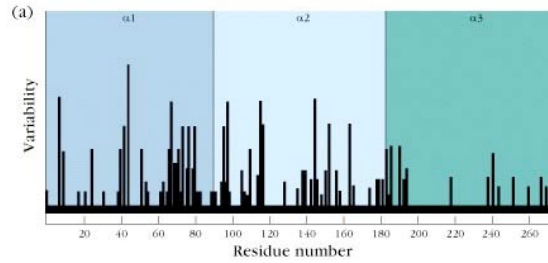




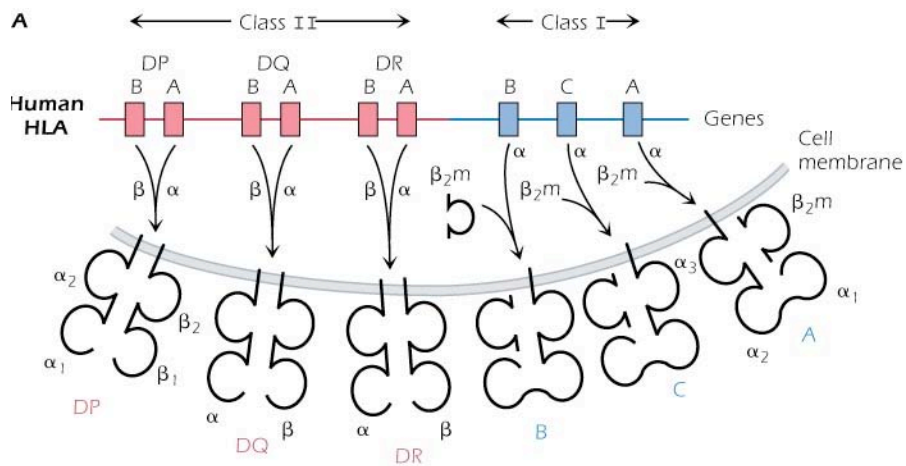
## MHC Polymorphisms

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

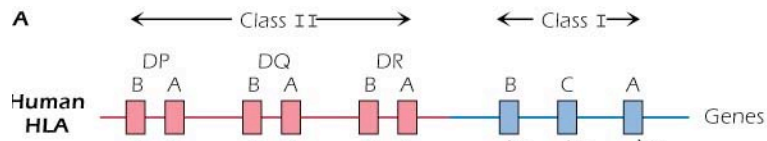
# MHC Polymorphisms



# 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
- No gene rearrangements with the MHC!

## 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?

