

Lecture 2

## ANTIGENS, ANTIGEN RECOGNITION AND PRESENTATION

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## Antigens

Definition:

- A molecule, or part of a molecule that can be specifically recognized by the immune system

Antigens are recognized by the mechanisms of adaptive immunity:

- Receptors on T and B cells
- Immunoglobulins

## The structure of antigens

- Proteins, peptide chains, carbohydrates, glycoproteins, synthetic molecules, etc..
- Receptors recognize the structure of molecules:
  - Aminoacid sequence,
  - 3D conformation,
  - Type of aa., charge,
  - Modifications and additional residues.

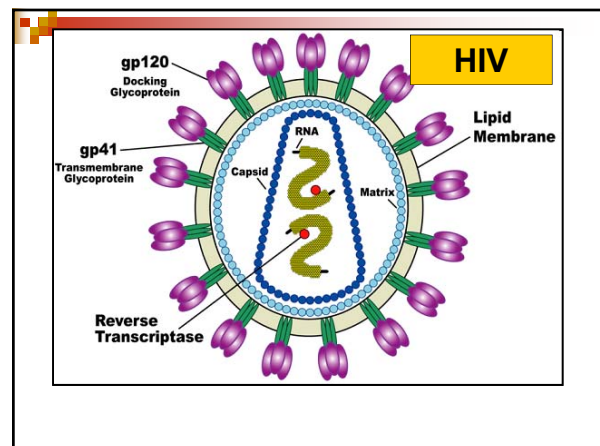
## Immunogenicity:

The ability of a molecule to elicit a specific immune response

## Epitopes – the antigenic

- Cytotoxic T cells via MHC-I: 8-10 aa. peptides
- Helper T cells via MHC class II: 12-20 aa. peptides
- B cells via BCR: folded 3D conf. of the protein

- One antigen may contain more than one epitope, or repeat epitopes.
- The diversity of epitopes on a certain antigen is responsible for the polyclonal immune response.
- Different receptors on cells recognize different forms of the antigens.



## Haptens

- Small particles, not immunogenic by themselves.
- Need a carrier protein to be recognized.
- Antibodies may be produced against the hapten itself or the hapten-carrier conjugate (neoantigen).
- Significance of haptens:
  - Immunity to drugs
  - Drug-induced autoimmune diseases
  - Contact hypersensitivity, delayed type hypersensitivity

1 structure

## Antigen Presentation

Uptake  
Processing  
Introduction  
of antigens to effector cells  
**Stimulation**  
Antigen Presenting Cells (APCs)

3 presentation

## Modes of antigen presentation

In terms of involved mechanisms:

- Via MHC class I
- Via MHC class II
- Cross presentation
- Recognition of antigens by B-cell receptors.

In terms of antigen source:

- Presentation of intrinsic (intracellular) antigens
- Presentation of extrinsic (extracellular) antigens

3 presentation

## Major histocompatibility complex (MHC)

- Known in human as Human Leukocyte Antigen (HLA)
- Transmembrane complex of several protein chains and domains
- Encoded by genes on the chromosome 6.
- Responsible for antigen presentation by Antigen Presenting Cells (APCs)
- Three classes:
  - MHC class I ≡ HLA -A, -B, -C, -E ...
  - MHC class II ≡ HLA-DP, -DQ, -DR
  - MHC class III ≡ complement C2, C4, factor B, TNF, HSPs

2 MHC

## MHC genes

HLA class I region loci

HLA-A, HLA-B, HLA-C, HLA-E, HLA-F, HLA-G, HLA-H, HLA-I, HLA-J, HLA-K, HLA-L, HLA-M, HLA-N, HLA-O, HLA-P, HLA-Q, HLA-R, HLA-S, HLA-T, HLA-U, HLA-V, HLA-W, HLA-X, HLA-Y, HLA-Z

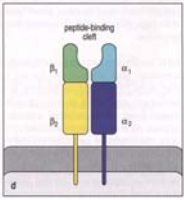
## MHC class I

- Products of the A,B,C,E,F,G loci
- Transmembrane complex which consists of:
  - Three  $\alpha$  domains 1-3
  - $\beta$ 2-microglobulin
  - Transmembrane region
  - Cytoplasmic tail
- Peptide binding groove

2 MHC

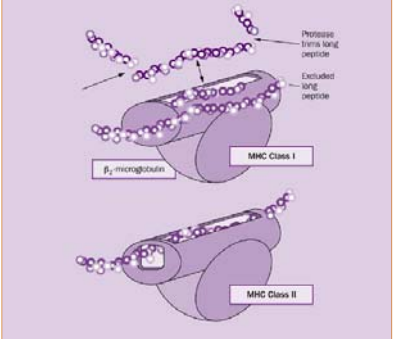
## MHC class II

- Products of the gene are: DP, DQ, and DR in humans
- Heteridimer:
  - $\alpha$  chain ( $\alpha 1$  and  $\alpha 2$  domains + c-tail)
  - $\beta$  chain ( $\beta 1$  and  $\beta 2$  domains + c-tail)
- Peptide binding groove

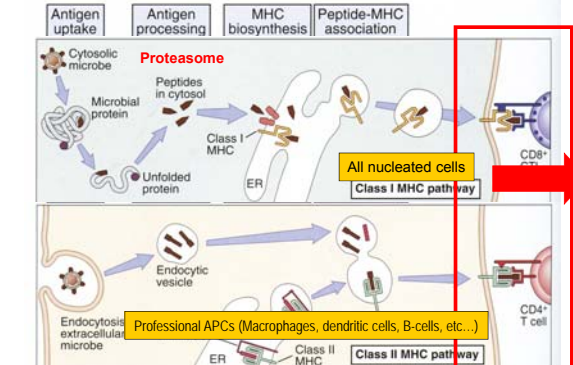


2 MHC

## PEPTIDE BINDING BY MHC CLASS I AND CLASS II MOLECULES

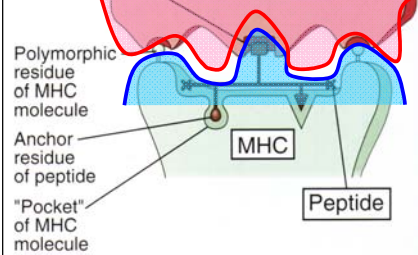


## Pathways of antigen processing



## MHC – TCR interaction

Good fit → better presentation  
 Poor fit → worse presentation

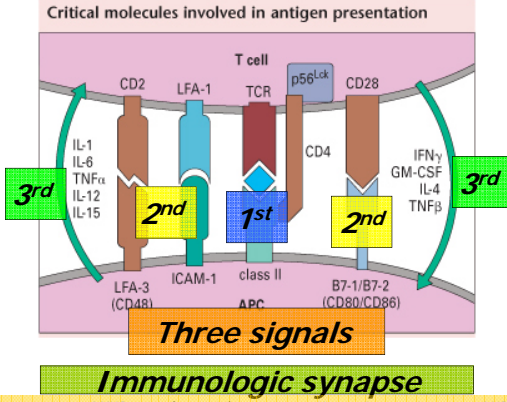


3 presentation

Disease	HLA-Specificity/Gene	Approximate Relative Risk
Autoimmune chronic hepatitis	HLA-DR3	14
Addison's Disease	HLA-DR3	9
Ankylosing Spondylitis	HLA-B27	100
Celiac Disease	HLA-DQ2	30
Diabetes Mellitus, type 1	HLA-DQ6	10
Graves Disease	HLA-DR3	4
Hemochromatosis	HLA-HFE (A3)	-
Multiple sclerosis	HLA-DR3	10
Narcolepsy	HLA-DR15/DQB1*0602	100
Postinfectious arthritides	HLA-B27	10-20
Rheumatoid arthritides	HLA-DR1, 4	7
Psoriasis vulgaris	HLA-Cw6	5
Reiter's Syndrome	HLA-B27	35

3 presentation

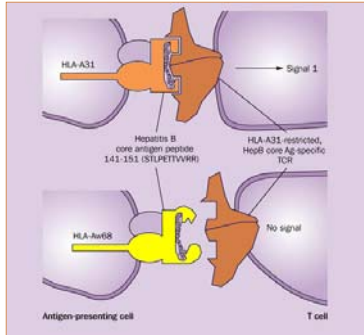
## Critical molecules involved in antigen presentation



3 presentation

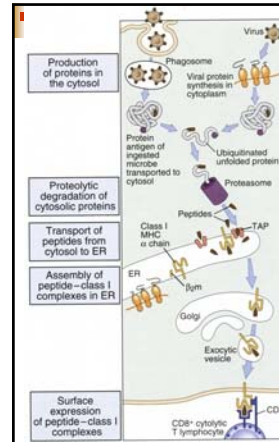
**MHC RESTRICTION**

- A T cell recognizes a peptide antigen only when it is bound to a particular MHC molecule
- Role in the T cell recruitment in the thymus



**Cross-presentation**

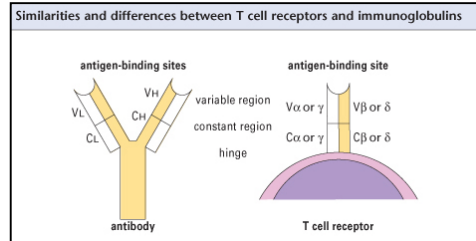
- Extracellular antigens are presented by MHC class I
- Essential role in antitumor immunity
- Role in immunity to infectious pathogens:
  - E.g. vaccines with viral antigens elicit cellular response



**T-cell Receptor (TCR)**

- A membrane receptor for antigens presented by APCs
- Heterodimer which consists of **alpha and beta** or **gamma and delta** chains linked to each other by SH-SH bridge
- **Complementarity determining regions (CDRs):** portions of the alpha and beta chains fold into a structure that resembles the antigen-binding portion (Fab) of an antibody, they are responsible for antigen binding
- **CD3 complex:** polypeptide invariant chains (gamma, delta, epsilon, and zeta) associated with antigen binding domain and capable of transmitting a signal into the cell upon binding to an antigen

4 recognition



4 recognition

Read more about the MHC class II-mediated antigen presentation!

**B-cell receptor**

- Is a surface IgM on mature B lymphocytes
- Recognizes folded proteins or glycoproteins (3D structure).
- Each cell recognizes one epitope, the activation of this receptor induces the internalization of the receptor degradation and the antigen presentation by MHC-II to helper T cells

1. Introduction 2. MHC 3. presentation 4. recognition 5. Subpopulations 6. Index

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## T-dependent and T-independent antigens

- TD:
  - Proteins
  - B cells require the help of T cells
  - Proteins are presented on MHC-II of APC, induced Th cells activate B cells that recognized the antigen by BCR
  - The help from T cells includes: binding of costimulatory molecules, sending cytokine signals, inducing class switching by CD40-CD40L signals.

- TI:
  - Polysaccharides, lipids, nucleic acids (do not undergo processing by APC)
  - B cells are stimulated directly by the antigen.
  - Co-stimulatory signal from C3d is required to activate the B cell.
  - Induce low affinity IgM, rarely lead to class switching and memory.

## SUPERANTIGENS

- Molecules capable of binding MHC and TCR in an atypical non-specific manner.
- Activate T cells independently from their specificity
- Provide to massive clone-nondependent activation of lymphocytes,
- Examples:
  - staphylococcal enterotoxins (SEB) responsible for some types of acute food poisoning,
  - toxic shock syndrome toxin-1 (TSST-1) responsible for tampon sepsis-induced shock
  - exfoliative dermatitis toxin.

5 superantigens