B cell recognition and response of antigens

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Chapter 1　B cell response to T cell-dependent antigen

The developmental process that results in production of plasma cells and memory B cells can be divided into three broad stages:

--Generation of mature, immunocompetent B cells (maturation):

Ig-gene rearrangements,

negative selection (10% B cell will be re-circulating B cell pool)

the antigen-independent phase of B-cell development.

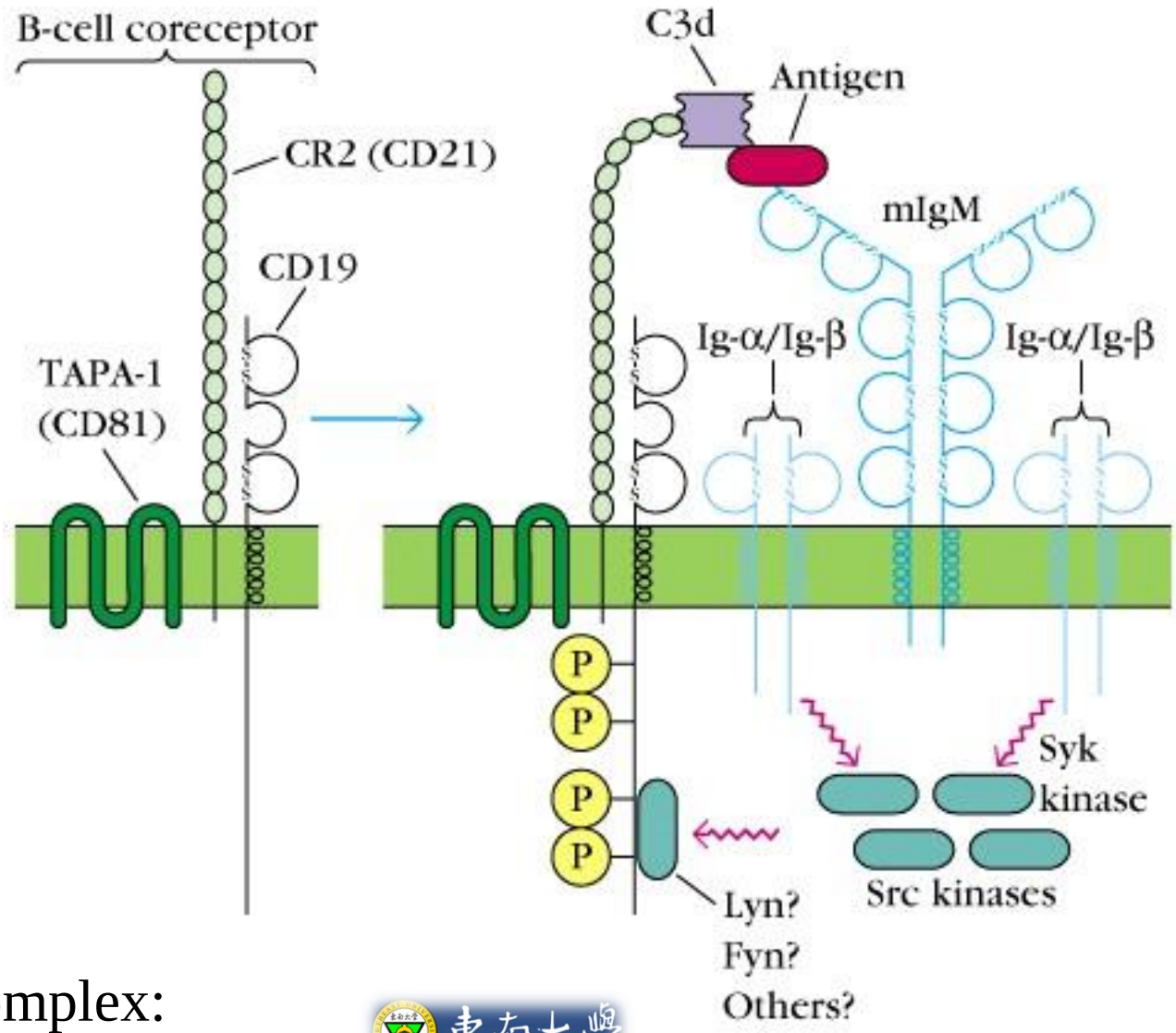
--Activation of mature B cells when they interact with antigen:

recognition, activation, somatic hypermutation and affinity maturation

--Differentiation of activated B cells into plasma cells and memory B cells

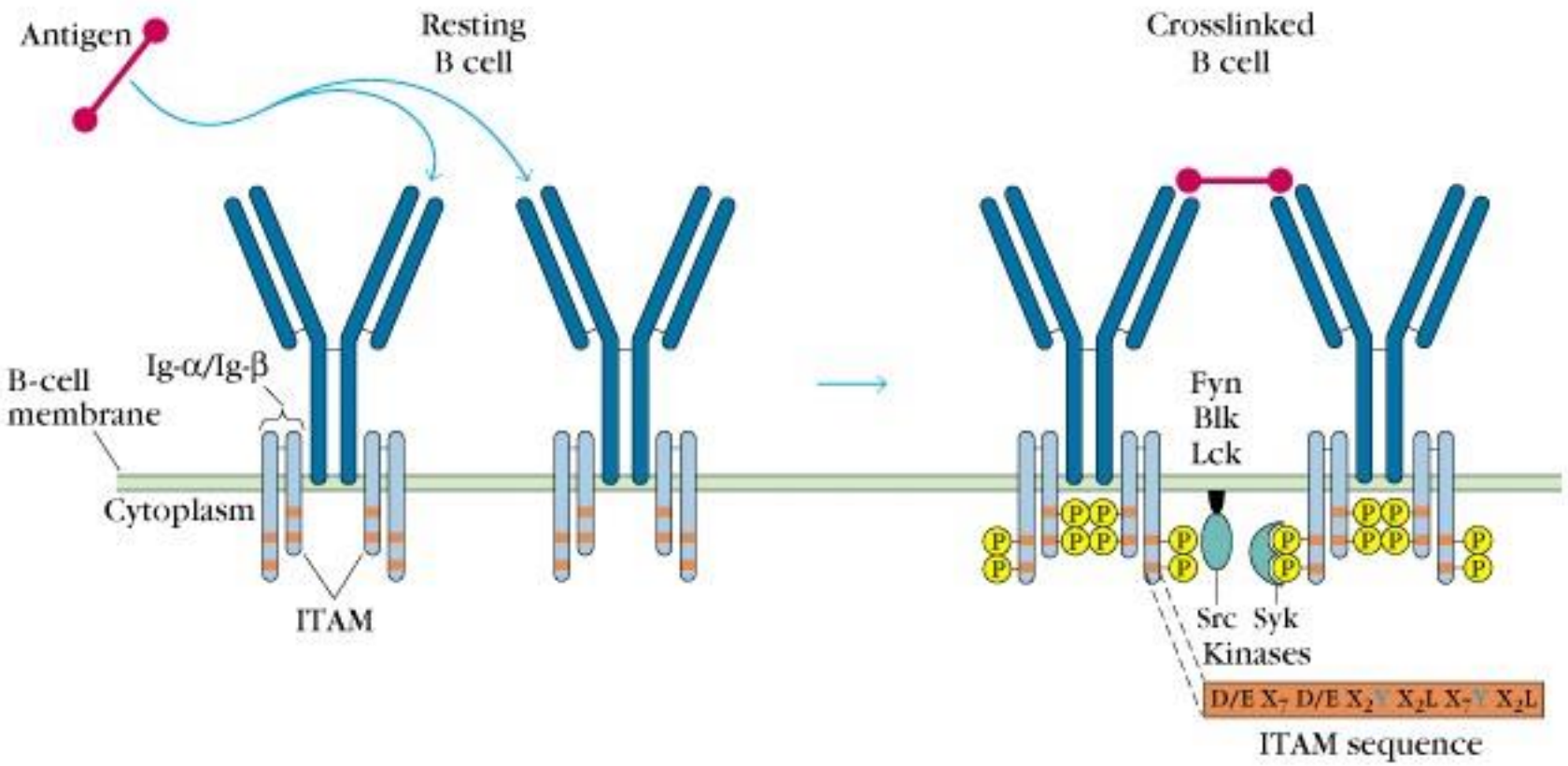
germinal center

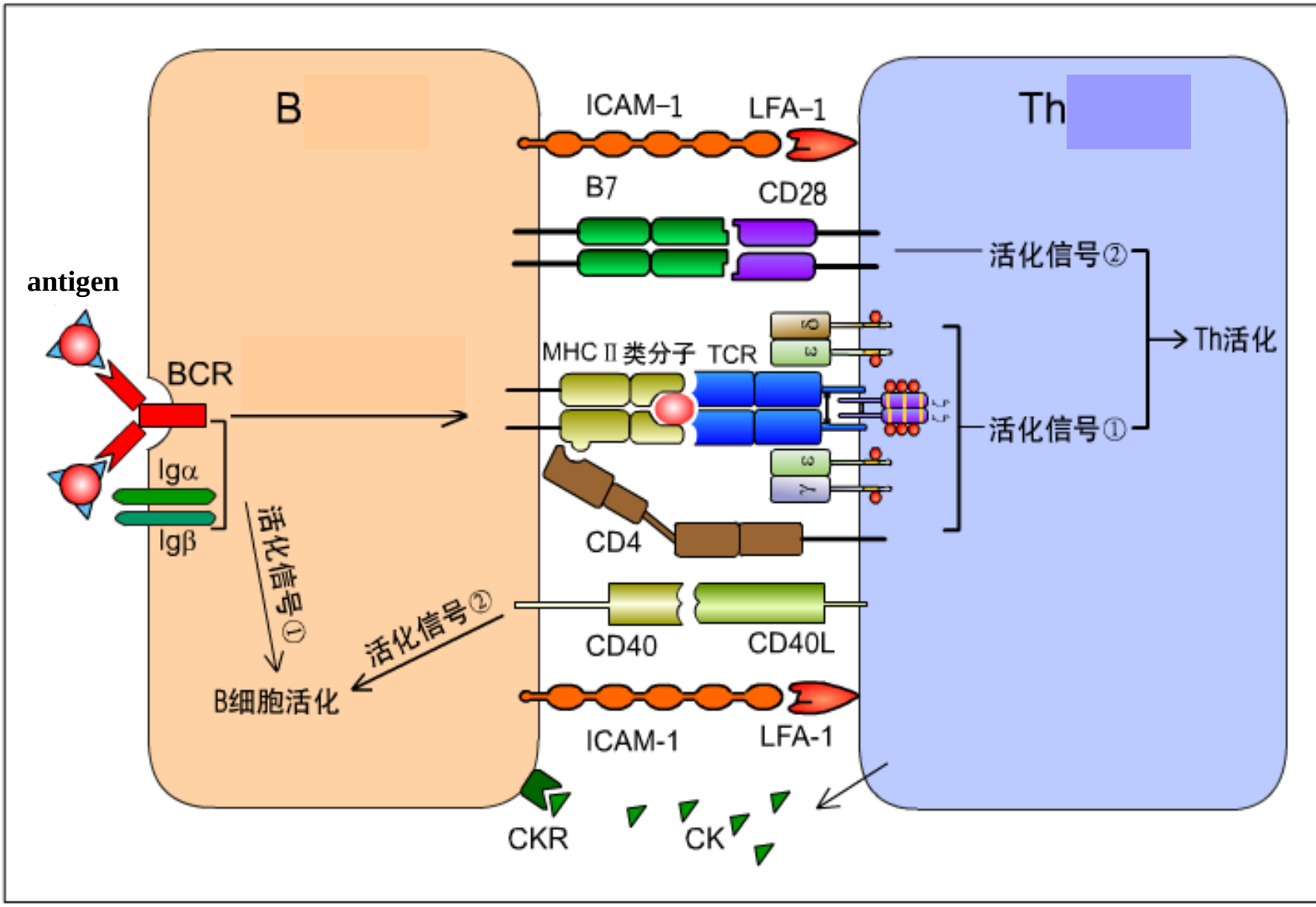
Recognition of B cell:



BCR complex:

Crosslinking:



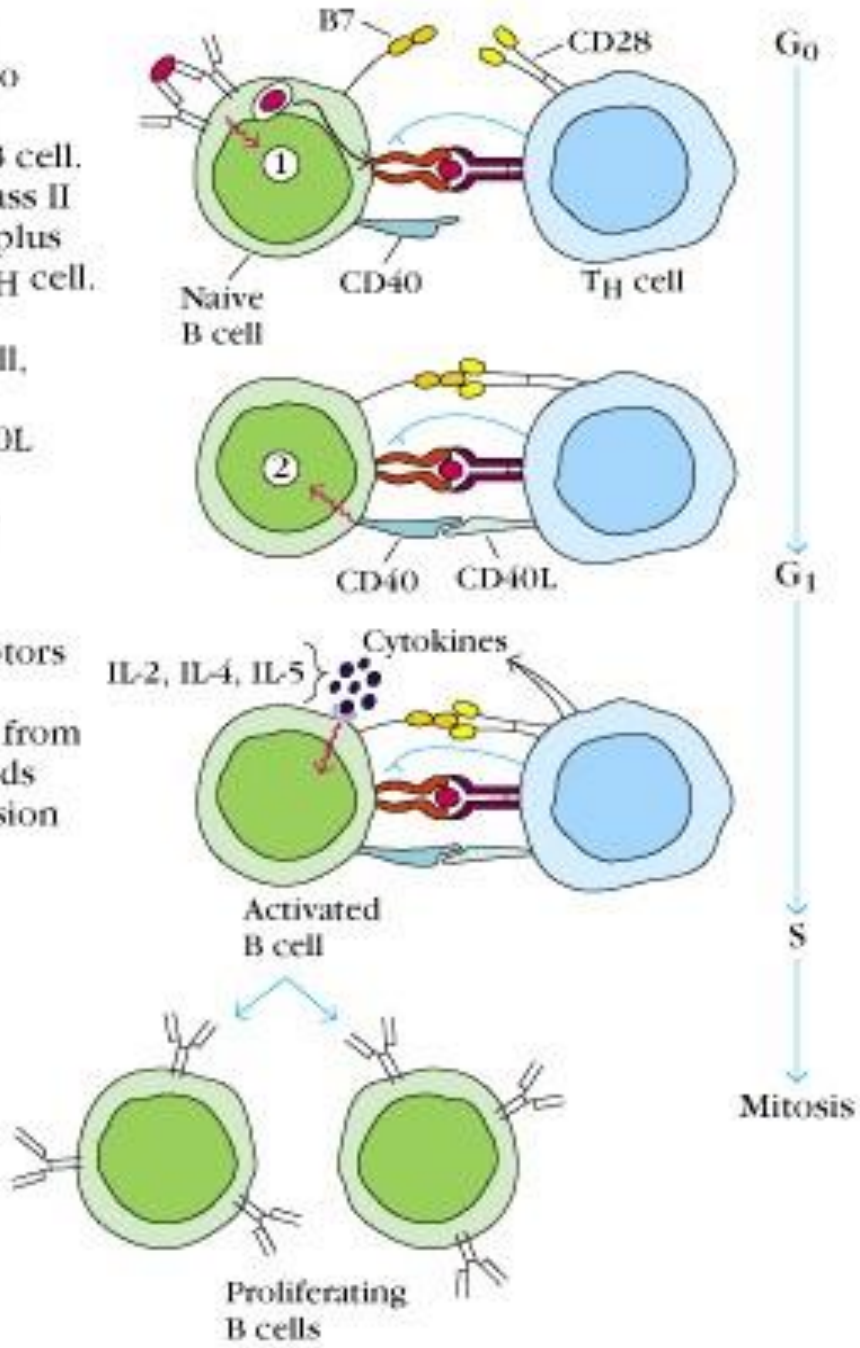


Interaction between B cell and TH cell

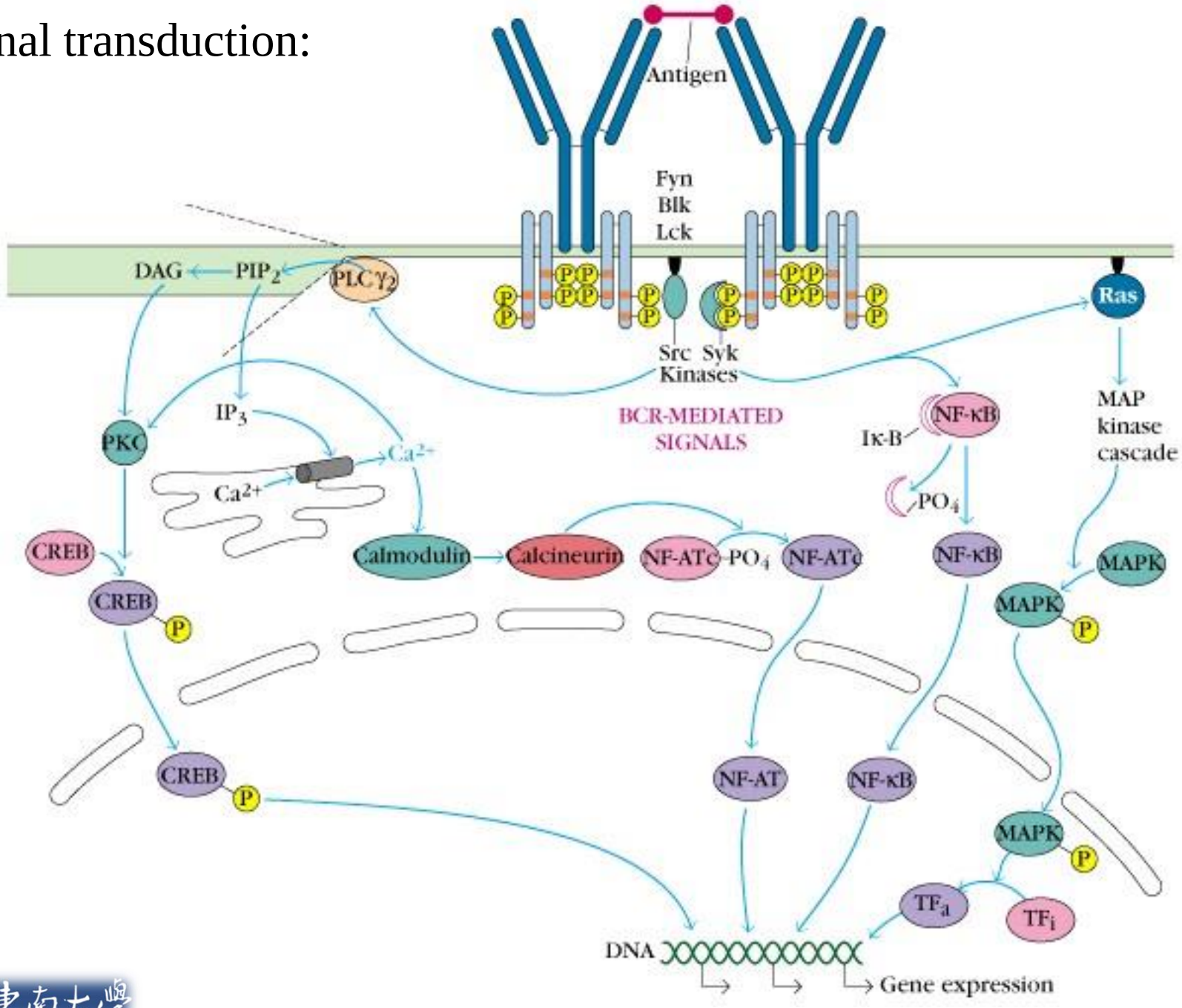
(a)1. Antigen cross-linkage of mIg induces signal ① , which leads to increased expression of class II MHC and co-stimulatory B7 on B cell.
2. T_H cell recognizes antigen-class II MHC on B-cell membrane. This plus co-stimulatory signal activates T_H cell.

(b)1. Following activation of T_H cell, it begins to express CD40L.
2. Interaction of CD40 and CD40L provides signal ②.
3. B7-CD28 interactions provide costimulation to the T_H cell.

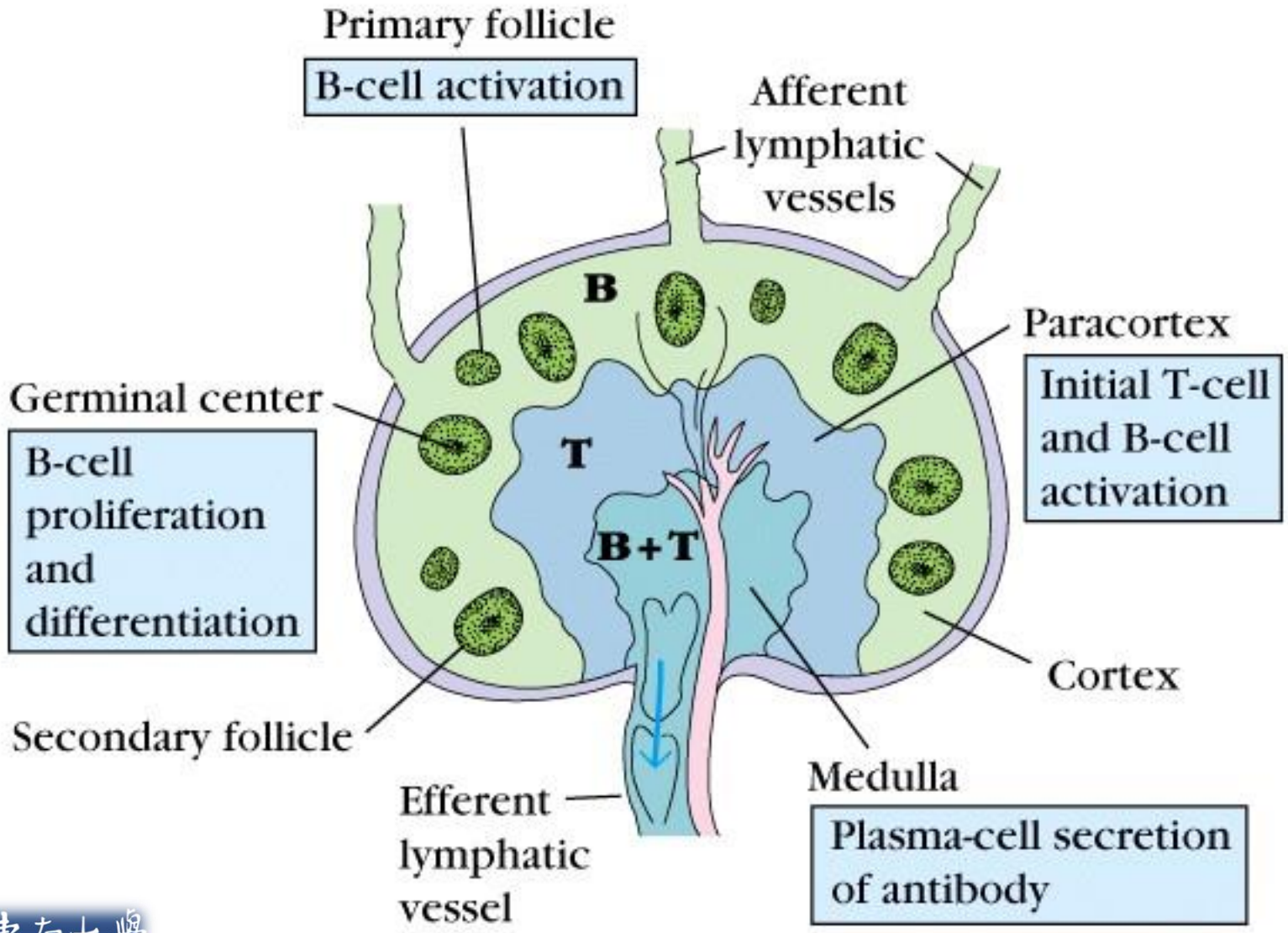
(c)1. B cell begins to express receptors for various cytokines.
2. Binding of cytokines released from T_H cell in a directed fashion sends signals that support the progression of the B cell to DNA synthesis.

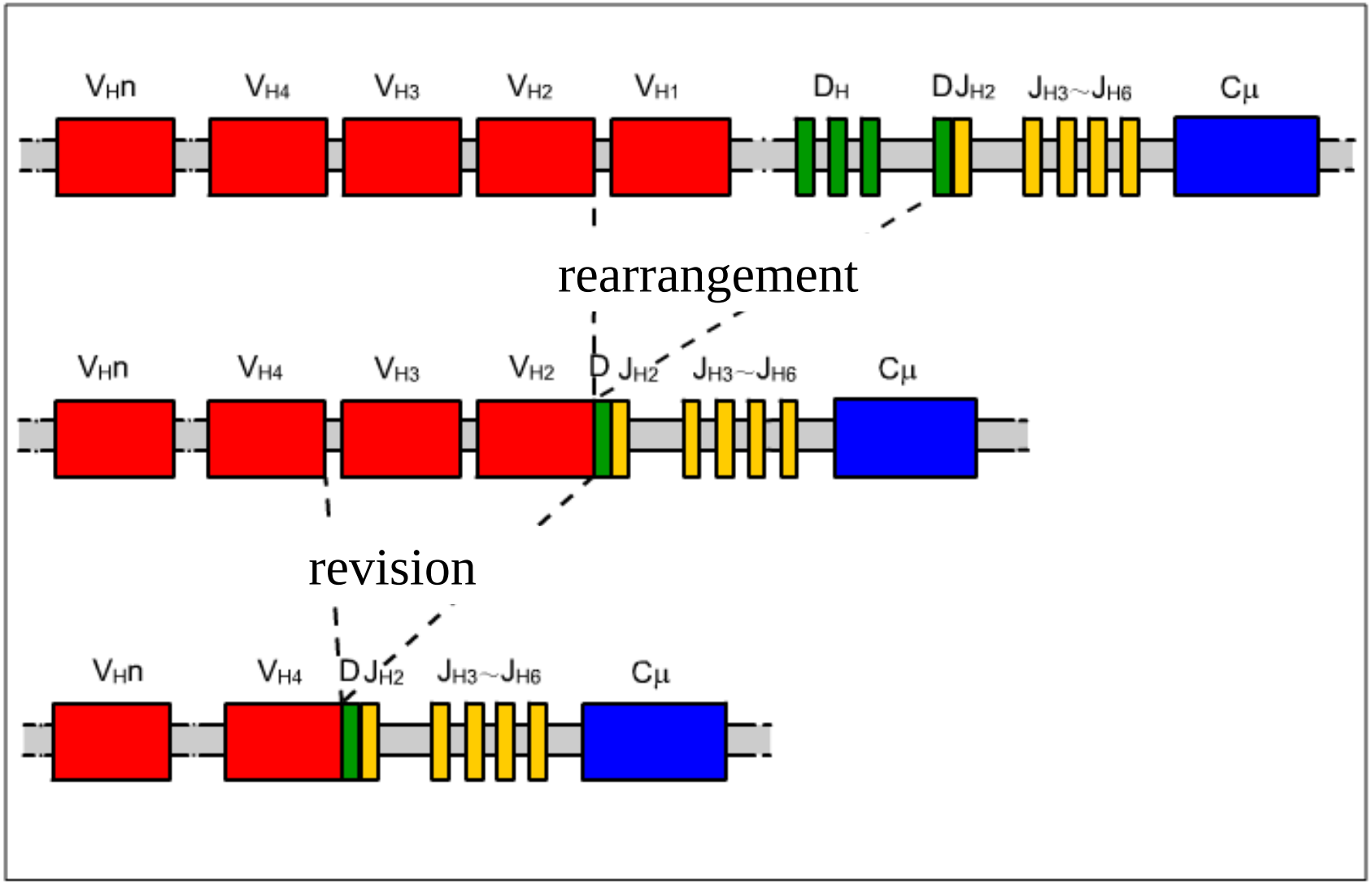


Signal transduction:



Germinal center:





BCR rearrangement and revision

Immunology

Somatic hypermutation and affinity maturation:

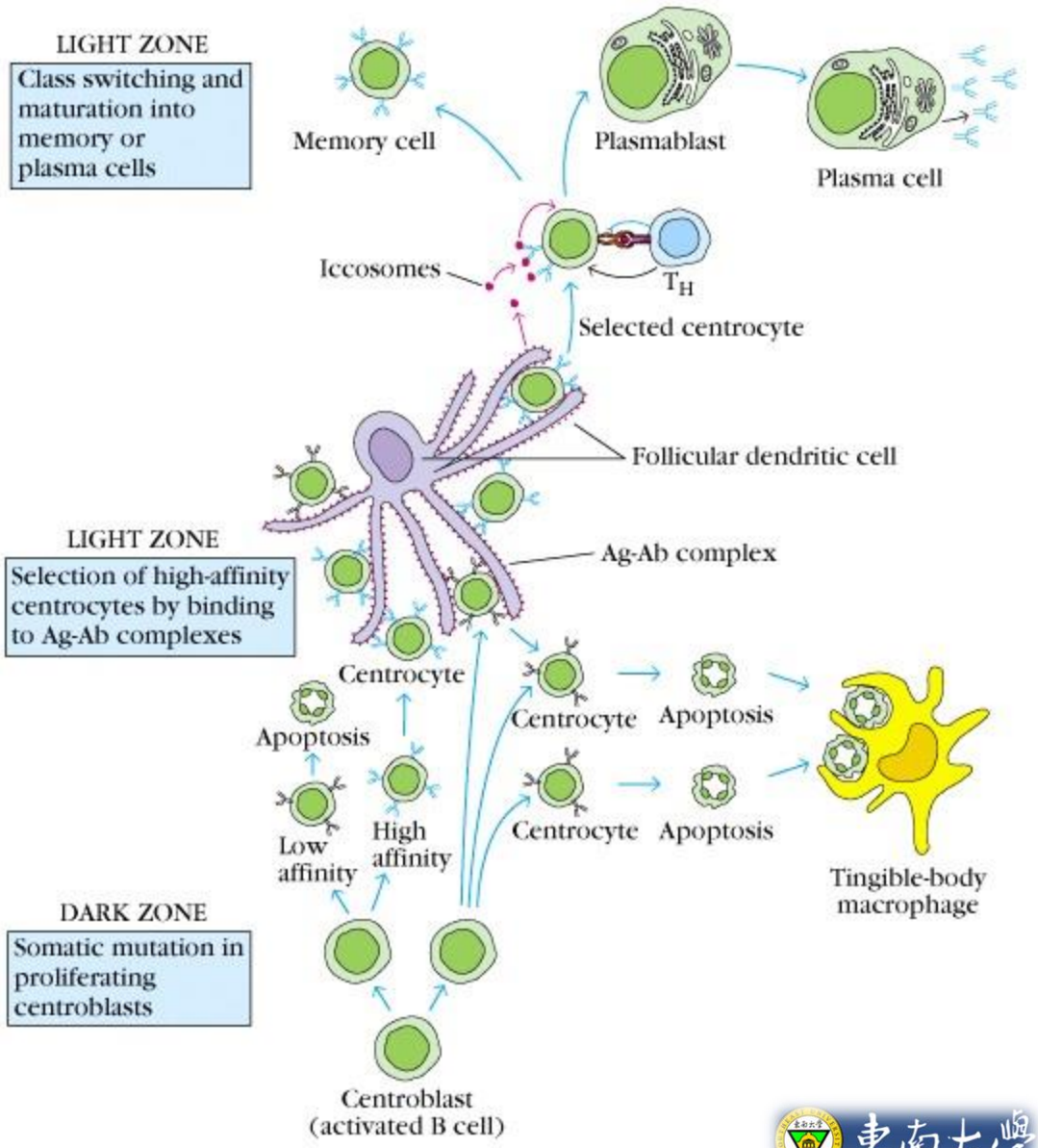
Overview of cellular events within secondary follicles of peripheral lymph nodes.

Follicular dendritic cells bind antigen-antibody complexes along their long extensions.

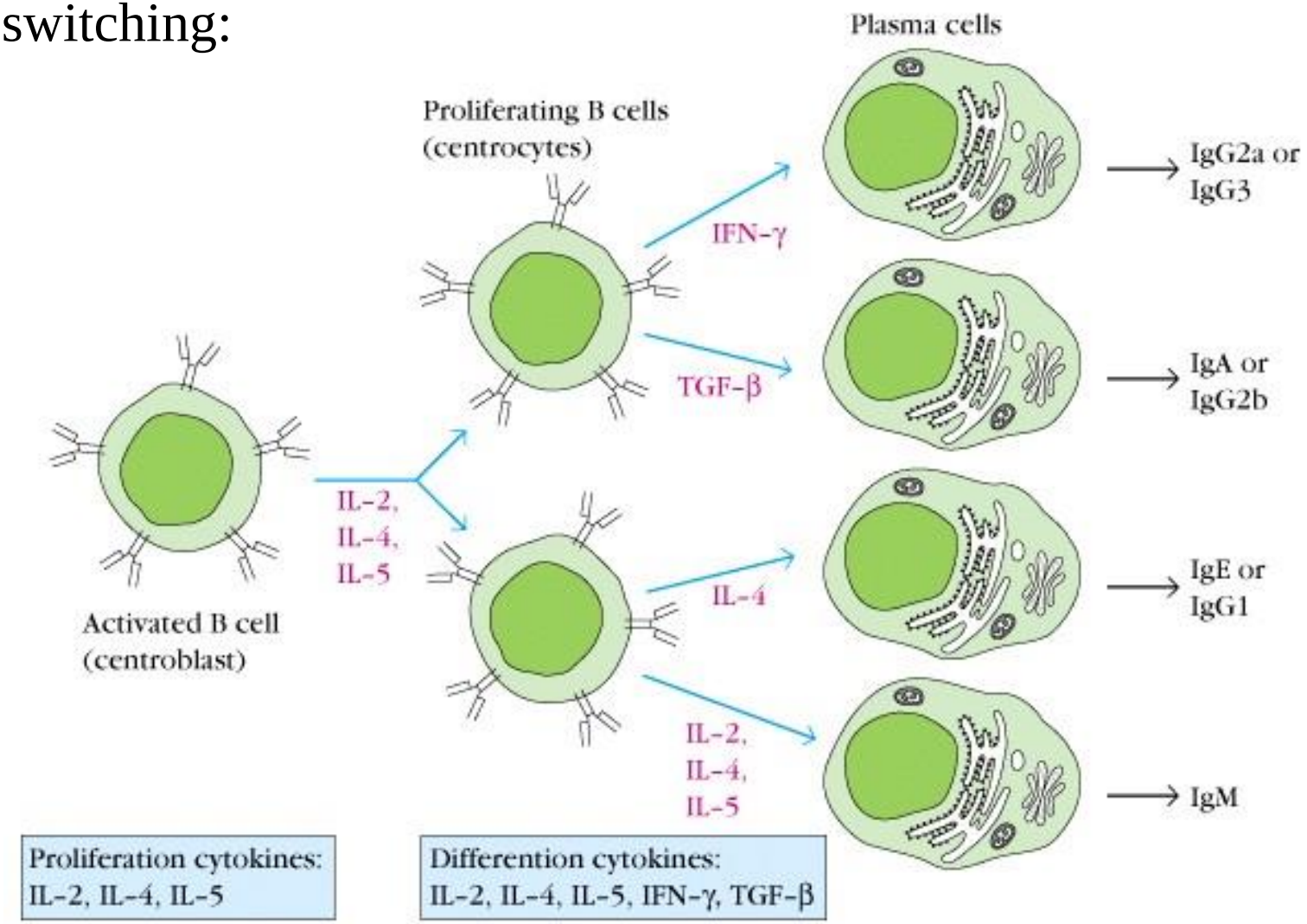
Small B cells (centrocytes) bearing high-affinity membrane immunoglobulin (antibodies shown in blue) are thought to interact with antigen presented as antigen-antibody complexes on the follicular dendritic cells;

unselected centrocytes bearing low-affinity mIg (antibodies shown in black) die by apoptosis, and the debris is phagocytosed by tingible-body macrophages.

Selected centrocytes, which may undergo class switching, then mature into memory B cells or plasmablasts; the latter develop into plasma cells.



Class switching:



The interactions of numerous cy t o k i n e s with B cells generate signals required for proliferation and class switching during the differentiation of B cells into plasma cells.

Binding of the proliferation cytokines, which are released by activated TH cells, provides the progression signal needed for proliferation of activated B cells.

Memory B cells:

TABLE 11-7 COMPARISON OF NAIVE AND MEMORY B CELLS

Properties	Naive B cell	Memory B cell
Membrane markers		
Immunoglobulin	IgM, IgD	IgM, IgD(?), IgG, IgA, IgE
Complement receptor	Low	High
Anatomic location	Spleen	Bone marrow, lymph node, spleen
Life span	Short-lived	May be long-lived
Recirculation	Yes	Yes
Receptor affinity	Lower average affinity	Higher average affinity due to affinity maturation*
Adhesion molecules	Low ICAM-1	High ICAM-1

*Affinity maturation results from somatic mutation during proliferation of centroblasts and subsequent antigen selection of centrocytes bearing high-affinity mIg.

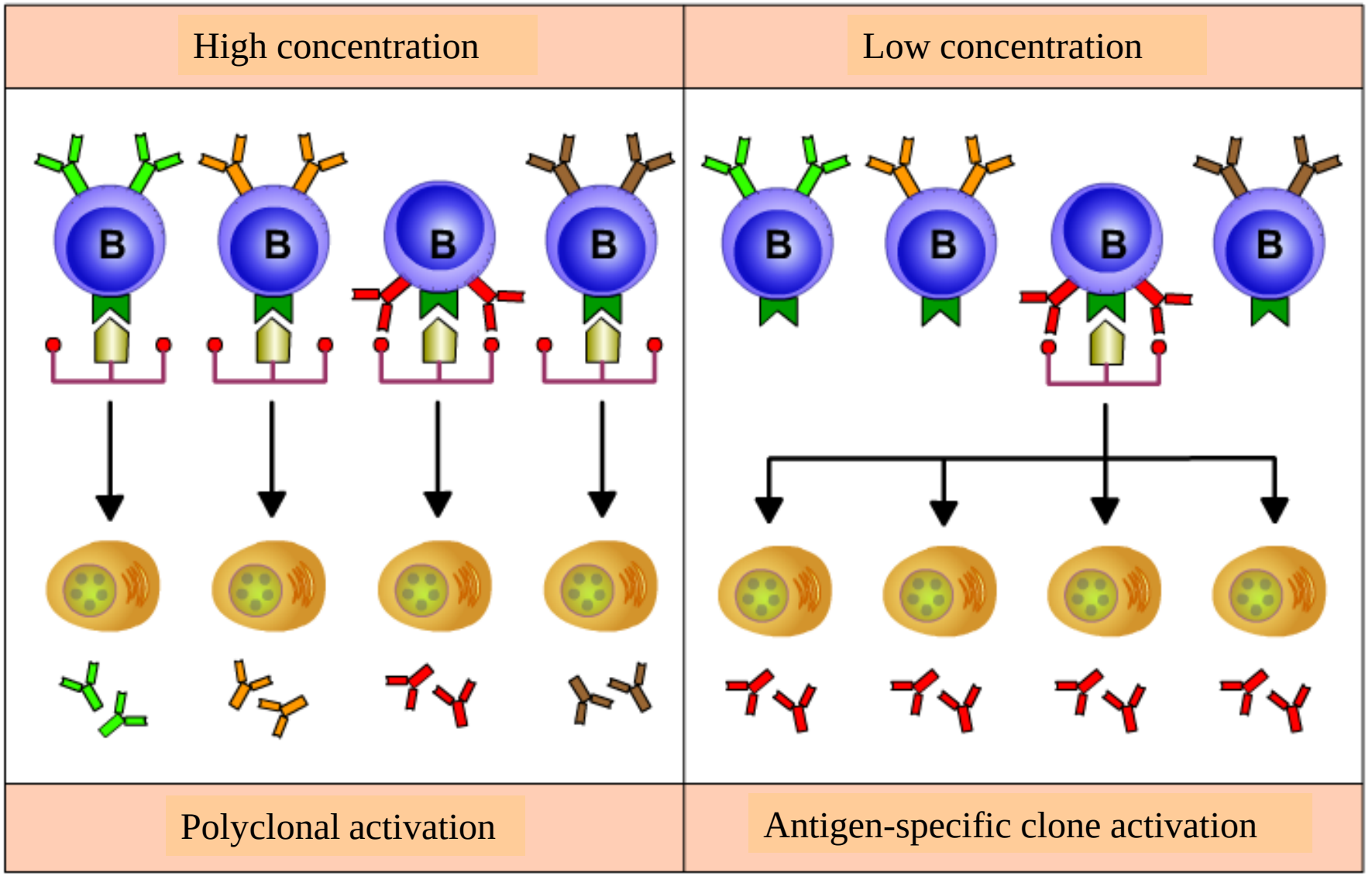
Chapter 2 B cell response to T cell-independent antigens

Most TI-1 antigens:

are polyclonal B-cell activators **(mitogens);** that is, they are able to activate B cells regardless of their antigenic specificity.

At high concentrations, some TI-1 antigens will stimulate proliferation and antibody secretion by as many as one third of all B cells. The mechanism by which TI-1 antigens activate B cells is not understood well.

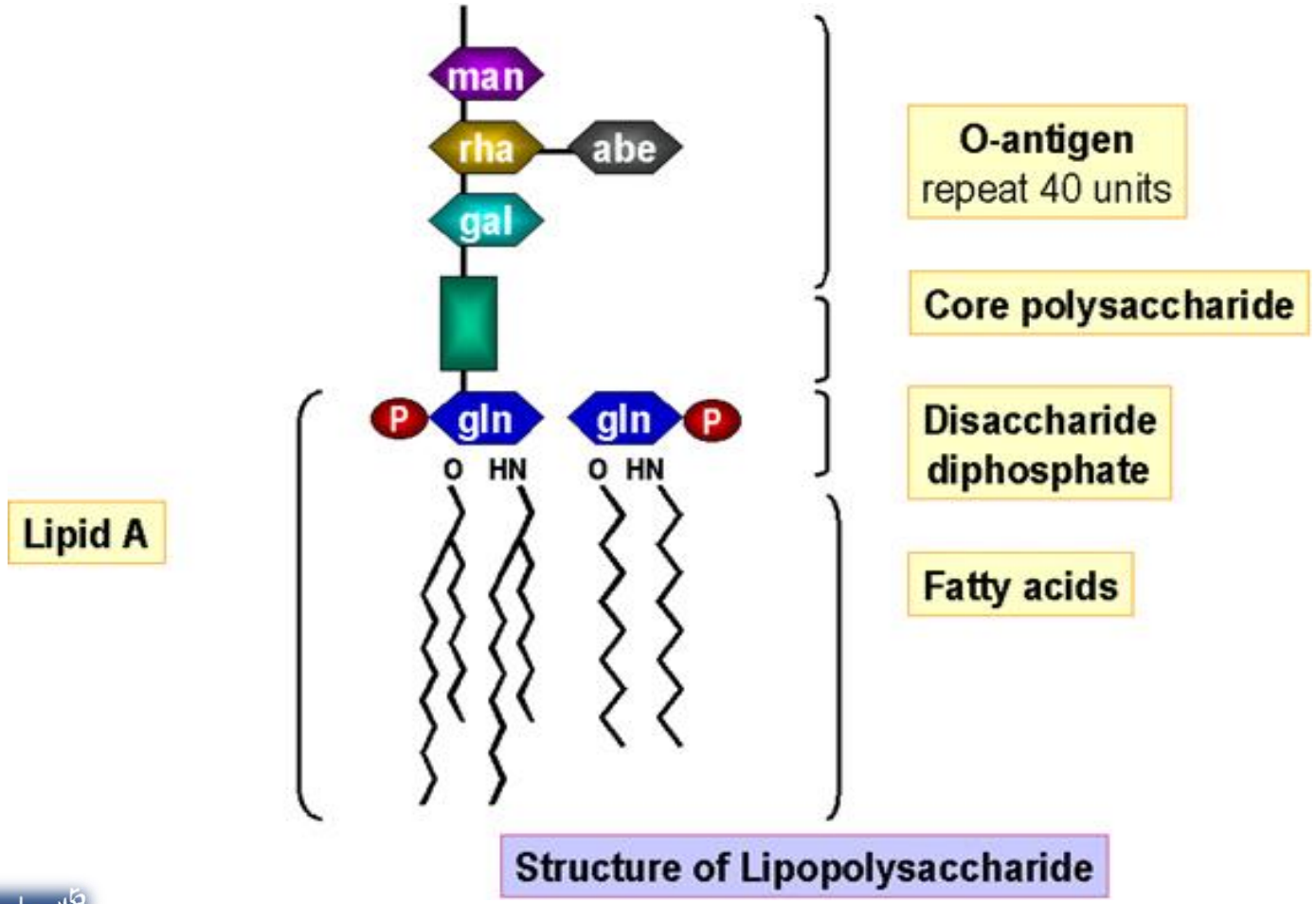
At lower concentrations of TI-1 antigens, only those B cells specific for epitopes of the antigen will be activated. These antigens can stimulate antibody production in nude mice (which lack a thymus and T cells).



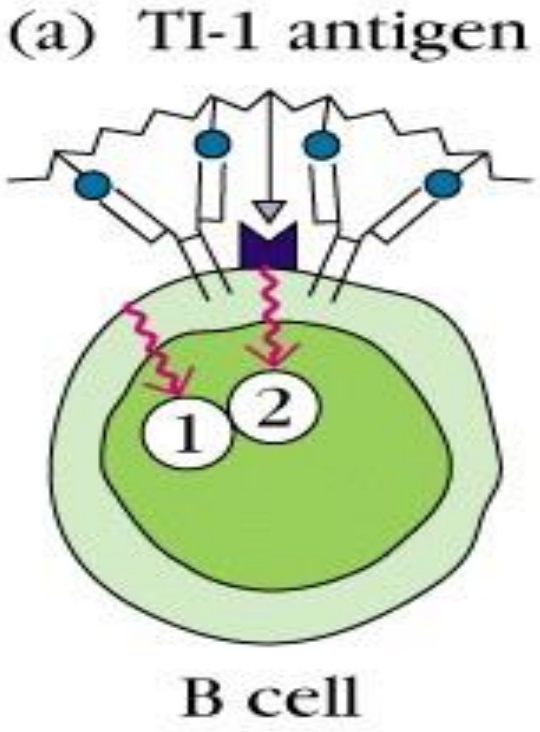
Activation of B1 cells stimulated by TI-1 antigen

Immunology

脂多糖(lipopolysaccharid,LPS)



Structure of Lipopolysaccharide



The prototypic TI-1 antigen is **lipopolysaccharide (LPS),** a major component of the cell walls of gram-negative bacteria.

At low concentrations, LPS stimulates the production of antibodies specific for LPS.

At high concentrations, it is a polyclonal B-cell activator.

TI-2 antigens :

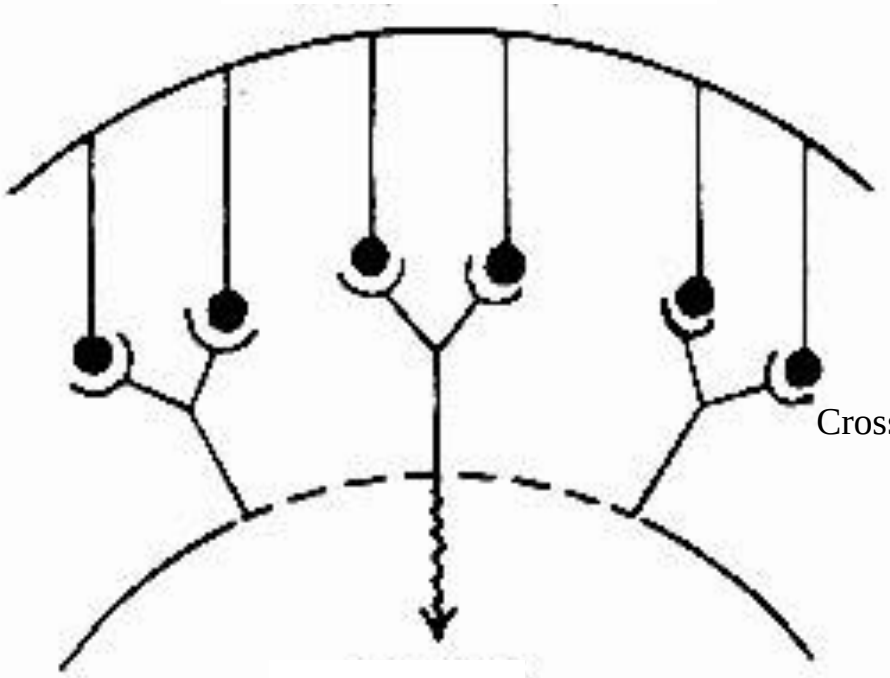
activate B cells by extensively crosslinking the mIg receptor. However, TI-2 antigens differ from TI-1antigens in three important respects:

--First, they are not B-cell mitogens and so do not act as polyclonal activators.

--Second, TI-1 antigens will activate both mature and immature B cells, but TI-2 antigens activate mature B cells and inactivate immature B cells.

--Third, although the B-cell response to TI-2 antigens does not require direct involvement of T cells, cytokines derived from T cells are required for efficient B-cell proliferation and for class switching to isotypes other than IgM.

TI-2 antigen



Cross-link numerous BCR molecules

B1 cell

TI-2 antigen posses highly repetitive epitopes

TABLE 11-2 PROPERTIES OF THYMUS-DEPENDENT AND THYMUS-INDEPENDENT ANTIGENS

Property	TD antigens	TI antigens	
		Type 1	Type 2
Chemical nature	Soluble protein	Bacterial cell-wall components (e.g., LPS)	Polymeric protein antigens; capsular polysaccharides
Humoral response			
Isotype switching	Yes	No	Limited
Affinity maturation	Yes	No	No
Immunologic memory	Yes	No	No
Polyclonal activation	No	Yes (high doses)	No

The response to TI antigens is generally weaker, no memory cells are formed, and IgM is the predominant antibody secreted, reflecting a low level of class switching.

These differences highlight the important role played by TH cells in generating memory B cells, affinity maturation, and class switching to other isotypes.

Chapter 3 rules of antibody production

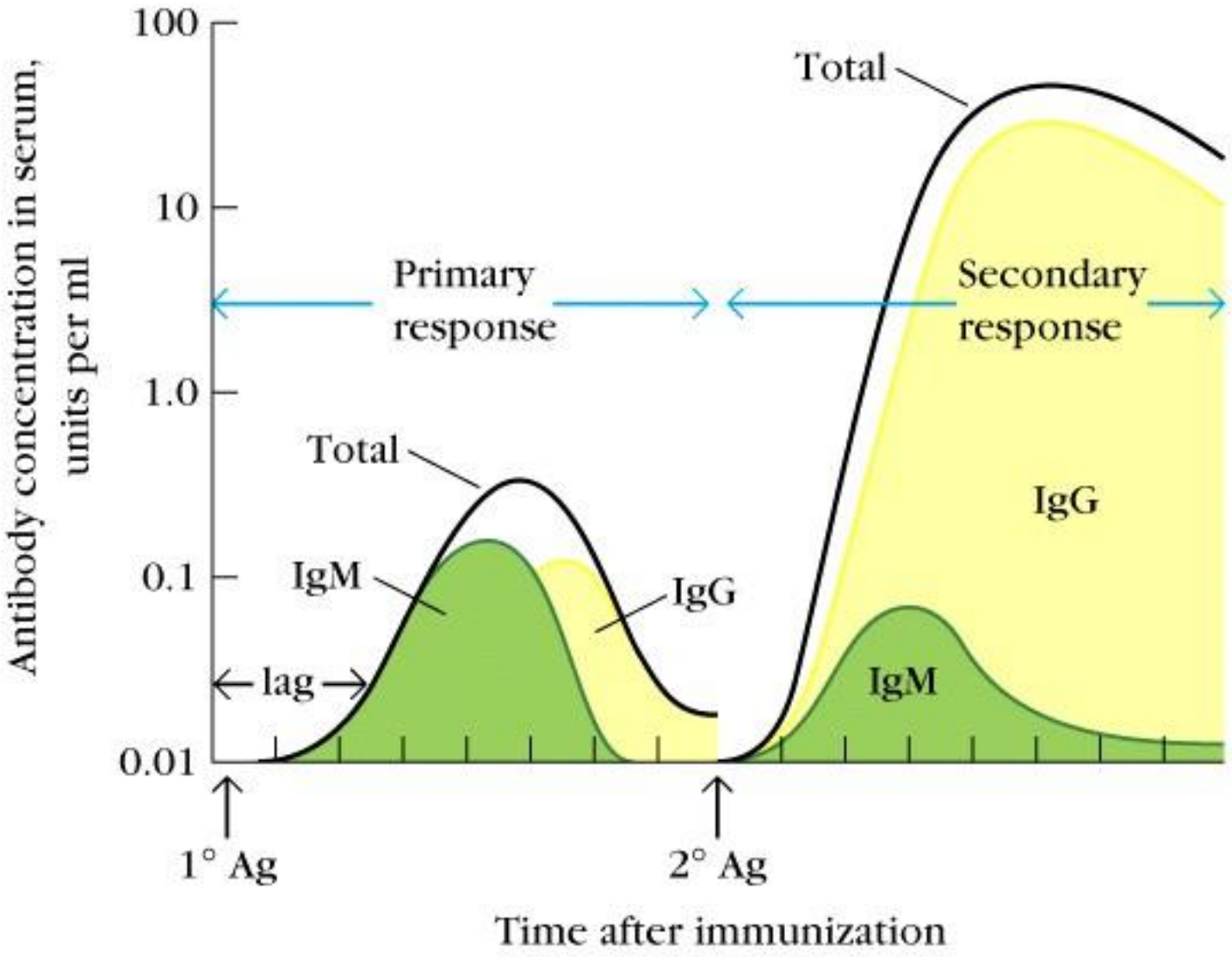

100
10
1.0
0.1
0.01
Antibody concentration in serum, units per ml
Total
Primary response
Secondary response
Total
IgG
IgM
IgG
lag
IgM
1° Ag
2° Ag
Time after immunization

TABLE 11-4 COMPARISON OF PRIMARY AND SECONDARY ANTIBODY RESPONSES

Property	Primary response	Secondary response
Responding B cell	Naive (virgin) B cell	Memory B cell
Lag period following antigen administration	Generally 4–7 days	Generally 1–3 days
Time of peak response	7–10 days	3–5 days
Magnitude of peak antibody response	Varies depending on antigen	Generally 100–1000 times higher primary response
Isotype produced	IgM predominates early in the response	IgG predominates
Antigens	Thymus-dependent and thymus-independent	Thymus-dependent
Antibody affinity	Lower	Higher