Basic mechanisms of immune defense

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What is immunology?

- Immunity
  - Freedom from disease, in particular from infections
- Immune system
  - A collection of molecules, cells, organs in the body mediating immunity
- Immune responses
  - A coordinated immune reaction against infections
- Immunology
  - The study of the immune system in health and disease

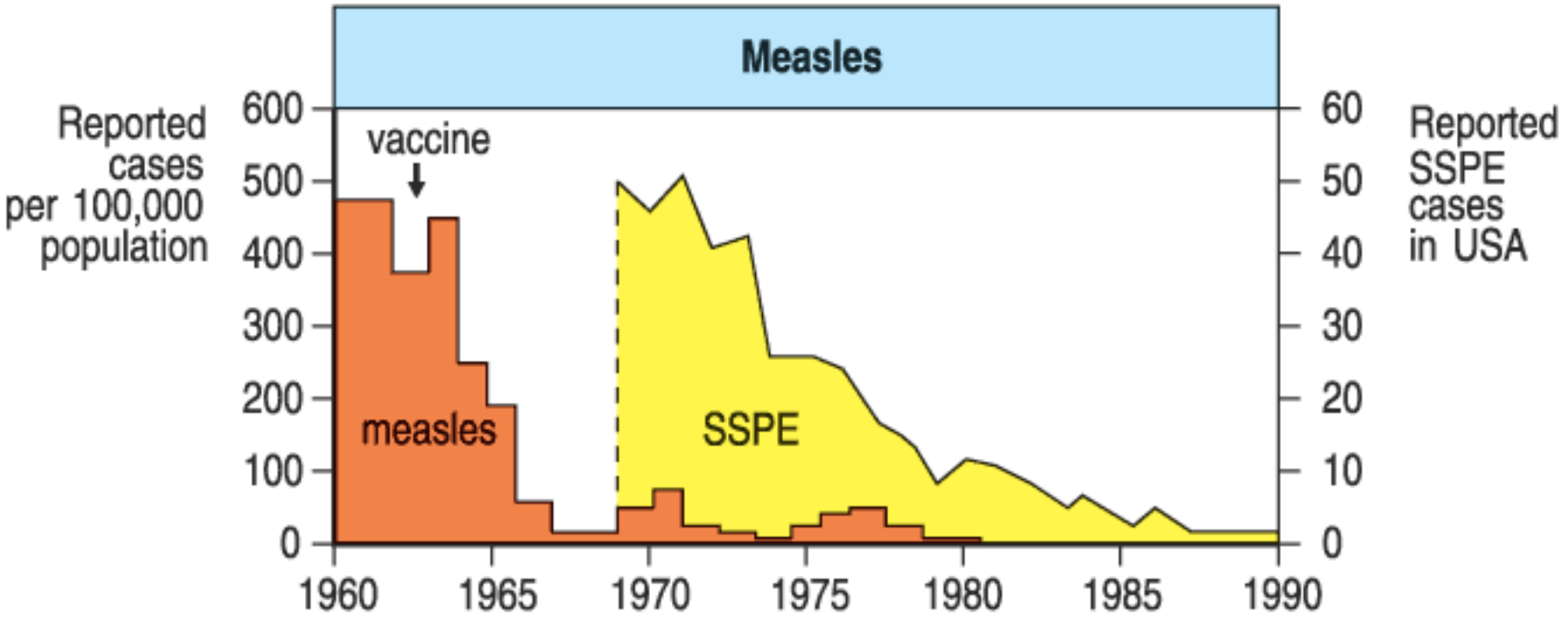
Importance of the immune system in health and disease

Role of the immune system	Implications
Defense against infections	Deficient immunity results in increased susceptibility to infections; exemplified by AIDS Vaccination boosts immune defenses and protects against infections
Defense against tumors	Potential for immunotherapy of cancer
The immune system recognizes and responds to tissue grafts and newly introduced molecules	Immune responses are barriers to transplantation and gene therapy
The immune system can injure cells and induce pathologic inflammation	Immune responses are the cause of allergic, autoimmune, and other inflammatory diseases

Effectiveness of vaccination

Disease	Maximum number of cases (year)	Number of cases in 2009	Percent change
Diphtheria	206,939 (1921)	0	-99.99
Measles	894,134 (1941)	61	-99.99
Mumps	152,209 (1968)	982	-99.35
Pertussis	265,269 (1934)	13,506	-94.72
Polio (paralytic)	21,269 (1952)	0	-100.0
Rubella	57,686 (1969)	4	-99.99
Tetanus	1,560 (1923)	14	-99.10
Hemophilus influenza type B	~20,000 (1984)	25	-99.88
Hepatitis B	26,611 (1985)	3,020	-87.66

Effectiveness of vaccination

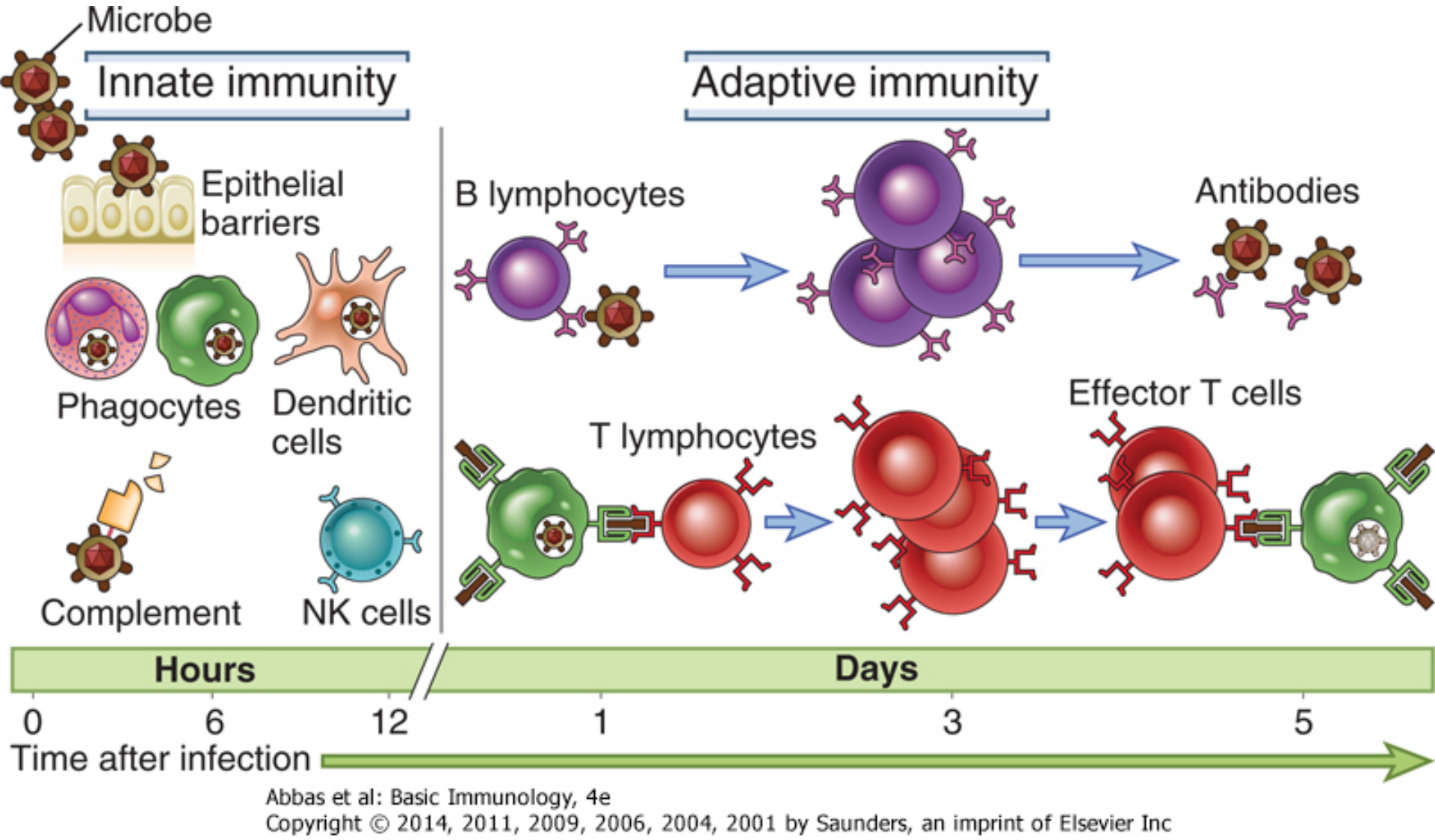


Some diseases for which effective vaccines are not yet available		
Disease	**Estimated annual mortality**	**Estimated annual incidence**
Malaria*	1,086,000	300–500 million
Schistosomiasis	14,000	no numbers available
Worm infestation	16,000	no numbers available
Tuberculosis	1,498,000	~8 million
Diarrheal disease	2,213,000	~4,100 million
Respiratory disease	4,039,000	~362 million
HIV/AIDS	2,673,000	~2 million
Measles†	875,000	~44 million

It is more than protection from infections

- Cancer immunotherapy
  - Recent progress show remarkable efficiency
- Monoclonal antibodies as drugs
  - Fastest growing class of new therapeutic molecules
- Antibodies in diagnostics
  - Sensitive and specific detection of antigens of clinical relevance
- Antibodies in research and biotechnology
  - Identification, characterization, purification, manipulation etc.

Innate & adaptive immunity



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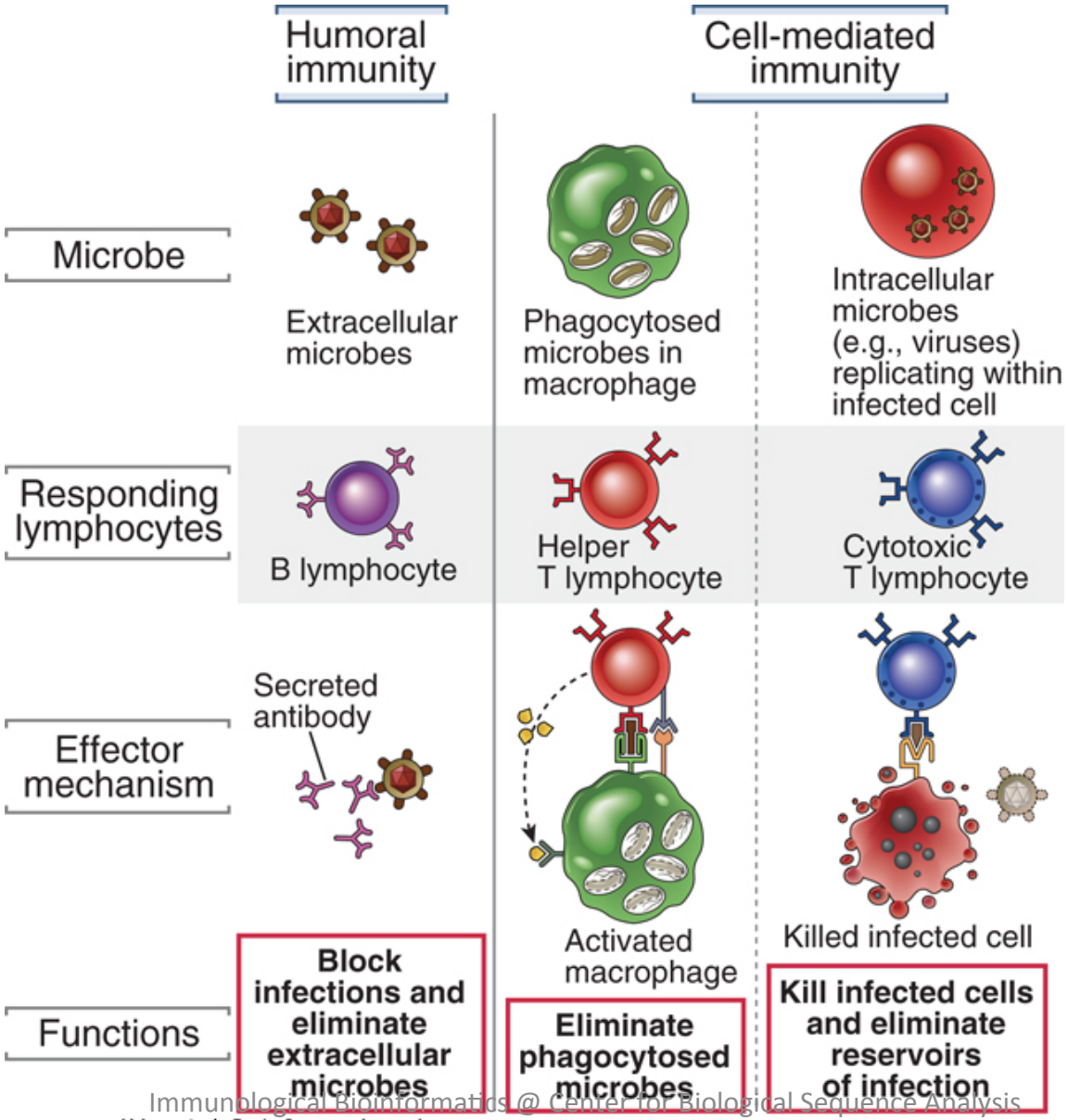
Types of adaptive immunity



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Active vs. passive immunization

- Active immunization (slow, long-lived)
  - Natural infection
  - Vaccination
- Passive immunization (immediate, short-lived)
  - Transfer of specific immune components (newborns)
    - Antibodies
    - T cells

Properties of adaptive immune responses

Feature	Functional significance
Specificity	Ensures that distinct antigens elicit responses that target those antigens
Diversity	Enables immune system to respond to a large variety of antigens
Memory	Leads to rapid and enhanced responses to repeated exposures to the same antigens
Clonal expansion	Increases number of antigen-specific lymphocytes to keep pace with microbes
Specialization	Generates responses that are optimal for defense against different types of microbes
Contraction and homeostasis	Allows immune system to respond to newly encountered antigens
Nonreactivity to self	Prevents injury to the host during responses to foreign antigens

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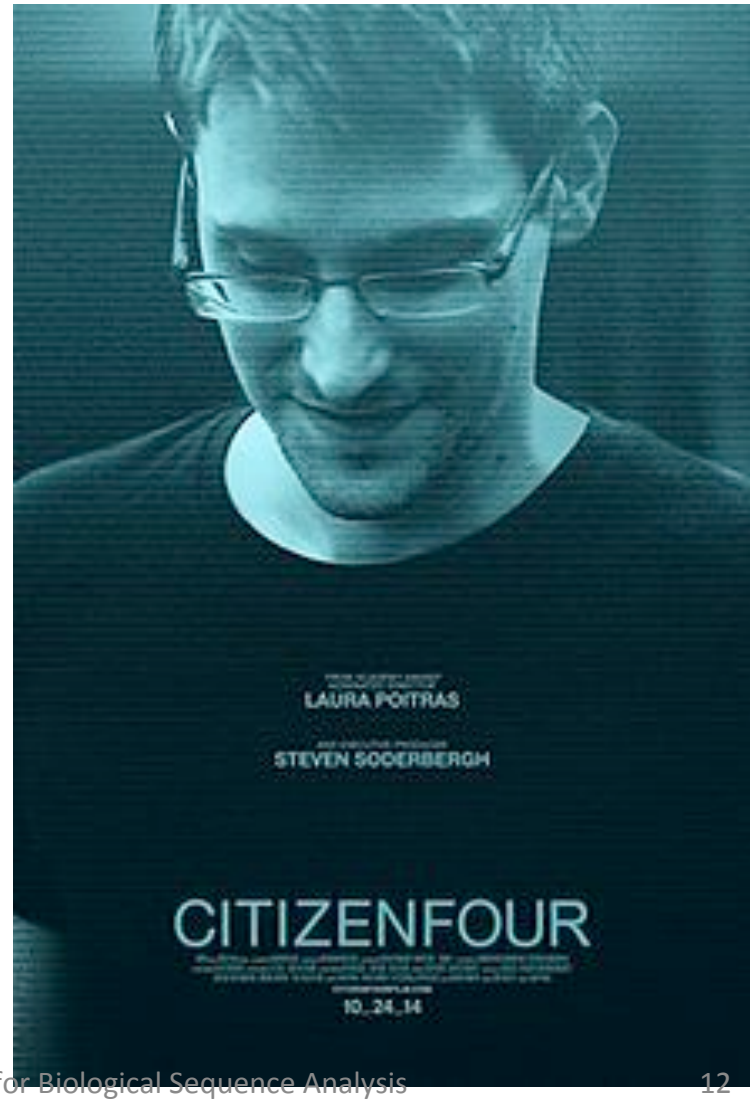
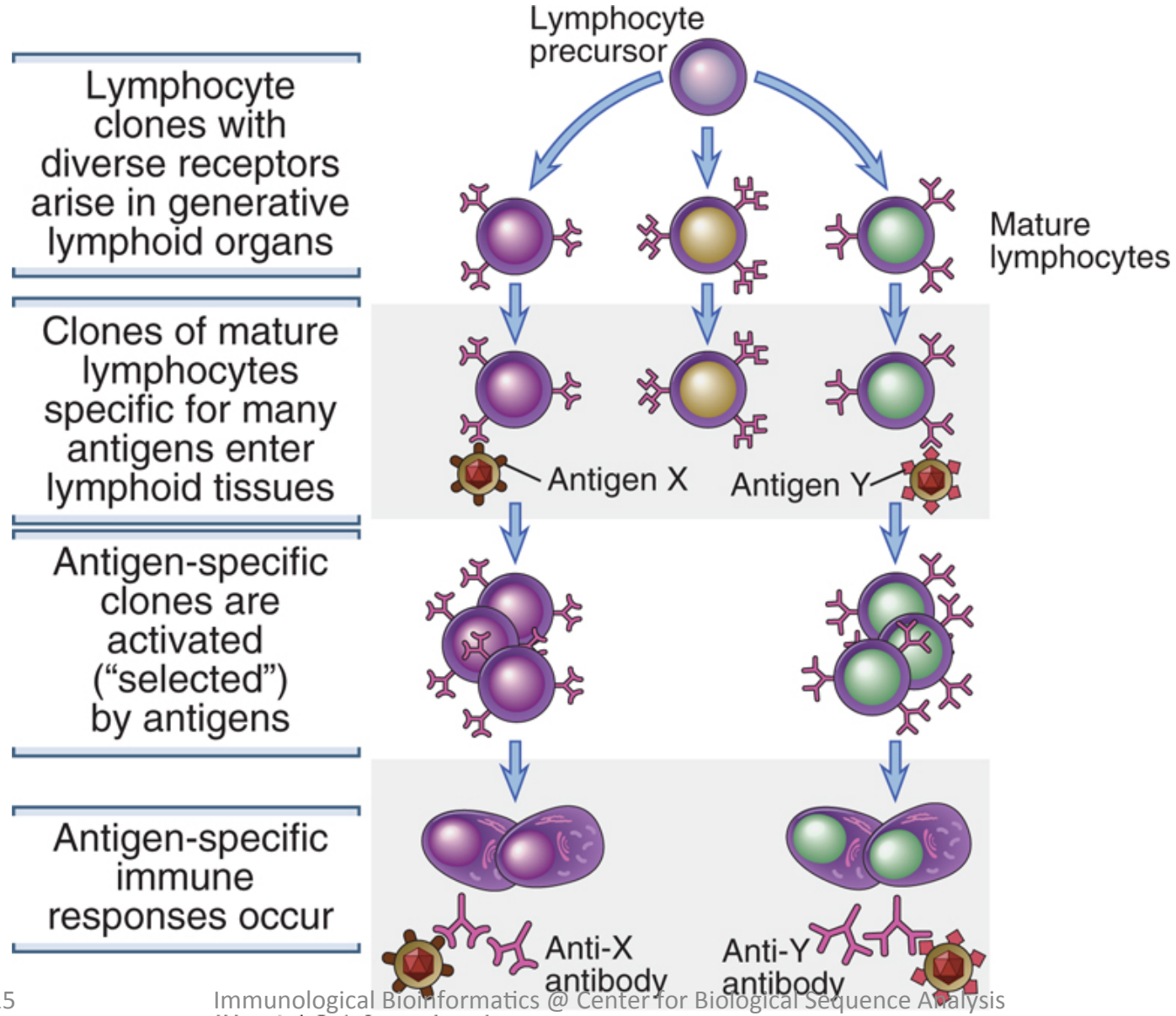
To be, or not to be - encrypted



Clonal Selection



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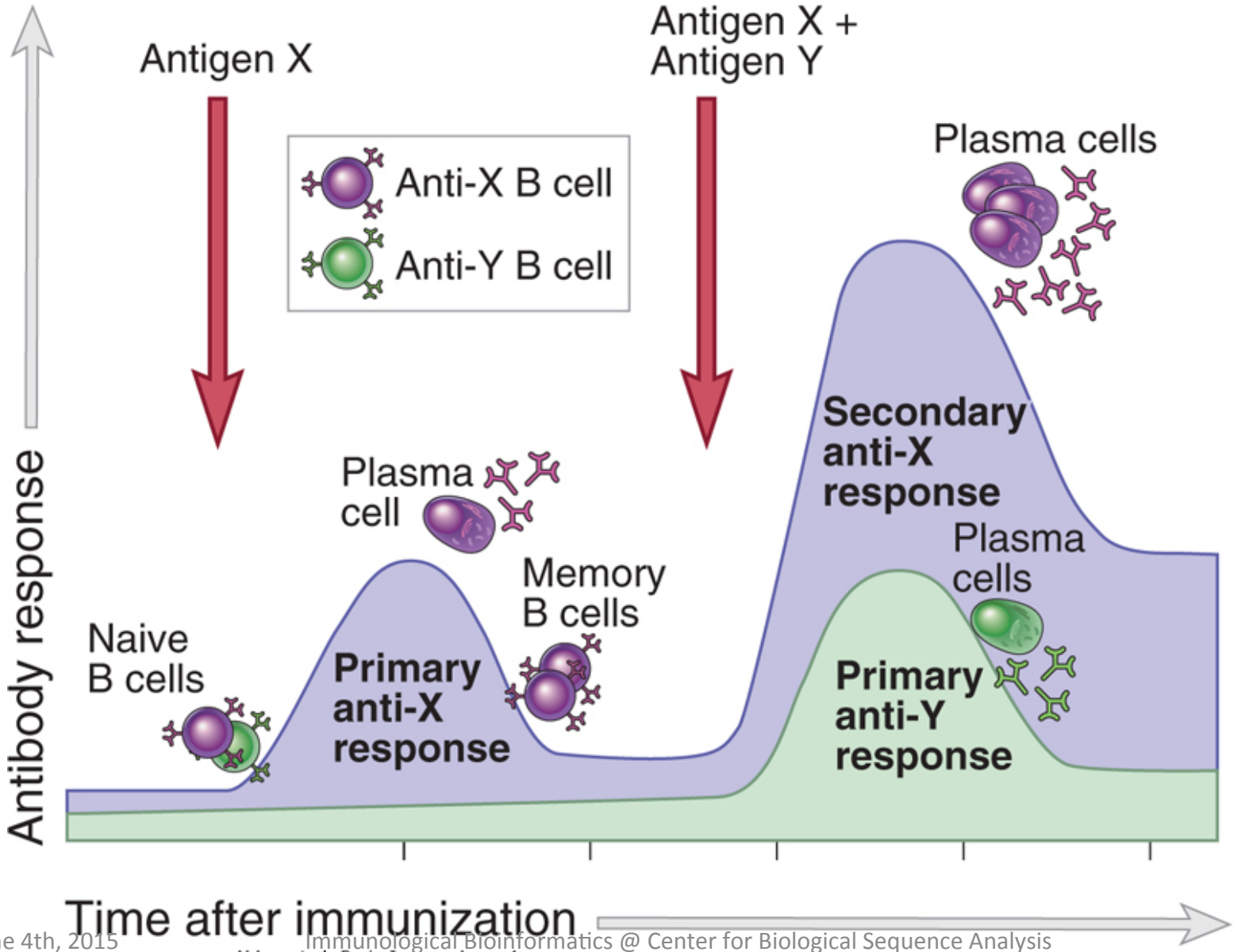
Primary & secondary immune responses



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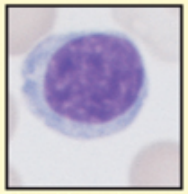
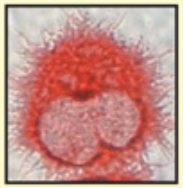
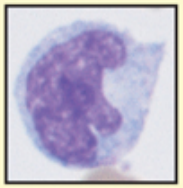
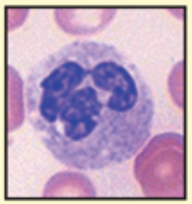
Principal cells of the immune system

Cell type	Principal function(s)
Lymphocytes: B lymphocytes; T lymphocytes; natural killer cells  *Blood lymphocyte*	Specific recognition of antigens: B lymphocytes: mediators of humoral immunity T lymphocytes: mediators of cell-mediated immunity Natural killer cells: cells of innate immunity
Antigen-presenting cells: dendritic cells; macrophages; follicular dendritic cells   *Dendritic cell* *Blood monocyte*	Capture of antigens for display to lymphocytes: Dendritic cells: initiation of T cell responses Macrophages: effector phase of cell-mediated immunity Follicular dendritic cells: display of antigens to B lymphocytes in humoral immune responses
Effector cells: T lymphocytes; macrophages; granulocytes  *Neutrophil*	Elimination of antigens: T lymphocytes: helper T cells and cytotoxic T lymphocytes Macrophages and monocytes: cells of the mononuclear phagocyte system Granulocytes: neutrophils, eosinophils

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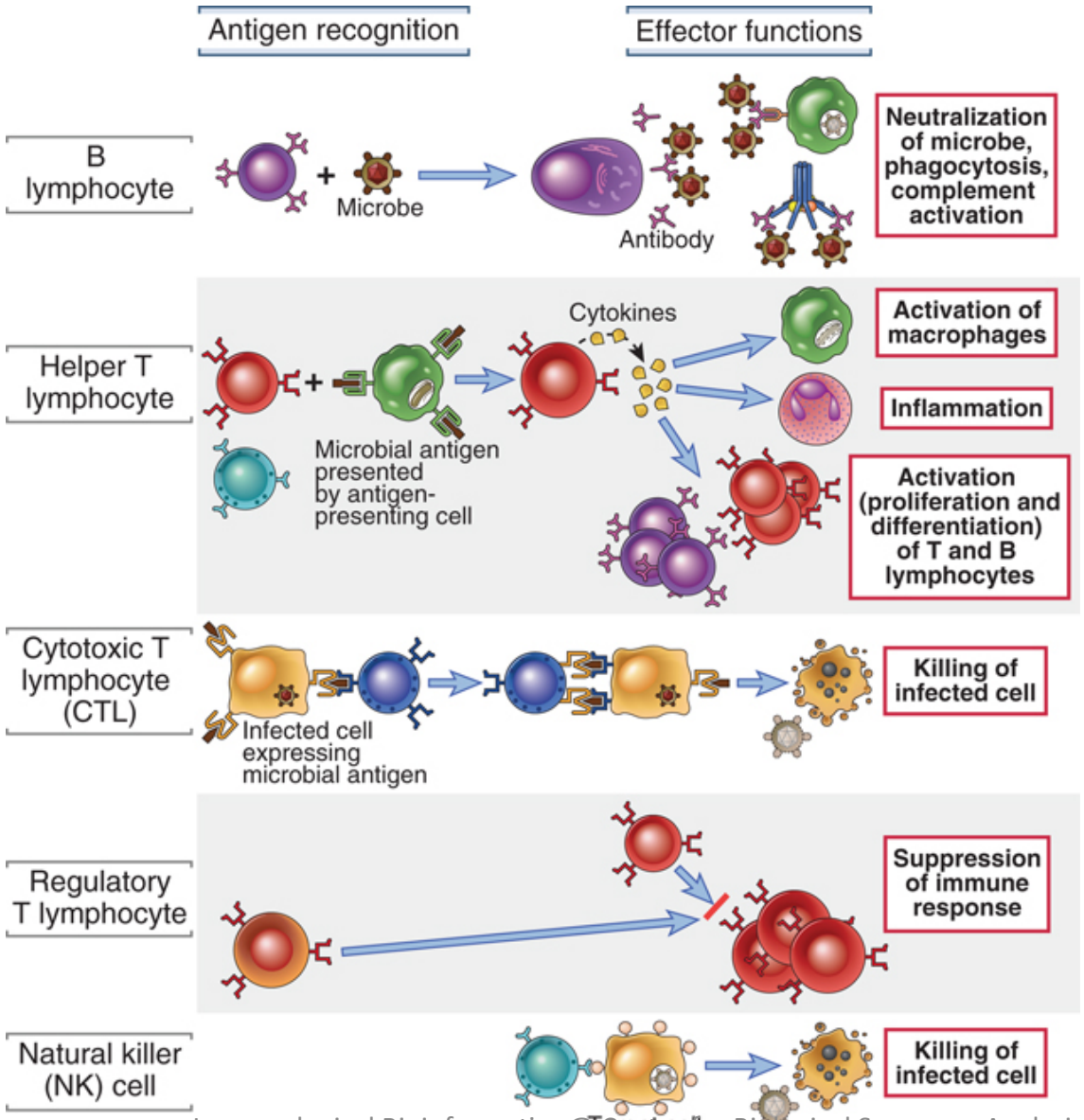
Classes of lymphocytes



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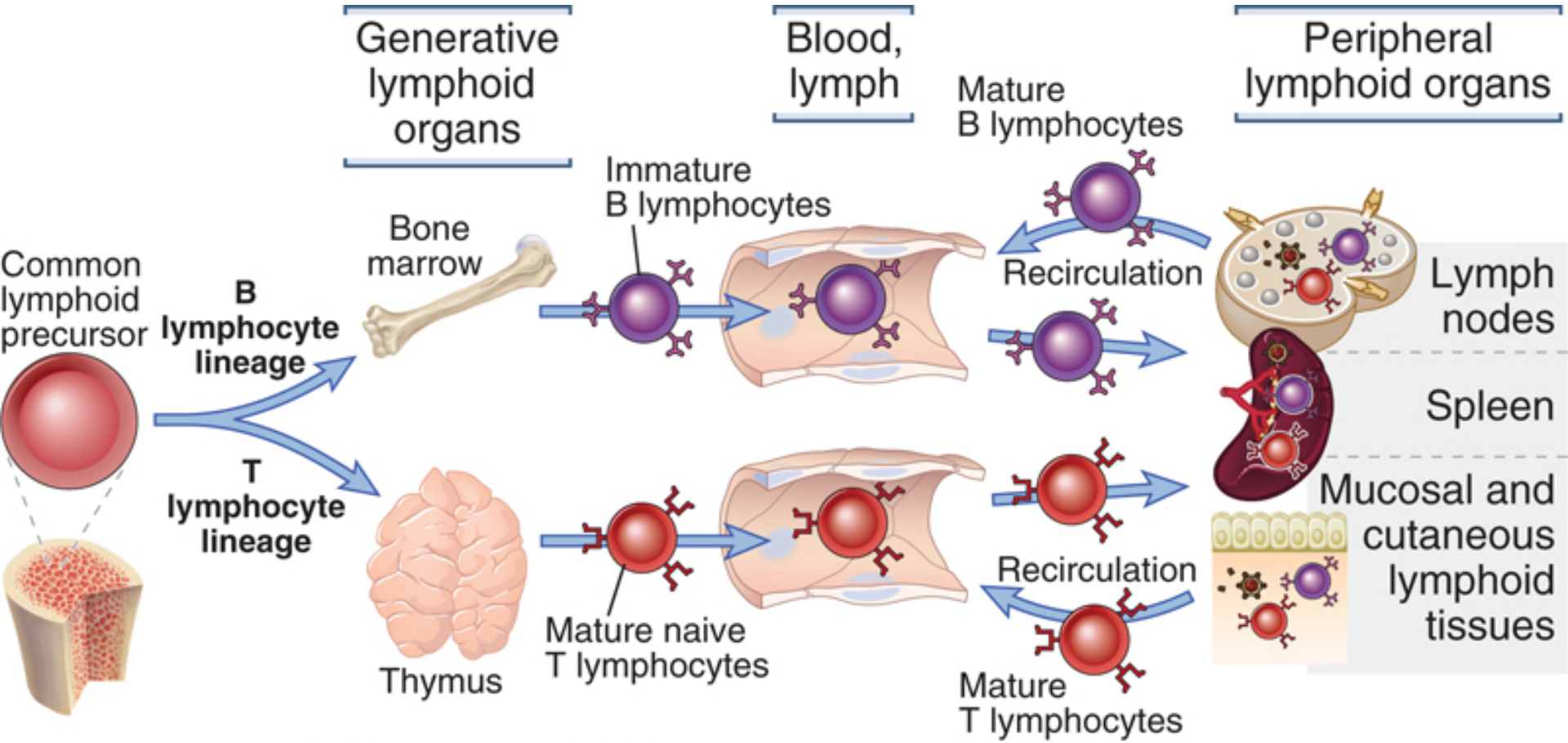
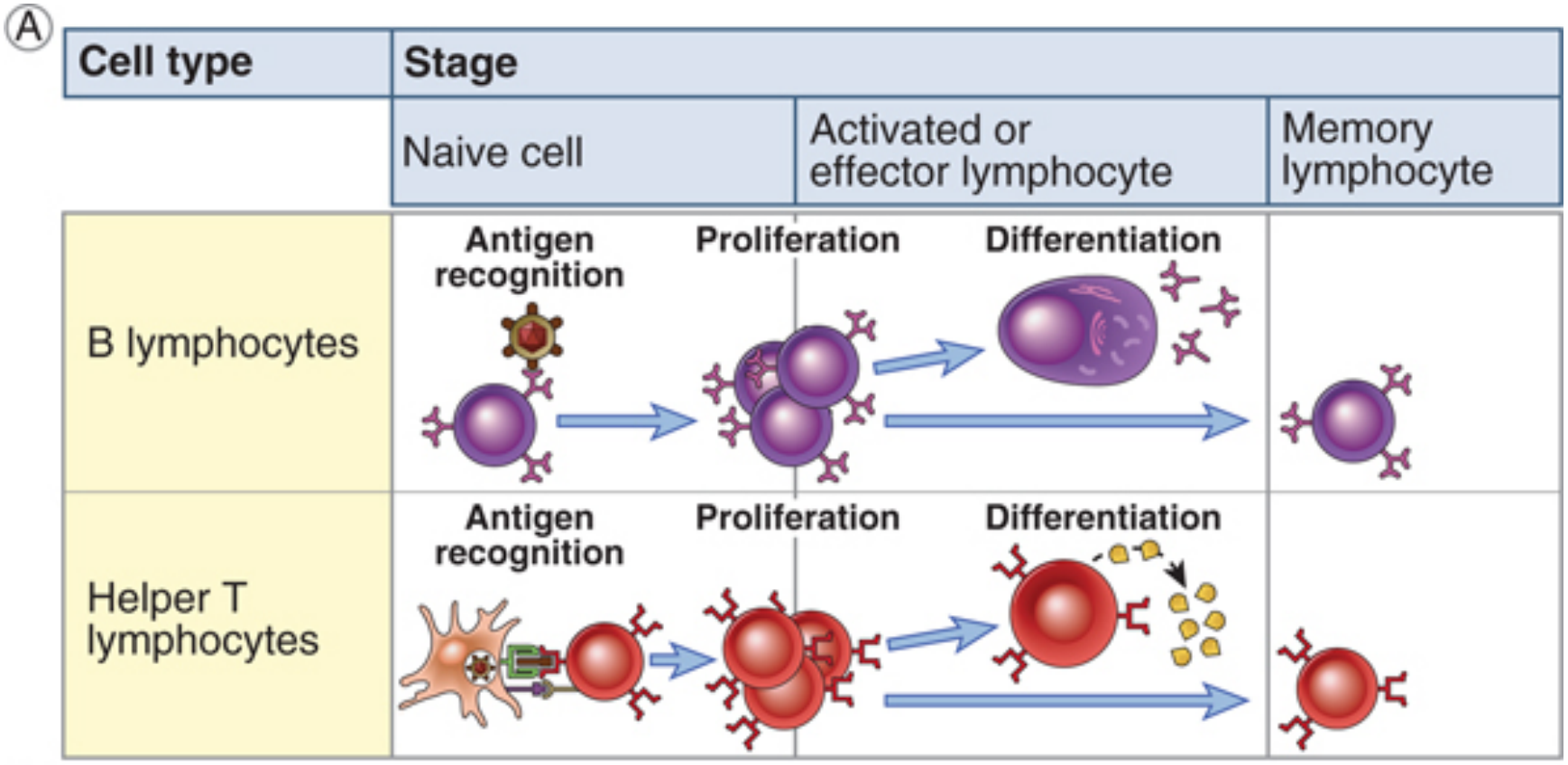
Maturation of lymphocytes



Stages in the life history of lymphocytes



Stages in the life history of lymphocytes

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	Naive cell	Activated or effector lymphocyte	Memory lymphocyte
T lymphocytes			
Migration	Preferentially to peripheral lymph nodes	Preferentially to inflamed tissues	Heterogenous: one subset to lymph nodes, one subset to mucosa and inflamed tissues
Frequency of cells responsive to particular antigen	Very low	High	Low
Effector functions	None	Cytokine secretion; cytotoxic activity	None
B lymphocytes			
Membrane immunoglobulin (Ig) isotype	IgM and IgD	Typically IgG, IgA, or IgE	Typically IgG, IgA, or IgE
Affinity of Ig produced	Relatively low	Increases during immune response	Relatively high
Effector functions	None	Antibody secretion	None

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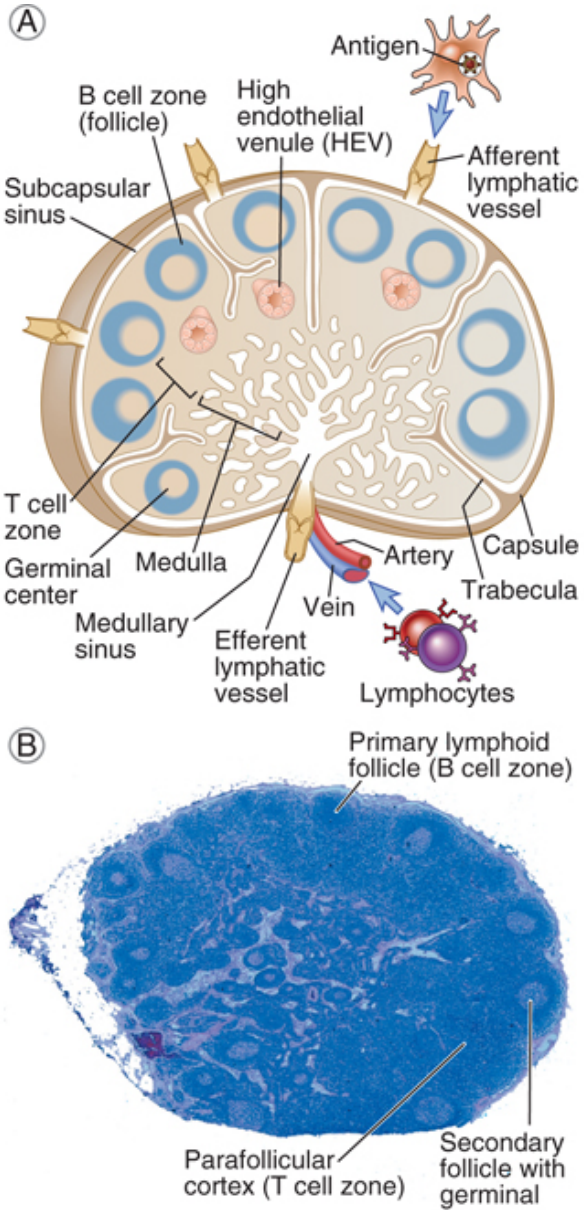
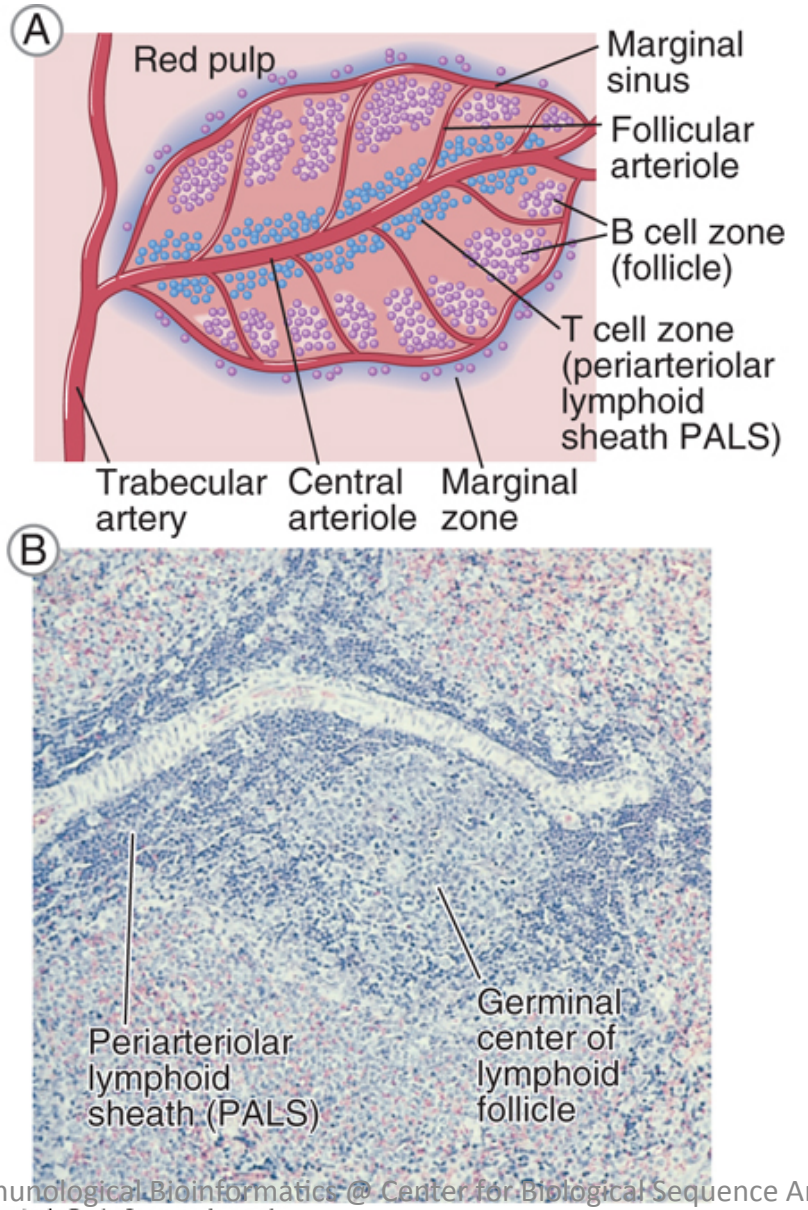
Antigen presenting cells (APC)

- Professional APC presents antigen to T cells
  - Dendritic cells
  - Macrophages
  - B cells
    - Capture antigen and process it
    - Presents it in association with MHC (Signal 1)
    - Express co-stimulatory molecules (Signal 2)
- Follicular dendritic cells (FDC) presents antigen to B cells
  - Reservoir of conformationally intact antigen

Morphology of lymph nodes.



Morphology of the spleen.



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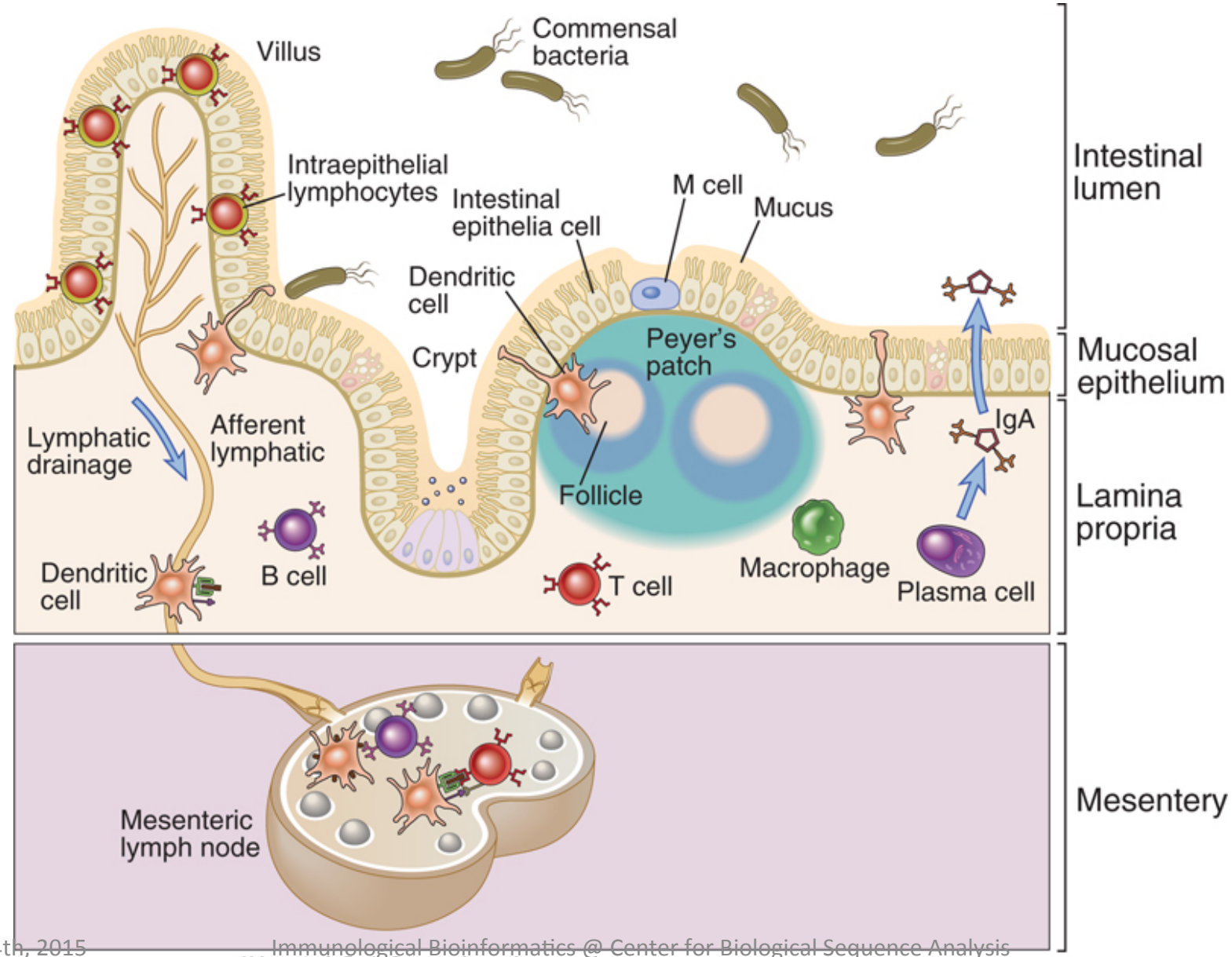
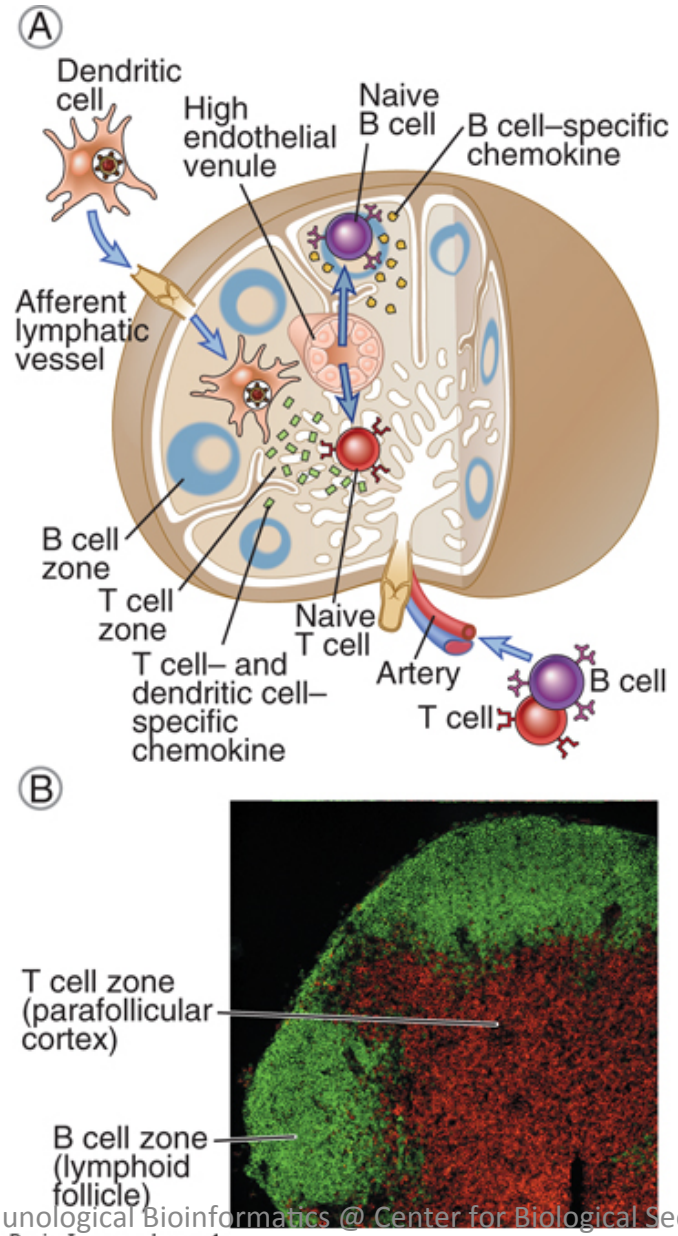
Mucosal immune system



Segregation of T and B lymphocytes



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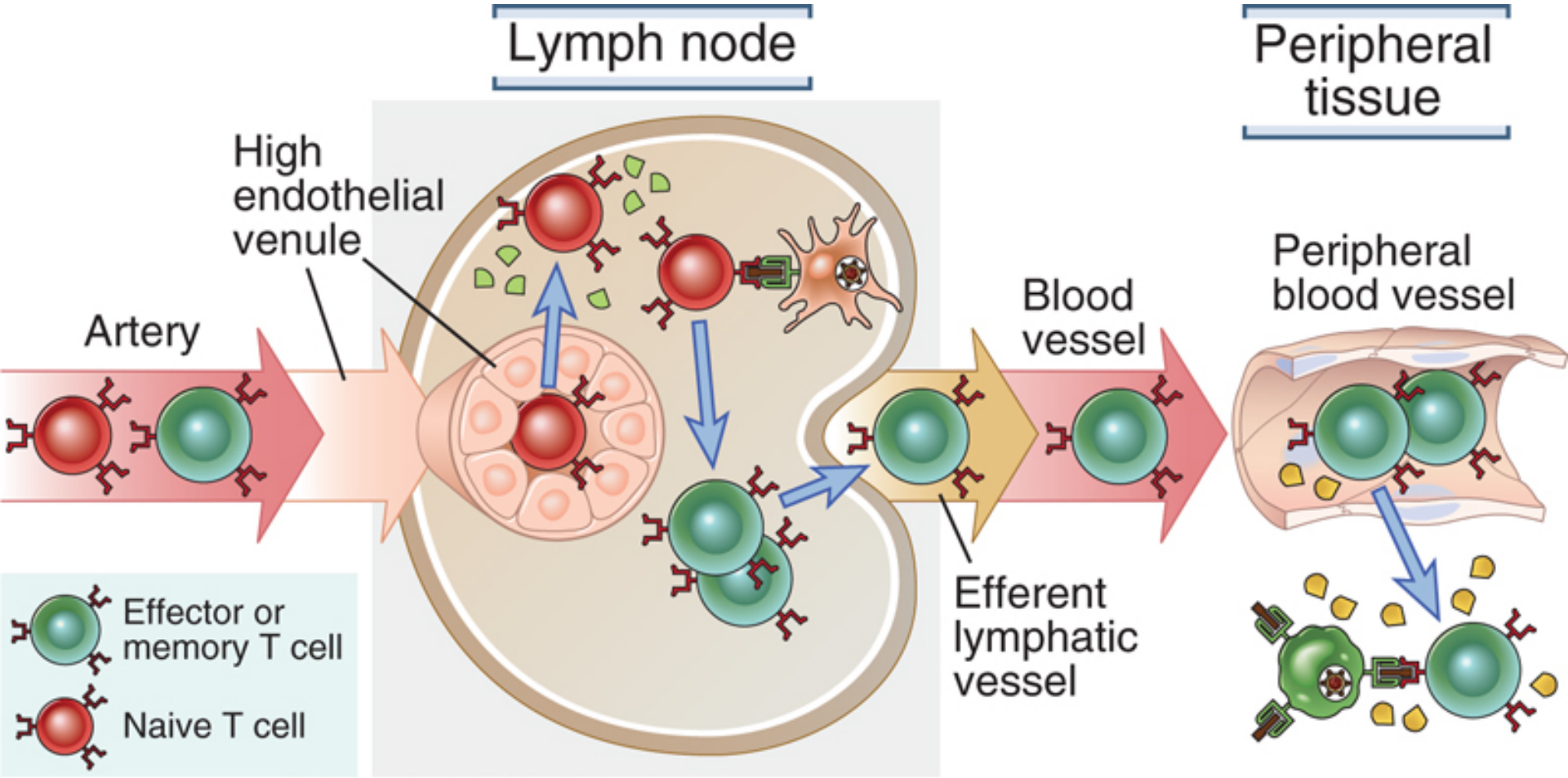
Migration of T lymphocytes



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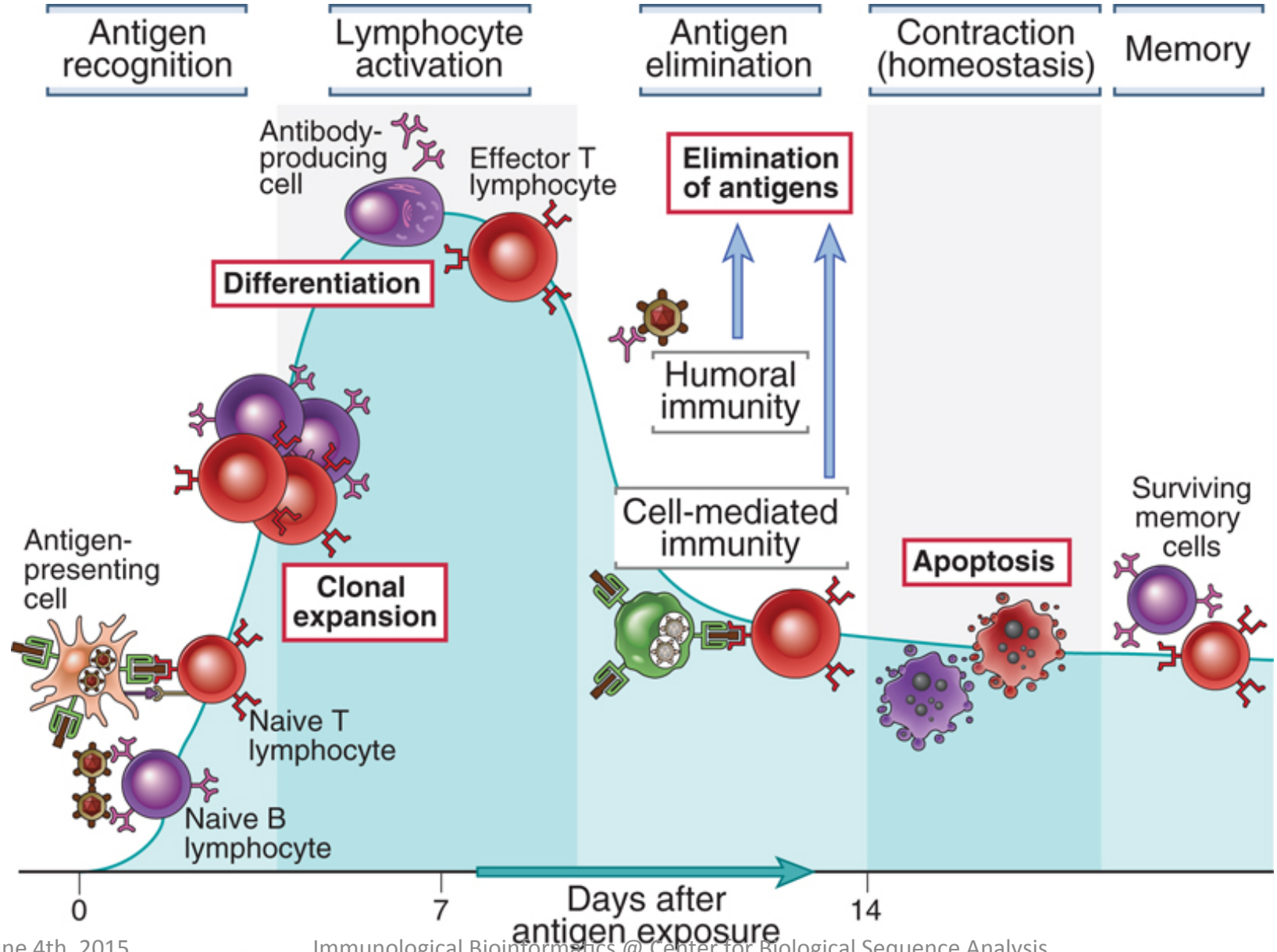
Innate immune responses

- Immediate
  - Barriers
  - Complement
- Early induced
  - Phagocytosis
  - Cytokine secretion
  - Inflammation
- Activate the adaptive immune system
  - APC migrate to regional lymph tissue
  - Makes antigen available to B & T cells
    - Signal 1 – antigen specific
  - Becomes stimulatory
    - Signal 2 – co-stimulation

Adaptive immune responses

- T helper cells respond to extracellular antigens
  - Orchestrates the immune response
  - Stimulate other immune cells (innate as well as adaptive)
  - Recruits immune cells
- Antibodies eliminate extracellular threats
  - Neutralize
  - Opsonize
  - Activate complement
- T cytotoxic cells eliminate intracellular threats
  - Detect intracellular threats
  - Neutralize / kills

Phases of adaptive immune response



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