

# T Cell Receptors

# T Cell Receptors

- Structure
- Function

# T cells

- Called T cells because they develop in the thymus
- T cells are involved in cell-mediated immunity
- Distinguishing feature is T cell Receptor (TcR)
- Many different types of T cells: helper, cytotoxic, memory, regulatory, and  $\gamma\delta$

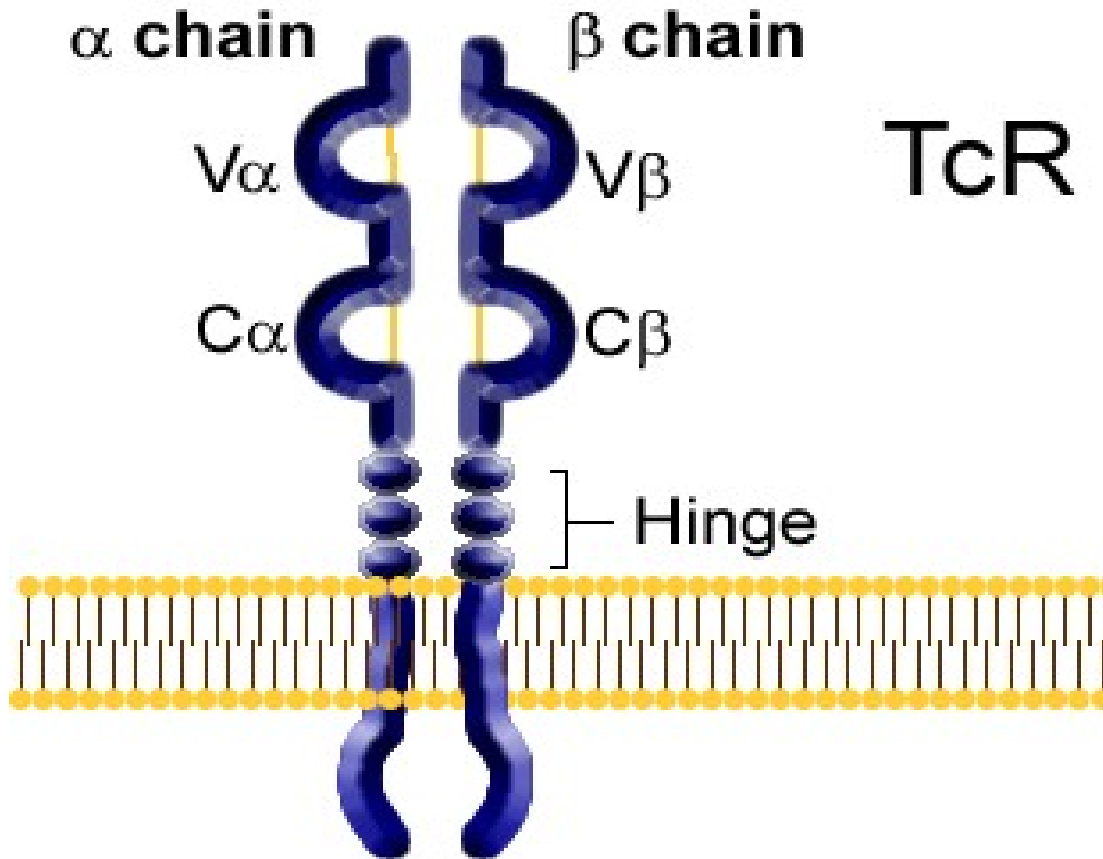
# T cell Receptors are heterodimers

i.e. two disulphide-linked polypeptides and have  
structurally similar domains like immunoglobulin

**TCR 1**  
 $\gamma\delta$  TCR

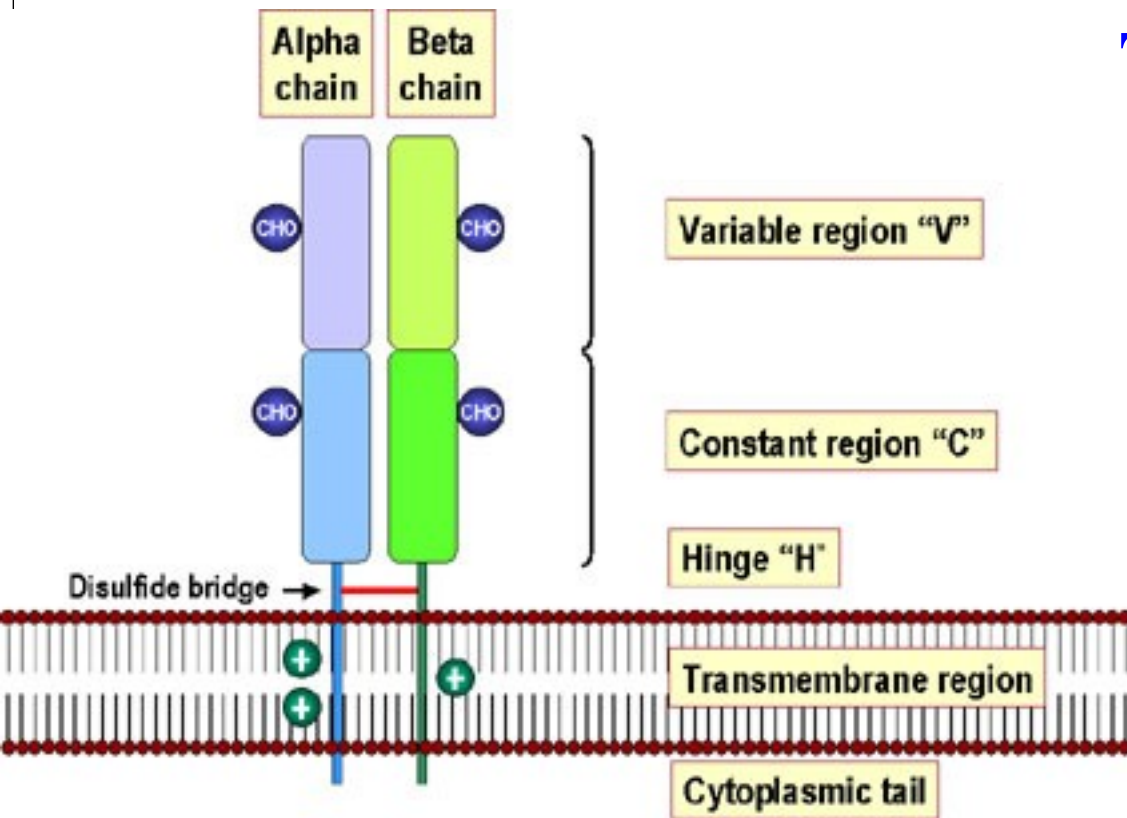
**TCR 2**  
 $\alpha\beta$  TCR

# The $\alpha\beta$ TCR

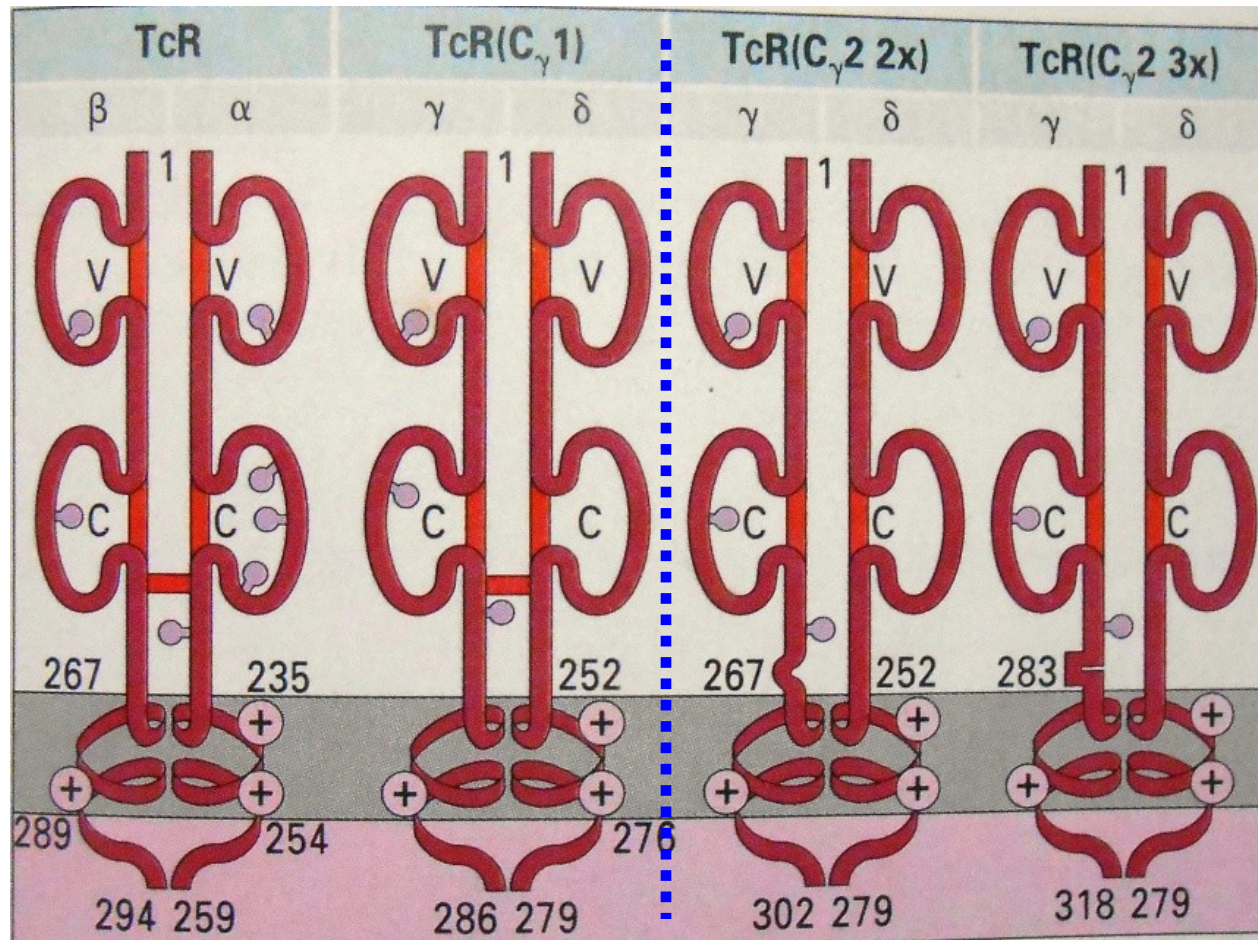


The TCR  $\alpha$  and  $\beta$  chains comprise two external immunoglobulin-like domains (V and C)

# Structure of T-Cell Receptor



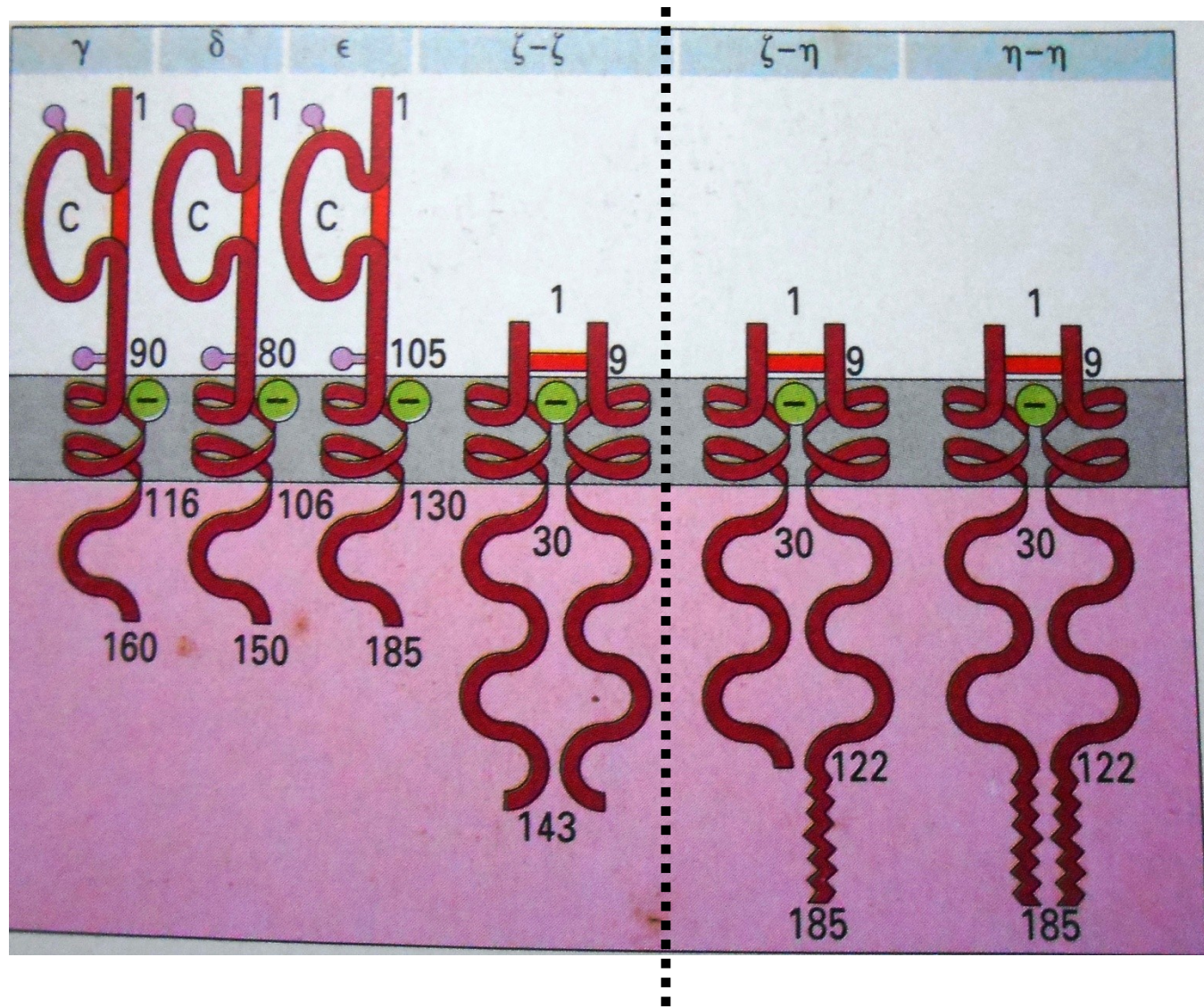
**The transmembrane segment contains two ( $\alpha$ ) and one ( $\beta$ ) positively charged residues and a short cytoplasmic tail. The  $\alpha$  and  $\beta$  chains are disulphide linked.**



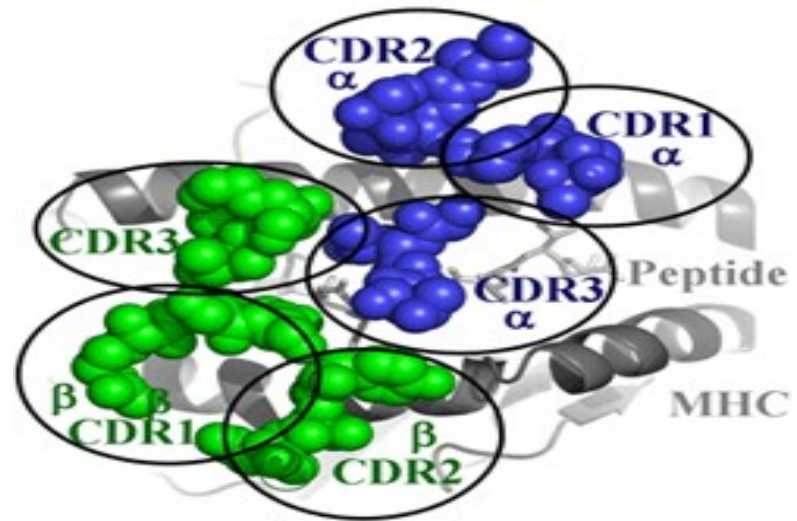
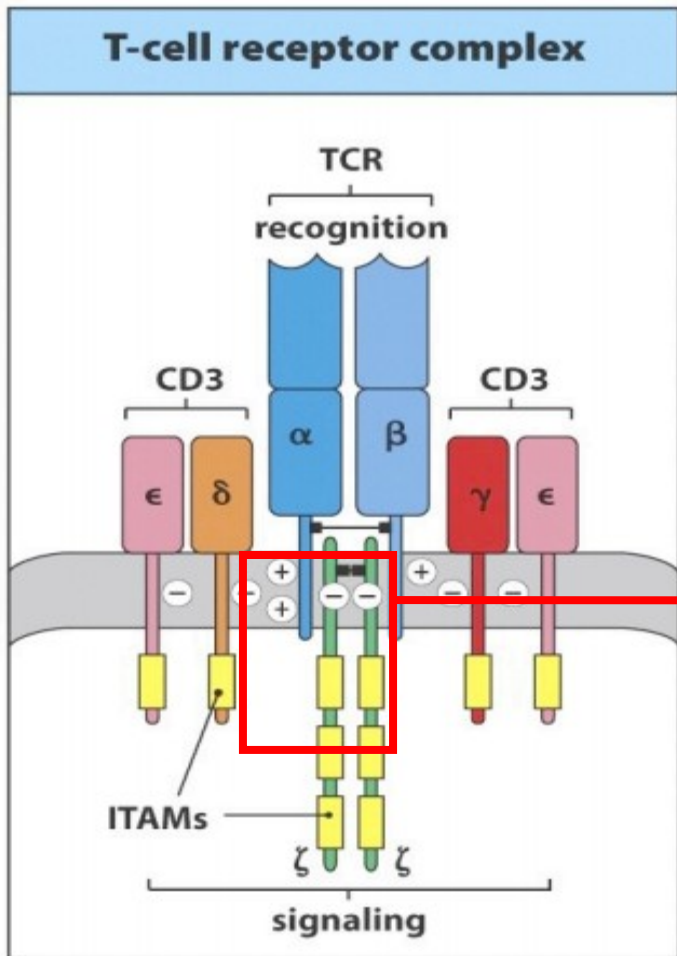
**The human TCR  $\gamma\delta$  receptor can several forms. The form containing a C $\gamma$ 1 constant region contains an interchain disulphide bond, whereas, C $\gamma$ 2 forms are not disulphide linked. The duplication or triplication of a section of the  $\gamma$  chain generates different forms of the g protein.**



# The CD3 Molecule





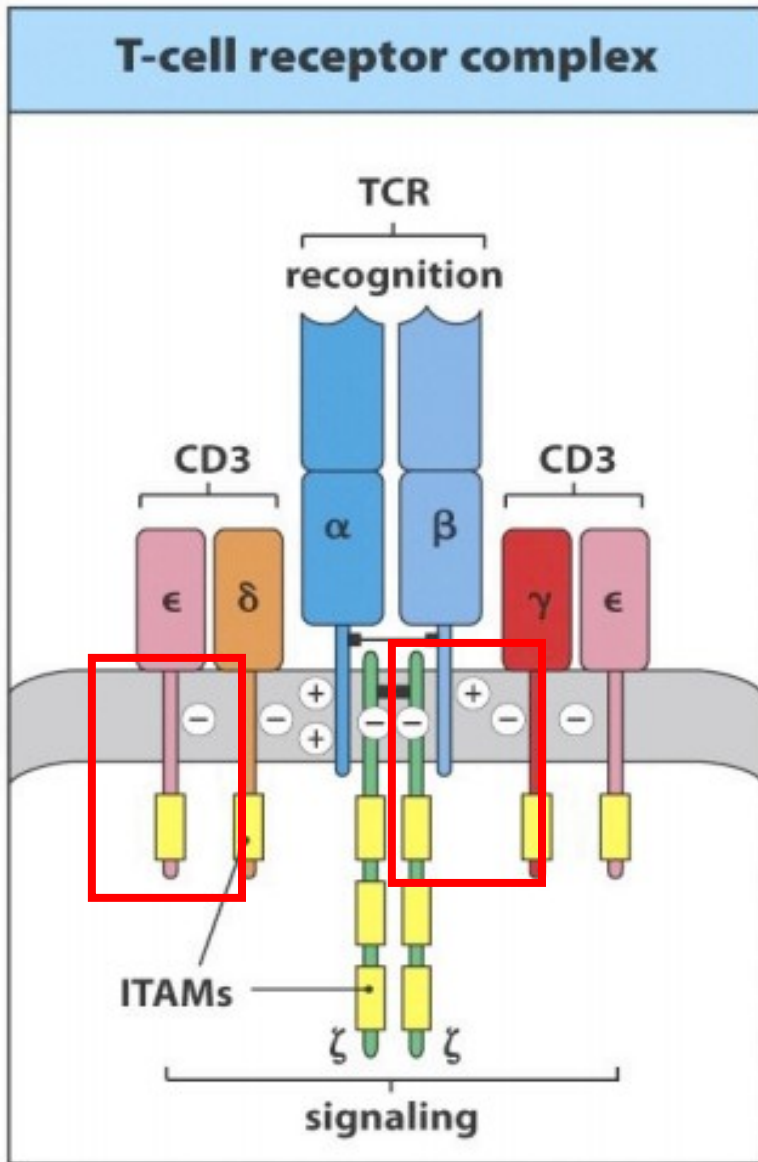


**TCR Complex**  
**TCR  $\alpha\beta/\gamma\delta$  + CD3 ( $\gamma\delta 2\epsilon 2\zeta$ )**

- Variable region binding to antigen: Major Histocompatibility Complex (MHC)

Figure 7.8 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

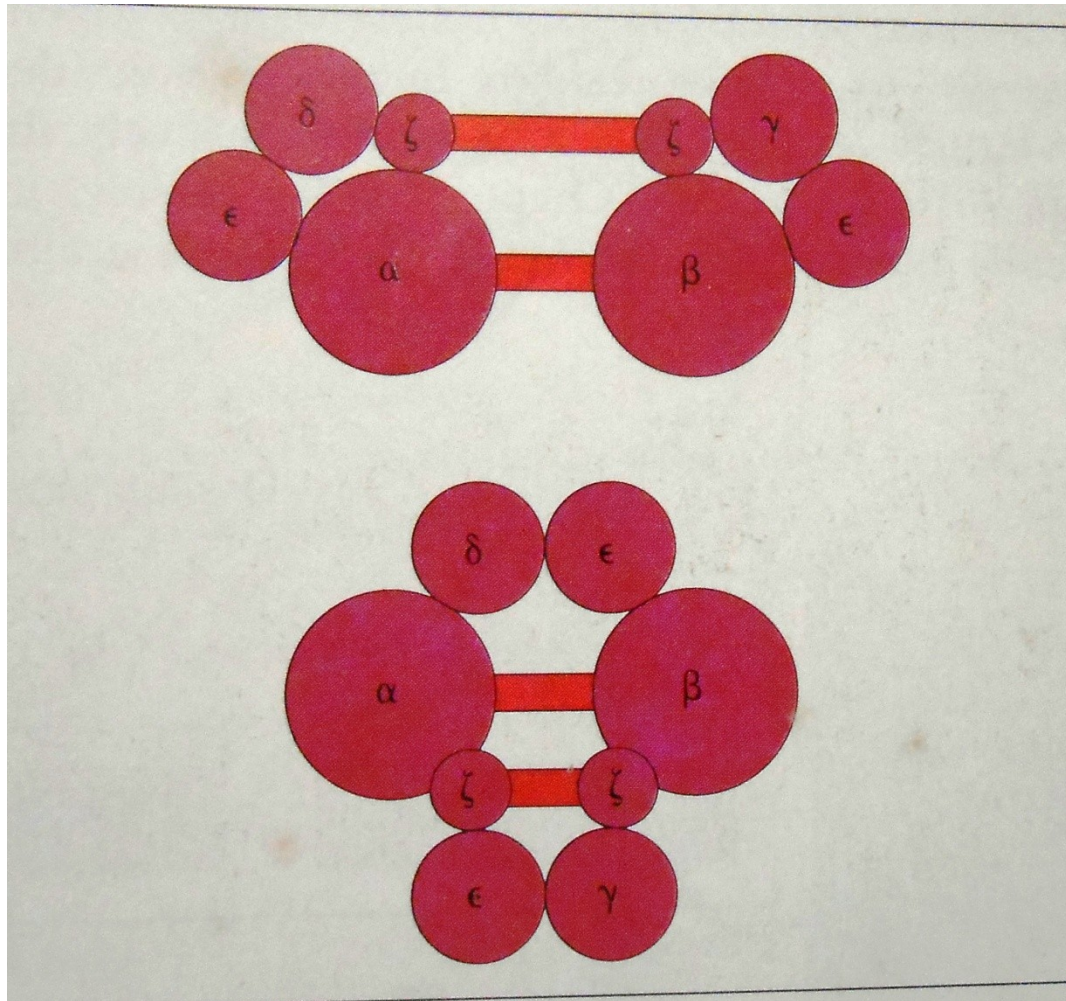
- Each polypeptide has 3 CDRs in the Variable region and Majority of variability in CDR3



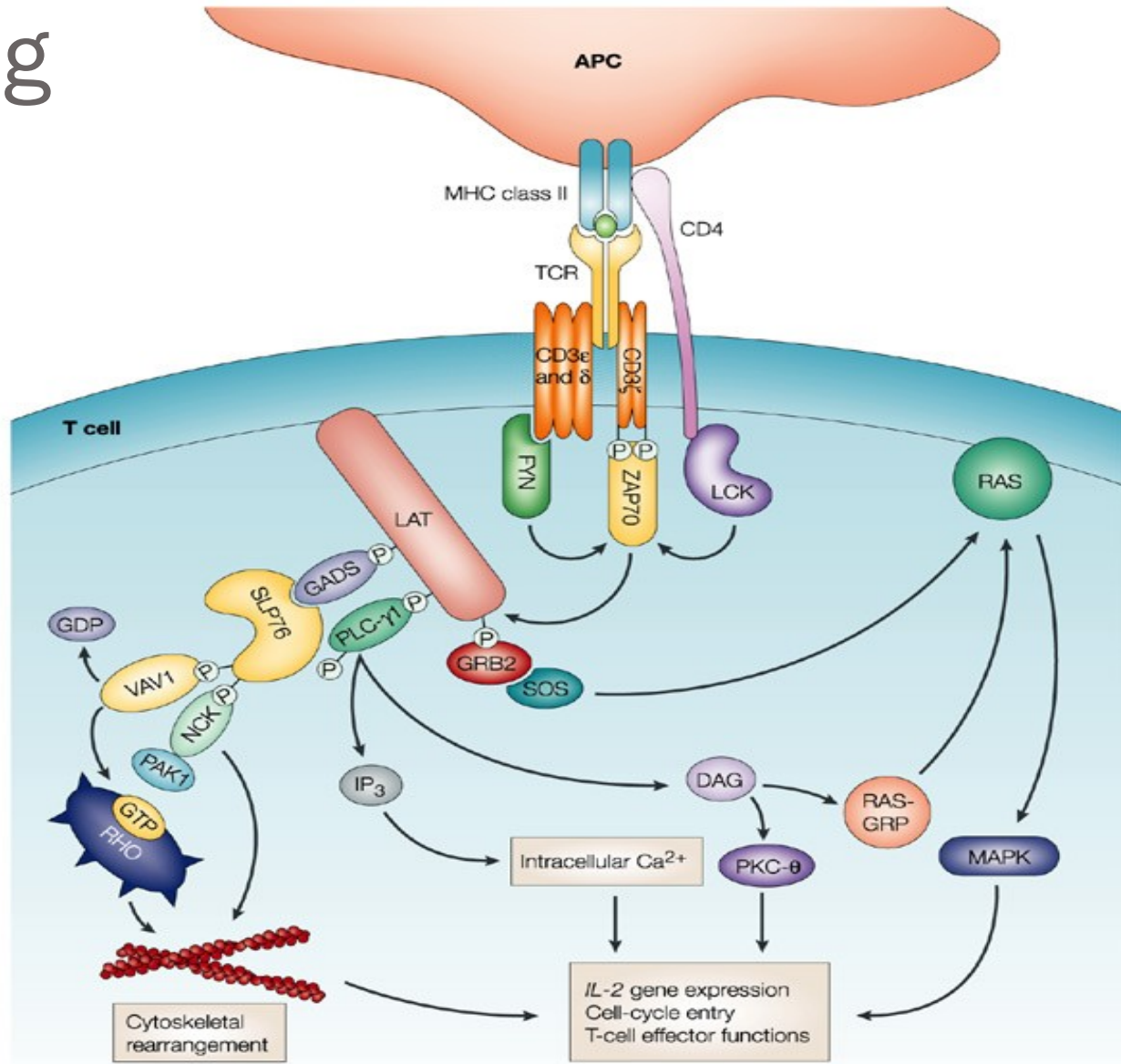
- TcR does NOT actually do any intracellular signaling by itself:
- The **CD3 complex** helps to take the signal from the **TcR** into the cell
- Monomeric  $\gamma$ ,  $\delta$ , and  $\epsilon$  chains
- $\zeta_2$  homodimer or  $\zeta\eta$  heterodimer
- Transmembrane proteins

Figure 7.8 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

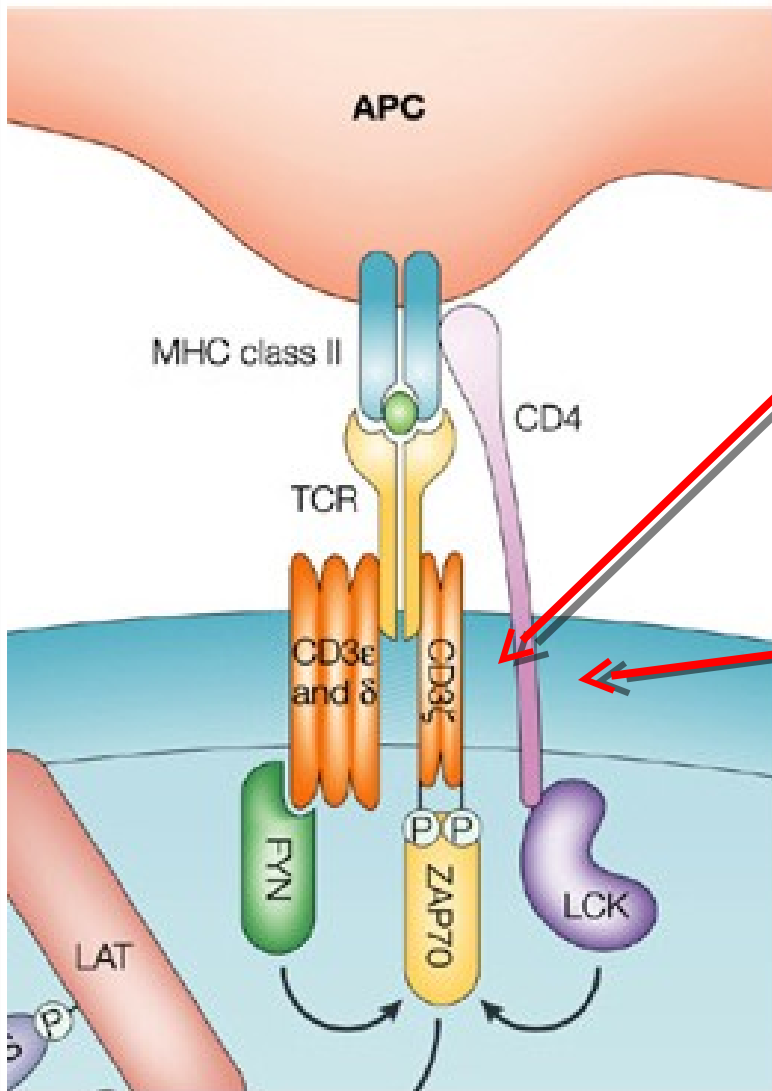
# Molecular arrangements of the TCR-CD3 Complex



# Signalling



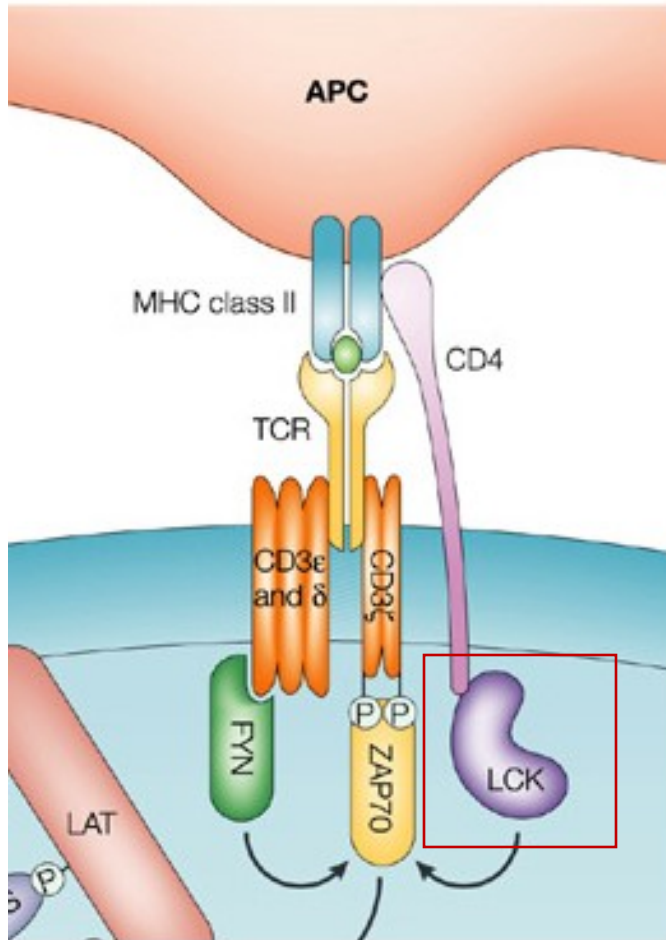
# Signalling



- CD3 (signalling complex) has no kinase activity
- CD4 or CD8 initiates the propagation of the signal



# Signaling

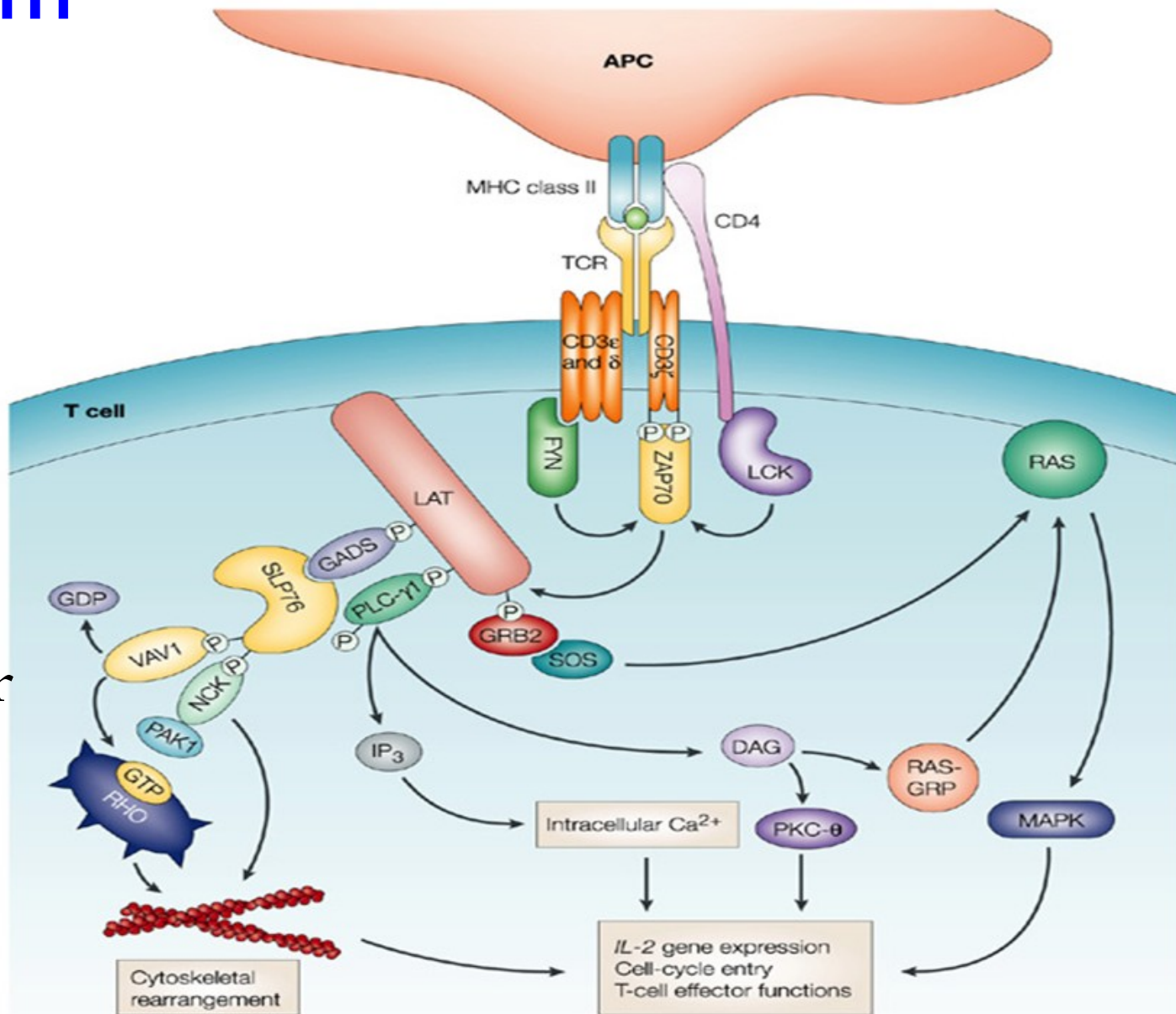


- Interaction of CD4/CD8 with MHCII/MHCI activates src-family protein tyrosine kinases (e.g. LCK)
- LCK phosphorylates immunoreceptor tyrosine activation motifs (ITAM) on the intracellular domain of the CD3 complex



# Signalling

- ITAM serves as docking site for other kinases
- Intracellular signalling cascade

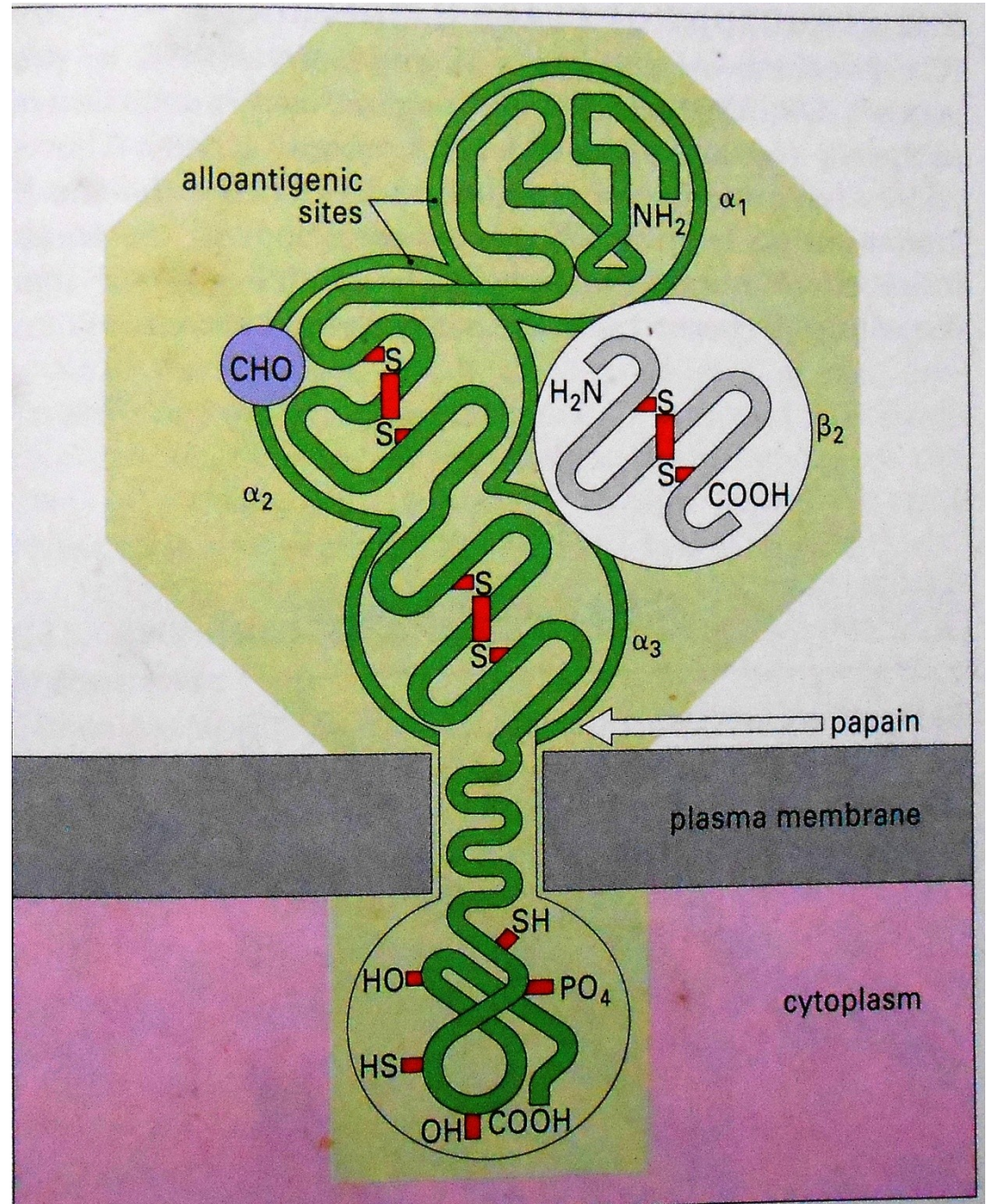


# Summary

- T-Cell Receptor Structure
  - Heterodimer consisting of **Alpha and Beta-chains** with **variable** and **constant regions**
  - The TCR is responsible for keeping the Antigen Presenting Cell in proximity. Signal transduction is done **co-receptors**.
  - Variable region is responsible for MHC-I/II interaction, it contains the **complementary determining regions** (CDR)

# MHC

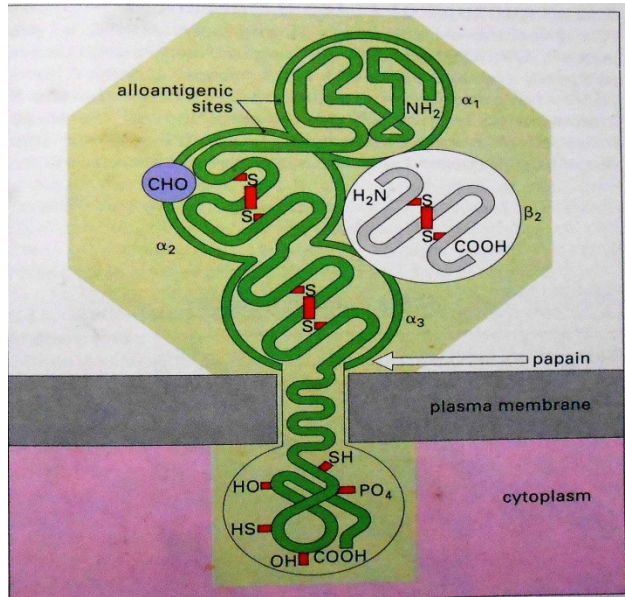
## The Major Histocompatibility Complex





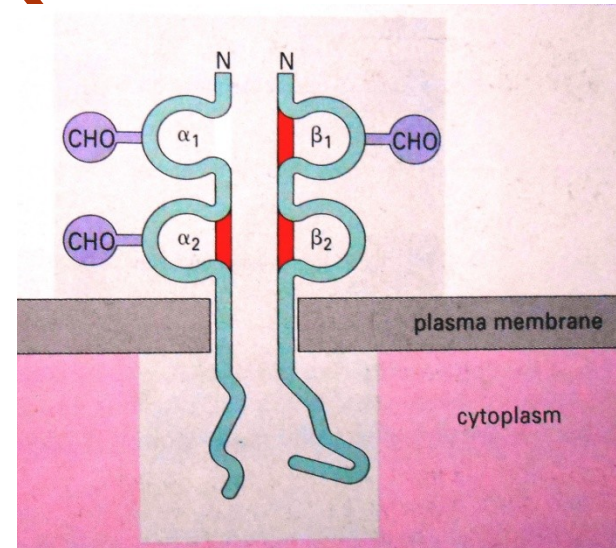
# MHC

## The Major Histocompatibility Complex



**Class I**

**Molecules (MHC I)**



**Class II**

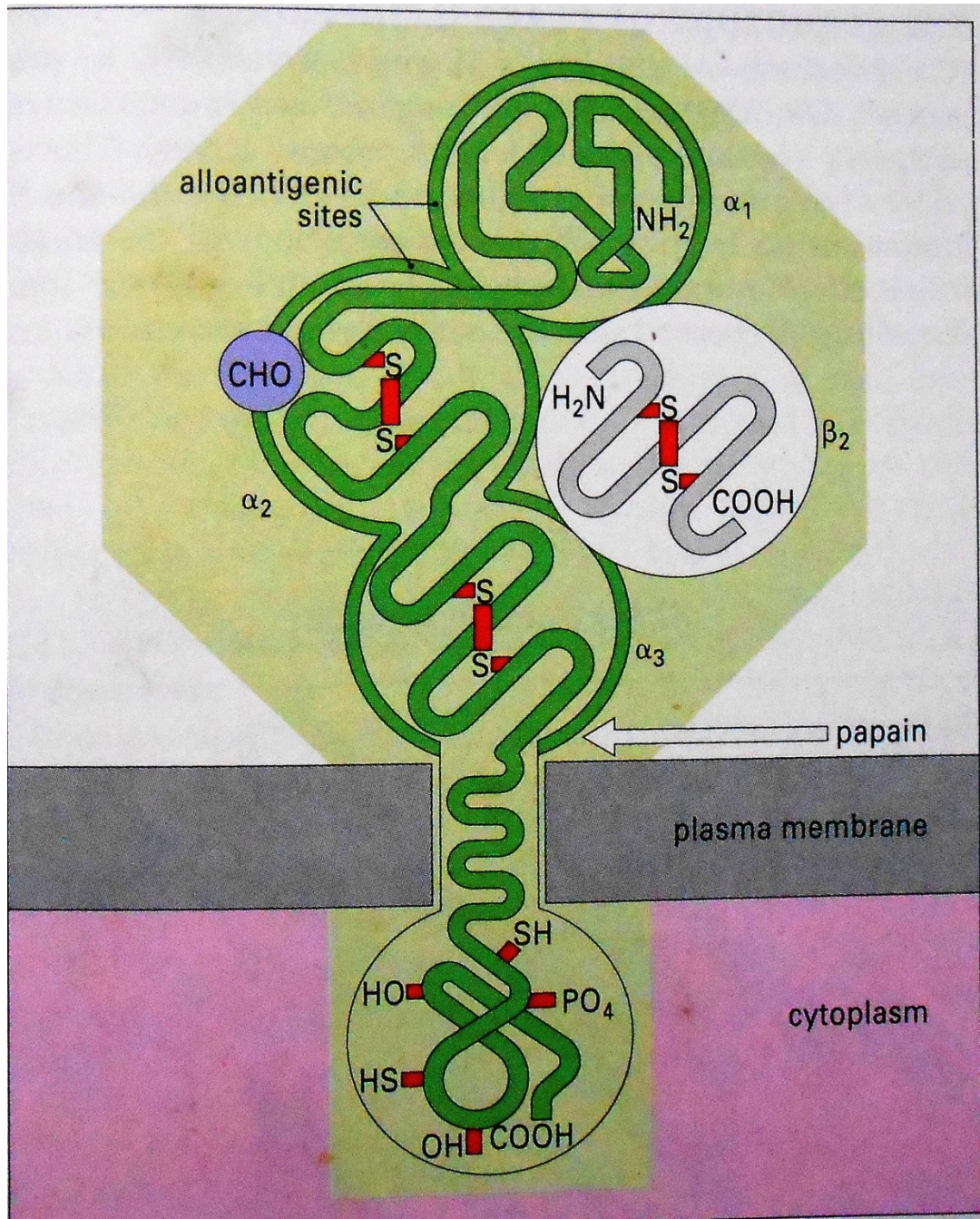
**Molecules (MHC II)**

# MHC class I antigen

It has 3 globular domains  $\alpha 1$ ,  $\alpha 2$  and  $\alpha 3$ .

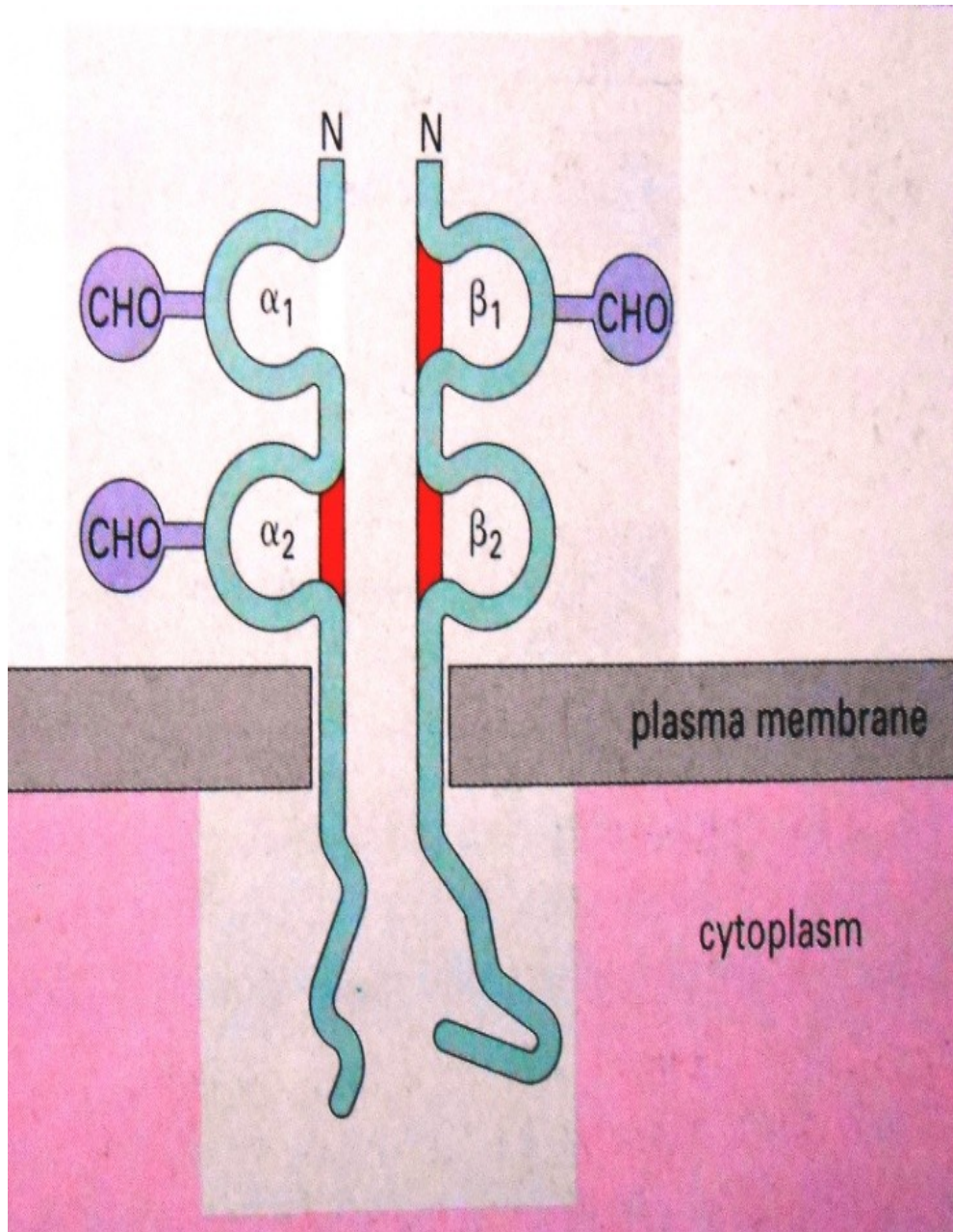
The  $\alpha 3$  domain is associated with **non-MHC-encoded peptide  $\beta 2$ -microglobulin** stabilized by S-S bond.

The  $\alpha 1$  and  $\alpha 2$  domains bind alloantigens and present to the T cells.





# MHC class II antigen



Consists of two non-identical peptides ( $\alpha$  &  $\beta$ ).

It peptide has 2 extracellular globular domains  $\alpha_1$ ,  $\alpha_2$  and  $\beta_1$ ,  $\beta_2$  respectively.

Each peptide has short cytoplasmic tails.

Except the  $\alpha_1$  other domains are stabilized by intrachain S-S bonds.

The  $\beta$  chain has the alloantigenic site.



# How T cells Work?