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DEPARTMENT OF BIOTECHNOLOGY
FACULTY OFENGINEERING & TECHNOLOGY

B-cell & T-Cell receptor

Content Outline

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B-cell receptor

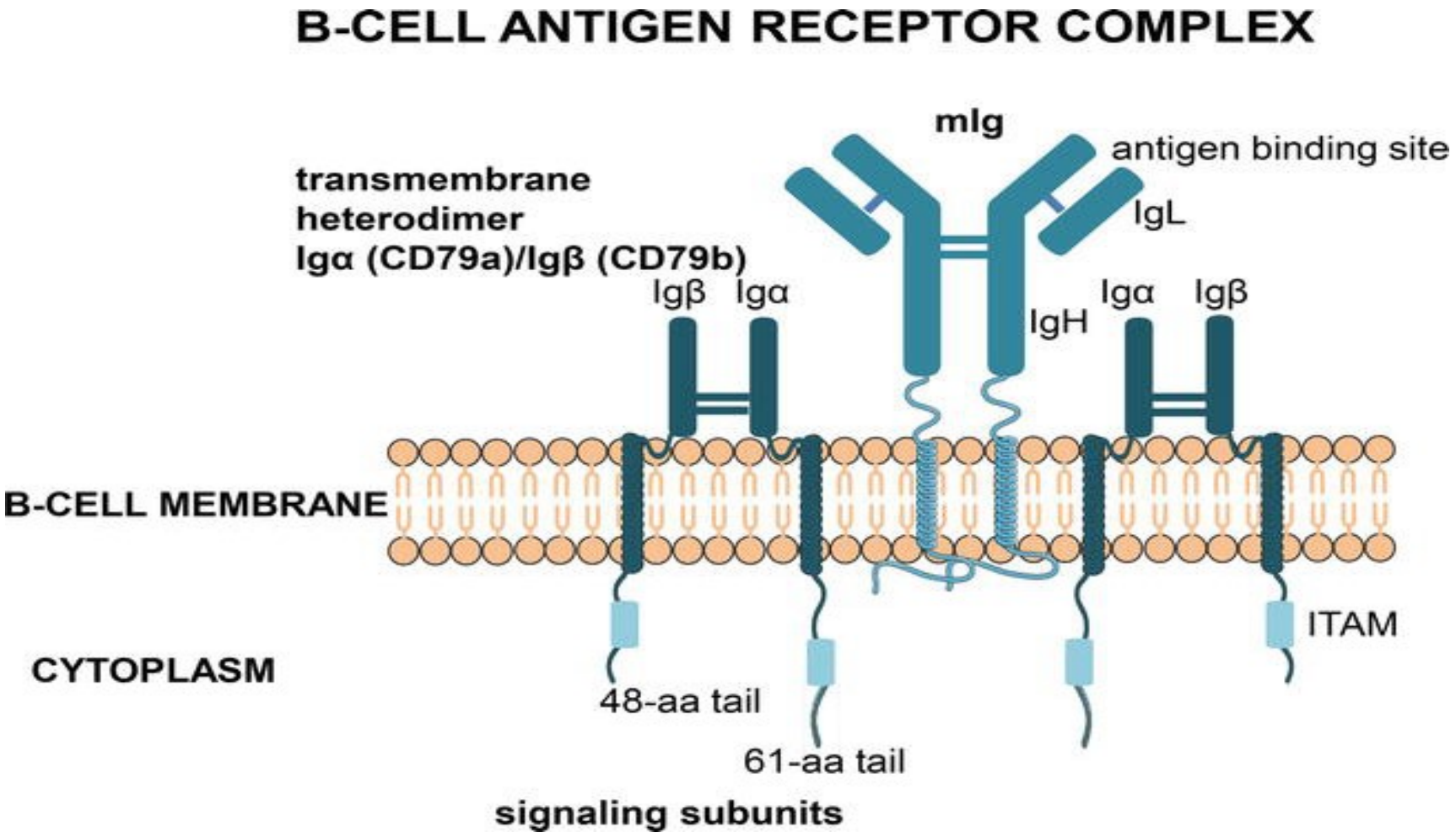
The **B cell receptor** (BCR) is a transmembrane protein on the surface of a **B cell**. **B cell receptors** are composed of immunoglobulin molecules that form a type 1 transmembrane **receptor** protein, and are typical located on the outer surface of these **lymphocyte cells**.

Structure

The B cell receptor (BCR) is a transmembrane protein complex composed of membrane bound immunoglobulin (mIg) and disulfide-linked heterodimers called Ig-α/Ig-β. Molecules of this heterodimer associate with a mIg molecule to form a BCR. The BCR is composed of two heavy (H) chains and two light (L) chains, either *IgLκ* or *IgLλ*. B cell receptors for antigen are almost identical in structure to secreted antibodies. The only structural difference is that the *C*-terminal region of the heavy chains contains a short hydrophobic stretch which spans the lipid bilayer of the membrane. In addition to antibody modules that recognizes antigen, B cell receptors have short transmembrane chains Ig-α and Ig-β. The Ig-α chain has long cytoplasmic tail containing 61 amino acids; the tail of the Ig-α chain contains 48 amino acids. The tails in both Ig-α and Ig-β are long enough to interact with intracellular signaling molecules.

•Mature B cells express two BCR isotypes, IgM and IgD. The BCR is composed of membrane immunoglobulin (mIg); a structure of four (in the case of IgD) or five (IgM) immunoglobulin domains in the heavy chain linked by a hinge, and a short intracellular domain consisting of just three amino acids: lysine, valine, lysine (KVK).

•The mIg itself does not contain any signalling motifs but instead is linked to the Igα/Igβ heterodimer, which contains immunoreceptor tyrosine-based activation motifs (ITAM); a conserved sequence of four amino acids in which a tyrosine is separated from a leucine or isoleucine by any two amino acids (YxxL/I) and generally repeated twice in the cytoplasmic domain of ITAM-containing proteins separated by between 7 and 12 amino acids, giving it the signature $YxxL_{7-12}YxxL$



B-cell receptors are complex consisting of various components: a membrane tethered Ig M and associated membrane bound proteins CD79A and CD79B

Receptor-ligand (antigen) Interactions

The precise pathways of signalling from the receptors to the interior of the cell are not yet fully understood but involve associated protein kinases. Engagement of the B cell receptor (BCR) by antigen initiates receptor aggregation at the cell surface followed by recruitment to lipid rafts. Lipid rafts are specialized membrane micro domains that facilitate assembly and activation of downstream signaling molecules. This step places the complex in proximity to the LYN tyrosine kinase, which phosphorylates tyrosine residues in the Igα/Igβ ITAM motifs (Tyrosine based activation motifs) and triggers recruitment of spleen tyrosine kinase (SYK) and Bruton tyrosine kinase (BTK). Activated SYK phosphorylates and recruits the B cell linker (BLNK) protein, which provides binding sites for phospholipase Cγ2 (PLCγ2), BTK, and VAV proteins, which are guanine nucleotide exchange factors. PLCγ2 generates the second messengers inositol triphosphate and diacylglycerol, which are necessary for calcium release from intracellular stores and protein kinase C activation. BCR signal transduction also leads to activation of the mitogen-activated protein (MAP) kinase pathway. B cell activation is further aided by a co-receptor complex that amplifies signals delivered by the BCR.

The members of this complex include CD19, the complement receptor type 2 (CR2 or CD21), and CD81. The CR2 enables the complement pathway to synergize with BCR signal transduction, which enhances B cell activation. Collectively, these signaling events lead to the activation of the transcription factors known as nuclear factor of activated T cells (NFAT), nuclear factor-κB (NF-κB), and activator protein 1 (AP-1). Activation of the BCR on naive and memory B cells results in their activation and migration to the draining lymph node or other lymphatic tissue. B cells can respond to three types of antigens, and the type of antigenic exposure dictates the quality of the ensuing response.

- The receptors on the surface of B cells (BCRs) can bind to soluble antigens only

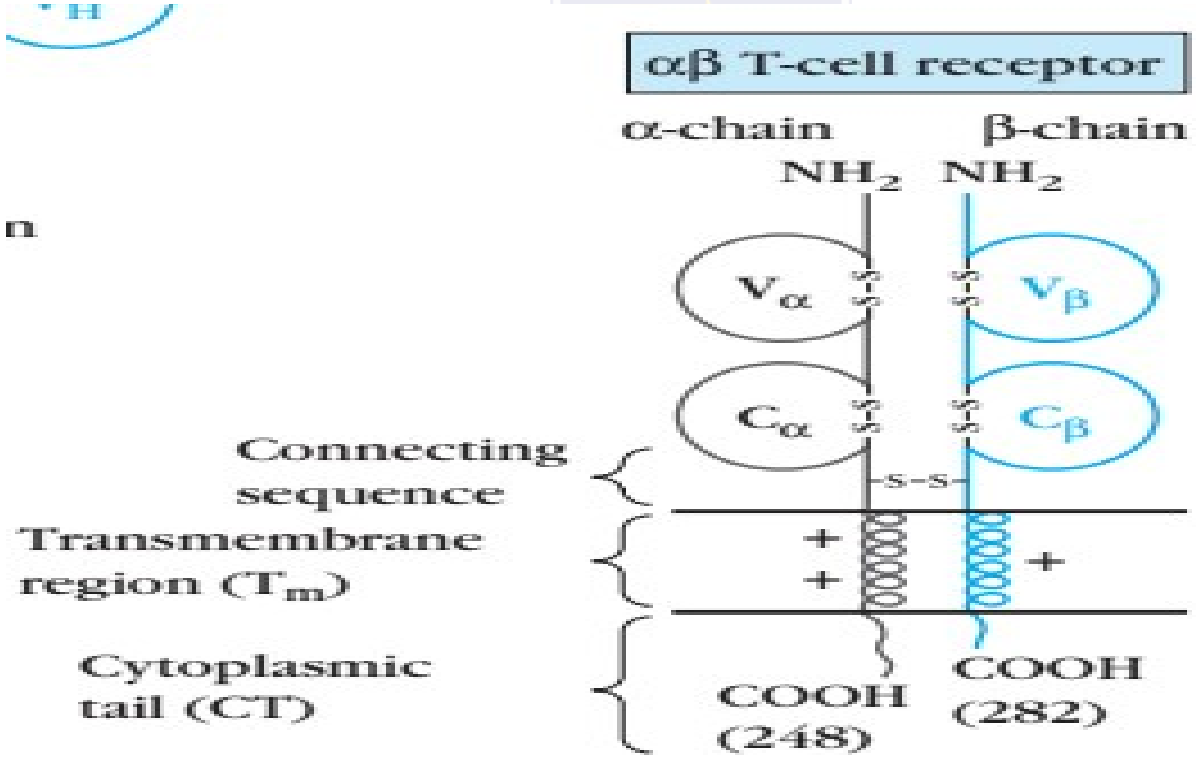
T-cell receptor

➢The T cell antigen receptor (TCR) is the principle defining marker of all T cells. Also associated with the TCR is a complex of proteins known as CD3, which participate in the transduction of an intracellular signal following TCR binding to its cognate MHC/antigen complex.

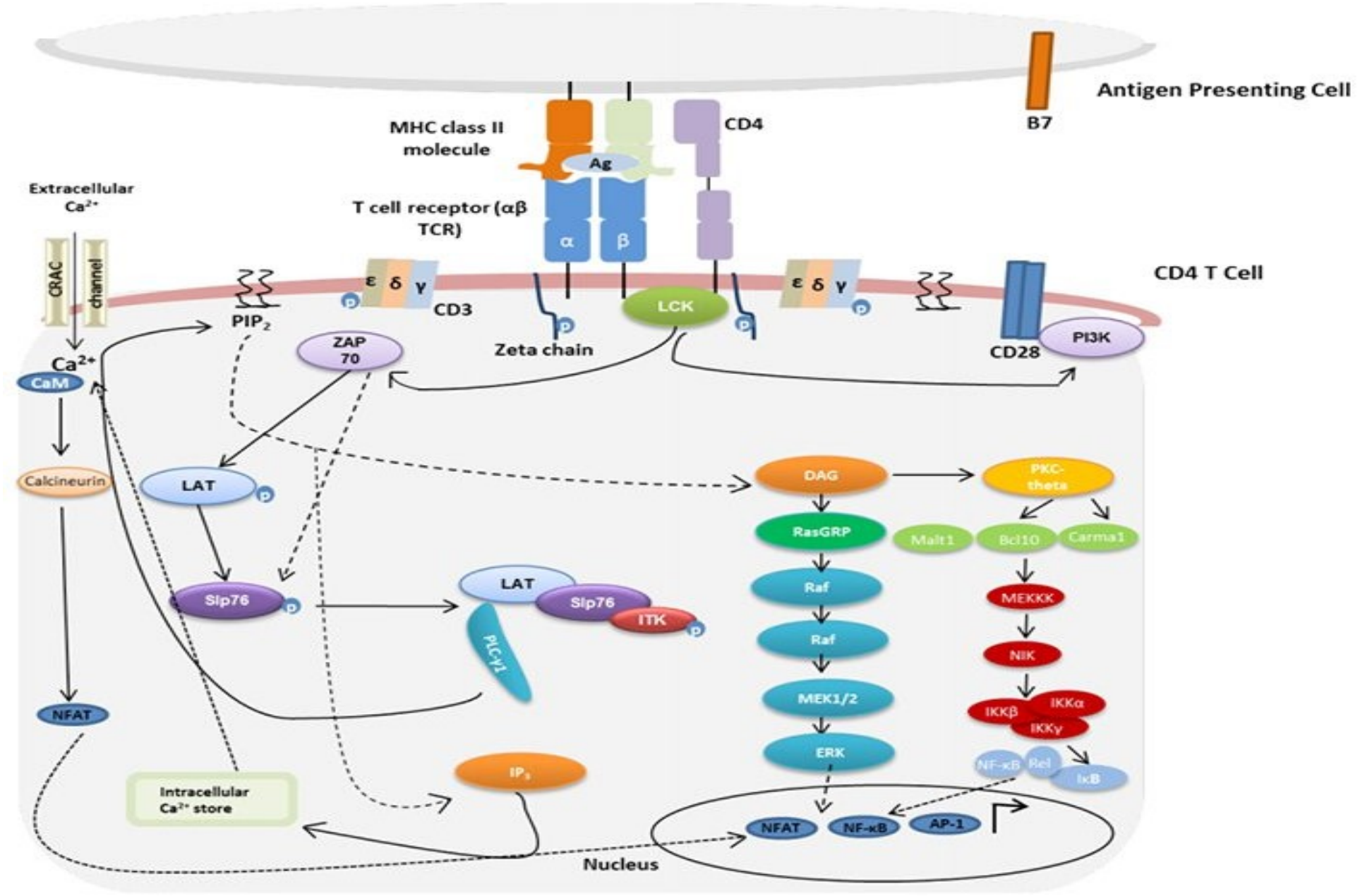
Structure

TCRs are heterodimers and fall into two classes: TCR-αβ and TCR-γδ; γδ T cells constitute 1–10% of the T-cell repertoire. The T cell receptor (TCR) is a T cell surface structure that is comprised of a disulfide-linked heterodimer of highly variable α and β chains expressed at the cell membrane as a complex with the invariant CD3 chains. Most T cells that bear this type of receptor are termed αβ T cells. A second receptor, the γδ TCR, is comprised of variable γ and δ chains expressed with CD3 on a smaller subset of T cells that recognize different types of antigens. Both of these types of receptors are expressed with a disulfide-linked homodimer of ξ chains. The TCR is a receptor for antigen on $CD4^+$ and $CD8^+$ T cells that recognizes foreign peptideself – MHC molecular complexes on the surface of antigen-presenting cells. **CD4** is a monomeric protein with four Ig-like domains; the two most membrane distal domains are thought to bind Class II MHC b2 domain.

CD8 is a disulfide-linked dimer; its a and b chains each have one Ig-like domain with a long extended region connecting it to the transmembrane region. CD8 binds to the a3 region of Class I MHC. The cytoplasmic tails of both CD4 and CD8 associate with a cytoplasmic tyrosine kinase, Lck, to initiate signal transduction.



TCR activation & Signaling



TCR signaling is activated upon interaction of the TCR with cognate peptide antigen bound to a major histocompatibility complex (MHC) molecule, and co-stimulation by co-receptor molecules such as CD28. AP-1, activator protein 1; Bcl10, B cell lymphoma 10; Ca^{2+}, calcium; CaM, calmodulin; Carma1, caspase recruitment domain membrane-associated guanylate kinase protein 1; CRAC, calcium release-activated Ca^{2+}; DAG, diacylglycerol; IP3, inositol trisphosphate; IKK, I kappa B kinase; ITK, interleukin-2 inducible tyrosine kinase; LAT, linker activation of T cells; LCK, leukocyte-specific tyrosine kinase; Malt 1, mucosa-associated lymphoid tissue protein 1; NFAT, nuclear factors of activated T cells; NF-κB, nuclear factor kappa B; NIK, NF-kappa-B-inducing kinase, PI3K, phosphatidylinositol-3 kinase; PIP2, phosphatidylinositol bisphosphate; PKC-theta, protein kinase C-theta; PLC-γ1, phospholipase C gamma 1; RasGRP, RAS guanyl nucleotide releasing protein; Slp76, SH2-domain containing leukocyte protein of 76 kDa; ZAP70, zeta-activated protein 70 kDa.

For detailed description click on this link

https://www.bio-rad-antibodies.com/t-cell-receptor-minireview.html

References & Further reading

References

1. **https://www.bio-rad-antibodies.com/t-cell-receptor-minireview.html**
2. **https://www.sinobiological.com/research/receptors/t-cell-receptor**
3. **https://www.britannica.com/science/immune-system/T-cell-antigen-receptors**

Further reading

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