



MHC ANTIGENS

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DEFINITION

- **MHC antigens are cell surface protein molecules coded by genes located as a cluster on a part of gene complex called as 'Major Histocompatibility Complex'.**
- **Antigens of selfness**
- **responsible for cell/tissue/organ graft acceptance or rejection depending upon the compatibility of MHC antigens between donor and recipient (Tissue matching – MHC typing)**

NOMENCLATURE

Species	MHC
Human	HLA
Dogs	DLA
Bovines (cow)	BOLA
Swine	SLA
Equine	ELA
Chicken	B
Mouse	H-2/TLA
	LA=Leukocyte Antigen

FEATURES

- **MHC code for three types of antigens**
 - **Class I – present on all nucleated cells**
 - **Class II – present on APCs (Dendritic cells, Macrophages, B cells, other cells)**
 - **Class III – complement components and sex limited proteins**
- **MHC molecules are membrane-bound.**
- **major self antigens which an offspring acquires from both the parents; no two individuals have identical set of MHC antigens, except homozygous twins**
- **highly polymorphic; alleles for MHC genes are co-dominant**

FEATURES (continued)

- Although there is a high degree of polymorphism for a species, an individual has maximum of six different class I MHC products and only slightly more class II MHC products.
- MHC polymorphism is determined only in the germline.
- A processed antigenic peptide must associate with a MHC molecule, otherwise no immune response can occur (**MHC restriction**).
- Peptide from cytosol associates with class I MHC and is recognized by Tc cells.
- Peptide from vesicles associates with class II MHC and is recognized by Th cells.

FEATURES (continued)

- Recognition of processed antigenic peptide associated with a MHC molecule by T cells requires cell to cell contact.
- Each MHC molecule has only one binding site, called as 'agerotope', which can bind to different peptides, but only one at a time.
- Because each MHC molecule can bind many different peptides, binding is termed **degenerate**
- There are no recombinational mechanisms for generating diversity of agerotope
- Cytokines (especially interferon- γ) increase level of expression of MHC

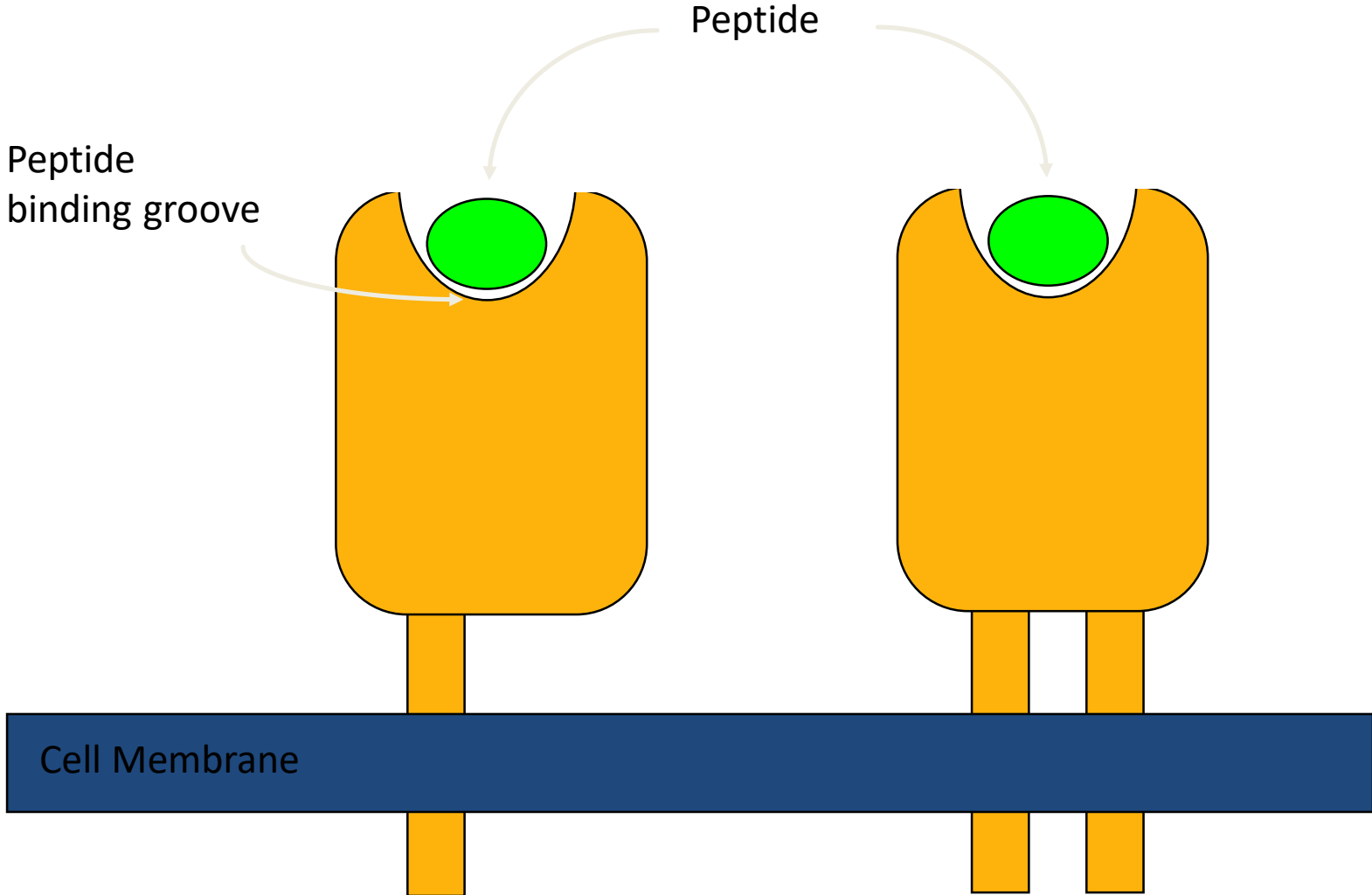
MHC molecules

MHC class I

MHC class II

Peptide

Peptide
binding groove

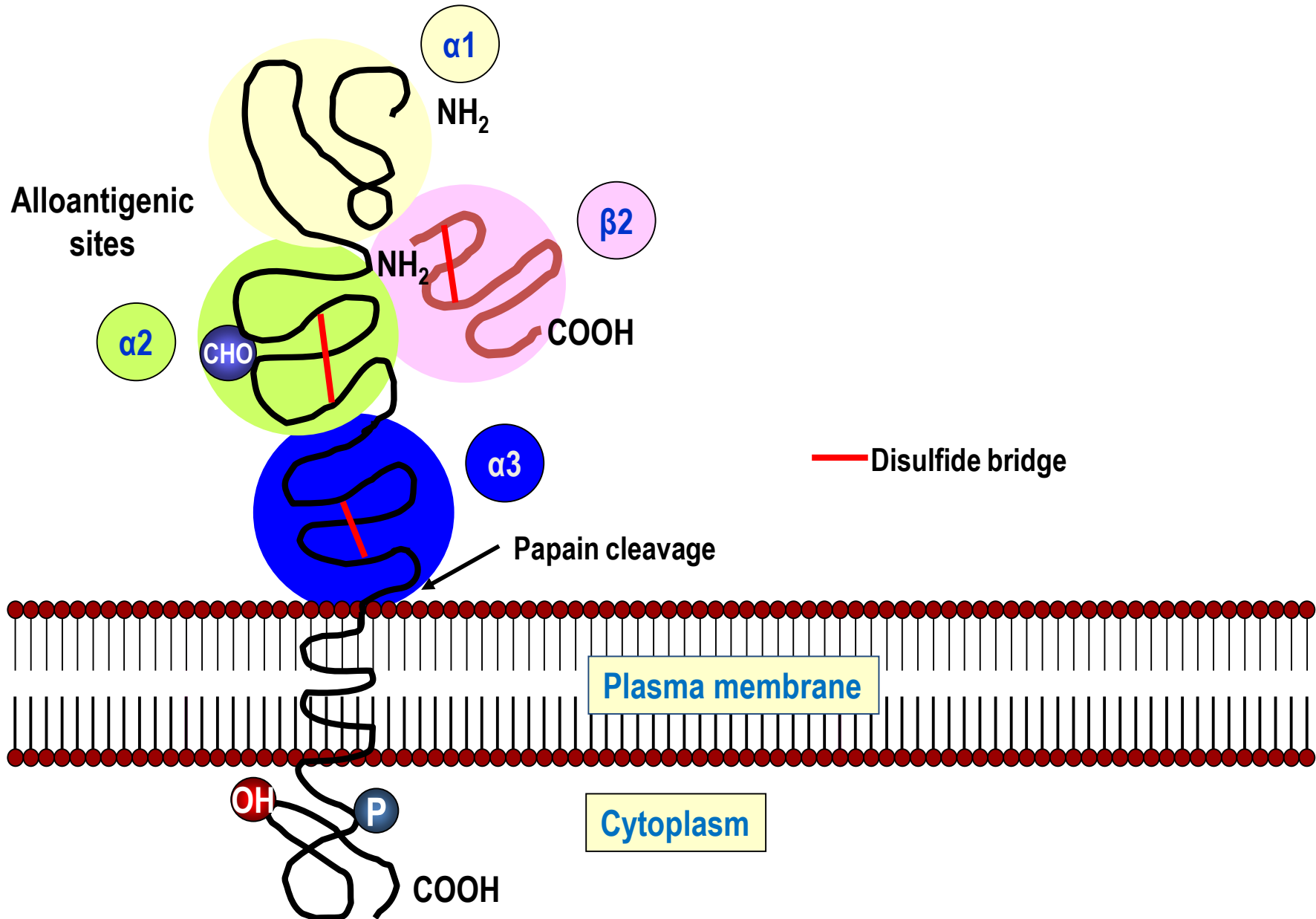


MHC CLASS-I ANTIGENS

FEATURES

- **expressed on surface of all nucleated cells**
- **recognized by TCR of Tc cells**
- **CD8 molecule on surface of Tc cells binds to class I MHC-peptide complex**
- **source of peptide is cytosolic compartment**

Structure of Class I MHC



Structure of Class I MHC

- Two polypeptide chains(heterodimer) - a MHC-encoded long α chain, and a non-MHC-encoded short β chain called $\beta 2$ microglobulin
- Four regions:
 - **Peptide-binding region** - a groove formed from $\alpha 1$ and $\alpha 2$ domains of the α chain
 - **Immunoglobulin-like region** – highly conserved $\alpha 3$ domain - site to which CD8 on T cell binds
 - **Transmembrane region** – stretch of hydrophobic amino acids spanning membrane
 - **Cytoplasmic region** – contains sites for phosphorylation and binding to cytoskeletal elements

Class I MHC - Agerotope

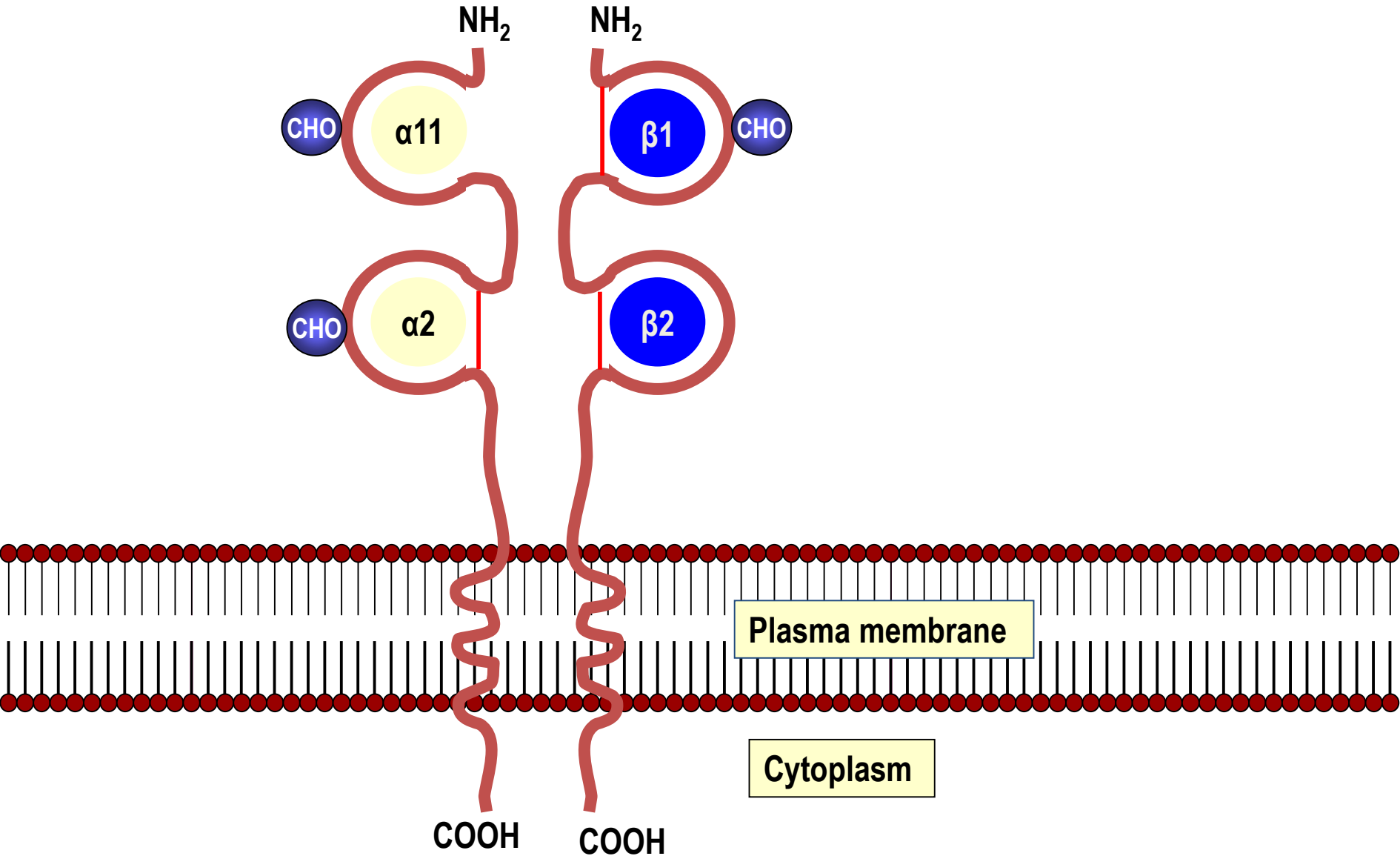
- a “groove” composed of an α -helix on two opposite walls and eight β -pleated sheets forming the floor
- a.a. residues lining groove are most polymorphic
- 8-10 amino acids long peptide can be lodged in groove
- specific amino acid on peptide required for “anchor site” in groove

MHC CLASS-II ANTIGENS

FEATURES

- **expressed on surface of APCs and thymic epithelium**
- **recognized by TCR of Th cells**
- **CD4 molecule on surface of Th cells binds to class II: MHC-peptide complex**
- **source of peptide is vesicular compartment**

Structure of Class II MHC



Structure of Class II MHC

- Two polypeptide chains, α and β , of roughly equal length (homodimer).
- Four regions:
 - **Peptide-binding region** – a groove formed from the $\alpha 1$ and $\beta 1$ domains of the α and β chains – site of polymorphism
 - **Immunoglobulin-like region** – conserved $\alpha 2$ and $\beta 2$ domains – $\beta 2$ is site to which CD4 on T cell binds
 - **Transmembrane region** – stretch of hydrophobic amino acids spanning membrane
 - **Cytoplasmic region** – contains sites for phosphorylation and binding to cytoskeletal elements

Class II MHC Agerotope

- a “groove” composed of an α -helix on two opposite walls and eight β -pleated sheets forming the floor
- a.a. residues lining groove are most polymorphic
- Open ended groove which can bind to 13-25 amino acids long peptide, not all of which need to lie in groove
- specific amino acid on peptide required for “anchor site” in groove

Differences between Class-I and II MHC

Characteristic	MHC-I	MHC-II
Location	All nucleated cells	APCs and Thymic epithelium
Structure	Heterodimer	Homodimer
Ag presentation	Tc cells	Th cells
Intracellular source of antigenic peptide presented	Cytosol	Vesicle
Binding CD molecule on T cells	CD8	CD4
Type of binding groove	Closed	Open
Groove forming domains	$\alpha 1$ and $\alpha 2$ domains of α chain	$\alpha 1$ and $\beta 1$ domains of the α and β chains, respectively
Size of peptide that can be accommodated in groove	8-10 aa residues	13-25 aa residues