The Major Histocompatibility Complex (MHC)

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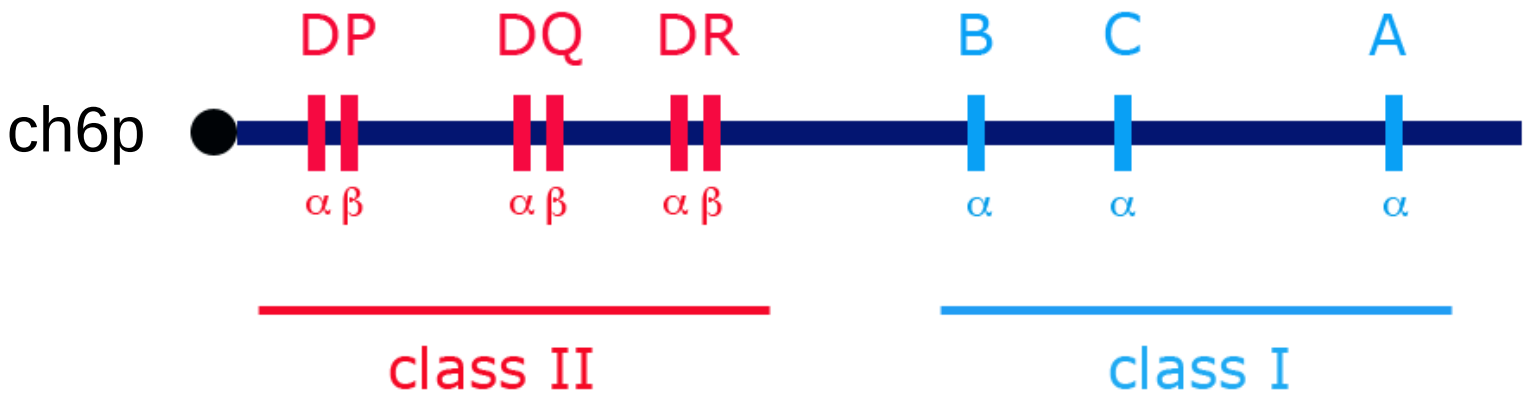
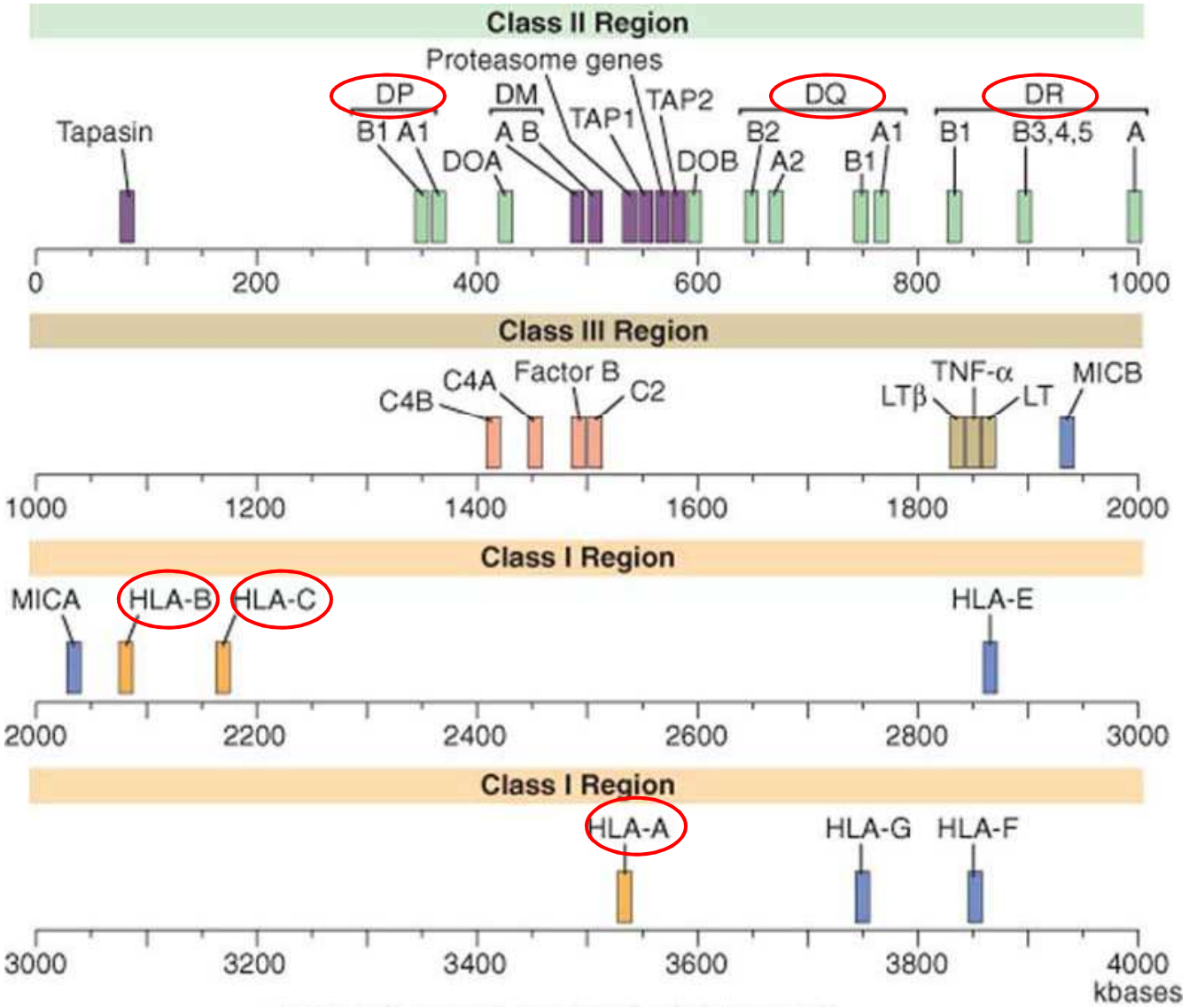
(MHC)

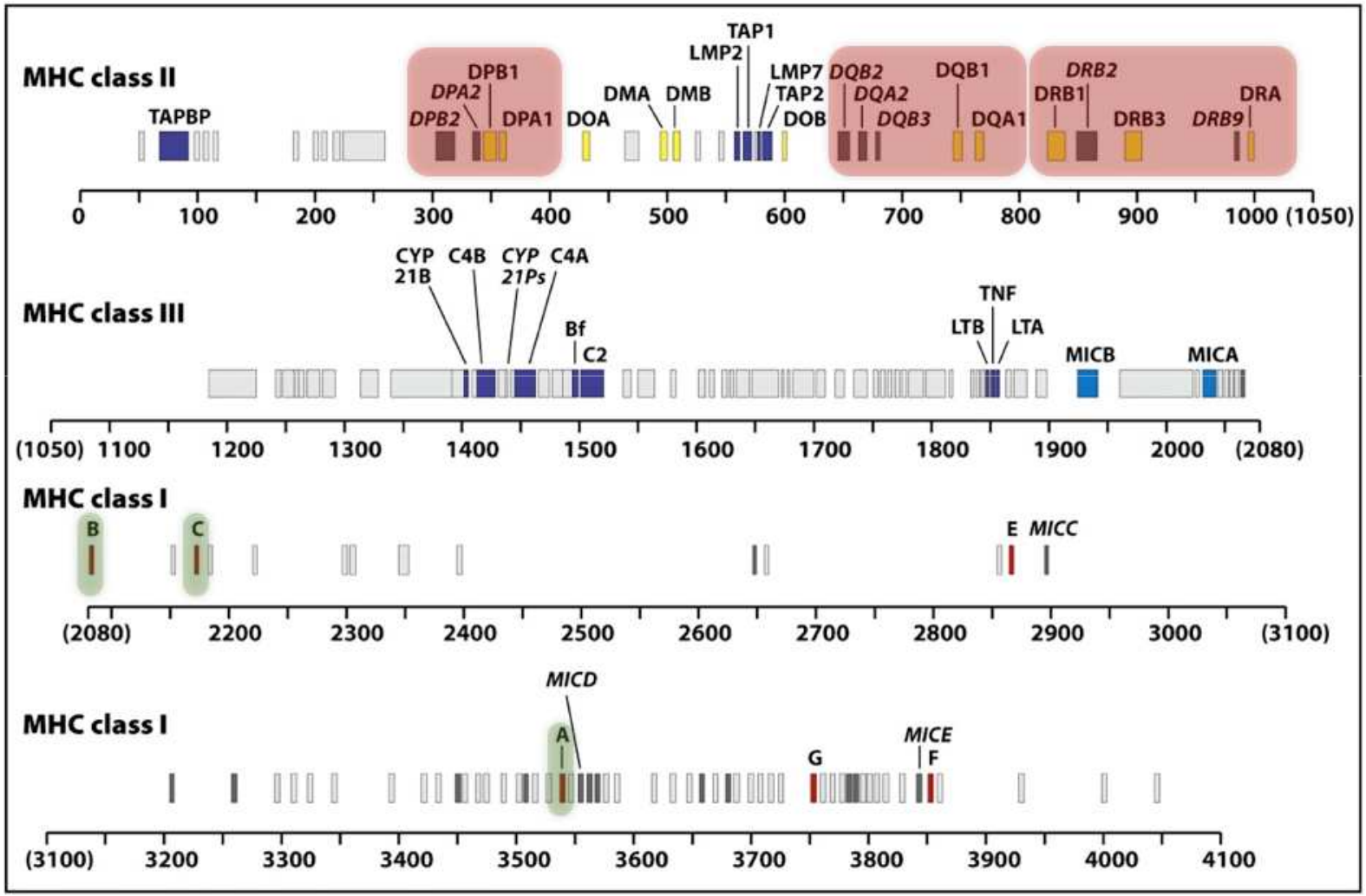


Human Leucocyte Antigens
(HLA)

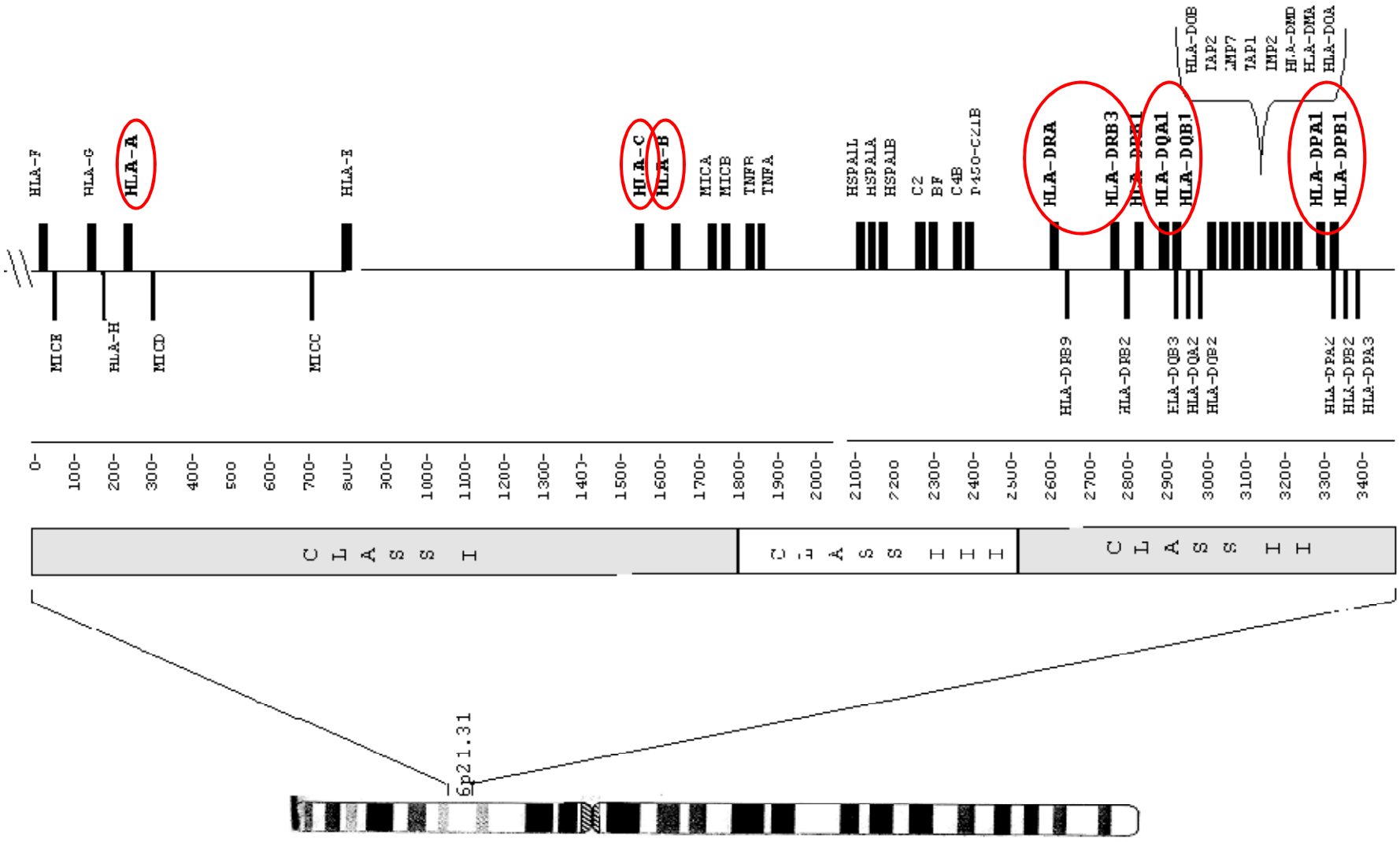
Map of the human MHC (short arm Chr 6)



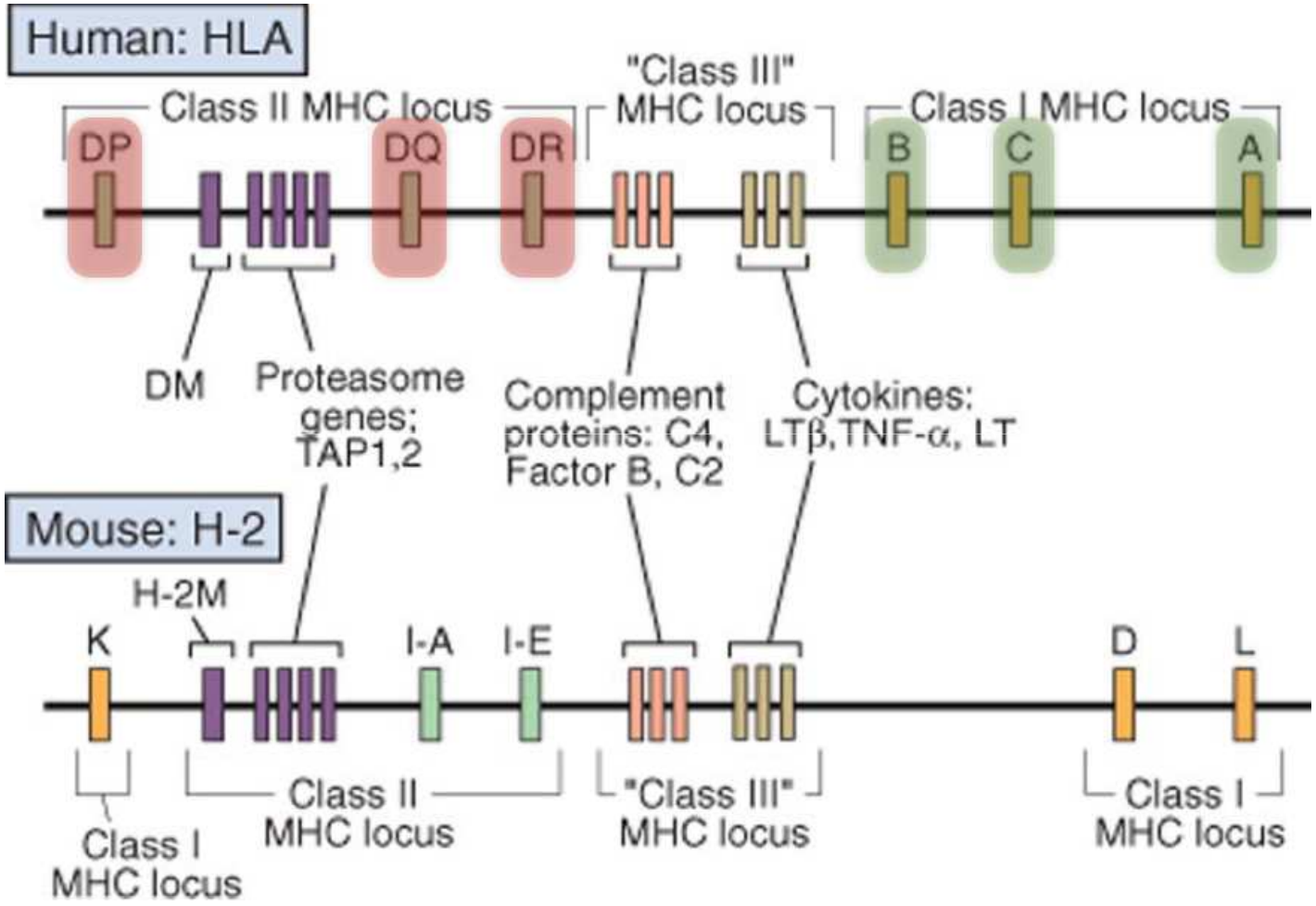
Map of the human MHC (short arm Chr 6)



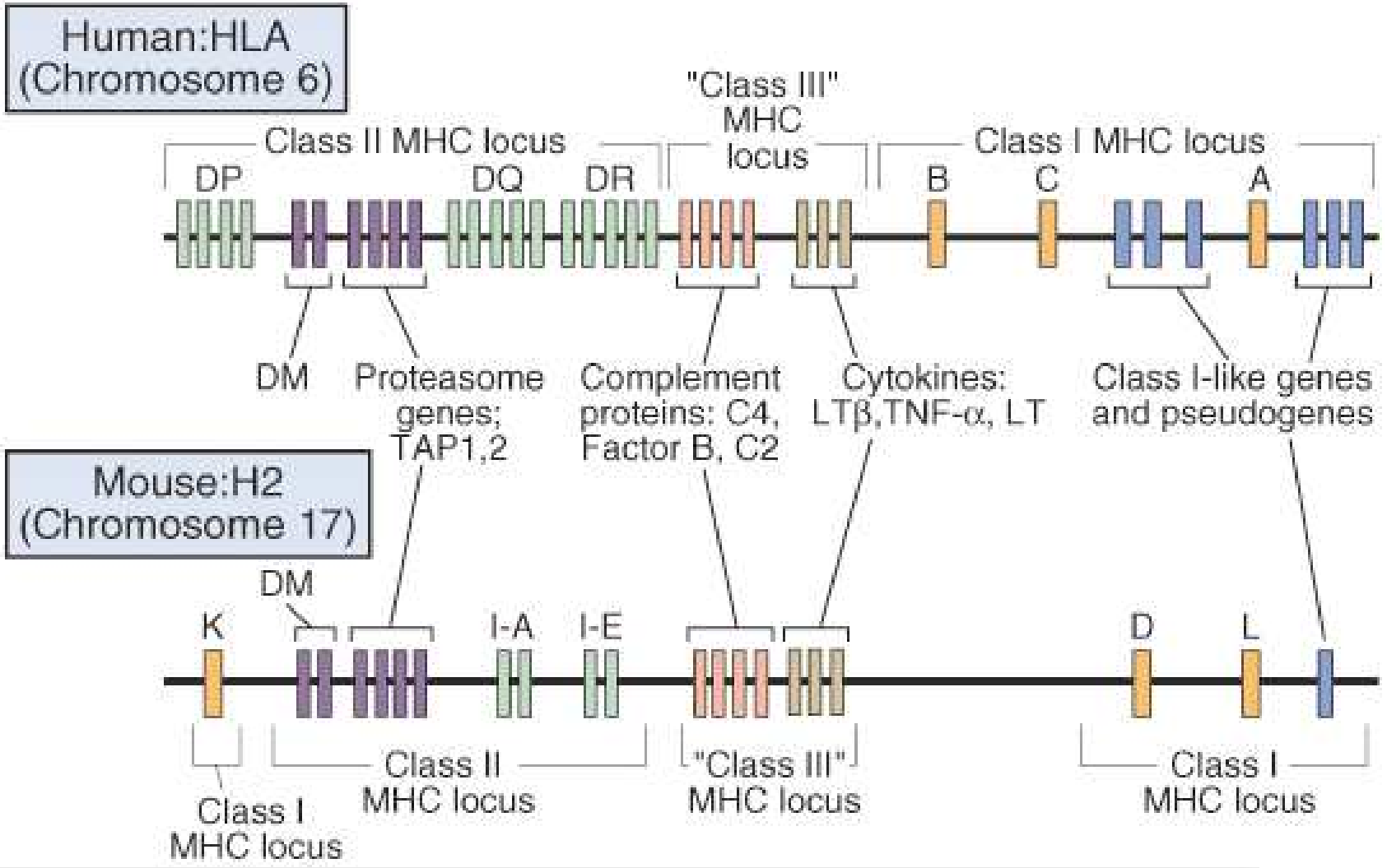
Map of the human MHC (short arm Chr 6)



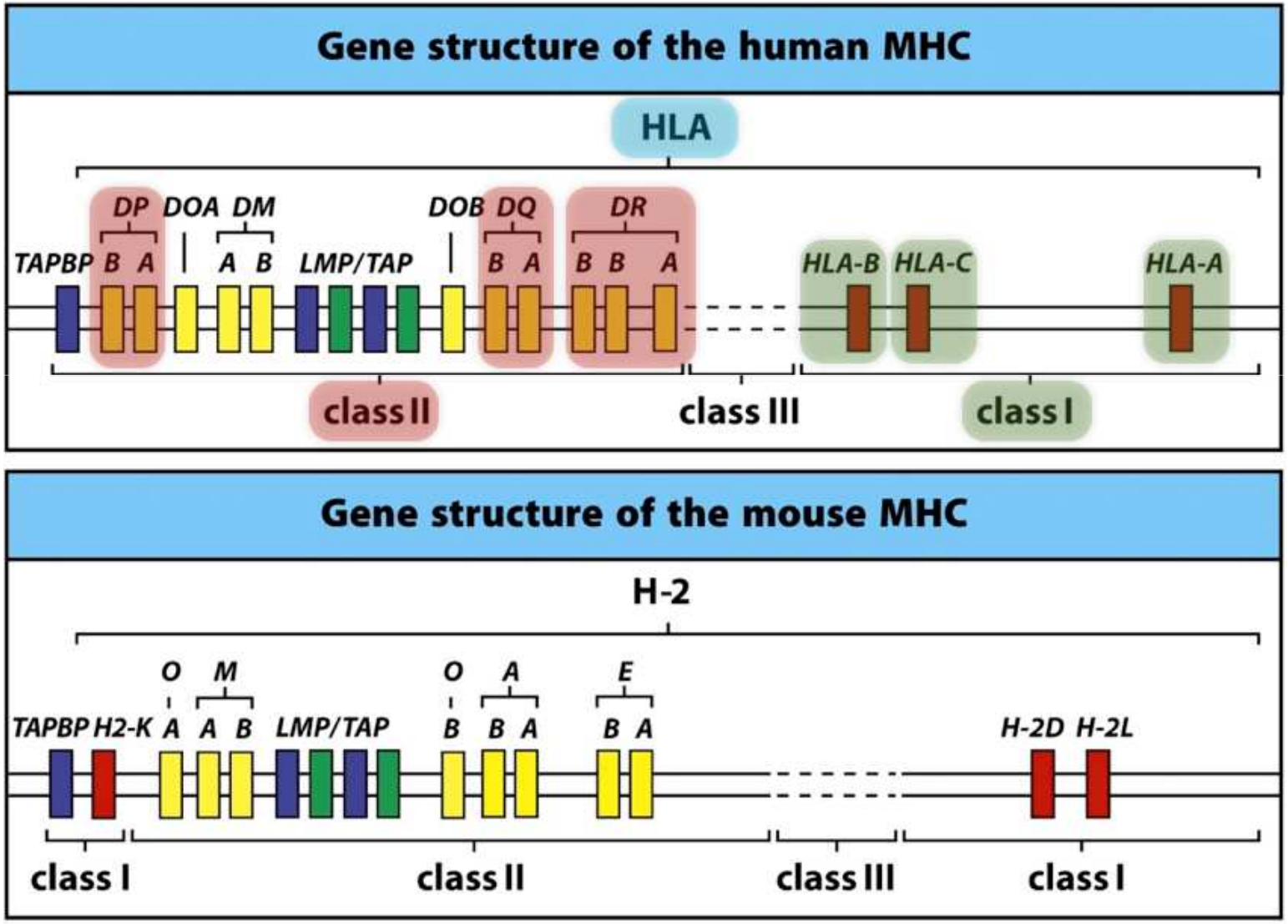
Maps of human and murine MHC loci



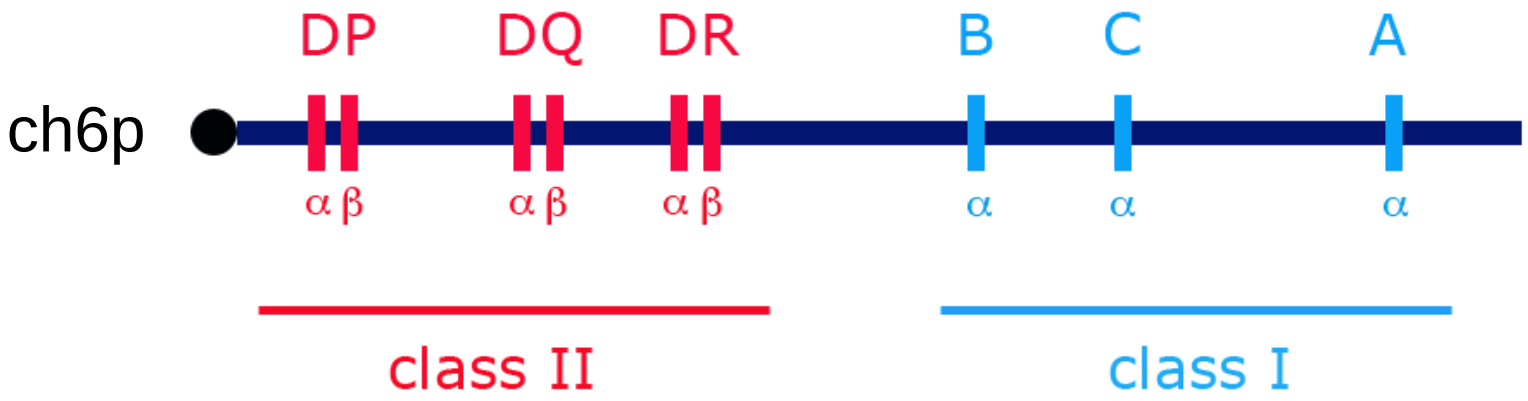
Maps of human and murine MHC loci



Maps of human and murine MHC loci



Major Histocompatibility Complex
(MHC)



Human Leucocyte Antigens
(HLA)

MHC

polygenic: 9 main genes (DP⟨ / ®, DQ⟨ / ®, DR⟨ / ®, B, C, A)

polymorphic: multiple alleles for each gene

codominant: both maternal and paternal alleles expressed

Allelic polymorphism

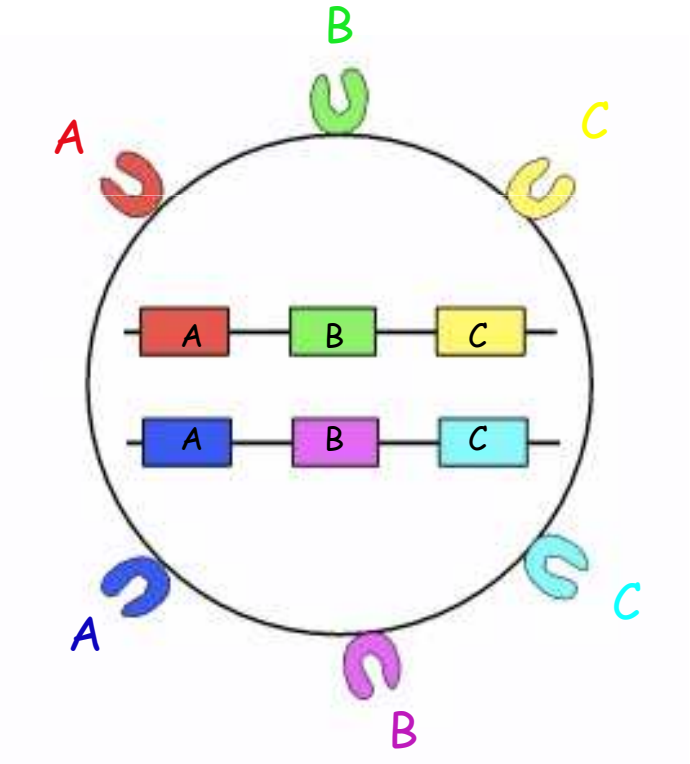
HLA-A locus:	580	
HLA-B locus:	921	
HLA-C locus:	312	
HLA-DPα locus:	23	
HLA-DPβ locus:	127	
HLA-DQα locus:	34	
HLA-DQβ locus:	86	
HLA-DRα locus:	3	(~ monomorphic)
HLA-DRβ locus:	577	

Co-dominance

both paternal and maternal MHC alleles are expressed

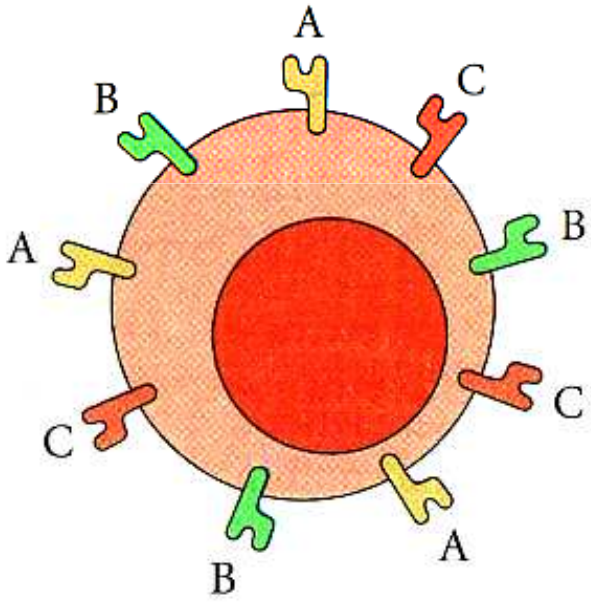
MHC class I

Paternal A, B, C
Maternal A, B, C



Expression of human MHC molecules

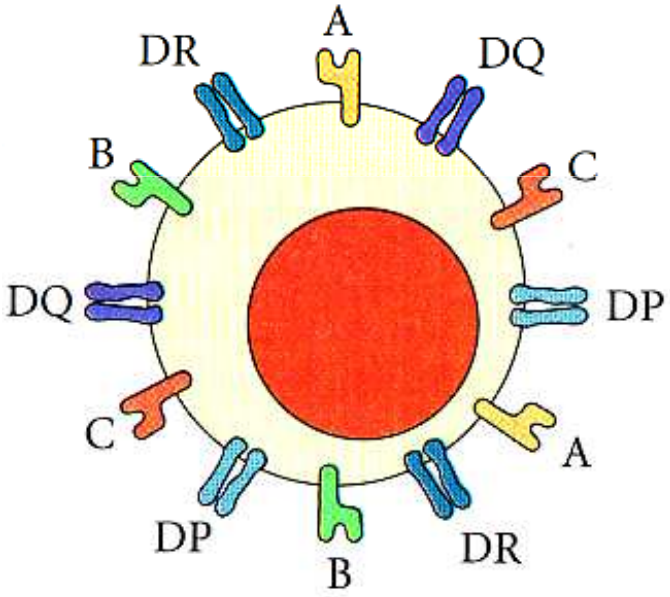
All nucleated cells



Class I

Antigen Presenting Cells

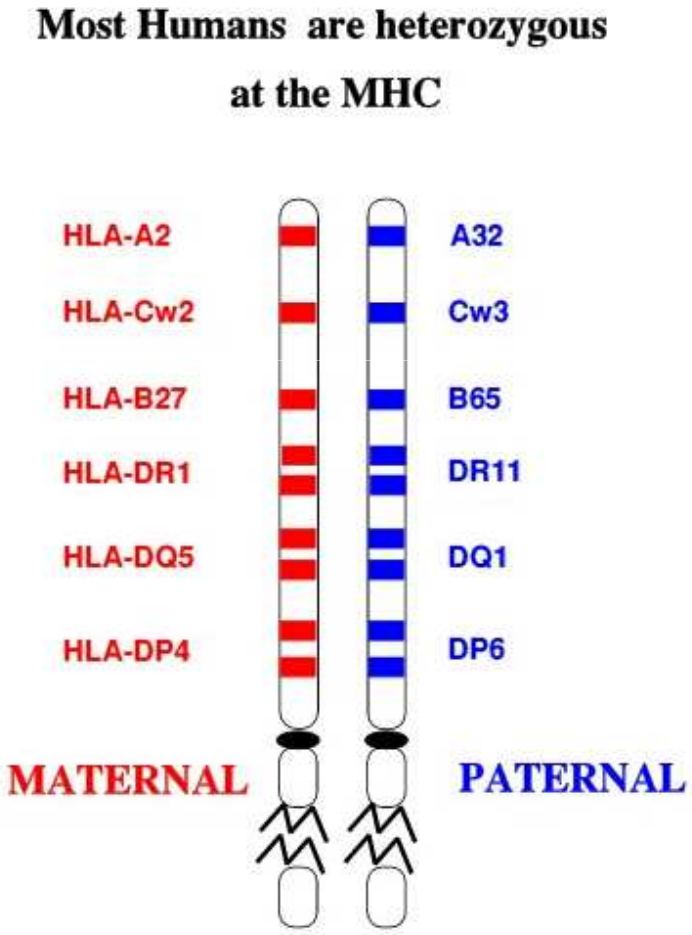
(Dendritic cells, macrophages, monocytes, B lymphocytes, Langherans cells)



Class I + Class II

Haplotype

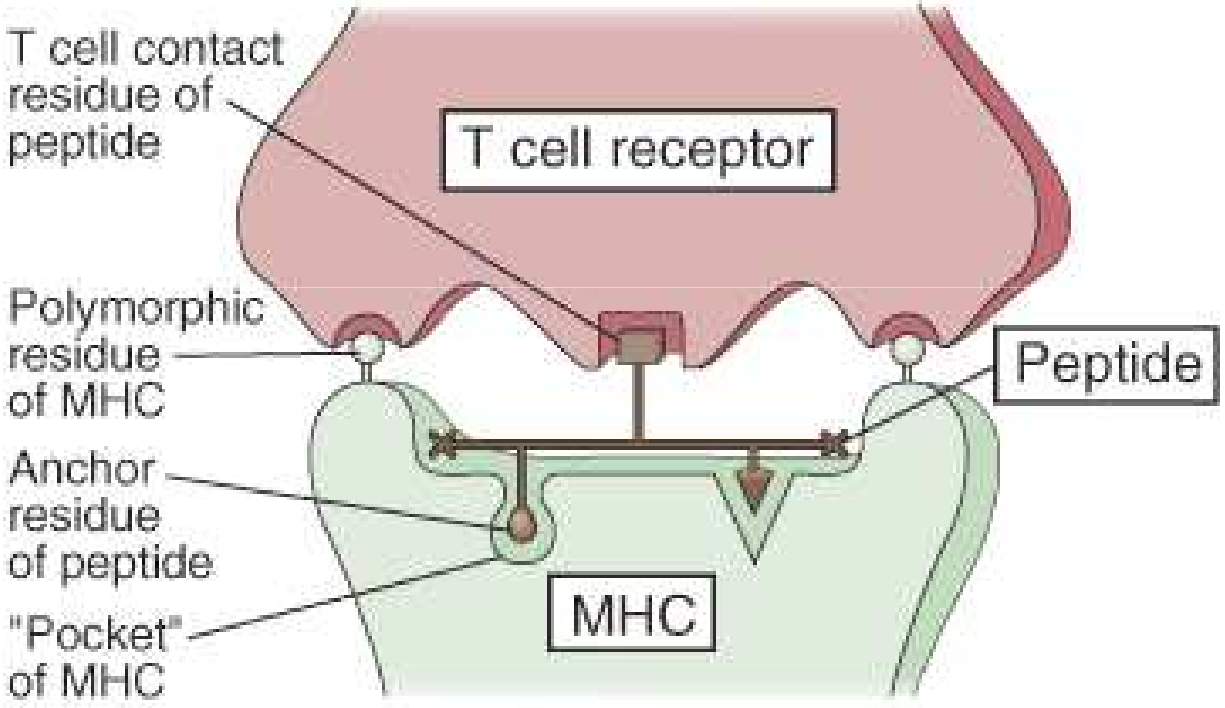
the set of inherited MHC alleles on each chromosome



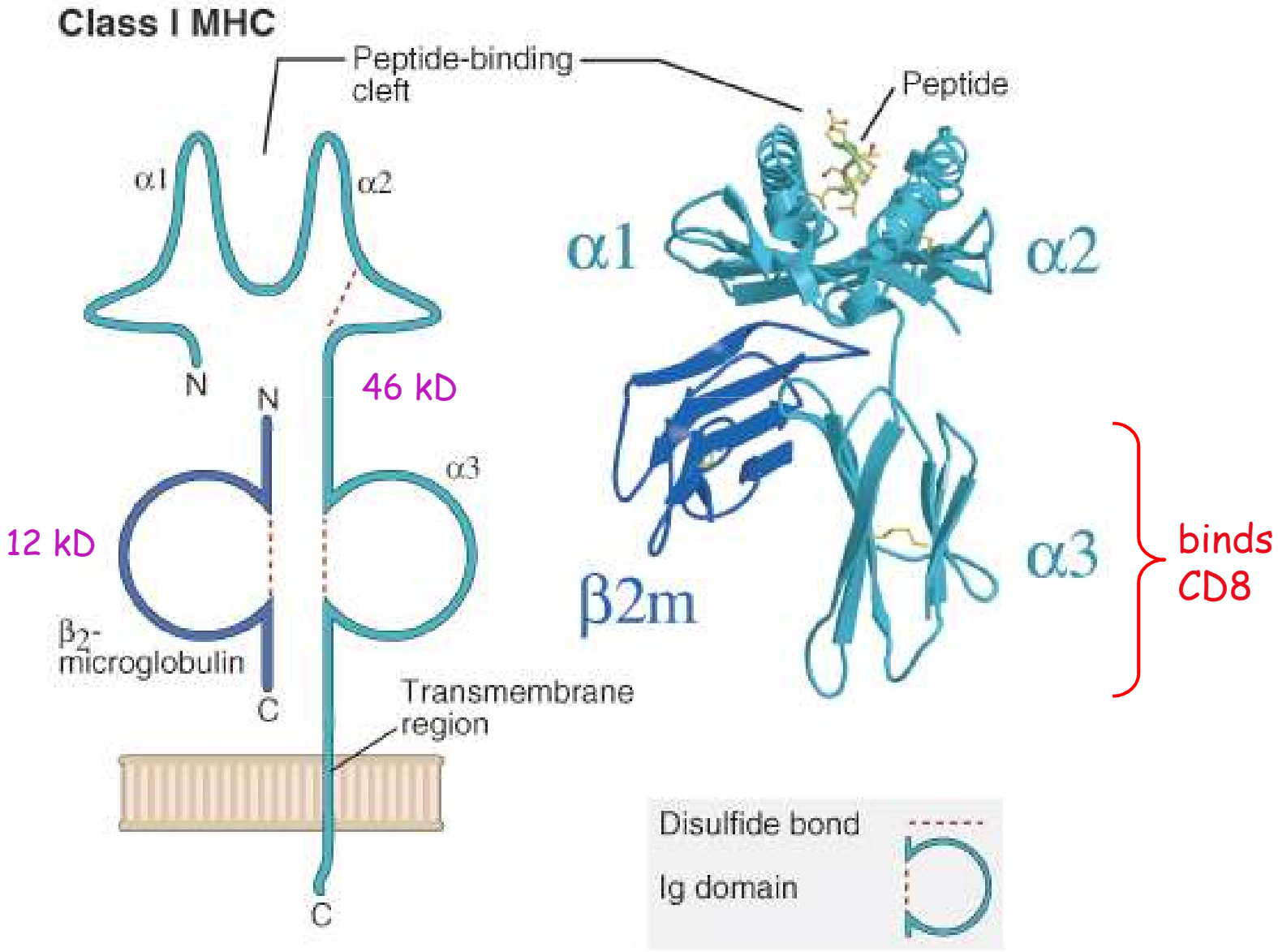
Number of different MHC molecules on each cell

	n.	codom	$\alpha+\beta$ mix	+ loci extra	TOT
Class I	3	x2	-	-	= 6
Class II	3	x2	x2	+x	~ 18-20

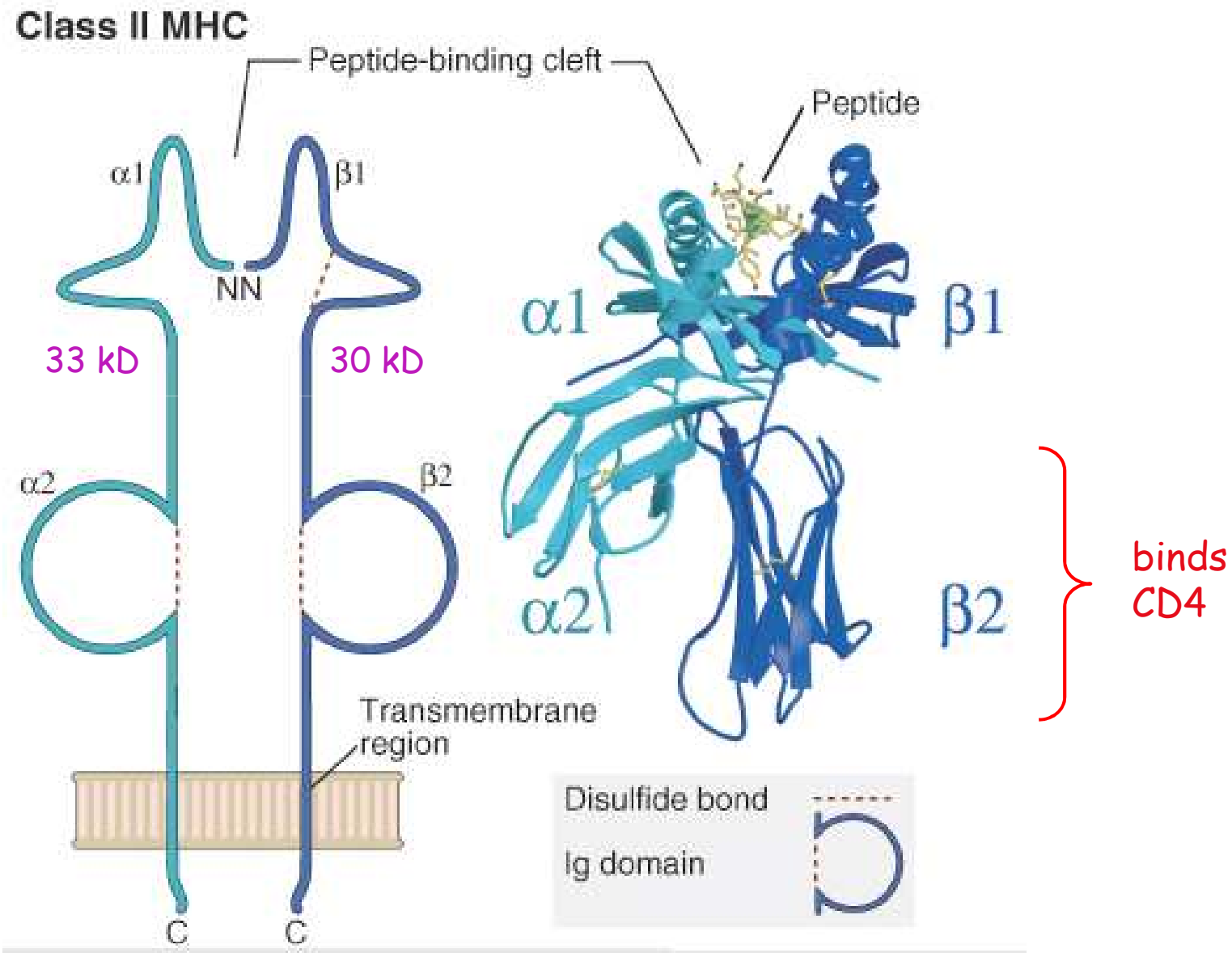
MHC/peptide - TCR interaction



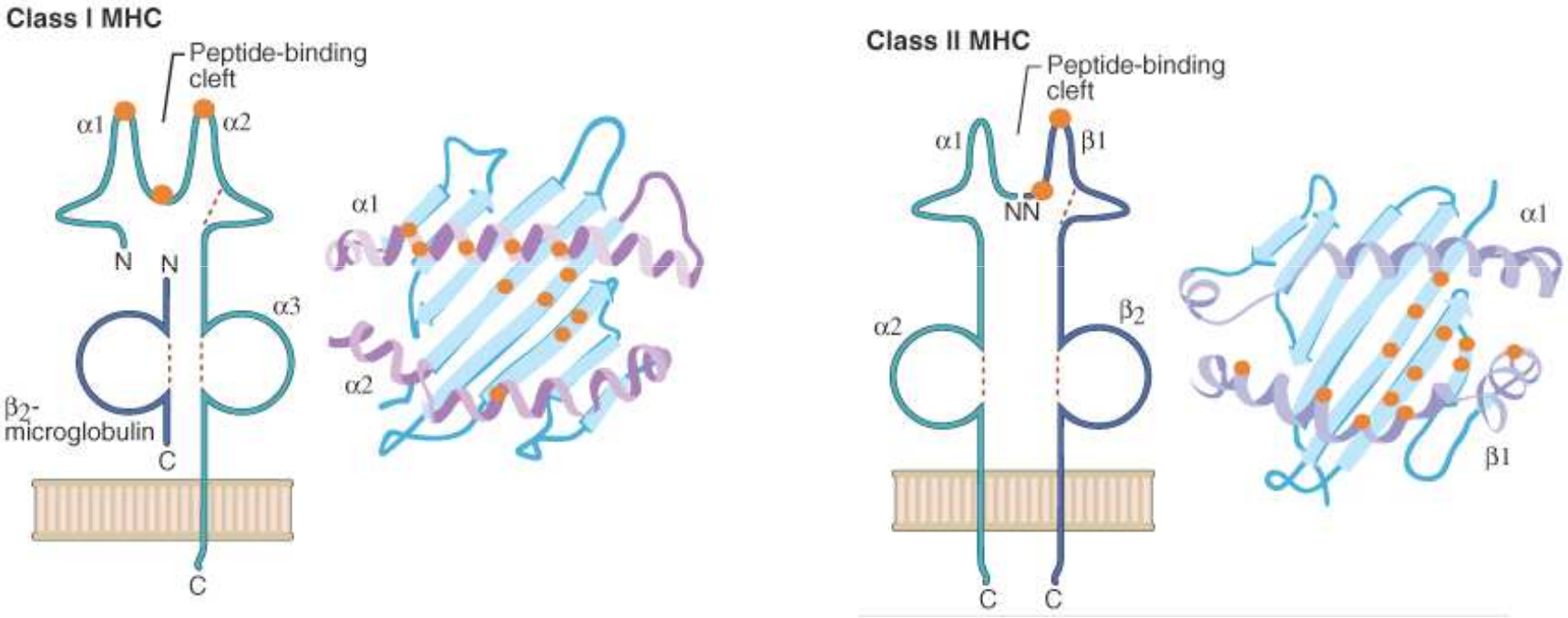
Structure of a Class I MHC molecule



Structure of a Class II MHC molecule

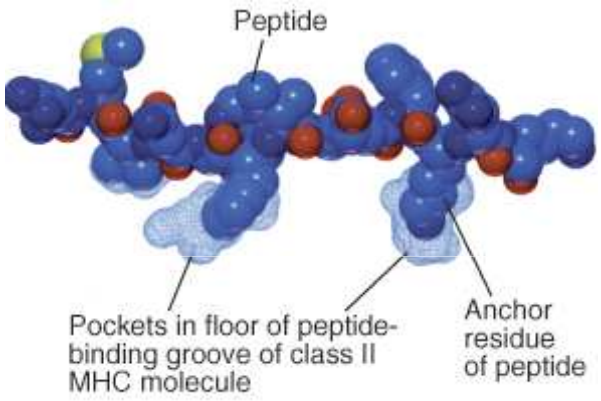


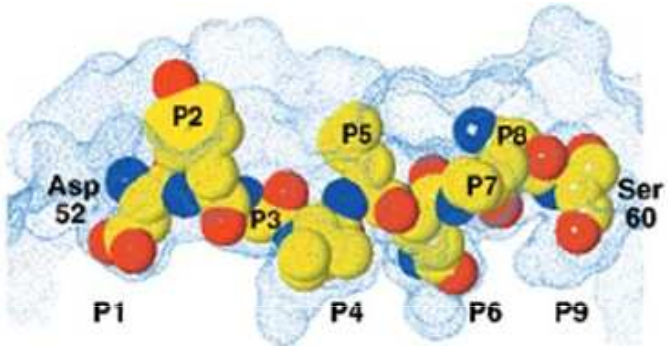
Polymorphic residues in MHC molecules



Non-polymorphic regions: Class I α3 binds CD8, Class II β2 binds CD4

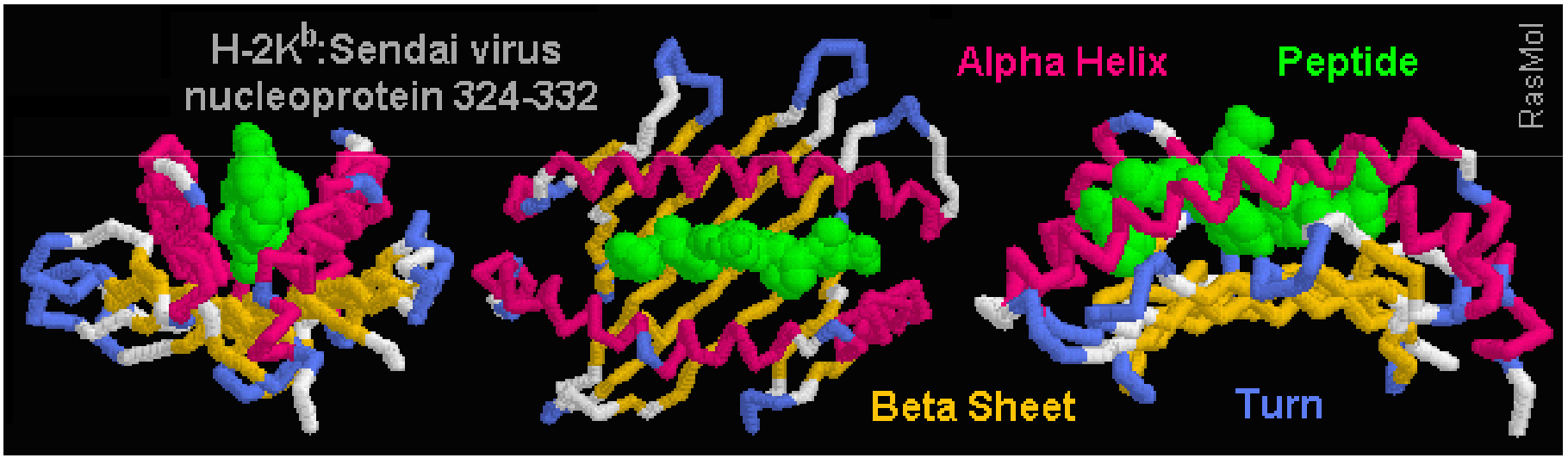
Peptides



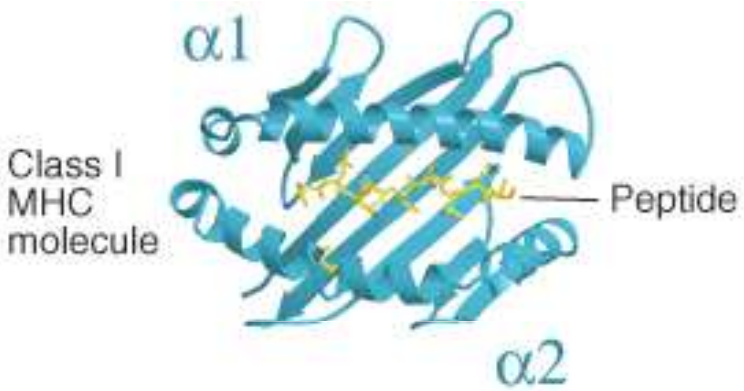


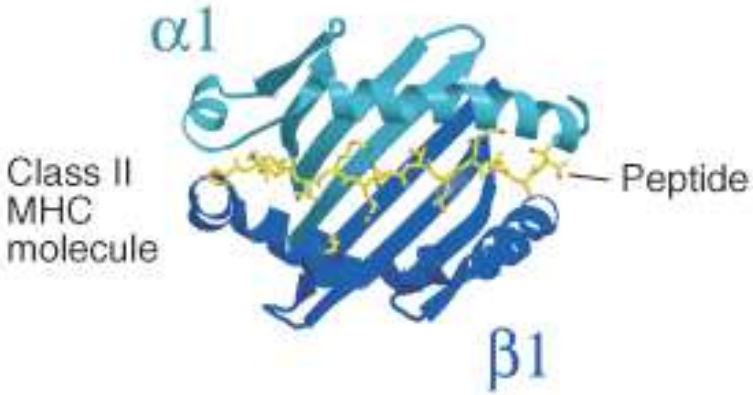
- Peptides loaded on MHC molecules are normally self peptides
- Each individual MHC molecule can bind different peptides
- Slow on-rate (15-30 min) and extremely slow off-rate (days)

Viral peptide in a Class I groove

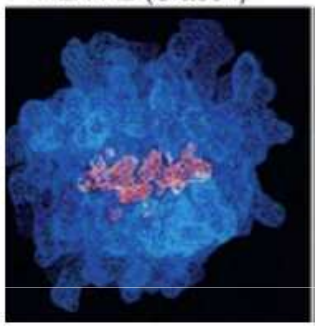


Antigenic peptides in the MHC pockets

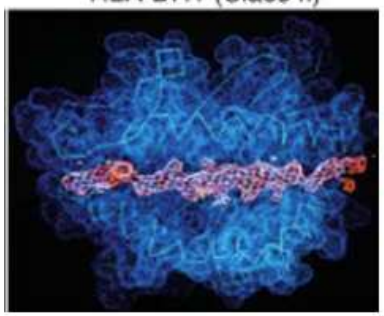




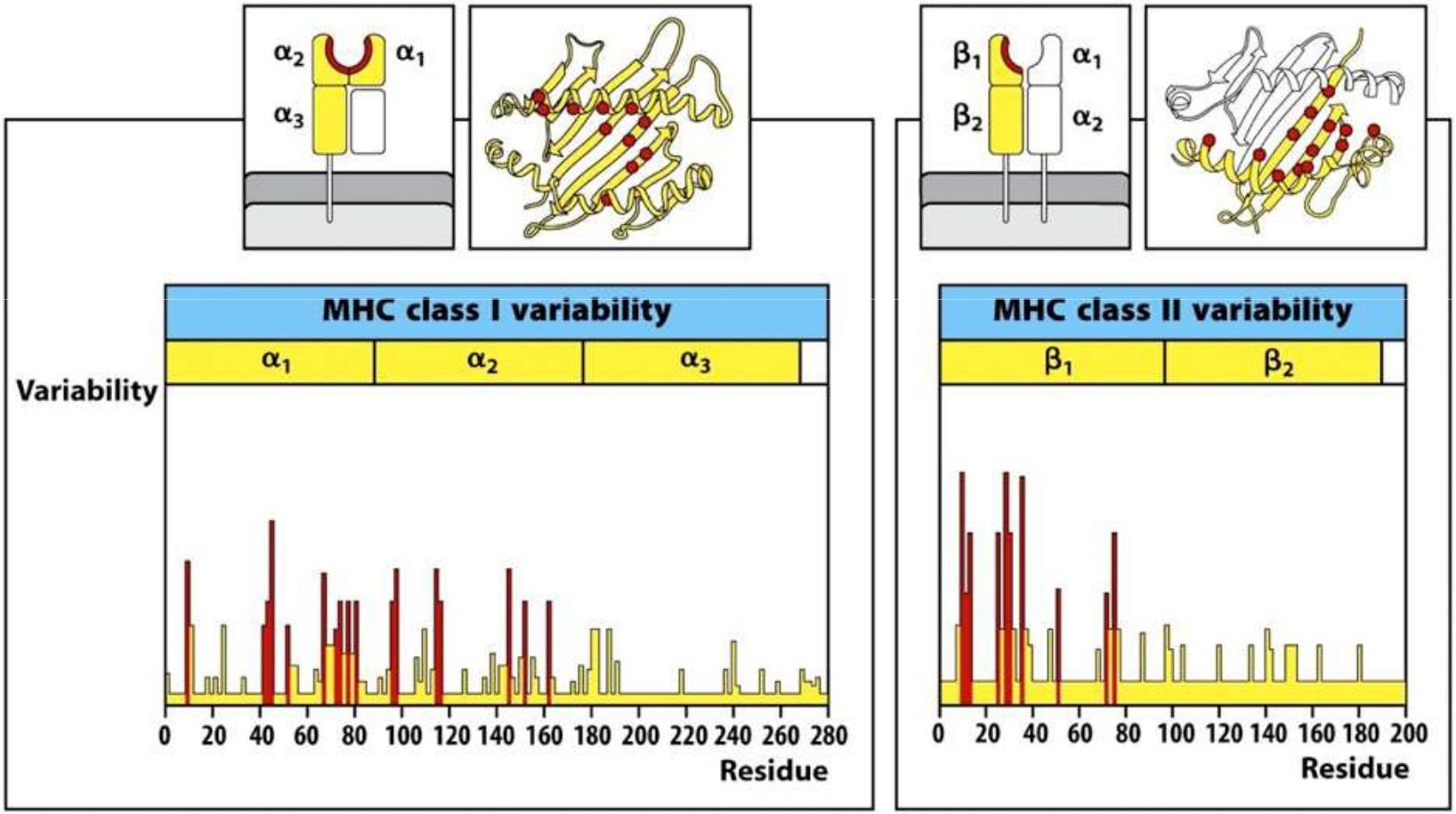
HLA-A2 (Class I)



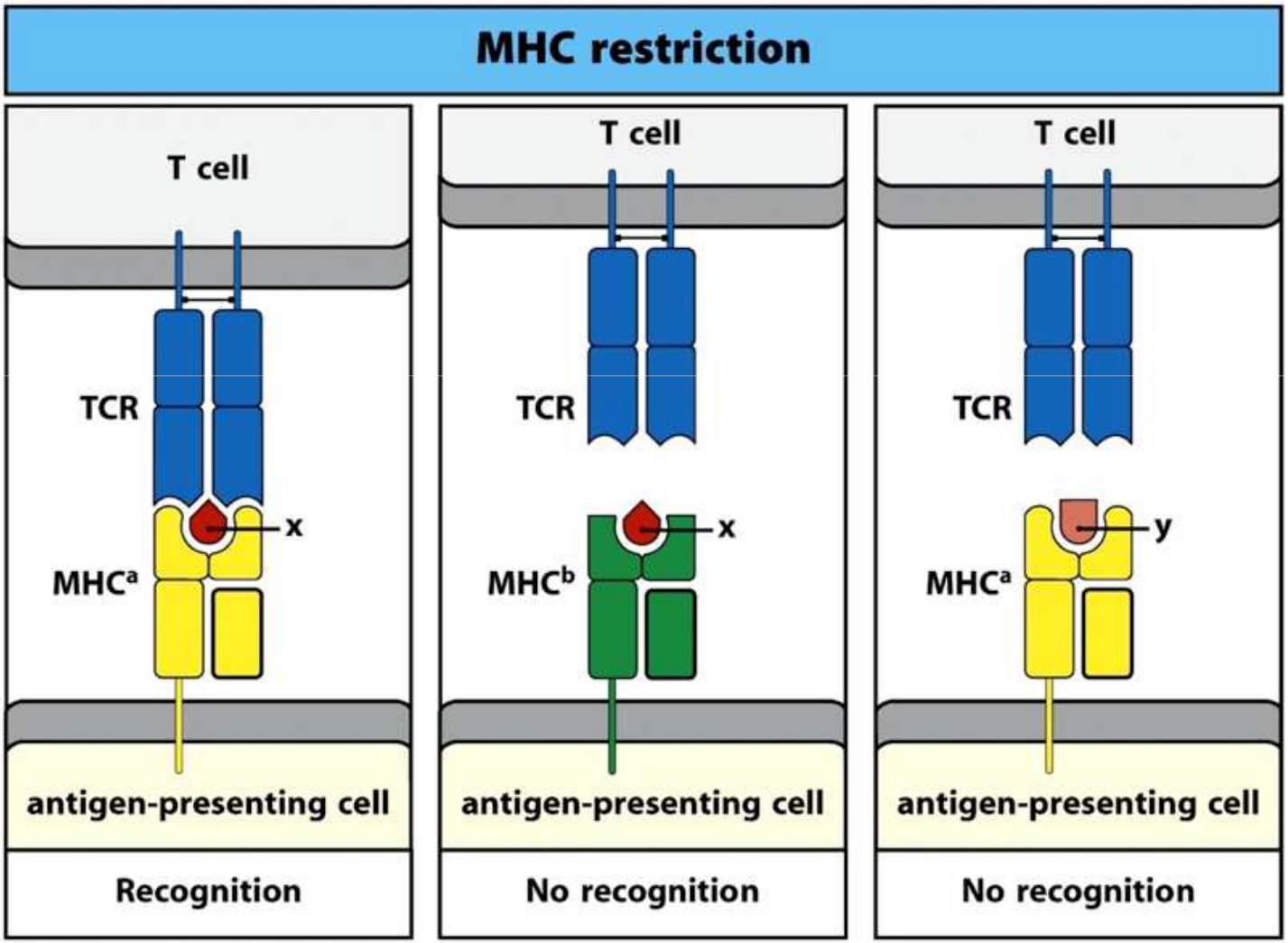
HLA-DR1 (Class II)



Allelic polymorphism dictates peptide specificity



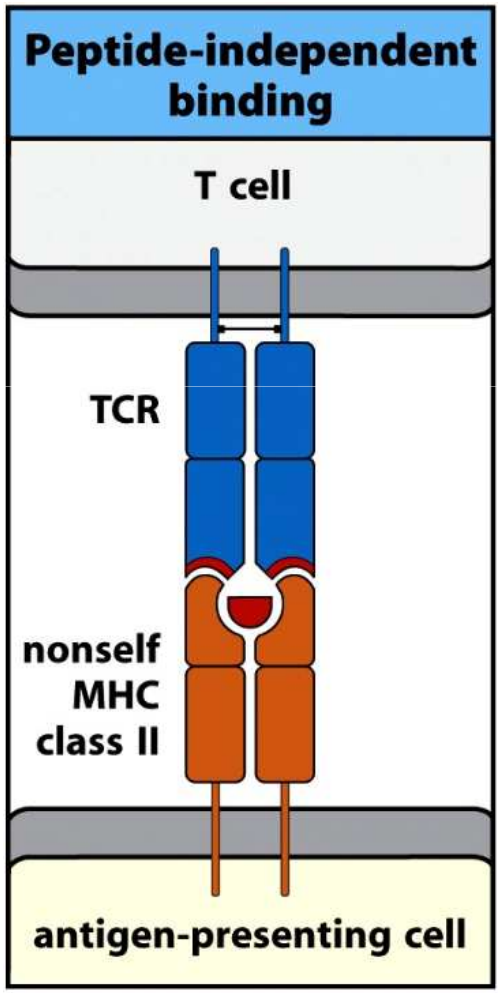
peptide recognition by the TCR is MHC - "restricted"



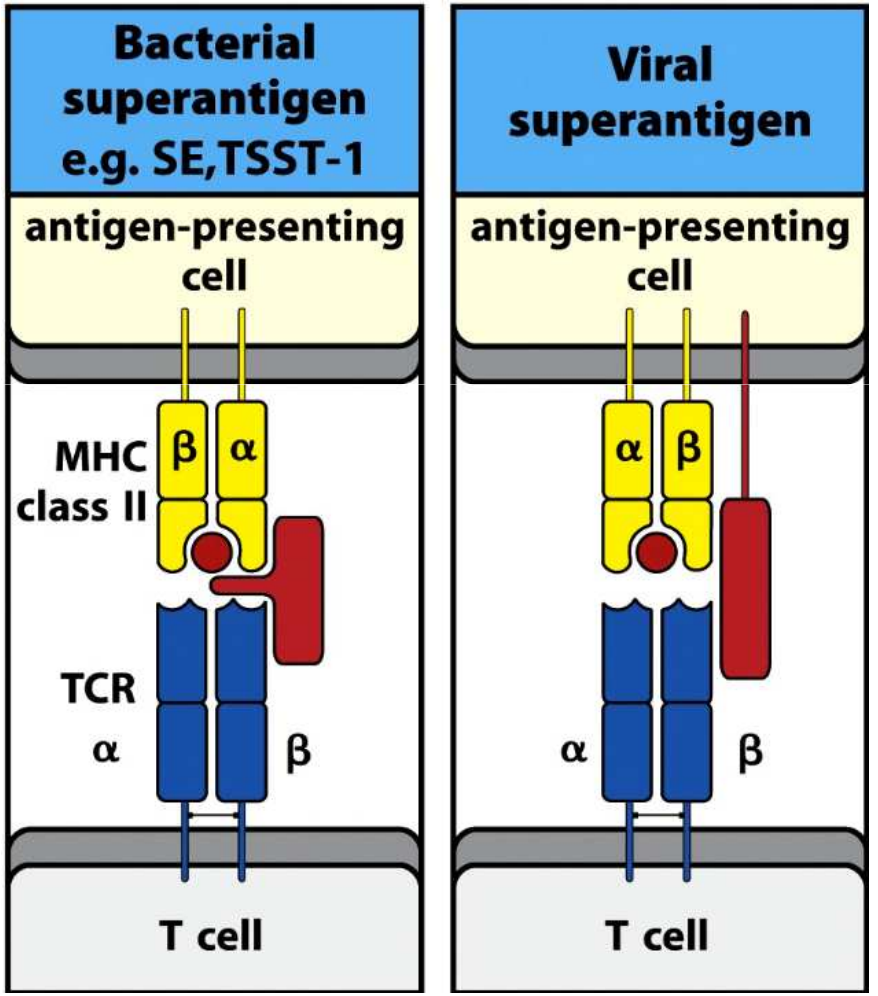
Alloantigens: non-self MHC molecules. 1-10% of all T lymphocytes recognizes allogenic MHC - transplant rejection

Superantigens: bacterial or viral proteins/lipid/sugars that associate extracellularly with the MHC-II and are recognized by 5-10% of all T lymphocytes - endotoxic shock

Alloreactivity



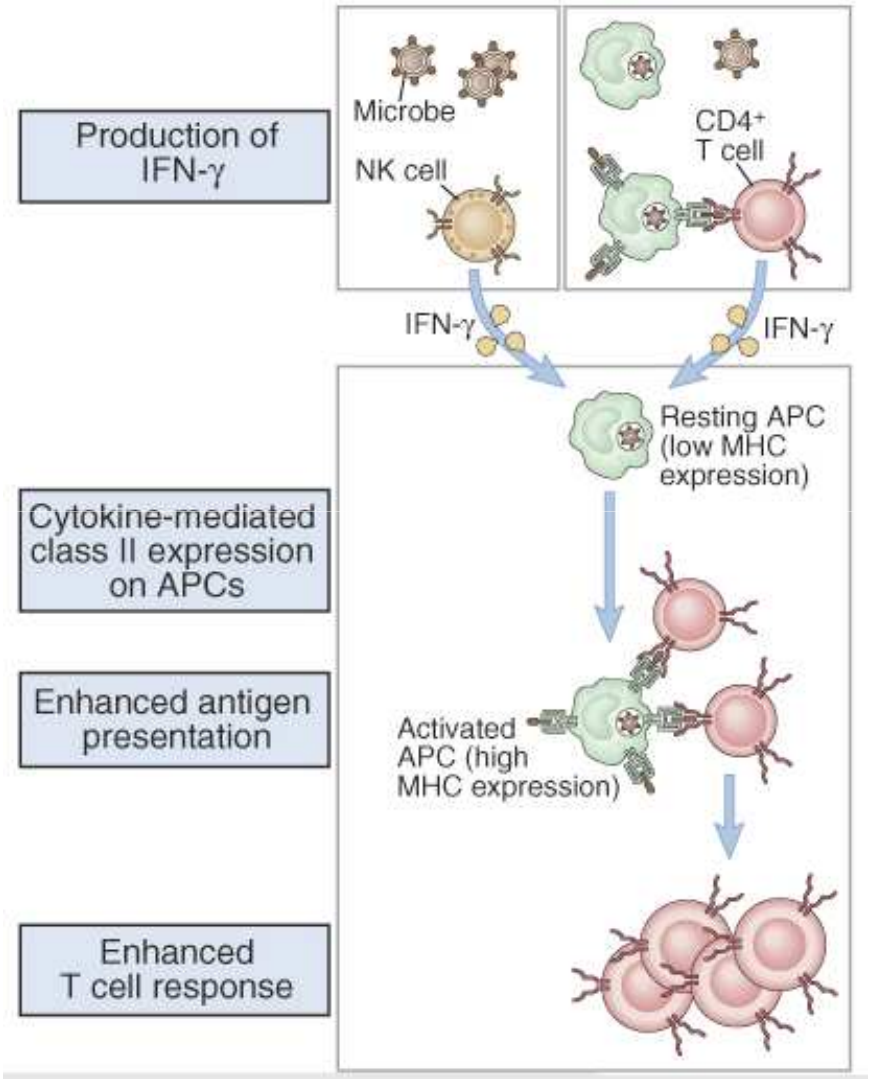
Superantigens



Features of MHC molecules

Feature	Class I MHC	Class II MHC
Polypeptide chains	α (44-47 kD) β_2-Microglobulin (12 kD)	α (32-34 kD) β (29-32 kD)
Locations of polymorphic residues	α1 and α2 domains	α1 and β1 domains
Binding site for T cell coreceptor	α3 region binds CD8	β2 region binds CD4
Size of peptide-binding cleft	Accommodates peptides of 8-11 residues	Accommodates peptides of 10-30 residues or more
Nomenclature		
Human	HLA-A, HLA-B, HLA-C	HLA-DR, HLA-DQ, HLA-DP
Mouse	H-2K, H-2D, H-2L	I-A, I-E

γIFN enhances MHC class II expression



Mediated by Class II transactivator (CIITA)

γIFN also enhances the expression of TAP genes and proteasome genes, such as LMP-2 and LMP-7

MHC-Ib recognition by NK cells

- MICA and MICB on epithelial cells are recognized by the complex DAP10/NKG2D on NK cells (activatory signal)
- HLA-G and HLA-E are recognized by the complex CD94/NKG2A on NK cells (inhibitory signal)