

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 $\gamma\delta$

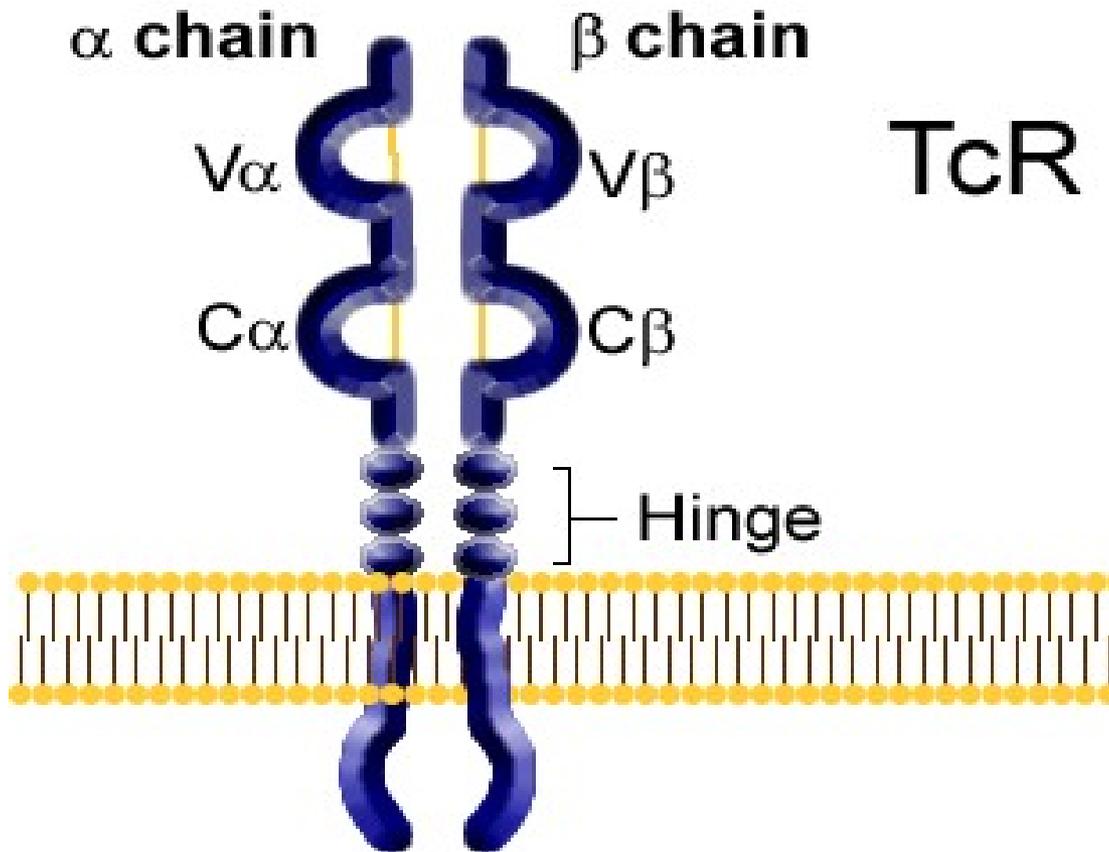
T cell Receptors are heterodimers

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

TCR 1
 $\gamma\delta$ TCR

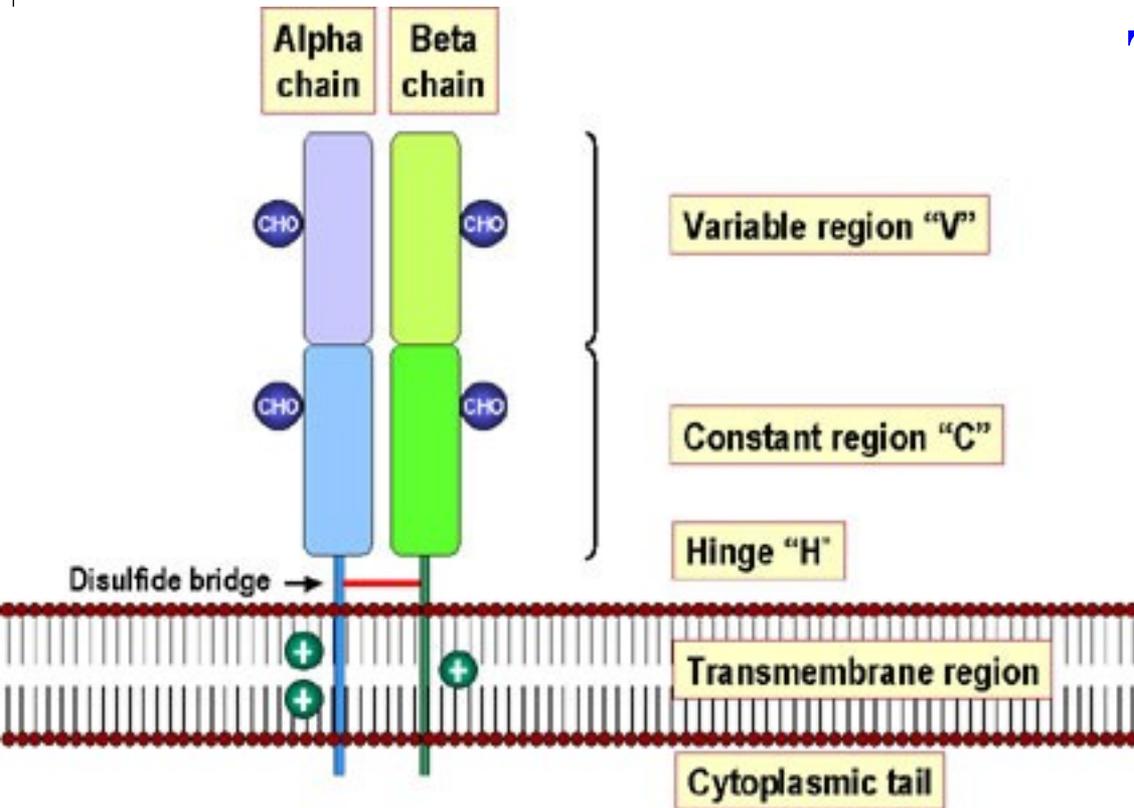
TCR 2
 $\alpha\beta$ TCR

The $\alpha\beta$ TCR

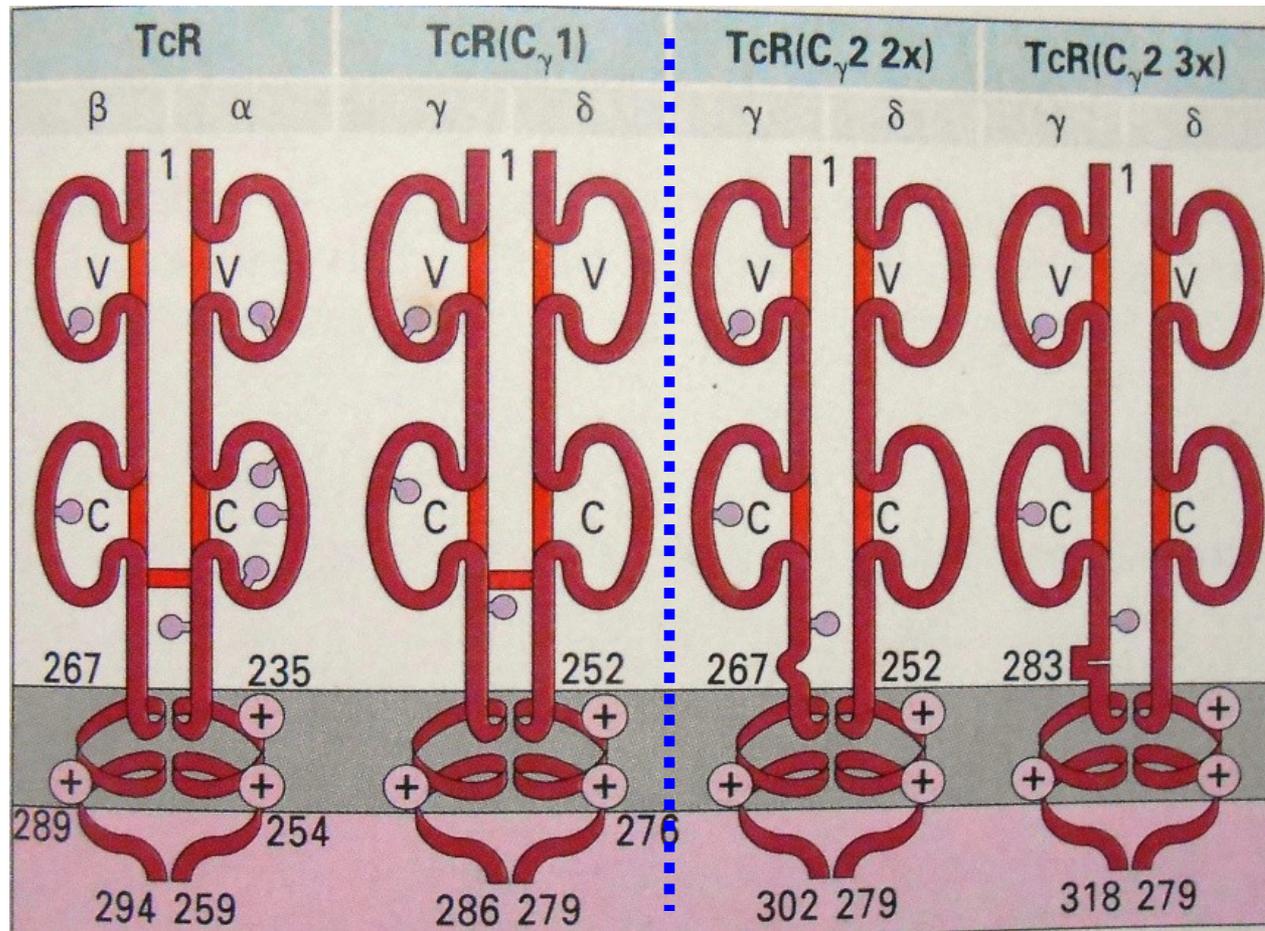


The TCR α and β chains comprise two external immunoglobulin-like domains (V and C)

Structure of T-Cell Receptor

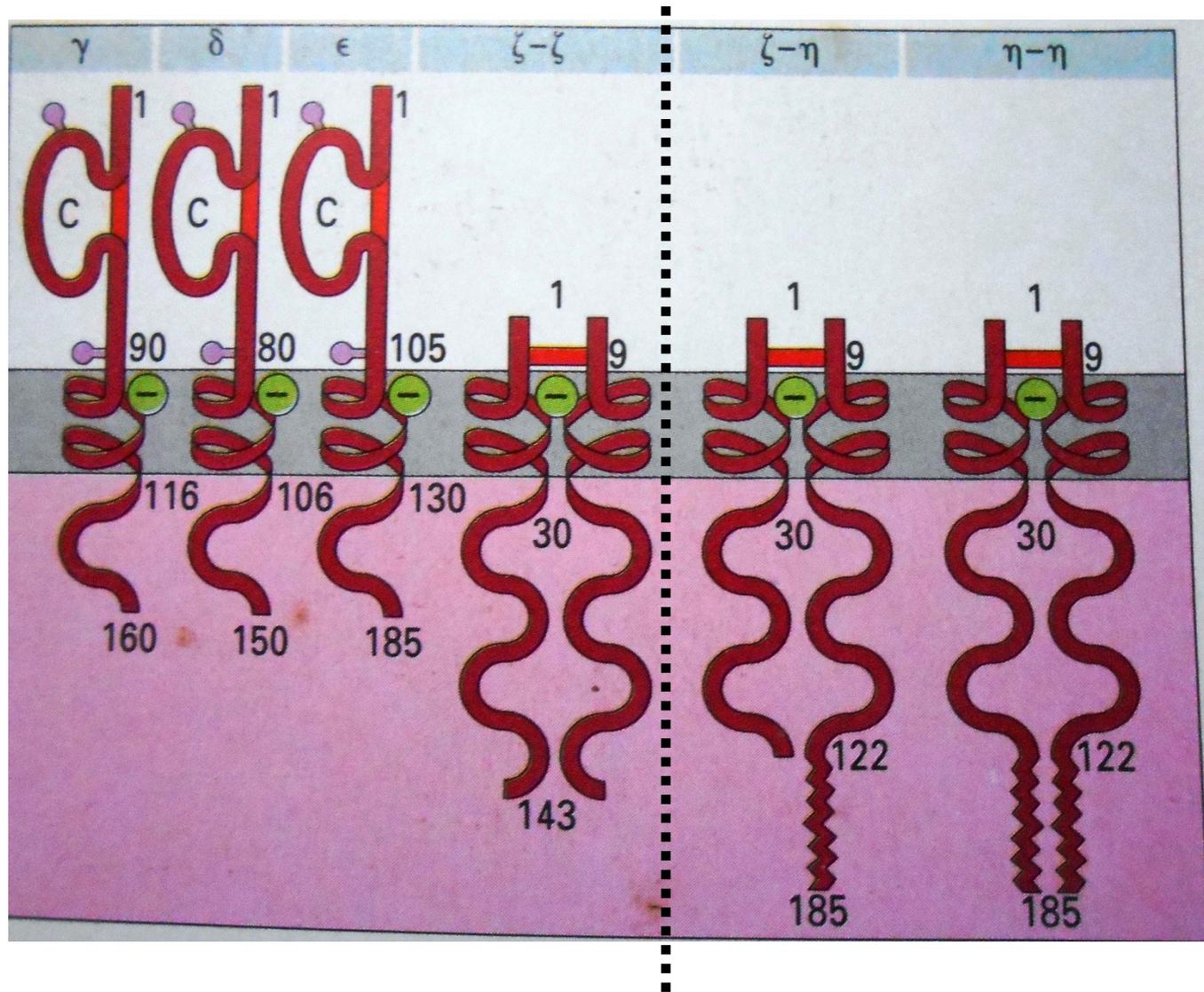


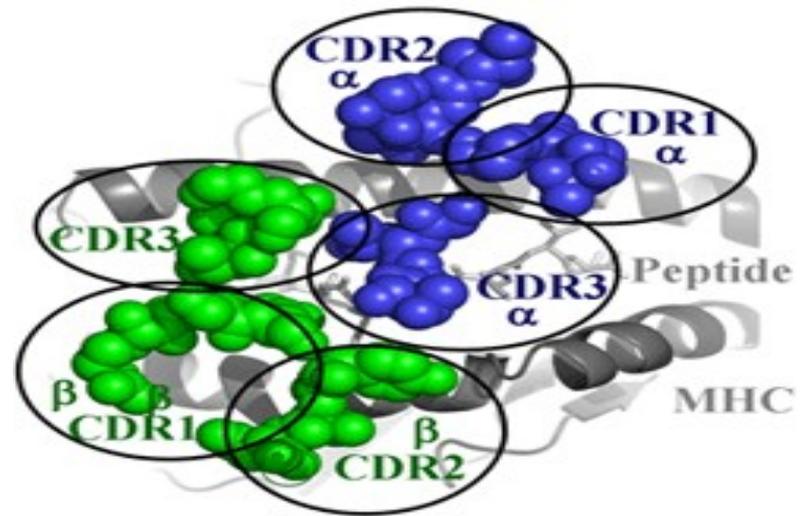
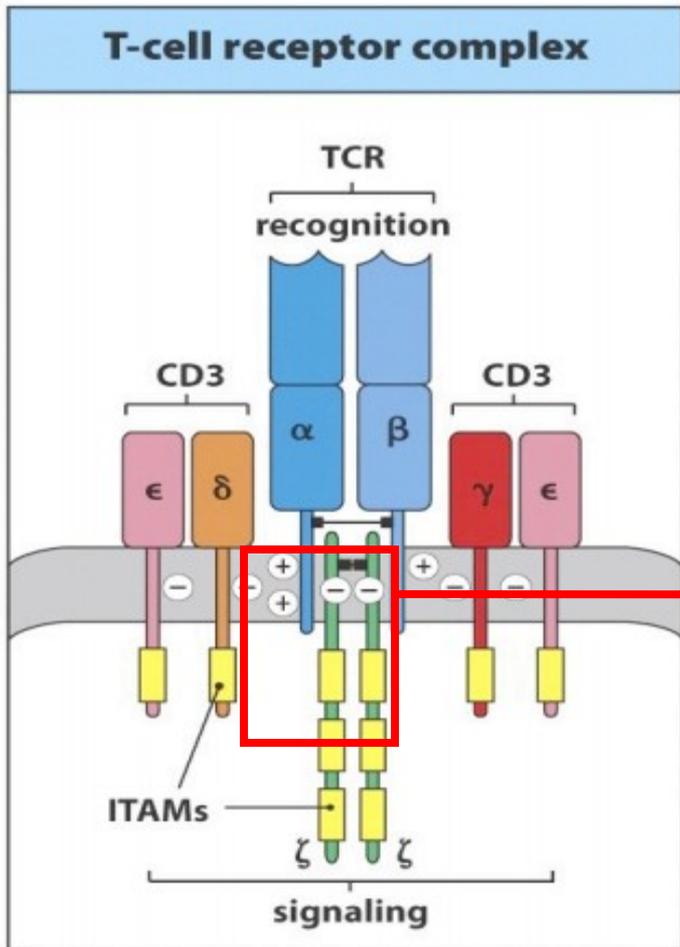
The transmembrane segment contains two (α) and one (β) positively charged residues and a short cytoplasmic tail. The α and β chains are disulphide linked.



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

The CD3 Molecule



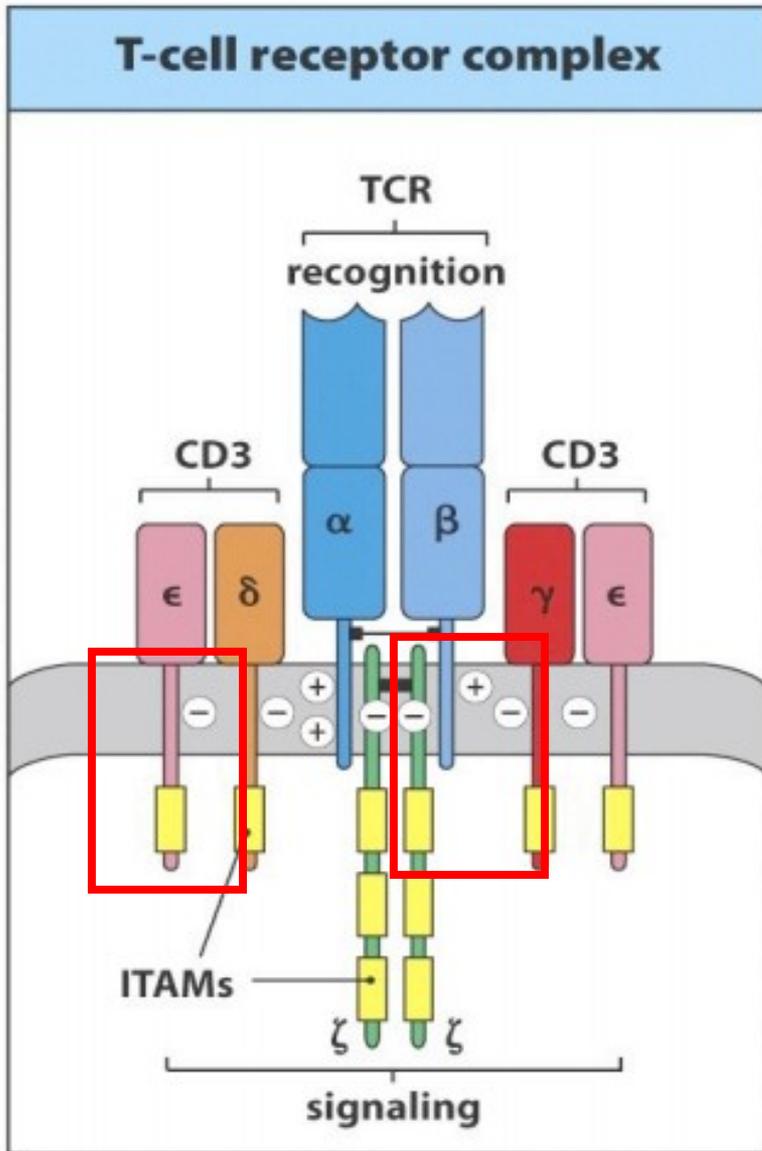


TCR Complex
TCR $\alpha\beta/\gamma\delta$ + CD3 ($\gamma\delta 2\epsilon 2\zeta$)

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

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

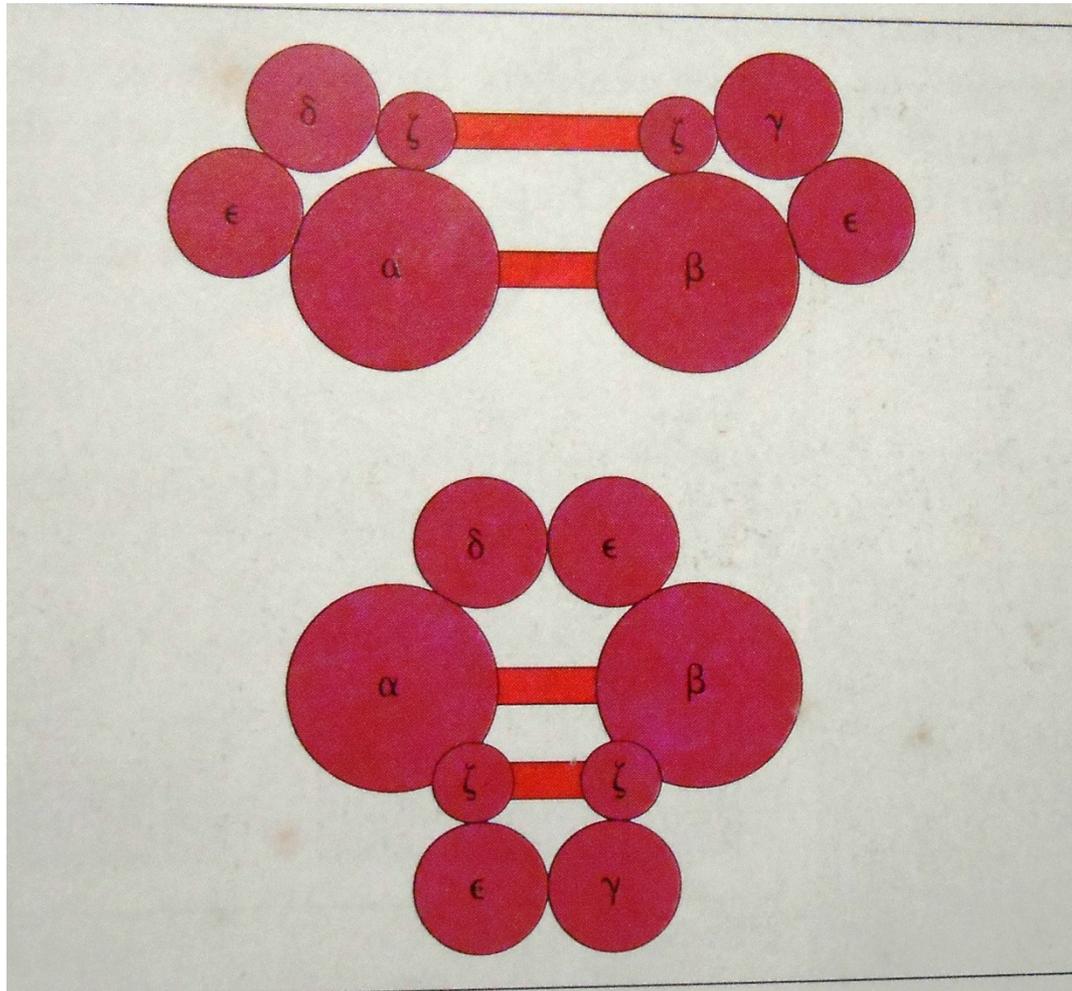
- Each polypeptide has 3 CDRs in the Variable region and Majority of variability in CDR3



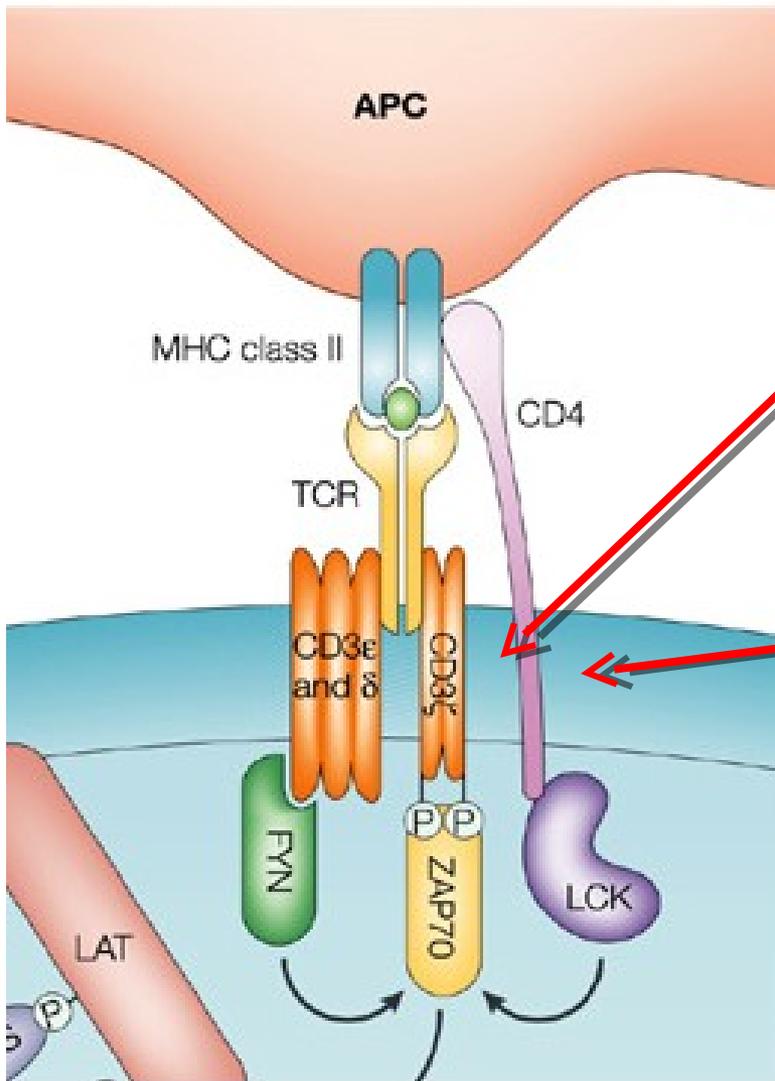
- TcR does NOT actually do any intracellular signaling by itself:
- The **CD3 complex** helps to take the signal from the **TcR** into the cell
- Monomeric γ , δ , and ϵ chains
- ζ_2 homodimer or $\zeta\eta$ heterodimer
- Transmembrane proteins

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

Molecular arrangements of the TCR-CD3 Complex

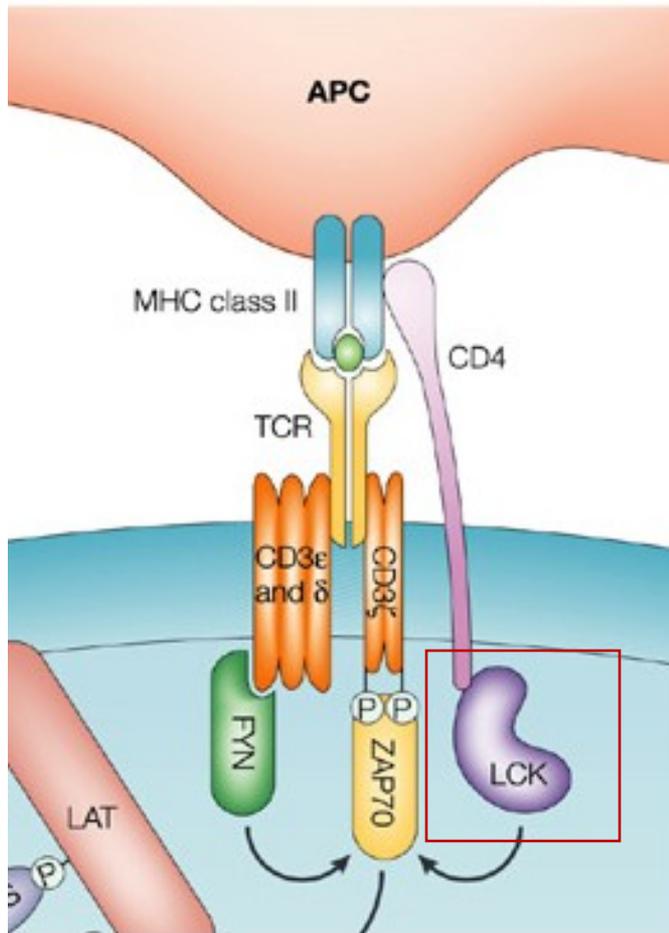


Signalling



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

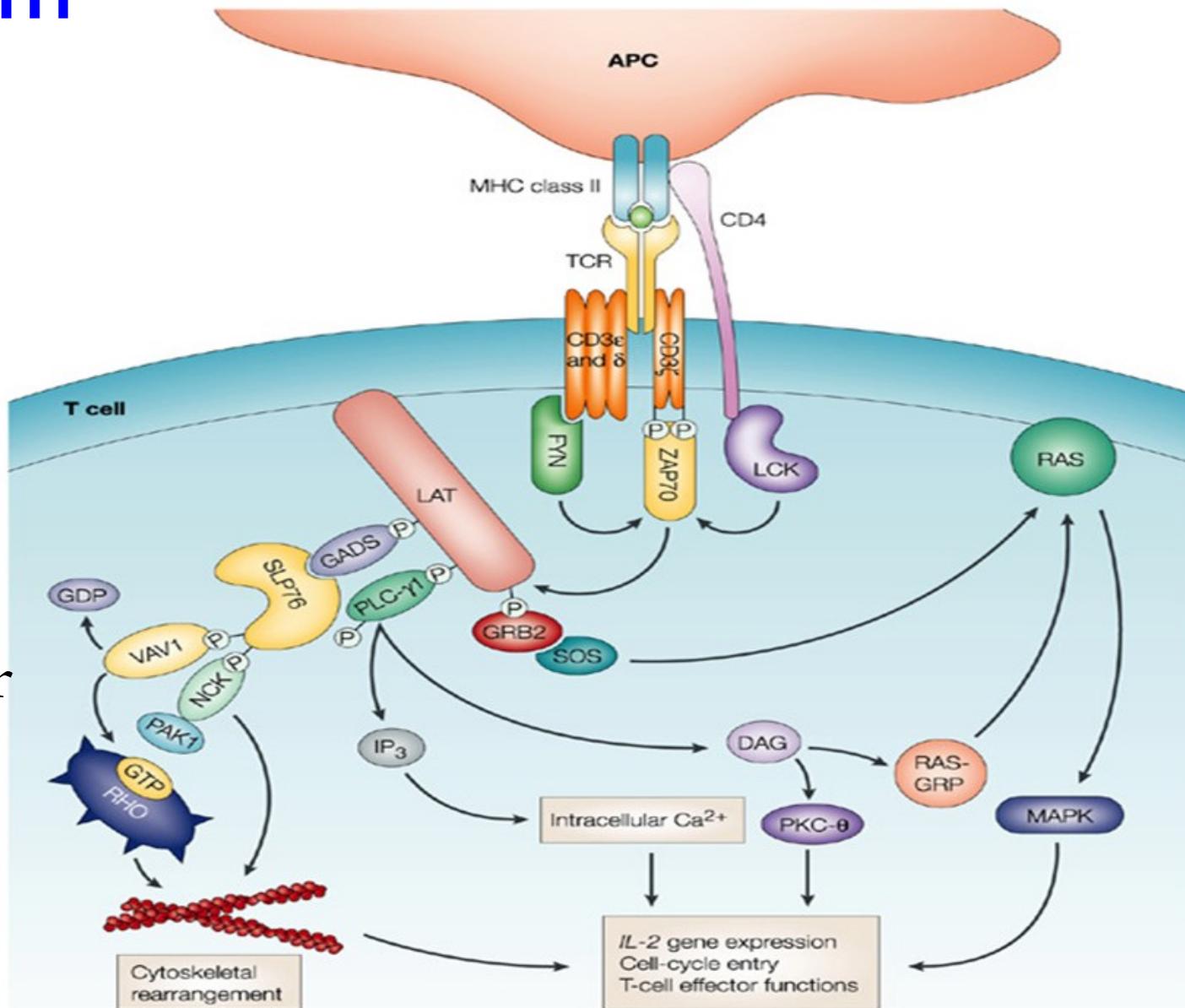
Signaling



- 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

Signaling

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

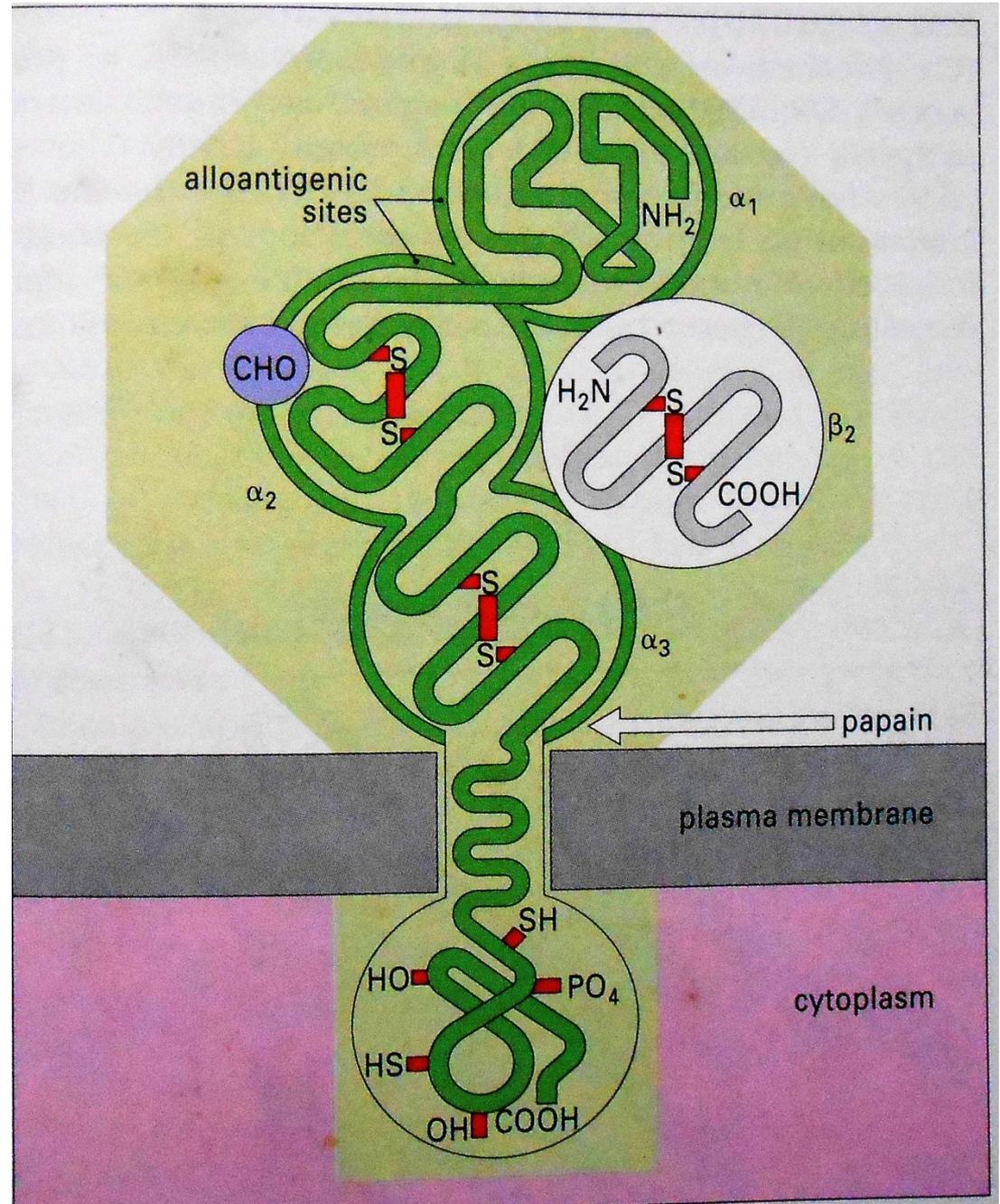


Summary

- 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)

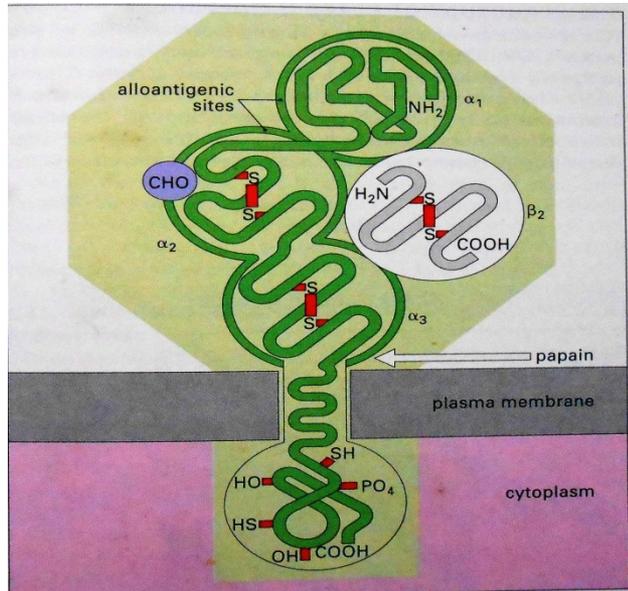
MHC

The Major Histocompatibility Complex



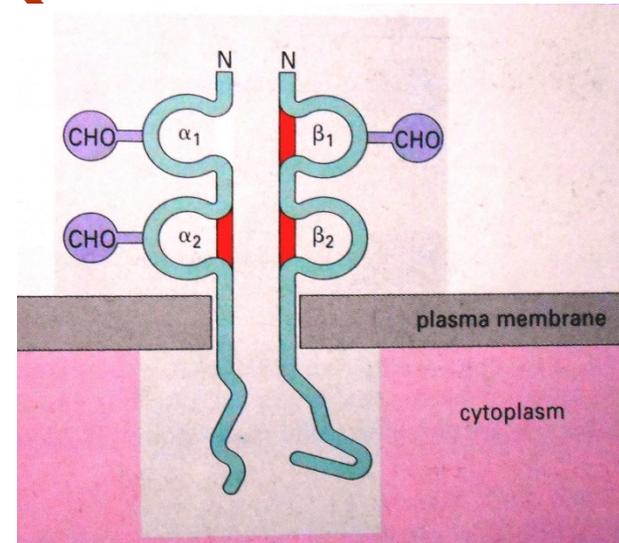
MHC

The Major Histocompatibility Complex



Class I

Molecules (MHC I)



Class II

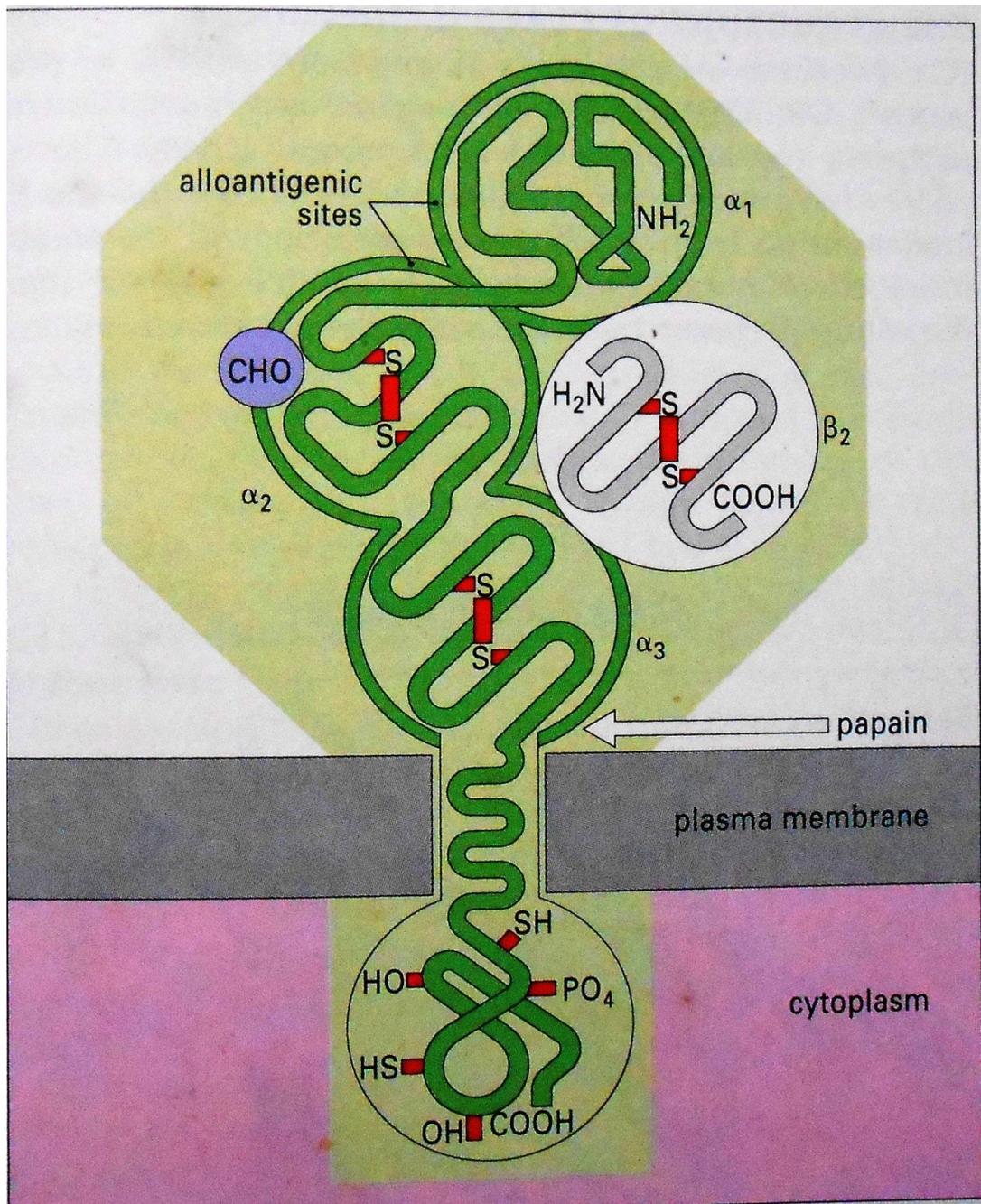
Molecules (MHC II)

MHC class I antigen

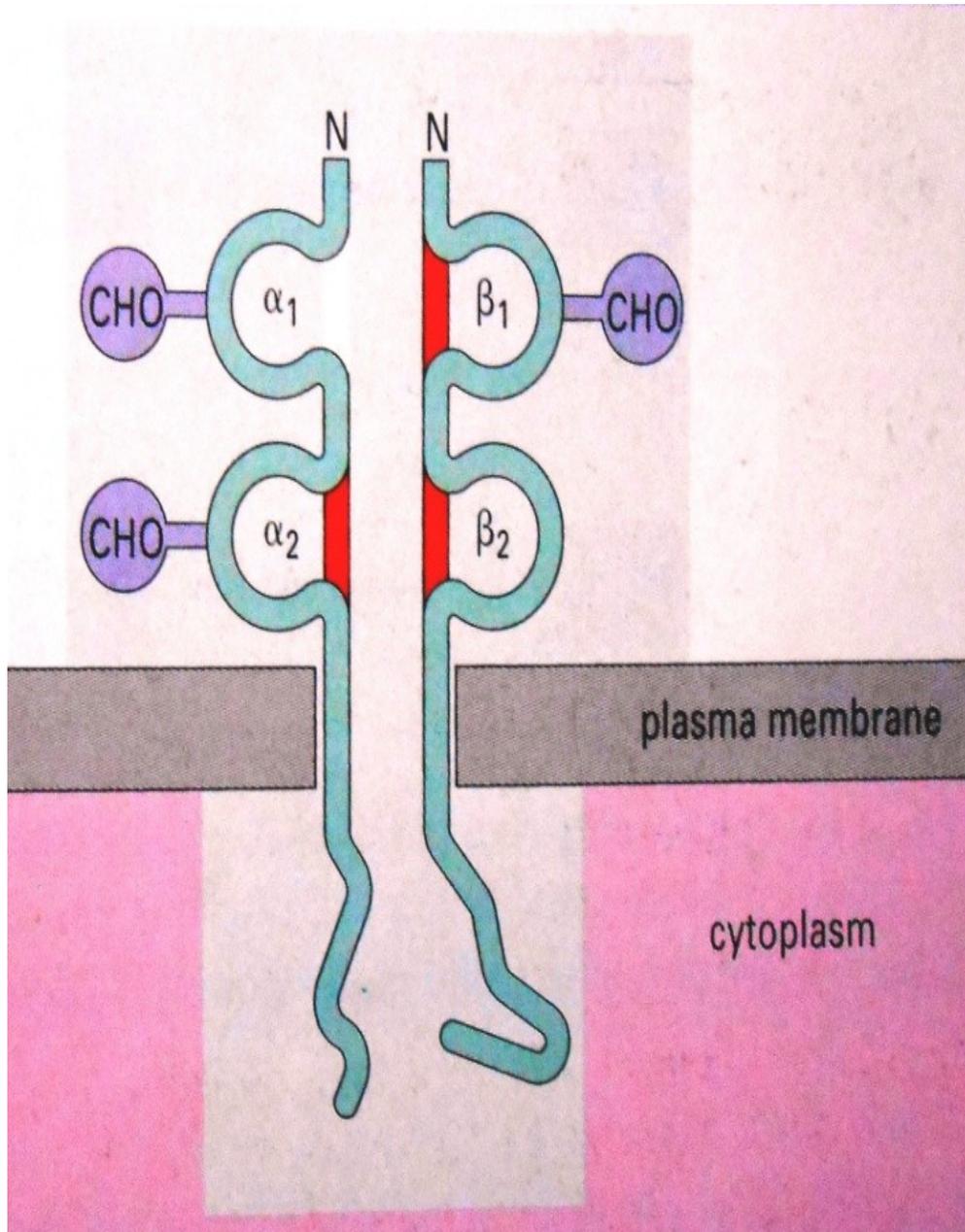
It has 3 globular domains $\alpha 1$, $\alpha 2$ and $\alpha 3$.

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 (α & β).

It peptide has 2 extracellular globular domains $\alpha 1$, $\alpha 2$ and $\beta 1$, $\beta 1$ respectively.

Each peptide has short cytoplasmic tails.

Except the $\alpha 1$ other domains are stabilized by intrachain S-S bonds.

The β chain has the alloantigenic site.

How T cells Work?