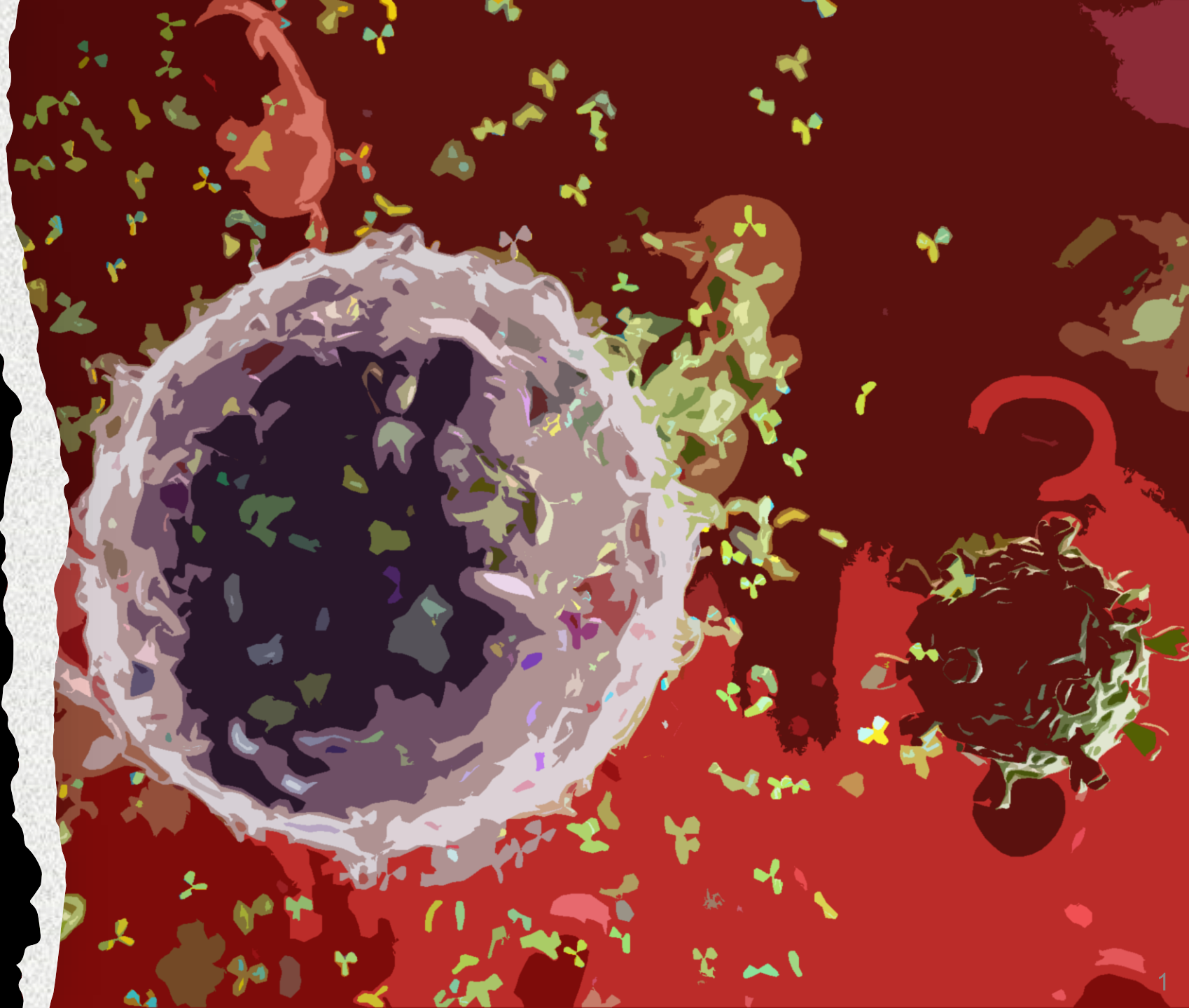
MD627 707
Essential Immunology

ADAPTIVE IMMUNITY



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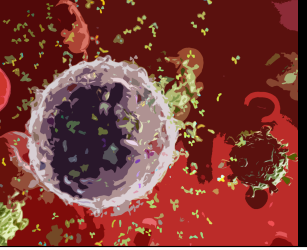
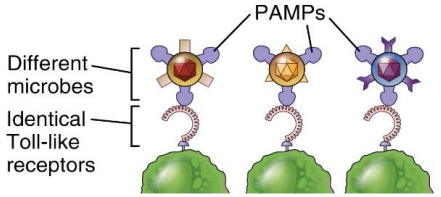
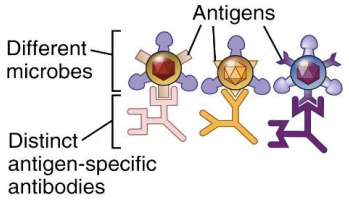
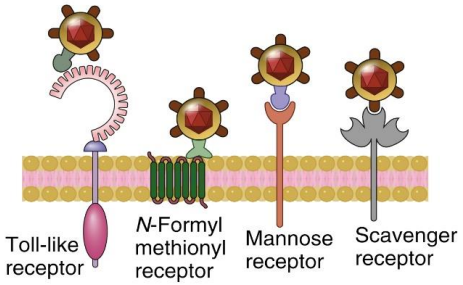
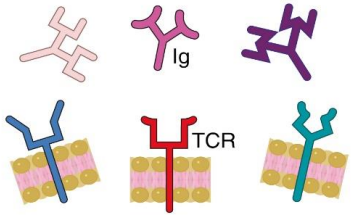
Faculty of Medicine, Khon Kaen University



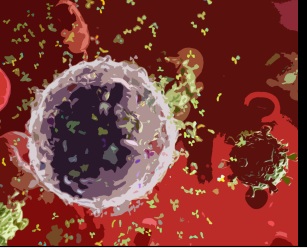
RECAP

Feature	Innate immunity	Adaptive immunity
Specificity	For structures shared by classes of microbes (pathogen-associated molecular patterns) 	For structural detail of microbial molecules (antigens); may recognize nonmicrobial antigens 
Number of microbial molecules recognized	About 1000 molecular patterns (estimated)	$>10^7$ antigens
Receptors	Encoded in germline; limited diversity (pattern recognition receptors) 	Encoded by genes produced by somatic recombination of gene segments; greater diversity 
Number and types of receptors	<100 different types of invariant receptors	Only 2 types of receptors (Ig and TCR), with millions of variations of each
Distribution of receptors	Nonclonal: Identical receptors on all cells of the same lineage	Clonal: clones of lymphocytes with distinct specificities express different receptors
Genes encoding receptors	Germline encoded, in all cells	Formed by somatic recombination of gene segments only in B and T cells
Discrimination of self and nonself	Yes; healthy host cells are not recognized or they may express molecules that prevent innate immune reactions	Yes; based on elimination or inactivation of self-reactive lymphocytes; may be imperfect (hence the possibility of autoimmunity)

Clonal….

- **(high) specificity**
- **diversity**
- improve themselves from time to time

MEMORY



RECAP

I. Cell-mediated immune response (CMIR) => using cell to action

- Elimination of extracellular pathogens mediate with T helper (CD3+CD4+) cells

Enhancement of immunity using cytokine

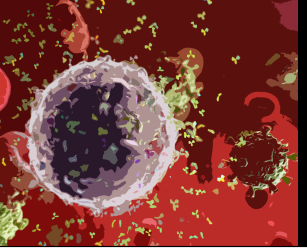
- Elimination of intracellular pathogens and tumor cell mediate with T cytotoxic (CD3+CD8+) cells

Specifically attack cells with abnormal Ag on the surface

II. Humoral immune response (HIR)

- Elimination of extracellular pathogens, toxins, virus mediate with B cells (CD19+) cells and plasma cells producing antibodies

All about antibody



RECAP

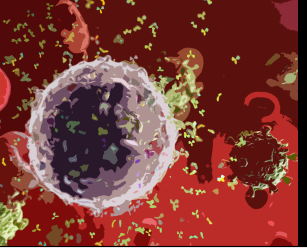
Enhancement of overall bacterial killing (esp. intracellular bacteria)

Enhancement of defense against parasite & wound healing

Recruiting neutrophils & increased barrier function (esp GI tract)

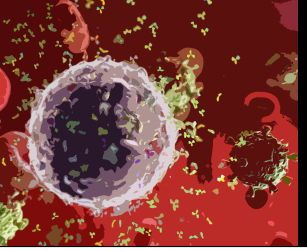
Enhancement of B-cell development (esp T-dependent antibody pathway)

Effector T cells	Defining cytokines	Principal target cells	Major immune reactions	Host defense
Th1	IFN-γ	Macrophages	**Classical** Macrophage activation	Intracellular pathogens
Th2	IL-4 IL-5 IL-13	Eosinophils	Eosinophil and mast cell activation; ~~alternative~~ macrophage activation	Helminths
Th17	IL-17 IL-22	Neutrophils	Neutrophil recruitment and activation	Extracellular bacteria and fungi
Tfh	IL-21 (and IFN-γ or IL-4)	B cells	Antibody production	Extracellular pathogens

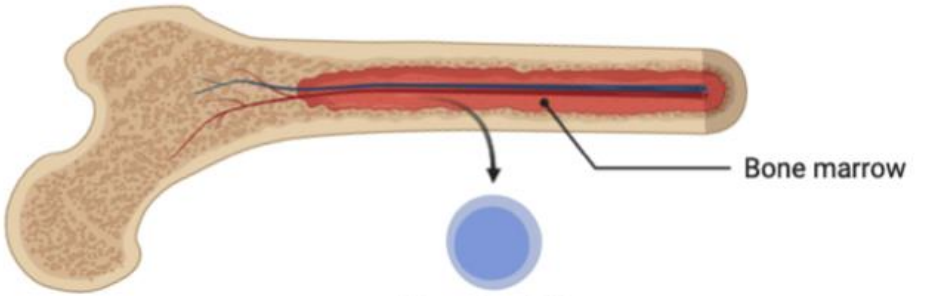


OBJECTIVES

1. Production and maturation of adaptive immunity
2. Activation of T-cell and its effector functions
3. Activation of B-cell and its effector functions
4. Selection and affinity maturation of B-cell
5. Phase of exposure



PRODUCTION



Hematopoietic stem cell

Myeloid progenitor cell

Lymphoid progenitor cell

Megakaryocyte

Eosinophil

Basophil

Erythrocytes

Monocyte

Neutrophil

T cell

B cell

NK cell

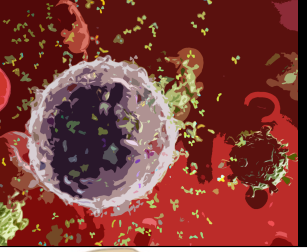
Platelets

Dendritic cell

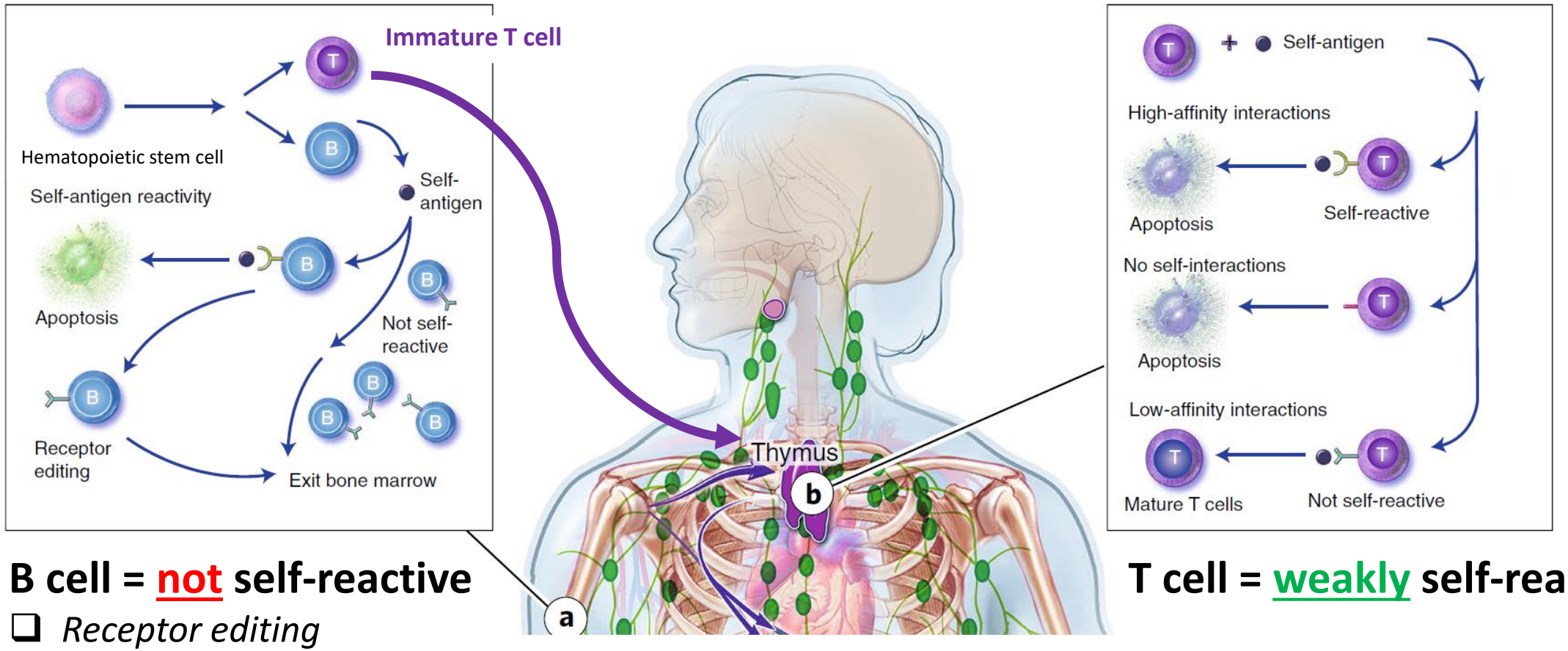
Macrophage

Plasma cell

+ Innate lymphoid cells (ILCs)



MATURATION



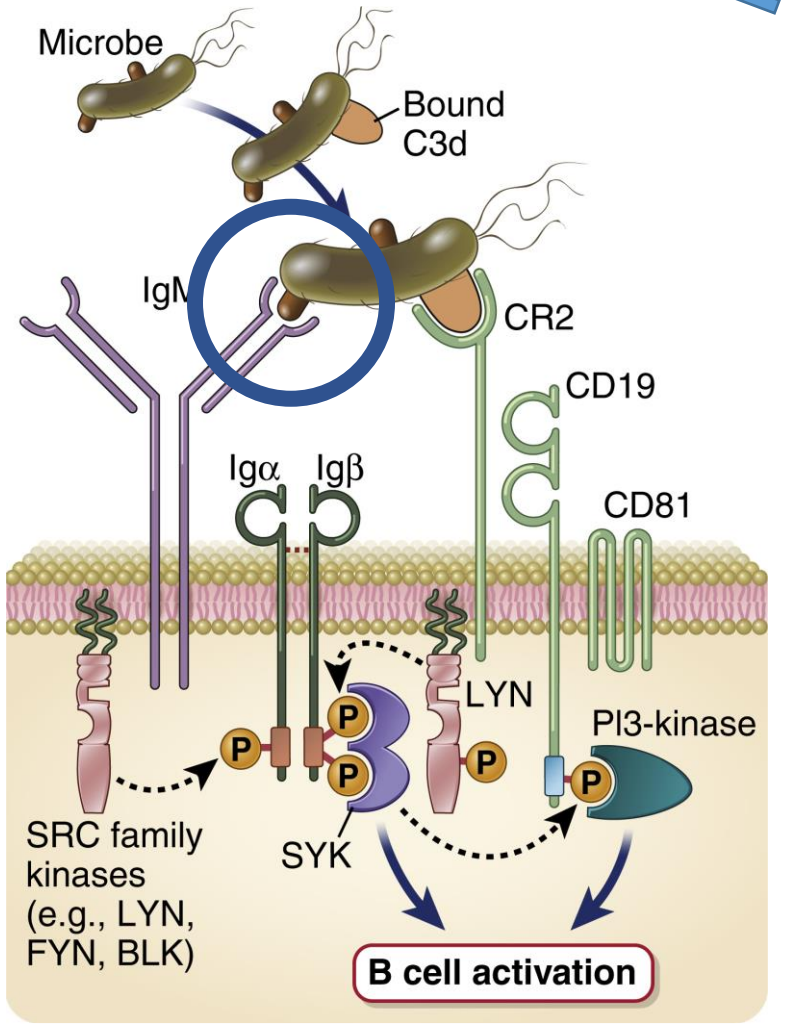
B cell = not self-reactive

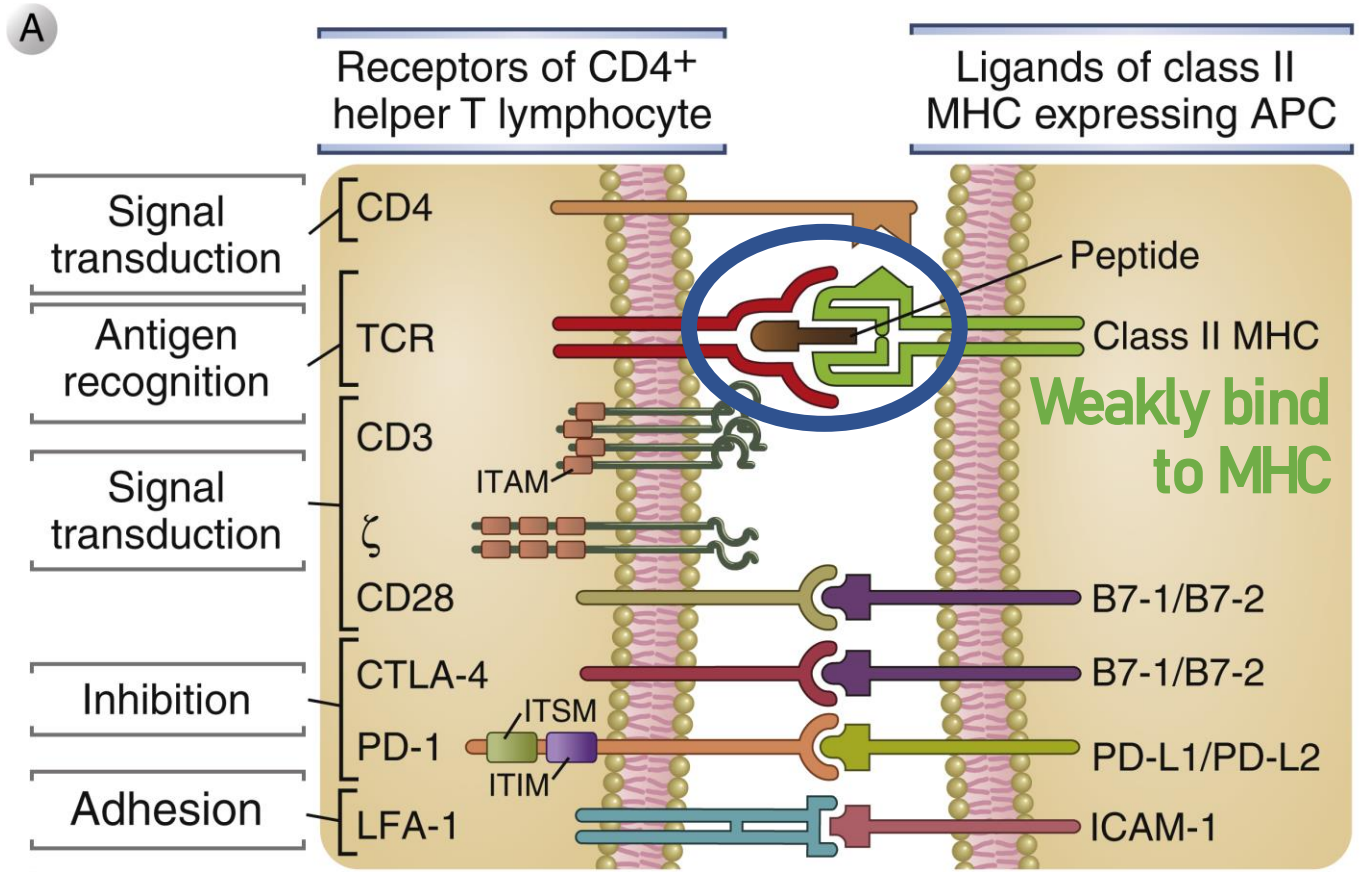
- ❑ *Receptor editing*
- ❑ *Negative selection*

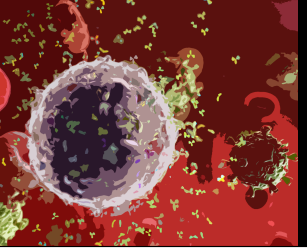
T cell = weakly self-reactive

PRODUCTION

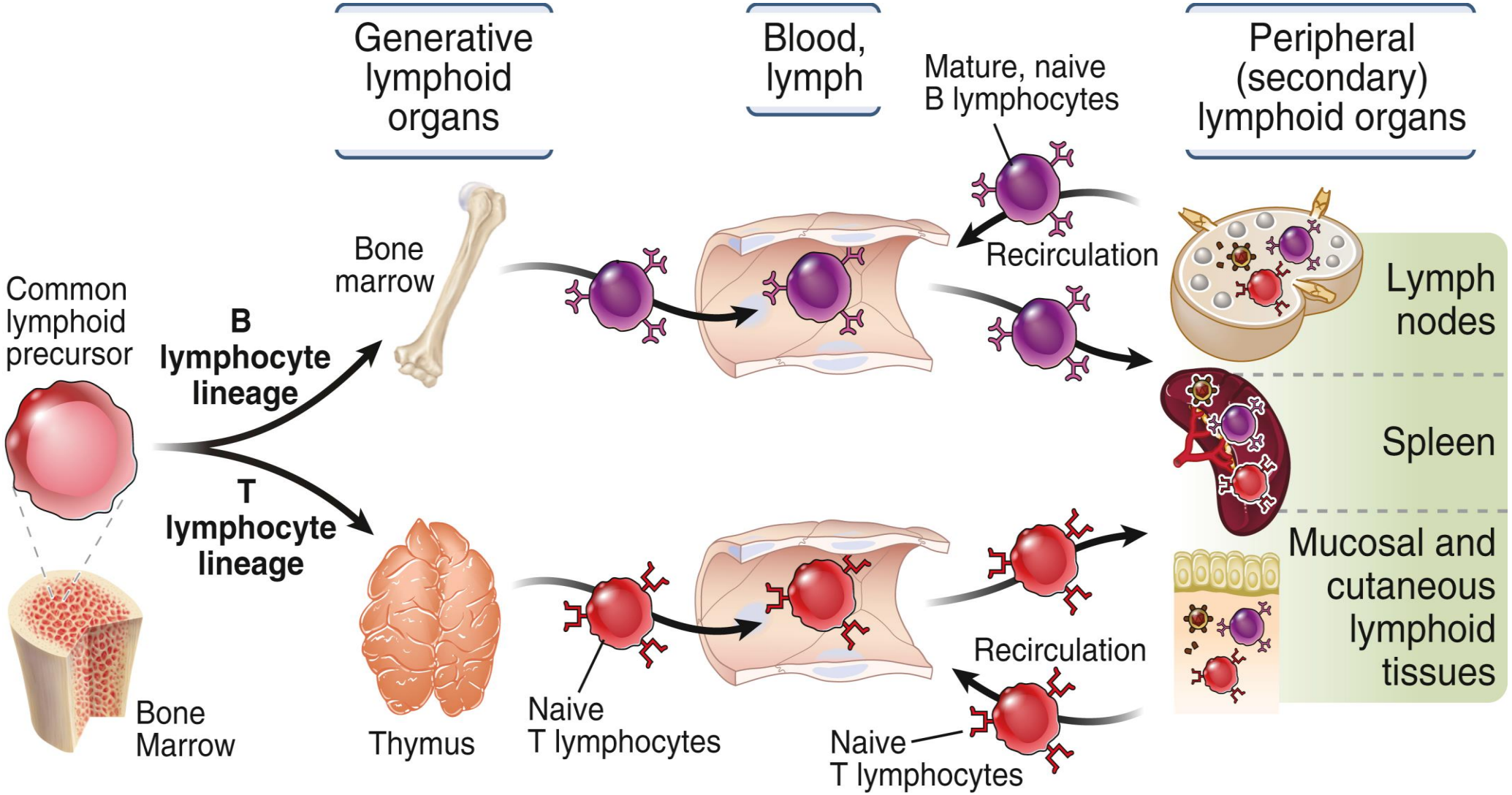
B-cell receptor (BCR) ← Bind to non-self antigen → T-cell receptor (TCR)

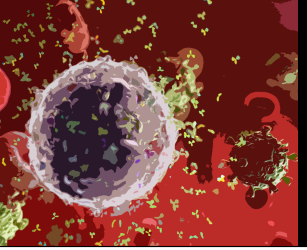






IMMUNE CELL PRODUCTION





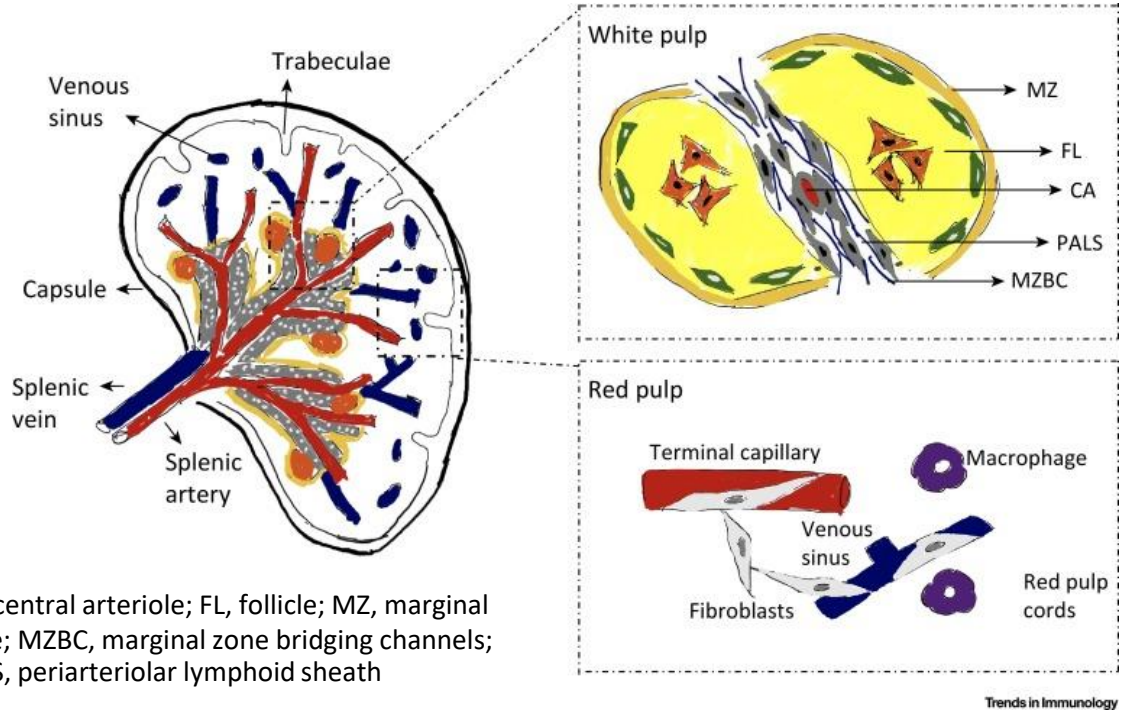
IMMUNE CELL PRODUCTION

Generative / primary / central lymphoid organs

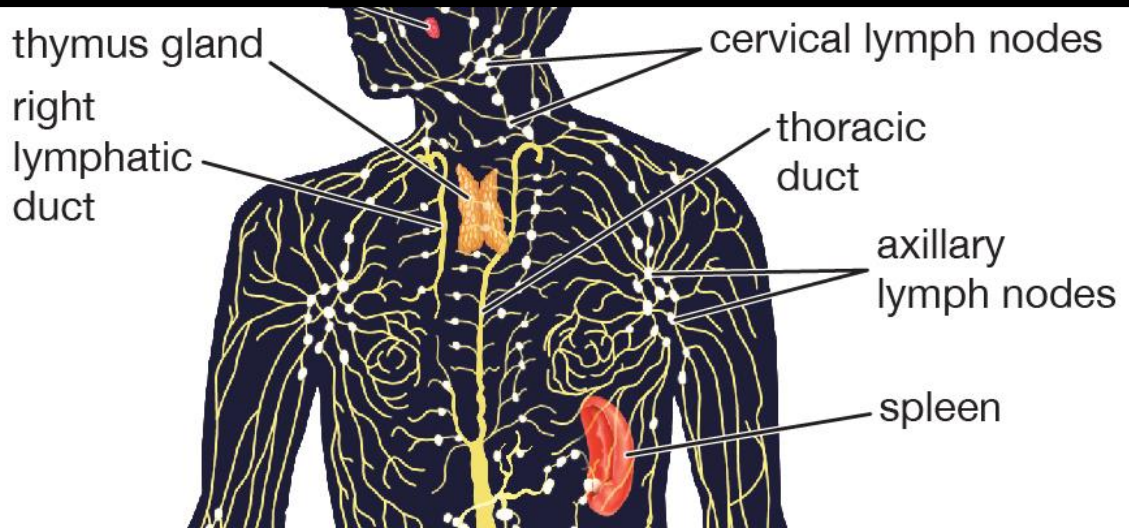
- Creation and maturation
  - B cells = Bone marrow
  - T cells = Bone marrow and thymus

Peripheral / secondary lymphoid organs

- Activation and development
  - Spleen (main filter for blood-borne pathogens)

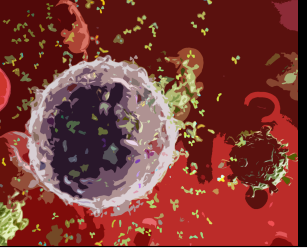


CA, central arteriole; FL, follicle; MZ, marginal zone; MZBC, marginal zone bridging channels; PALS, periarteriolar lymphoid sheath



a region **supporting adaptive immune responses** and consisting of distinct T and B cell compartments

contains macrophages and erythrocytes and plays a major role in **surveillance of blood-borne pathogens**, elimination of old erythrocytes, and iron recycling



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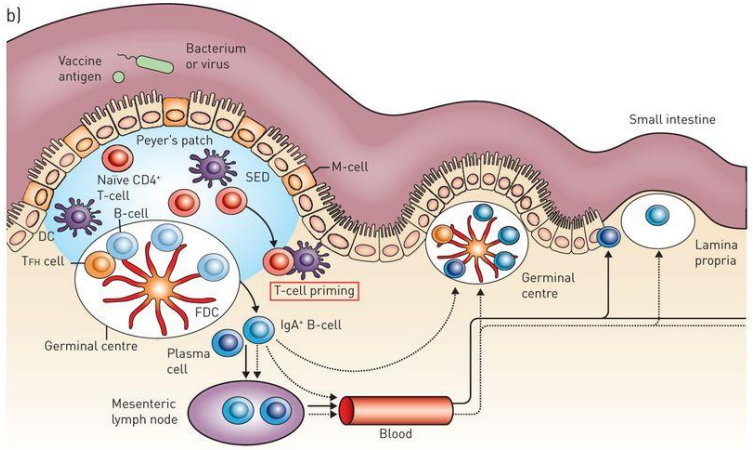
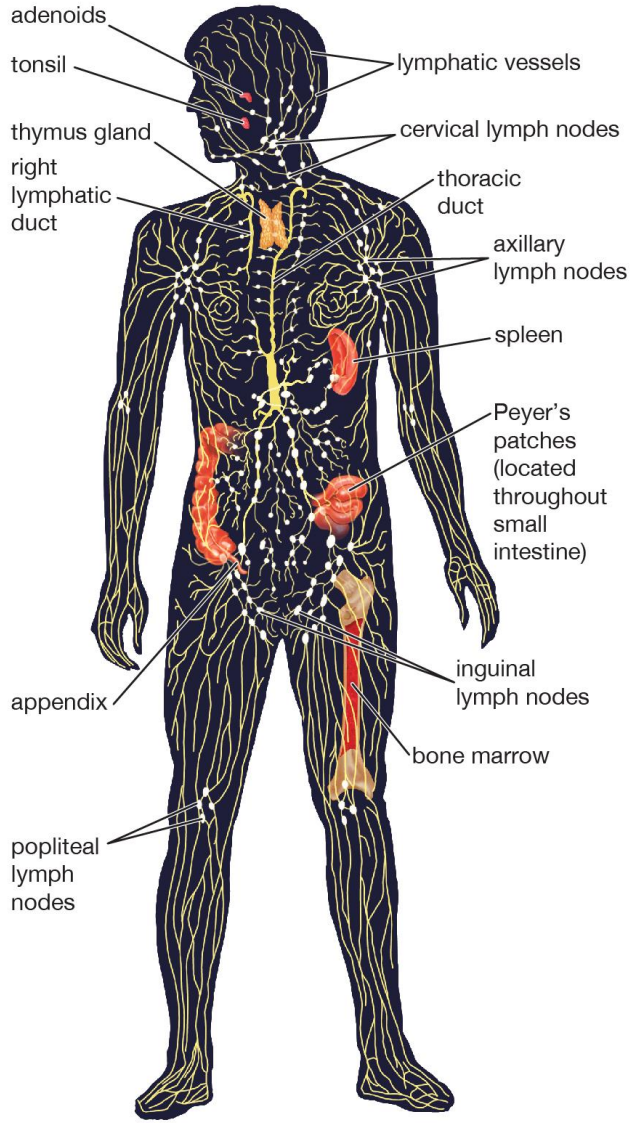
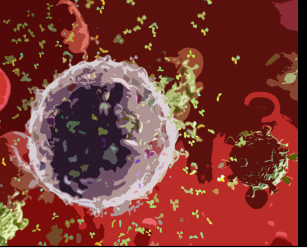
Peripheral / secondary lymphoid organs

- Activation and development
  - Spleen (main filter for blood-borne pathogens)
  - Lymph nodes (Surveillance for cutaneous antigens)
  - Mucosal-associated lymphoid tissue (MALT) in lung
  - Gut-associated lymphoid tissue (GALT) in intestine







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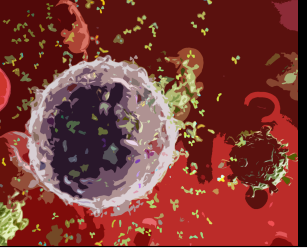
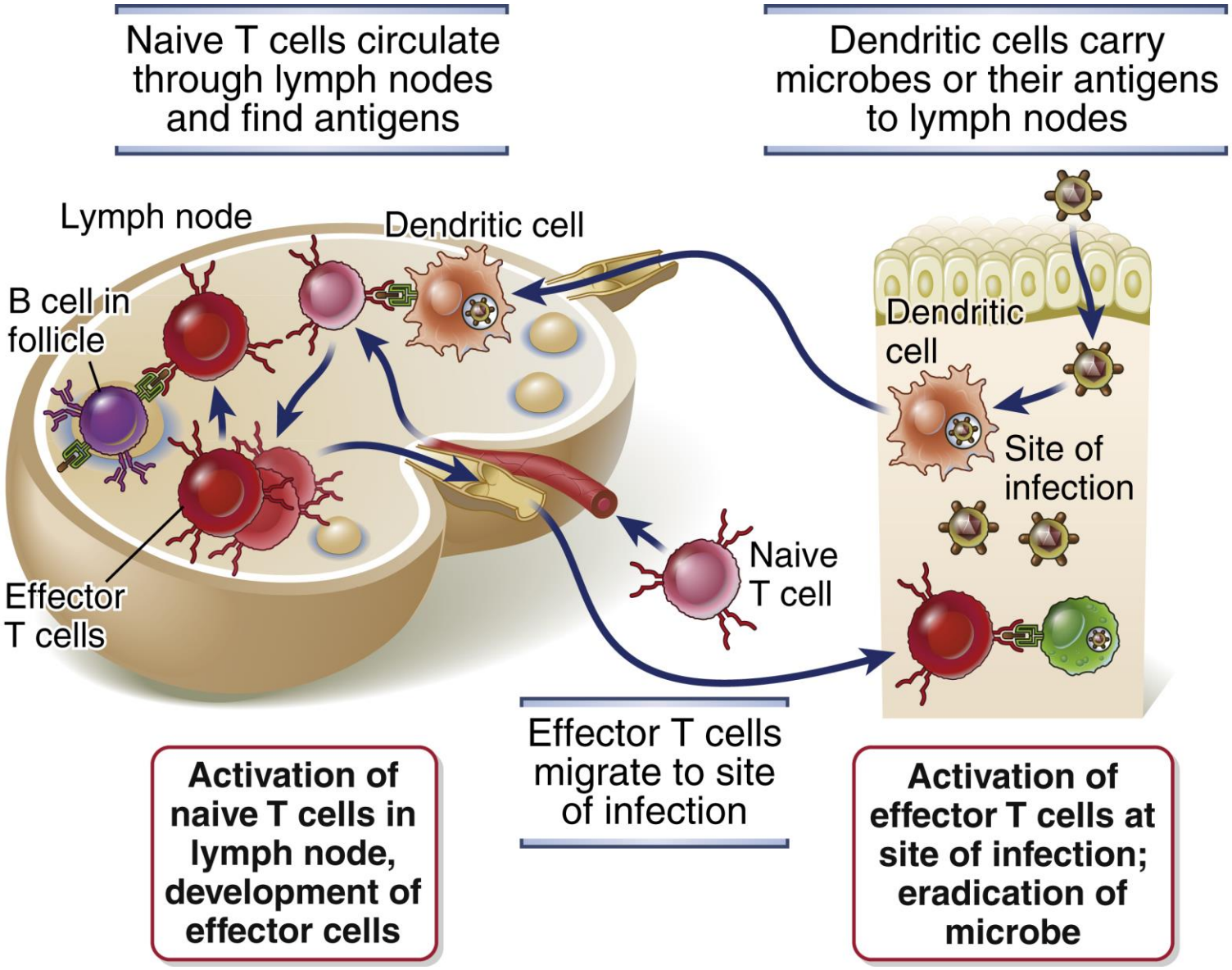


T-CELL ACTIVATION

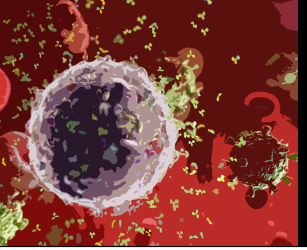


1. Stock naïve T cell in lymph node

2. DC collect antigens and carry to lymph node nearby

3. DC present antigen to naïve T cell and turn to effector T cells

4. Effector T cell move to site of action



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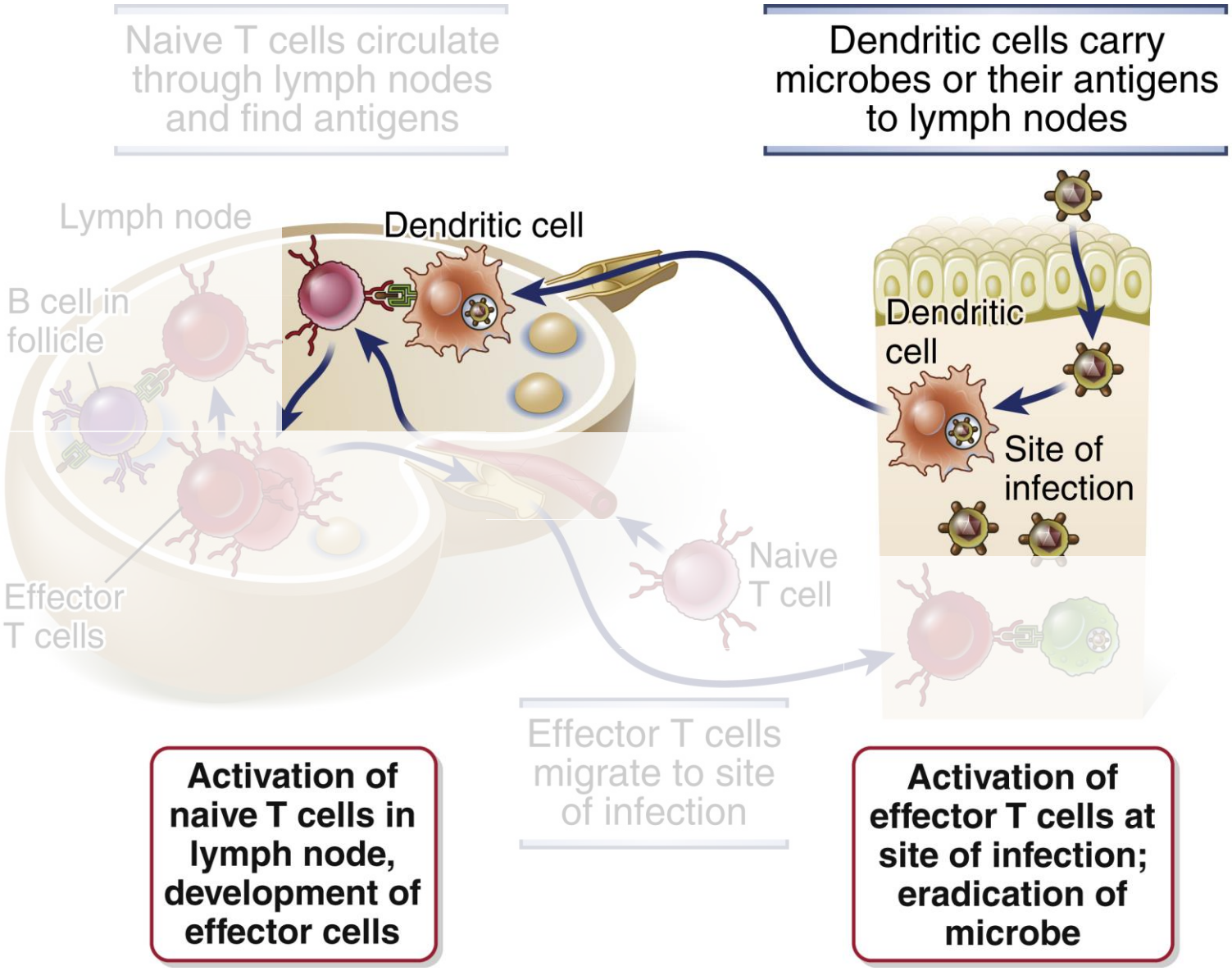

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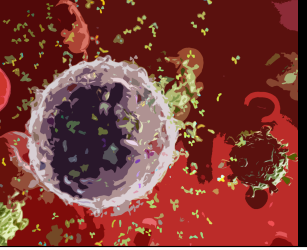
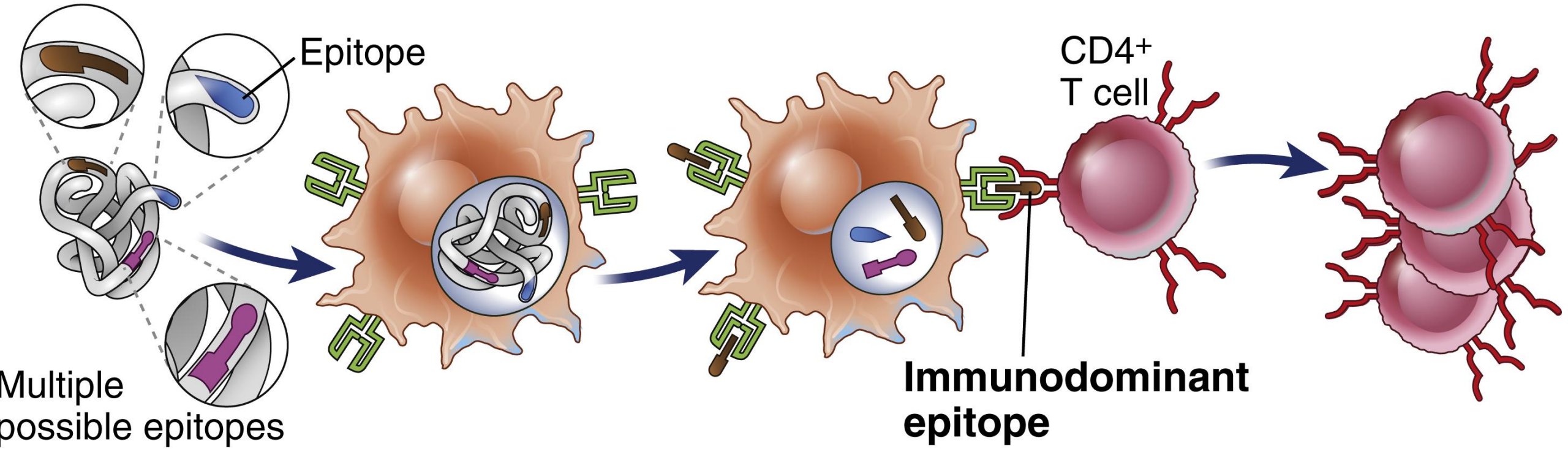


ANTIGEN PRESENTATION

Internalization of antigen into APC	Antigen processing	Processing generates multiple peptides, one of which can bind to class II allele	T cells respond to immunodominant peptide epitope



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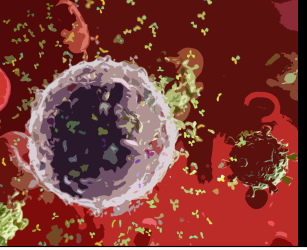

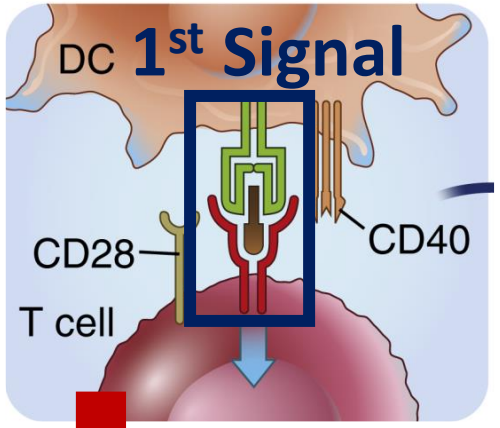

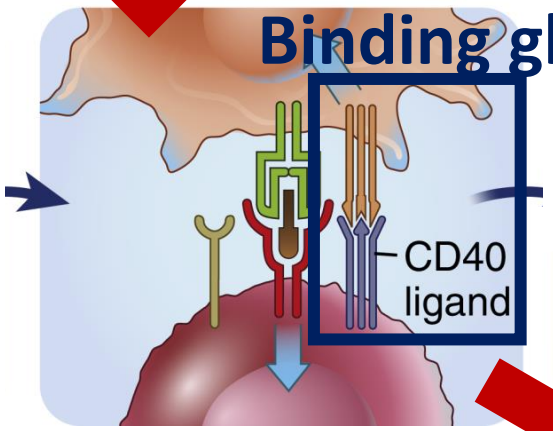

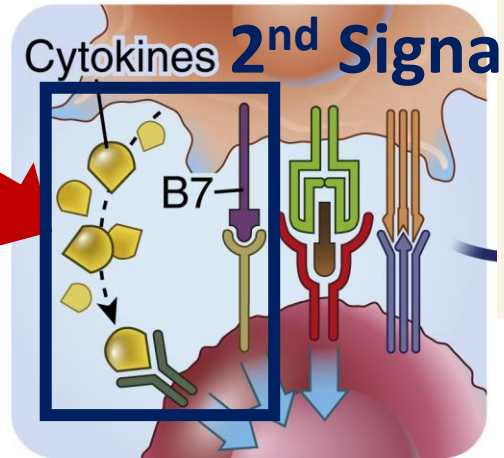

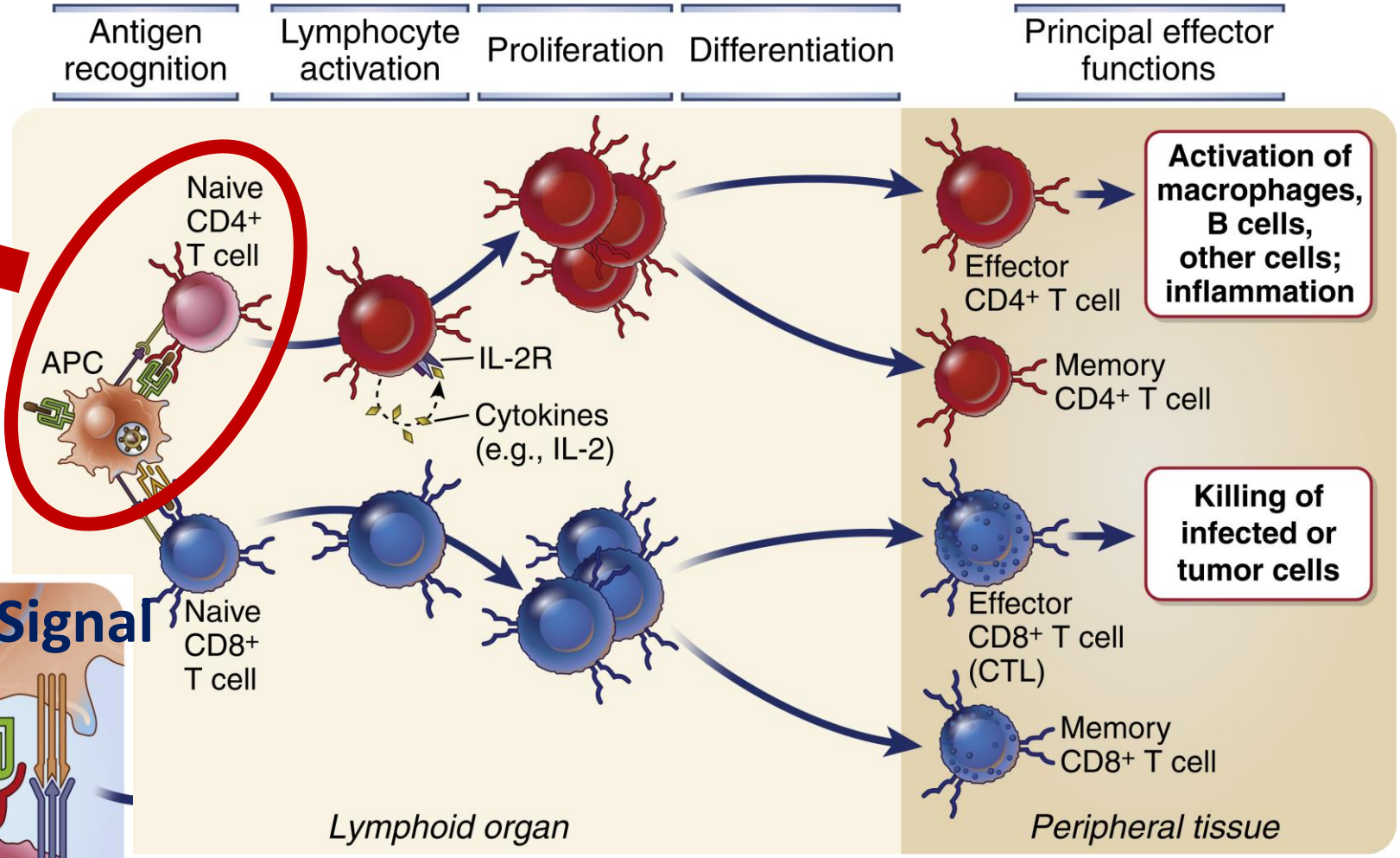

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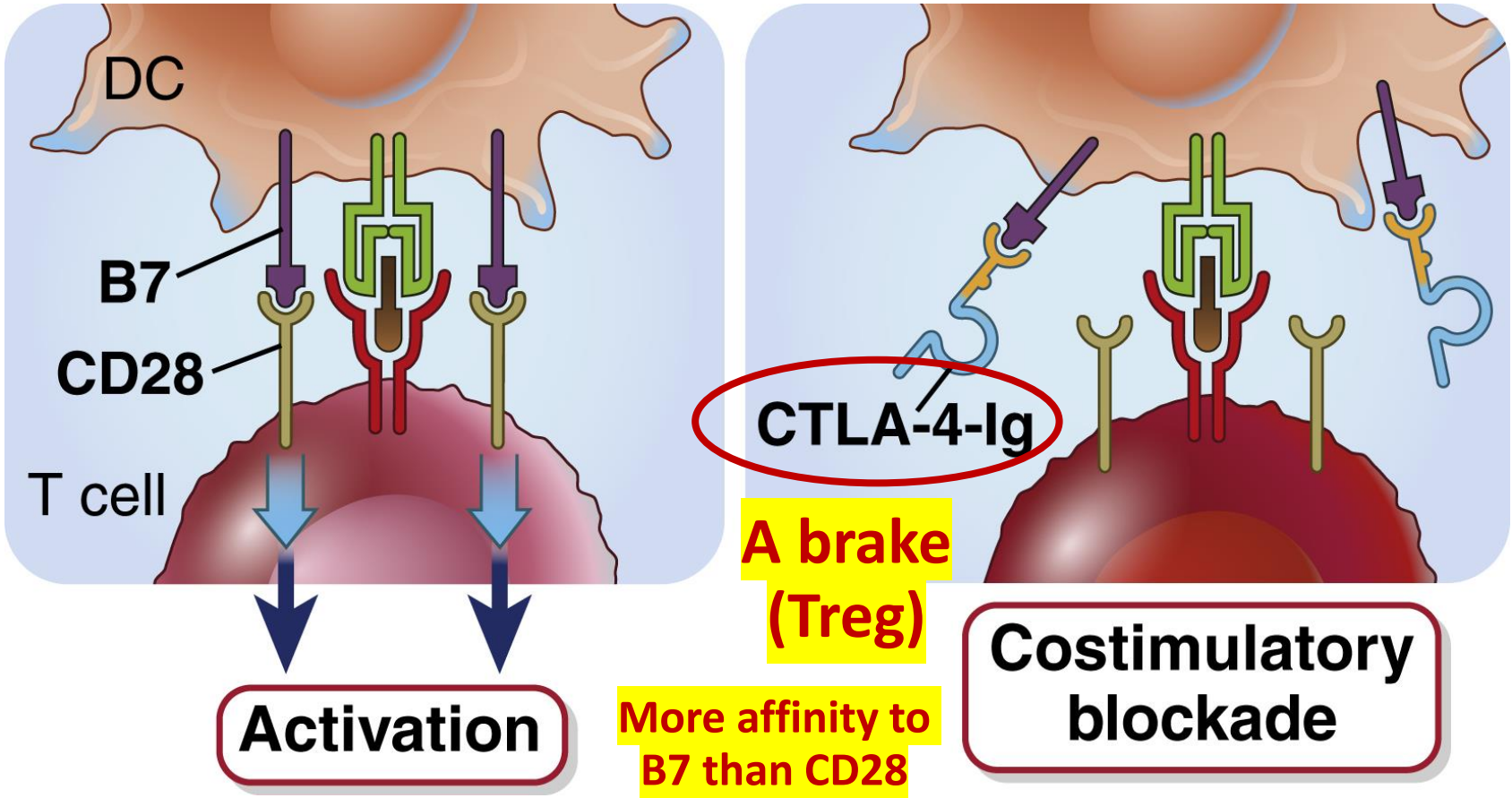
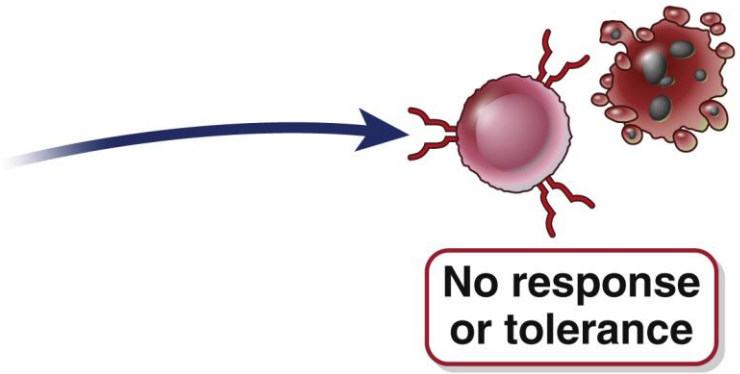
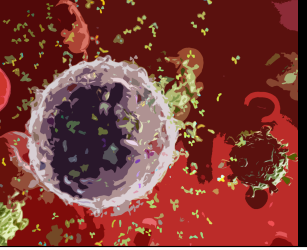


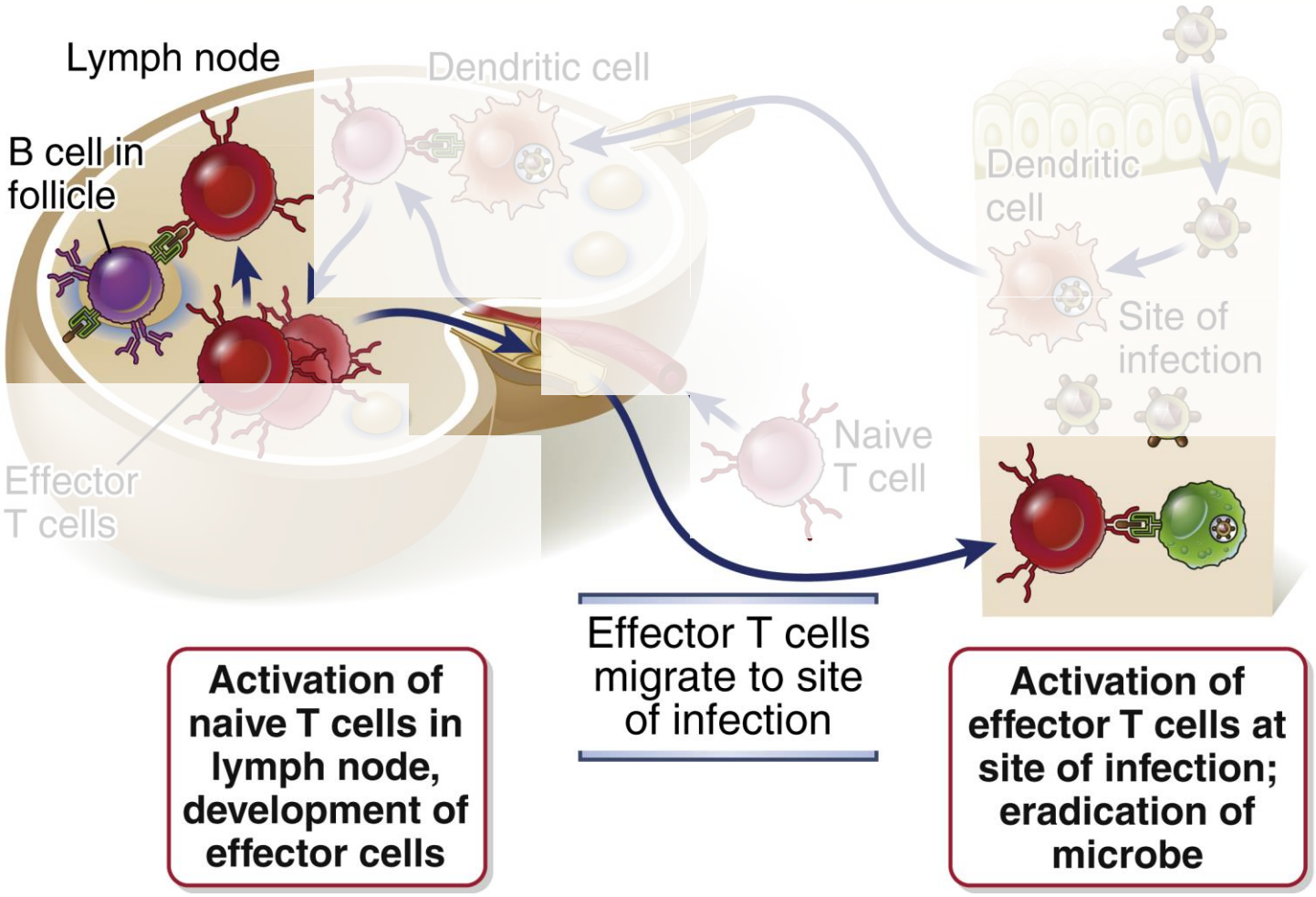
Completed 2 signals from APC are crucial



Anergy



T-CELL ACTIVATION



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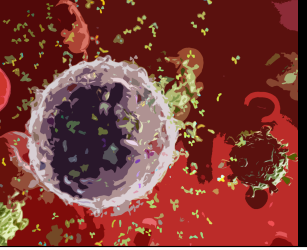
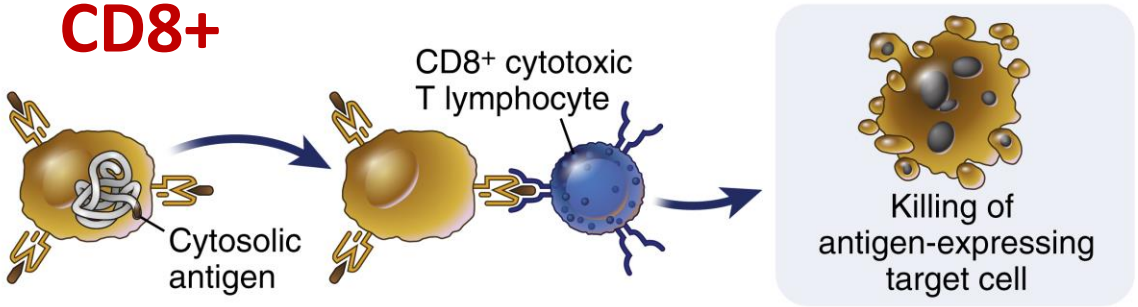


EFFECTOR T-CELLS

Antigen uptake or synthesis | Antigen presentation | T cell effector functions

Class I MHC pathway: antigen presentation to cytotoxic T lymphocytes

CD8+

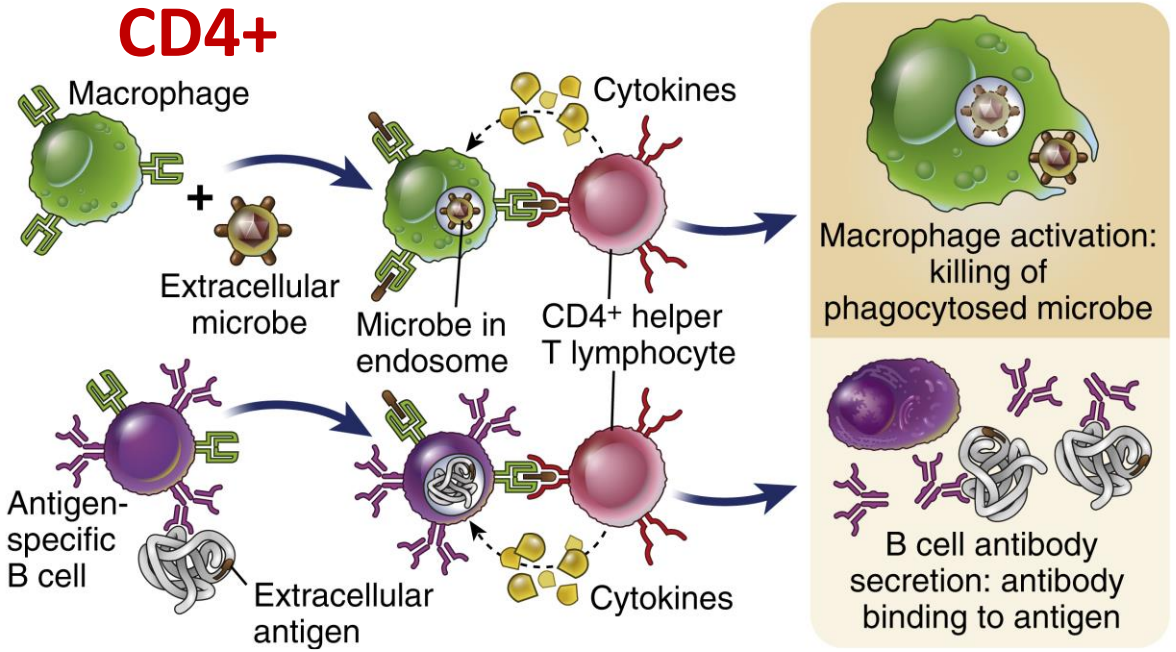


- Intracellular bacterial infection
- Viral infection
- Cancer/tumor

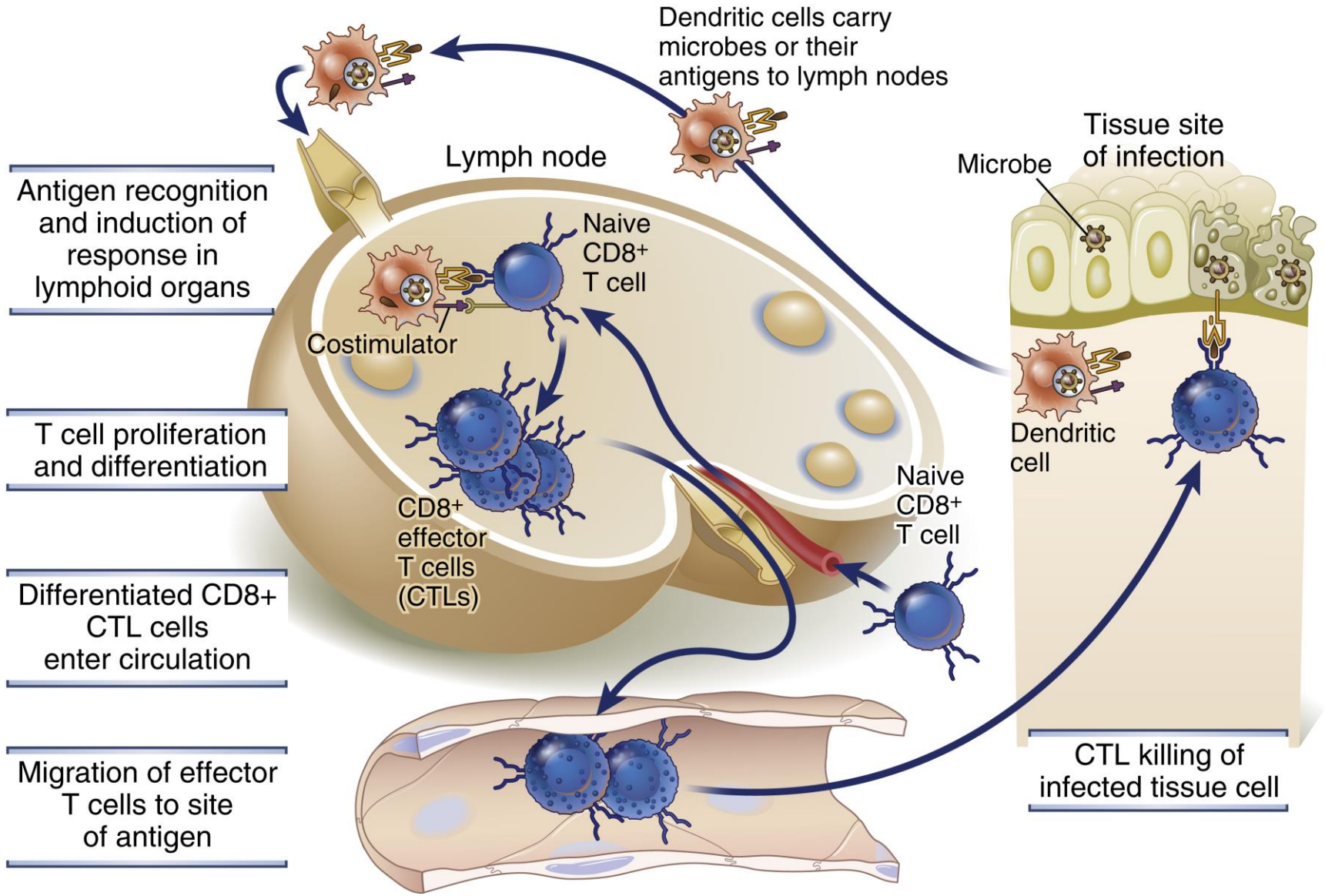
Antigen uptake or synthesis | Antigen presentation | T cell effector functions

Class II MHC pathway: antigen presentation to helper T cells

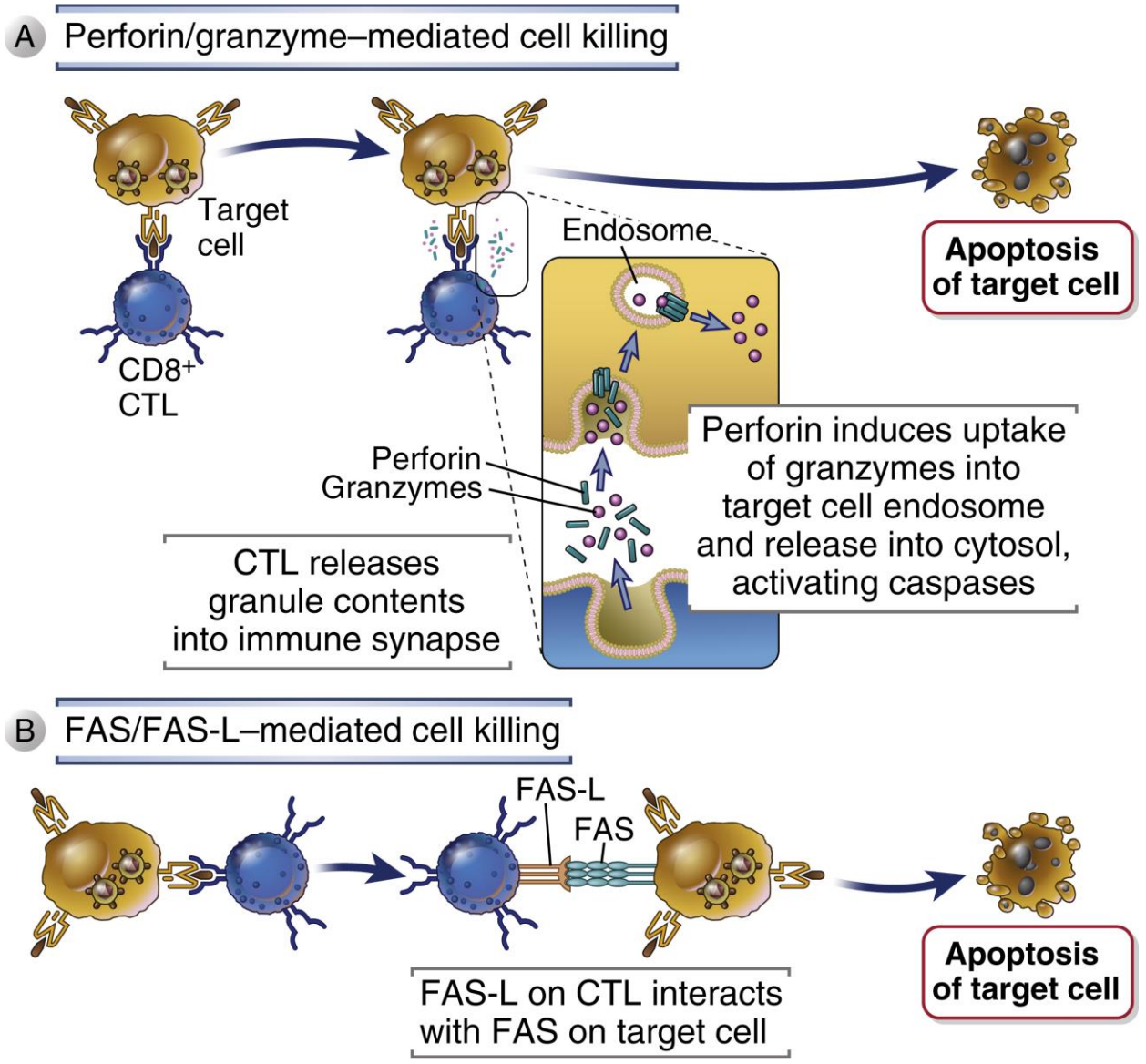
CD4+

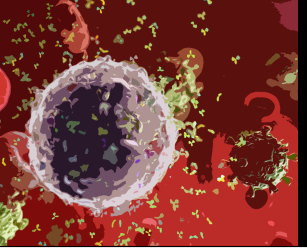


EFFECTOR T-CELLS (CTL)



EFFECTOR T-CELLS (CTL)





T-CELL TAKE HOME MSG.

Bone Marrow

Immature T-cell

Thymus

Mature/Naïve T-cell

Positive selection
- Weakly bind to MHC

Negative selection
- Strongly bind to self antigen

Blood circulation

Naïve/Memory

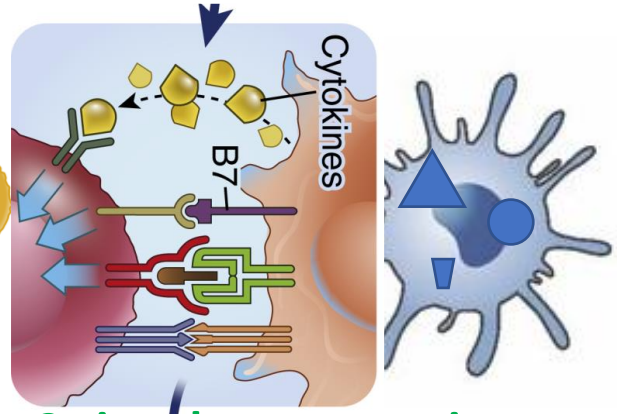
Lymph node/spleen

Memory

Recirculation

CTL
CD8 = MHC I

Th
CD4 = MHC II



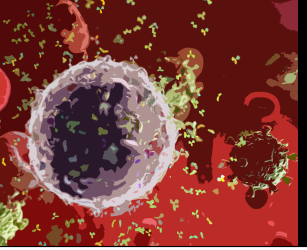
2 signals presentation
1. TCR = Ag on MHC
2. Co-stimulation

Cytokine secretion
Th1 = enhance mac/inflame
Th2 = healing
Th17 = PMN recruitment

Cell mediated killing
Perforin/granzyme
Apoptosis induce

Infected Tissue


TAKE A BREAK
WITH Q&A



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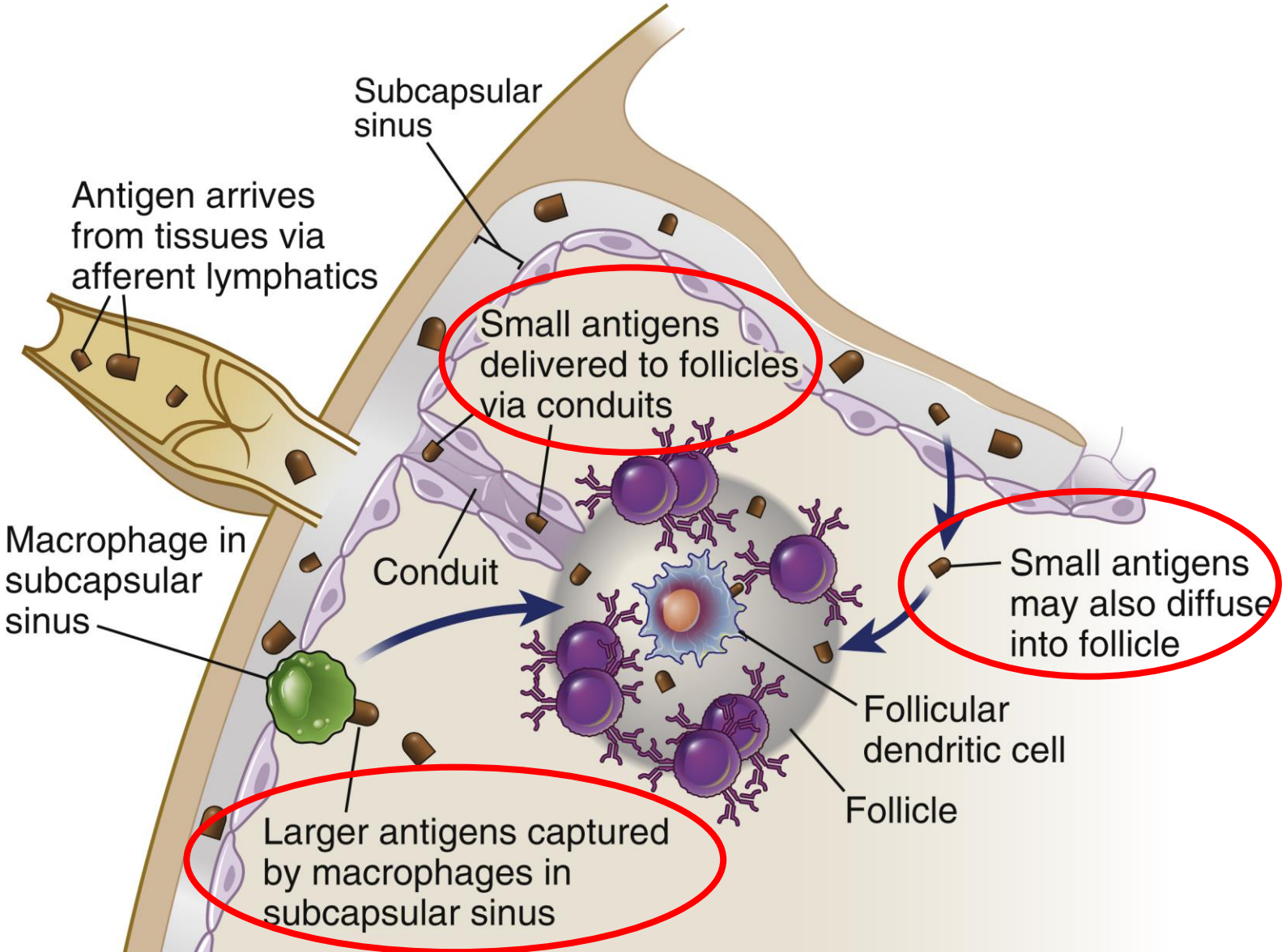
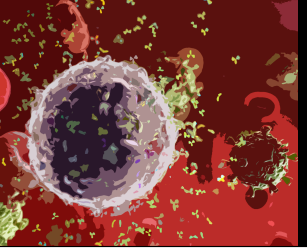
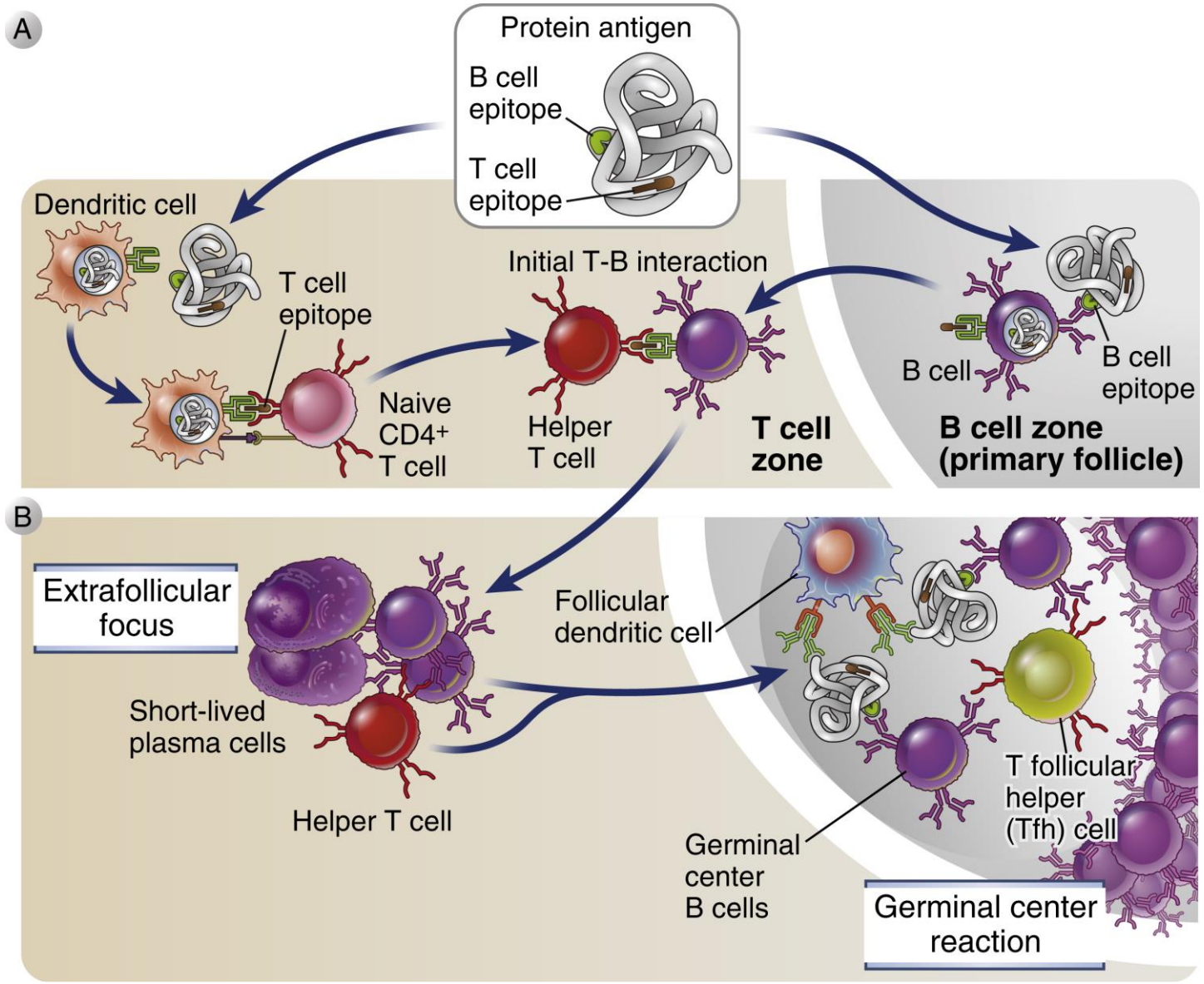
5. Phase of exposure

ANTIGEN DELIVERY

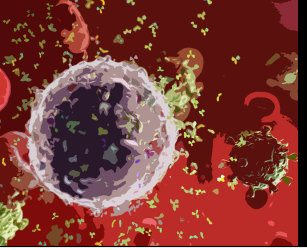




B-CELL ACTIVATION



1. Antigen recognition and process
2. Antigen presentation to activated T helper cell
3. B cell proliferation and development to **short-lived plasma cells** with **isotype switching**
4. Activated T helper and activated B cells move to follicle to form **germinal center (GC)** and initiate **affinity maturation**, additional **isotype switching**, **memory B cell** generation, and generation of **long-lived plasma cells**



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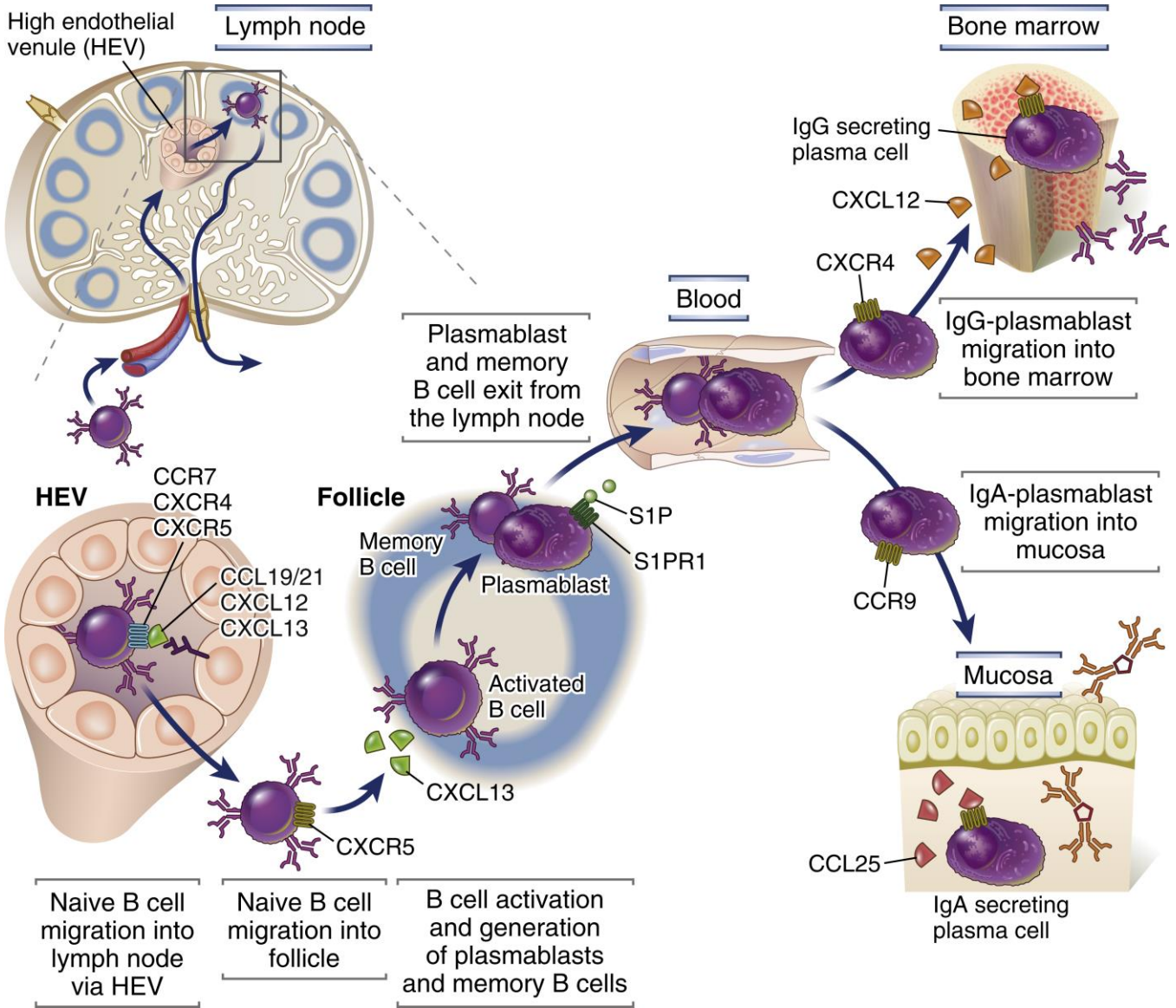

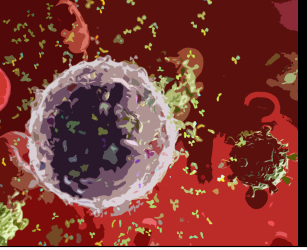

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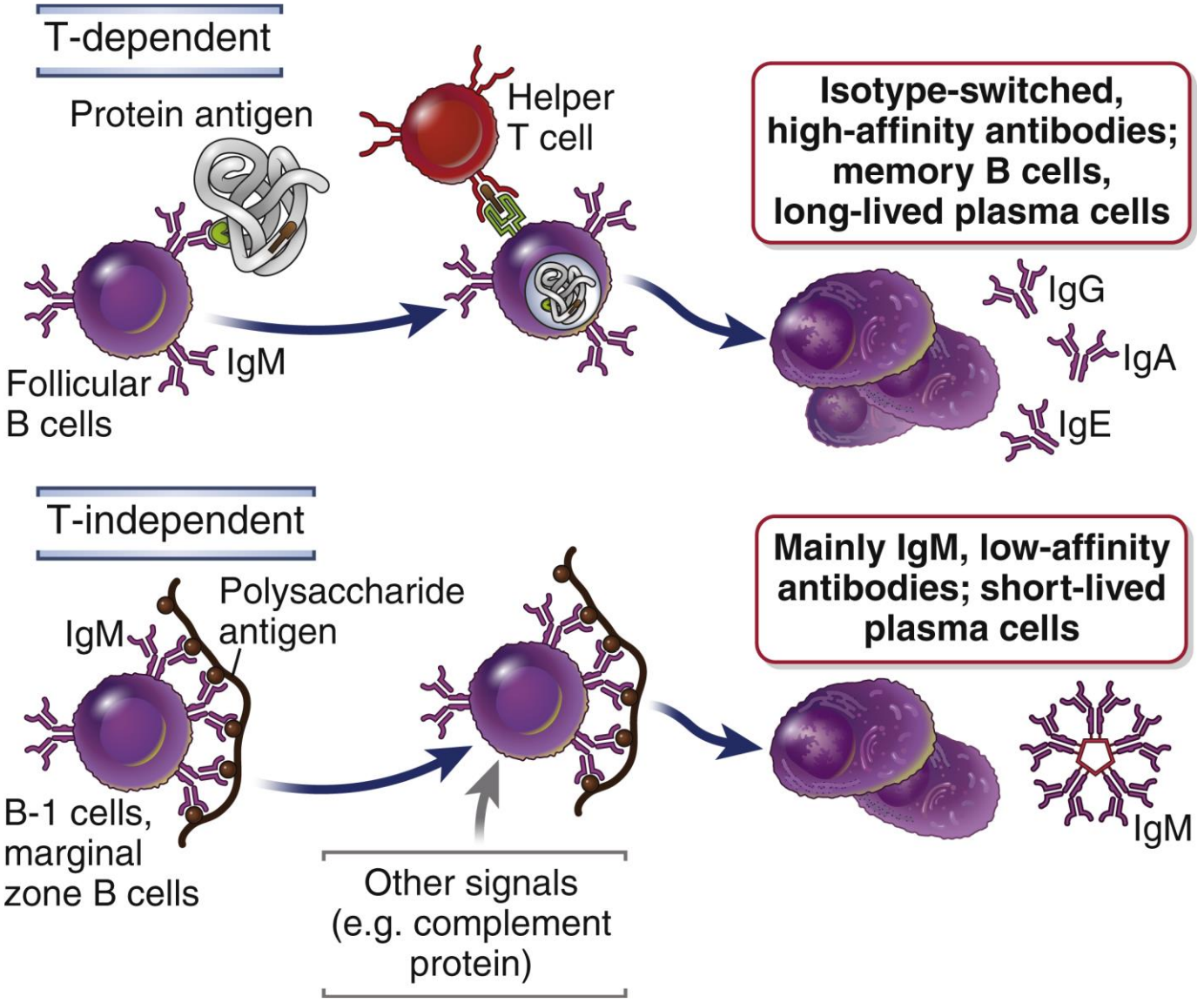
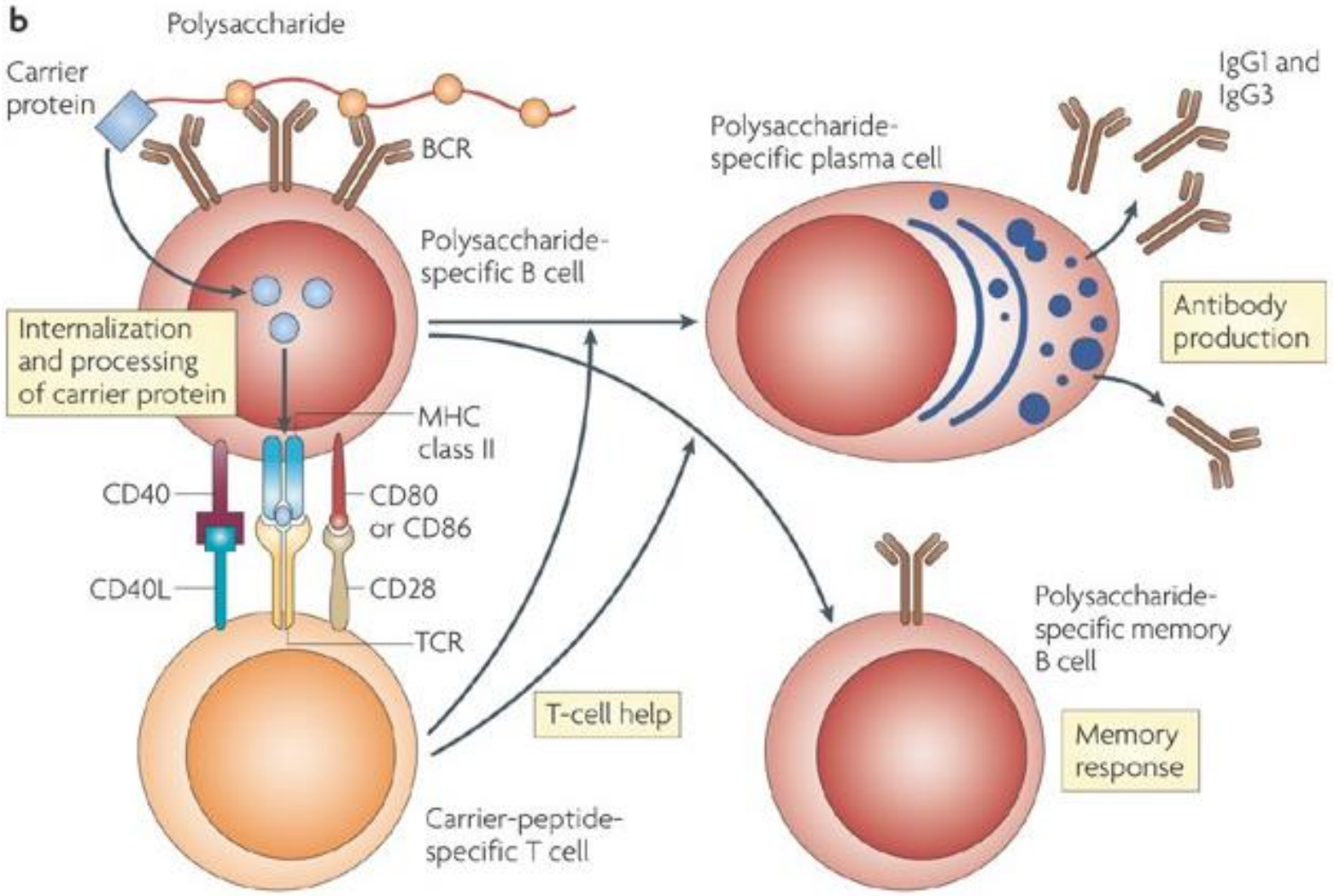


B-CELL ACTIVATION



CD40L, CD40 ligand; TCR, T-cell receptor.

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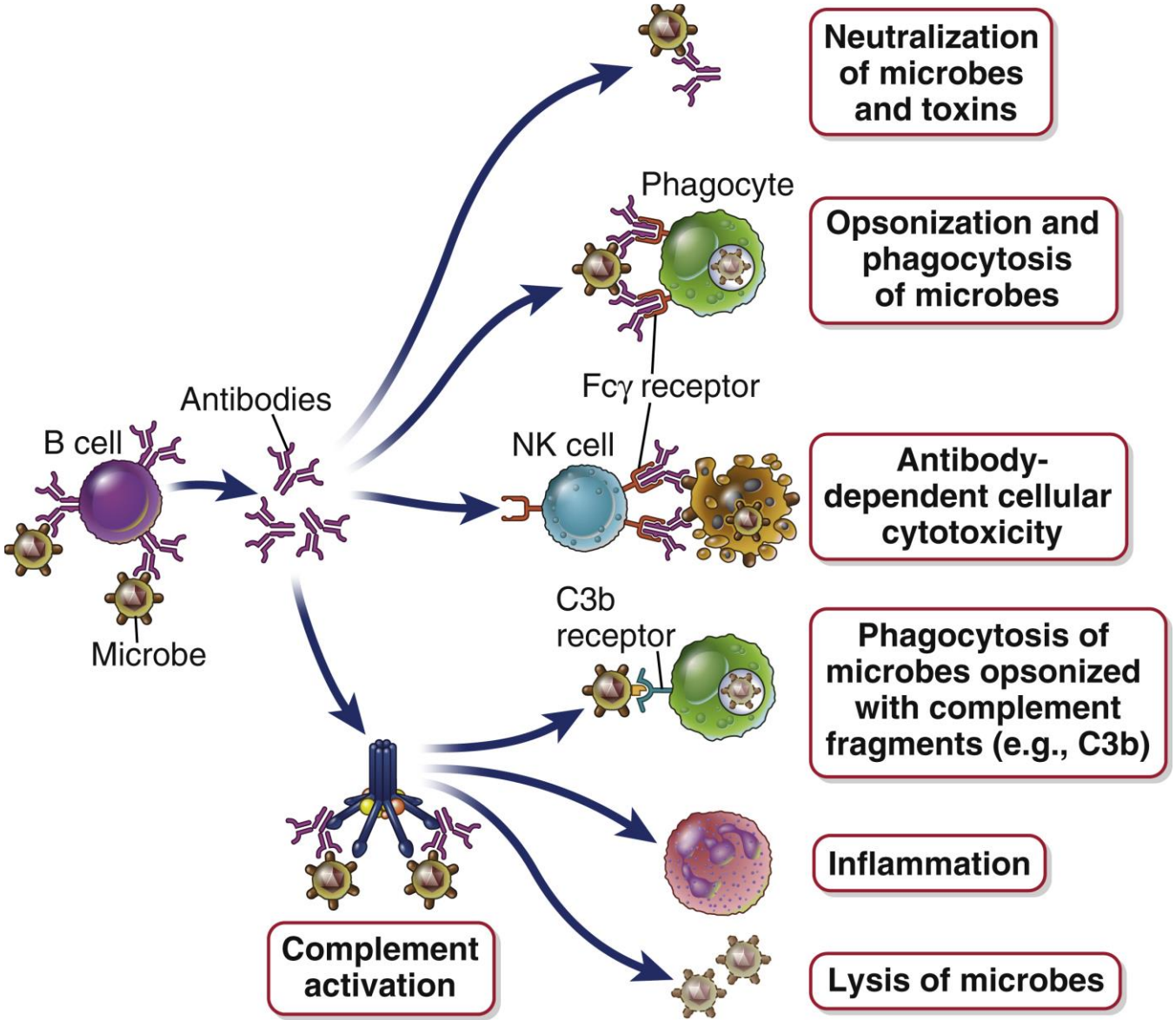
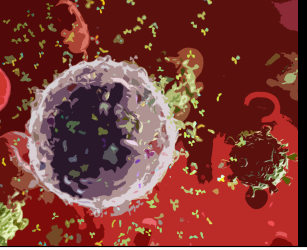
The carrier protein from **protein–polysaccharide conjugate vaccines** is processed by the polysaccharide-specific B cell, and peptides are presented to carrier-peptide-specific T cells, resulting in T-cell help for the production of both plasma cells and memory B cells.

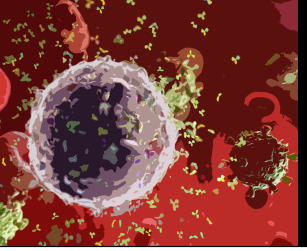
EFFECTOR B-CELL



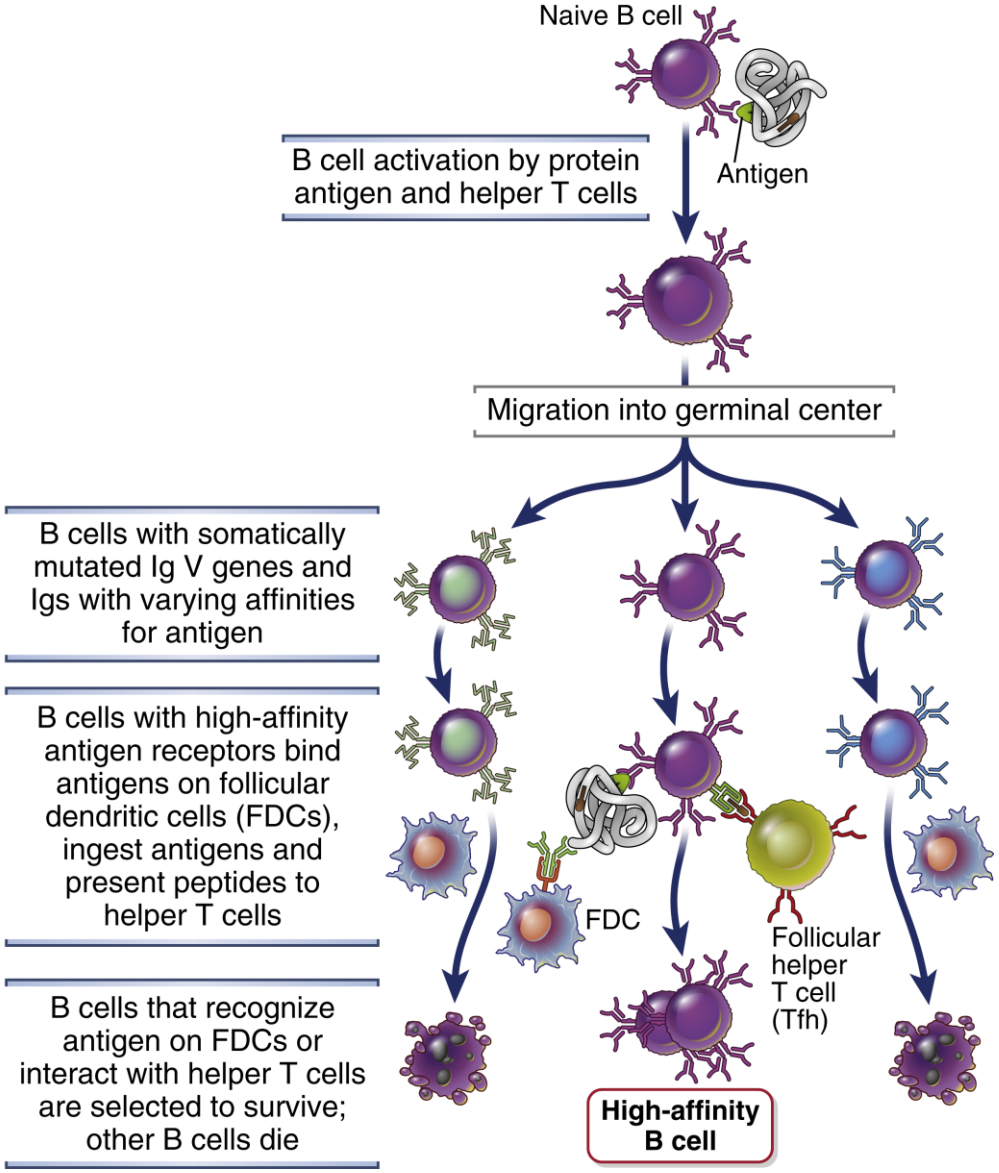


OBJECTIVES

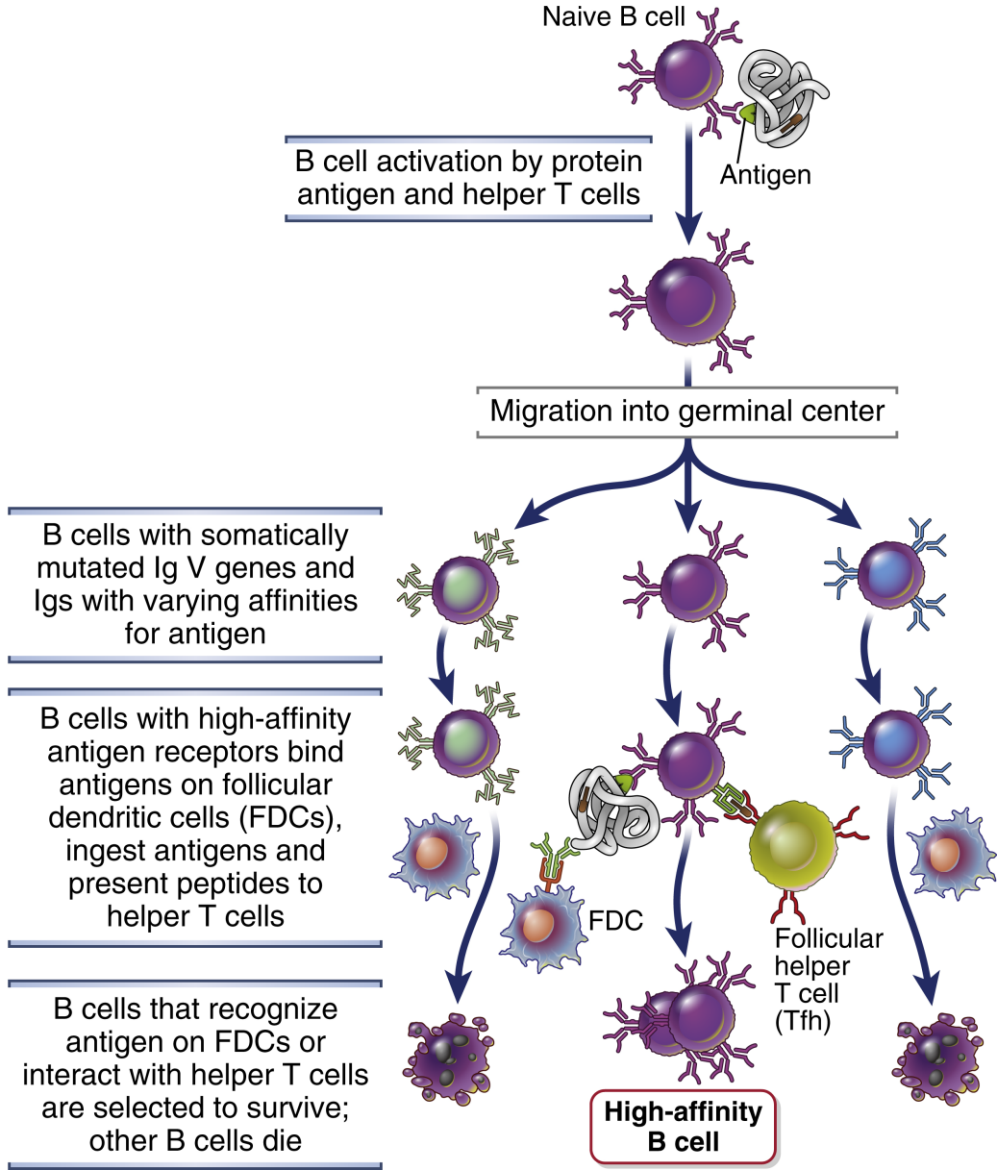
1. Production and maturation of adaptive immunity
2. Activation of T-cell and its effector functions
3. Activation of B-cell and its effector functions
4. **Selection and affinity maturation of B-cell**
5. Phase of exposure

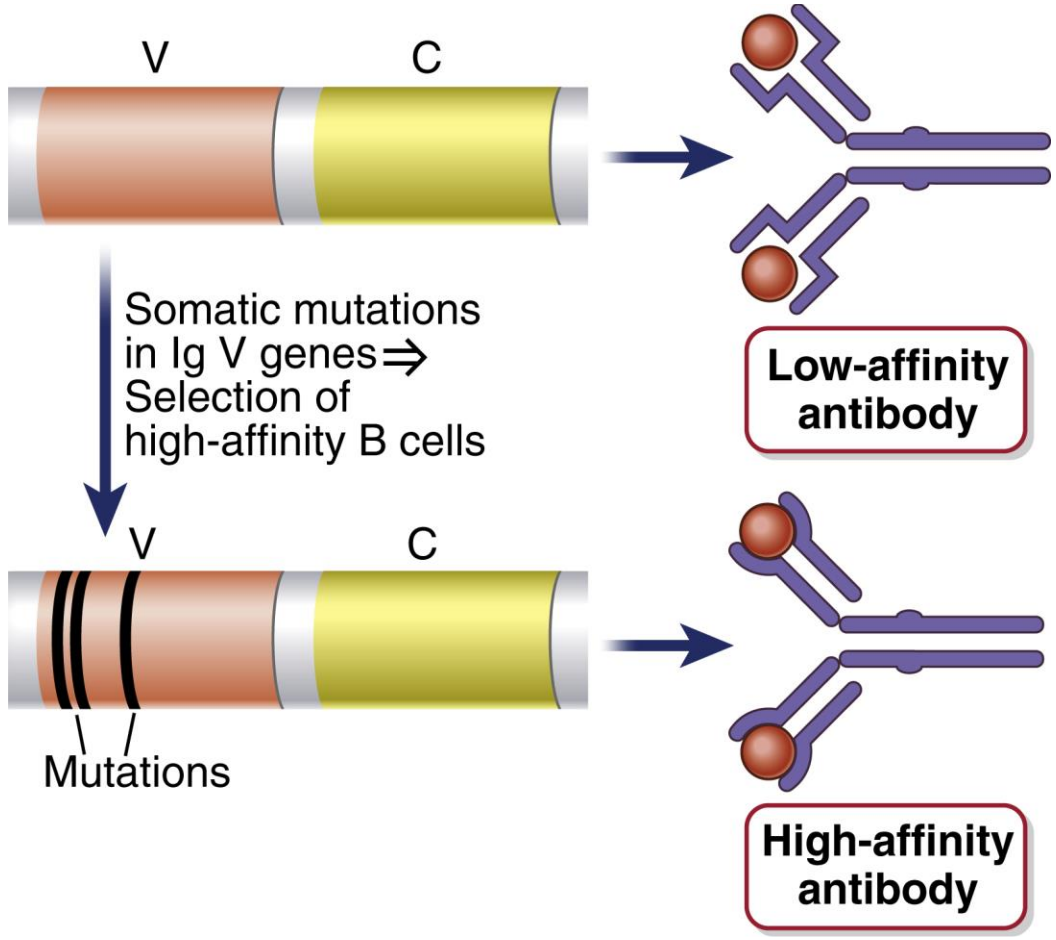


SELECTION OF B-CELL



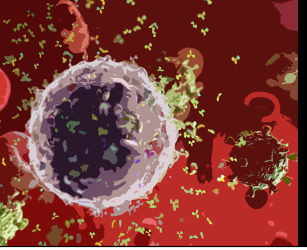
AFFINITY MATURATION B-CELL





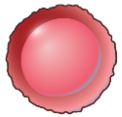
Somatic hypermutation

Ig V genes undergo point mutations at an extremely high rate.



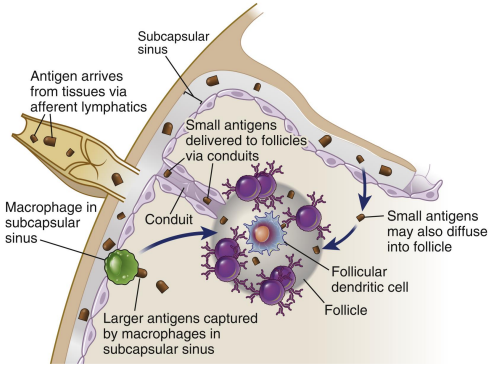
B-CELL TAKE HOME MSG.

Bone Marrow

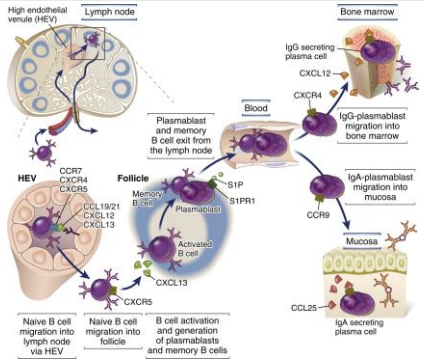


Immature B-cell

Mature/ naïve B-cell



Antigen delivery



Plasma/memory cell storage

T-independent antigen

1. Recognition
2. Development (IgM)

T-dependent antigen

1. Recognition
2. Presentation
3. Development

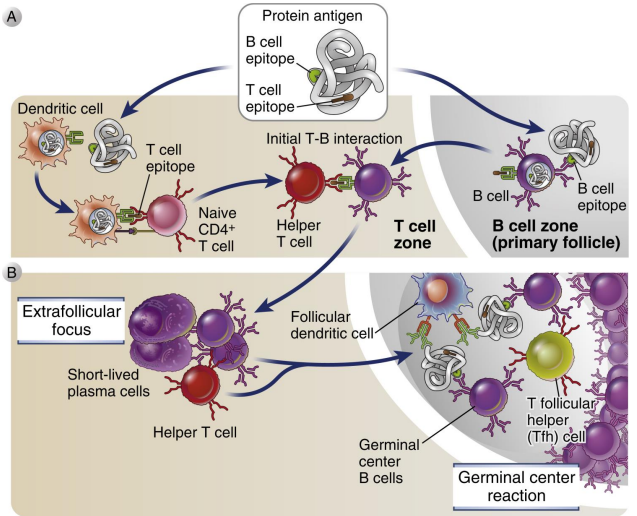
(switching, short-lived plasma cell)

4. GC formation

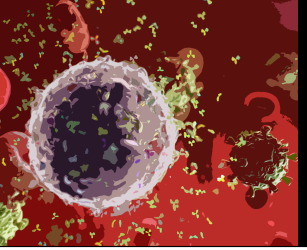
(switching, long-lived plasma cell, memory)

Blood circulation

Antibody



Lymph node / spleen



OBJECTIVES

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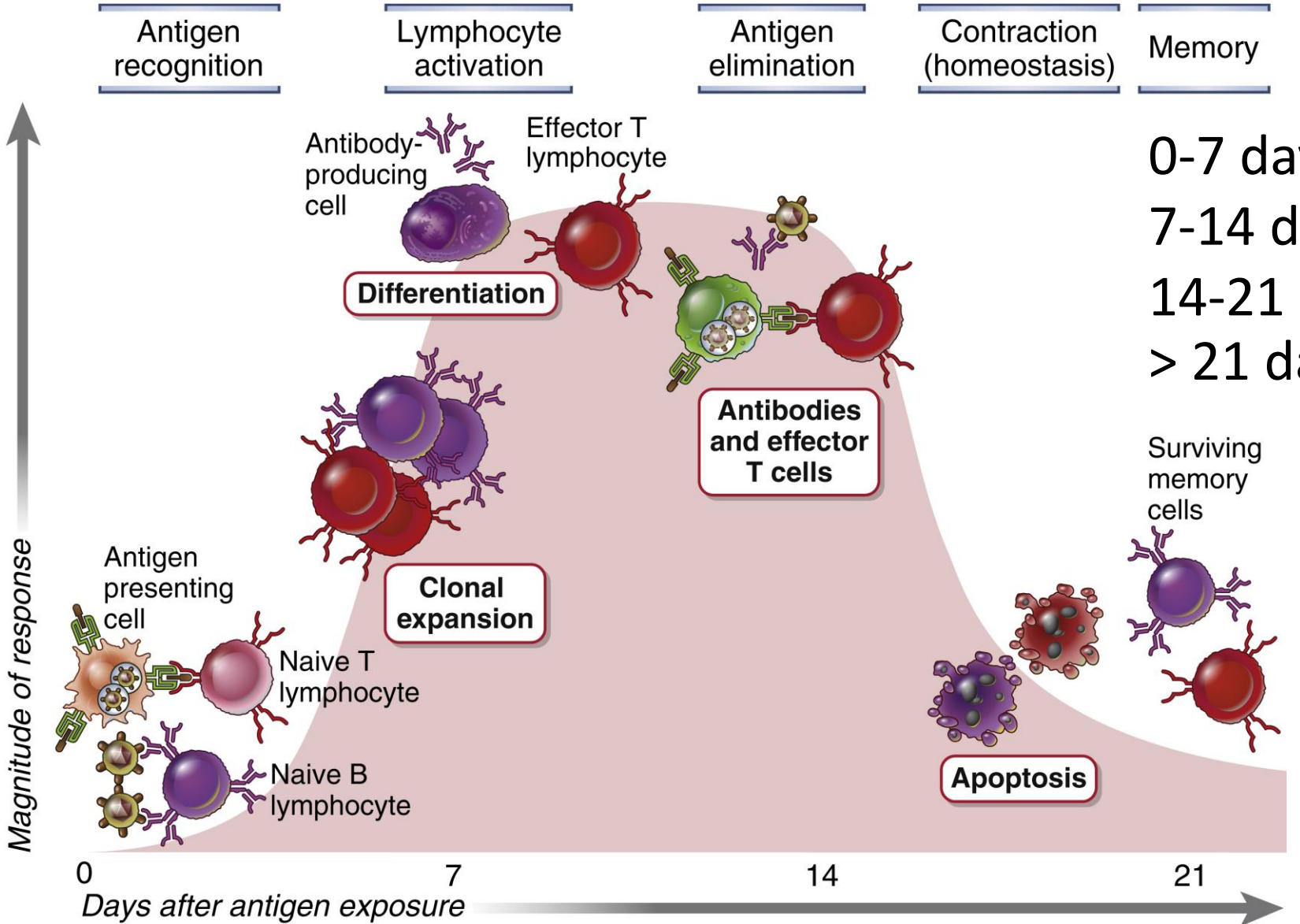
PHASE OF EXPOSURE



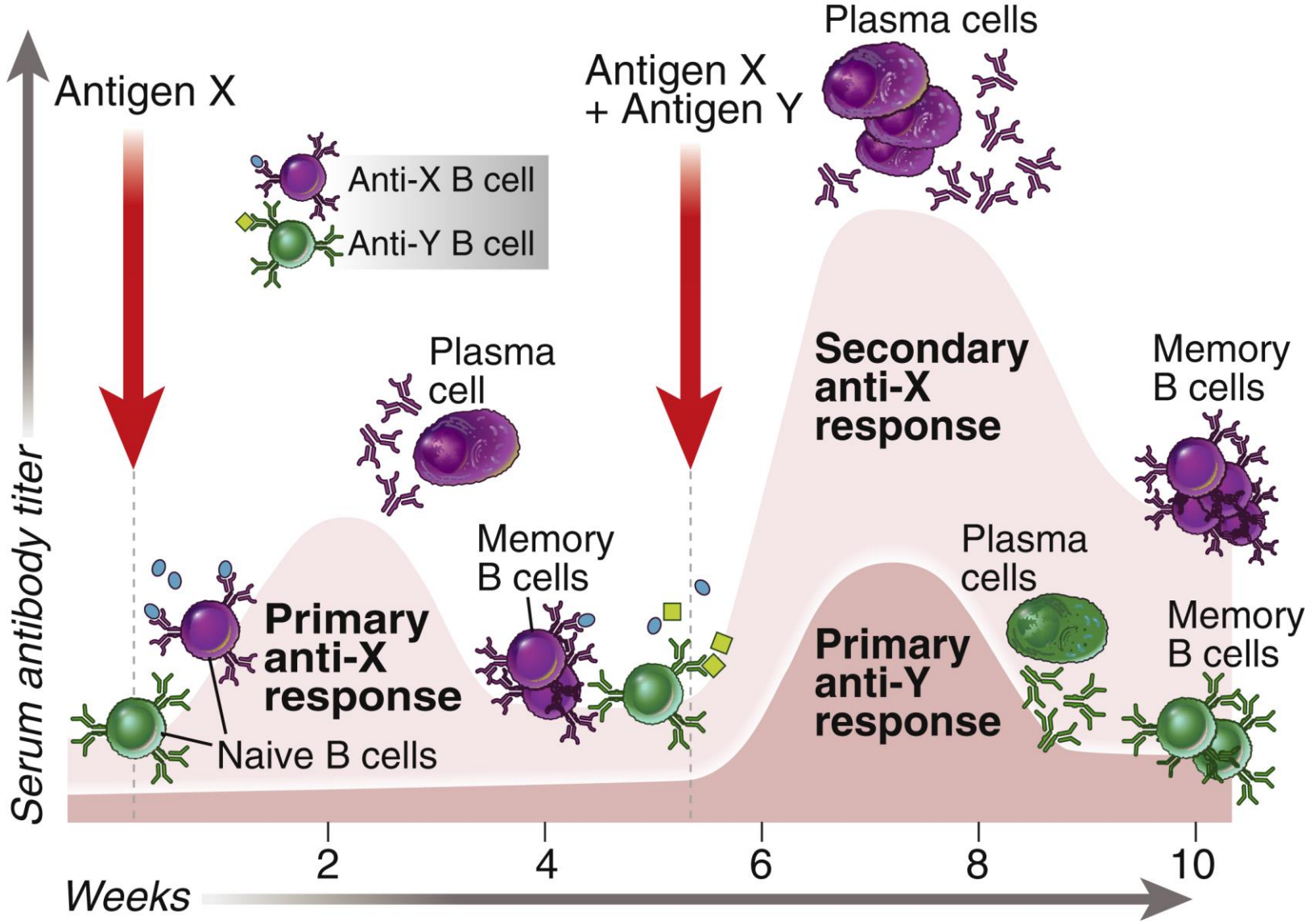
0-7 days = priming/activation

7-14 days = peak immune

14-21 days = decline immune

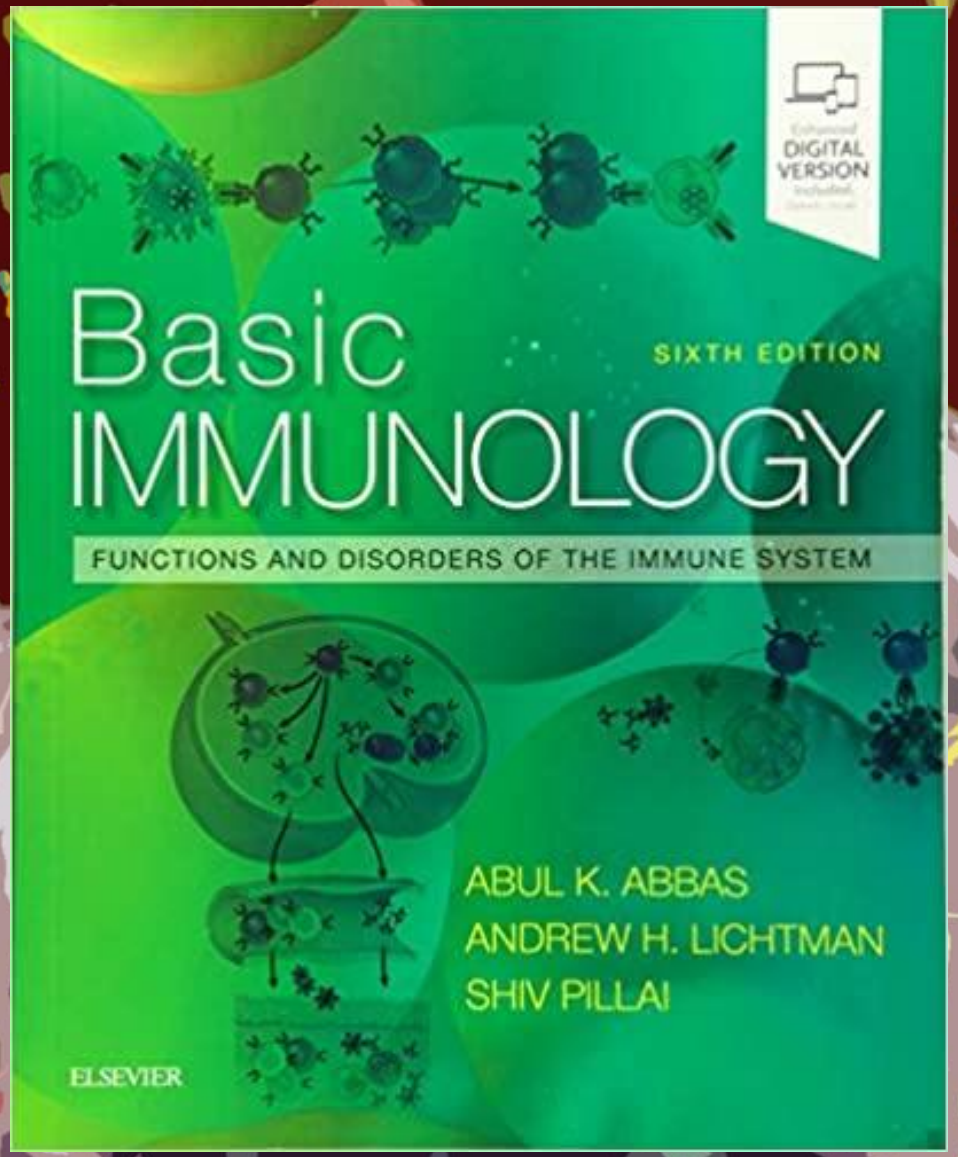
> 21 days = memory

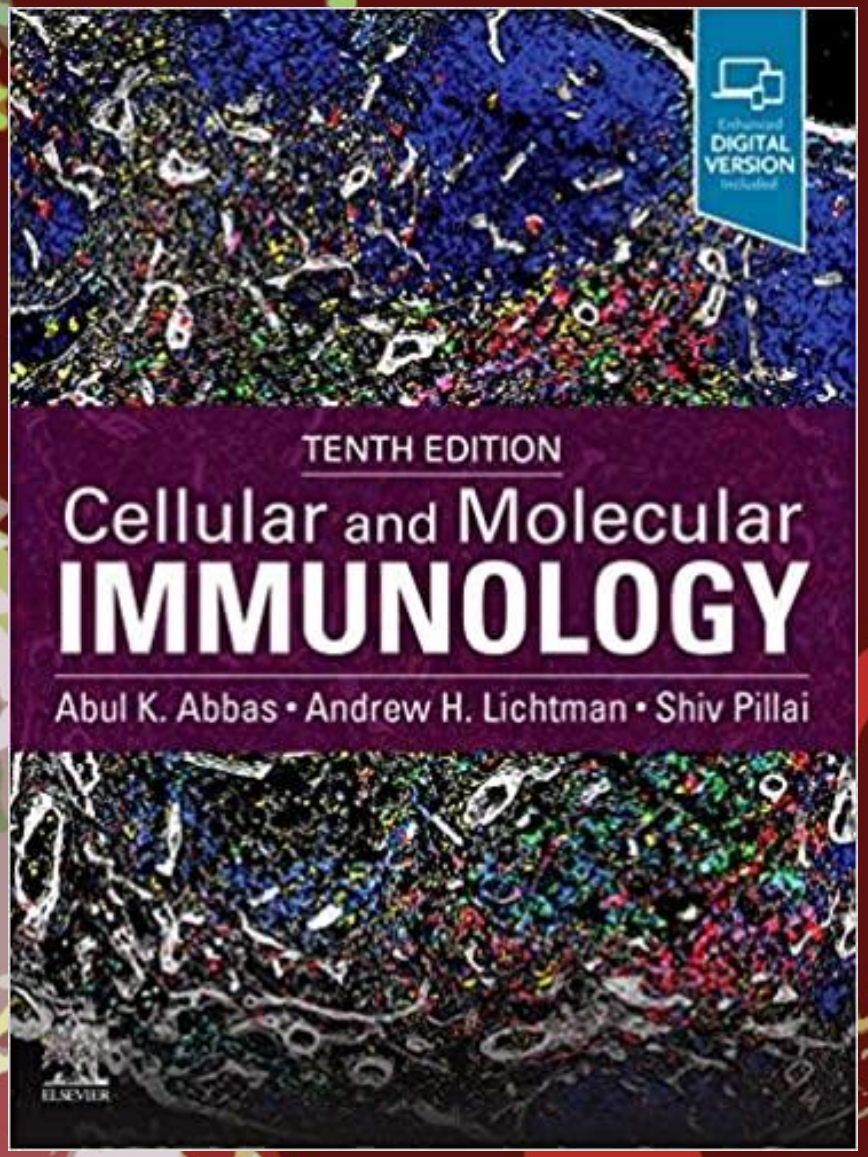
1ST VS 2ND EXPOSURE



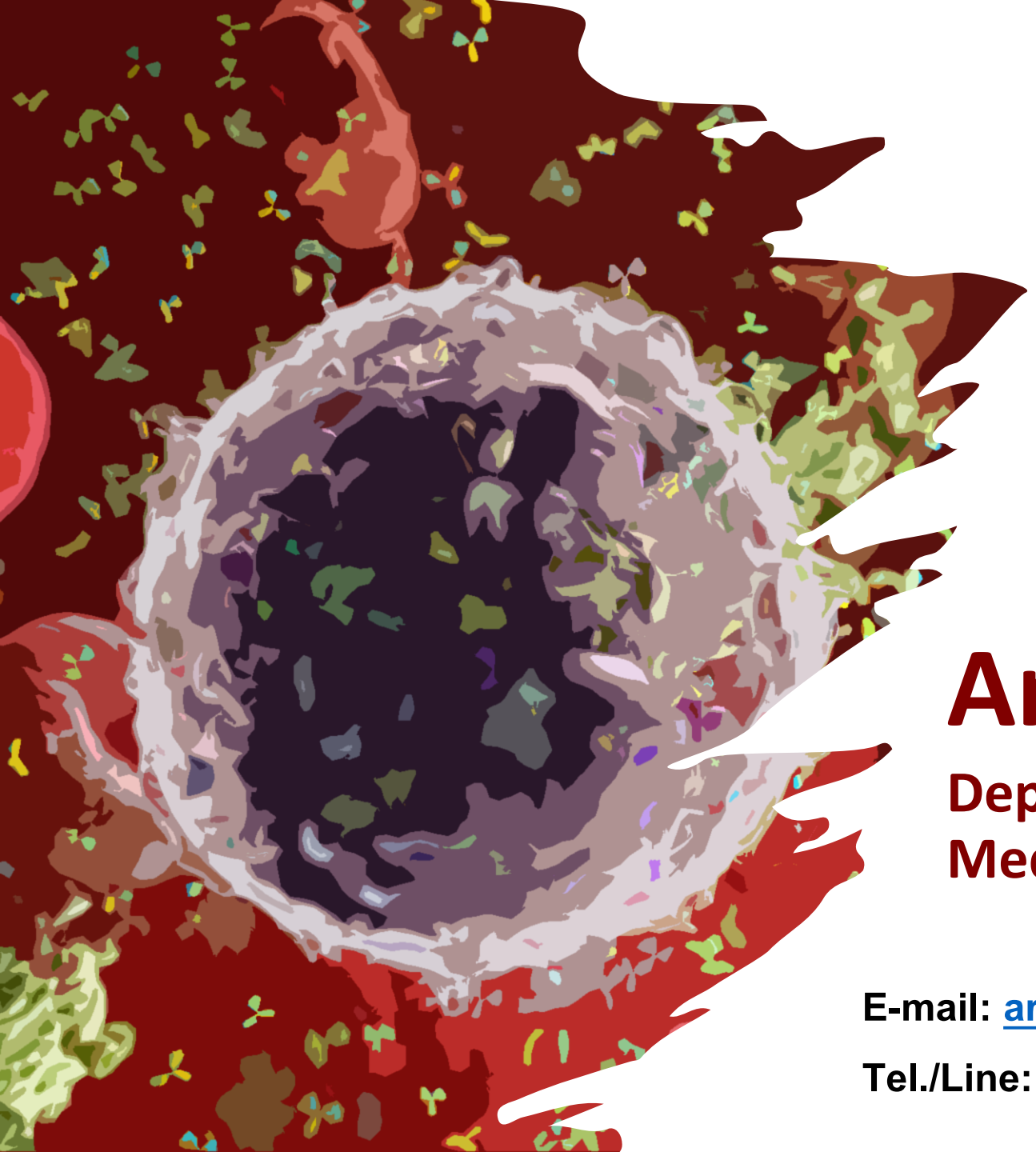
Memory cells are ready to respond immediately (skip the priming step)

Learning sources






Q & A



THANK YOU FOR YOUR ATTENTIONS

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