

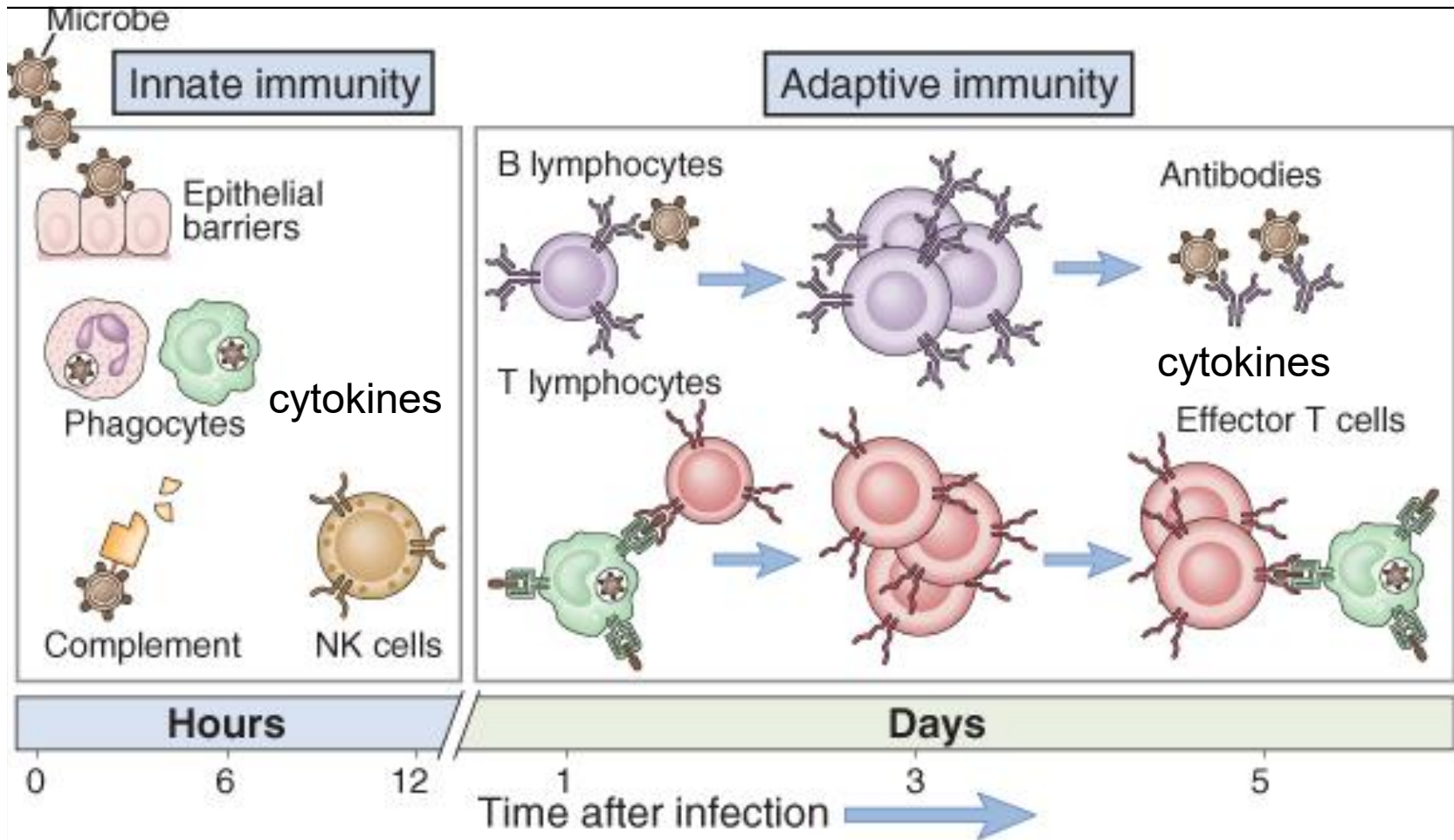
**Corso di Immunologia - III anno**  
**Prof. Giovanni Bernardini**

**Lezione 14/10/2026**

**“Il sistema immunitario:  
componenti dell'immunità acquisita”**

**Il materiale presente in questo documento viene distribuito esclusivamente  
ad uso interno e per scopi didattici.**

# The immune response consists of TWO “PHASES”



# I COMPONENTI CELLULARI DELL'IMMUNITA' ACQUISITA o SPECIFICA:

- LINFOCITI T

- LINFOCITI B

# The **adaptive** response :

is **antigen-specific**

develops on a **clonal** basis

is capable of **memory**

} T and B lymphocytes

**ANTIGEN** recognition ability is at the basis of  
**ADAPTIVE** immunity

**ANTIGEN:** any molecular structure recognized by T and B lymphocyte antigen receptors

**ANTIGEN:** any molecular structure recognized by T and B lymphocyte antigen receptors

Antigenicity depends on:

1- Chemical nature: proteins are good antigens; polysaccharides and lipids much less, and only for B cells

2 - Structural complexity

3- Conformation: important for B but not for T cell recognition

4-Difference from self

# The ANTIGEN RECEPTORS of B and T LYMPHOCYTES

## BCR= B cell receptor

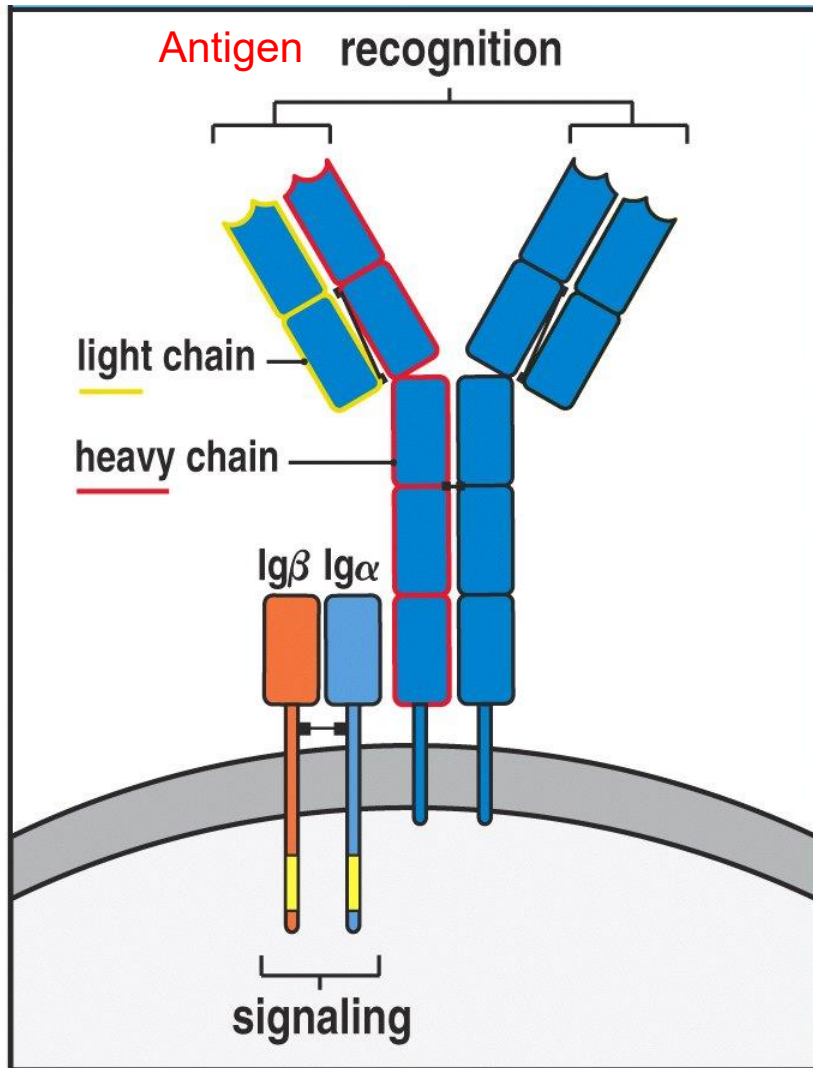


Figure 6-8 Immunobiology, 6/e. (© Garland Science 2005)

## TCR=T cell receptor

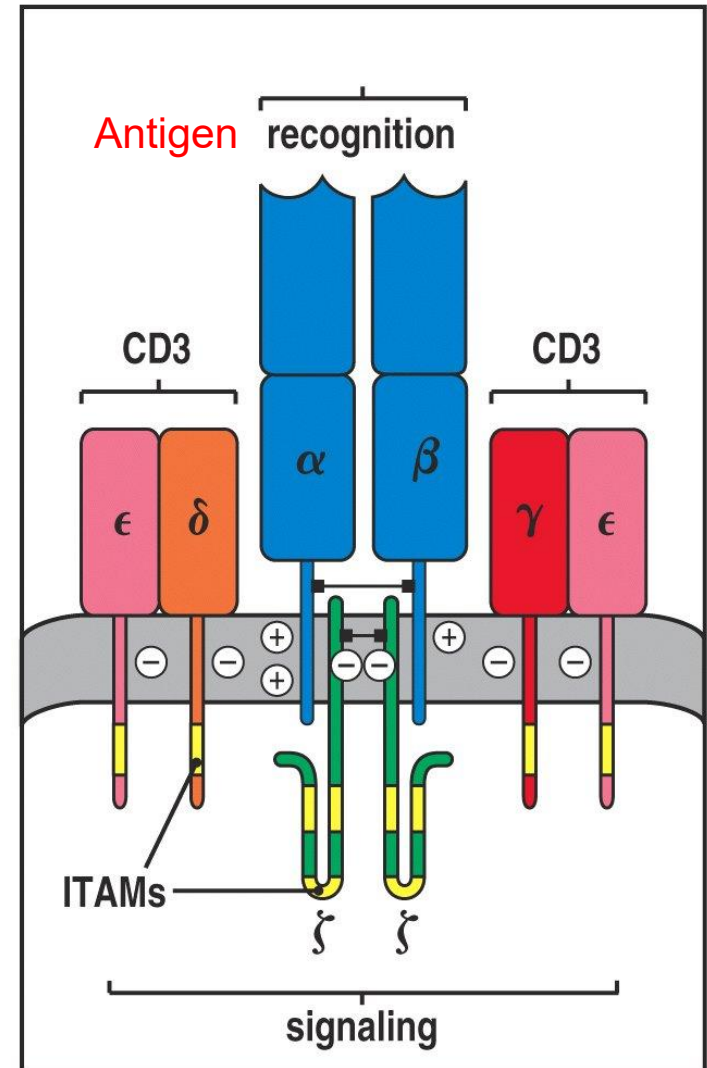
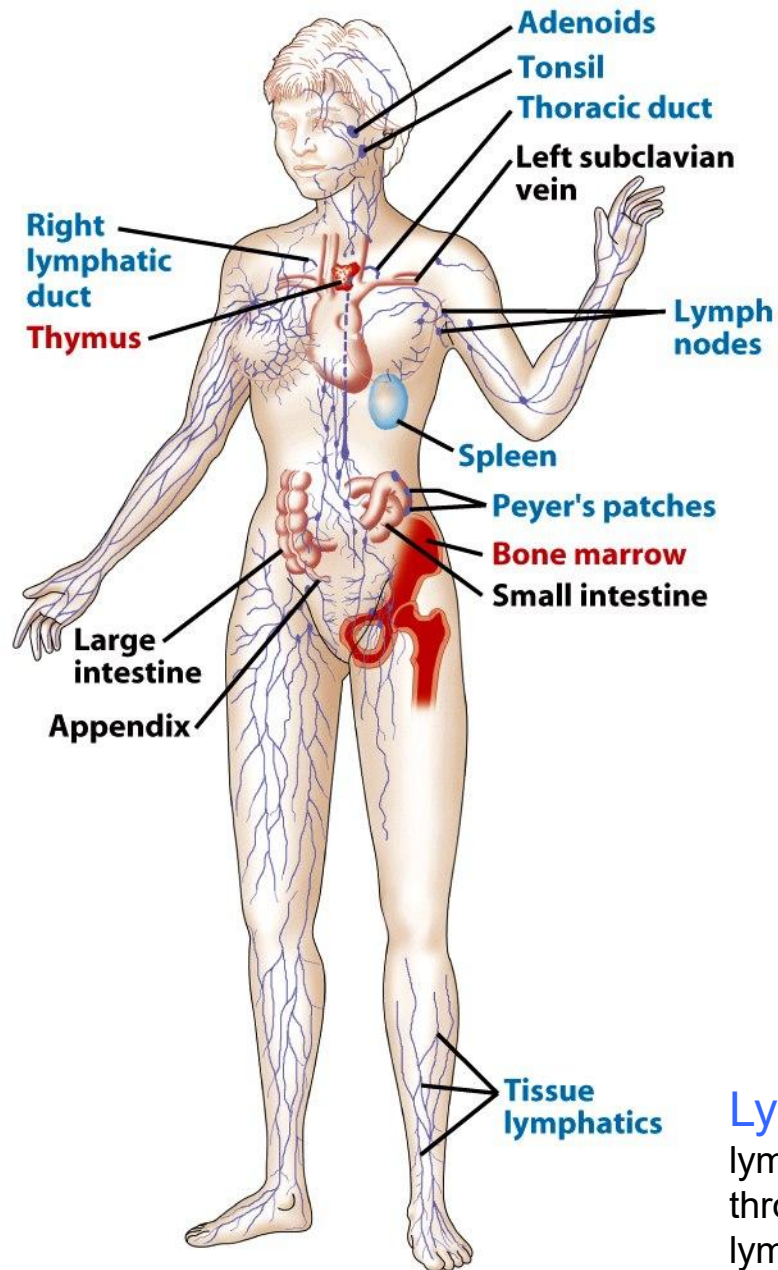


Figure 6-9 Immunobiology, 6/e. (© Garland Science 2005)

# Where does the encounter with antigen occur?



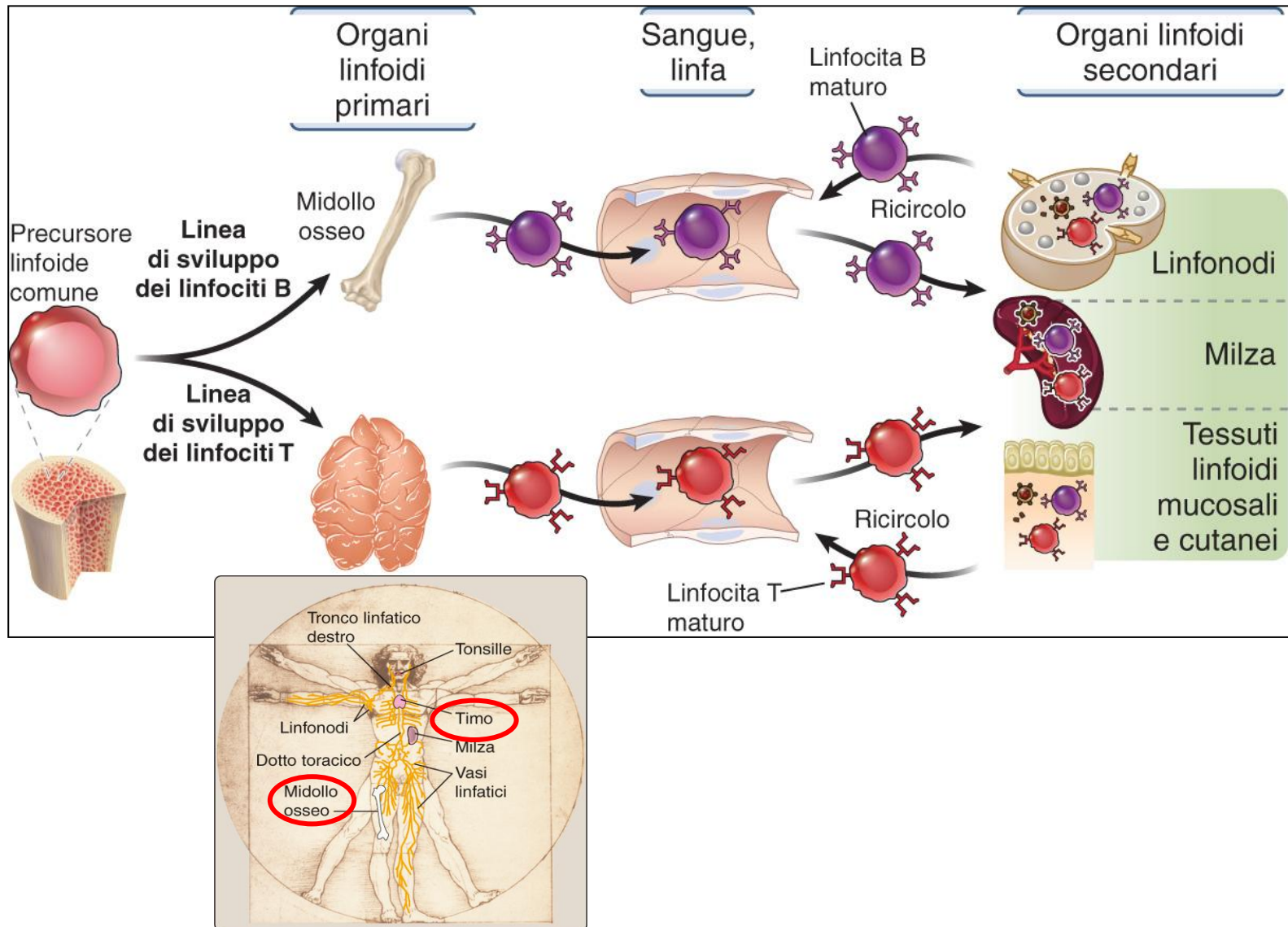
Primary and **secondary**

## LYMPHOID ORGANS

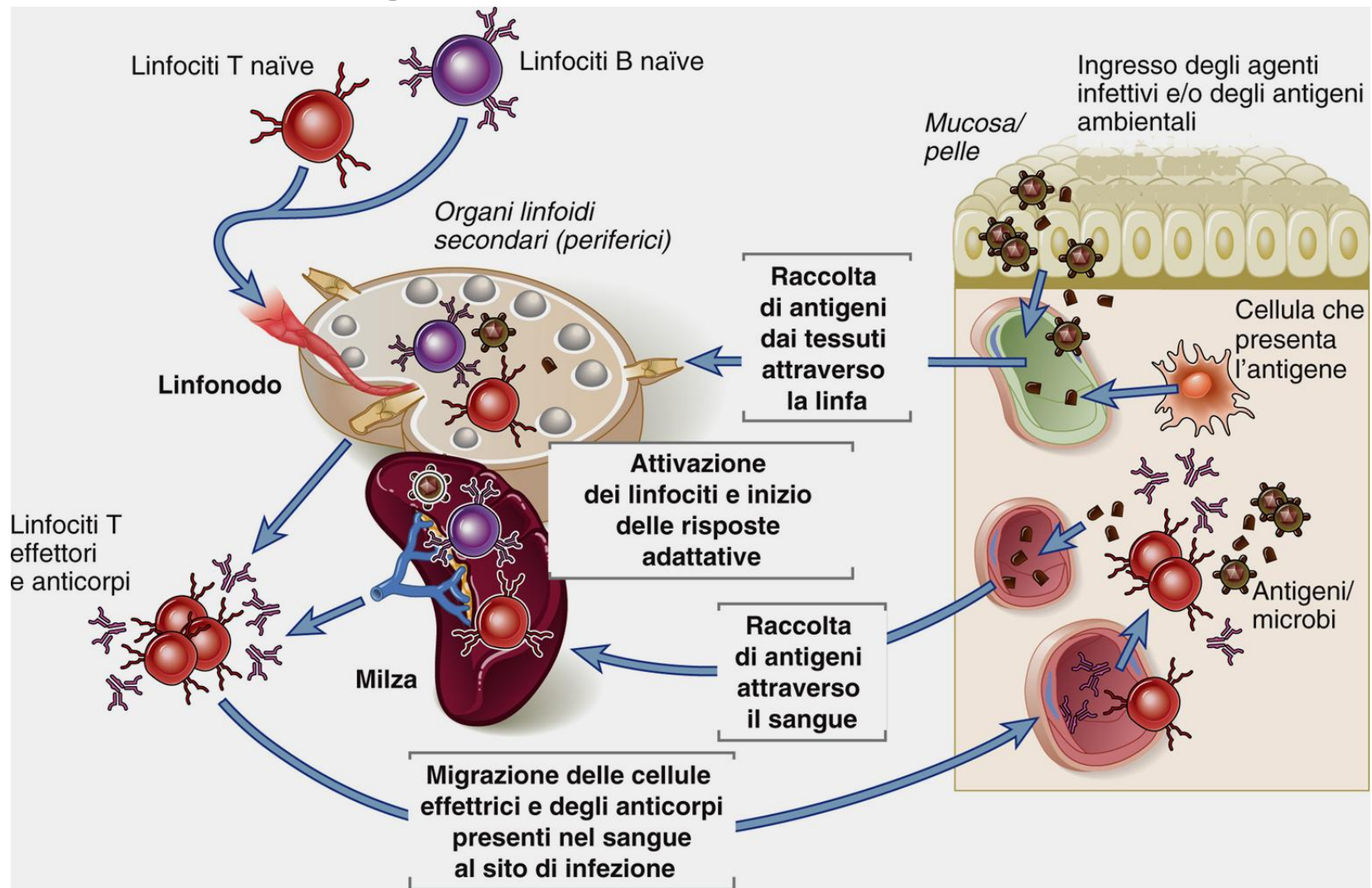
- Lymph nodes  
- Spleen  
- Mucosal and cutaneous immune system

**Lymph nodes:** are encapsulated nodular aggregates of lymphoid tissues located along lymphatic channels throughout the body. Fluid, called lymph, is drained to the lymph nodes from tissues

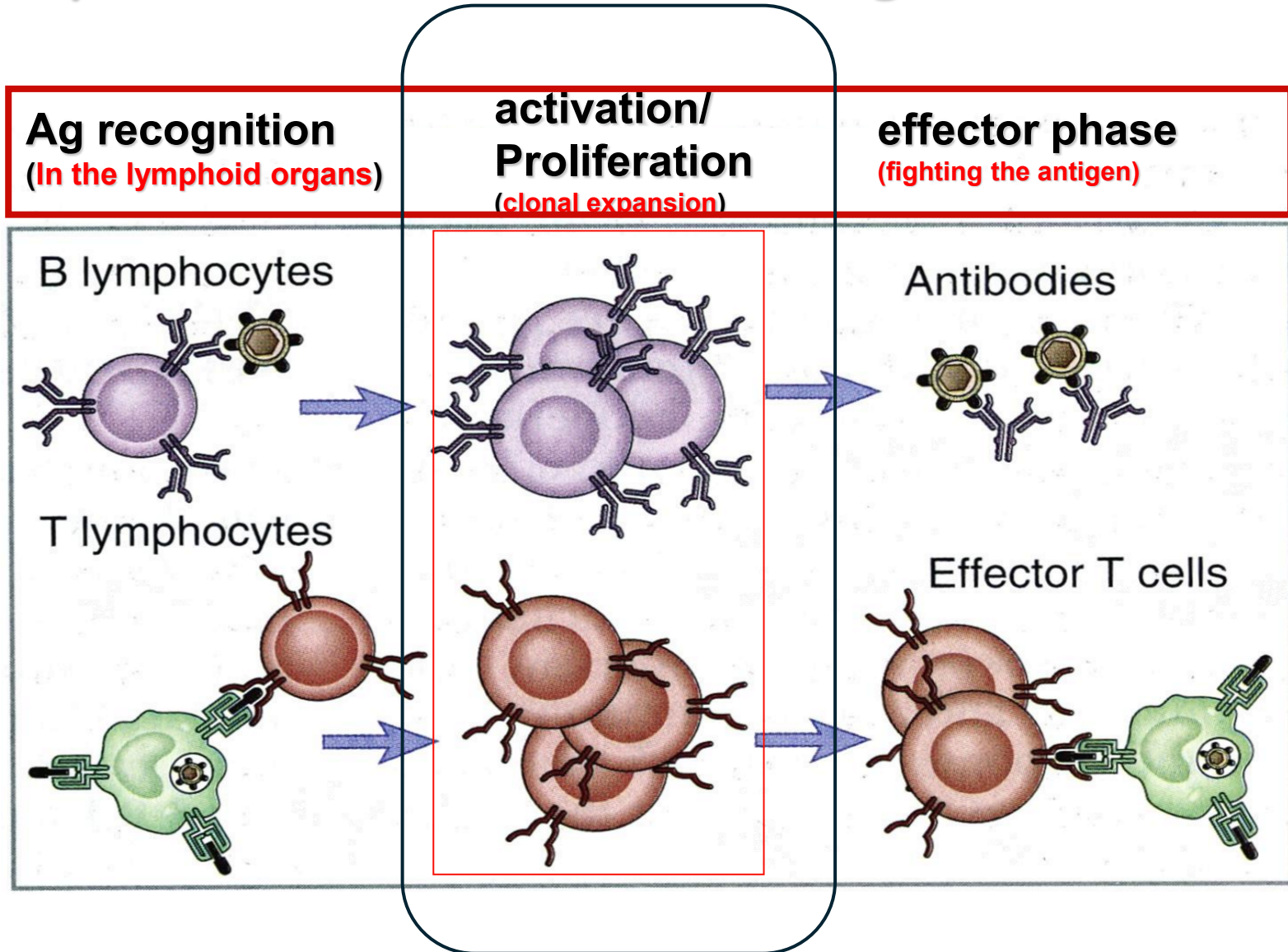
# Gli organi linfoidi sono la sede di maturazione e attivazione dei LINFOCITI T e B



# La risposta immunitaria adattativa inizia negli organi linfoidi secondari



# T and B lymphocytes specific for the antigen have to proliferate before becoming effector cells



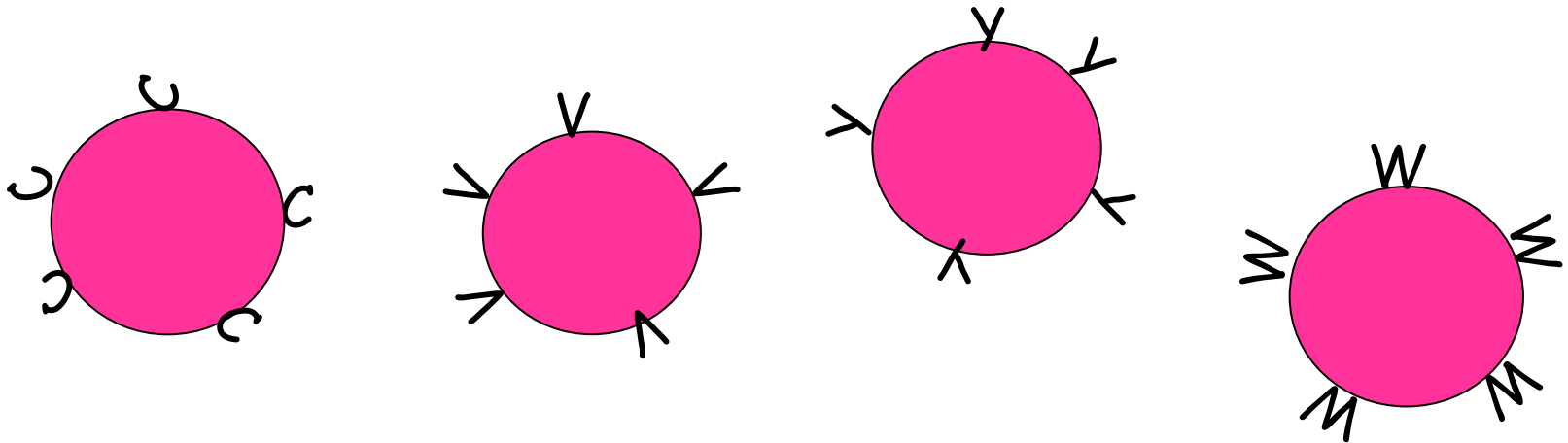
Naive lymphocytes: express antigen receptors but don't perform functions that are required to eliminate antigens

Effector lymphocytes: are the differentiated progeny of naive cells that have the ability to produce molecules that function to eliminate antigens. The effector cells in the B lymphocyte lineage are antibody-secreting cells called plasma cells.

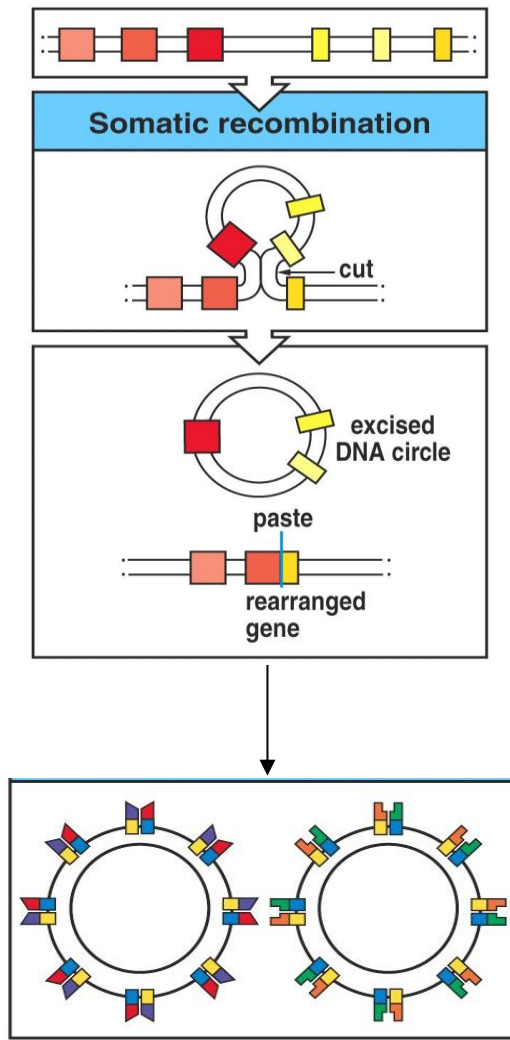
Memory cells: generated from the progeny of antigen-stimulated lymphocytes; they survive for long periods in the absence of antigen. When memory cells encounter the same antigen that induced their development, memory cells rapidly respond to initiate secondary immune response.

**T** and **B lymphocytes** recognize foreign antigen using specific receptors

Each lymphocyte expresses only one type of antigen receptor which is different from that of other lymphocytes



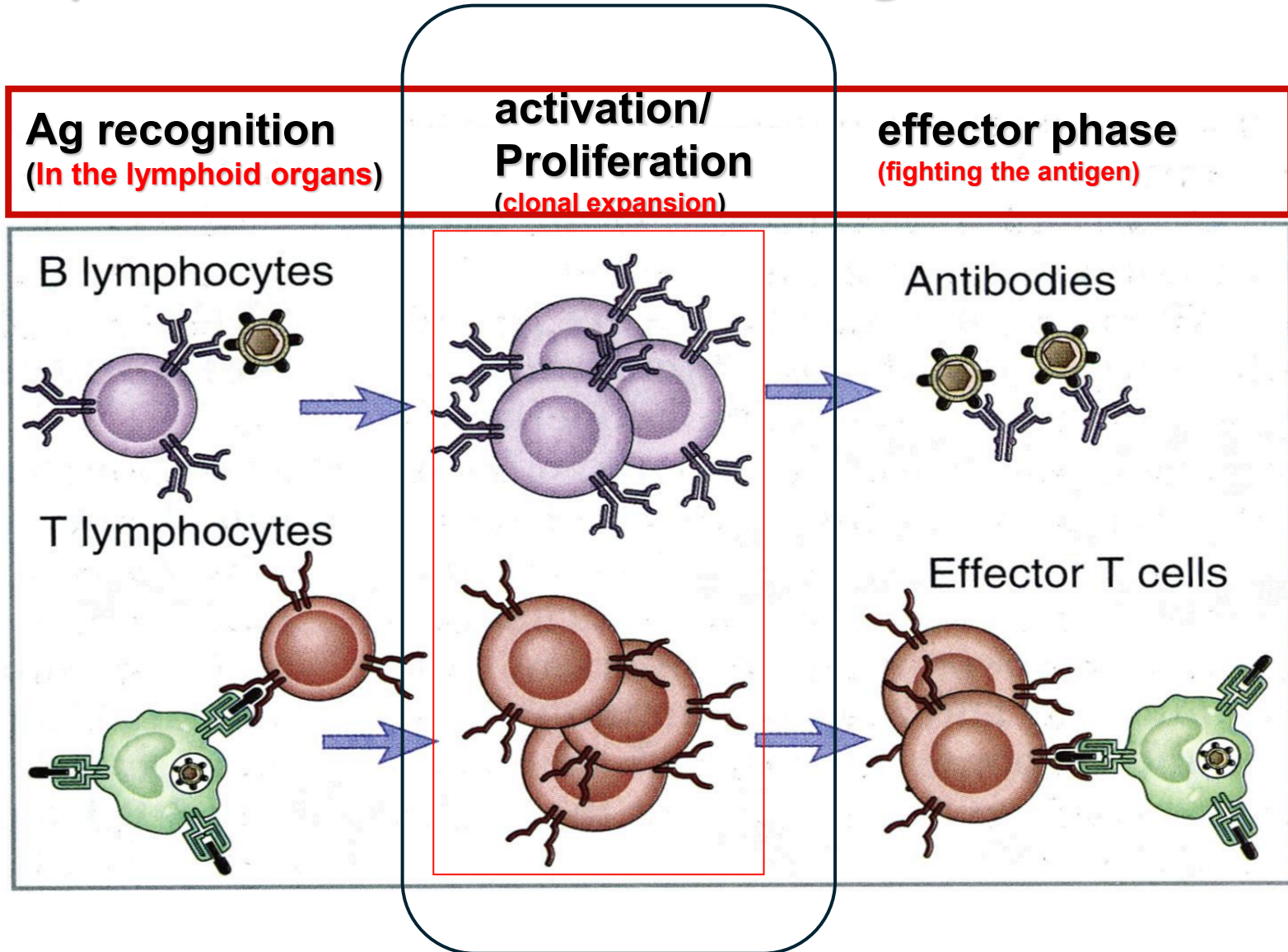
# When and how are antigen receptors formed?



Antigen receptors are formed during lymphocyte maturation through entirely random gene recombination events

Upon completion of recombination, each lymphocyte will express only one type of antigen receptor

# T and B lymphocytes specific for the antigen have to proliferate before becoming effector cells

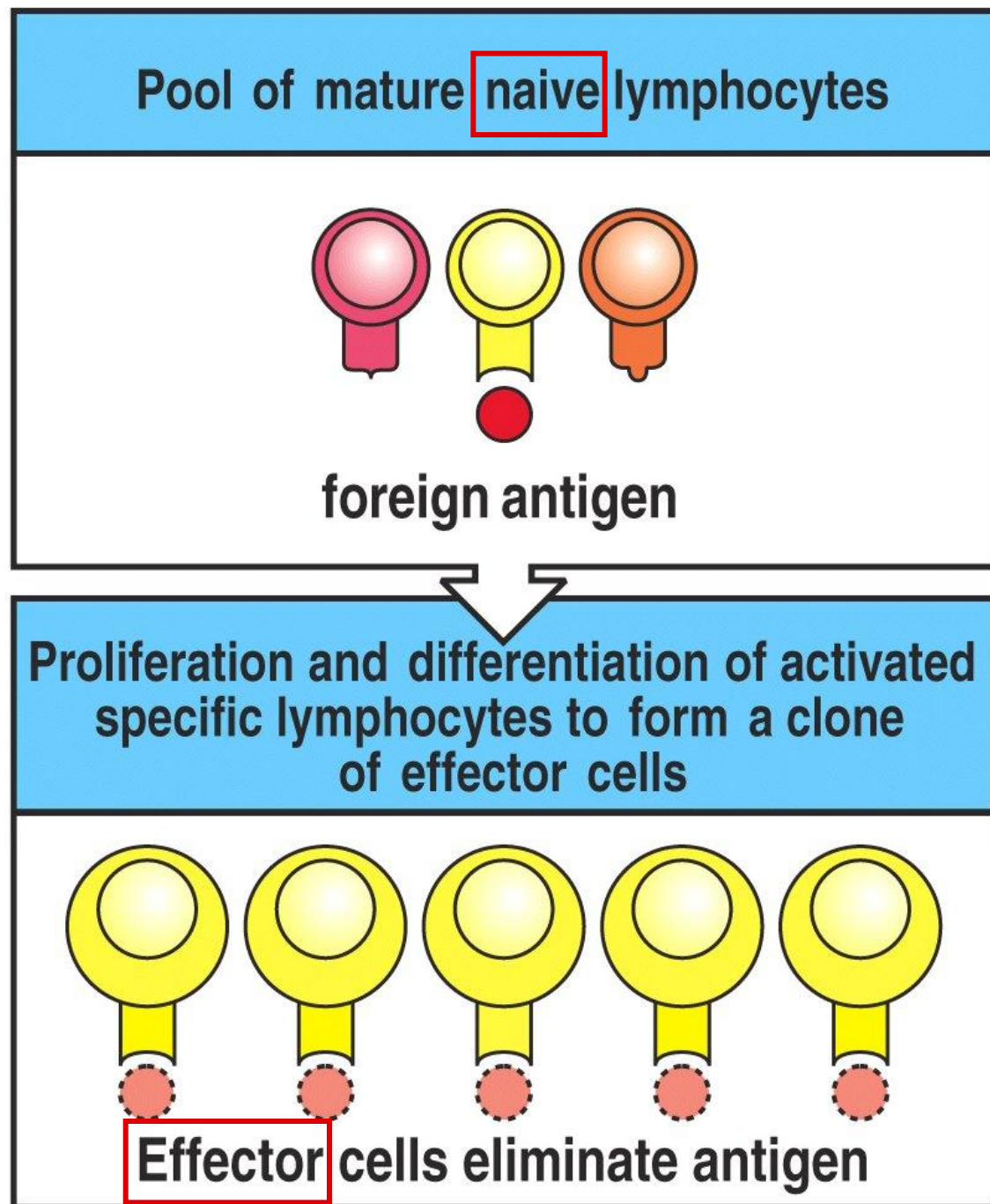


# The clonal selection theory:

**Antigen** induces the  
MASSIVE expansion  
(up to  $10^4$  x)!  
of lymphocytes expressing  
the specific receptor

The progeny bears the same  
antigenic specificity of the  
parental lymphocyte

**A clone!**



# La teoria della **selezione clonale** dei linfociti

Ogni individuo possiede un grande numero di linfociti diversi, ma quanto grande?

**$10^{10}$ - $10^{18}$  LINFOCITI MATURI**

La **selezione clonale** dei linfociti è indotta dal patogeno!



Macfarlane Burnet. Nobel price for Medicine 1960

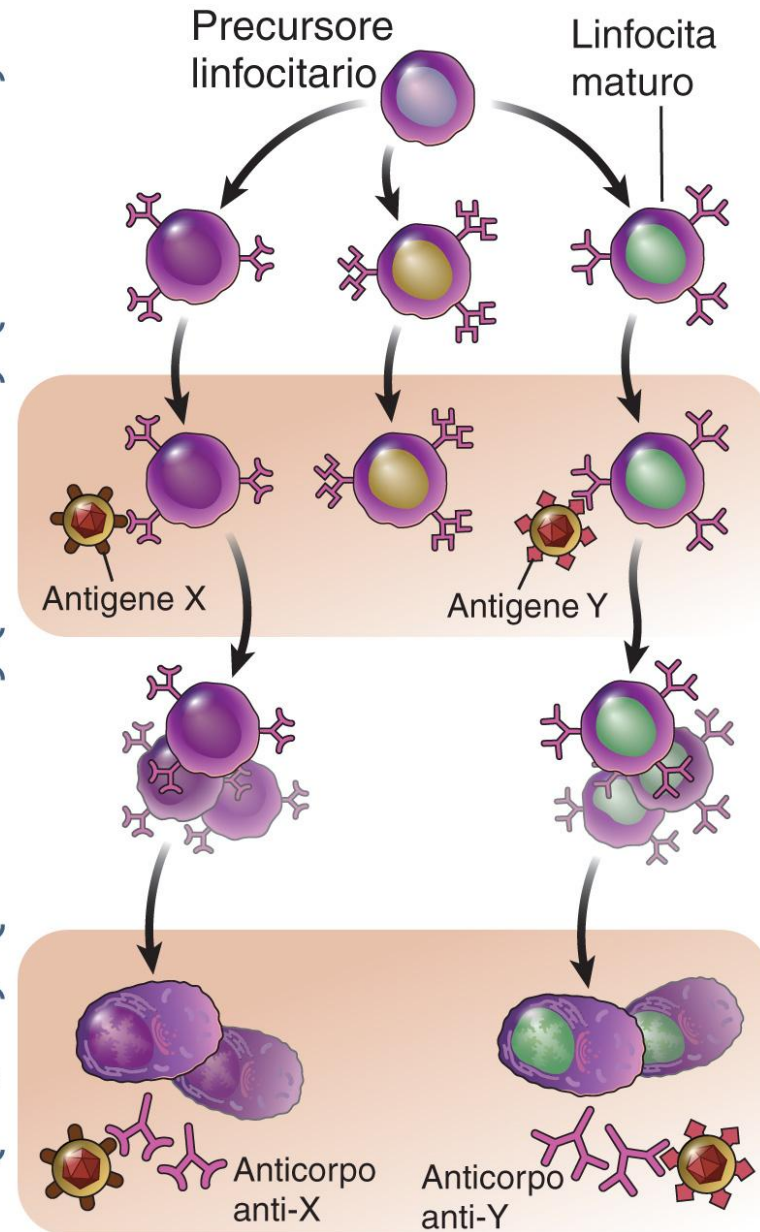
Sir Frank Macfarlane Burnet  
Courtesy of The National Library of Medicine

Negli organi linfoidi primari si sviluppano cloni linfocitari con recettori vari

I cloni di linfociti maturi, specifici per molti antigeni, entrano nei tessuti linfoidi

I cloni antigene-specifici vengono attivati ("selezionati") dagli antigeni

Si attivano le risposte immunitarie antigene-specifiche



## **Postulates of the clonal selection hypothesis**



**Each lymphocyte bears a single type of receptor with a unique specificity**



**Interaction between a foreign molecule and a lymphocyte receptor capable of binding that molecule with high affinity leads to lymphocyte activation**



**The differentiated effector cells derived from an activated lymphocyte will bear receptors of identical specificity to those of the parental cell from which that lymphocyte was derived**

The central problem of the IMMUNE SYSTEM is  
to correctly discriminate:

**SELF**

All normal constituents  
of the body

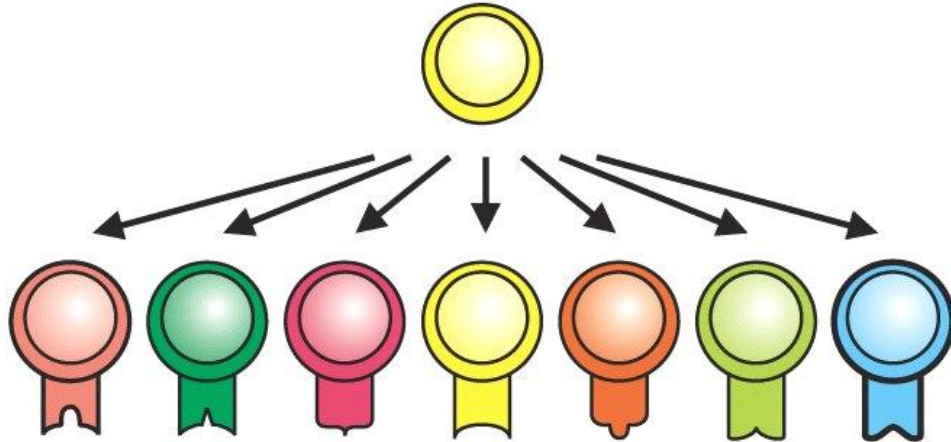
FROM

**NON SELF**

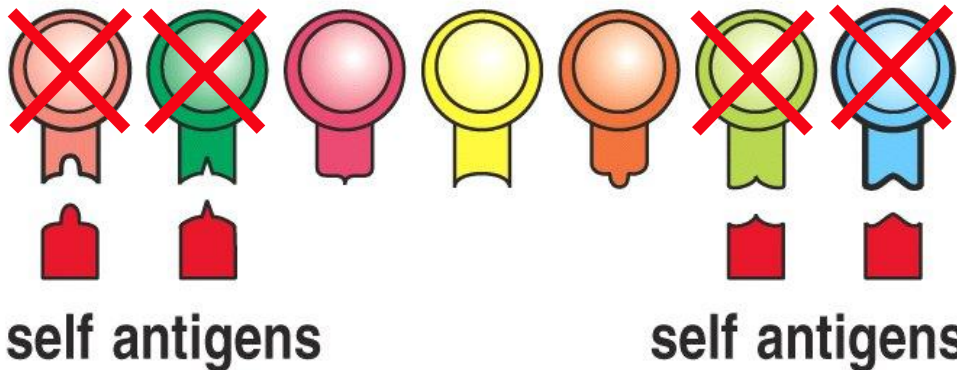
Pathogen constituents,  
altered constituents of  
the body

To react to **NON SELF**  
To be tolerant to **SELF**

A single progenitor cell gives rise to a large number of lymphocytes, each with a different specificity

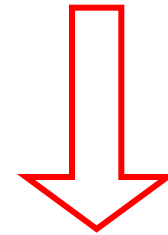


Removal of potentially self-reactive immature lymphocytes by clonal deletion



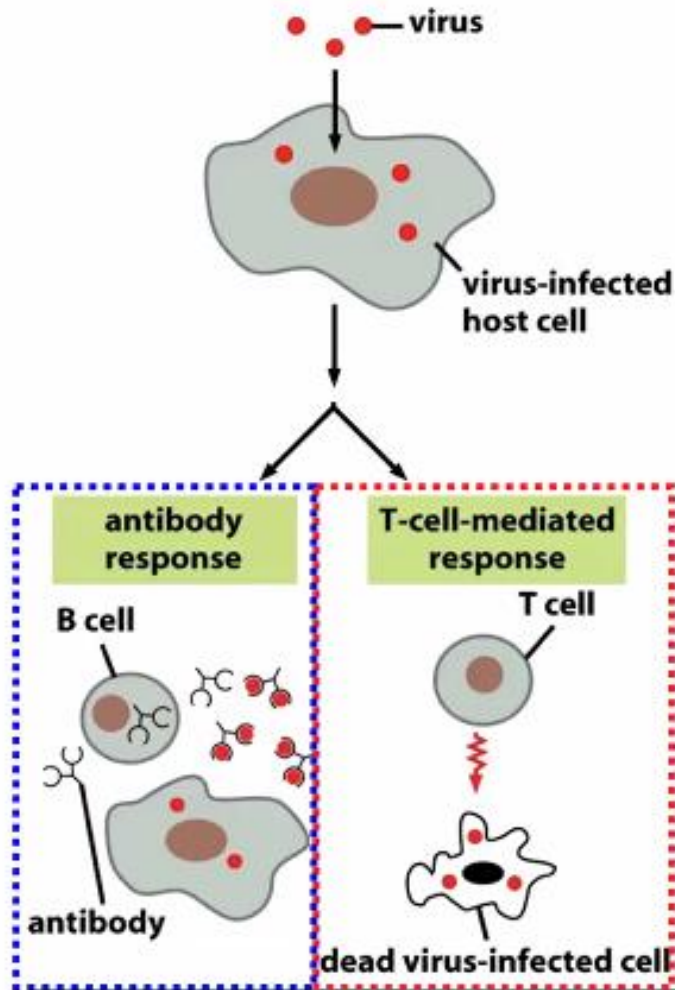
The immune system is tolerant to self!

Antigen receptors are formed during lymphocyte maturation, by random genetic events



Cells expressing receptors strongly reacting with self antigens do not complete the maturation process

# The two arms of adaptive immune system:



To efficiently prevent viral infection it is necessary to activate both arms of defense of the immune system



## Humoral immunity – B cells

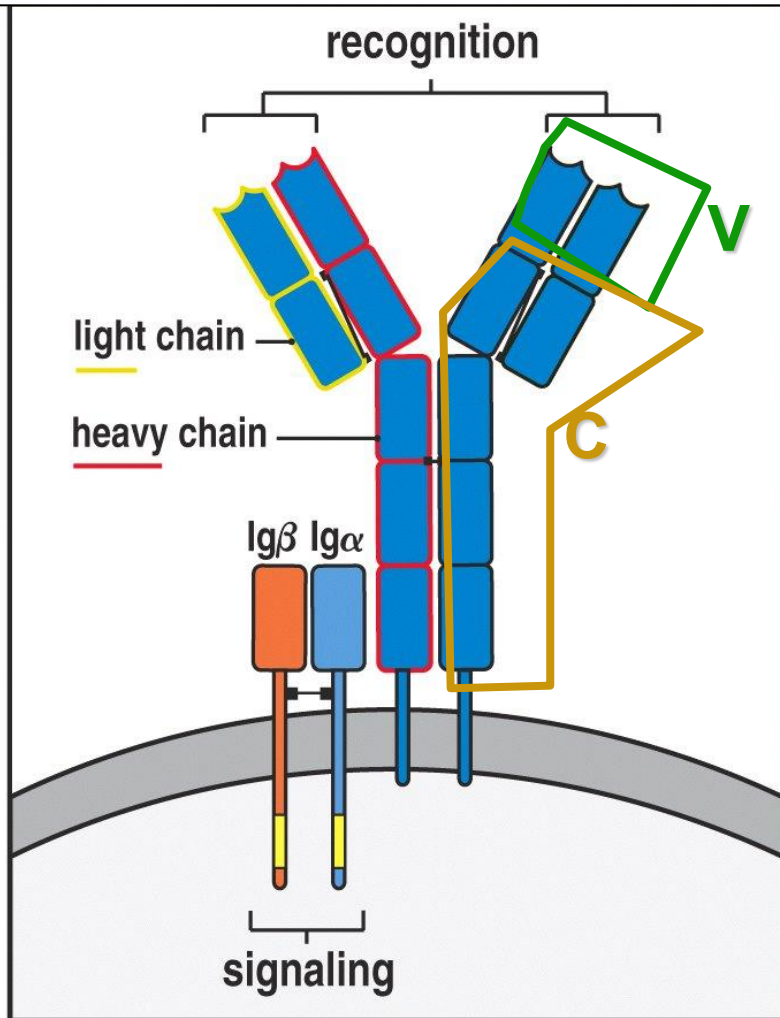
antibody-mediated  
neutralises extracellular  
pathogens  
prevents infection

## T cell mediated immunity

cytotoxic effector cells (CD8<sup>+</sup>)  
kill infected cells  
T helper & effector cells (CD4<sup>+</sup>)  
produce anti-viral cytokines &  
provide "help" to B and CD8 T cells

# Some basic B cell facts

## BCR (B cell receptor)



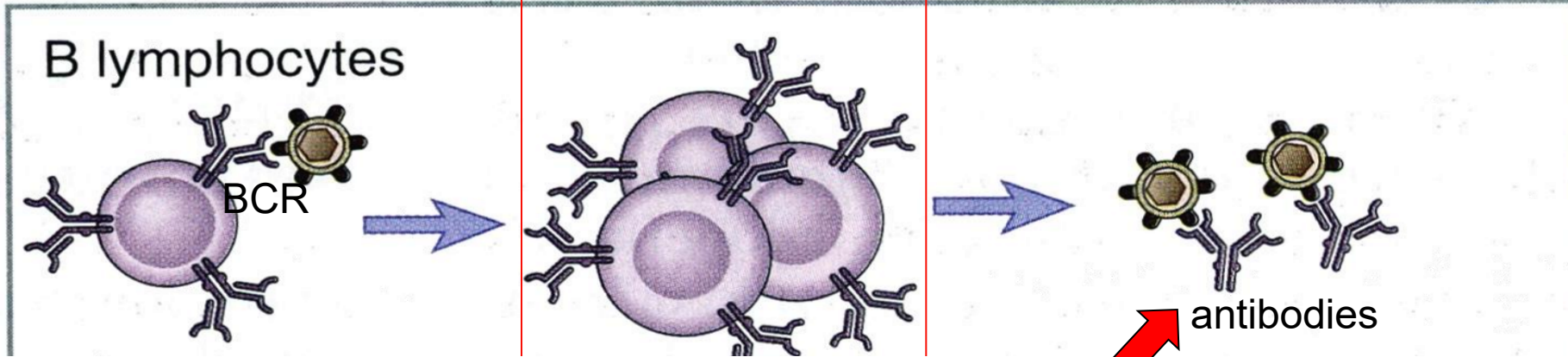
- First made in the liver of the **foetus** at around **8 - 9 weeks**
- Then the **Bone Marrow** takes over and carries on throughout life
- We make **10 - 20%** of total number each day (we also lose that number!)
- Each B cell has approx. **100,000** specific receptors for an antigen on its surface

# The main function of B lymphocytes is that of producing **ANTIBODIES** (=Immunoglobulins)

Antigen recognition

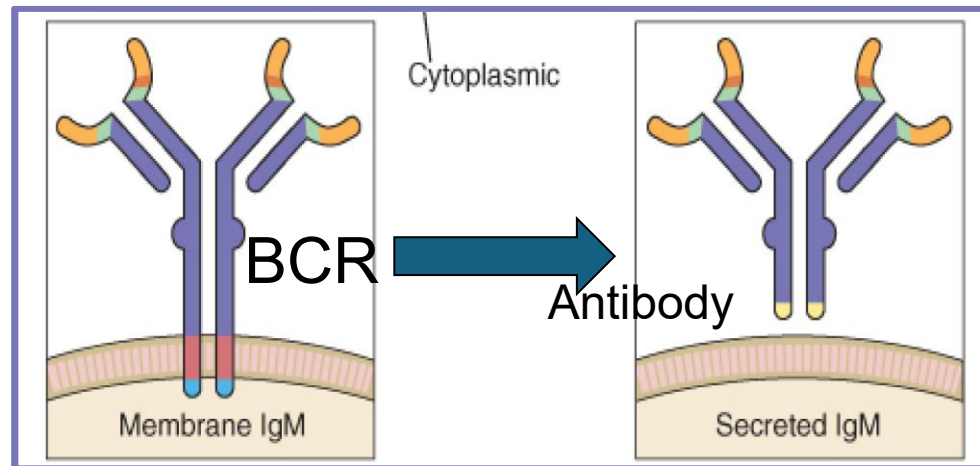
Proliferation

Effector function/ production of antibodies (immunoglobulins)



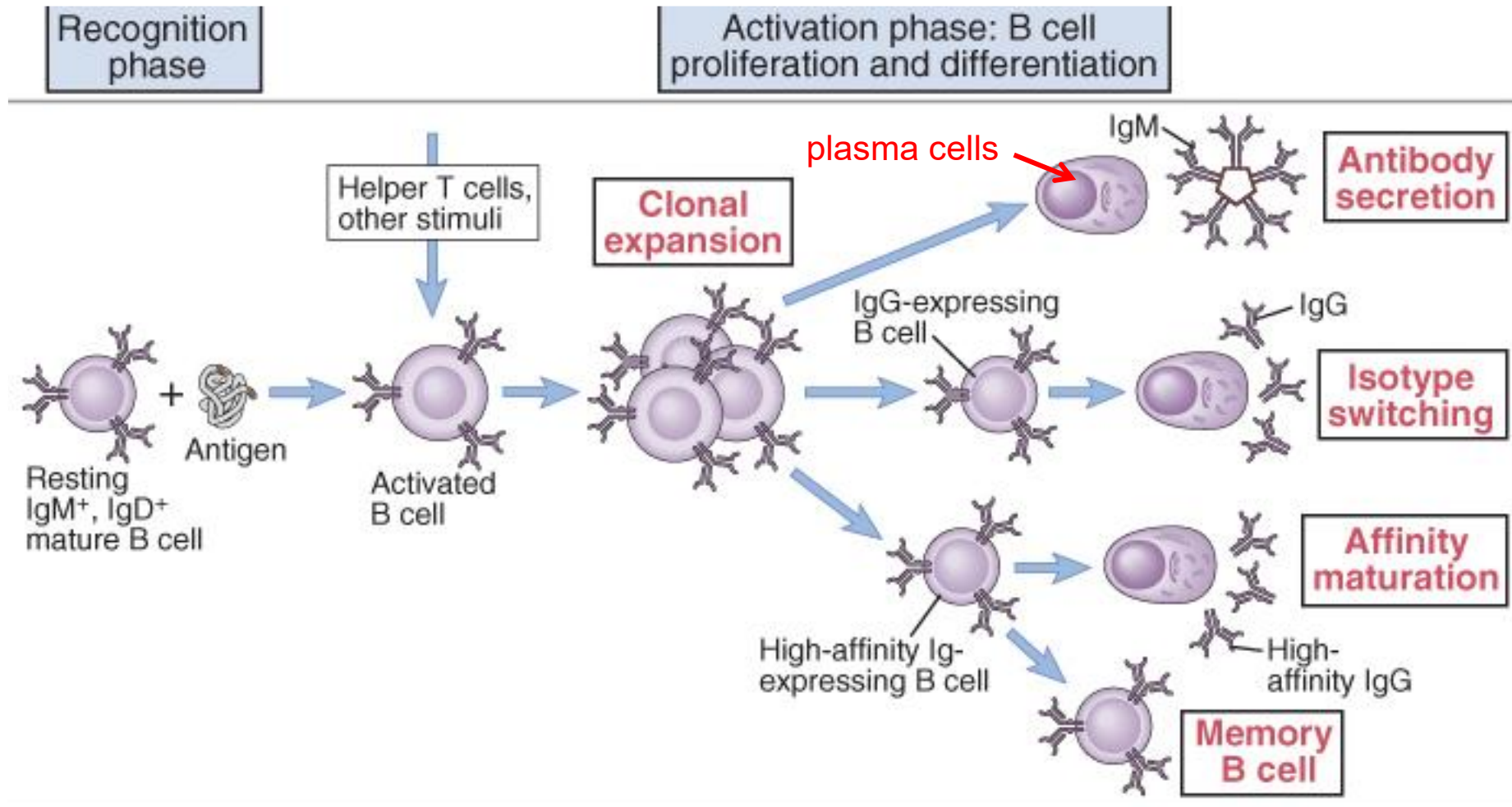
Antibody

The BCR is expressed on the cell surface and after the B cell activation it is secreted in a soluble form and it is called antibody or immunoglobulin (Ig).

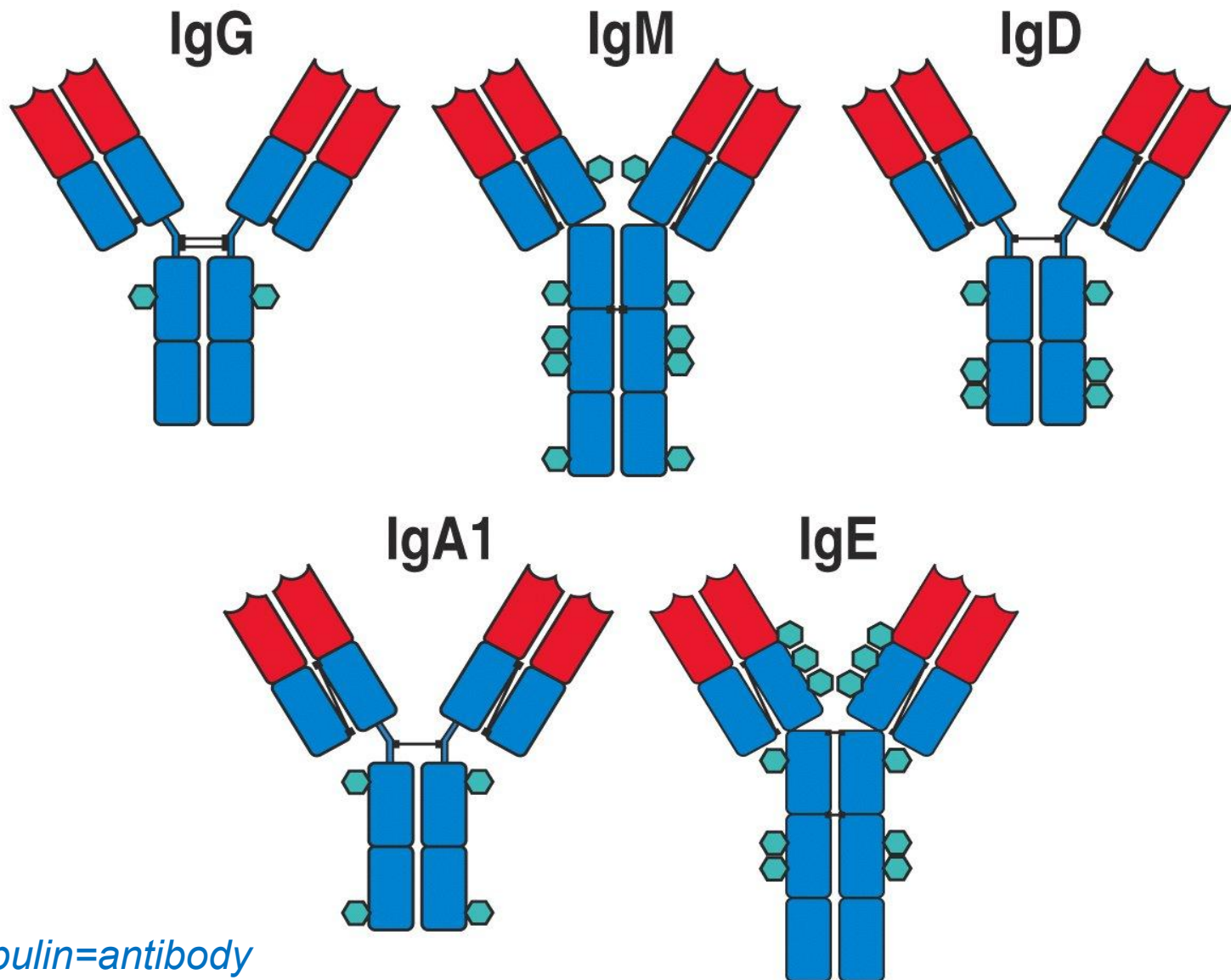


# PHASES OF HUMORAL IMMUNE RESPONSES

Naive B cells recognize antigens, and under the influence of helper T cells, the B cells are activated to proliferate, giving rise to clonal expansion and to differentiate into antibody secreting plasma cells. Some of them become long-lived memory cells.



Five different immunoglobulins (Ig) classes (isotypes) are produced by B cells



*Immunoglobulin=antibody*

Figure 4-18 Immunobiology, 6/e. (© Garland Science 2005)

Five different immunoglobulins (Ig) classes:

- 1. distinct distribution in our body
- 2. distinct features

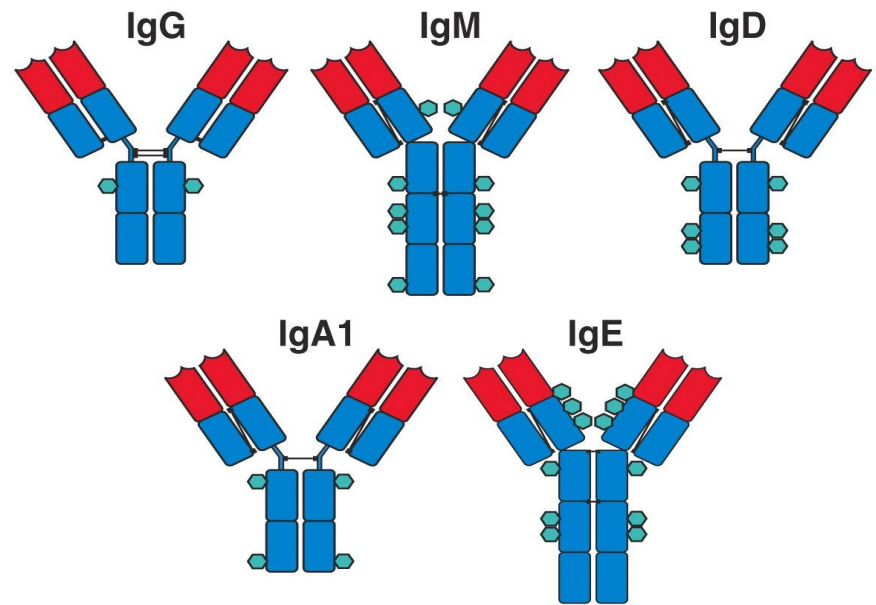
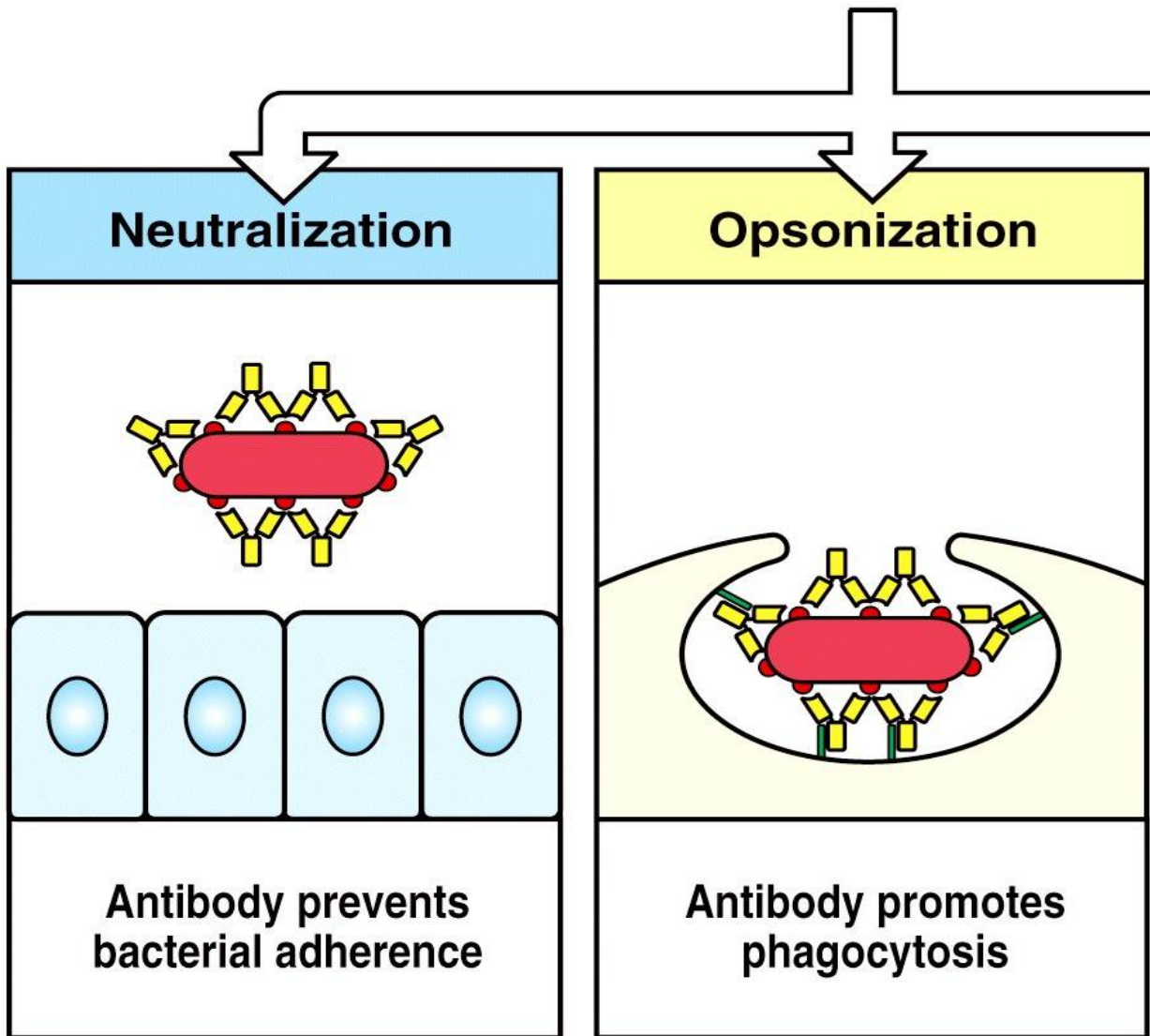


Figure 4-18 Immunobiology, 6/e. (© Garland Science 2005)

# Le funzioni effettrici degli anticorpi

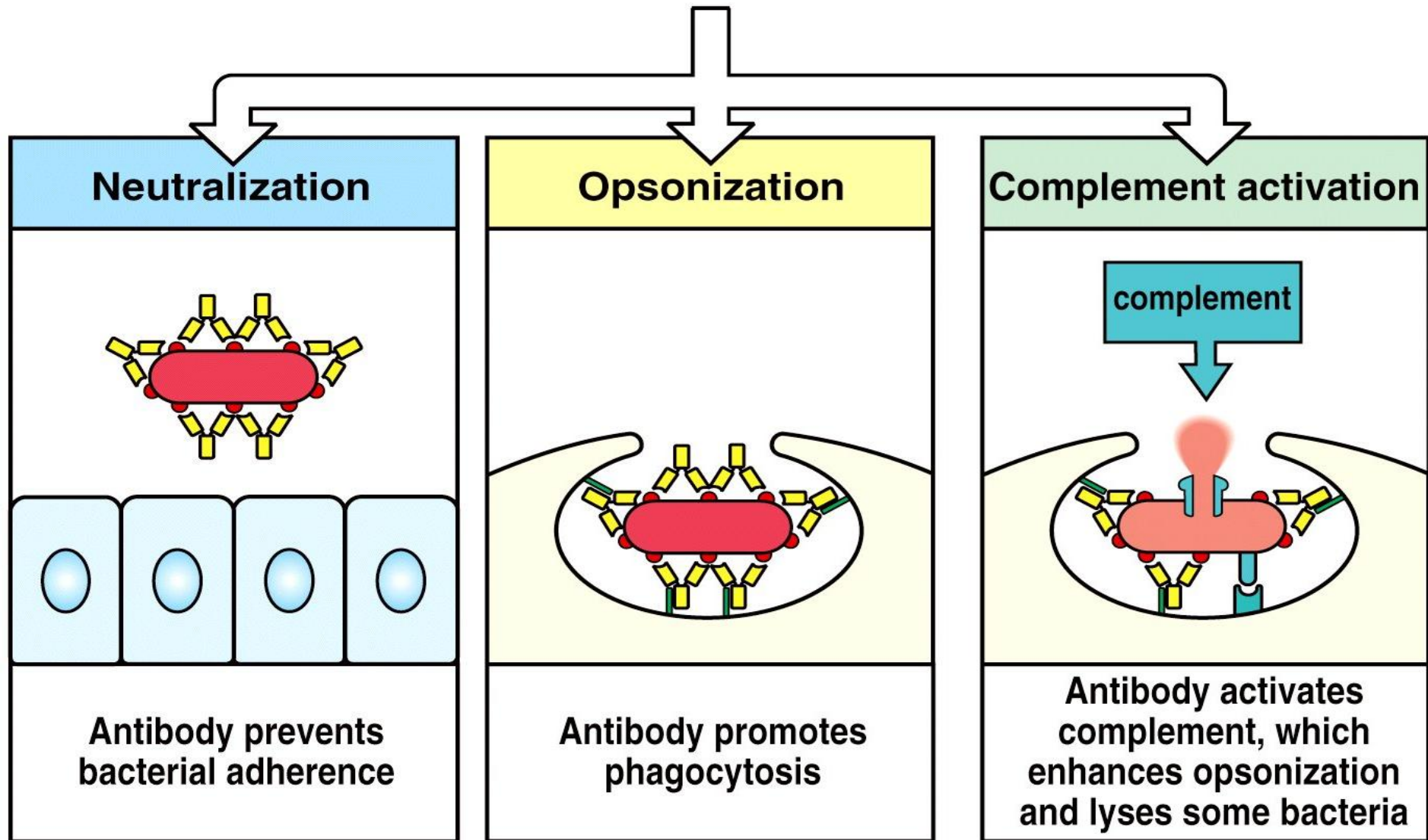


**Opsonizzare** =  
preparare al pasto

Gli anticorpi sono Le principali sostanze in grado di funzionare da **OPSONINE**.

I patogeni opsonizzati vengono fagocitati in maniera più efficiente (10-50 volte di più degli stessi patogeni non opsonizzati).

# Le funzioni effettrici degli anticorpi



Antibody titer in serum: IgG, IgA, and IgM levels slowly increase until young adulthood and remain stable thereafter

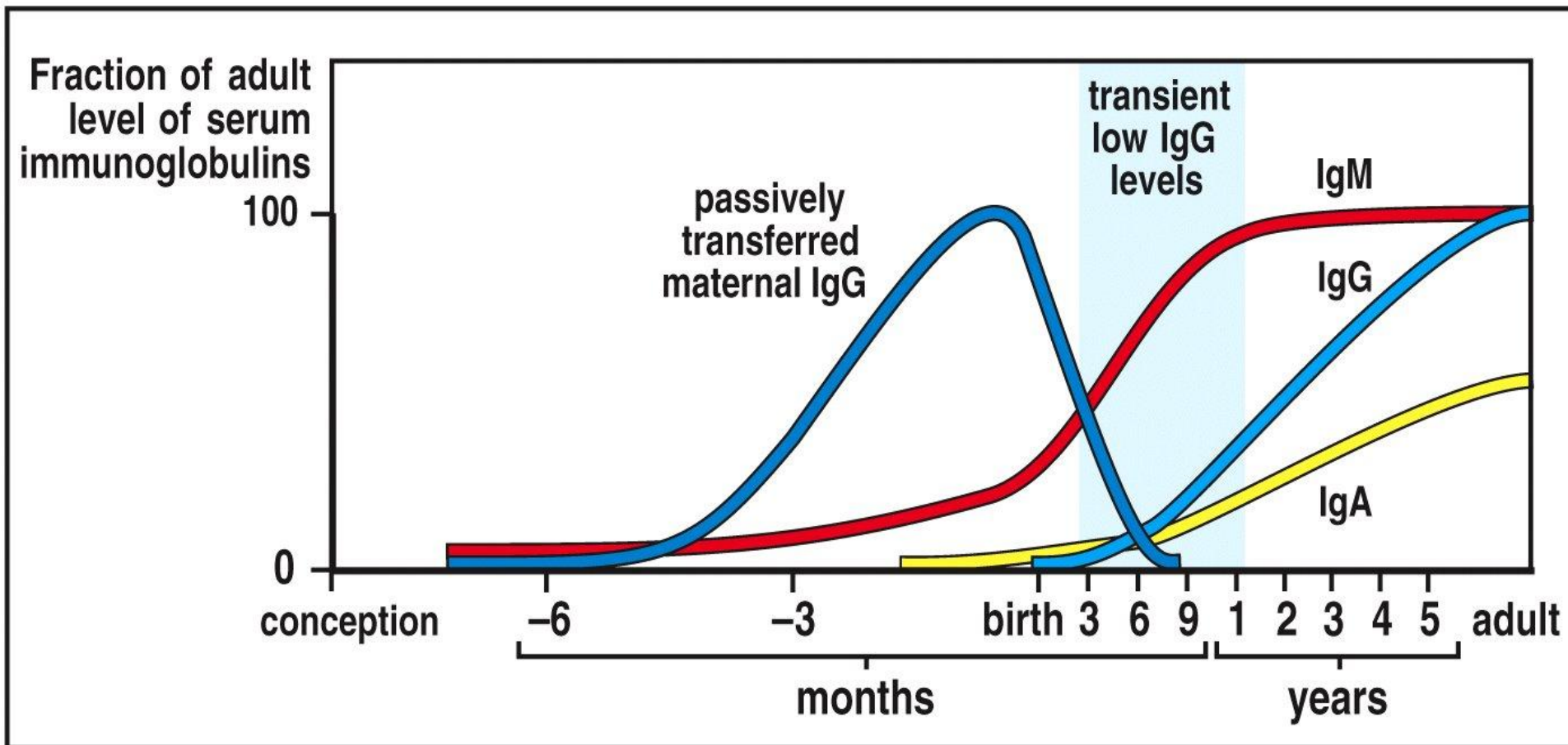
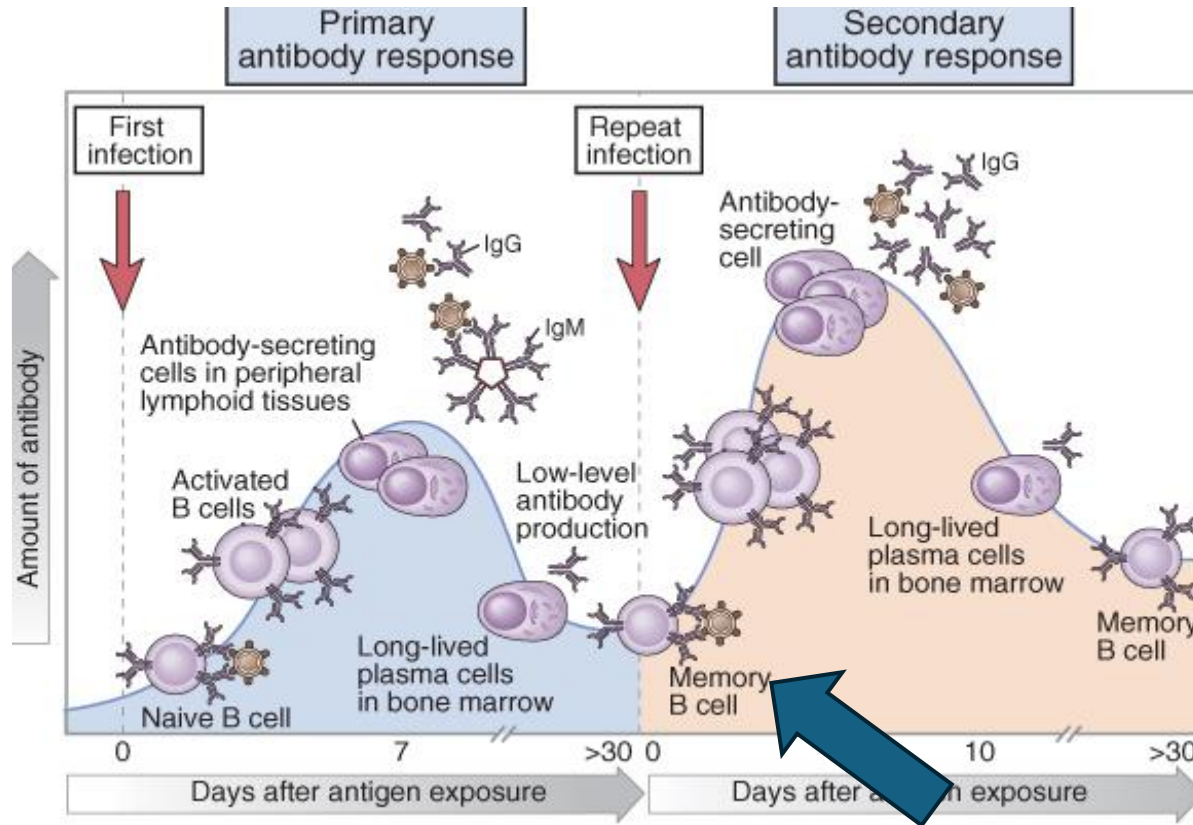


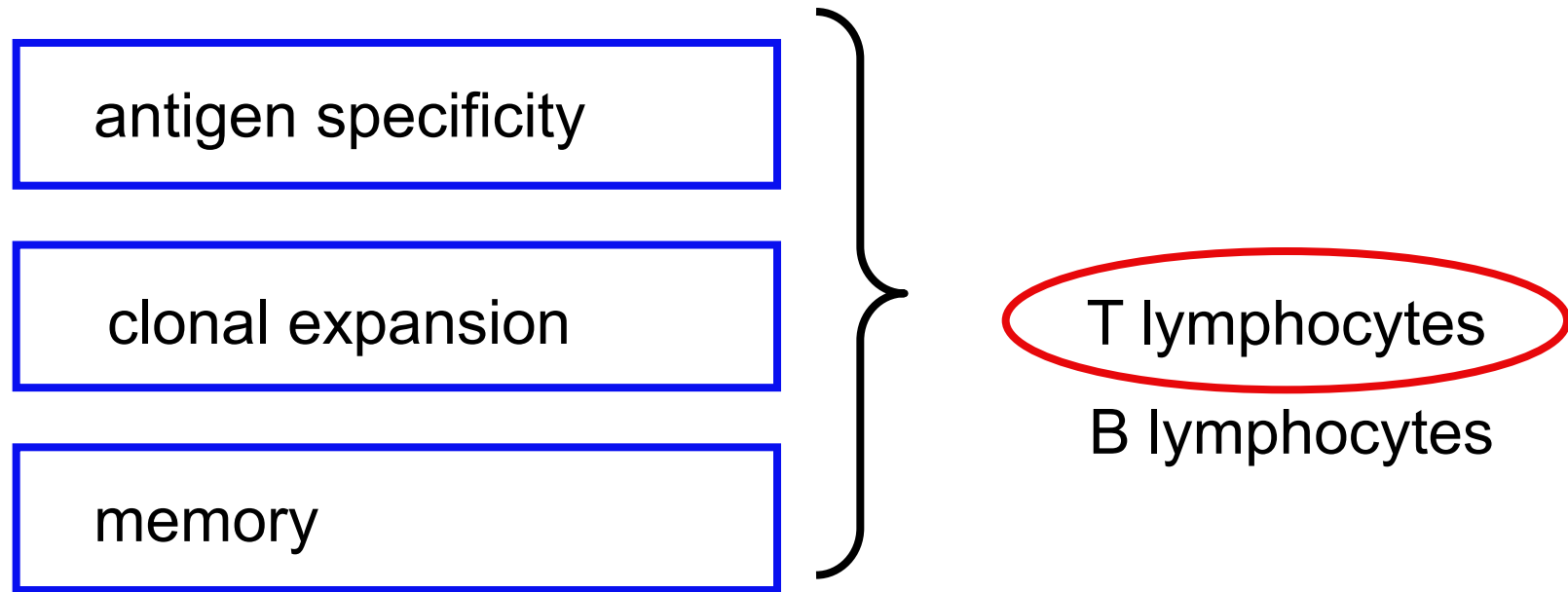
Figure 11-11 Immunobiology, 6/e. (© Garland Science 2005)

# Features of primary and secondary antibody responses



|                        | Primary response       | Secondary response                                                                                    |
|------------------------|------------------------|-------------------------------------------------------------------------------------------------------|
| Lag after immunization | Usually 5-10 days      | Usually 1-3 days                                                                                      |
| Peak response          | Smaller                | Larger                                                                                                |
| Antibody isotype       | Usually IgM, few IgG   | Relative increase in IgG and, under certain situations, in IgA or IgE (heavy chain isotype switching) |
| Antibody affinity      | Lower average affinity | Higher average affinity (affinity maturation)                                                         |

# The adaptive immune response:



T lymphocytes are divided into two main subsets:

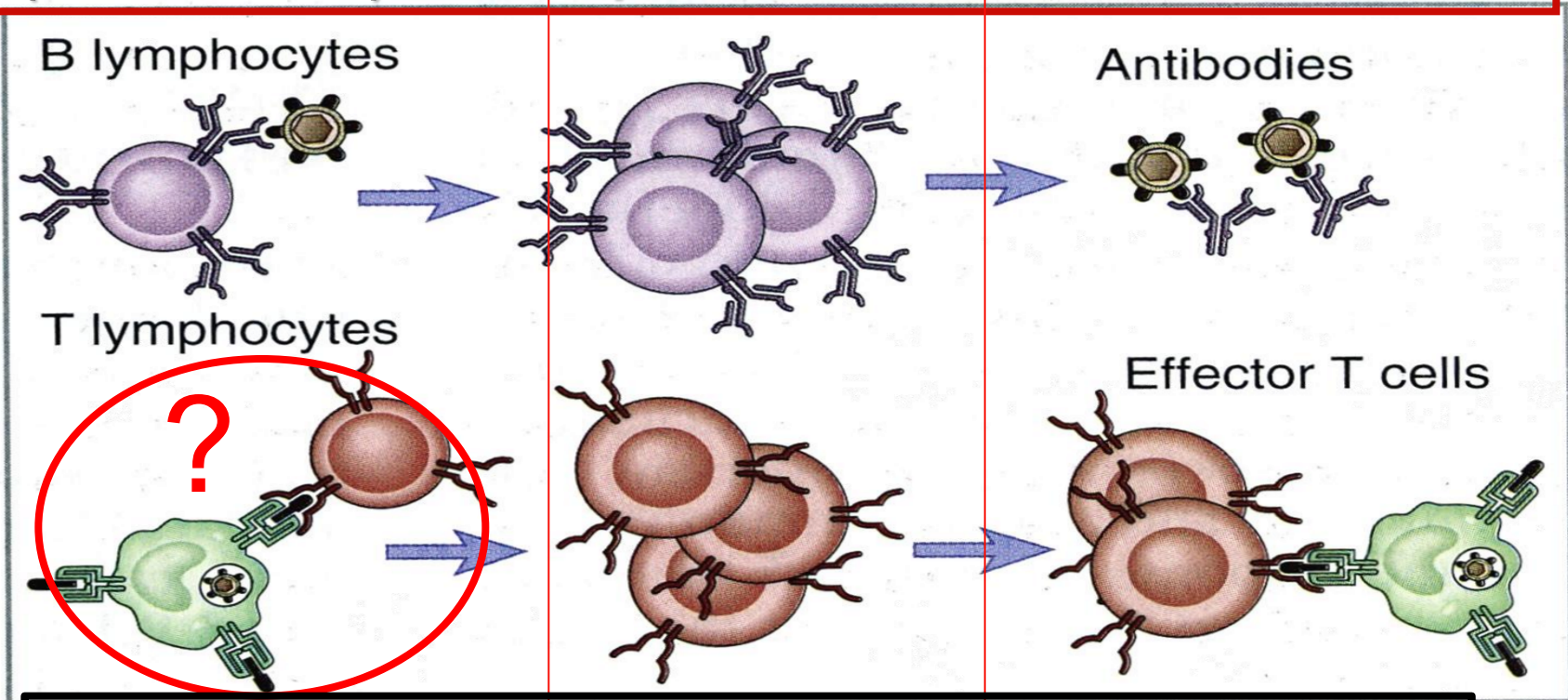
CD4<sup>+</sup> T lymphocytes

CD8<sup>+</sup> T lymphocytes

**Ag recognition  
("naive" cells)**

**activation/  
proliferation**

**effector phase**



T lymphocytes are divided into two main subsets:

CD4<sup>+</sup> T lymphocytes

CD8<sup>+</sup> T lymphocytes

Le diverse molecole espresse sulla superficie delle cellule ematopoietiche sono designate con la sigla CD seguita da un numero (ad es. CD1, CD2, ecc.).

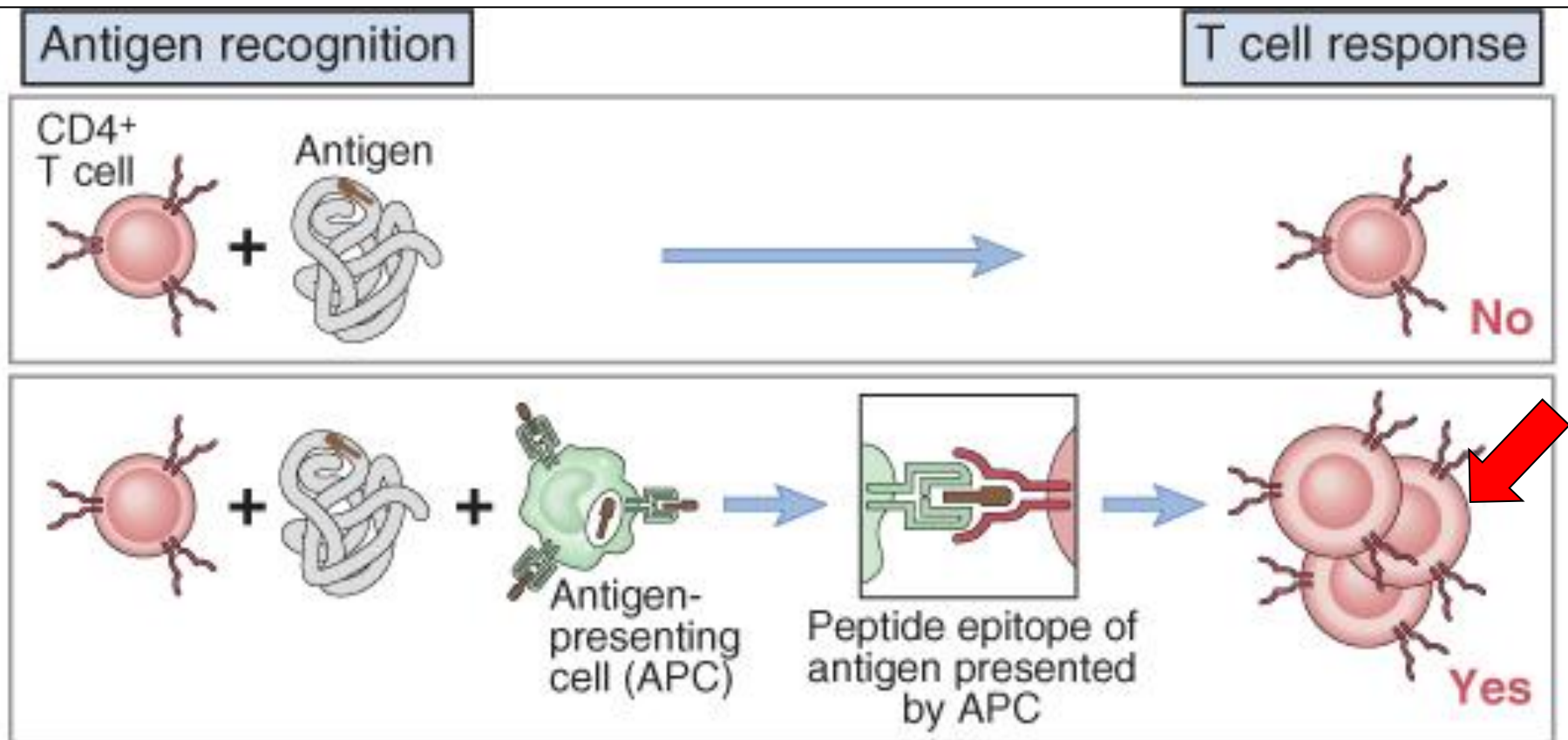
**CD =**  
**C**luster **D**esignation  
**C**luster **D**ifferentiation

Ogni CD viene identificato mediante l'utilizzo di anticorpi monoclonali.

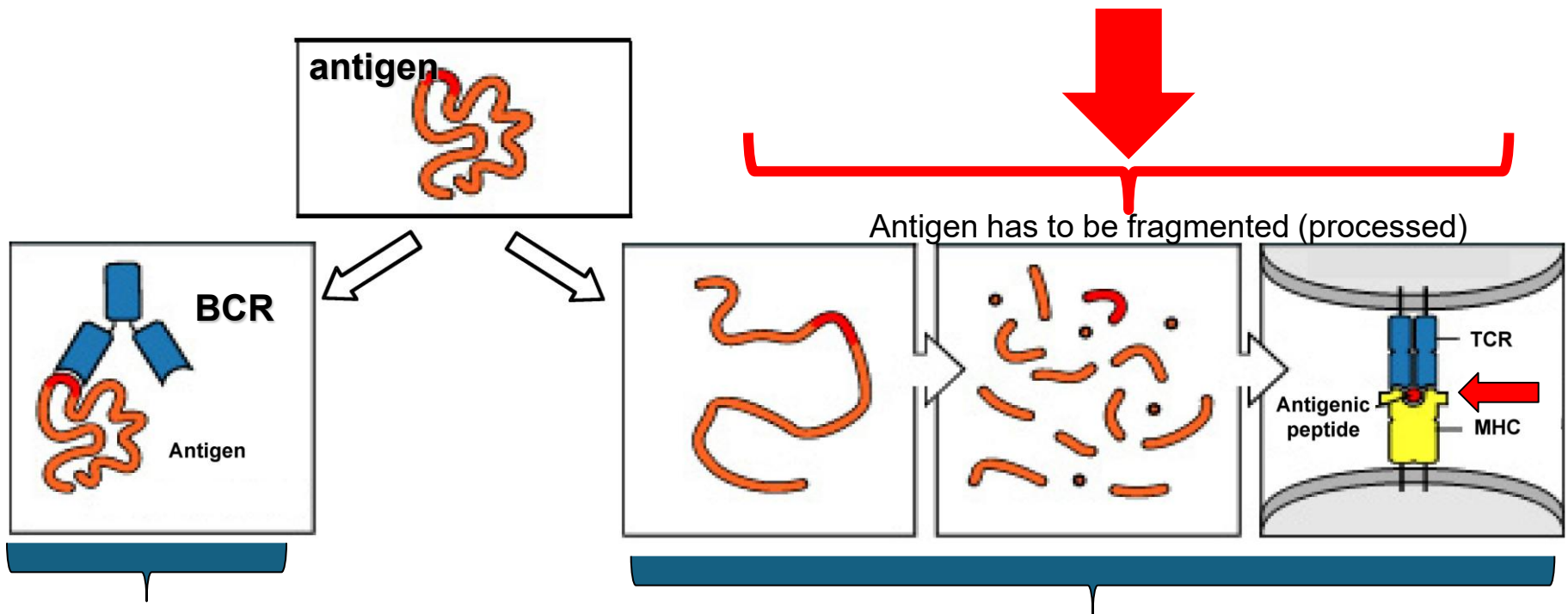
Attualmente sono stati identificati e caratterizzati circa 400 diversi CD.

# Antigen recognition of T cells is:

- **MHC**-restricted
- requires **processing** by accessory cells (**APC**)



# T cells and B cells “see” antigen differently!



BCR (or Ig) binds the antigen directly

BCR binds different type of antigens  
(lipids, proteins, polysaccharides)

Affinity=  $10^{-7}/10^{-11}$

Augments during response

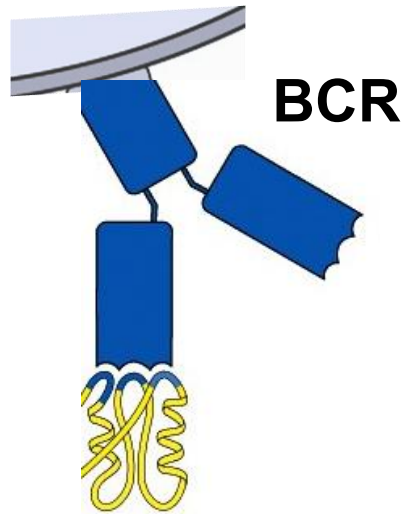
TCR binds the antigen associated to MHC molecules

TCR binds only proteins

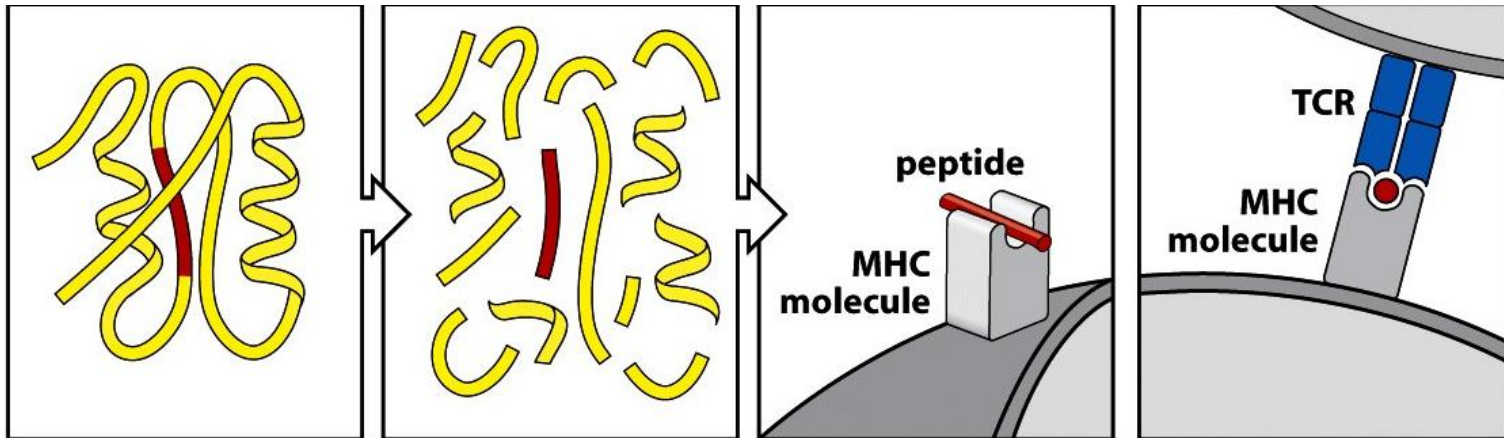
Affinity=  $10^{-5}/10^{-7}$

MHC= Major Histocompatibility Complex

**I LINFOCITI B RICONOSCONO L' ANTIGENE IN FORMA NATIVA**

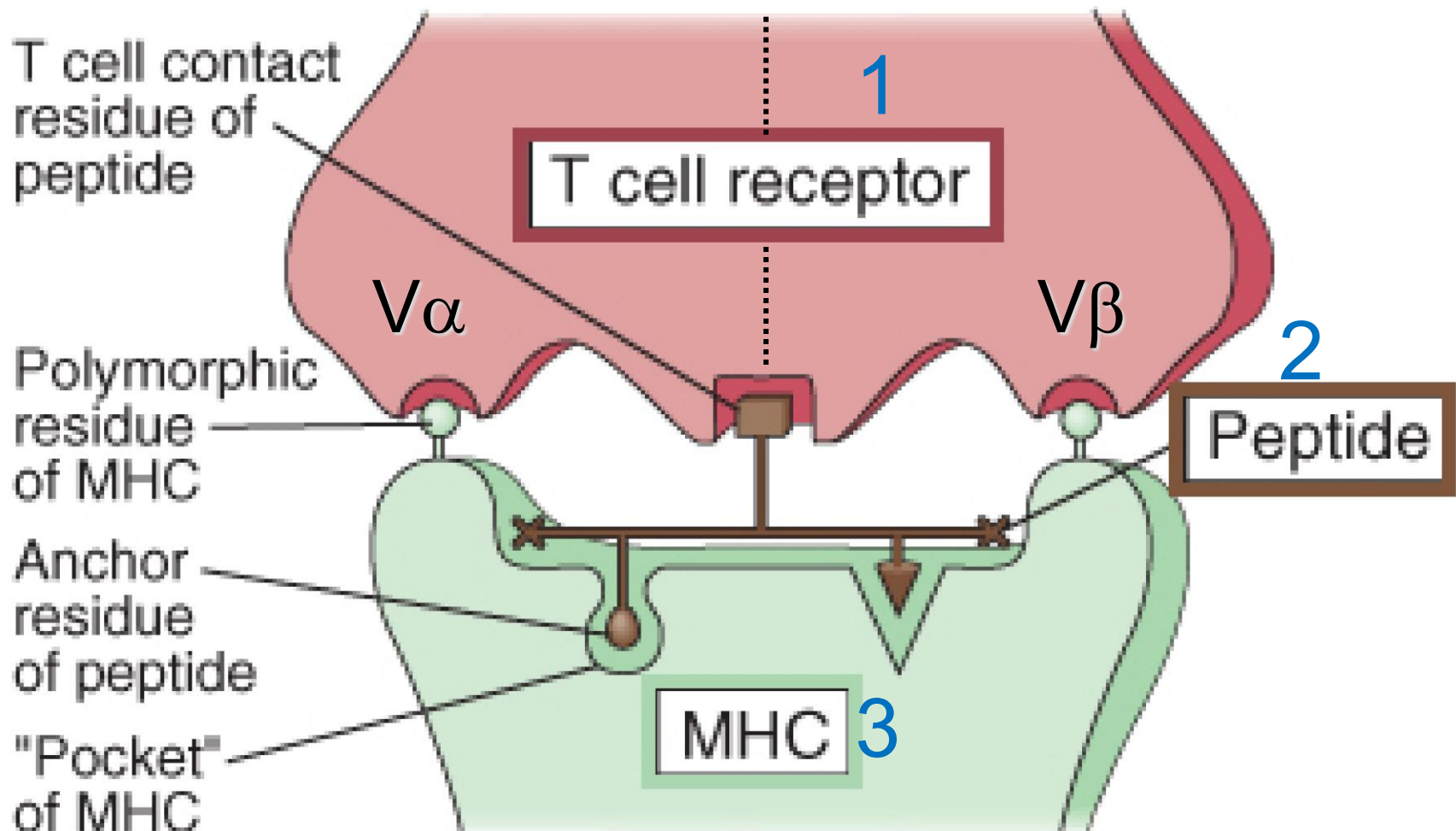


**I LINFOCITI T RICONOSCONO L' ANTIGENE PROTEICO IN FORMA DENATURATA.....**

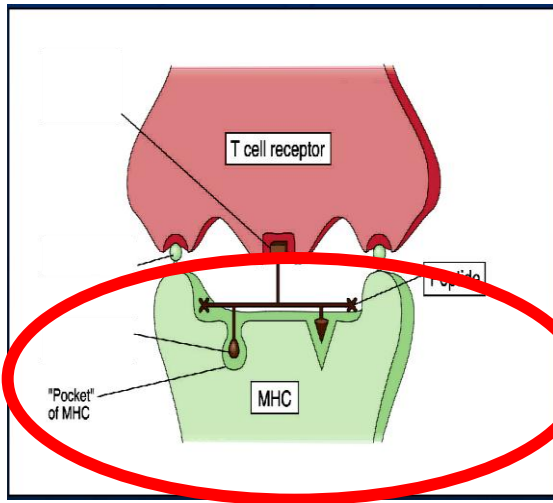


**... e hanno bisogno dell'intervento di cellule accessorie!**

# T cell antigen recognition depends on a **TRIMOLECULAR** interaction



*MHC*: the major histocompatibility complex



## MHC: Major Histocompatibility Complex

It is a group of tissue molecules that have been discovered for their importance in the transplantation rejection reactions and are essential for T cell antigen recognition.

# Nobel prize in Medicine, 1996

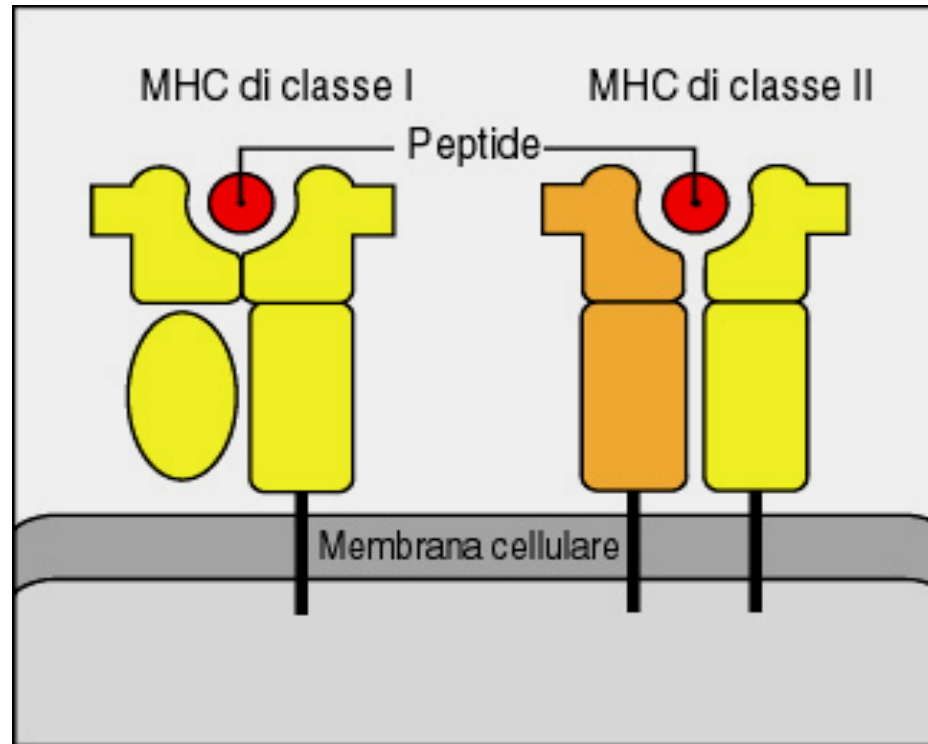


Peter Doherty

Rolf Zinkernagel

*«for their discoveries concerning the specificity of the cell mediated immune defence»*

Esistono due tipi di molecole MHC ....



.... entrambe espresse sulla membrana delle **APC**

# Where are MHC/HLA molecules expressed?

| Tissue                         | MHC class I | MHC class II |
|--------------------------------|-------------|--------------|
| <b>Lymphoid tissues</b>        |             |              |
| T cells                        | +++         | +*           |
| B cells                        | +++         | +++          |
| Macrophages                    | +++         | ++           |
| dendritic cells                | +++         | +++          |
| Epithelial cells of the thymus | +           | +++          |
| <b>Other nucleated cells</b>   |             |              |
| Neutrophils                    | +++         | -            |
| Hepatocytes                    | +           | -            |
| Kidney                         | +           | -            |
| Brain                          | +           | -†           |
| <b>Non-nucleated cells</b>     |             |              |
| Red blood cells                | -           | -            |



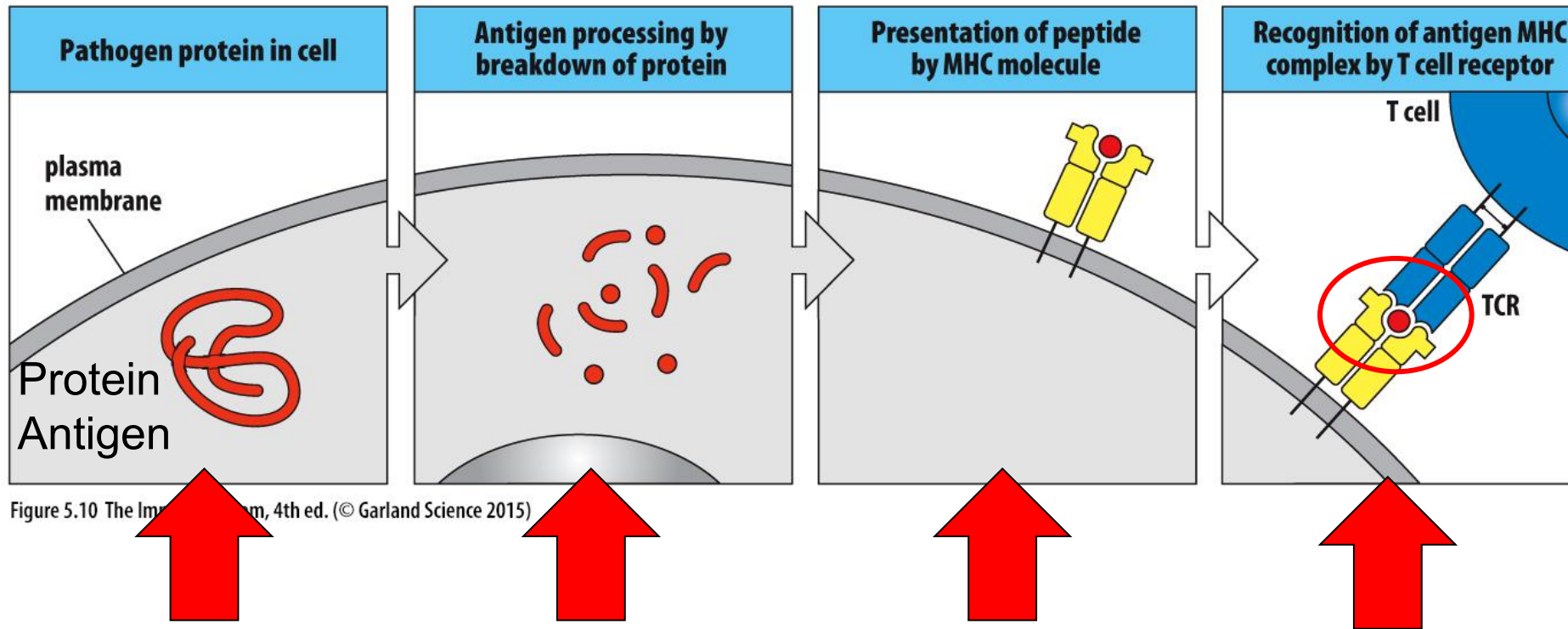
**APC**  
*Antigen Presenting Cells*



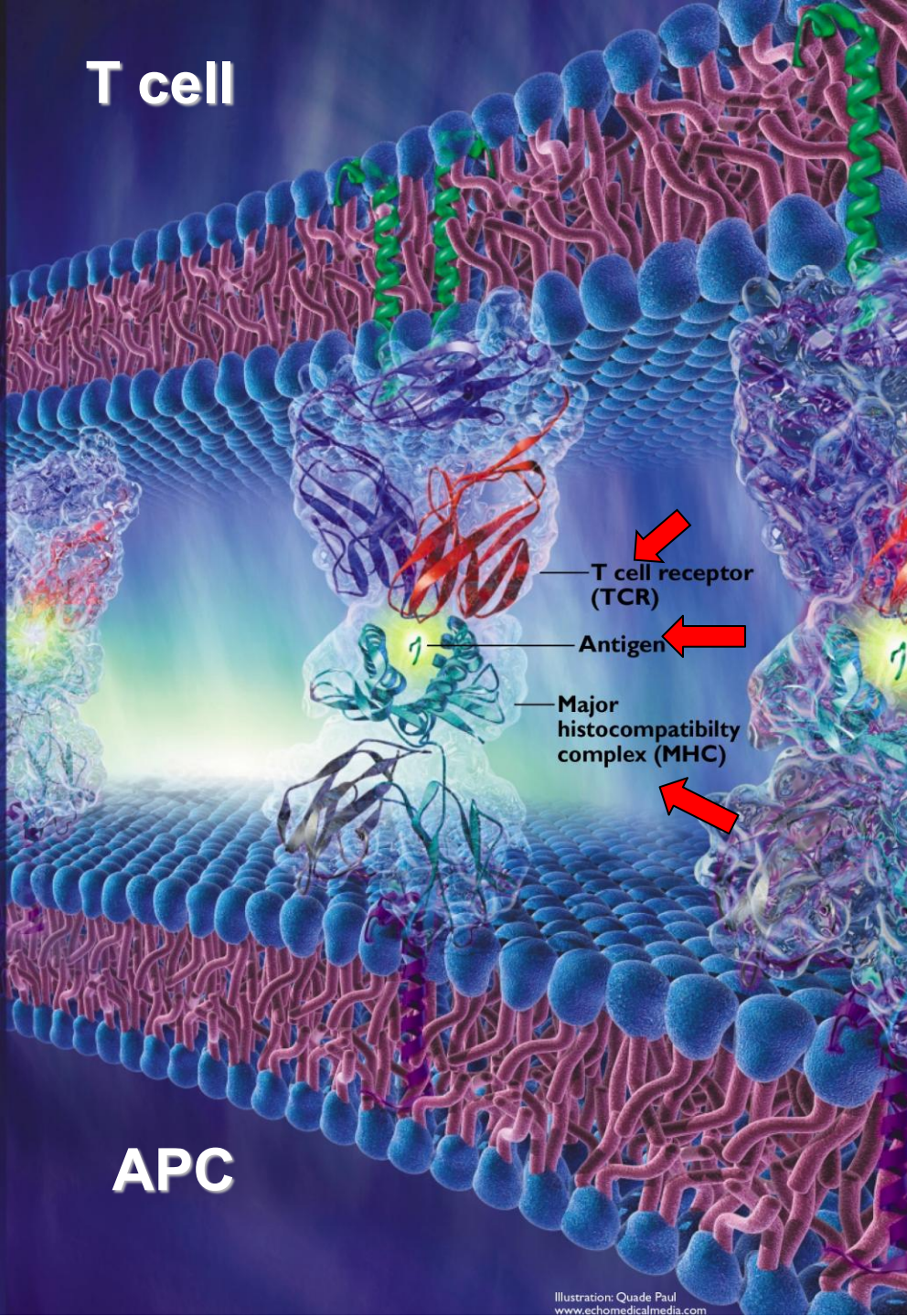
## ***APC, Antigen presenting cells***

- Macrophages, B lymphocytes, and dendritic cells***
- Express on their cell surface MHC I and MHC II molecules.***
- APCs present antigens to T cells (both CD4<sup>+</sup> and CD8<sup>+</sup> lymphocytes)***

- The antigen is processed by Antigen Presenting Cells (APC)



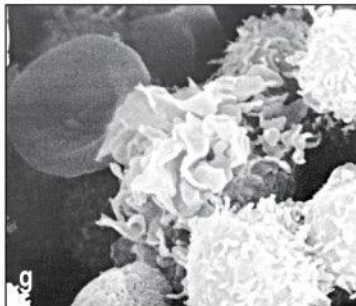
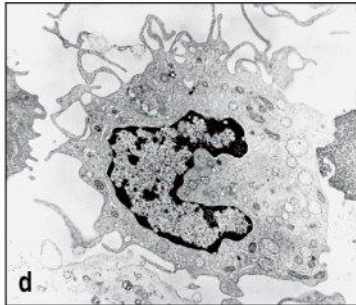
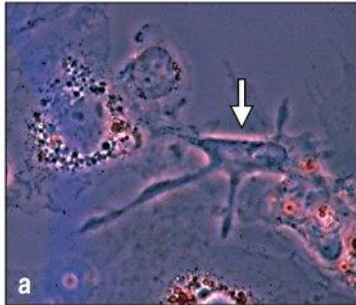
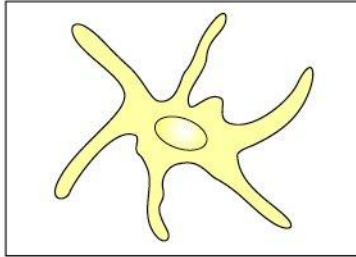
**T cell**



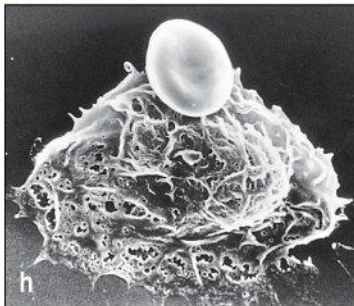
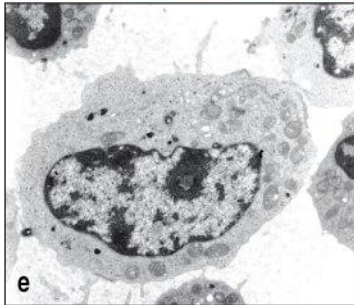
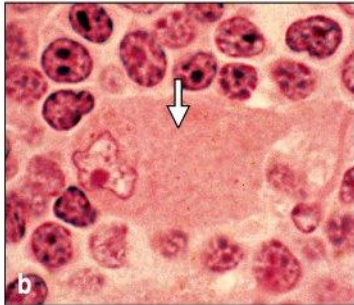
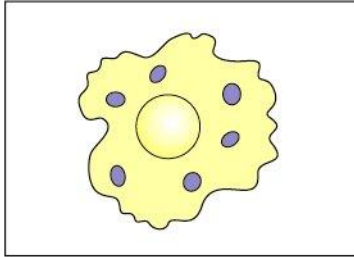
**T cell recognition  
occurs at the  
surface of Antigen  
Presenting Cells  
(APCs)**

**APC**

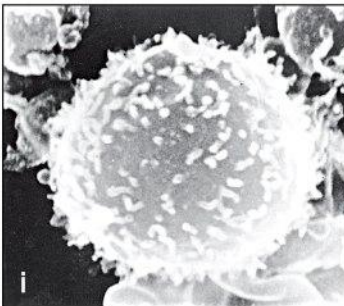
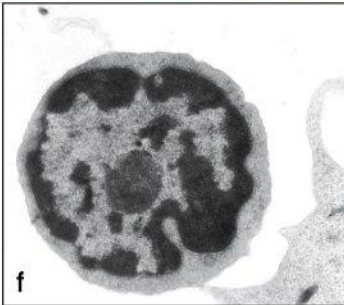
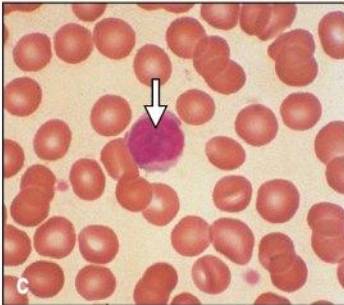
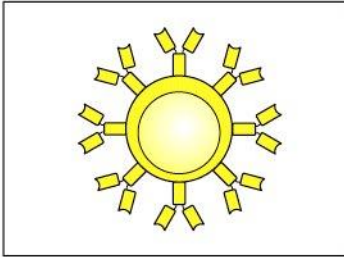
## Dendritic cells



## macrophages



## B lymphocytes



## Three types of professional

### Antigen Presenting Cells

➤ Express MHC class I and MHC class II

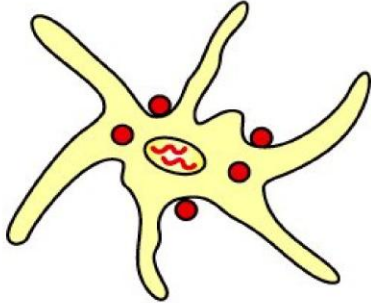
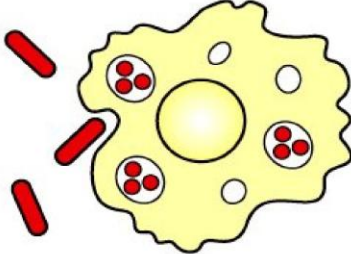
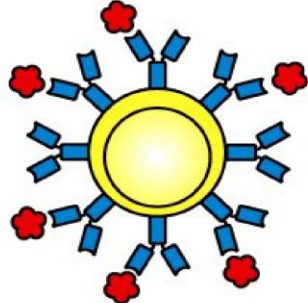
➤ present antigens to BOTH CD4<sup>+</sup> and to CD8<sup>+</sup> T lymphocytes

➤ CD4<sup>+</sup> T lymphocytes bind the antigen associated to MHC class II molecules

➤ CD8<sup>+</sup> T lymphocytes bind the antigen associated to MHC class I molecules

Figure 1-22 Immunobiology, 6/e. (© Garland Science 2005)

# The 3 types of professional APCs are functionally different!

|                | Dendritic cells                                                                    | Macrophages                                                                        | B cells                                                                             |
|----------------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
|                |   |  |  |
| Antigen uptake | +++ Macropinocytosis and phagocytosis by tissue dendritic cells<br>Viral infection | Phagocytosis<br>+++                                                                | Antigen-specific receptor (Ig)<br>++++                                              |

**B lymphocytes present their specific antigen very efficiently**

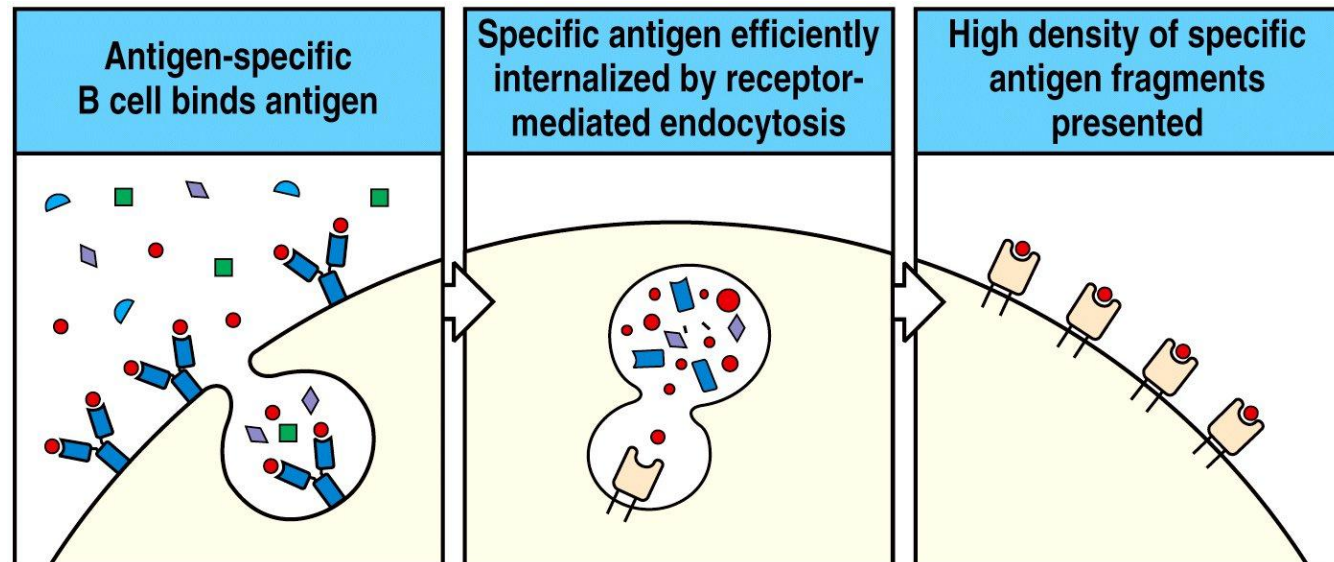
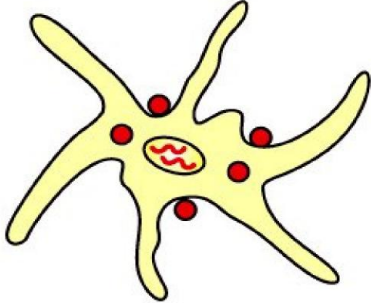
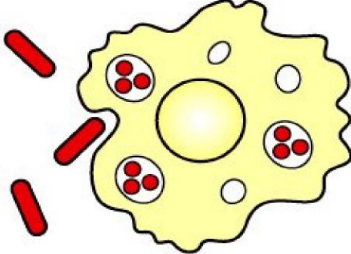
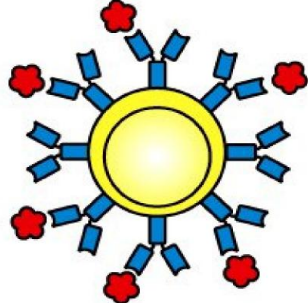


Figure 8-17 Immunobiology, 6/e. (© Garland Science 2005)

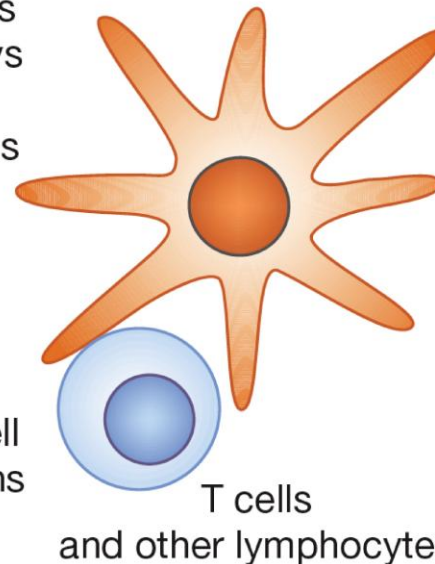
# The 3 types of professional APCs are functionally different!

|                | Dendritic cells                                                                    | Macrophages                                                                        | B cells                                                                             |
|----------------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
|                |   |  |  |
| Antigen uptake | +++ Macropinocytosis and phagocytosis by tissue dendritic cells<br>Viral infection | Phagocytosis<br>+++                                                                | Antigen-specific receptor (Ig)<br>++++                                              |

**Dendritic Cells (DC) are the most important Antigen Presenting Cell type**

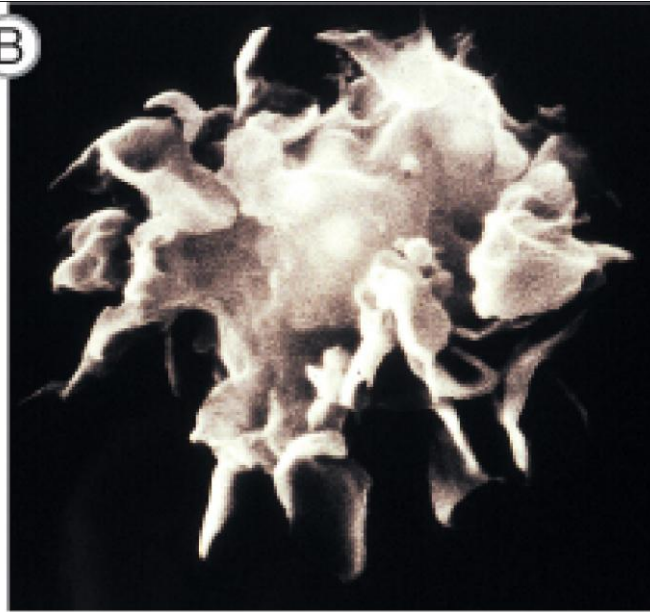
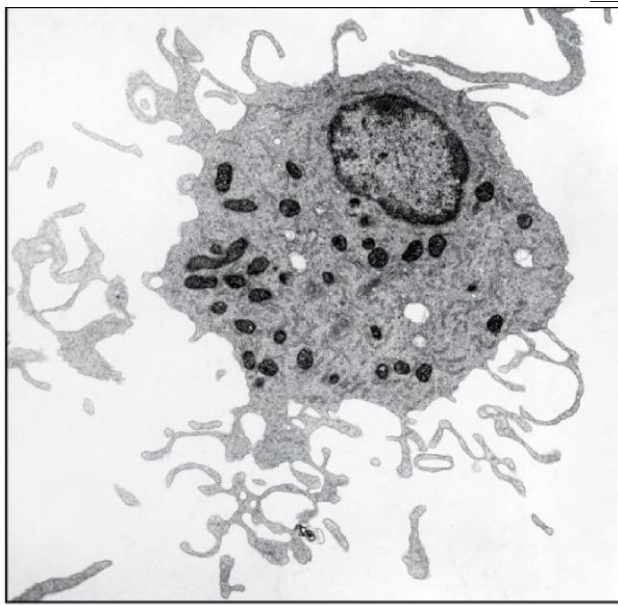
Antigen uptake receptors and processing pathways for **presentation** of peptide-MHC complexes

**Location** at body surfaces and in the T-cell areas of lymphoid organs



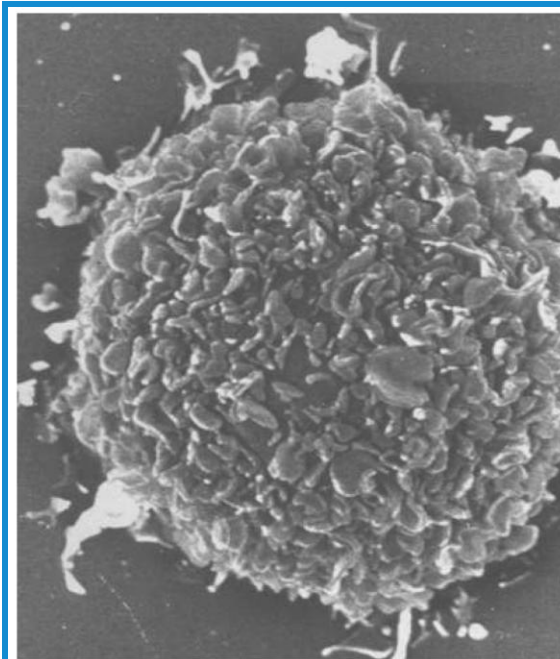
**Maturation** or differentiation in response to microbial and other stimuli

**Subsets** with distinct pattern recognition receptors and functions

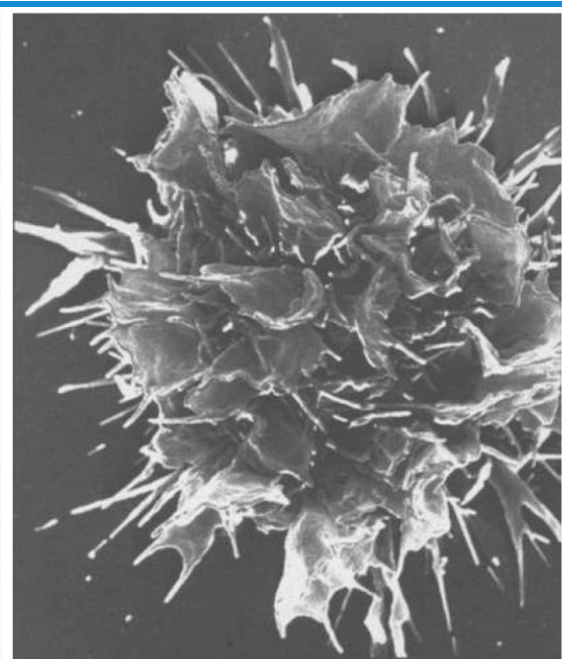


**Dendritic cells originate in the bone marrow, and are present:**

- ❖ **at body surfaces,**
- ❖ **in all peripheral organs**
- ❖ **in the T cell-dependent areas of lymphoid organs**



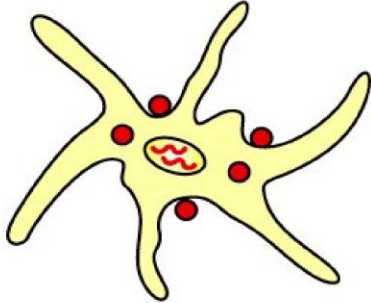
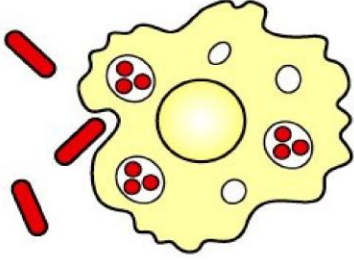
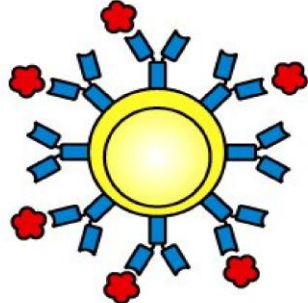
immature DC



mature APC

**Dendritic cells MATURE in response to microbial and other stimuli**

# The 3 types of professional APCs are functionally different!

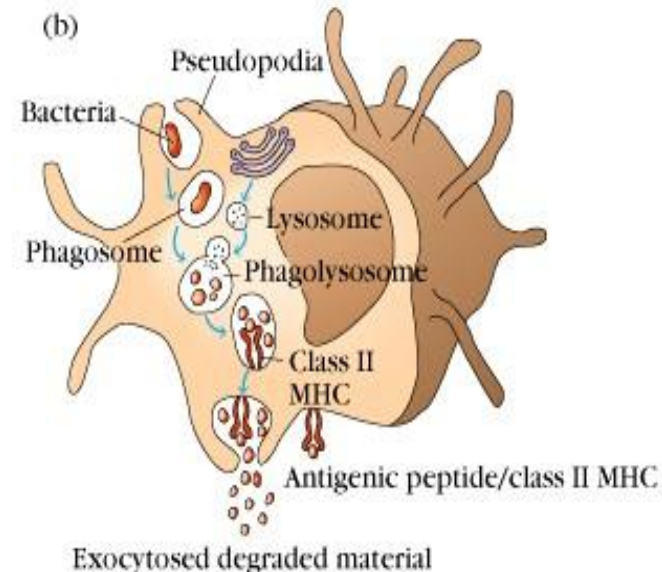
|                | Dendritic cells                                                                    | Macrophages                                                                        | B cells                                                                             |
|----------------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
|                |   |  |  |
| Antigen uptake | +++ Macropinocytosis and phagocytosis by tissue dendritic cells<br>Viral infection | Phagocytosis<br>+++                                                                | Antigen-specific receptor (Ig)<br>++++                                              |

**Macrophages present exogenous antigens obtained through phagocytosis**

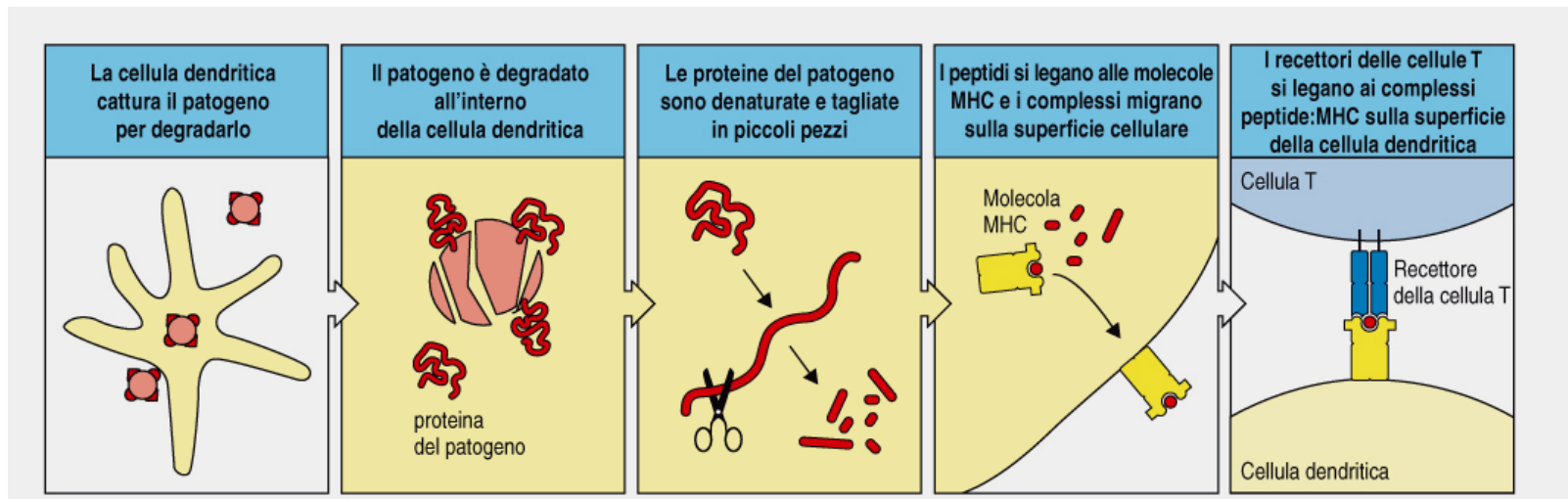
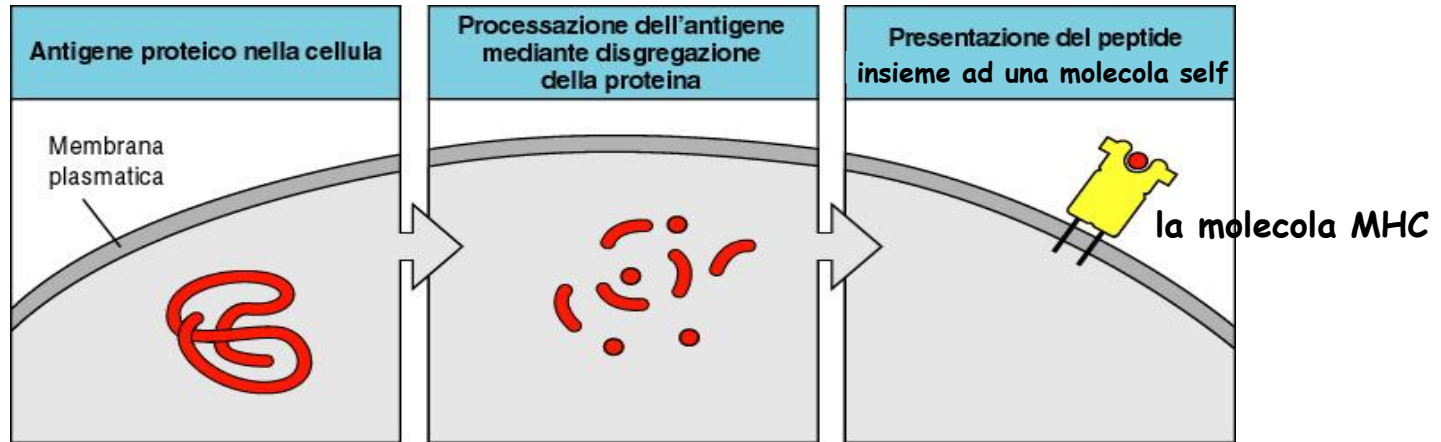
(a)



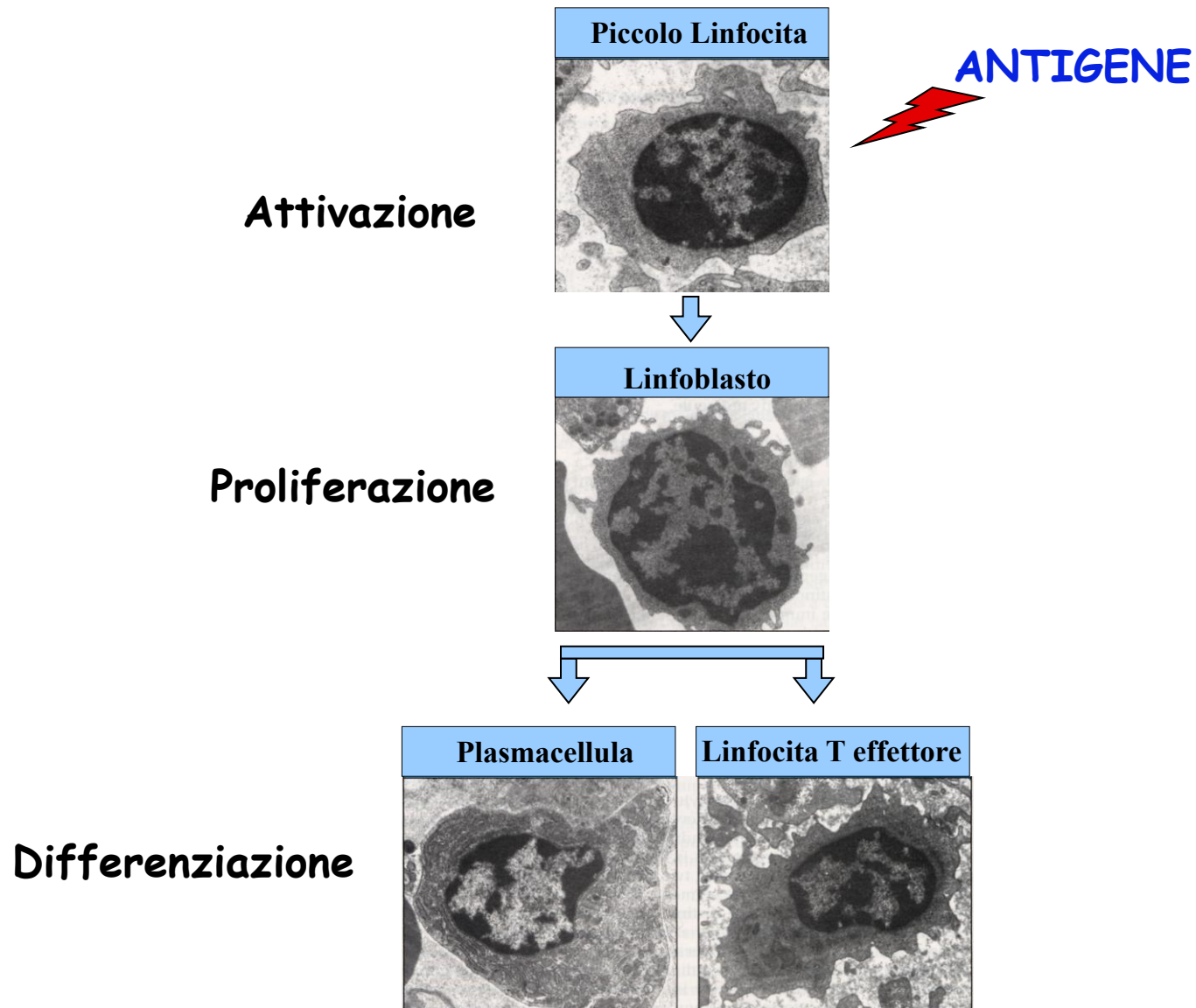
(b)



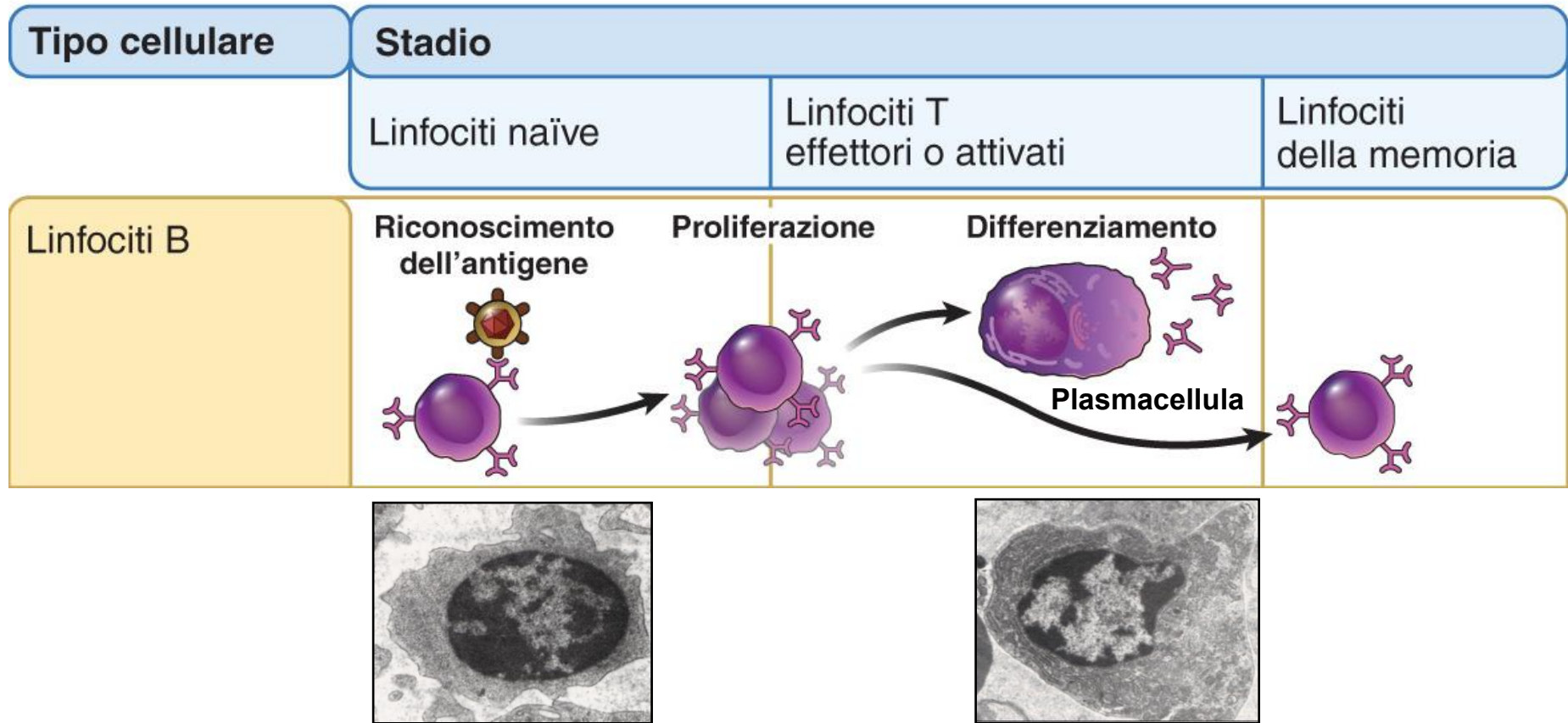
# Le cellule accessorie processano e presentano l'antigene proteico ai linfociti T (Antigen Presenting Cells)



# Le cellule dell'immunità adattativa: i Linfociti

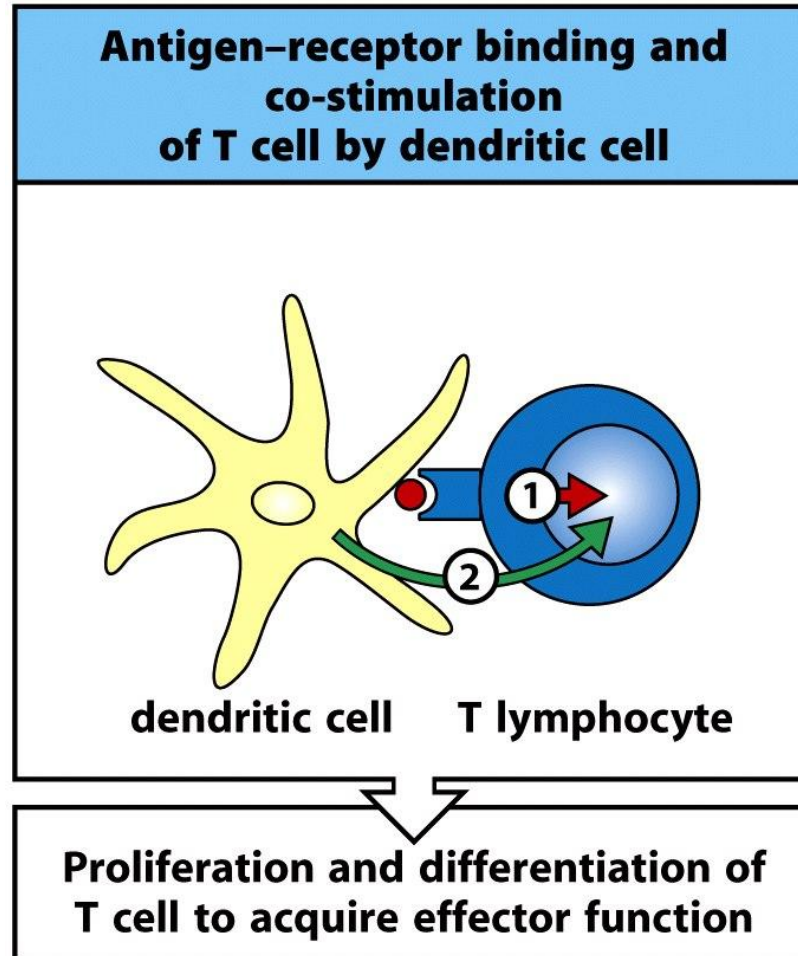


# La funzione dei linfociti B



- Il **Linfocita B** si differenzia in plasmacellula e secerne anticorpi

# L'attivazione dei linfociti T richiede due segnali!



**non self**

**Characteristics  
of the immune  
system**

**self**



**immune system**

**antigen**

adaptive response

innate response

**primary  
contact**

**+**

**+**

**secondary  
contact**

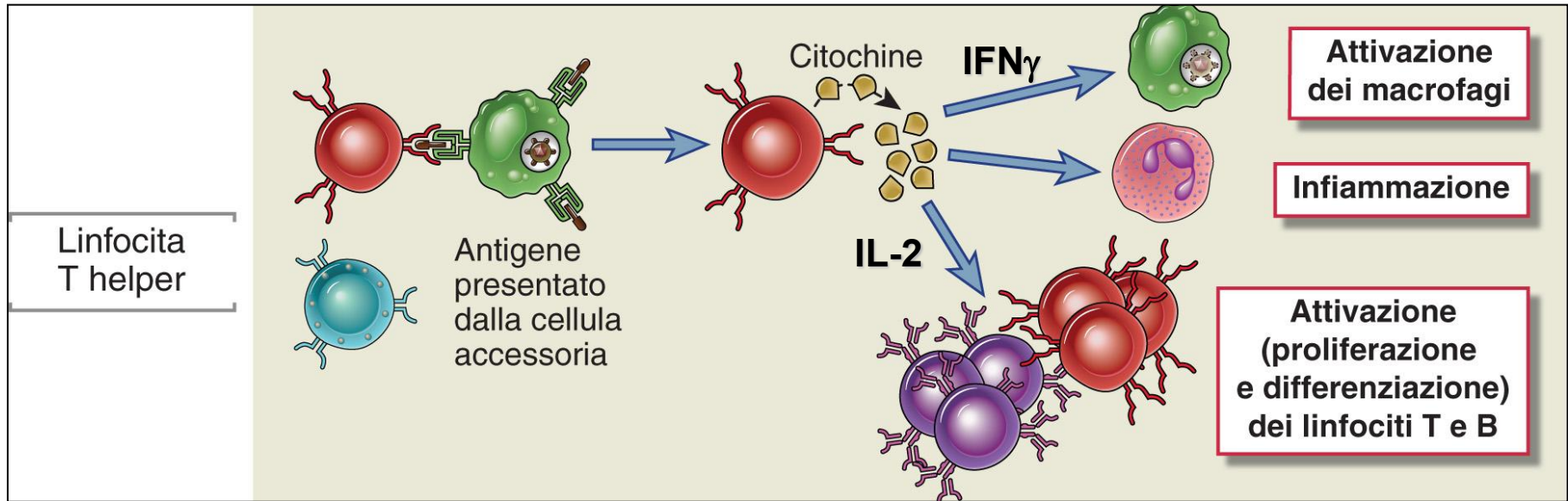
**+++**

**+**

**-specific  
-memory**

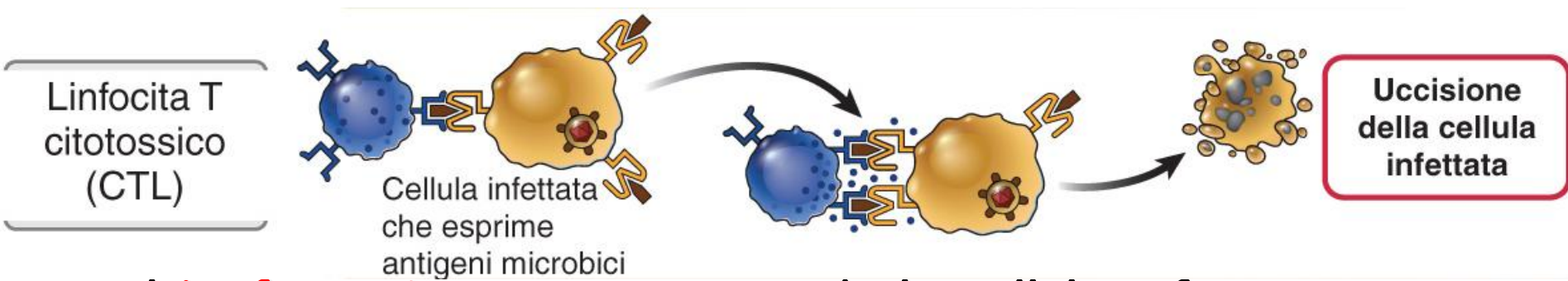
**-non specific  
-no memory**

# Meccanismi effettori dei linfociti T



- Il **Linfocita T helper** rilascia citochine e guida le risposte degli altri linfociti e delle cellule dell'immunità innata.

# Meccanismi effettori dei linfociti T



- Il **Linfocita T citotossico** uccide le cellule infettate.

Cytotoxic T-Lymphocyte  
killing a target cell  
infected with influenza  
virus

# Meccanismi utilizzati dai principali componenti del SI per eliminare i patogeni:

## Meccanismo utilizzato

## Diretto contro:

---

### Fagocitosi

- Monociti/macrofagi
- Granulociti neutrofili

Batteri extracellulari e funghi

### Meccanismo litico

- Cellule NK
- Linfociti T citotossici

Cellule infettate da virus

- Granulociti eosinofili

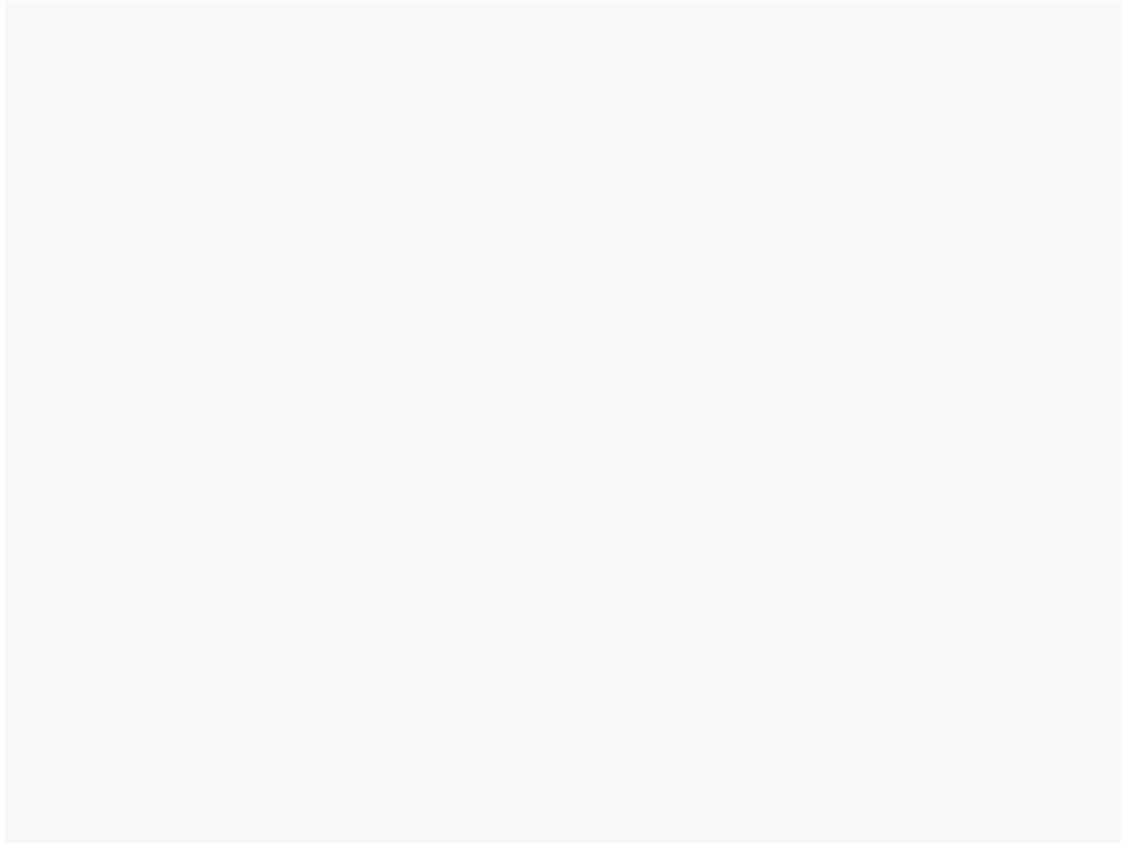
Elminti

### Neutralizzazione

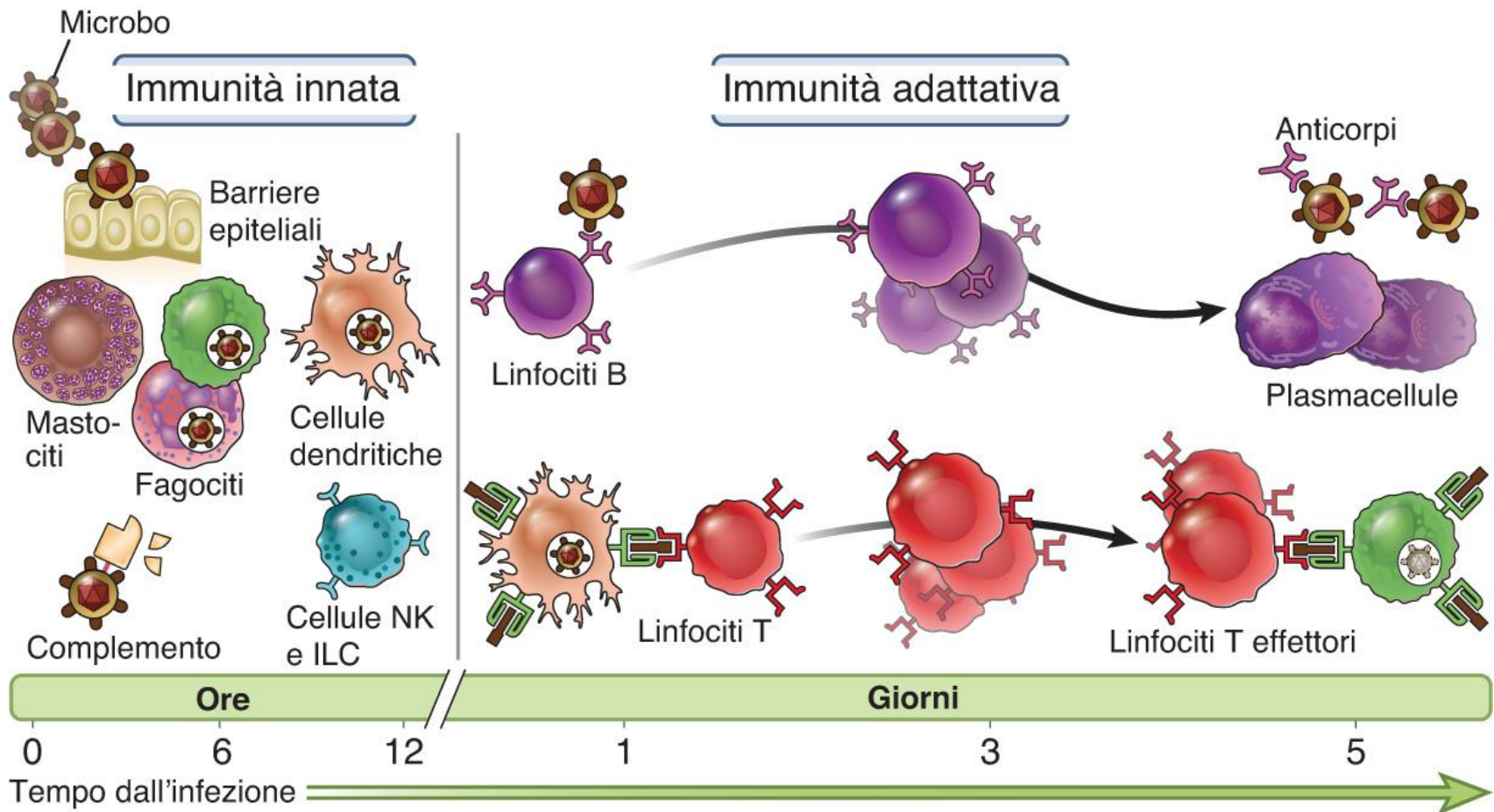
- Anticorpi

Esotossine, virus

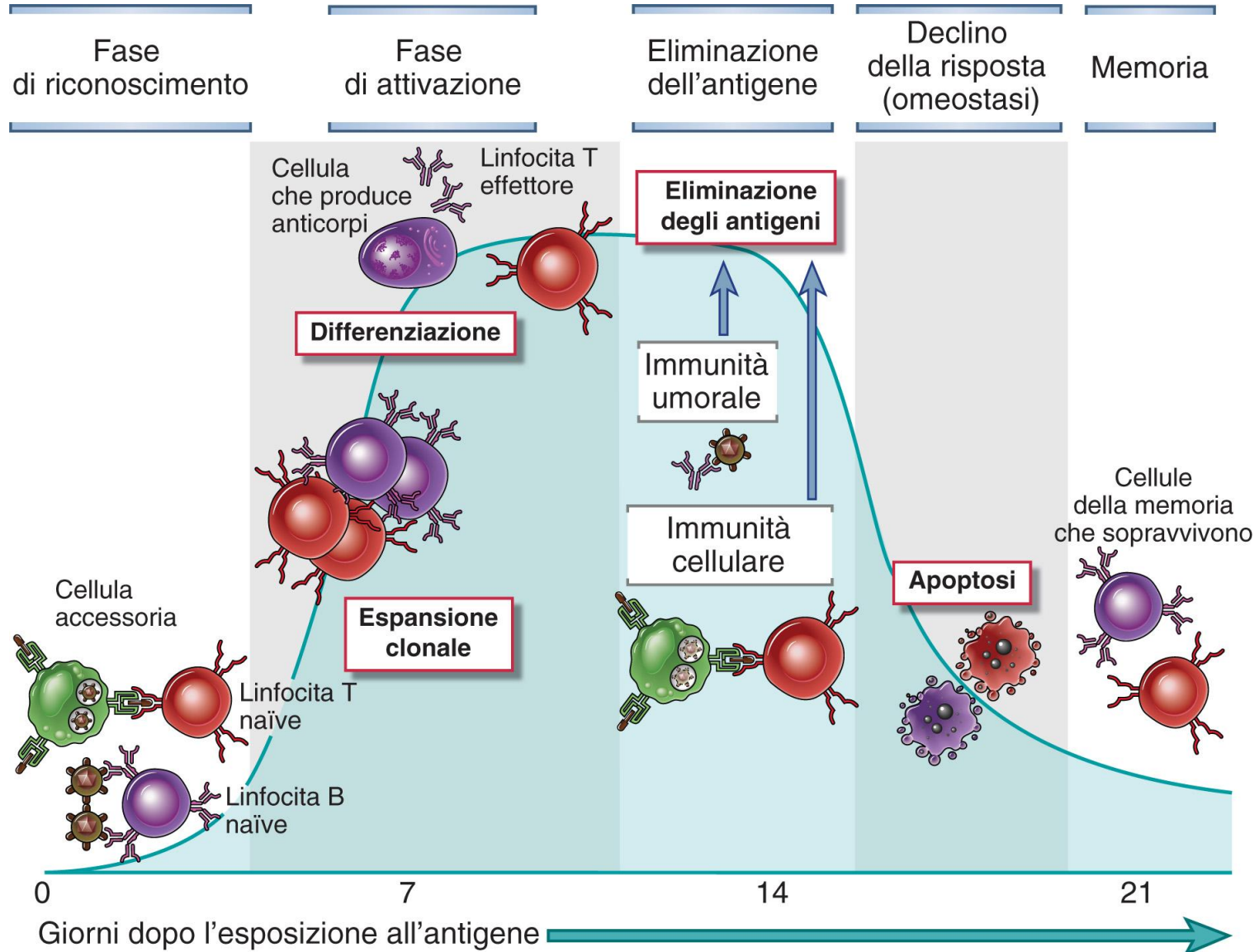
# Le diverse fasi della risposta immunitaria



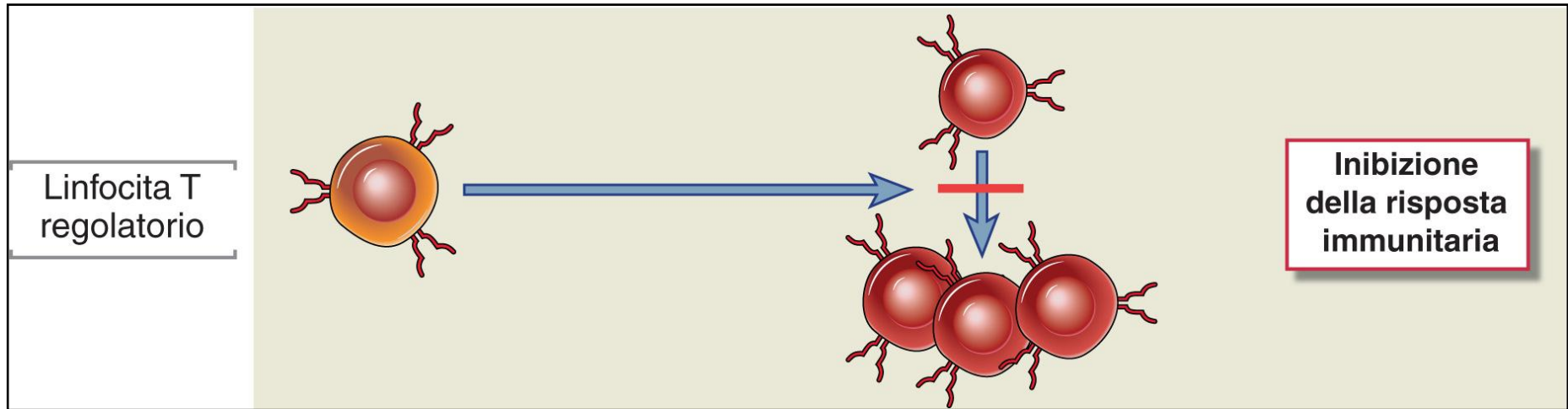
# La risposta immunitaria



# Le diverse fasi della risposta immunitaria

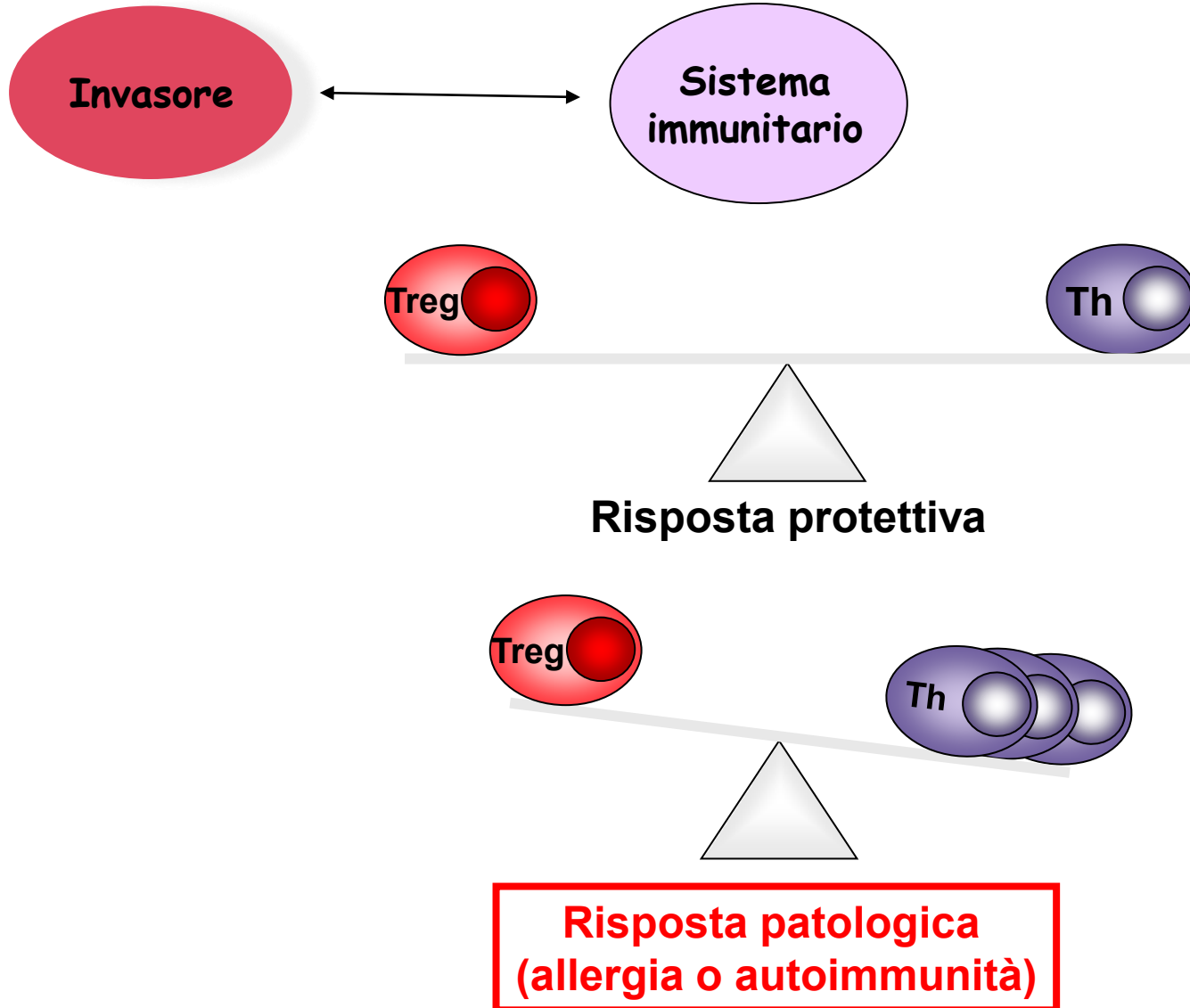


# Meccanismi effettori dei linfociti T regolatori



- I **Linfociti T regolatori** rilasciano citochine e sopprimono le risposte delle cellule dell'immunità innata e degli altri linfociti

**Il sistema immunitario può essere causa di malattia:**  
**Un prezzo da pagare per una difesa efficace contro le infezioni!**





# GLI ANTICORPI: I PROTAGONISTI DELLE RISPOSTE UMORALI DELL'IMMUNITA' SPECIFICA

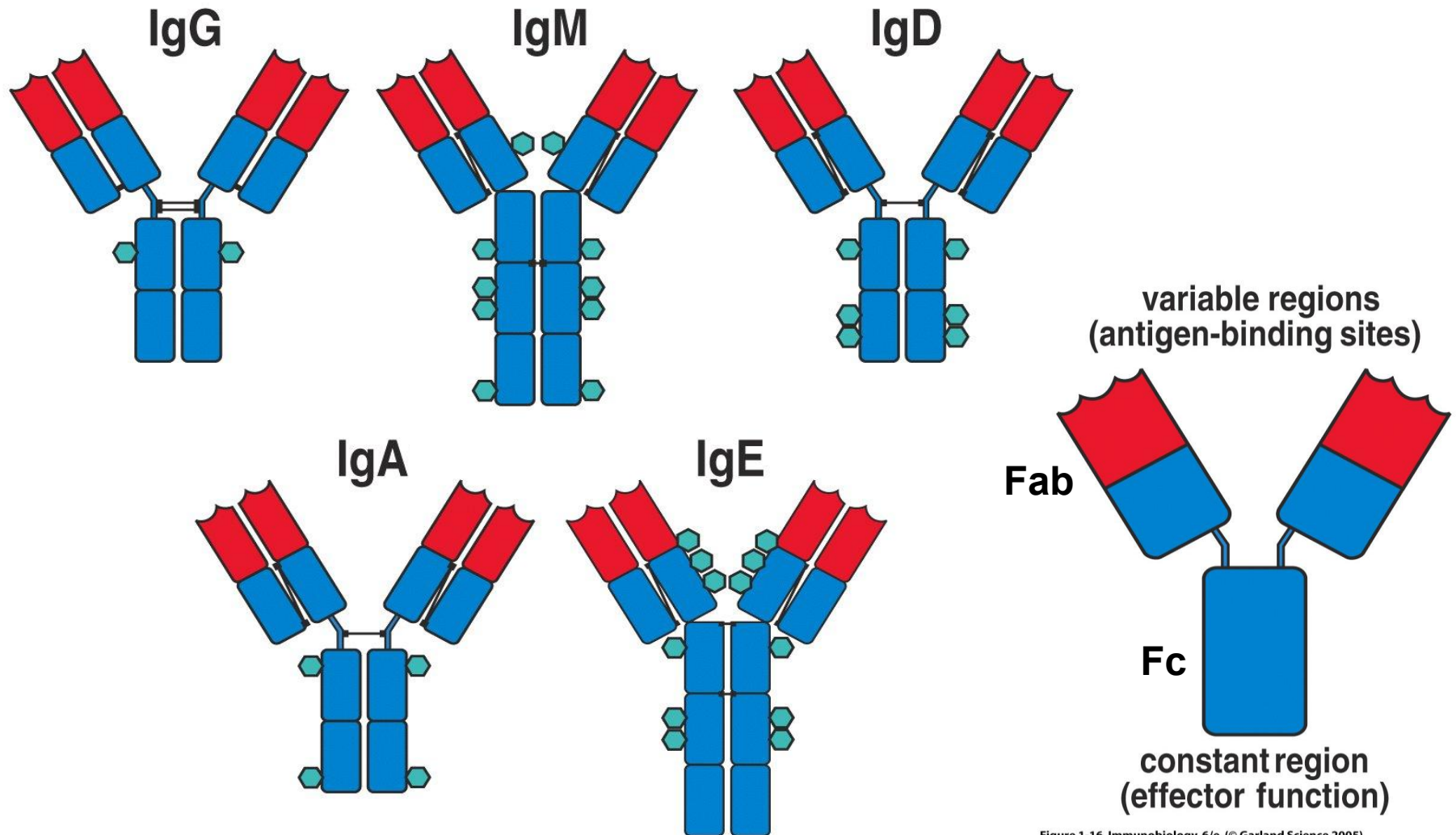
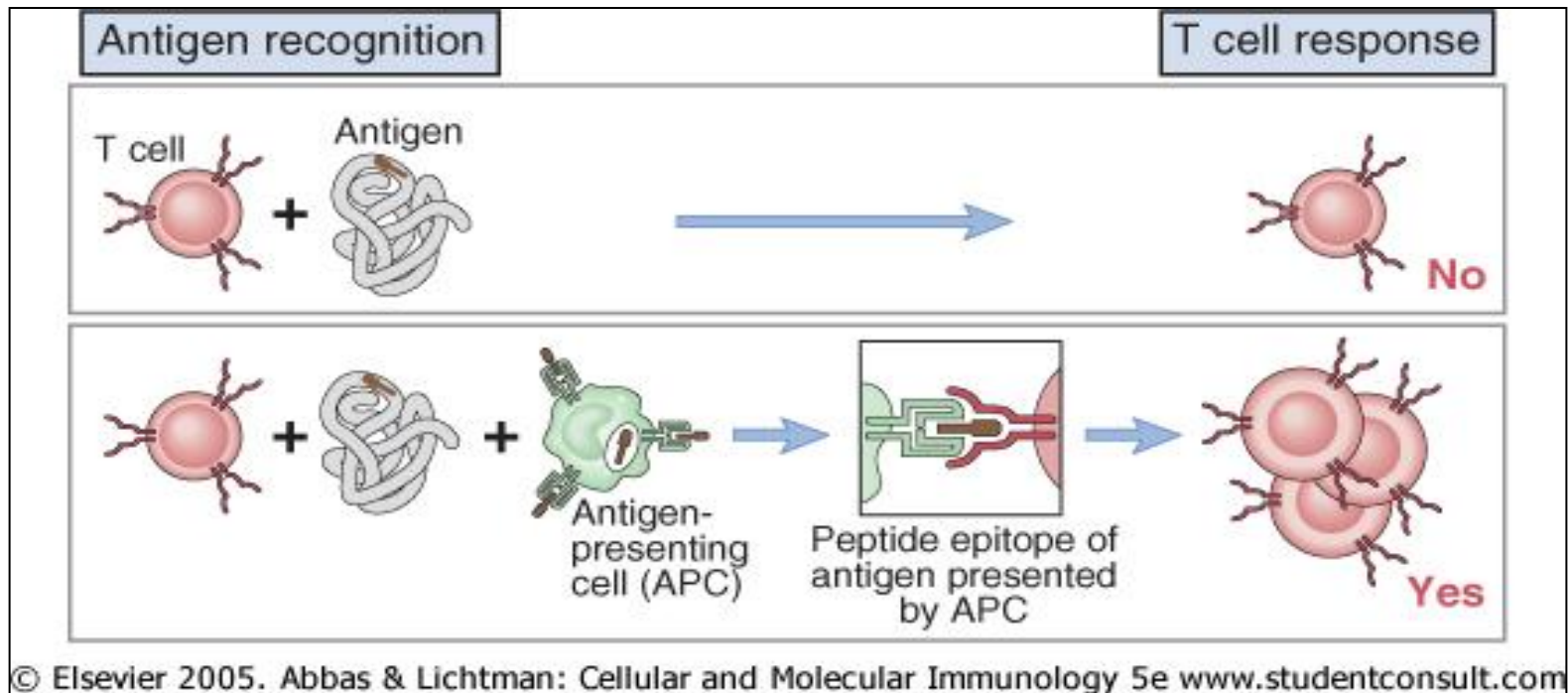


Figure 1-16 Immunobiology, 6/e. (© Garland Science 2005)

# Characteristics of antigen recognition by T cells

- T cells recognize antigen after fragmentation (processing) and association with MHC/HLA molecules
- HLA class I molecules (HLA-A, B, C) present peptides of antigens to **CD8+ cytotoxic T lymphocytes**
- HLA class II molecules (HLA-DR, DP, DQ) present peptides of antigens to **CD4+ helper T lymphocytes**
- All nucleated cells of the body express HLA class I molecules
- Only 3 cell types (B lymphocytes, macrophages, and dendritic cells) express HLA class II molecules => professional Antigen Presenting Cells (APC)

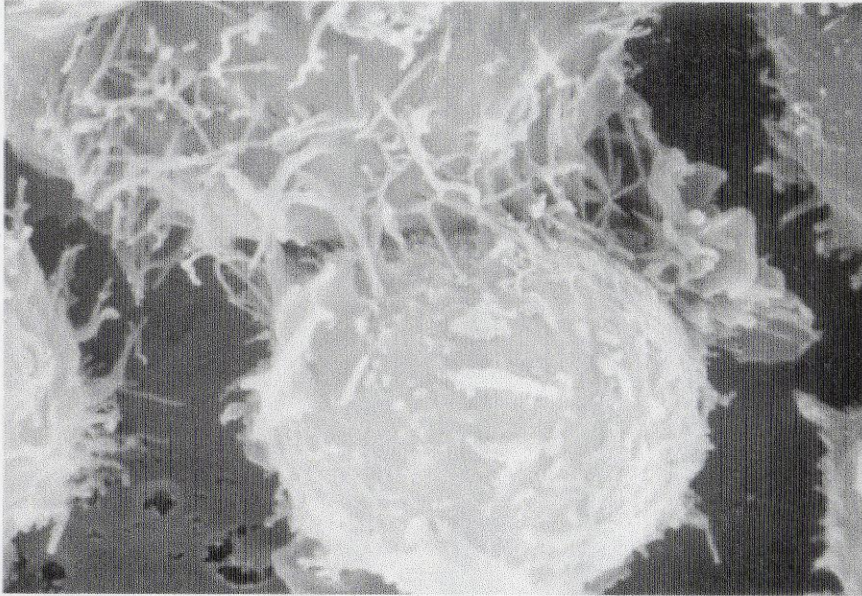
**Il linfocita T non è in grado di riconoscere l'antigene nella sua conformazione nativa.....**



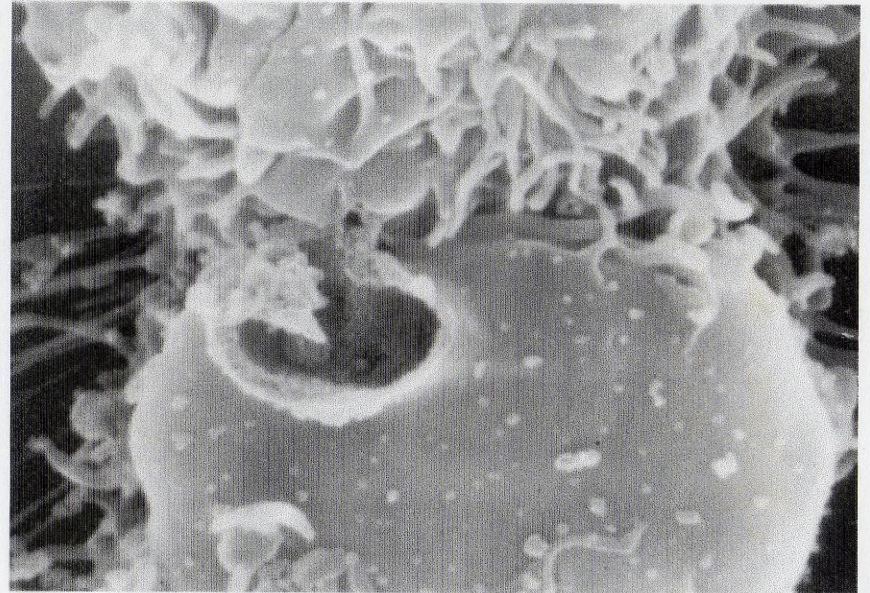
**....ma ha bisogno dell'intervento di cellule accessorie!**

# Il bacio della morte

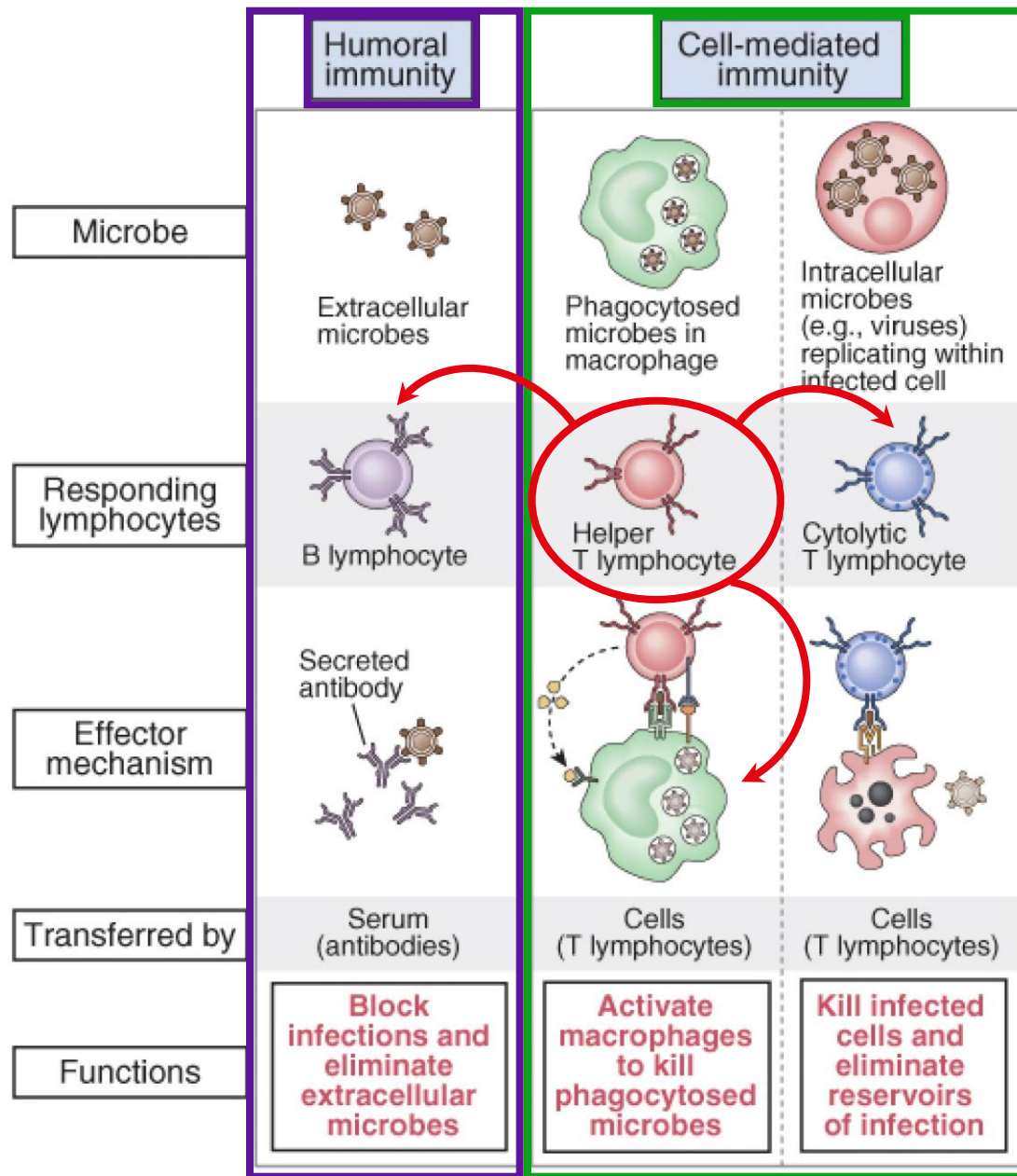
(a)



(b)



# CD4+ T cells (Helper) coordinate and regulate the immune response



# STRUCTURE OF MHC/HLA MOLECULES

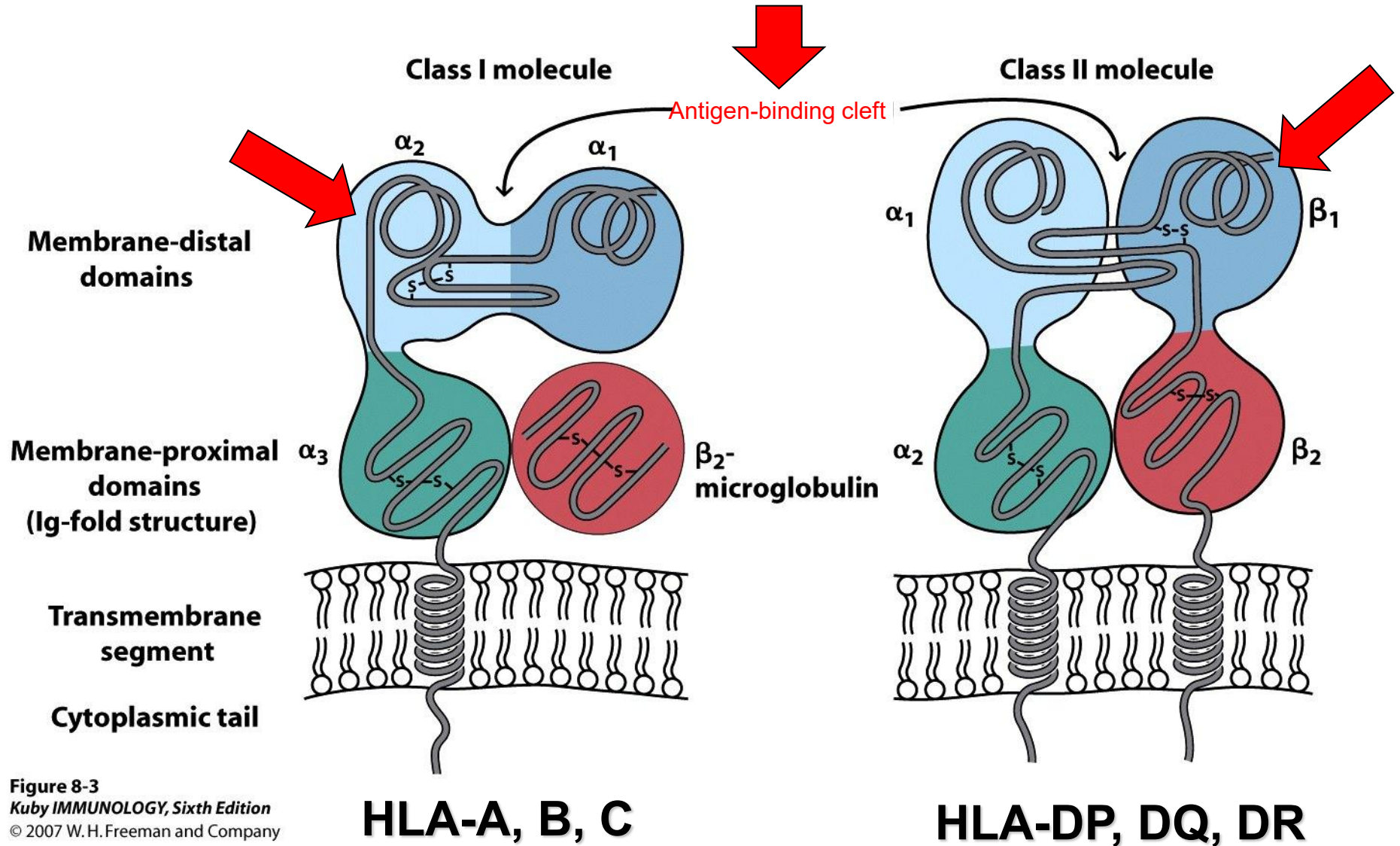


Figure 8-3  
Kuby IMMUNOLOGY, Sixth Edition  
© 2007 W. H. Freeman and Company

# Antigen Presenting Cells

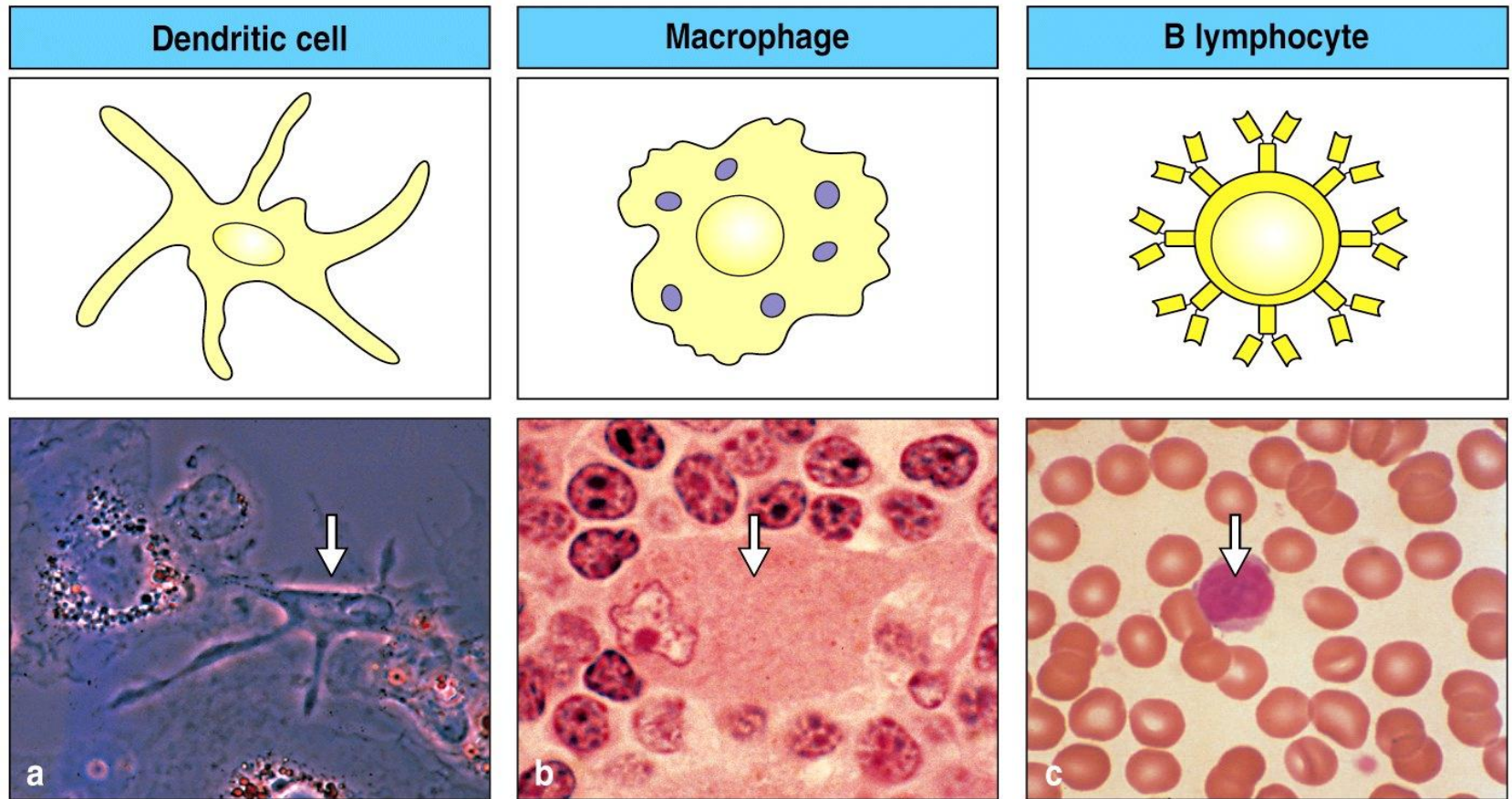
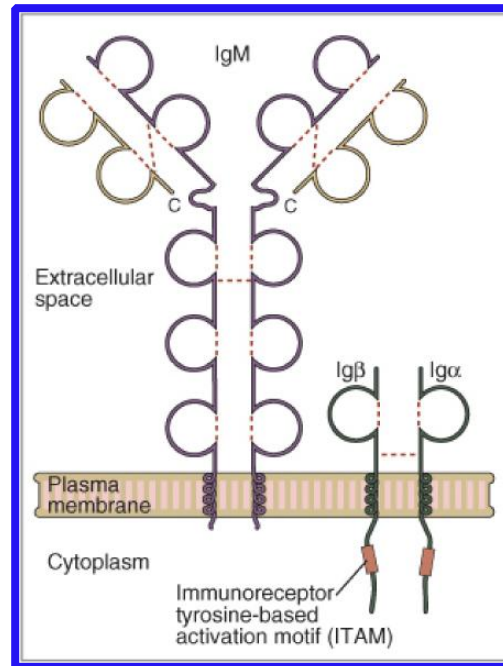


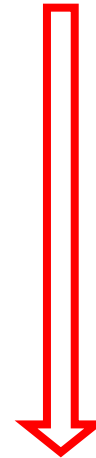
Figure 1-22 part 1 of 3 Immunobiology, 6/e. (© Garland Science 2005)

**Cellule dendritiche, macrofagi e linfociti B sono APC professionali**, ossia sono cellule specializzate nel presentare gli antigeni ai linfociti T

**B cells make antibodies!**



**BCR** (it is expressed on the B cell surface)



**Antibody** (it is secreted from the B cell)

