#### **IMMUNOLOGY** TOPIC : T CELL RECEPTORS

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# T CELL RECEPTORS AND TCR-CD3 COMPLEX

### T cell receptor

- T cell receptor is different from B cell antigen binding receptor.
- a) The TCR is a membrane bound and does not appear in a soluble form as the B cell receptor does
- b) The antigen binding interaction of TCR is weaker than that of antibodies
- c) Most TCR are specific not for antigen alone but for antigen combined with a molecule encoded by the Major histocompatibility complex

 The molecule responsible for T cell specificity is a heterodimer composed of either α and β or γ and δ chains.

• The TCR is associated on the membrane with a **multicomponent signal transducing complex , CD3 ,** whose function is similar to that of the Ig- $\alpha$  /Ig –  $\beta$  complex of the

B cell receptor

- The αβ TCR , like the antibody, is characterized by its high degree of specificity and thus is considered a signature molecule of the adaptive immune system.
- By contrast , certain receptors on γδ T cells appear to recognize classes of antigens present on groups of pathogens and so function in a manner more consistent with innate immunity.

#### STRUCTURE OF TCR

- Two types of TCR are seen αβ TCR and γδ TCR each chain in a TCR has 2 domains has 65 to 70 amino acids and an intrachain disulphide bond
- The amino terminal domain in both chains show marked sequence variation but the sequence of the other part of chain is conserved

- The variable and constant domain of the TCR are structurally similar to the V and C domain of the immunoglobulin
- TCR variable region has 3 hypervariable regions, which are similar to CDRs in immunoglobulin light and heavy chain
- The 2 chains of the TCR are held together by a single disulphide bond at the lower end followed by a transmembrane region of 21-22 amino acids

- The trans membrane region of both the chains contains positively charged amino acids, which enable the chain of the heterodimer to interact with CD3 signal transducing complex.
- At the carboxy terminal end of the TCR chain has 5-12 amino acids which extend into cytoplasm

 The hypervariable region of TCR consisting of 3 CDRs is the antigen binding site, of which CDR1 and CDR2 contact primarily the α – helical region of the MHC.  The antigenic peptides held in the cleft of the MHC molecules are found to interact with CDR3 located in the center of the antigen binding site of TCR

#### ANTIGEN RECOGNITION BY T CELLS

- TCR recognizes short peptides that are derived from the antigen and are bound to MHC molecules on the surface of APC.
- 2 ways that foreign proteins can get into APCs
  . By the whole microbe growing inside of cell
  (e.g. viruses)
  - . By being endocytosed by phagocytes

- These proteins are degraded by cellular poteases, and the resulting peptides are loaded on MHC molecules
- These complexes , after transport to the surface of the cell , are what antigen specific T cells recognize.

#### T CELL RECEPTOR COMPLEX TCR : CD3

• CD3 is a complex of **5 invariant polypeptide** chains that associate to form 3 dimers :

- a heterodimer of delta and epsilon,
- and a homo dimer of 2 zeta chains
- or a heterodimer of zeta and eta chains



**FIGURE 9-9** Schematic diagram of the TCR-CD3 complex, which constitutes the T-cell antigen-binding receptor. The CD3 complex consists of the  $\zeta\zeta$  homodimer (alternately, a  $\zeta\eta$  heterodimer) plus  $\gamma\epsilon$  and  $\delta\epsilon$  heterodimers. The external domains of the  $\gamma$ ,  $\delta$ , and  $\epsilon$  chains of CD3 are similar to the immunoglobulin fold, which facilitates their

also may occur between the oppositely charged transmembrane regions in the TCR and CD3 chains. The long cytoplasmic tails of the CD3 chains contain a common sequence, the immunoreceptor tyrosine-based activation motif (ITAM), which functions in signal transduction.  About 90 percentage of the CD3 complex s incorporate the zeta – zeta homodimer; the remainder has the zeta-eta heterodimer

# ITAM

- The cytoplasmic tails of the CD3 chains contain a motif called the immunoreceptor tyrosine based activation motif (ITAM)
- ITAMS are found in a number of other receptors, including the Ig α / Ig β heterodimer of the BCR complex and the Fc receptors for IgE and IgG.
- The ITAM sites have been shown to interact with tyrosine kinases and to play an important role in signal transduction.

- The zeta chain has a distinctly different structure, with a very short external region of only 9 amino acids, a transmembrane region, and a long cytoplasmic tail containing 113 amino acids.
- The transmembrane region of all the CD3 polypeptide chains contain a negatively charged amino acid residue that interacts with 1 or 2 positively charged amino acids in the transmembrane region of the TCR chain

In CD3 ,the γ, δ and ε chains contain a single ITAM, whereas the zeta and eta chains contain 3 copies.

## TCR and CD3 complex

- TCR is closely associated with CD3 complex
  - Group of 5 proteins
  - Commonly called "invariant" chains of TCR
- Role of CD3 complex
  - CD3 necessary for cell surface expression of TCR
  - transduces signal after Ag interaction with TCR

