Antibody classes

- In mice and humans the different types of antibodies **(isotypes)** are known as **IgM, IgG , IgA, IgD,** and **IgE.**

    They are called different isotypes because they have **different heavy chain**.

- Subtypes of certain isotypes exist both in humans and mice **(G1, G2, G3, G4,** and **A1, A2)**.

- We can call G1, G2, G3, G4, and A1, A2 as separate **subclasses.**

The respective **heavy chain in each Ig** is described by Greek letters:

1. **mu (μ)** IgM
2. **gamma (γ)** IgG
3. **alpha (α)** IgA
4. **delta (δ)** IgD
5. **epsilon (ε)** IgE

Antibodies of **each isotype** have **different properties** in terms of **complement fixation** and **binding** to **immunoglobulin (Ig) receptors** on cell surface**.**

There are **two** light chain isotypes:

kappa (κ)

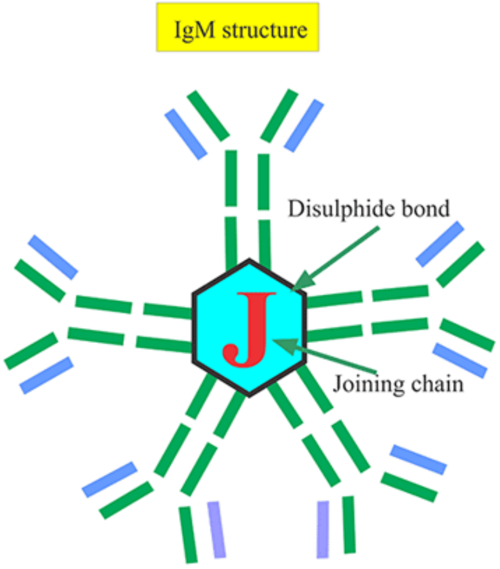
lambda (λ)

One B cell will only ever express **one** light chain isotype.

It means that antibody produced by a B cell will **always have same** light chain isotype.

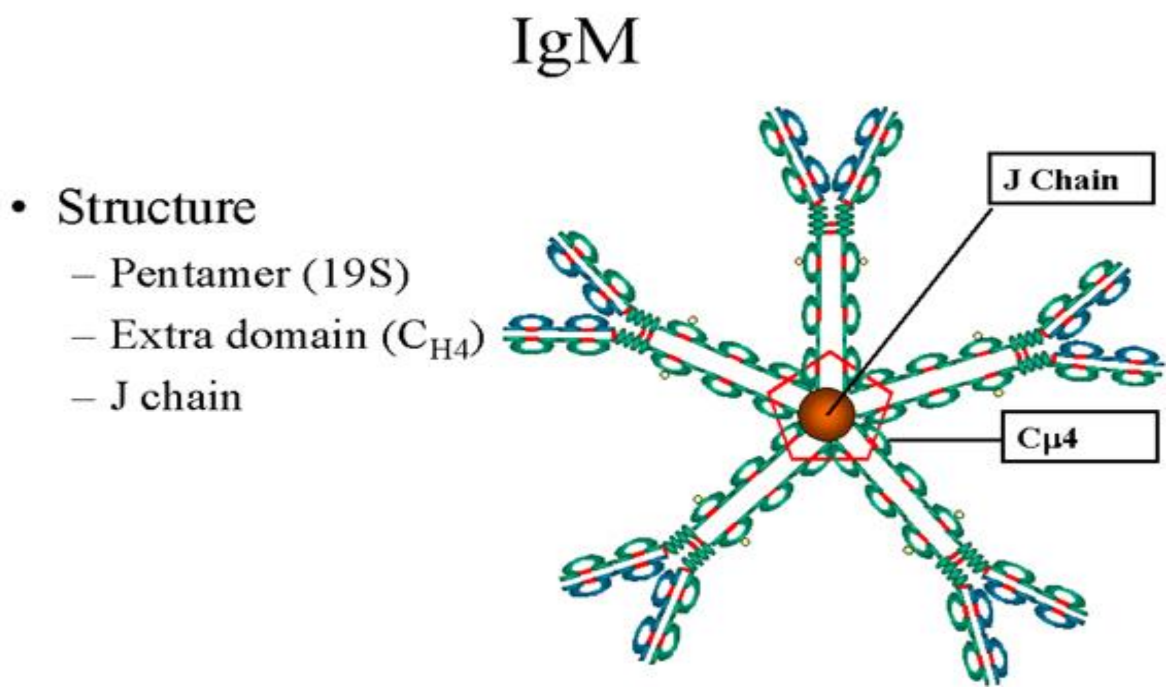
- Some antibody classes form **multimeric structures**, pentamers (five units) in the case of IgM and dimers or trimers in the case of IgA.

- These multimeric structures are associated with a small protein called the **joining (J) chain** required for stabilization of the complexes.



IgM:

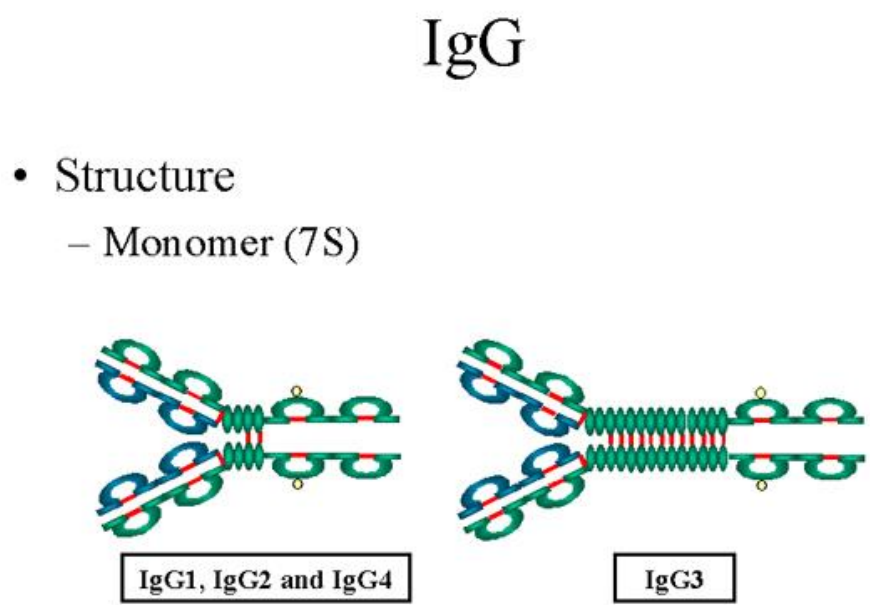
- **μ** heavy chain has 4 C (constant) domains and there is no hinge
- <u>pentamer</u>: J chain + disulfide bonds



Structure of Immunoglobulins

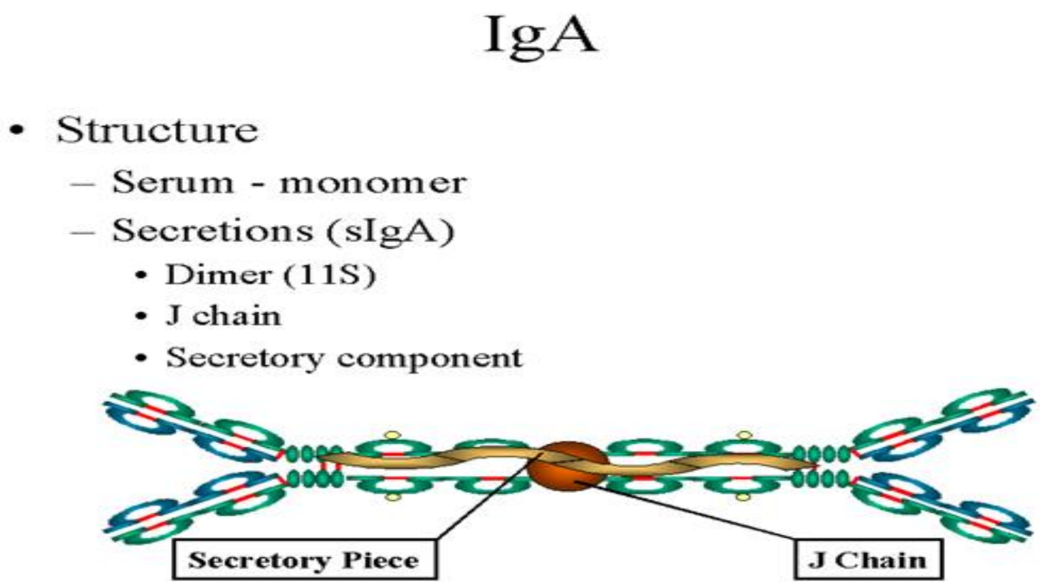
IgG:

- γ heavy chain has 3 C domains + hinge
- four subclasses (IgG1, IgG2, IgG3, IgG4)
- <u>monomer</u>



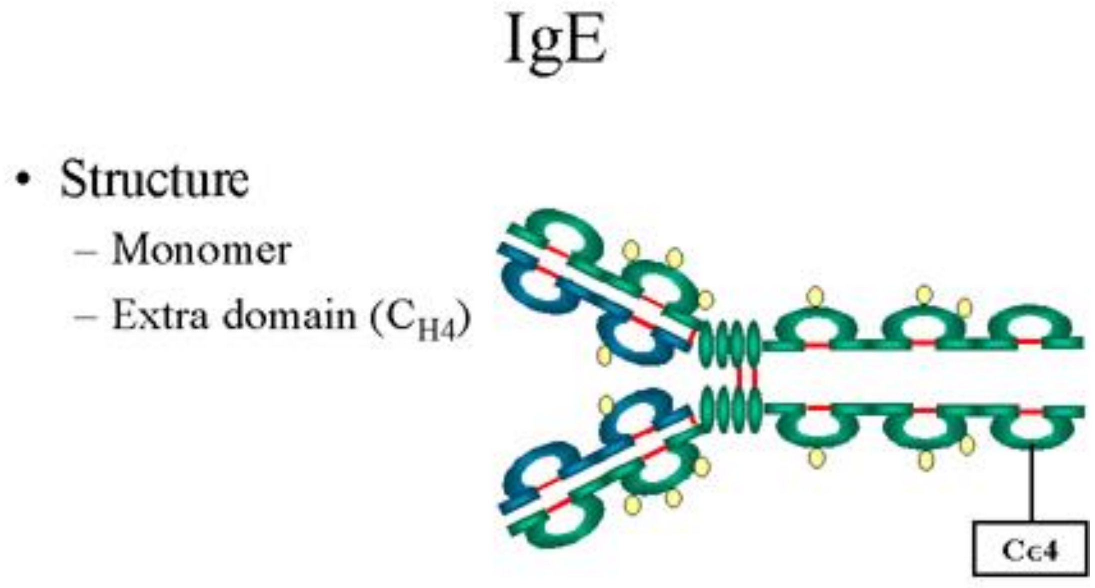
IgA:

- **α** heavy chain has 3 C domains + hinge
- monomer (serum), or dimer (secreted)
- Secreted form: J chain + secretory component



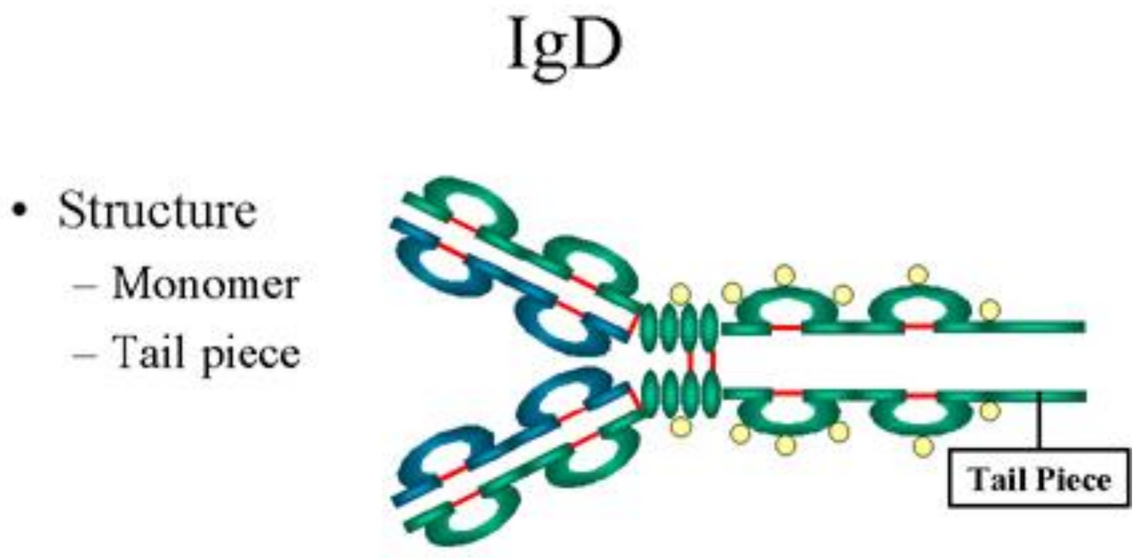
IgE:

- **ε** heavy chain has 4 C domains +hinge
- <u>monomer</u>



IgD:

- δ heavy chain has 3 C domains + hinge + tail piece



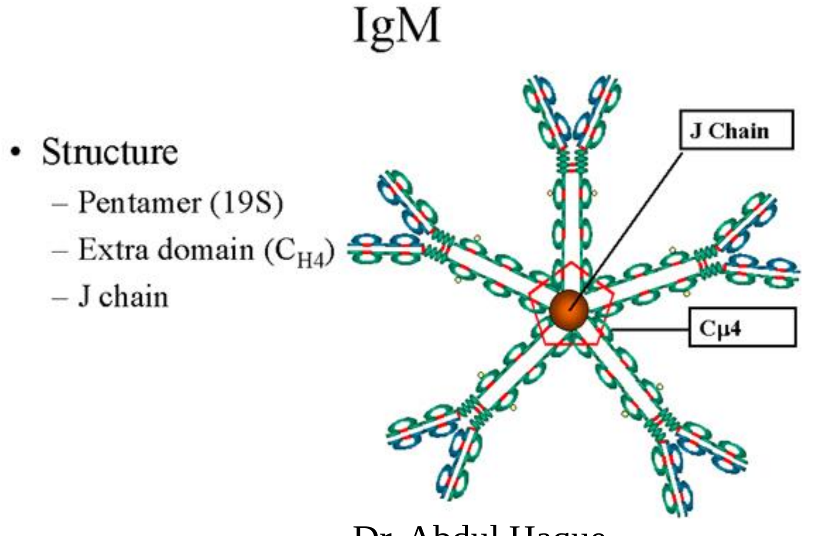
Biological activities of IgM

Key Points:

5-10% of total serum immunoglobulin

Pentamer with *valency* of 10 (ten binding sites)

Present on surface of **mature B cell (as monomer)**



-- **First immunoglobulin** produced during immune response; low affinity compared to IgG

-- **Large size** (pentamer) helps in **carrying** other proteins such as **CD5L** and for **agglutination**

-- Efficiently **agglutinates** (aggregates) *multivalent* antigen (due to ten binding sites)

-- Efficiently **activates complement**

*Plays a key role in providing **first** response to antigen*

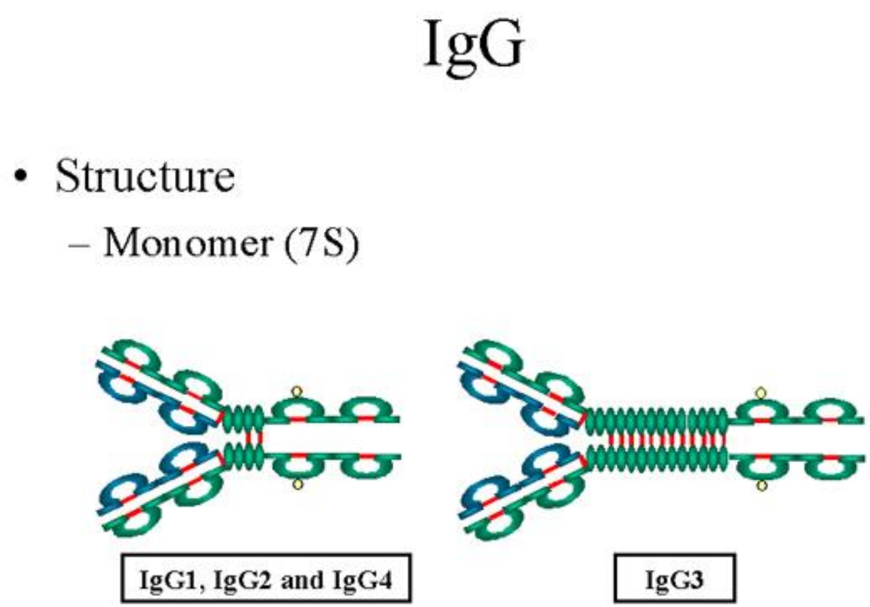
Does not - cross placenta

Biological activities of IgG

<u>Key Points:</u>

-- **80%** of total serum immunoglobulin

-- **Monomer** with *valency* of 2



-- **Four subclasses** differing in hinge region size and number of disulfide bonds.

Ig3 has the largest hinge.

-- **Present in serum and tissue** (by diffusion from serum)

-- Produced **later** in immune response

-- **Higher affinity** compared to IgM

-- **Binds Fcγ receptors** on immune cells (IgG1=IgG3>IgG4>IgG2)

-- **Crosses placenta** (passive immunity to fetus) (IgG1=IgG3=IgG4>IgG2).

Only Ig that cross placenta and reach fetal circulation.

-- **Activates complement** (IgG3>IgG1>IgG4>IgG2)

*Plays a key role in **neonatal immunity** and **response to/ clearance of antigen** from blood and tissue*

Is not:

- secreted along mucosa

- present on the surface of unactivated, mature B cells

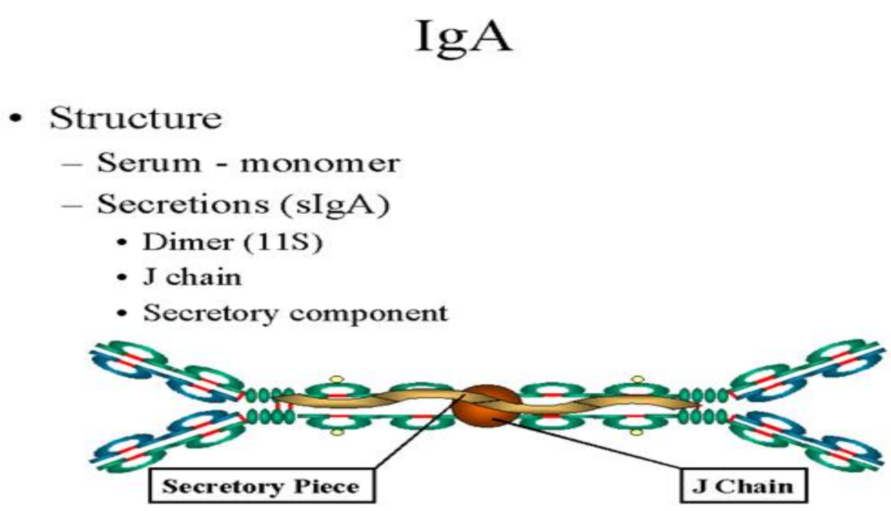
Biological activities of IgA

Key Points:

10-15% of total serum immunoglobulin

Monomer (serum), *valency* of 2

Dimer (secreted), *valency* of 4



-- Two subclasses (**IgA1, IgA2**) according to size of hinge region

-- Present in **serum** and **external secretions**

-- Produced **later** in immune response

-- **Higher affinity** compared to IgM

Plays a key role in defense along mucosal surfaces

Is not:

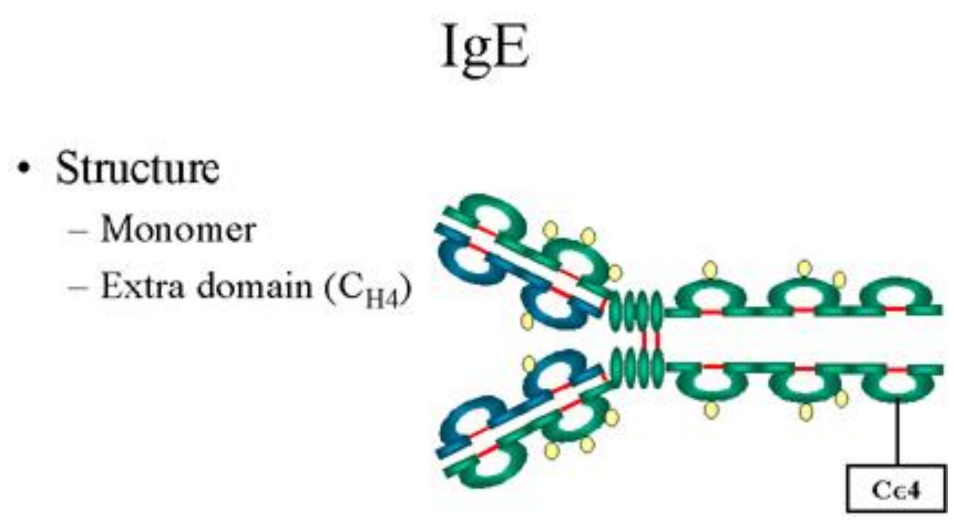
- transported across placenta
- a potent activator of complement
- present on the surface of un-activated, mature B cells

Biological activities of IgE

<u>Key Points:</u>

~0.002% of total serum immunoglobulin

Monomer with a *valency* of 2



-- Although these are present in serum, distribution is mainly **restricted to surface of blood basophils** and **tissue mast cells**, which express a **high affinity Fcε receptor**.

-- Produced **later** in immune response

-- **Higher affinity** compared to IgM

Plays a key role in allergic responses and defense against parasites

Is not:

- transported across placenta or secreted
- an activator of complement
- present on the surface of inactivated, mature B cells

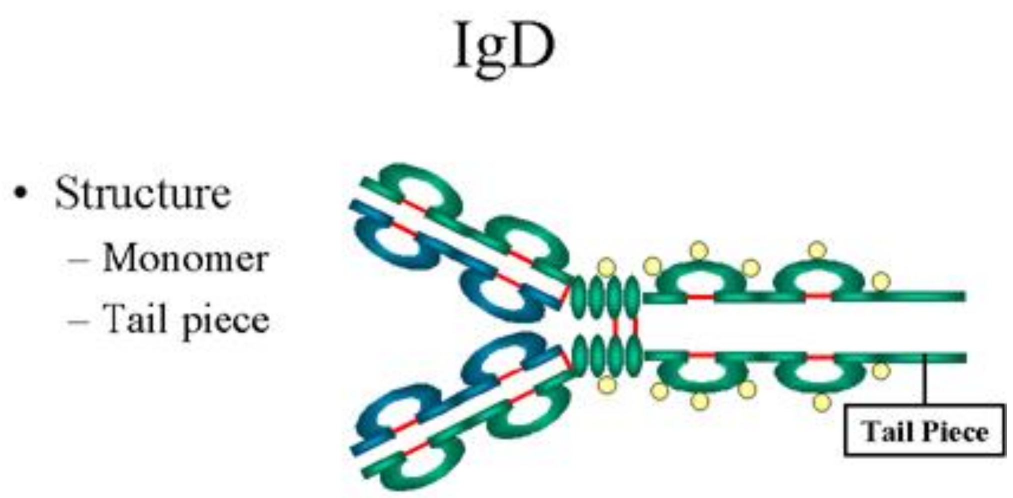
Biological activities of IgD

Key Points:

~0.2% of total serum immunoglobulin

Monomer with a *valency* of 2

Has a unique **tail piece**



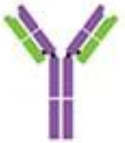
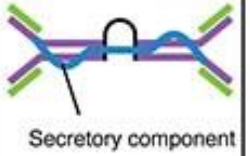
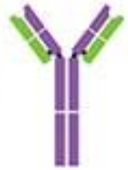
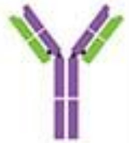
-- Distribution largely **restricted to surface of mature B cells** (coexpressed with surface IgM)

-- The function of IgD is to **signal** the B cells to be **activated**.

Is not:

-- transported across placenta or secreted

-- an activator of complement

The Five Immunoglobulin (Ig) Classes					
	IgM pentamer	IgG monomer	Secretory IgA dimer	IgE monomer	IgD monomer
					
Heavy chains	μ	γ	α	ε	δ
Number of antigen binding sites	10	2	4	2	2
Molecular weight (Daltons)	900,000	150,000	385,000	200,000	180,000
Percentage of total antibody in serum	6%	80%	13%	0.002%	1%
Crosses placenta	no	yes	no	no	no
Fixes complement	yes	yes	no	no	no
Fc binds to		phagocytes		mast cells and basophils	
Function	Main antibody of primary responses, best at fixing complement; the monomer form of IgM serves as the B cell receptor	Main blood antibody of secondary responses, neutralizes toxins, opsonization	Secreted into mucus, tears, saliva, colostrum	Antibody of allergy and antiparasitic activity	B cell receptor

The B cell receptor (BCR)

Key Points:

Expression of BCR is developmentally controlled on **mature B cell**

BCR consists of the following:

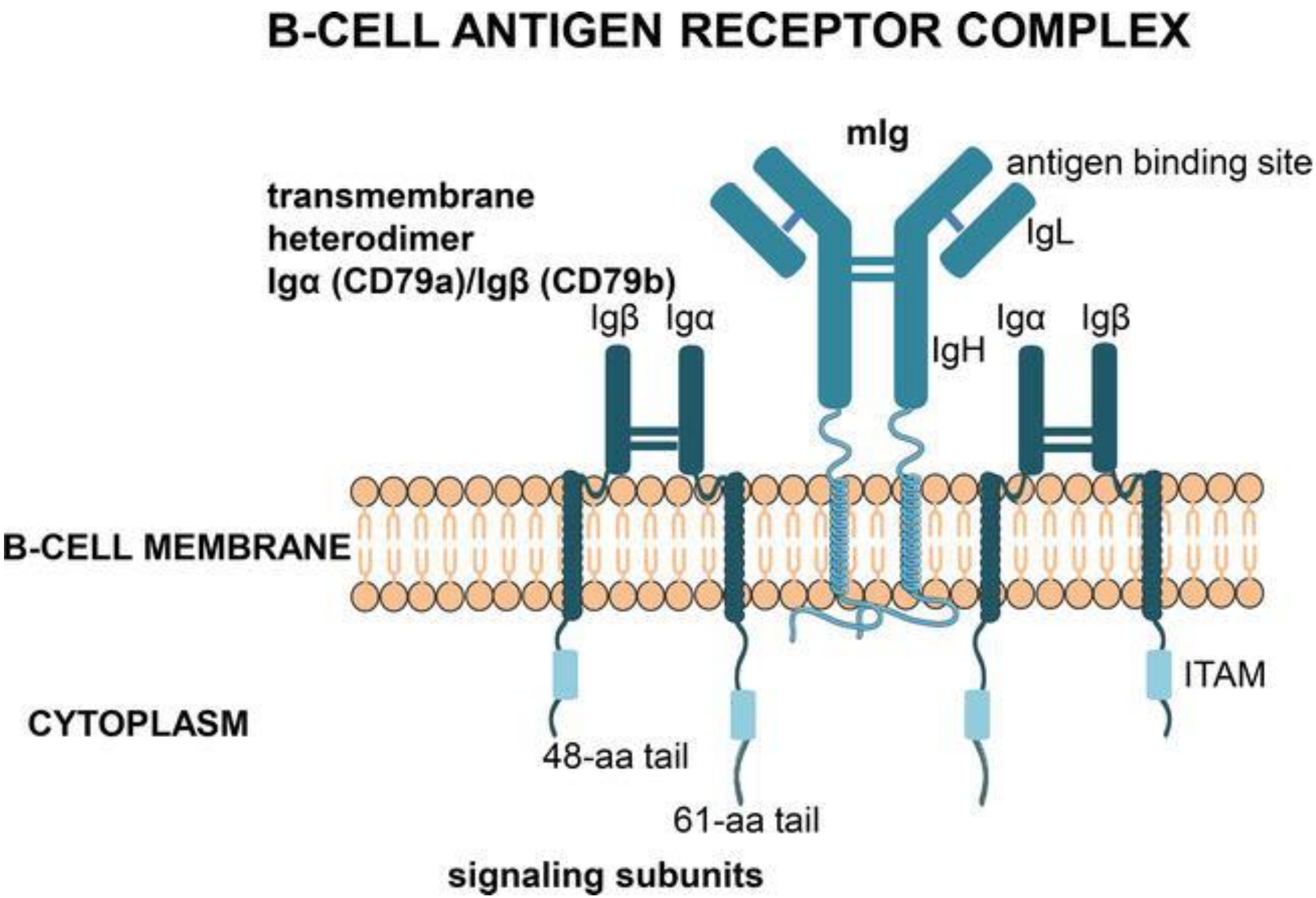
- ***Membrane-bound IgM* (mIgM):** contains transmembrane region and short cytoplasmic tail

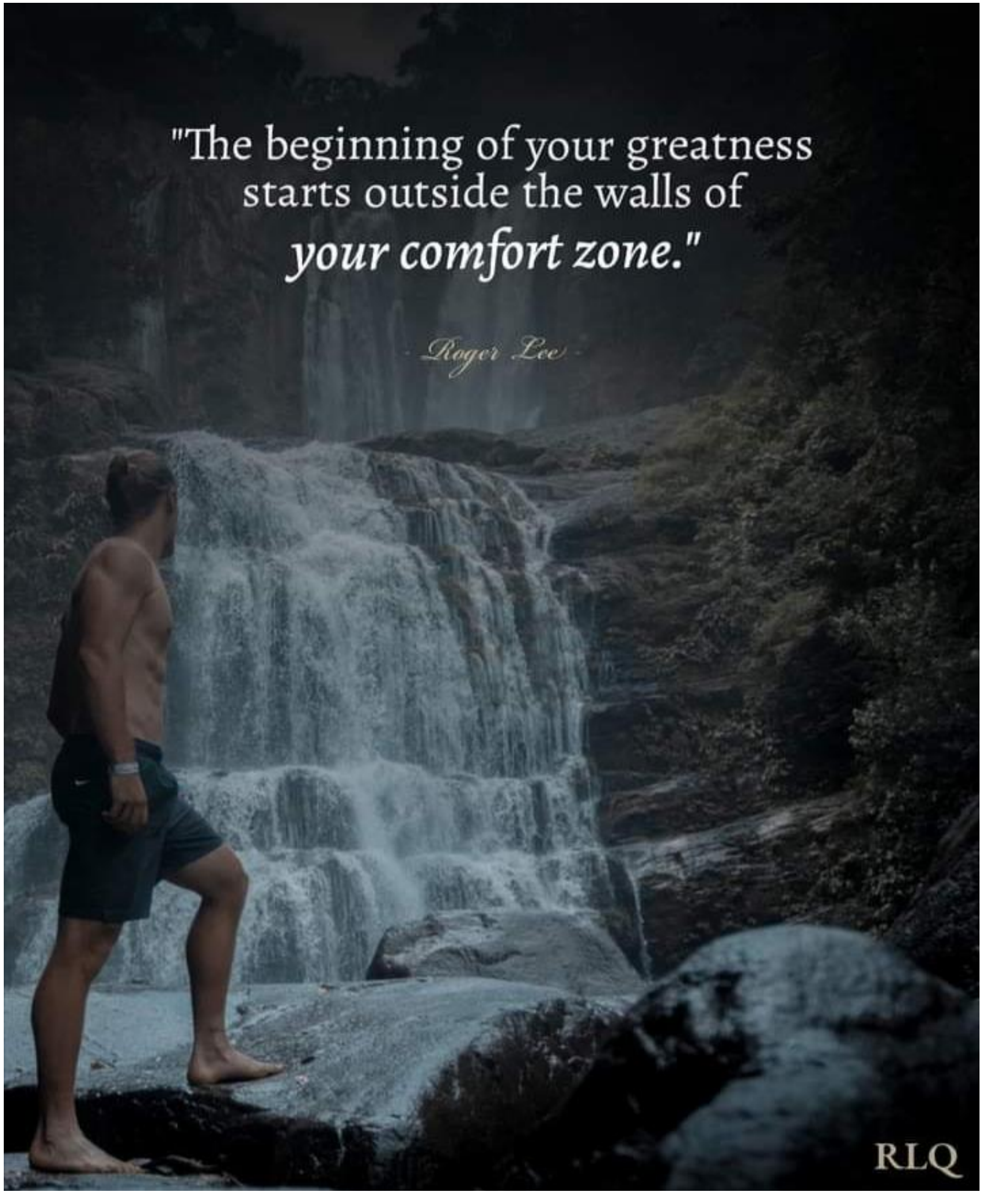
  or

  ***Membrane-bound IgD* (mIgD)** with a tail piece

- ***Ig-α/Ig-β heterodimer*:** transmembrane region and long cytoplasmic tail, interacts with intracellular signaling molecules. **Two** molecules flanking mIgM or IgD.

B cell receptor




"The beginning of your greatness
starts outside the walls of
your comfort zone."
- Roger Lee -
RLQ

Yanar Dag near Baku, Azerbaijan where fire never goes out due to leaking gases, especially methane


Thank You!