11.8E: T Cell Receptors

LEARNING OBJECTIVES

- Discuss the role of the T cell receptor (TCR)

T lymphocytes have a dual specificity: they recognize polymorphic residues of self major histocompatibility complex (MHC) molecules, which accounts for their MHC restriction; they also recognize residues of peptide antigens displayed by these MHC molecules, which is responsible for their specificity. MHC molecules and peptides form complexes on the surface of antigen presenting cells (APCs). The receptor that recognizes these peptide-MHC complexes is called the T Cell Receptor (TCR). Clones of T cells with different specificities express different TCRs.

The biochemical signals that are triggered in T cells following antigen recognition are transduced not by the TCR itself, but by invariant proteins (CD3, and zeta), which are non-covalently linked to the antigen receptor to form the TCR complex. T cells also express other membrane receptors that do not recognize antigens but participate in responses to antigens; these are collectively called 'accessory molecules'. The physiologic role of some accessory molecules is to deliver signals to the T cells that function in concert with signals from the TCR complex to fully activate the cell.
The antigen receptor of MHC-restricted CD4 helper T cells and CD8 cytolytic T cell is a heterodimer consisting of two transmembrane polypeptide chains, designated alpha and beta, covalently linked to each other by disulfide bonds. Each alpha and beta chain consists of one variable domain (V), one constant domain (C), a hydrophobic transmembrane region, and a short cytoplasmic region. The V regions of the TCR contain short stretches of amino acids where the variability between different TCRs is concentrated, and these form the hypervariable or complementarity-determining regions (CDRs). The recognition of peptide-MHC complexes is mediated by CDRs formed by both the alpha and beta chains of the TCR.

Key Points

- Many TCRs recognize the same antigen and many antigens are recognized by the same TCR.
- The TCR is composed of two different protein chains (that is, it is a heterodimer). In 95% of T cells, this consists of
an alpha (α) and beta (β) chain, whereas in 5% of T cells this consists of gamma and delta (γ/δ) chains.

- When the TCR engages with antigen and MHC, the T lymphocyte is activated through a series of biochemical events mediated by associated enzymes, co-receptors, specialized accessory molecules, and activated or released transcription factors.

### Key Terms

- **polymorphic**: relating to polymorphism (any sense), able to have several shapes or forms
- **major histocompatibility complex**: MHC is a cell surface molecule that mediate interactions of immune cells with other leukocytes or body cells. MHC determines compatibility of donors for organ transplants as well as one’s susceptibility to an autoimmune disease. In humans, MHC is also called human leukocyte antigen (HLA).