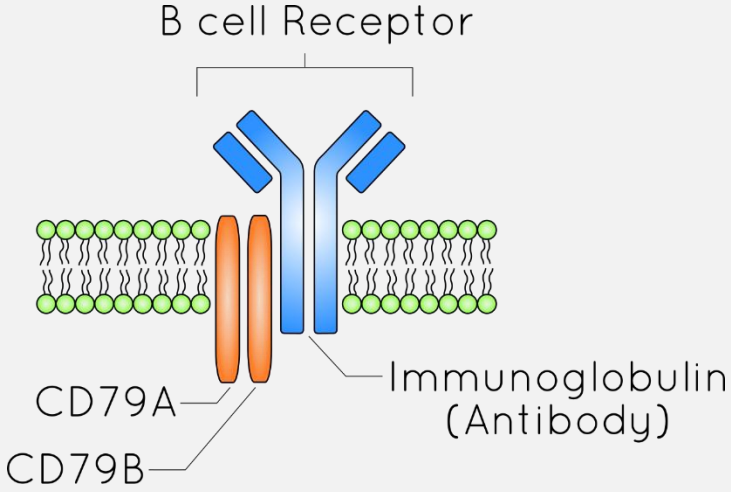
# B CELL RECEPTOR

## 1. Introduction

- The B-cell receptor complex is made up of **cell-surface immuno-globulin with one each of the invariant proteins Igα and Igβ**.
- The immunoglobulin recognizes and binds antigen but cannot itself generate a signal.
- The **BCR and antibodies are essentially the same molecule** — the only difference is that the BCR is membrane-bound, while antibodies are the **secreted** form after B cell activation.




- The **B cell receptor (BCR)** is a protein complex found on the surface of **B lymphocytes (B cells)** that allows them to recognize and bind to specific **antigens**. It plays a key role in the **adaptive immune response** by detecting pathogens and triggering B cell activation, proliferation, and antibody production.
- The **B cell receptor (BCR)** is a **membrane-bound immunoglobulin complex** present on the surface of **B lymphocytes (B cells)**.
- It plays a **critical role** in the adaptive immune system by recognizing specific **antigens** and initiating B cell activation.
- Each B cell expresses **one unique BCR** that recognizes a **single specific epitope** (antigenic determinant).

## 2. Structure of the B Cell Receptor

### A. Components

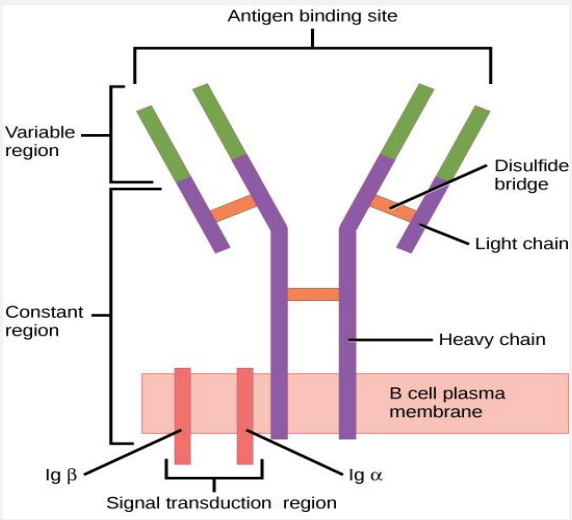
The BCR complex consists of **two main parts:**

**(i) Membrane-bound Immunoglobulin (mIg)**

- This is the **antigen-binding component** of the receptor.
- It is a **monomeric form** of an antibody molecule (usually **IgM** or **IgD** in naïve B cells).
- Structure:
  - **Two heavy (H) chains** and **two light (L) chains**.
  - Each chain has:
    - **Variable region (V region):** Determines antigen specificity.
    - **Constant region (C region):** Determines the immunoglobulin class.
  - The **antigen-binding site** is formed by the **variable regions** of one heavy and one light chain.
  - The **membrane-bound form** has a **hydrophobic transmembrane tail** anchoring it in the B cell membrane.

**(ii) Signaling Molecules (Igα and Igβ)**

- Also known as **CD79a (Igα)** and **CD79b (Igβ)**.
- These are **noncovalently associated** with the mIg.
- Functions:
  - Each contains **ITAMs (Immunoreceptor Tyrosine-based Activation Motifs)** in their cytoplasmic tails.
  - These motifs initiate intracellular signaling after antigen binding.
- Without Igα/Igβ, the membrane immunoglobulin **cannot be expressed or signal properly**.



**B. Structural Summary Table**

| Component | Composition | Function |
|---|---|---|
| **mIg (IgM or IgD)** | 2 heavy + 2 light chains | Antigen recognition |
| **Igα (CD79a)** | Transmembrane signaling protein | Signal transduction |
| **Igβ (CD79b)** | Transmembrane signaling protein | Signal transduction |

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## 3. Function of the B Cell Receptor

### A. Antigen Recognition

- BCRs recognize **native, unprocessed antigens** (unlike TCRs, which recognize processed peptides bound to MHC).
- Recognition is **highly specific**, determined by the variable regions of the mIg.
- Binding occurs via **non-covalent interactions** (hydrogen bonds, hydrophobic interactions, electrostatic forces).

### B. Signal Transduction

Once the BCR binds to its specific antigen, several intracellular events occur:

1. **Antigen Binding and Cross-linking:**
    - Binding of multivalent antigen leads to **BCR clustering** (cross-linking).
    - Brings Igα/Igβ molecules close together.
2. **Activation of Src-family kinases:**
    - **Lyn, Fyn, Blk** kinases phosphorylate ITAMs on Igα/Igβ.
3. **Recruitment of Syk kinase:**
    - **Syk** binds to phosphorylated ITAMs and becomes activated.
    - This triggers downstream signaling cascades.
4. **Intracellular signaling pathways:**
    - Activation of pathways like:
        - **PLCγ2 → $IP_3$ + DAG → $Ca^{2+}$ release and PKC activation**
        - **MAPK pathway → Gene transcription**
        - **NF-κB and NFAT activation**
5. **Cellular outcomes:**
    - B cell activation
    - Proliferation (clonal expansion)
    - Differentiation into:
        - **Plasma cells** (antibody-secreting cells)
        - **Memory B cells**

**C. Antigen Internalization and Presentation**

- After antigen binding, the BCR–antigen complex is **internalized by endocytosis**.
- The antigen is **processed** and presented on **MHC class II molecules**.
- **Helper T cells ($CD4^+$)** recognize the antigen–MHC complex and provide **co-stimulatory signals (via CD40–CD40L interaction)** to fully activate the B cell.

**4. BCR Diversity and Generation**

BCR diversity arises through several mechanisms during B cell development:

1. **V(D)J Recombination:**
   - Random recombination of **V (variable)**, **D (diversity)**, and **J (joining)** gene segments in heavy and light chains.
2. **Junctional Diversity:**
   - Addition or deletion of nucleotides at V-D-J junctions.
3. **Combinatorial Diversity:**
   - Random pairing of heavy and light chains.
4. **Somatic Hypermutation (in activated B cells):**
   - Point mutations in variable regions that increase affinity for antigen.

❖ Collectively, these mechanisms allow for **~$10^{11}$ possible BCR specificities**.

**5. BCR in B Cell Development**

| Stage | BCR Form | Key Events |
|---|---|---|
| **Pro-B cell** | None | Heavy chain gene rearrangement begins |
| **Pre-B cell** | Pre-BCR (μ heavy chain + surrogate light chain) | Signals for light chain rearrangement |
| **Immature B cell** | Membrane IgM | Tested for self-reactivity (central tolerance) |
| **Mature naïve B cell** | IgM and IgD | Circulates in periphery, ready for antigen encounter |

**6. Co-receptors and Regulation**

- The BCR works in conjunction with **co-receptors** that modulate the signaling threshold:
- **Positive regulators:**
    - **CD19, CD21 (CR2), CD81** form the **B cell co-receptor complex**, enhancing signaling.
- **Negative regulators:**
    - **FcγRIIB (CD32)** delivers inhibitory signals when antibodies are bound, preventing overactivation.