

# B cells and Antibodies

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# Adaptive immune system



**B Cells**

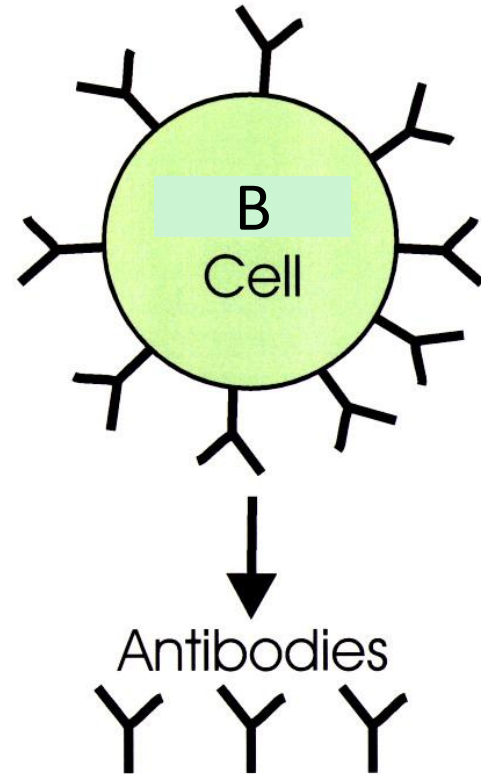
**T Cells**

# B cells

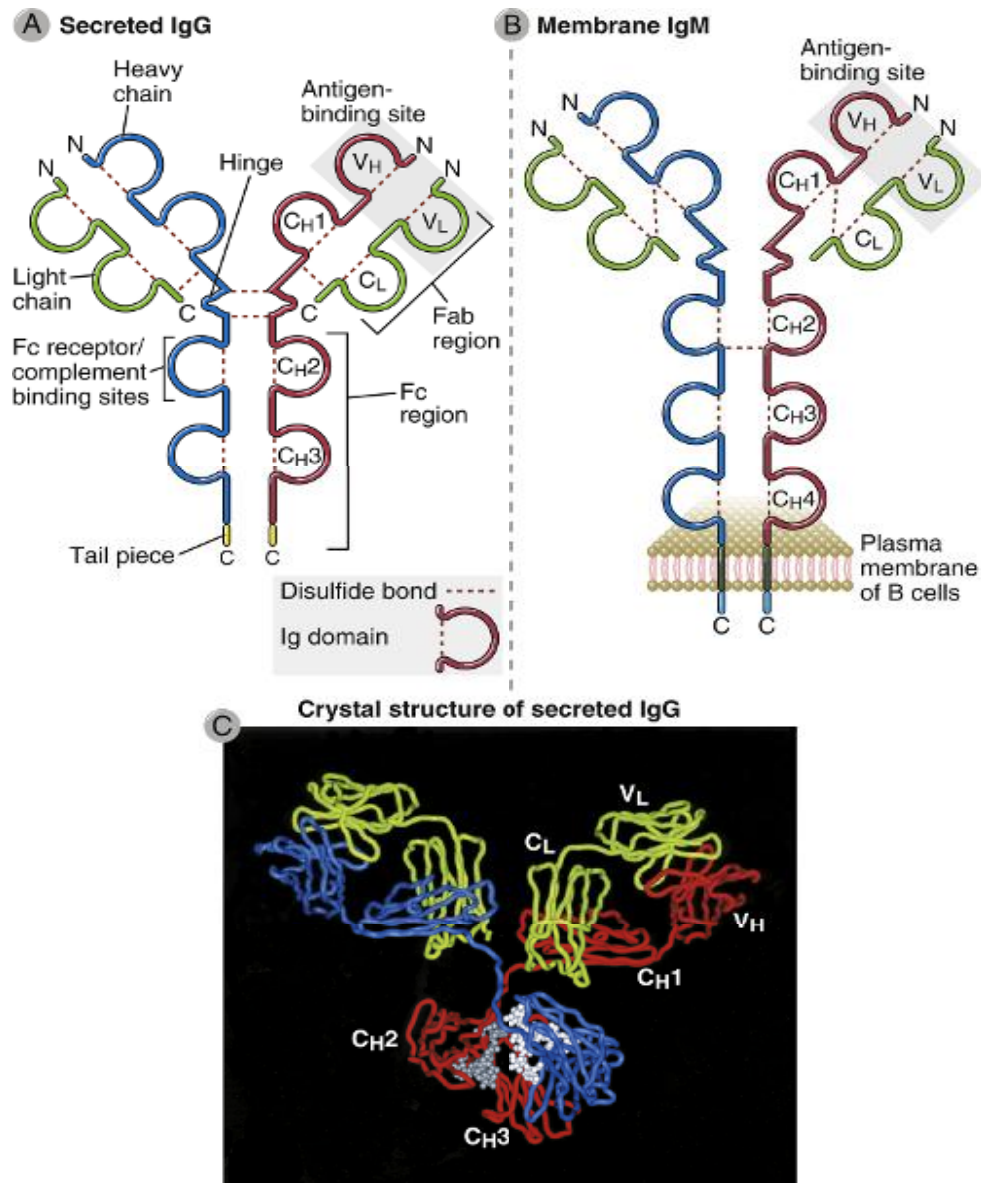
Made in the bone marrow

Select gene segments to make immunoglobulins (Ig)

Some Igs are on the surface, others are secreted.

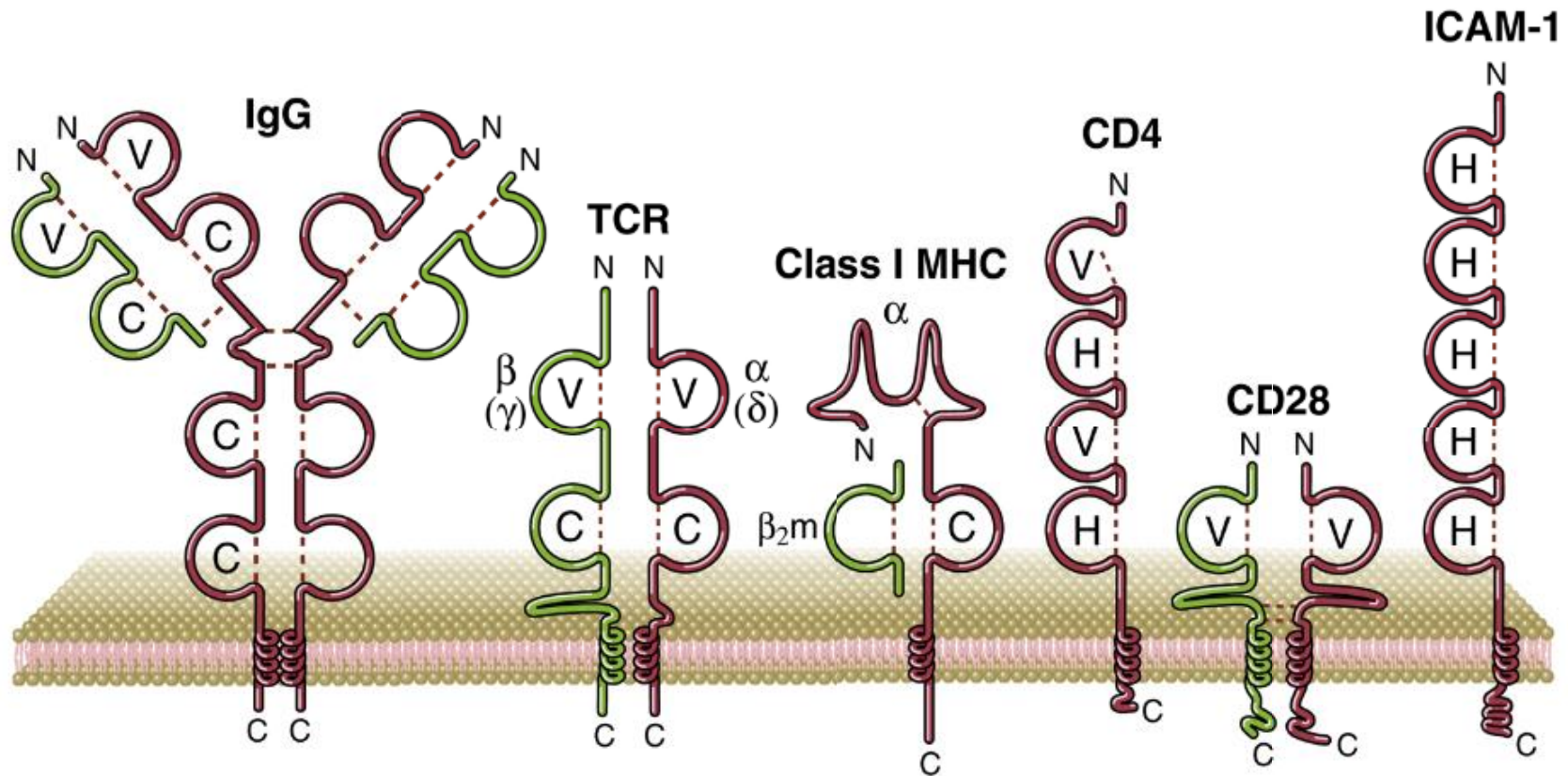


# Antibody Structure

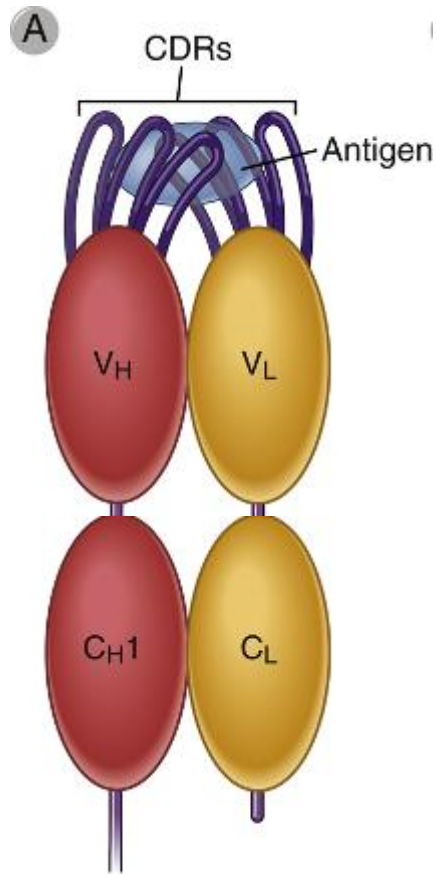




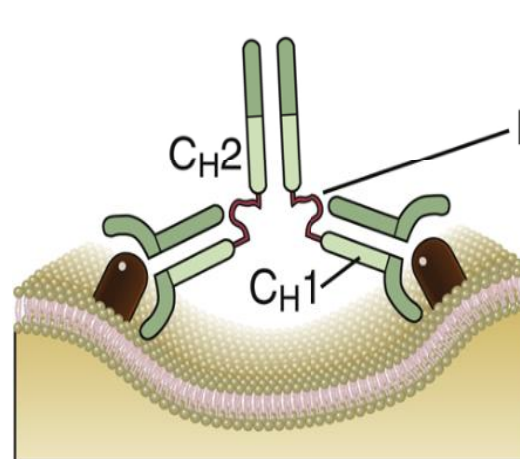
# Ig Superfamily proteins containing Ig domain



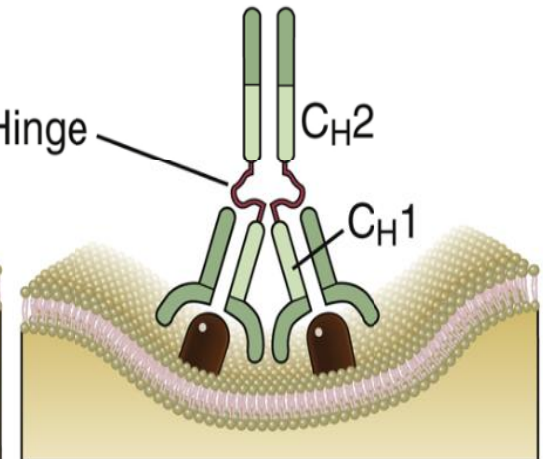
# Binding of Antigen



**A** Widely spaced cell surface determinants

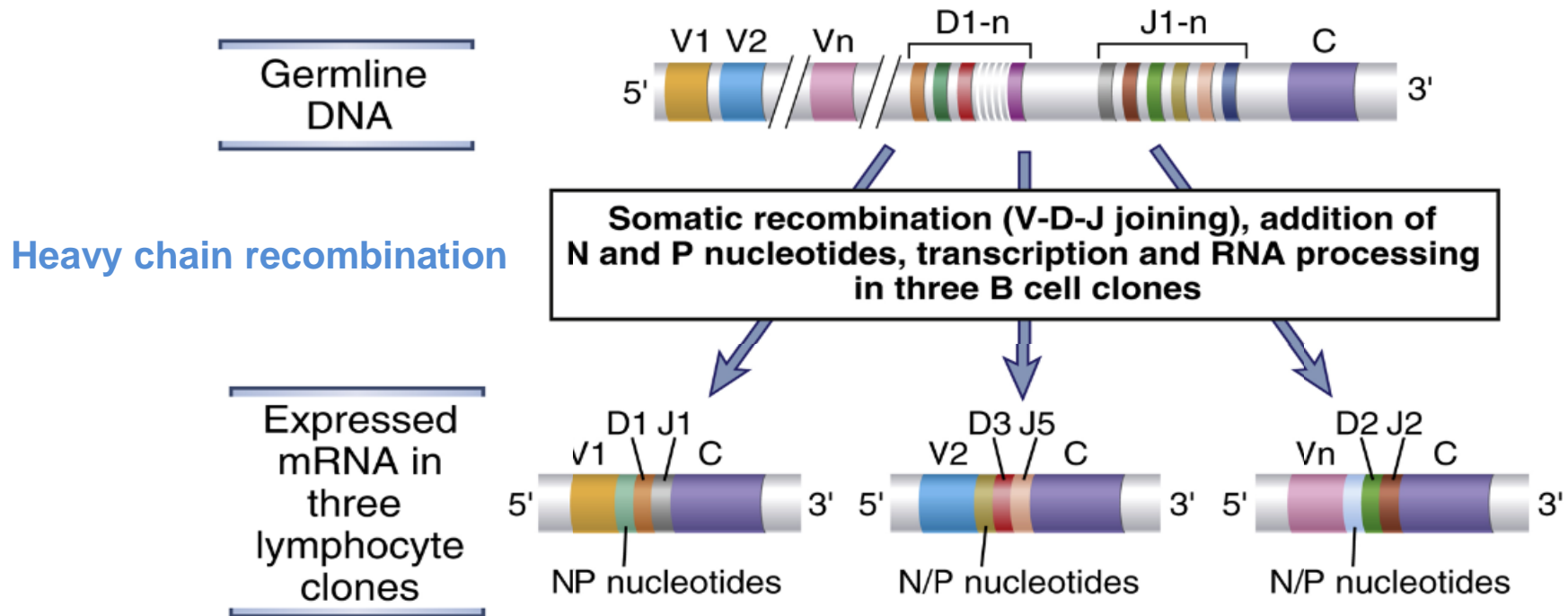


**B** Closely spaced cell surface determinants



CDR= Complementarity-determining regions

# Which Chromosome 14 is used to make Ig?



Gene rearrangement test:

Full Heavy/light chain?

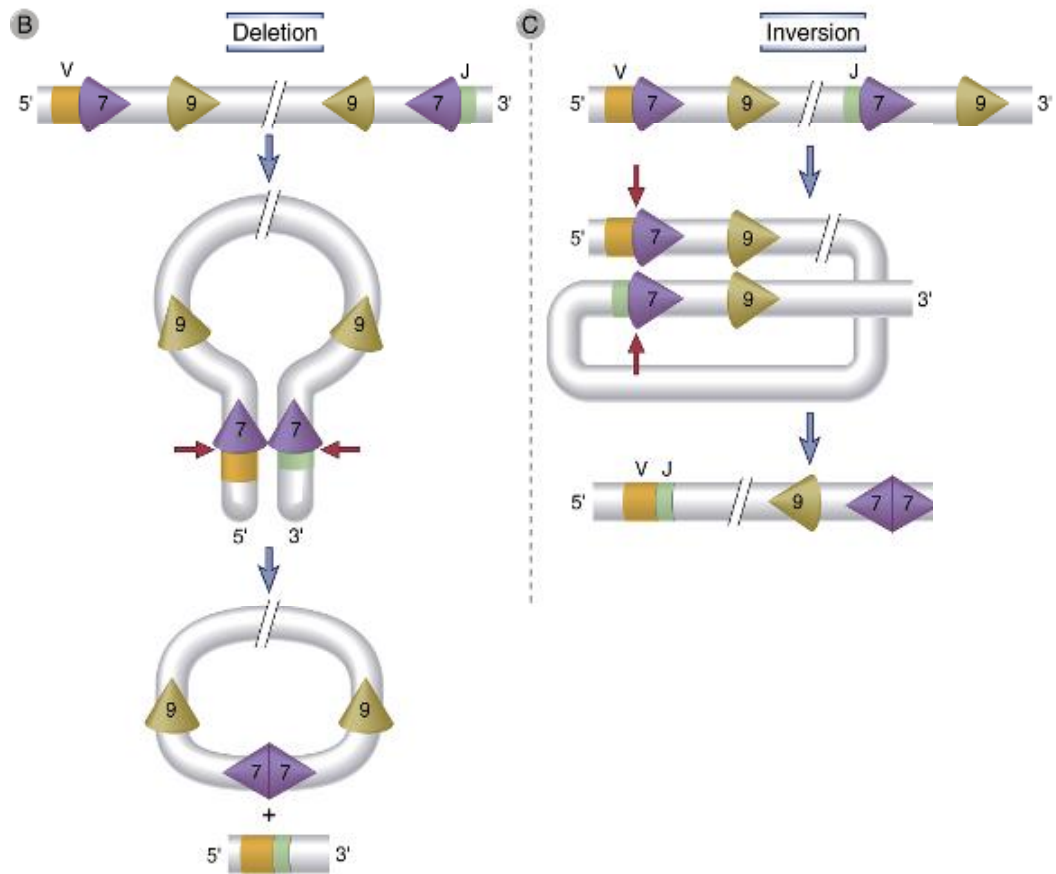
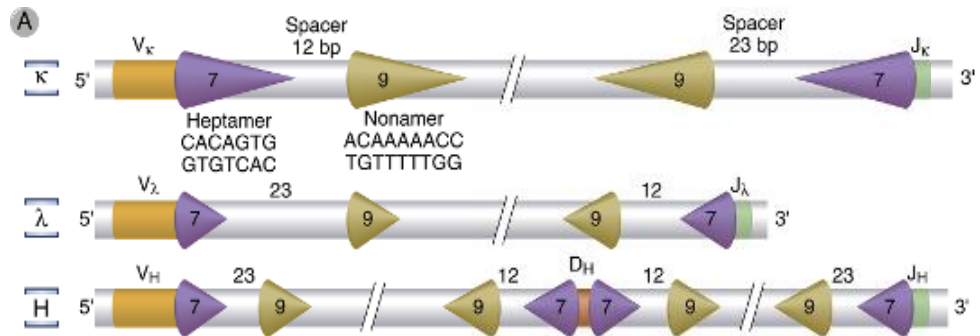
Did it load on cell surface?

If both copies fail:

B cell dies, by apoptosis

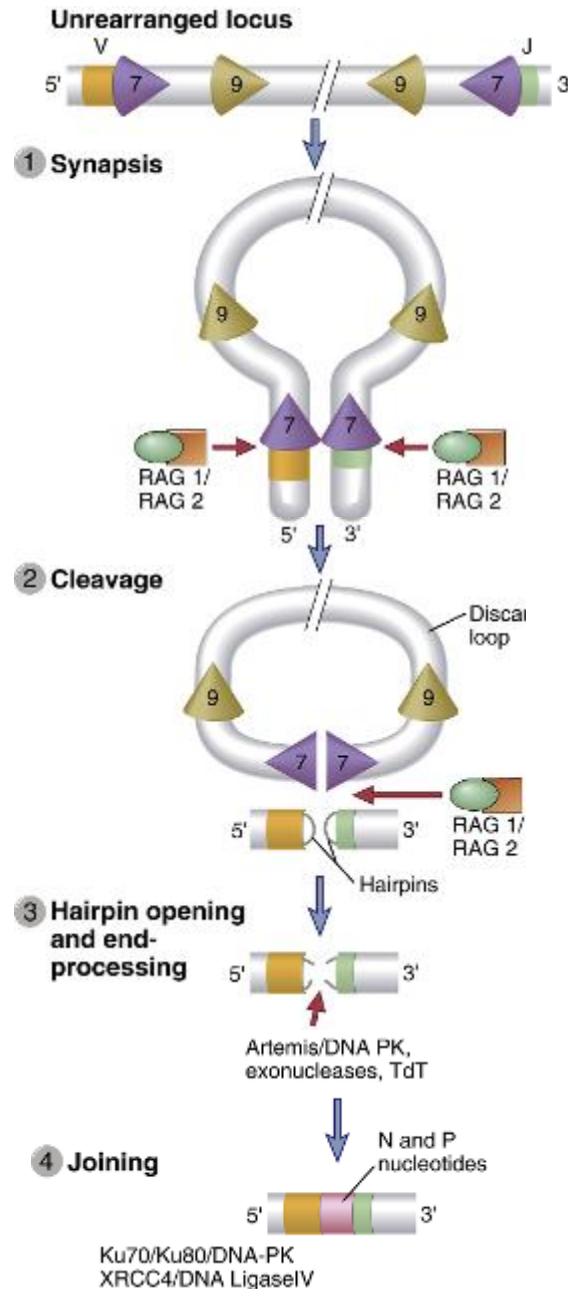
If yes, inactivate other copy of chromosome 14

# V(D)J Recombination

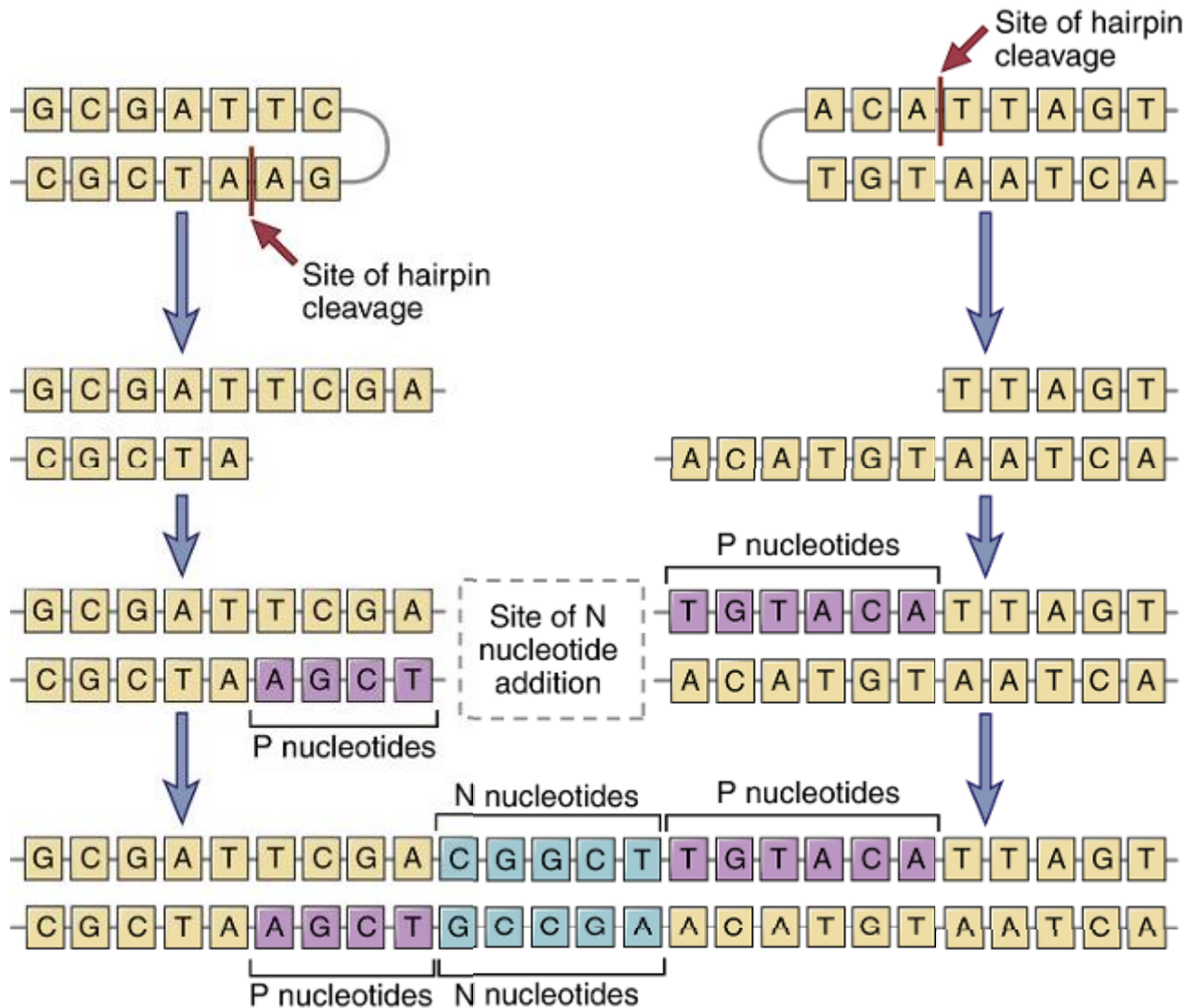




# Sequence of events in VDJ recombination



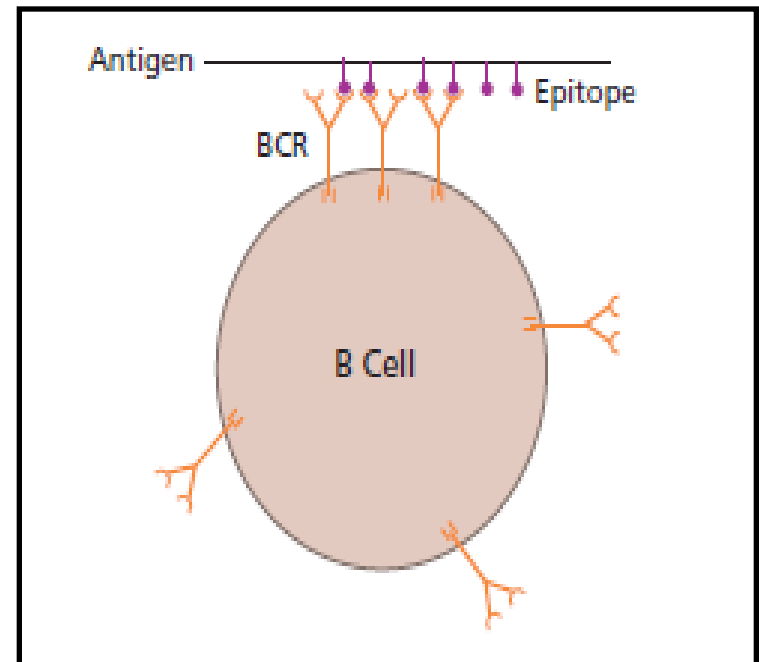
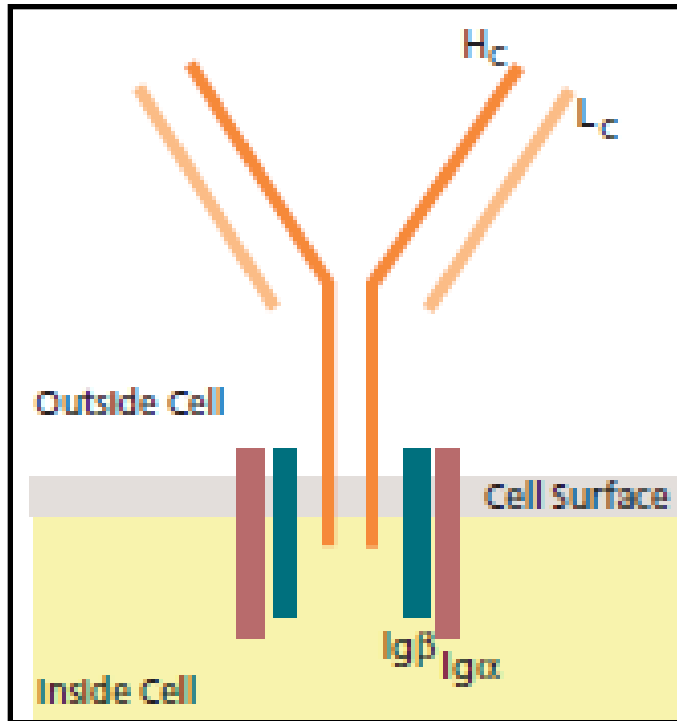
# Junctional Diversity



**One B cell** → **One antibody** (one heavy and one light chains)

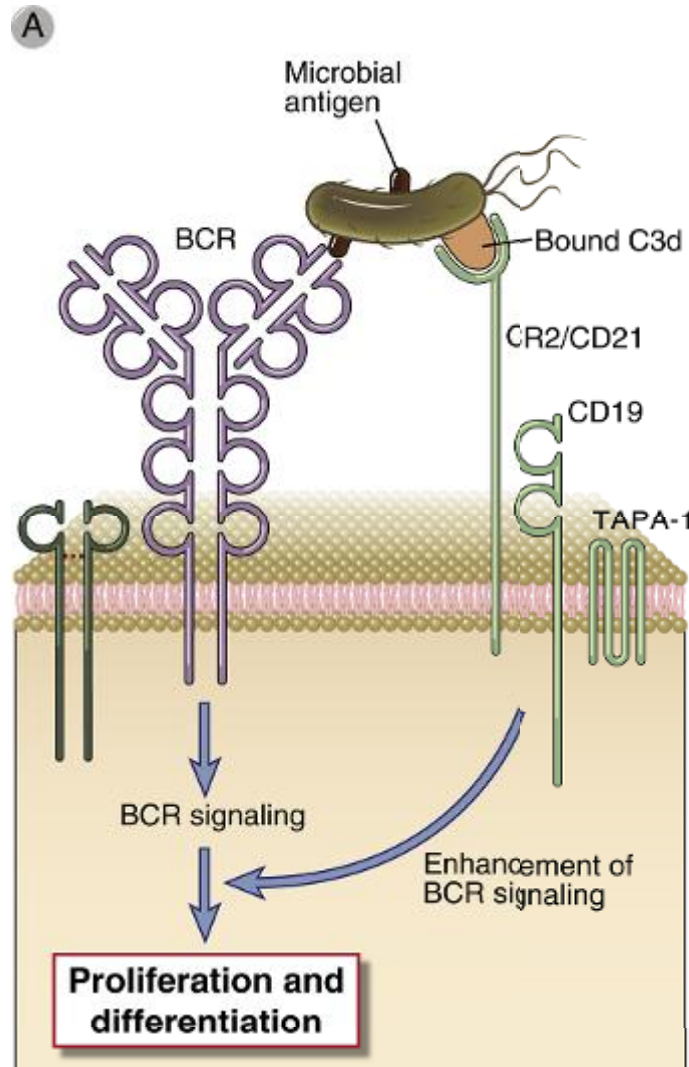
Recombination options so many! We can produce antibodies to **every** organic molecule available.

# BCR signaling



Accessory proteins are required for signaling  
but cross-linking of antibodies is key.

# Opsonization by complement system greatly amplifies BCR signaling



Complement receptor engagement tightens BCR binding and signaling



# How are B cells activated?

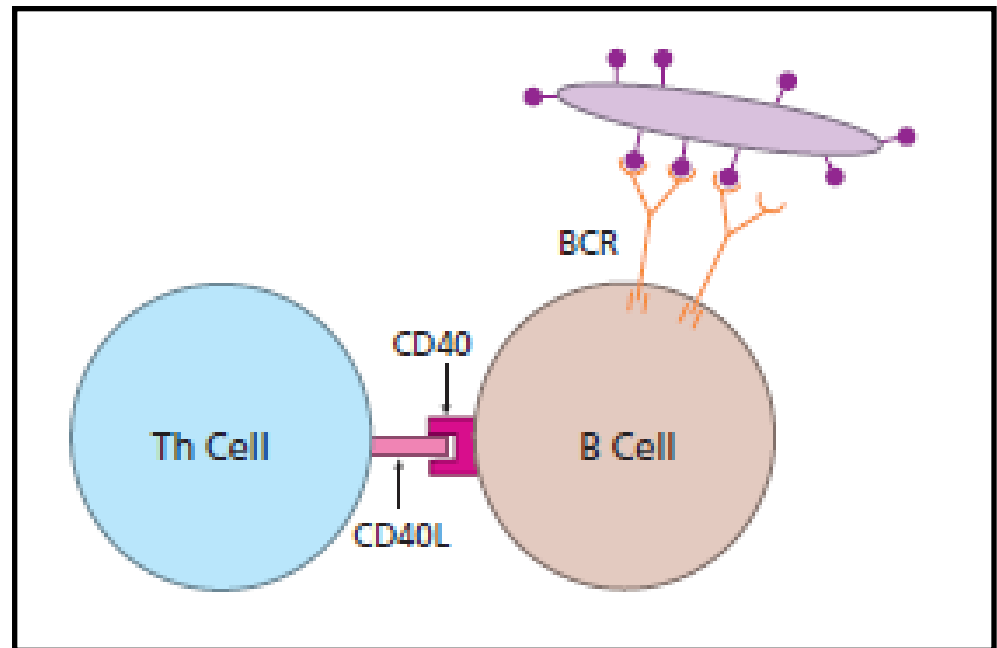
## Two-step activation system:

1- BCR engagement and clustering

2- Co-stimulatory signal

(T-cell-dependent: CD40L)

(T-cell independent: cytokines: IFN- $\gamma$ )



What is the purpose of T-cell-independent activation??

# B cell maturation

**1- Class Switching**

**2- Somatic hypermutation**

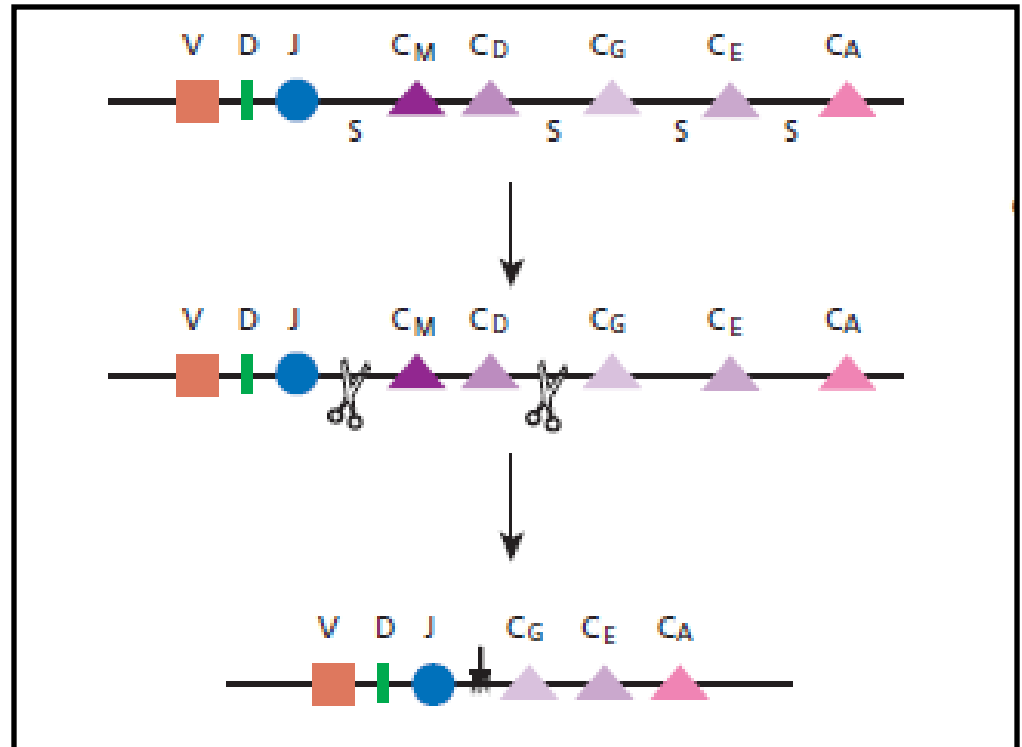
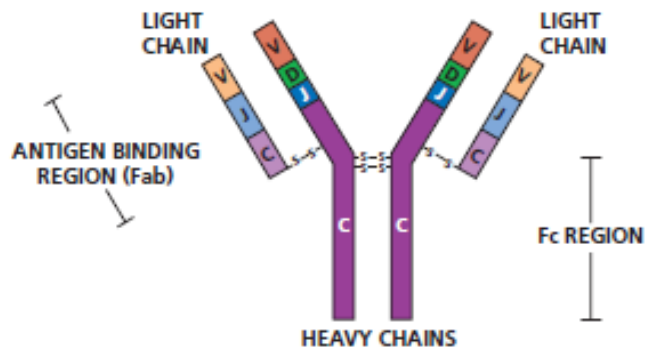
**3- Career Decision**

# Class Switching

Changing antibody class from IgM or IgD to IgG, IgA, or IgE.

Why?

**Class switch from IgM to IgG**



AID is a key enzyme for isotype switching

# Antibody classes and their function

## IgM Antibodies

Pentamer, first antibody to be produced.

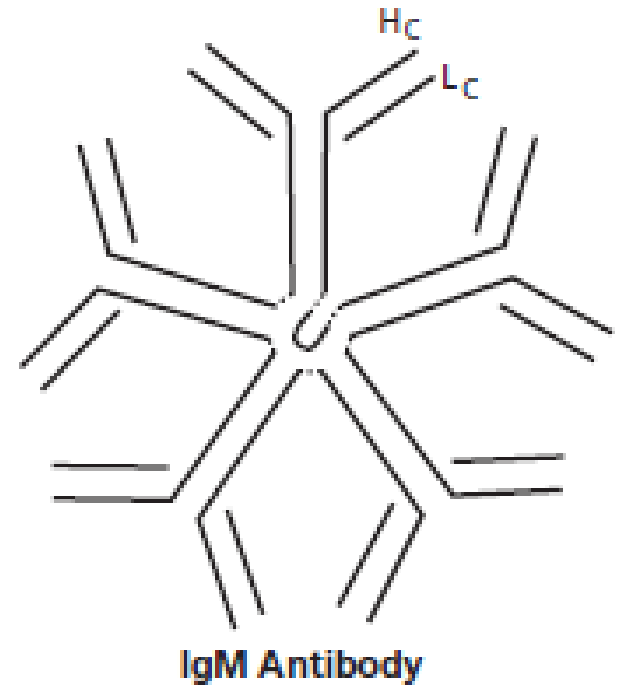
Can trigger classical complement pathway through bringing C1 molecules in close proximity.

C1s bind to Fc portion, get activated and subsequently activate the C3 convertase causing a complement cascade on the surface of the pathogen.

Why is the classical pathway needed?

Why IgM not IgG first??

Better complement fixer, better neutralizing ability



# IgG Class

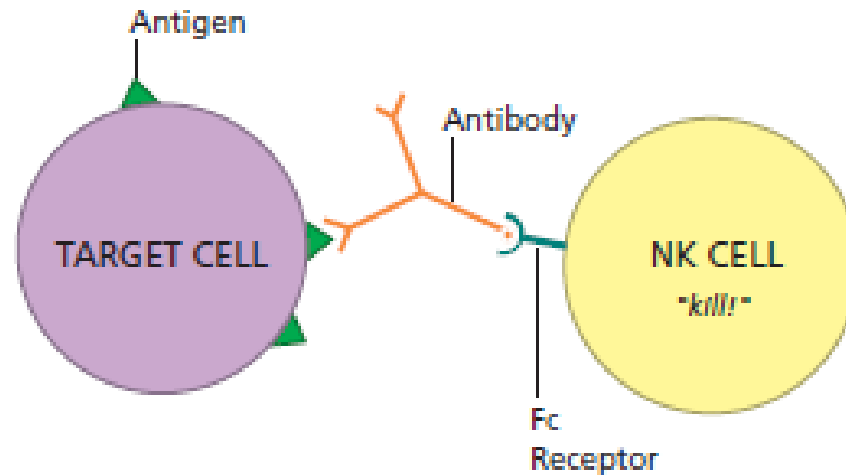
Called Gamma globulins. Decent complement fixers, good virus inactivators.

Can cross placenta, half-life 23 days, how long does IgM live??

Four subclasses: IgG1, IgG2, IgG3, IgG4

IgG1 is a good opsoniser. Macrophages and neutrophils have receptors for IgG1-Fc

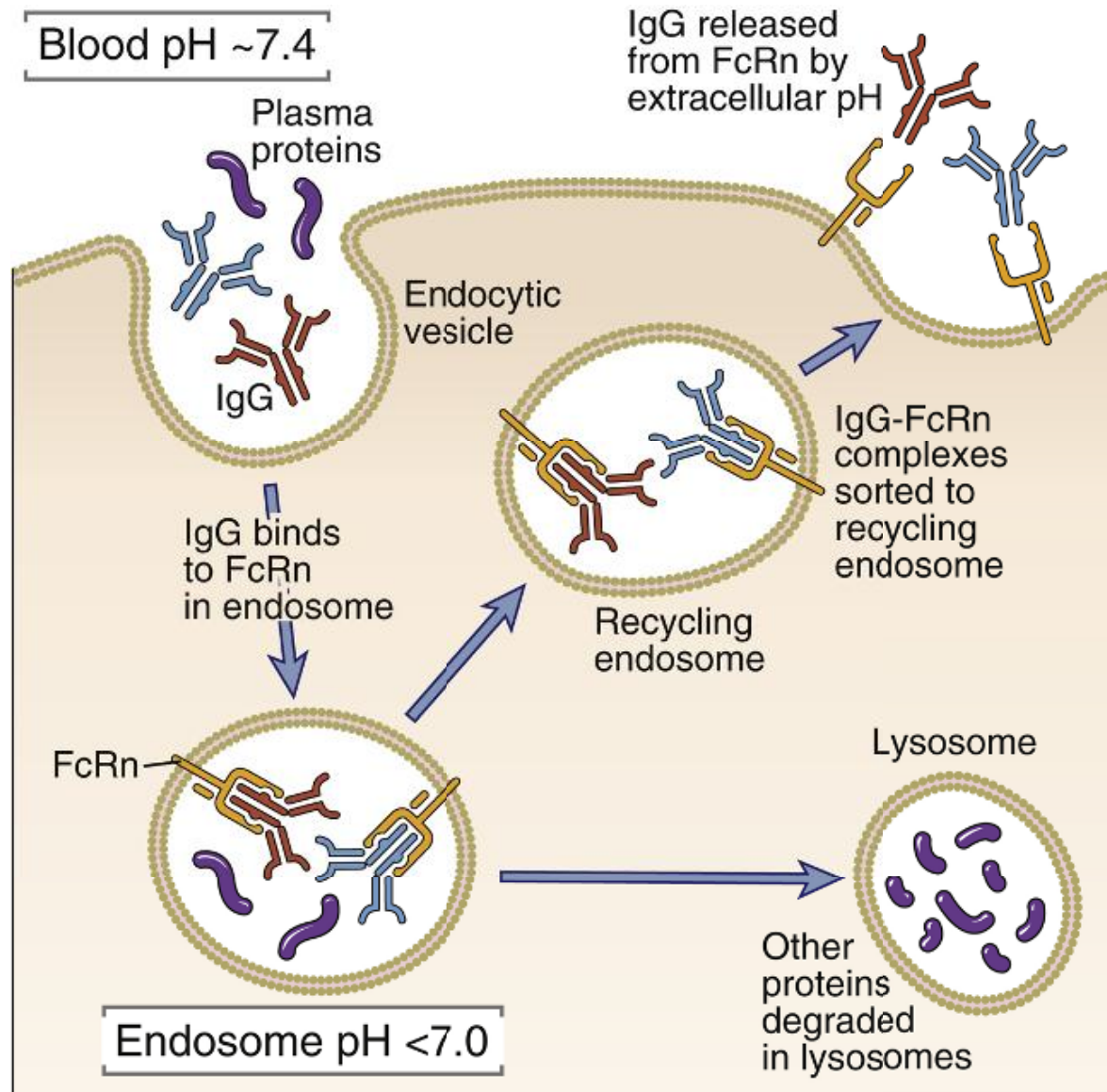
IgG3 fixes complement better than other subclasses. NK cells have receptors for it.



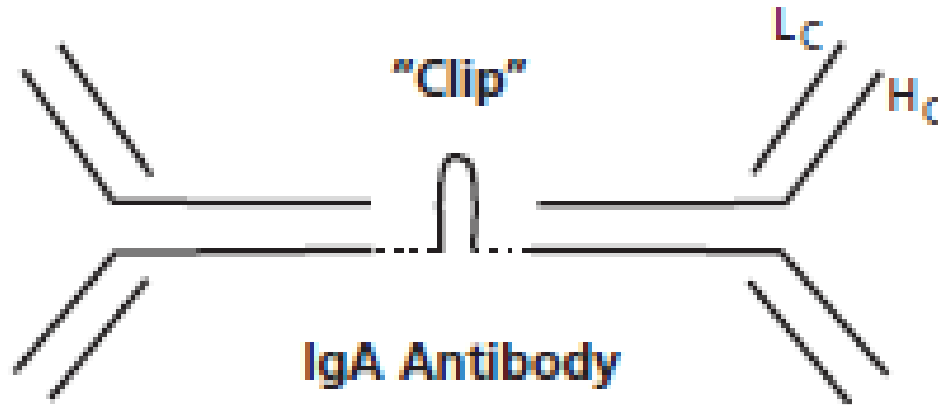
Antibody-dependent cellular cytotoxicity (ADCC)



# Reason behind longer half-life of IgG



# IgA class



Main Ab class that guards the mucosal surfaces of the body.

Its structure facilitates its transport to intestines, and makes it resistant to acids and enzymes

Dimeric structure helps clump bacteria together to be swept out with mucus or feces.

Secreted into the milk of nursing mothers. Why?

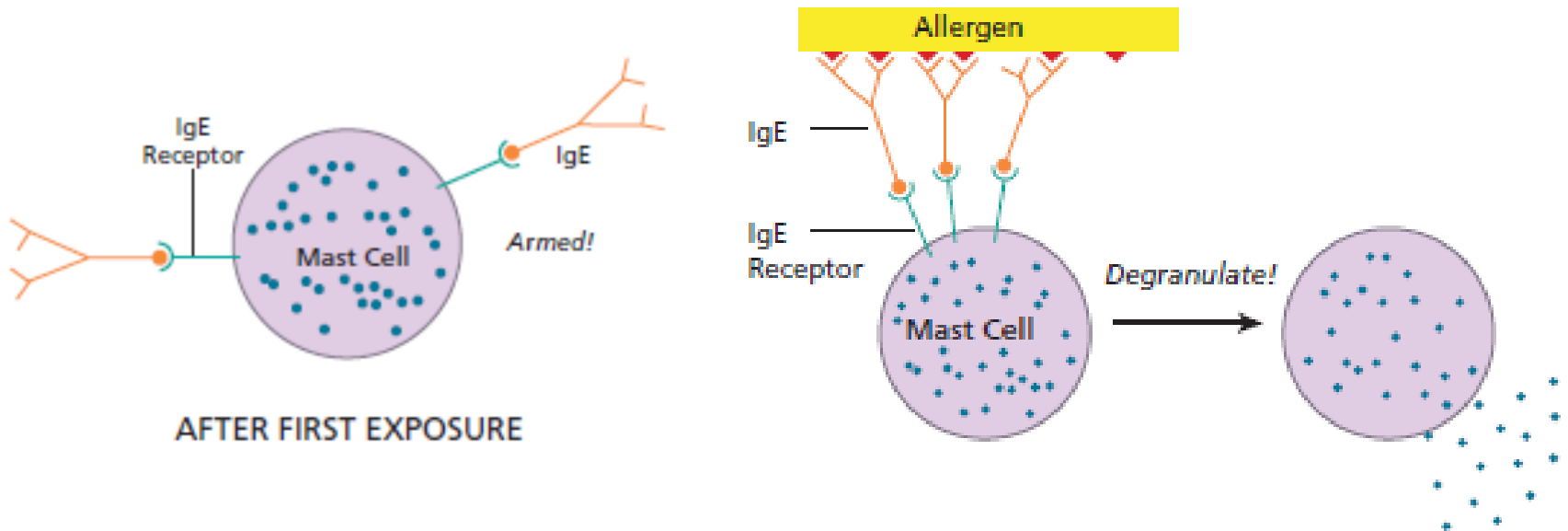
Good or bad complement fixers??

# IgE class

**1-Parasitic Infections:** IgE is made, Fab binds to parasite, Fc binds to mast cell

Mast cell releases histamine and cytokines such as TNF and IL-3,4,5 to kill parasites.

**2- Allergies:**



Allergic reaction, anaphylactic shock in some cases!

# Ab Classes and functions

ANTIBODY CLASS	ANTIBODY PROPERTIES
IgM	Great complement fixer Good opsonizer First antibody made
IgA	Resistant to stomach acid Protects mucosal surfaces Secreted in milk
IgG	OK complement fixer Good opsonizer Helps NK cell kill (ADCC) Can cross placenta
IgE	Defends against parasites Causes anaphylactic shock Causes allergies

Also, see **Table 5-2** Abul K. Abbas Textbook

# What triggers class-switch?

## Cytokines produced by Th cells

**IL-4** and **IL-5** favour a switch to **IgE** (Parasitic infections)

**IFN- $\gamma$**  favours switch to **IgG** (Fights bacteria and viruses)

**TGF- $\beta$**  favours a switch to **IgA** (Common colds, intestinal infections).



# Somatic Hypermutation

Mutation rate in our genome is approximately 1:100,000,000 b.p. per replication cycle.

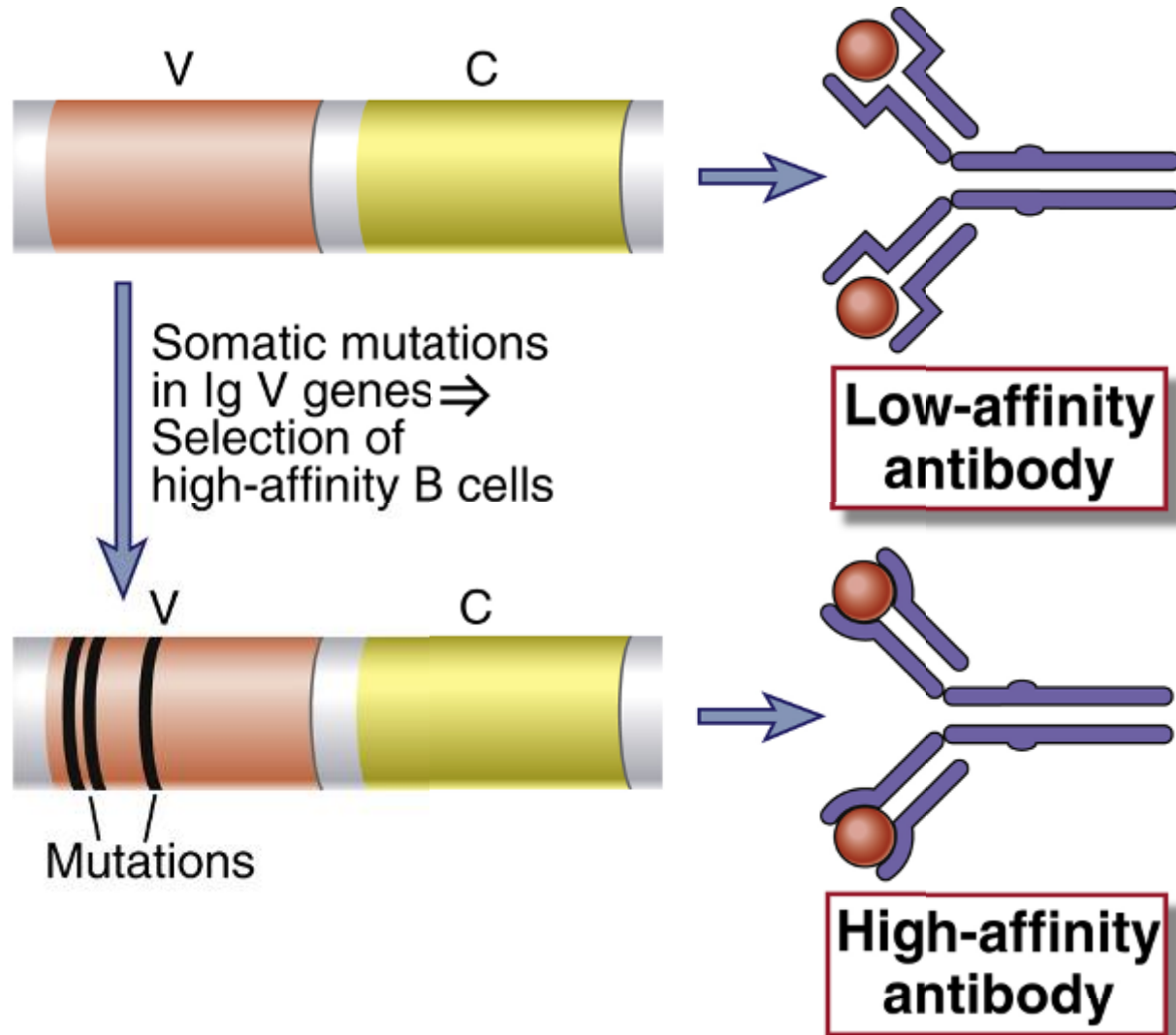
After VDJ segments have been selected, this region undergoes very high mutation rate:  
(As high as 1:1000 b.p. per generation).

This somatic hypermutation affects affinity of Fab region of B cell antibody.

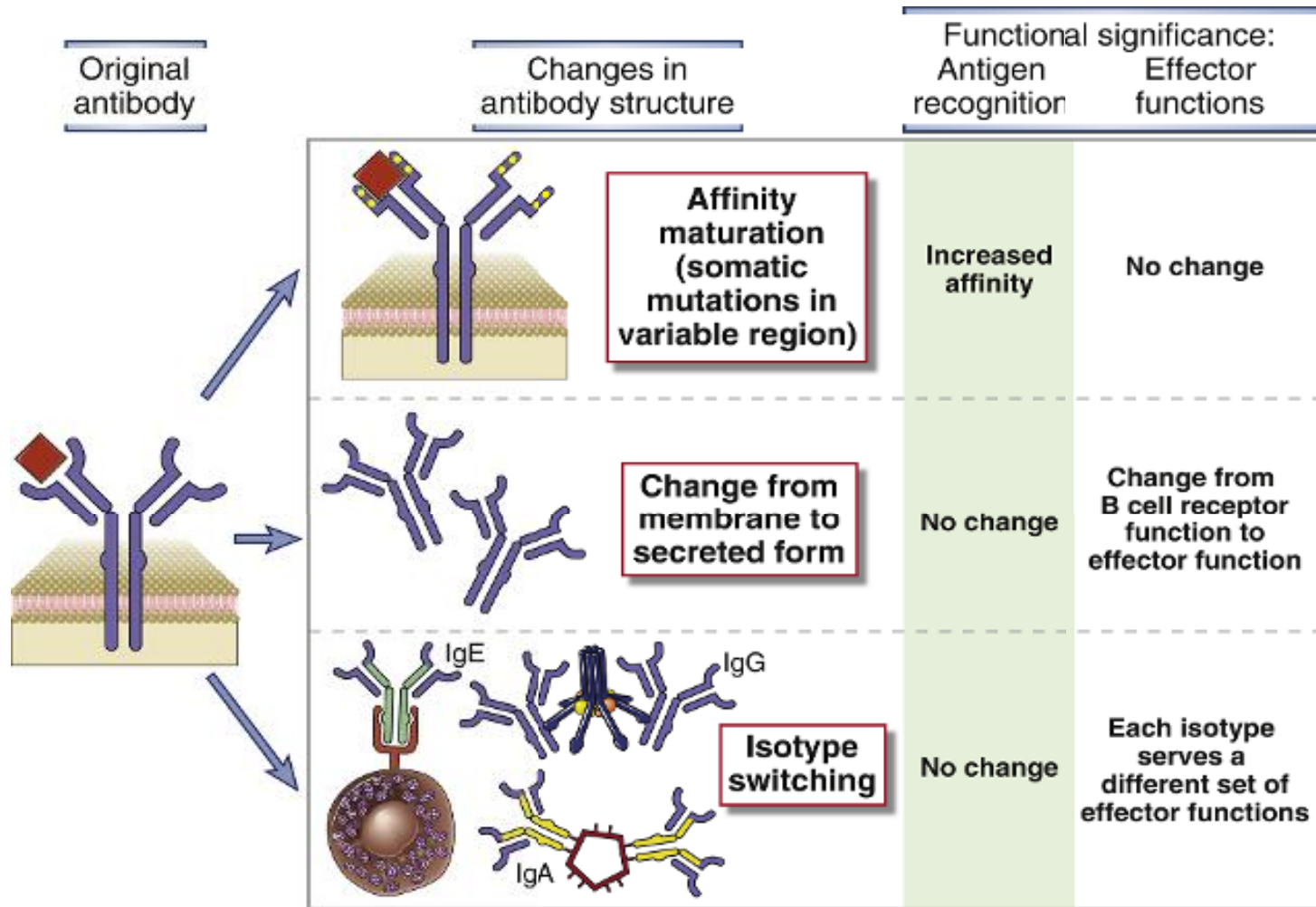
B cells with higher affinity are better stimulated by antigen presented by follicular DC and  
Can present it to  $T_{FH}$  which rescues B cells from apoptosis and promotes proliferation.

**B cells can change both their Fc region (Class-switch) and Fab region (somatic hypermutation) to become better adapted to fight invaders.**

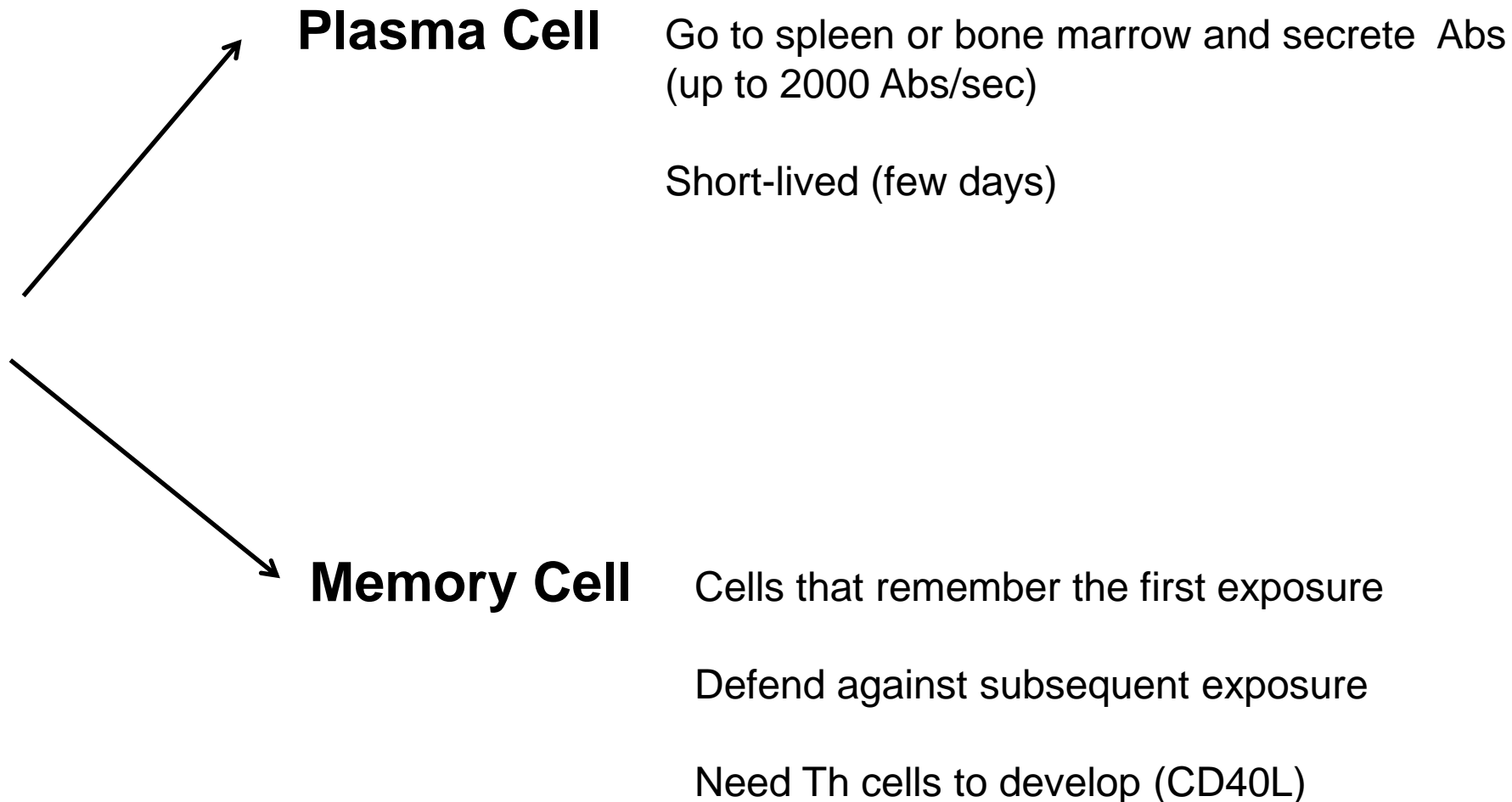
# Affinity Maturation



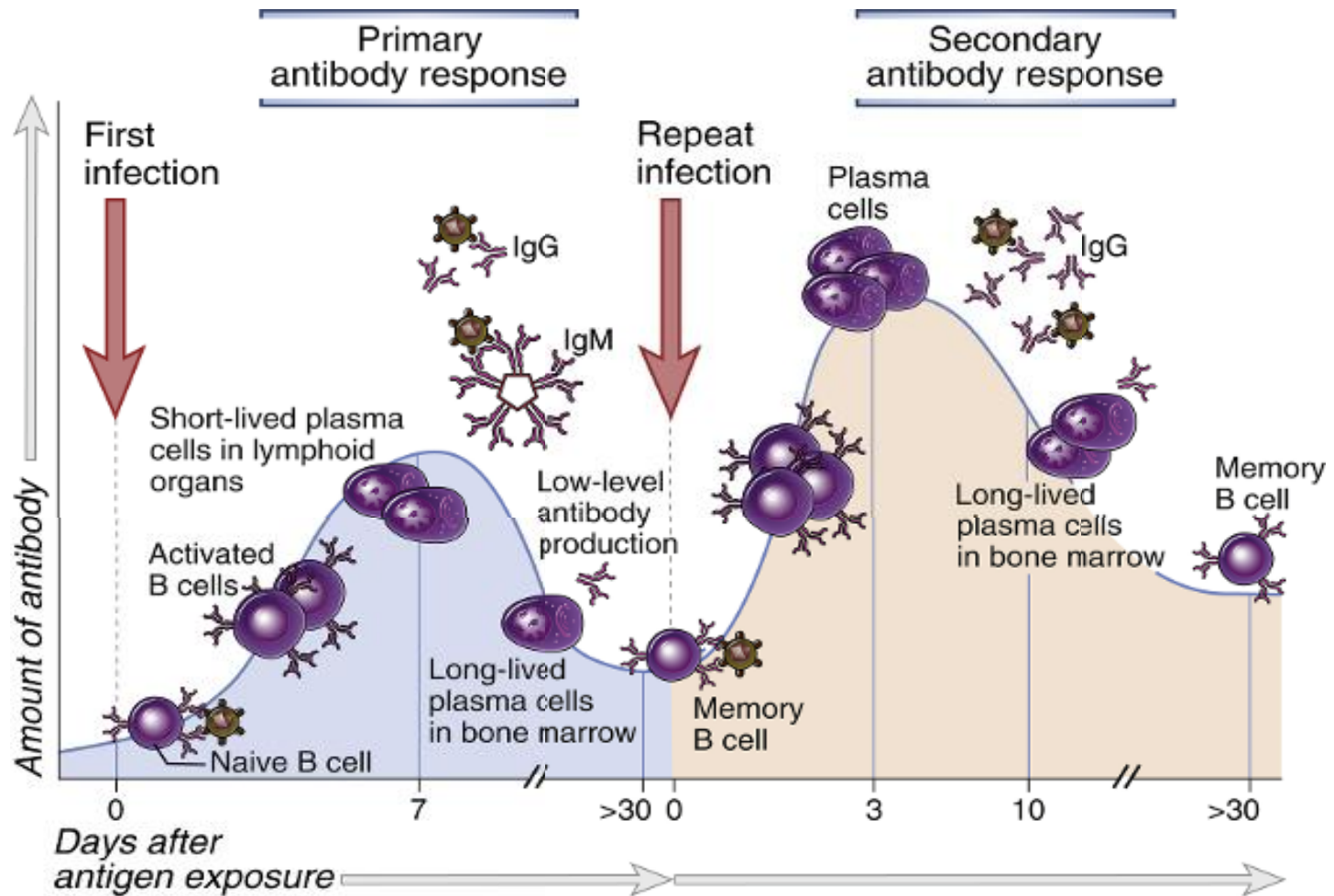
# Changes in Ab structure during humoral response



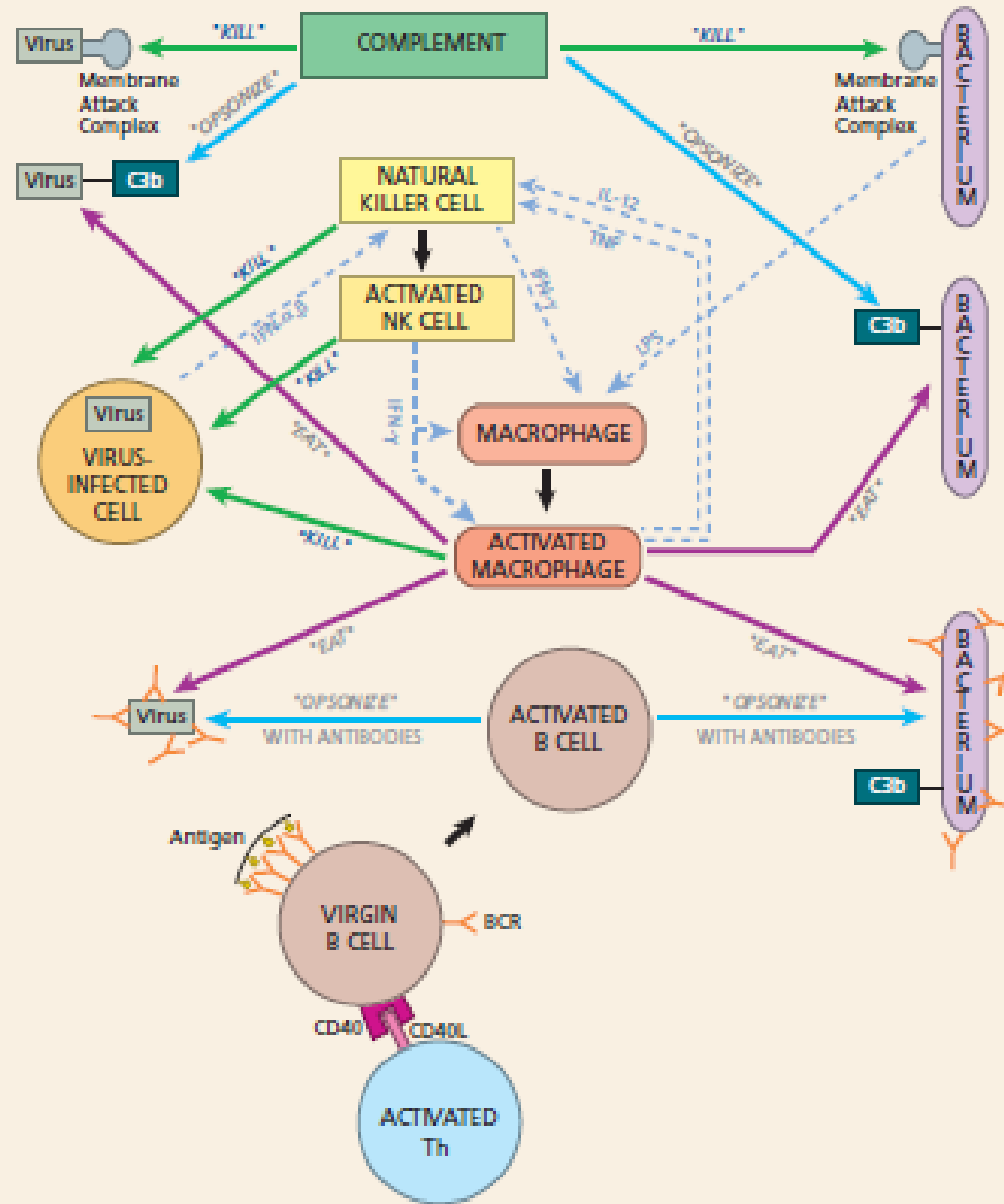
# B cells make a career choice



# Primary and Secondary Humoral Immune Responses







Thank you!

Questions???