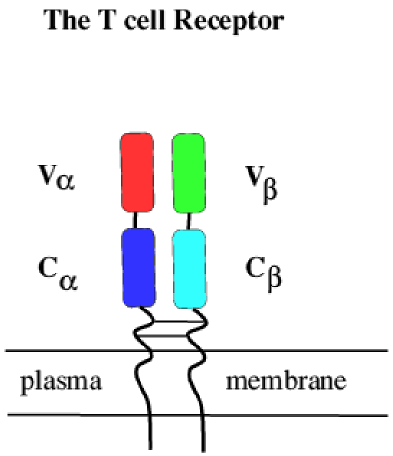
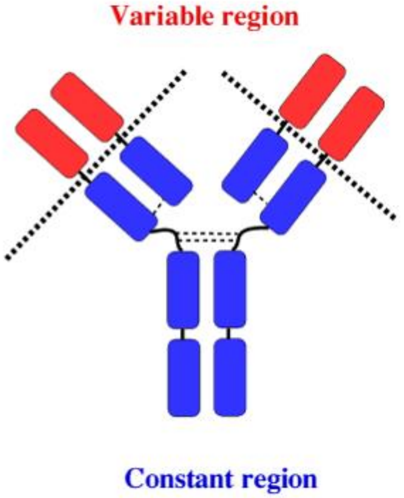
T cell receptor (TCR)

Structure of TCR

- Like B lymphocytes, T cells express an **antigen-specific receptor.**
- The **T cell receptor (TCR)** is in fact **very similar to Immunoglobulin.**
- It has 2 paired polypeptide chains both of which have constant and variable portions and both of which are composed of Ig-like domains.

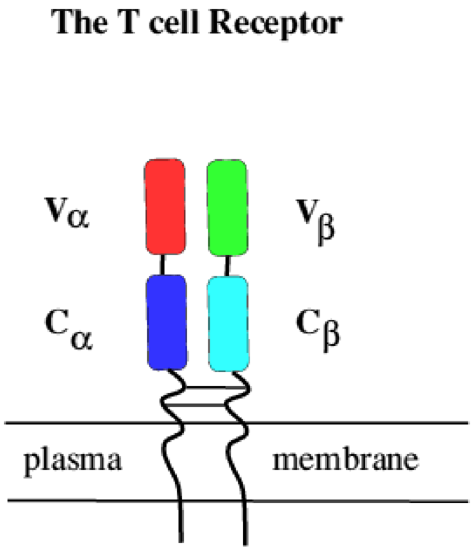


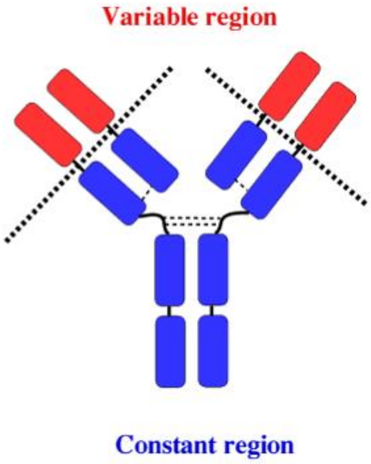


Two important differences are:

a) TCR is **monovalent**

b) It **exists only as a cell surface receptor** and has no counterpart to secreted antibody.

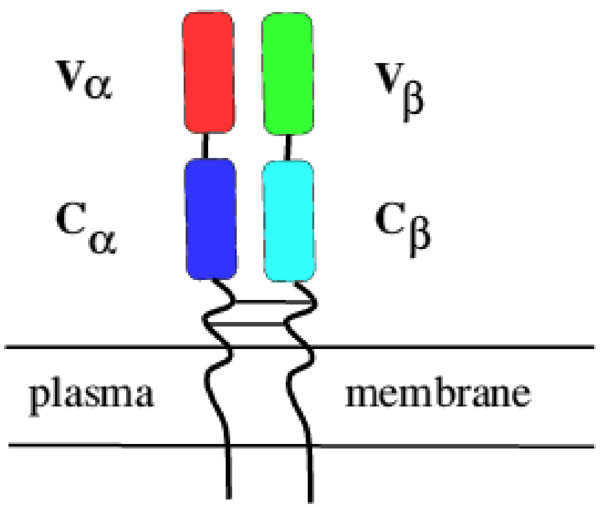




- TCRs are usually heterodimers of **α** and **β** chains or **γ** and **δ** chains

- Each chain has **variable** and **constant** domains.

The T cell Receptor



Variable domain:

It contains sequence variation (**3 CDRs** in **Vα** and **Vβ**).

Constant domain (with the short connecting sequence):

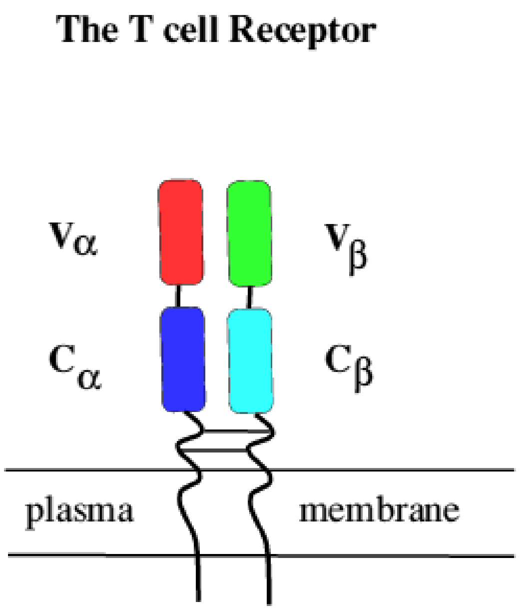
Forms a disulfide bond between the two chains

Transmembrane region:

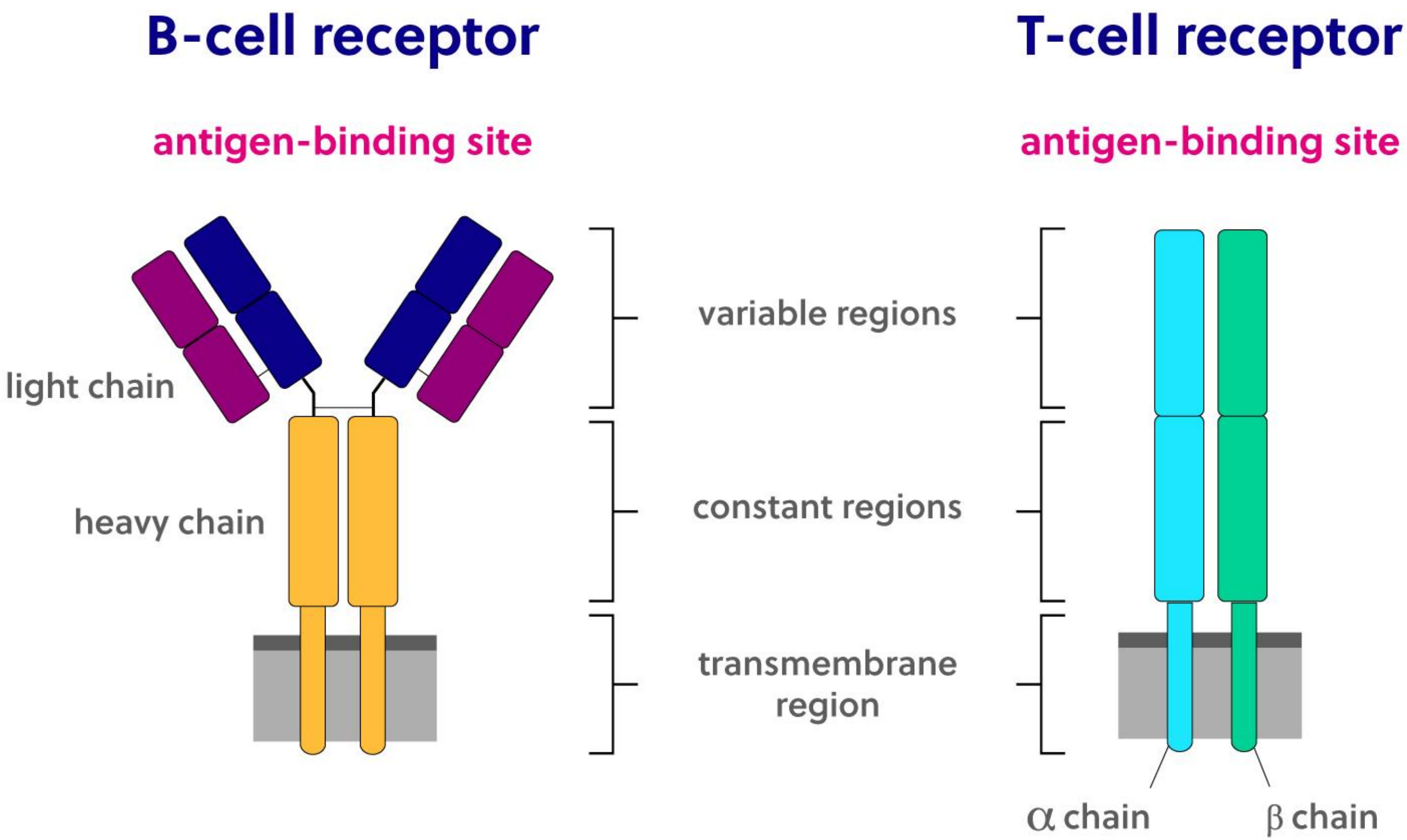
Site of interaction with **CD3**
(signal transducing complex)

Cytoplasmic tail:

5-12 aa at COOH end



Structure of T cell and B cell receptors



Specific characteristics of TCRs

αβ TCR

- Prototype T cells are **α β** T cells and form 90% of T cells.
  - **αβ TCR** interacts with **MHC** in **peptide-MHC complex** on APC cells and target cells.
  - Activated cells **proliferate**.
  - T cells with **high affinity receptors** are selected for the cell-mediated immune response.

γ δ TCRs

- There is another type….. **γ δ** T cells.
- These cells recognize antigens **not presented by MHC** (usually lipids).

  Example: phospholipid antigens on bacteria and parasites

- They secrete **cytokines** and **recruit αβ T cells.**

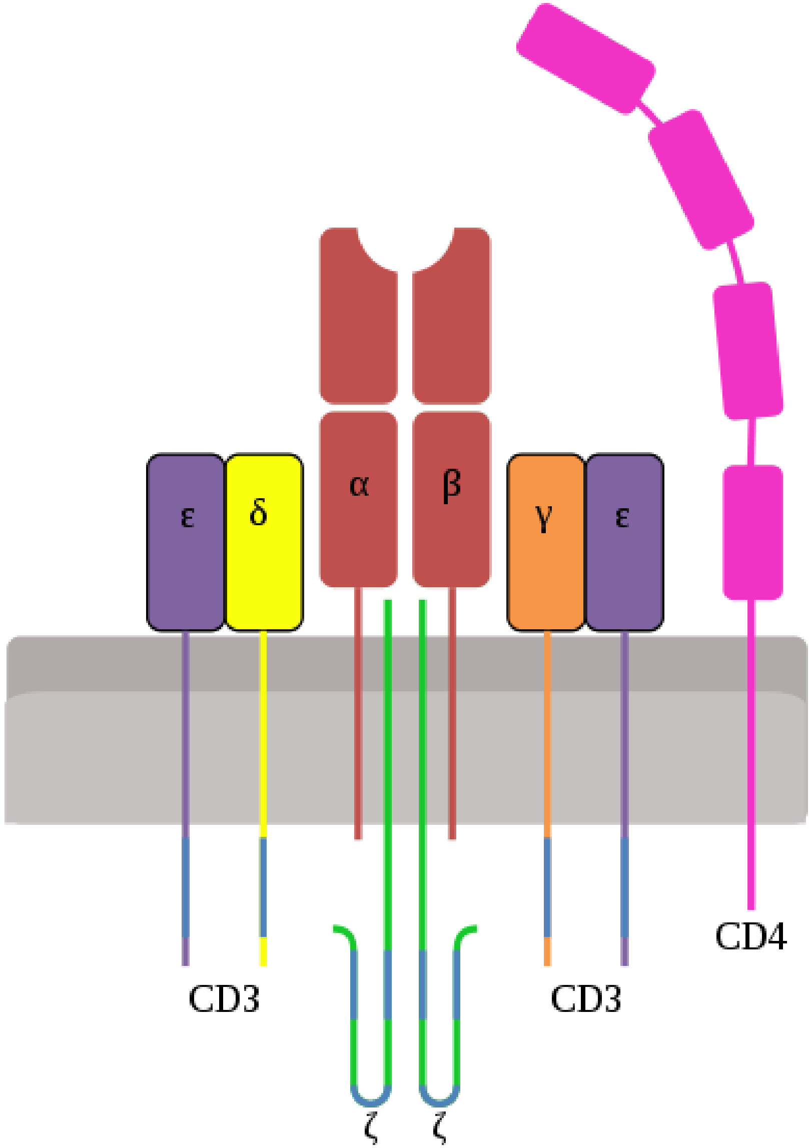
CD3 (signal transducing complex)

Expression and function of TCR requires **CD3 (signal transducing complex)**

This includes:

- Two **epsilon (€)** chains
- One **gamma (γ)** chain
- One **delta (δ)** chain

There are two **zeta (ζ)** chains also which are **not part** of TCR or CD3 but help them in their function.


α
β
ε
δ
γ
ε
CD3
CD3
CD4
ζ
ζ

Self-MHC restriction

- T cells activation is **specific** for **antigen plus MHC** and **not antigen alone.**

- T cells recognize antigen only when it is presented by a **self-MHC molecule**.

- This phenomenon is called **self-MHC restriction.**

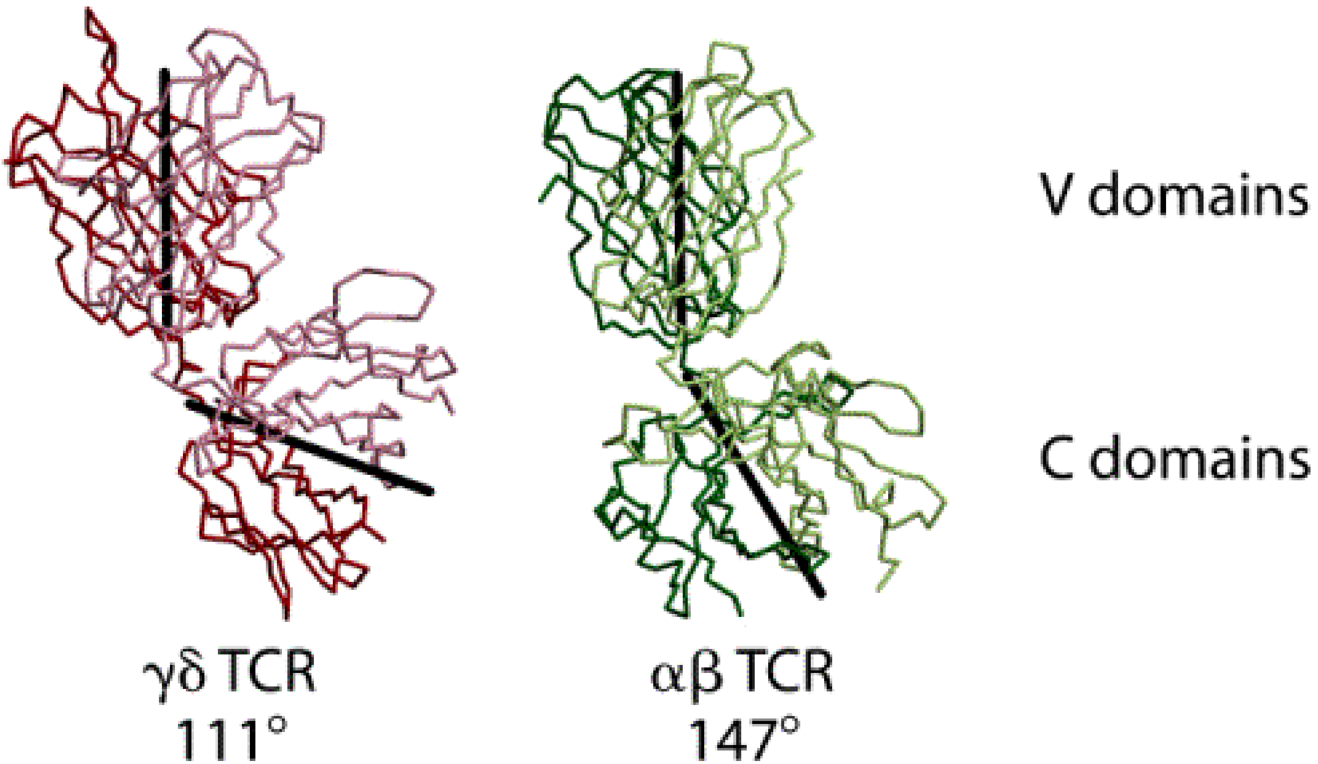
- **Self-MHC restriction** is mandatory for **α β** T cells (not mandatory in B cells).

Comparison of αβ TCR and γδ TCR

- **αβ TCR** and **γδ TCR** exhibit **different elbow angles** between the long axis of the variable and constant regions.

- It influences the interaction with **co-receptors** and results in **intracellular signaling differences**.

γδ TCR forms a **deep cleft** on the surface of the molecule where phospholipid can bind directly (no MHC presentation is required)



Organization and rearrangement of TCR Genes

In both **αβ** and **γδ TCRs,** functional TCR genes are produced by **rearrangement** similar to Ig genes.

The T cell receptor complex

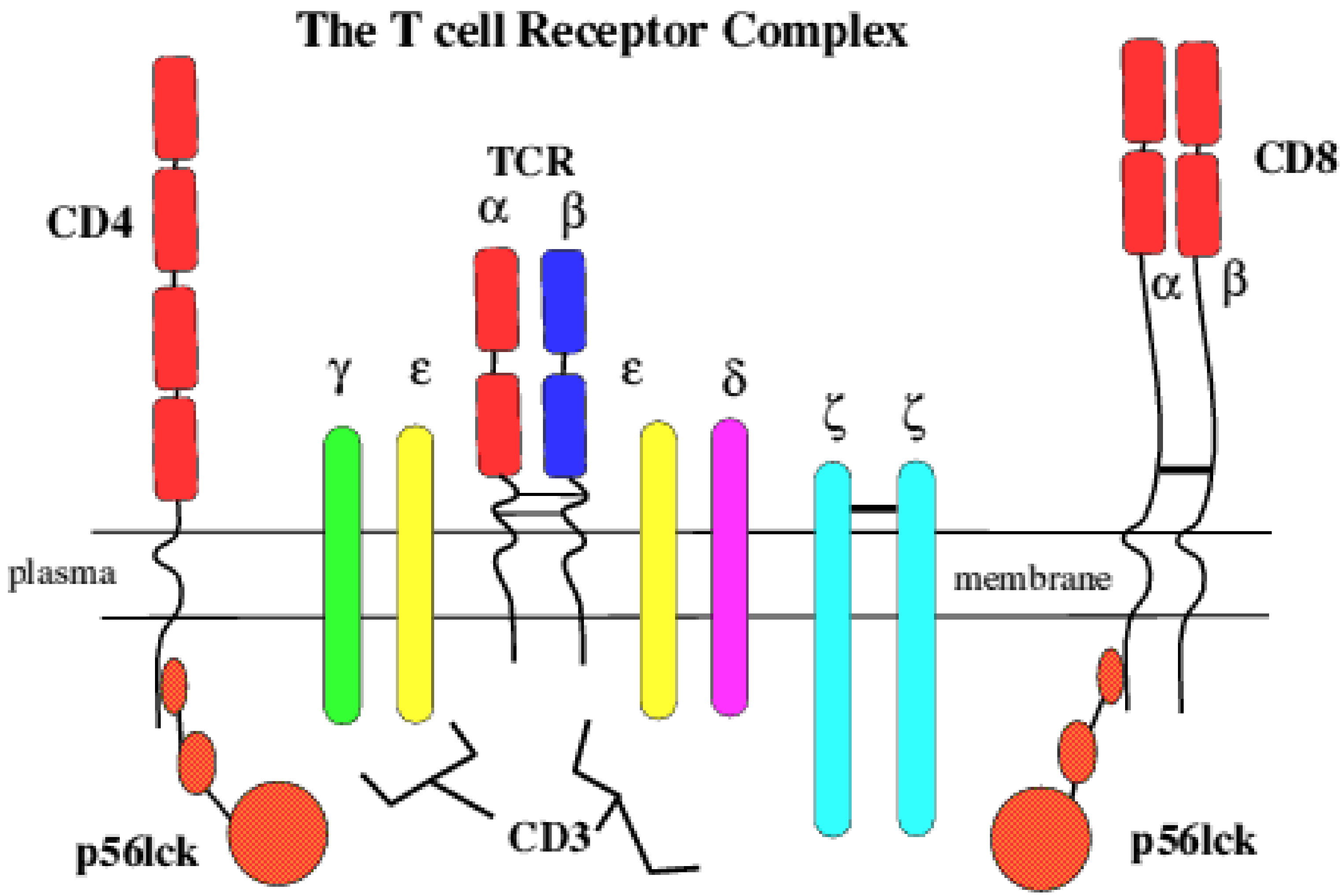
- The **TCR** is part of a complex signaling machinery which includes:

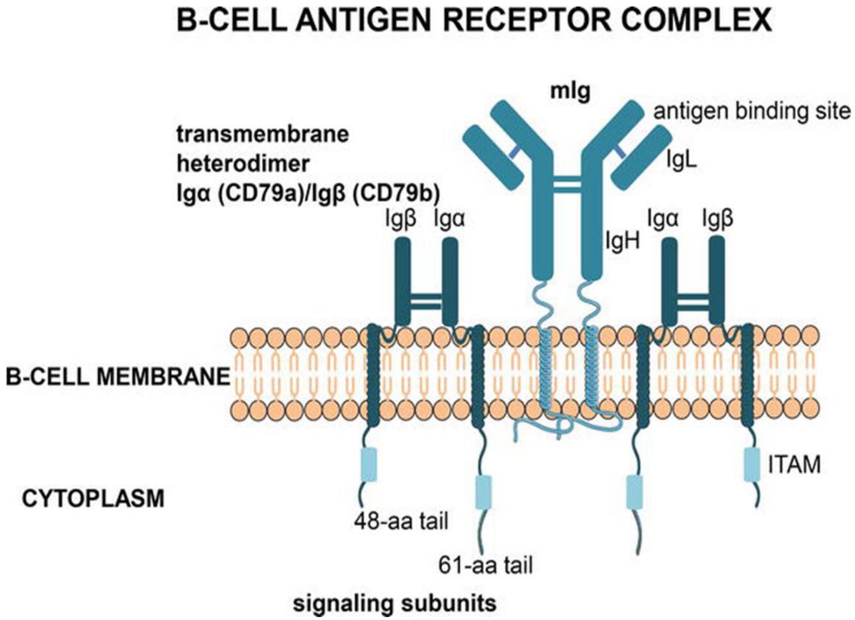
  -- the **TCR αβ dimer**

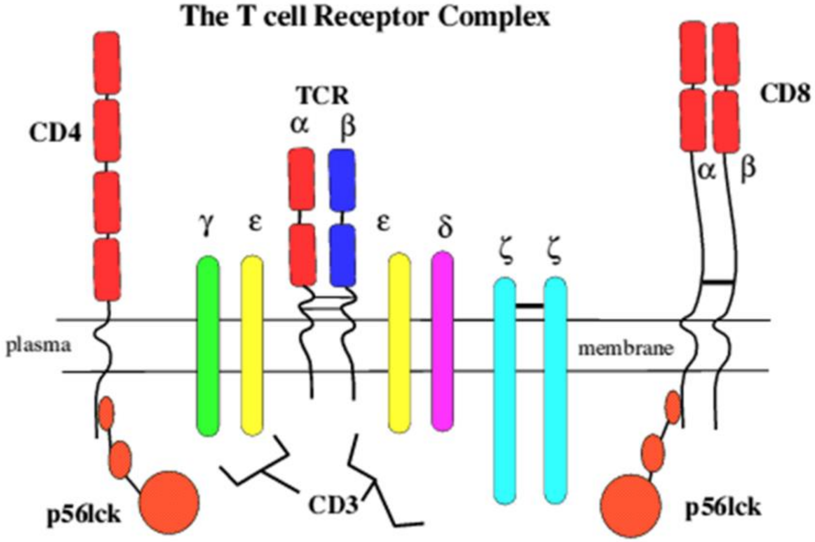
  -- the accessory molecules **CD4** or **CD8**

  -- **CD3** which is a signal transduction module made up of various chains.

  CD3 associates with **αβ** and **γδ TCR**.


The T cell Receptor Complex
CD4
TCR
α β
CD8
α β
γ ε
ε
δ
ζ ζ
plasma
membrane
p56lck
CD3
p56lck





Comparison of B cell receptor complex and T cell receptor complex

T cell accessory membrane molecules

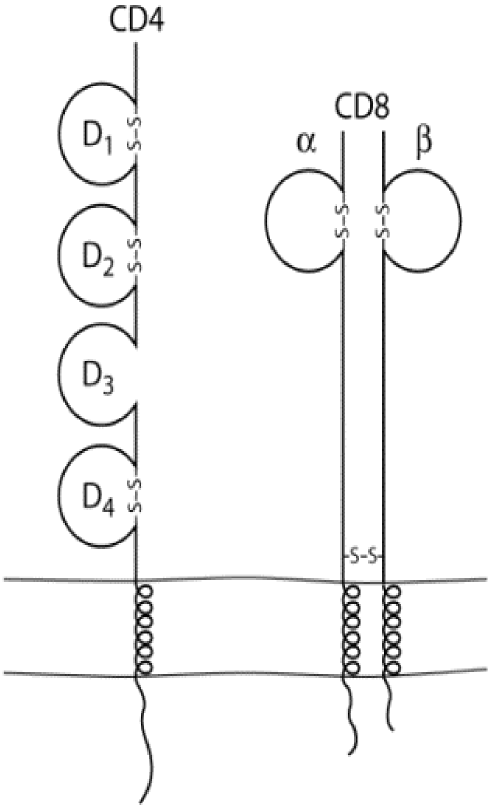
Function:

- Strengthen the **interaction** between **T cells** and **APCs** or target cells.

- **CD4** and **CD8** are important co-receptors for the recognition of **peptide-MHC.**

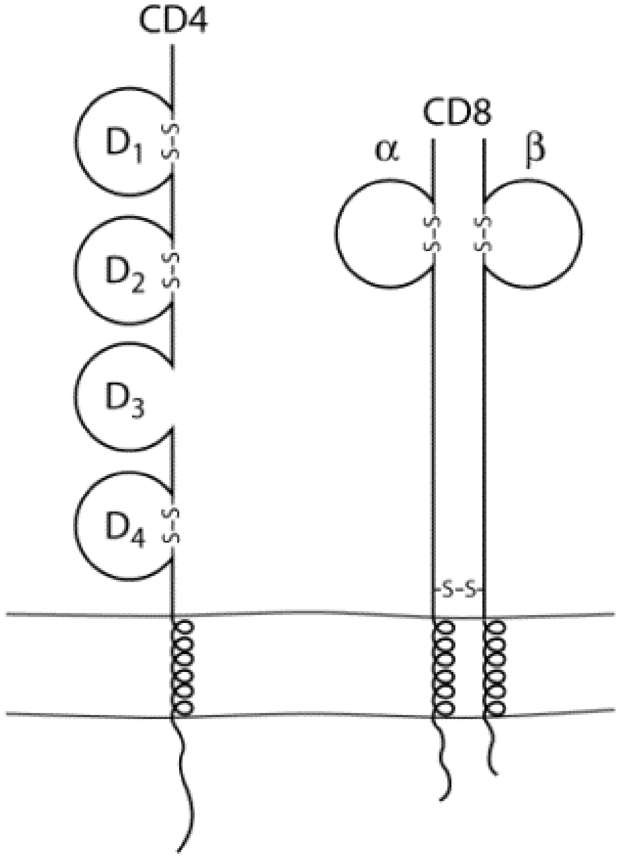
Structural features of CD4

- **55 kDa**, **monomeric** membrane glycoprotein with 4 extracellular Ig –like domains.
- **Hydrophobic** transmembrane region, long cytoplasmic tail with phosphorylatable serines



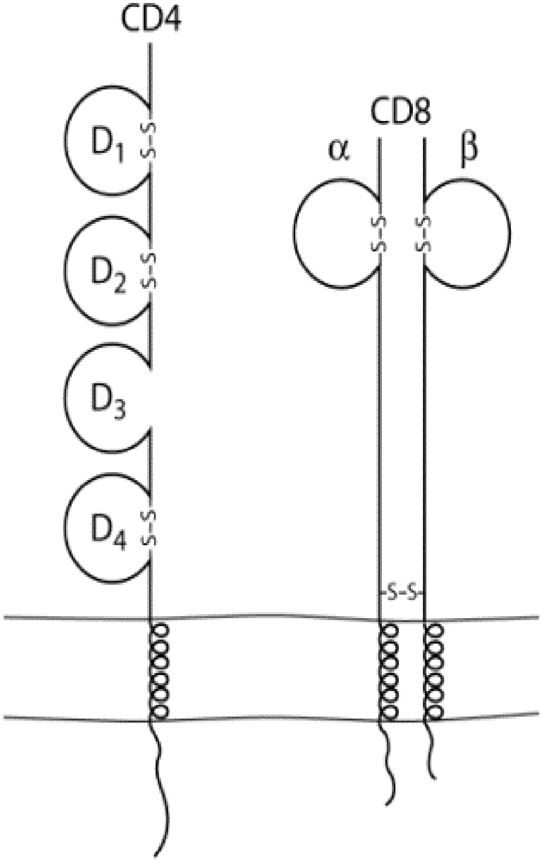
Structural features of CD8

- Disulfide linked **αβ** heterodimer or **αα** homodimer
- Small glycoprotein, **30-38 kDa**

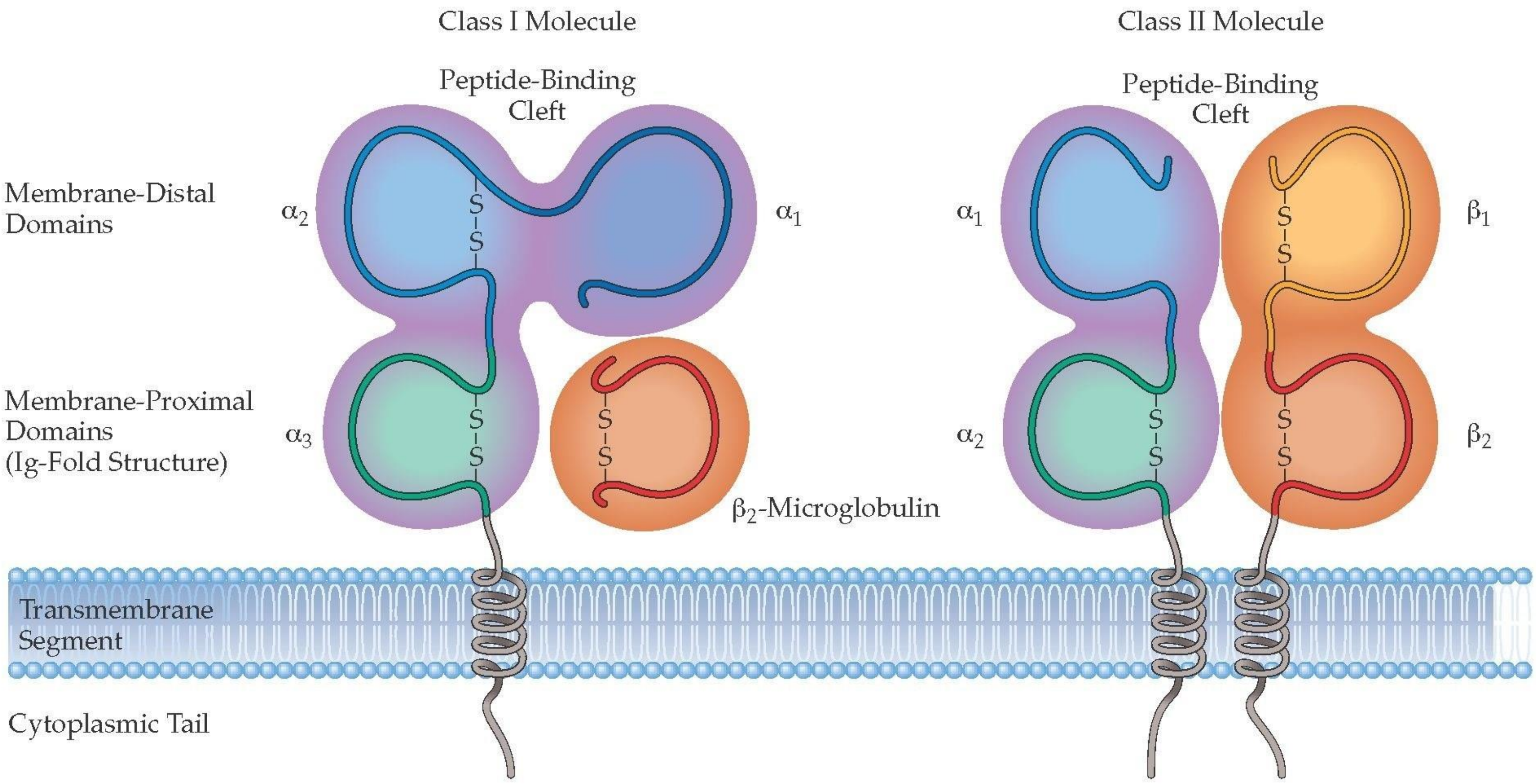


- **Hyrdrophobic** transmembrane region

- Cytosplasmic tail with **25-27 aa** (many can be phosphorylated)



- **CD8** binds by contacting **α2, α3, β2 microglobulin** domains in MHC I molecules.




"Success is not final,
failure is not fatal:
it is the COURAGE
TO CONTINUE
that counts."
WINSTON CHURCHILL
GH


Thank You!