

Objectives

By the end of this lecture, the student will able to:

1- Define terms of immunogen, Antigen, Epitopes and Haptens

2- What are the factors that influencing immunogenicity

3- Types of antigens

What does immunogen mean?

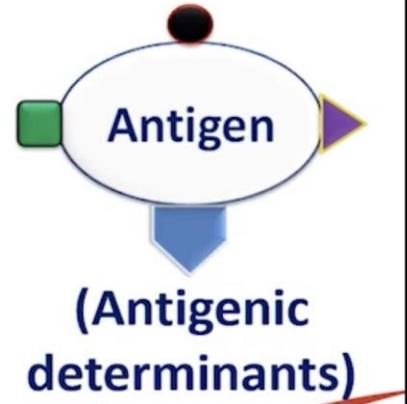
Any foreign substance that induce a specific immune response (humoral or cellular). All immunogens are antigens but not antigens are immunogens

What does antigen mean?

Any substance that reacts a specific with immune response

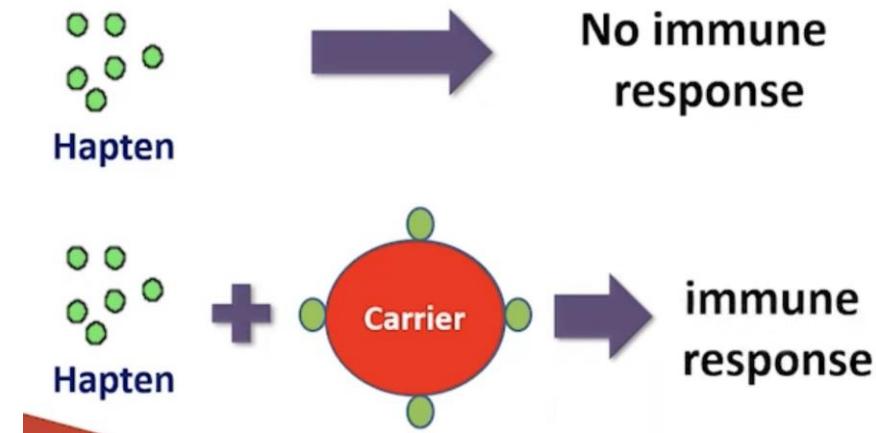
3) Epitope

In the large molecule of antigen, only small parts of the molecule (epitope) can interact with the immune system

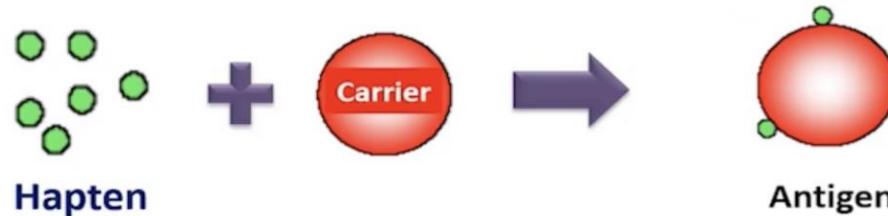


4) Hapten

Low molecular weight

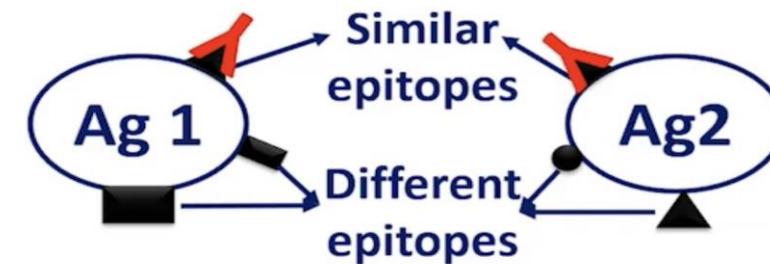


4) Hapten



This is a low molecular weight substance which is incapable of inducing immune response alone but when coupled with a carrier molecule (protein) it can act as an antigen

5) Heterophil Ag



- Antigens that share one or more similar epitopes.

Answer Exercise 1

Items	Antigen	Immunogen	Hapten
Foreigners	+	+	+
Immunogenicity	+	+	-
Reactivity	+	-	-
Example	Any Ag	Food protein	Penicillin



Factors influencing immunogenicity

1- Foreign to the body (non-self)

2- Molecular size (larger molecules are stronger antigenic)

3- Chemical structure (structure =complexity) more complex more antigenic

3- Chemical nature

Exotoxin

Which is more
antigenic?

Endotoxin

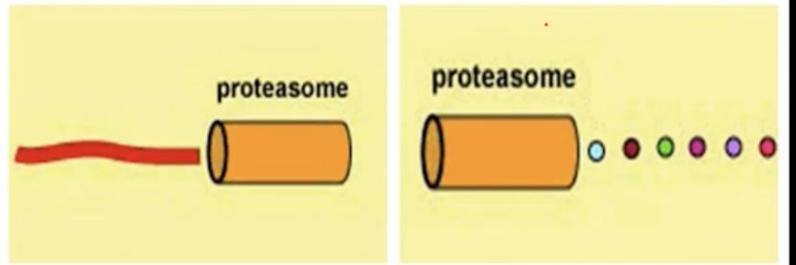
3- Chemical nature

Composition



4- Degradability

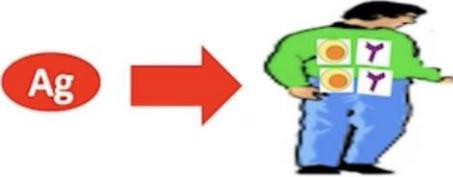
4- Degradability



5-Method of administration

- Dose (optimum dose)
- Method
- Route of administration (S.C or IM or Orally but not by IV =dilution)

6- Adjuvants (to help)



Ag + Adjuvants

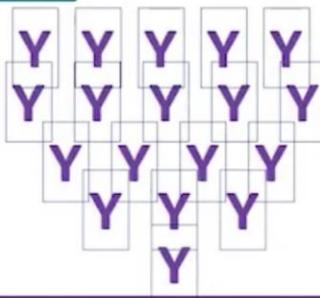


There are substances that can enhance the immunogenicity of antigen without altering their chemical nature

6- Adjuvants (to help)

Y Y Y
Y Y
Y

Vaccine without
adjuvants



Vaccine with
adjuvants

6- Adjuvants (to help)

Aluminum hydroxide and
Aluminum phosphate



6- Adjuvants (to help)

Toxoid of diphtheria

➤ Toxoid (alone)



1 year

➤ Toxoid
+
Aluminum
hydroxide



10 years

The main function of adjuvant is slow releasing of antigen at the site of injection.

7- Individual variation

Why most vaccines are given SC or I.M but never by IV?

Types of antigens

- Bacterial Ags like O,H,K,pili
- Viral Ags Capsid and envelope proteins
- Fungal Ag like cell wall
- ABO system (self Ags) and RH Ag
- Major histocompatibility complexes (MHC) or Human Leukocyte antigen (HLA)

Histocompatibility complex: a region of multiple loci that play major roles in determining whether transplanted tissue is with **histocompatibility** or **histoincompatibility**

- Major vs minor

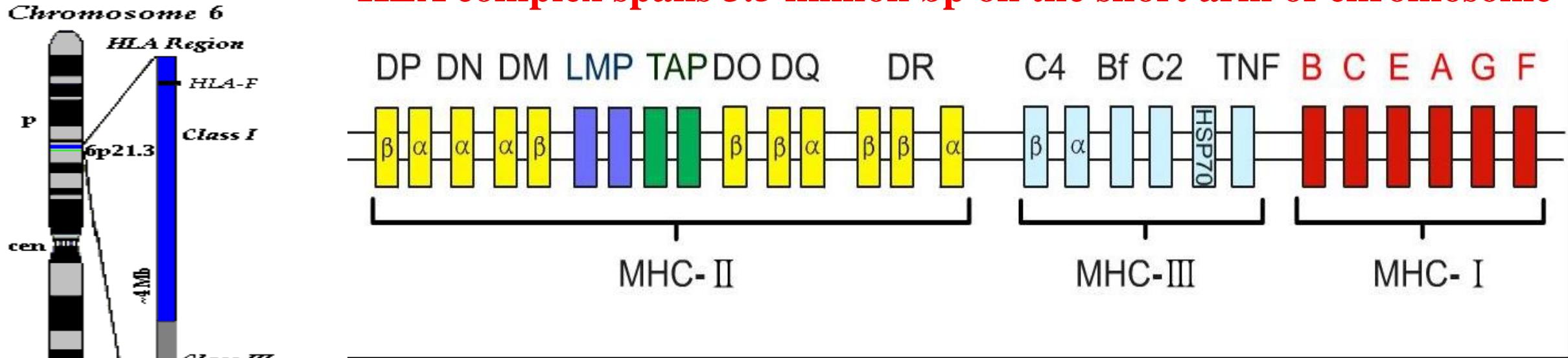
Major Histocompatibility Complex, MHC rapid graft rejection

Minor Histocompatibility complex, mHC slow graft rejection

human leukocyte antigen (HLA), MHC antigens in human

H 2 MHC antigen in mice

HLA complex spans 3.5 million bp on the short arm of chromosome 6

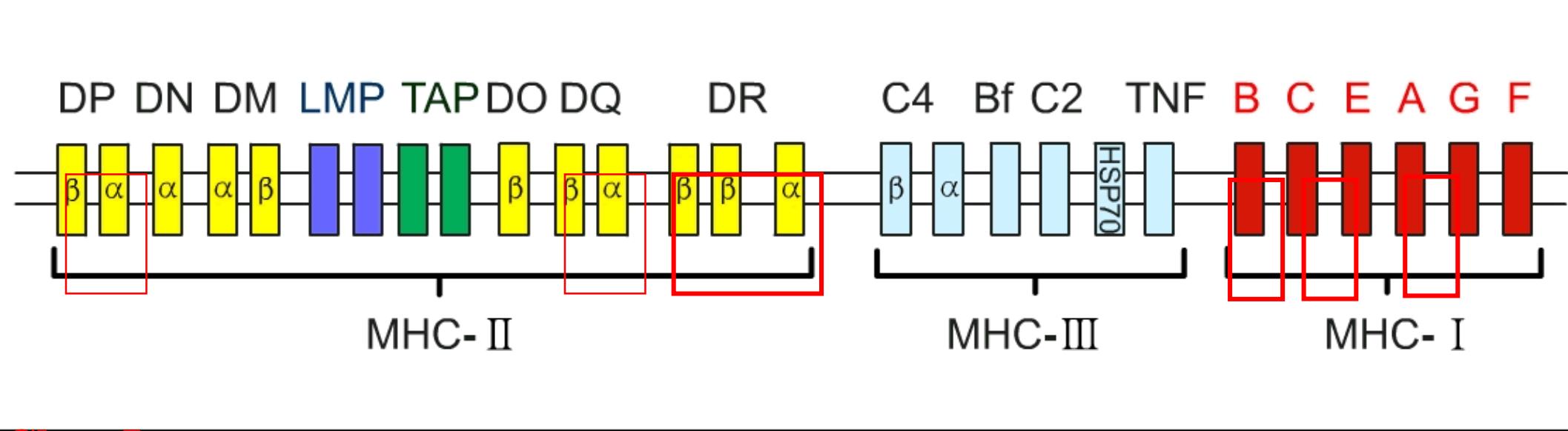


Gene structure of MHC on short arm of chromosome 6

This region of DNA contains over 100 genes (cluster of genes) and highly pleomorphic. The physiological function of these molecules is to display (present) peptides derived from protein antigens to T cells. Codominant expression: Both paternal alleles are expressed to increase number of different HLA molecules that can present peptides to T cells.

Functions of MHC

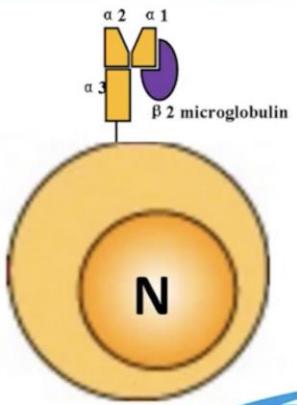
- 1- Antigen presentation
- 2- T cells activation
- 3- Organ transplantation & graft rejection
- 4- Paternity testing and forensic investigations
- 5- Complement synthesis
- 6- Disease association



- **Class I**
 - HLA-A,-B, and -C loci
 - encode the heavy chain (α chain) of HLA class I molecule
- **Class II**
 - HLA-DP,-DQ, and DR
 - Each has loci A and B , encode the α chain and β chain of HLA class II molecule, respectively
- **Class III** Various secreted proteins with immune functions in inflammation :TNF,C2,C4...
 - Other non classical genes and molecules:HLA-DM,CD1...

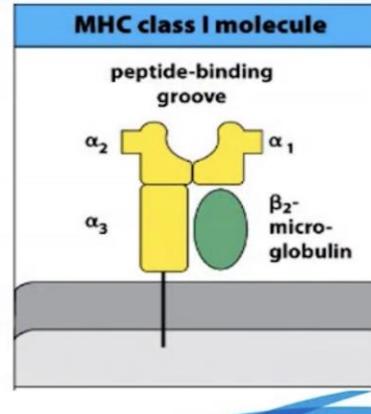
2) MHC-I

1
All Nucleated cells



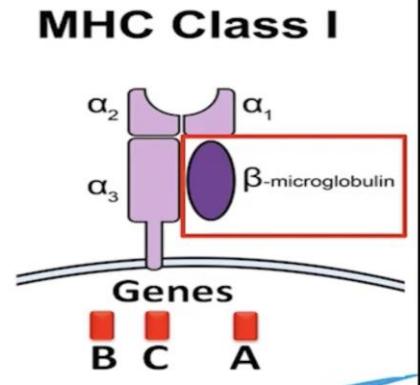
3) MHC I structure

2
 $\alpha(1,2,3)$ molecule & β2 Microglobulin



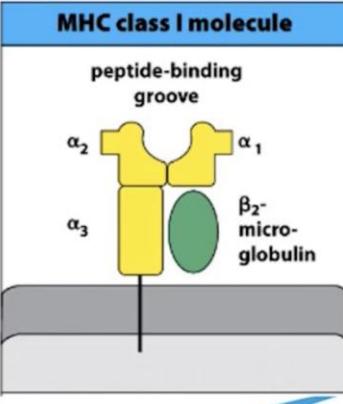
3) MHC I structure

3
Genes A,B,C (6)
β2 Microglobulin (15)



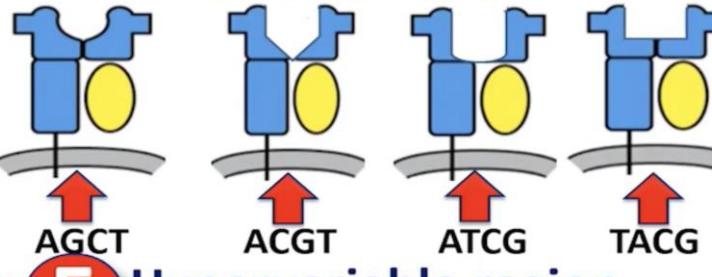
3) MHC I structure

4
The Ag binding site between α_1 & α_2 Hypervariable region



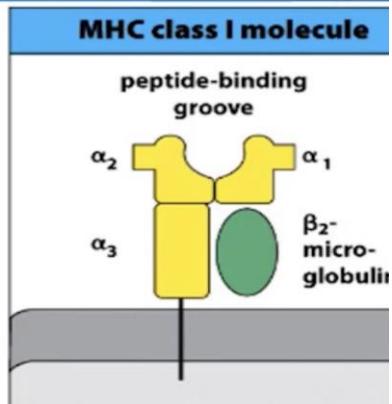
3) MHC I structure

Each molecule has a unique groove that differ from other

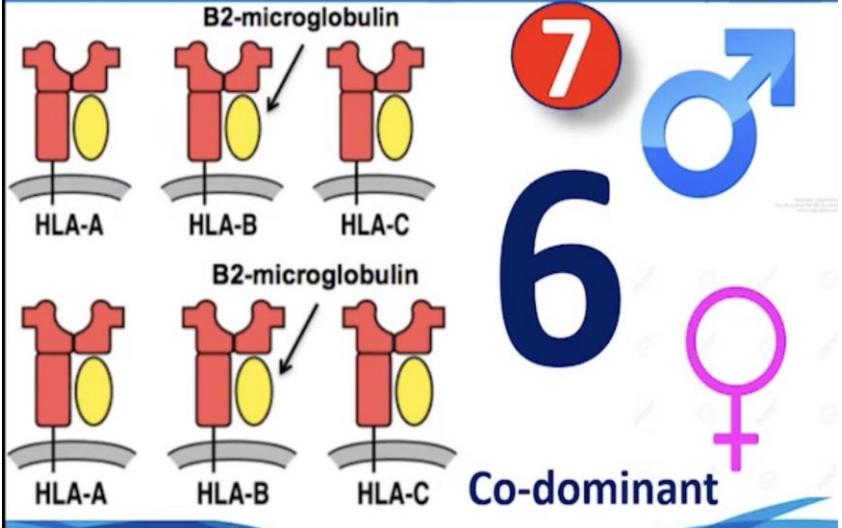


3) MHC I structure

6
 α_3 is constant !!

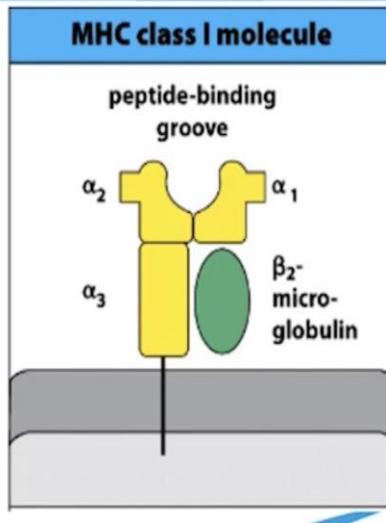


3) MHC I structure



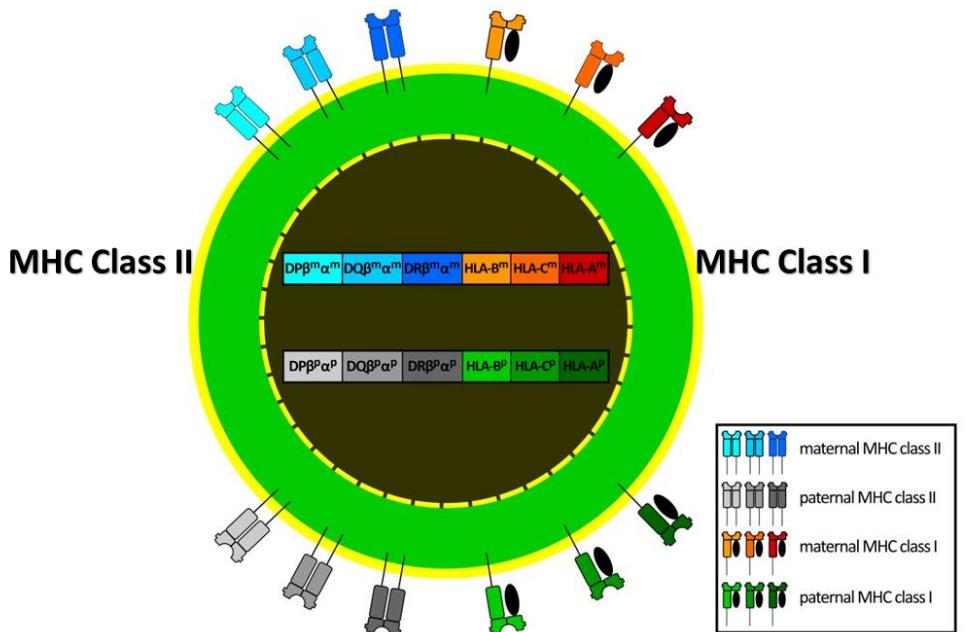
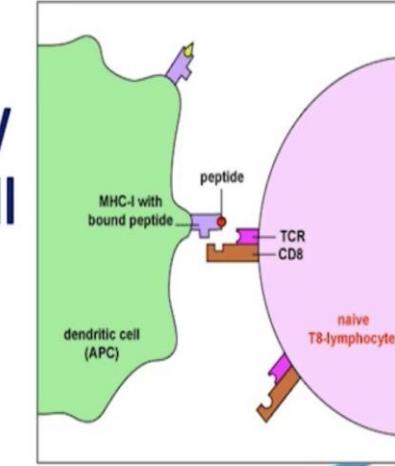
3) MHC I structure

8
Binds only with endogenous protein



3) MHC I structure

9
Recognized by T cytotoxic cell (MHC-I Restriction)



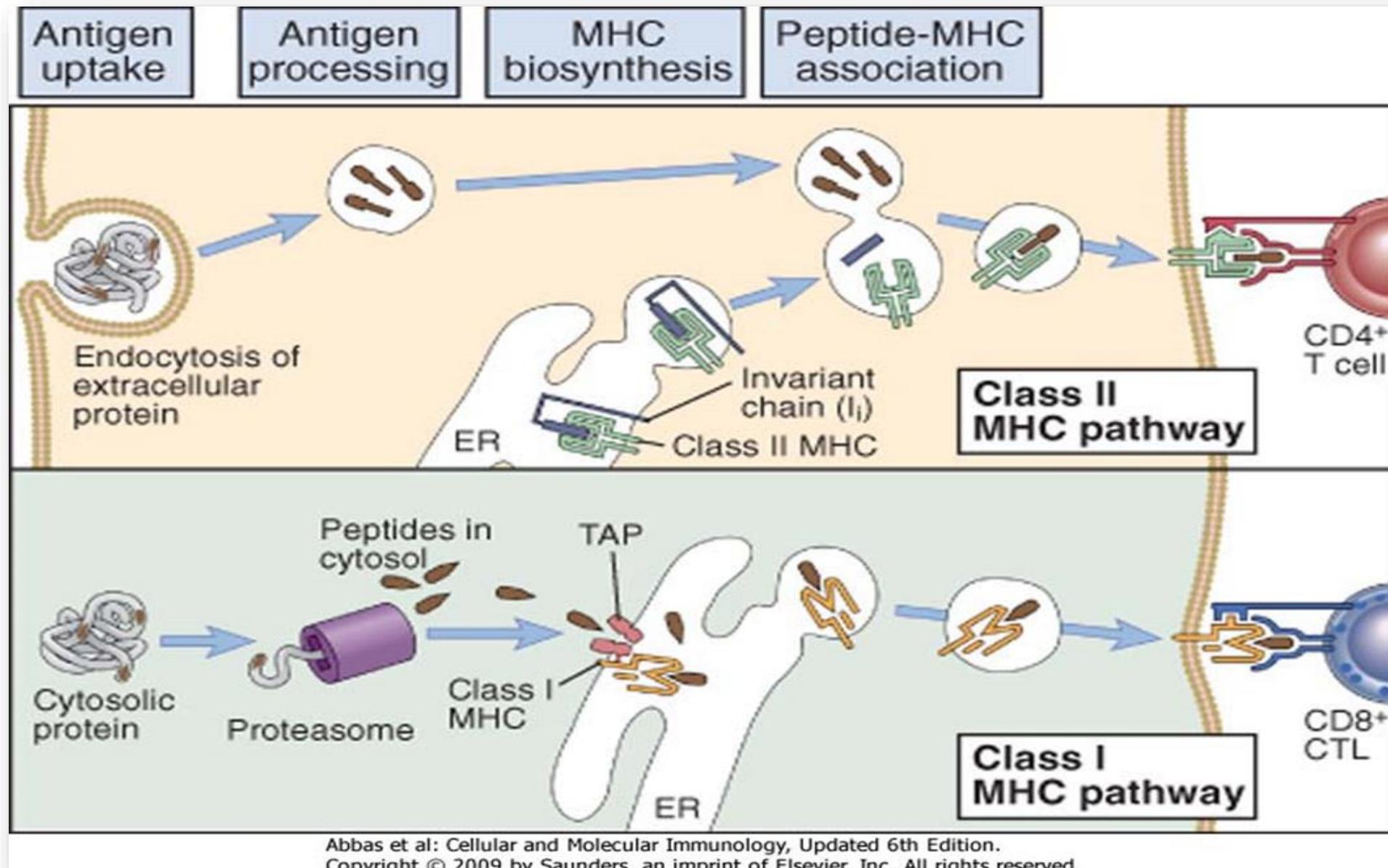
MHC nomenclature

HLA - A * 02

HLA prefix Hyphen gene separator allele number

Viruses inhibit infected host cells to express MHC-I

- MHC class I and II pathways

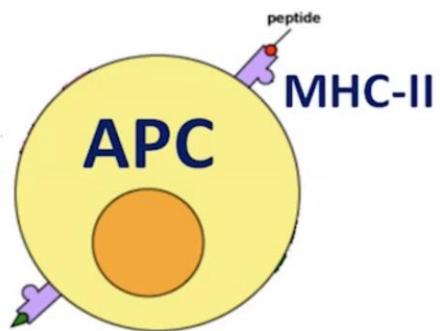


- MHC class 2

2) MHC-II

1

APC

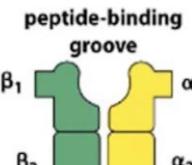


5) MHC II structure

2

Two polypeptide
 α & β

MHC class II molecule



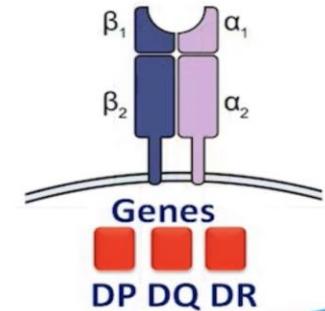
5) MHC II structure

3

Genes

DP,DQ,DR

MHC Class II



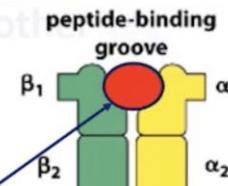
5) MHC II structure

4

The Ag binding site between
 α_1 β_1

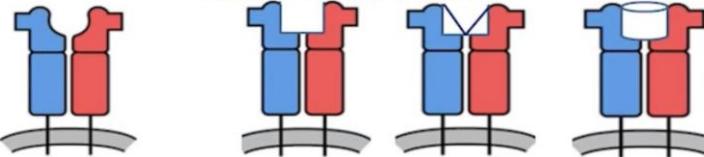
α_1 β_1

MHC class II molecule



3) MHC I structure

Each molecule has a unique groove that differ from other



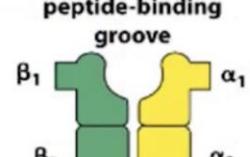
5 Hypervariable region

5) MHC II structure

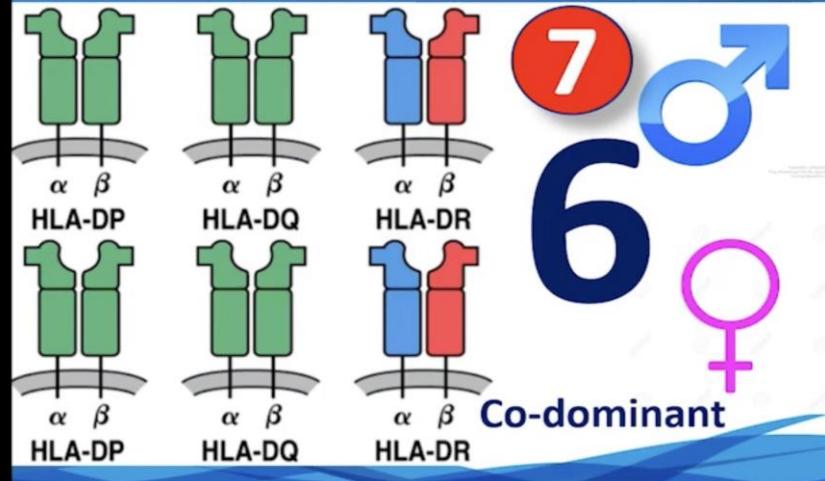
6

β_2 is constant
!!!!

MHC class II molecule



5) MHC II structure



5) MHC II structure

8
Binds only with exogenous protein

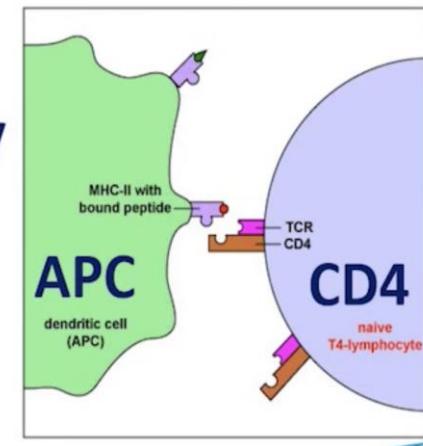
MHC class II molecule

peptide-binding groove

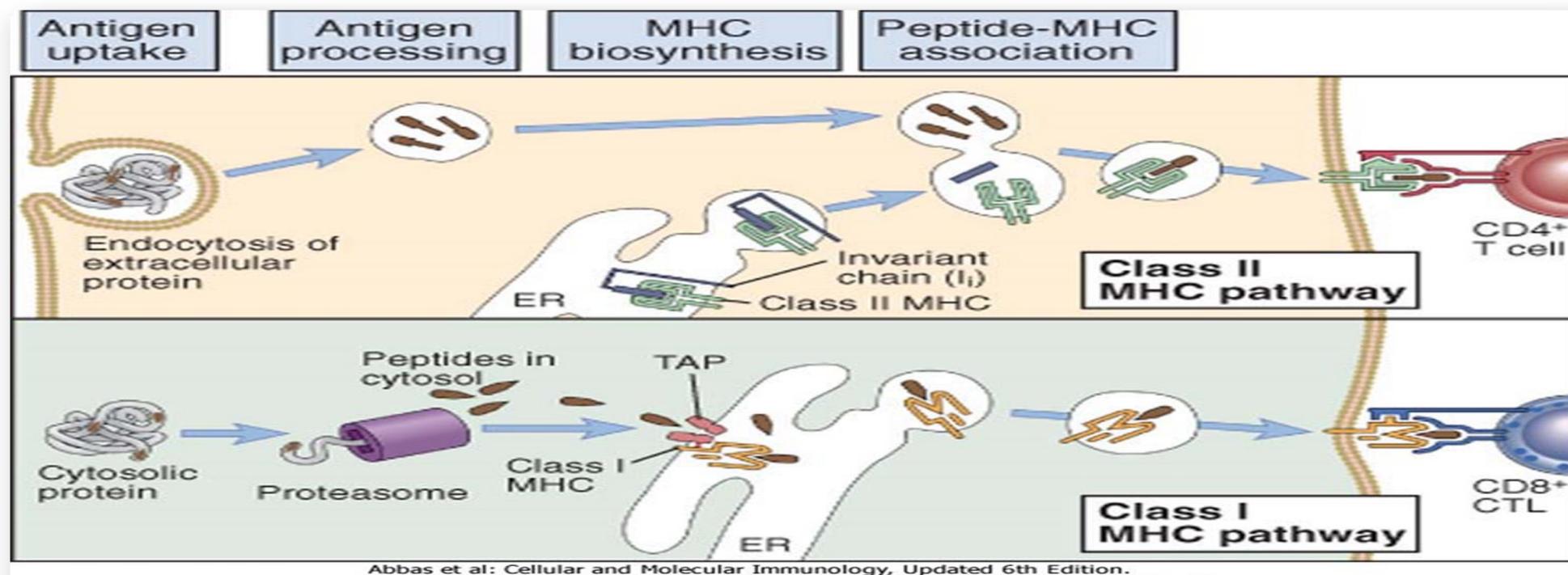
β_1 α_1
 β_2 α_2

5) MHC II structure

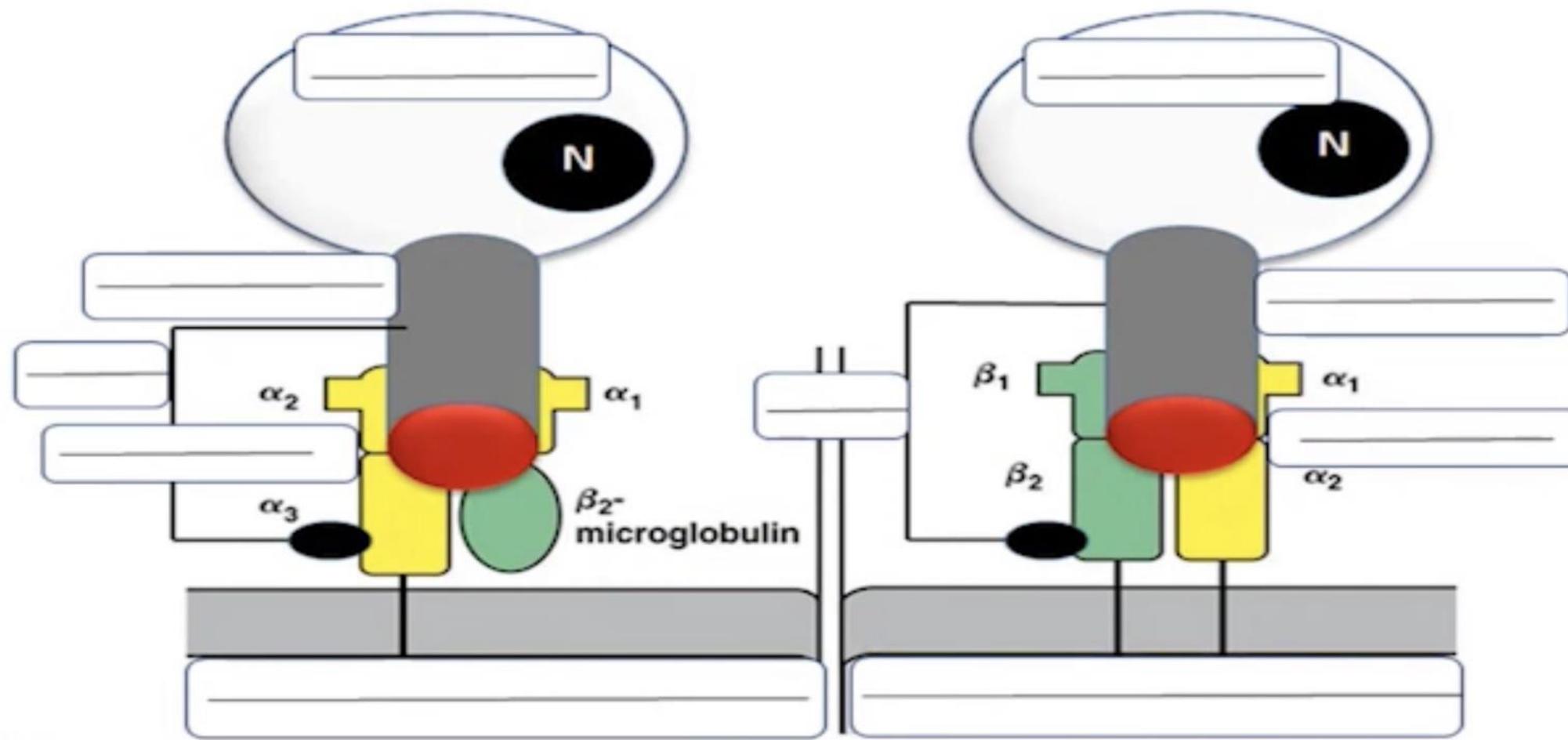
9
Recognized by T-helper cells (MHC-II restriction)



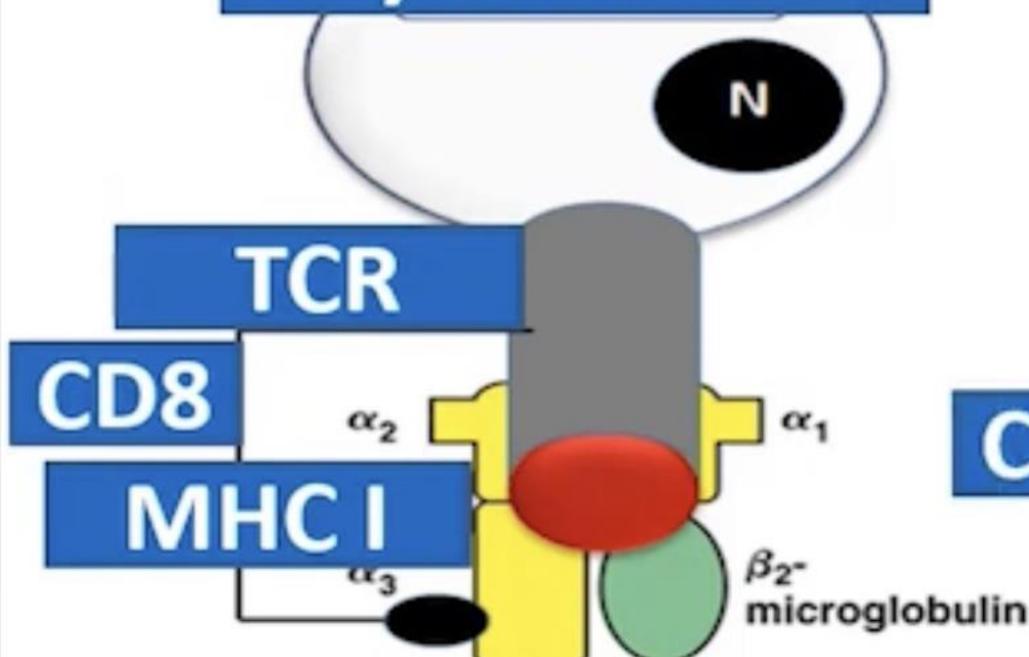
- MHC class II pathway



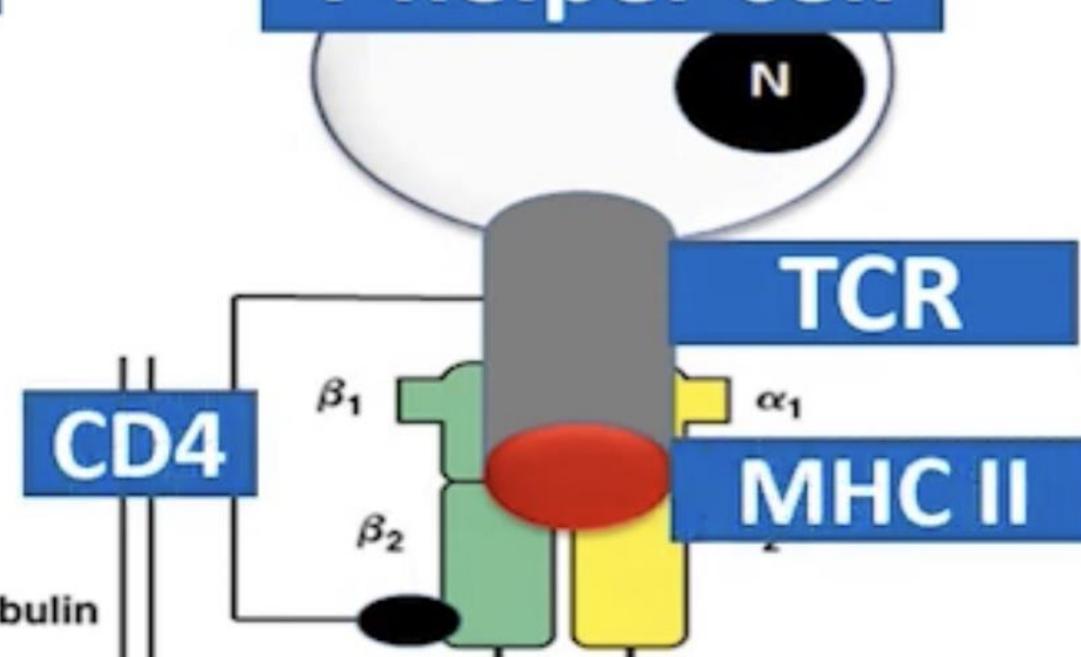
Label the following places



T cytotoxic cell



T helper cell



Our cells

APC

Items	MHCI	MHCII
1) Site		
2) Structure		
3) Ag binding site		

Items	MHCI	MHCII
4) Ag expression		
5) Recognized by		
6) Result		

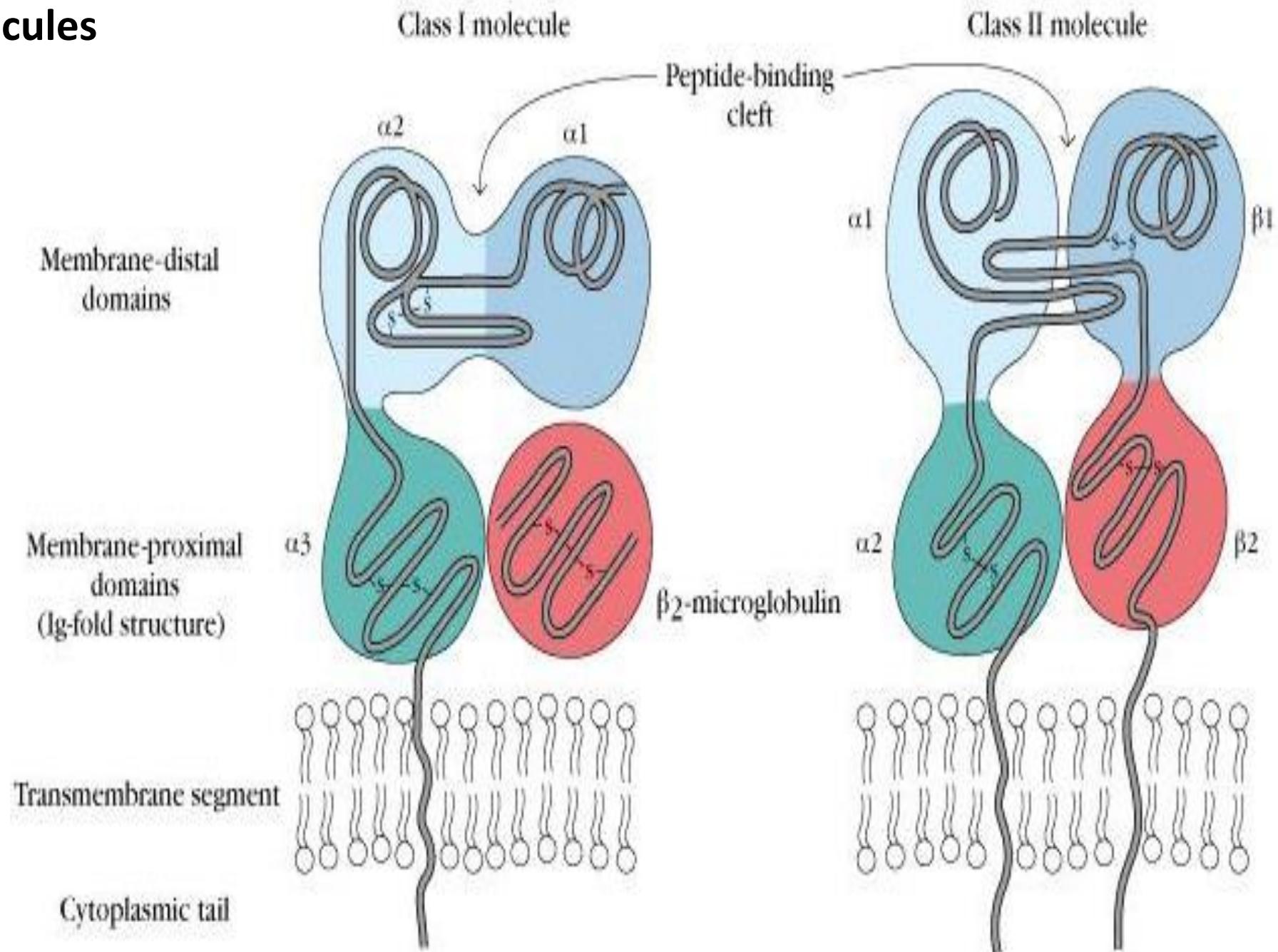


What will happen if a virus infects APC?

How immune system generates antibodies against viruses, while they will be killed by Cytotoxic T cells?

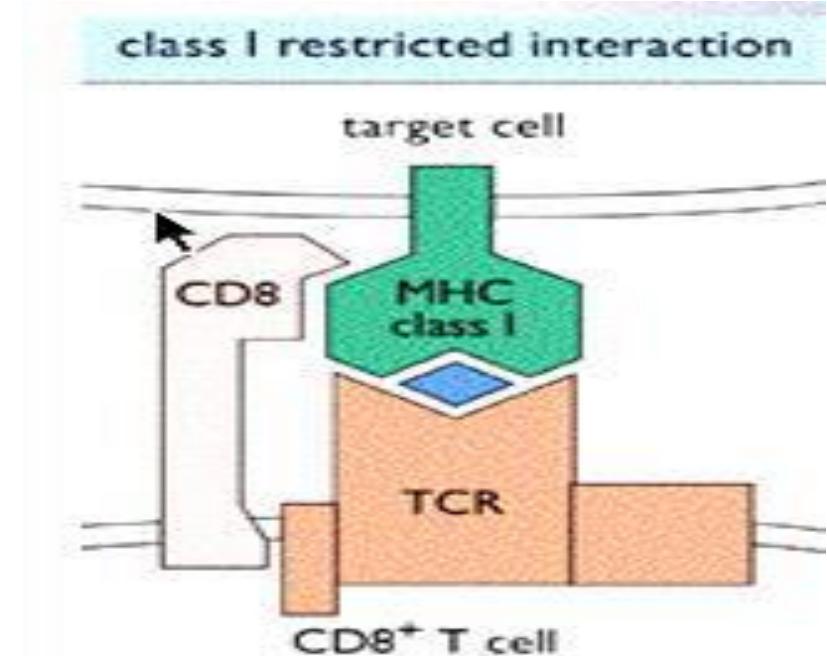
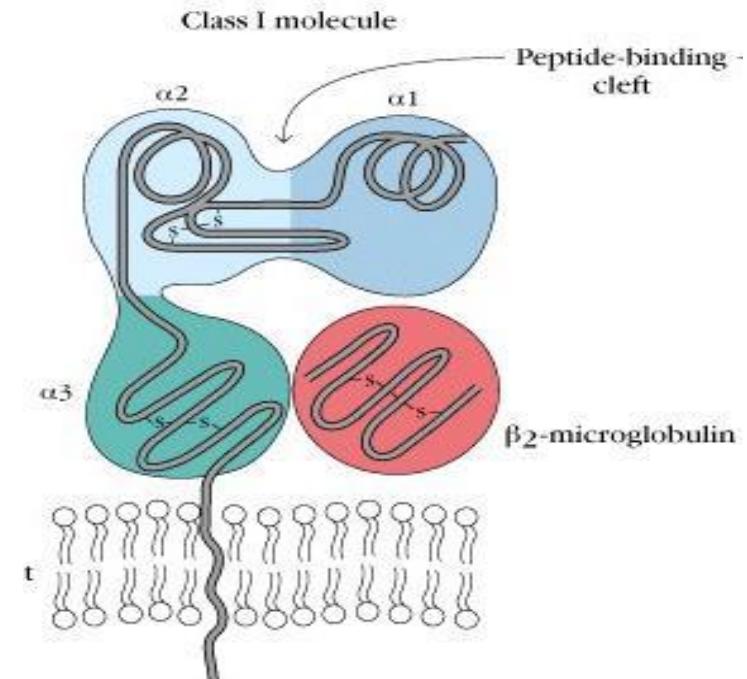
Discuss with your classmates, the importance of MHC.

Structure of MHC molecules



MHC class I Molecules

- α chain + β 2 microglobulin
 - α chain polymorphic, transmembrane
- α 1 and α 2 domains form **peptide binding cleft**
- α 3 interacts with **CD8 +ve** on T cells
 - β chain no polymorphism, one folded domain, stabilize class I molecules (gene on chromosome 15)
- Expressed on almost all nucleated cells
- Presentation of antigen (**endogenous**) to CD8 +ve T cells



How many different MHC classical class I proteins does each nucleated cell in a human heterozygous at the MHC locus express?

Six

Four

Two

Three

The alpha 3 domain In MHC-I contains a loop that serves as a binding site for what?

T cytotoxic cells (CD8)

T helper cells (CD4)

Macrophages

B cells

The characters of Hapten are

activate immune response alone

It is a foreign particle

Penicillin is example

It is a low molecular weight

Antigens

have low molecular weights of around

have one antigenic determinant

made up of many antigenic determinants

Usually made by lipids

A "foreign" molecule which can invoke the immune response is called

Hapten

Antigen

Adjuvant

Immunogen

What do APC's express on their surface?

MHC I

MHC I & MHC II

Antigen alone

MHCII

Cytotoxic T cells (CD8) recognizes?

Peptide antigen with MHC II molecules

Peptide antigen with MHC I molecules

Peptide antigen without MHC I

Peptide antigen outside MHC I

Cells that present peptides associated with class II MHC molecules to helper T cells are?

Macrophages

Dendritic cells

B cells

T cells

MHC class II restricted means

T helper cell binds to MHC I

T helper cell binds to MHC II

T Cytotoxic cell binds to MHC I

Peptide antigen outside MHC II

MHC class I restricted means

T helper cell binds to MHC I

T helper cell binds to MHC II

T Cytotoxic cell binds to MHC I

Peptide antigen outside MHC II