

Immunology

Innate immunity

Adaptive immunity

Interaction with pathogens

Mammalian immune system

Physical barrier: Skin, mucus, low gastric pH

Innate as well as adaptive immune system

Innate: Quick response, not long-lasting

Adaptive: Slower response, long-lasting, memory

Innate immune system dominant system in plants, lower animals

Both innate and adaptive immune systems contain humoral and cell-based components

Comparison of innate and adaptive immunity

	Innate	Adaptive
Response time	Minutes to hours	Days
Specificity	Limited and fixed	Highly diverse, adapts to improve during the course of response
Response to repeat infection	Same each time	More rapid and effective with each subsequent exposure
Major components	Barriers, phagocytes, pattern recognition molecules	T and B lymphocytes, antibodies

Components of innate immune system

Cell-based

Macrophages
Natural killer cells
Dendritic cells
Polymorphonuclear lymphocytes
Granulocytes
Mast cells

Humoral

Complement system
Interferons
Cytokines

Initial recognition of pathogens

Recognition of Pathogen-Associated Molecular Patterns (PAMPs)

Cell wall components of bacteria (Lipopolysaccharides, Lipoarabinomannan)

Double-stranded RNA in viruses

Recognized by Pattern recognition receptors (PRRs)

Toll-like-receptors (TLRs)

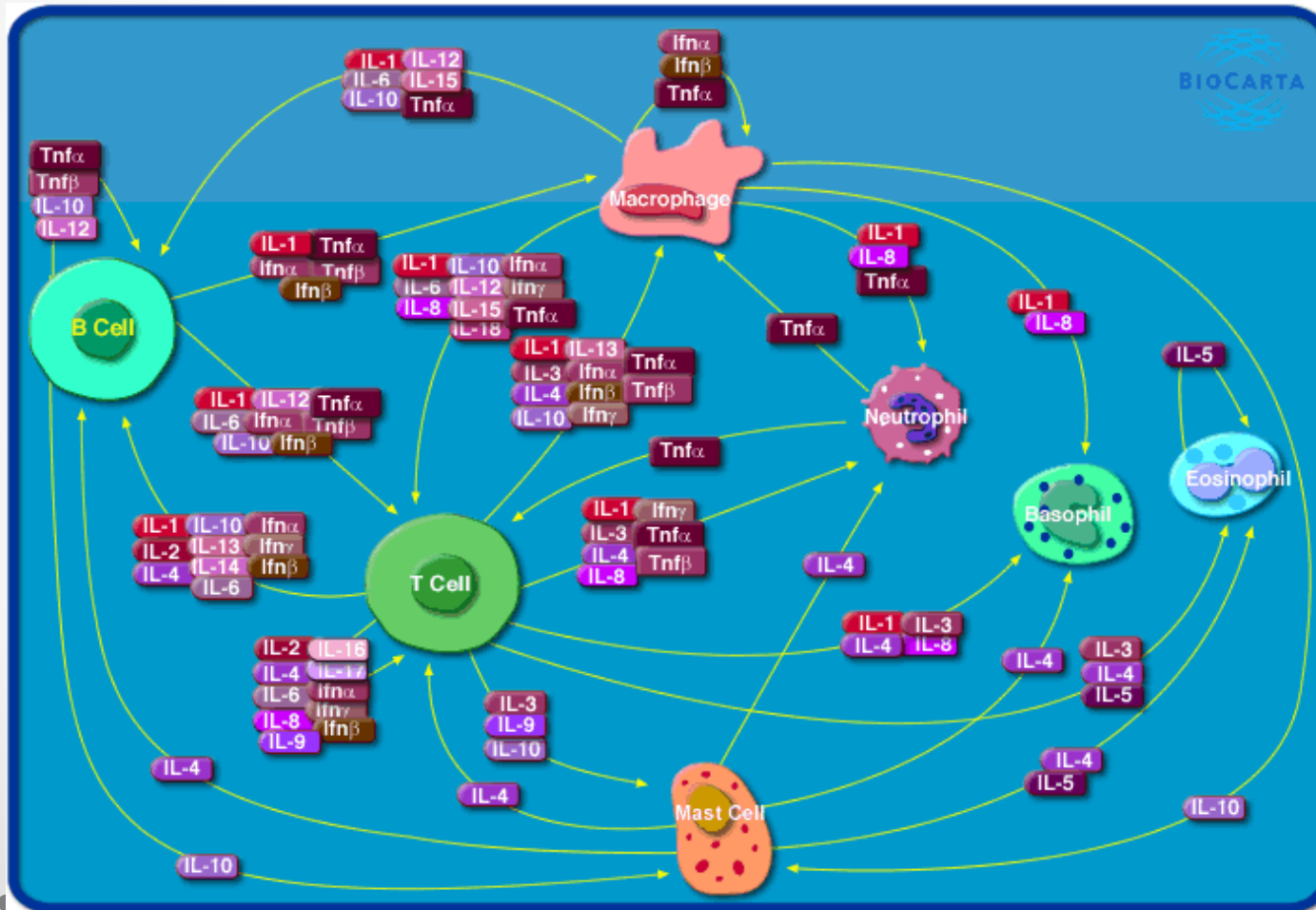
Initial recognition of pathogens by Toll-like receptors (TLRs)



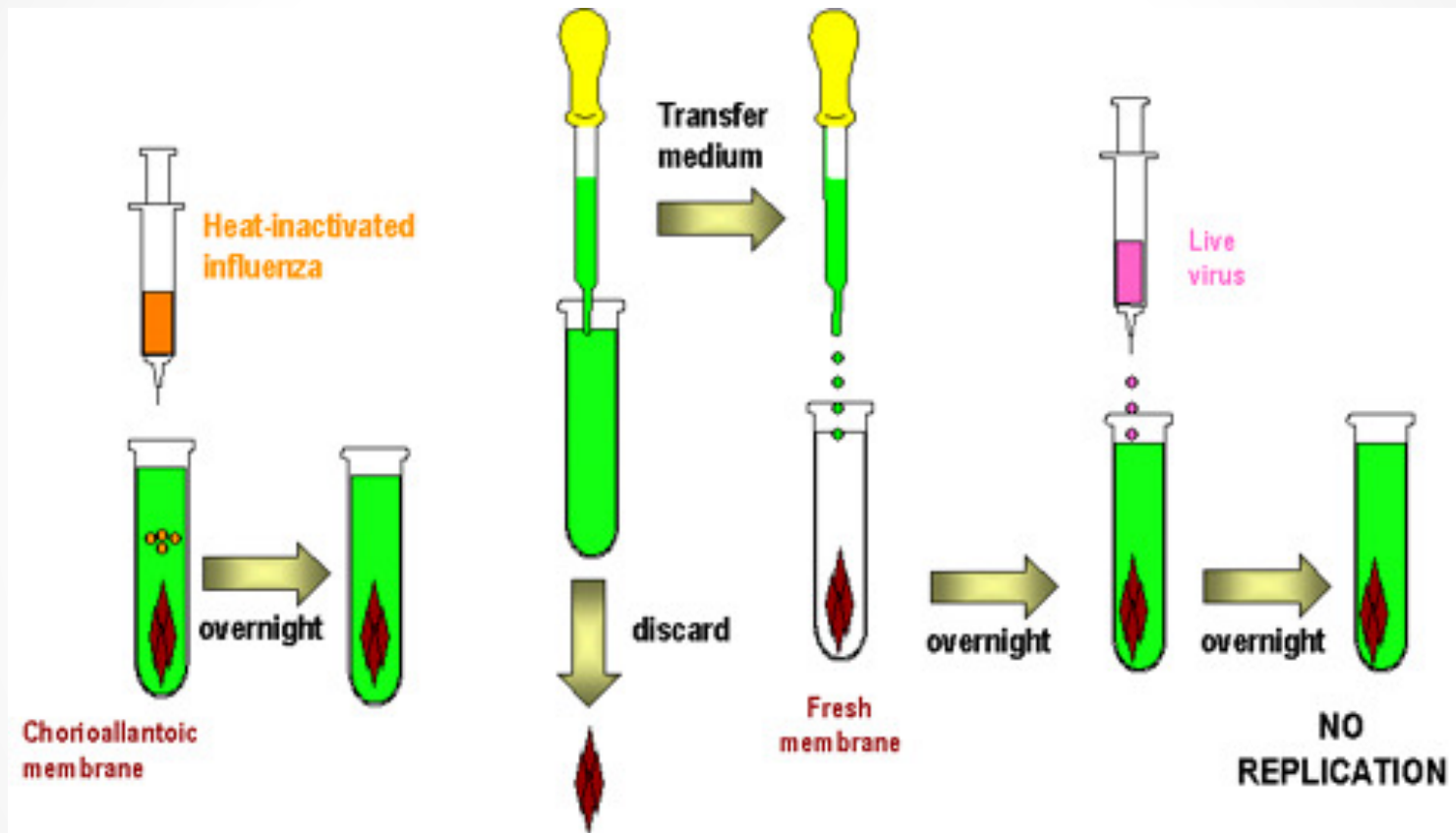
Leads to production of cytokines

Role of cytokines

Cytokines - Proteins/peptides that stimulate/inhibit inflammation, promote tissue repair, activate cells of immune system



Interferons set up anti-viral state



The Discovery of Interferon

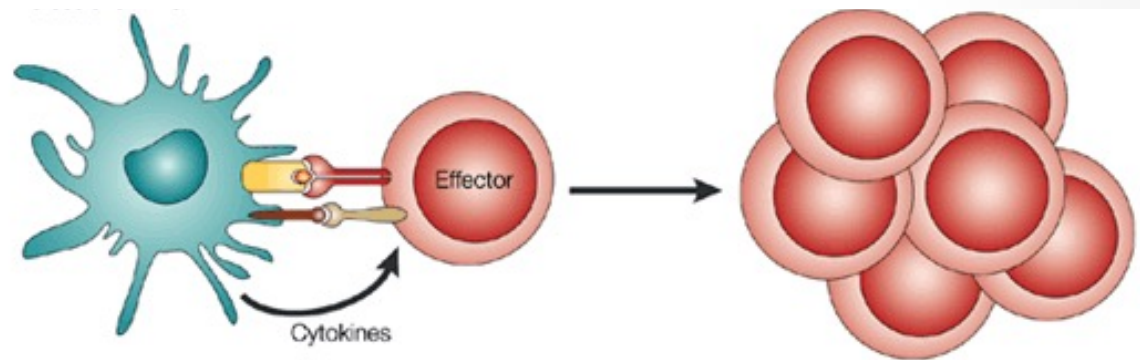
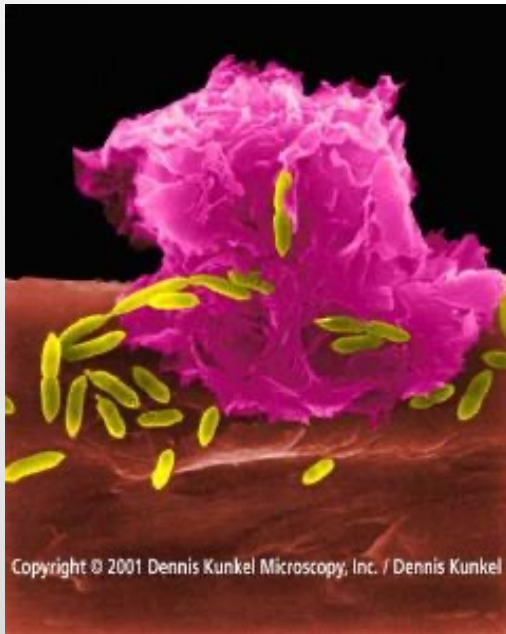
From Isaacs and Lindenmann, Proc. Roy Soc B, 1957

Cellular components of innate immune system

Macrophages, PMNL, Natural Killer cells

Can engulf bacteria/infected cells

Macrophages/dendritic cells present foreign antigens to B/T lymphocytes- Antigen presentation



Nature Reviews | Immunology

Components of adaptive immune system

Cell-based

B-lymphocytes (produce antibodies)
T-lymphocytes (helper and cytotoxic)

Humoral

Antibodies

Recognition of invading pathogen through “antigen”

Immune response tailored to suit the assault

Antigen - not only infectious material

Any “foreign” material

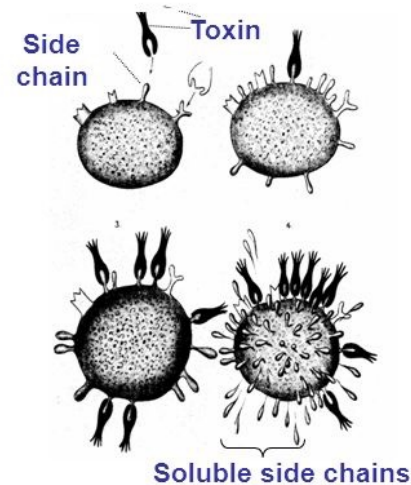
Distinction between “self” and “non-self”

Paul Ehrlich "Selective theory"

Modelle und Chemotherapie (Paul Ehrlich 1900)



- Ehrlich's Sidechain Theory (1900)
(Explains inducibility and specificity)
- Nobel price 1906
- First chemotherapy
(Salvarsan against Syphilis)



Division of Molecular Immunology, Universitätsklinikum Erlangen

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One B or T cell makes one type of receptor
Antigen binds one receptor, helps in proliferation

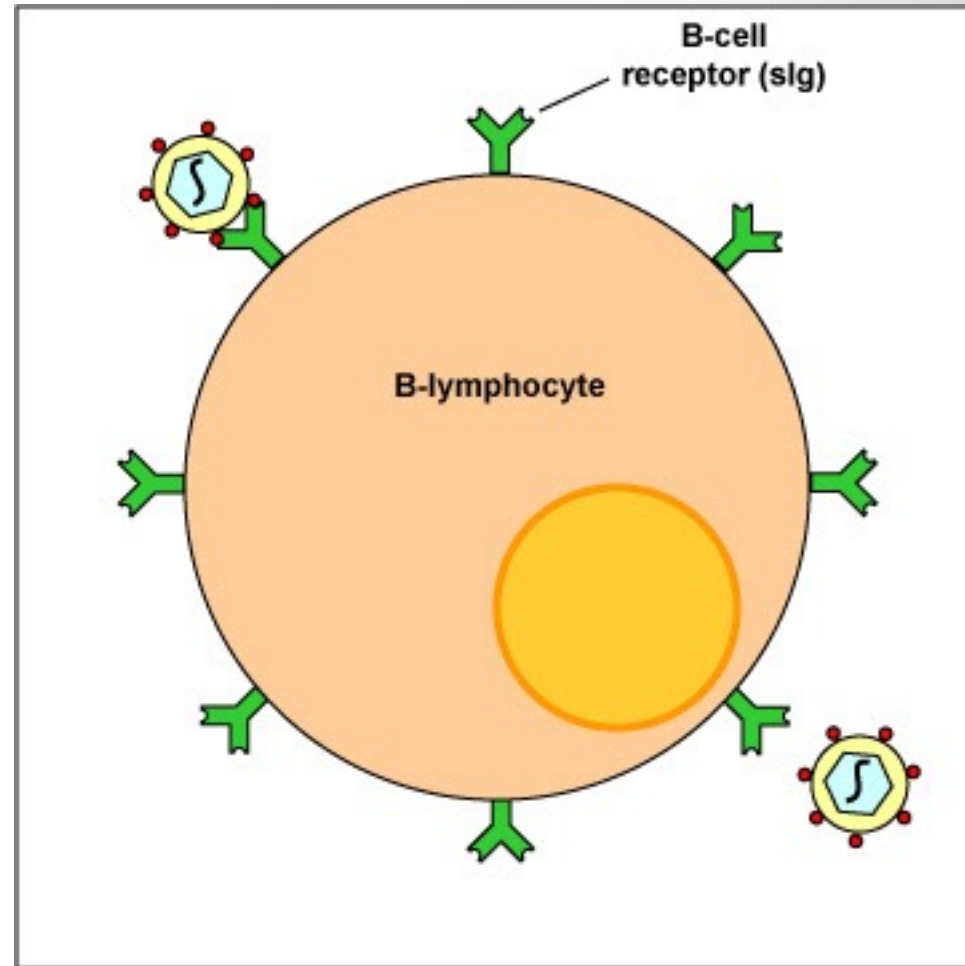
Components of adaptive immune system

B-lymphocytes

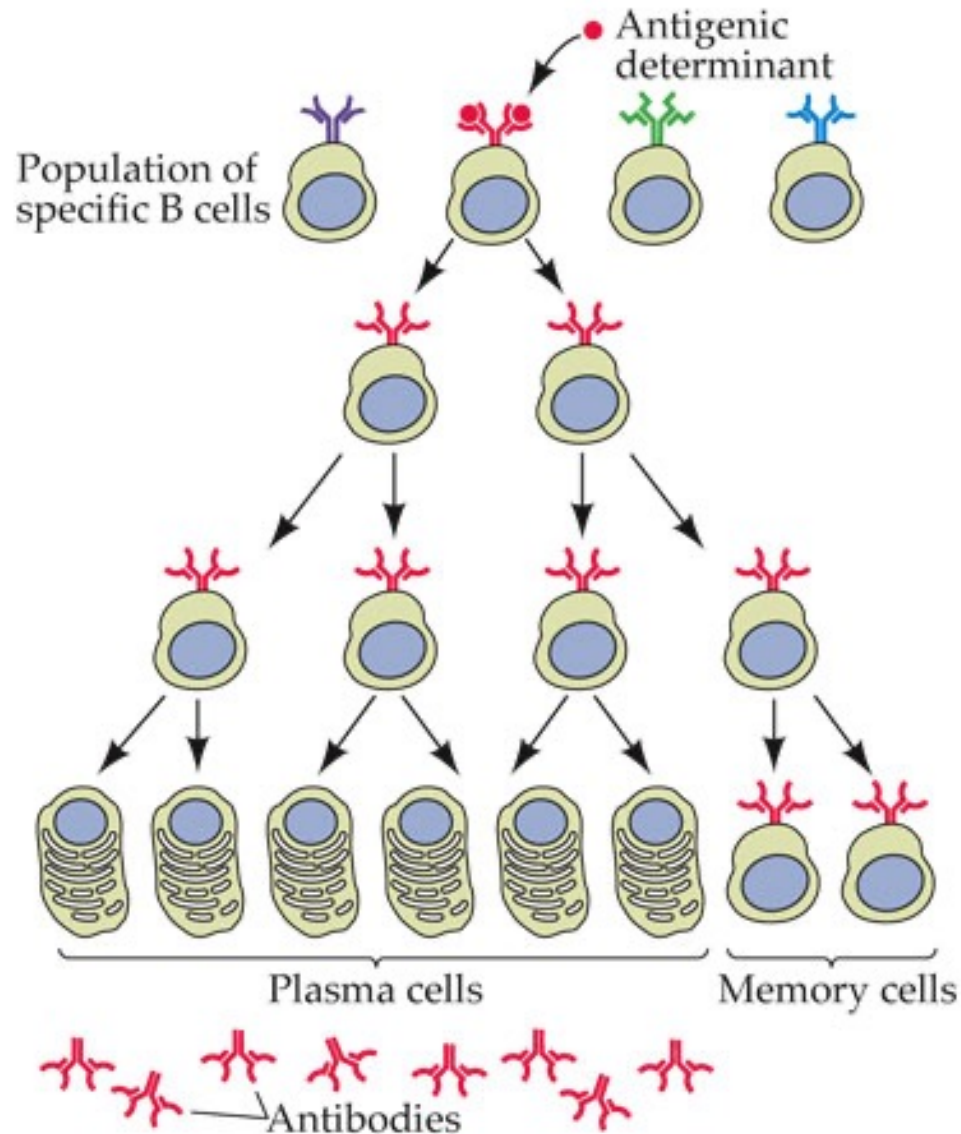
Produce antibodies

Each lymphocyte produces
one type of antibody or “receptor”

Theoretically able to bind any ligand

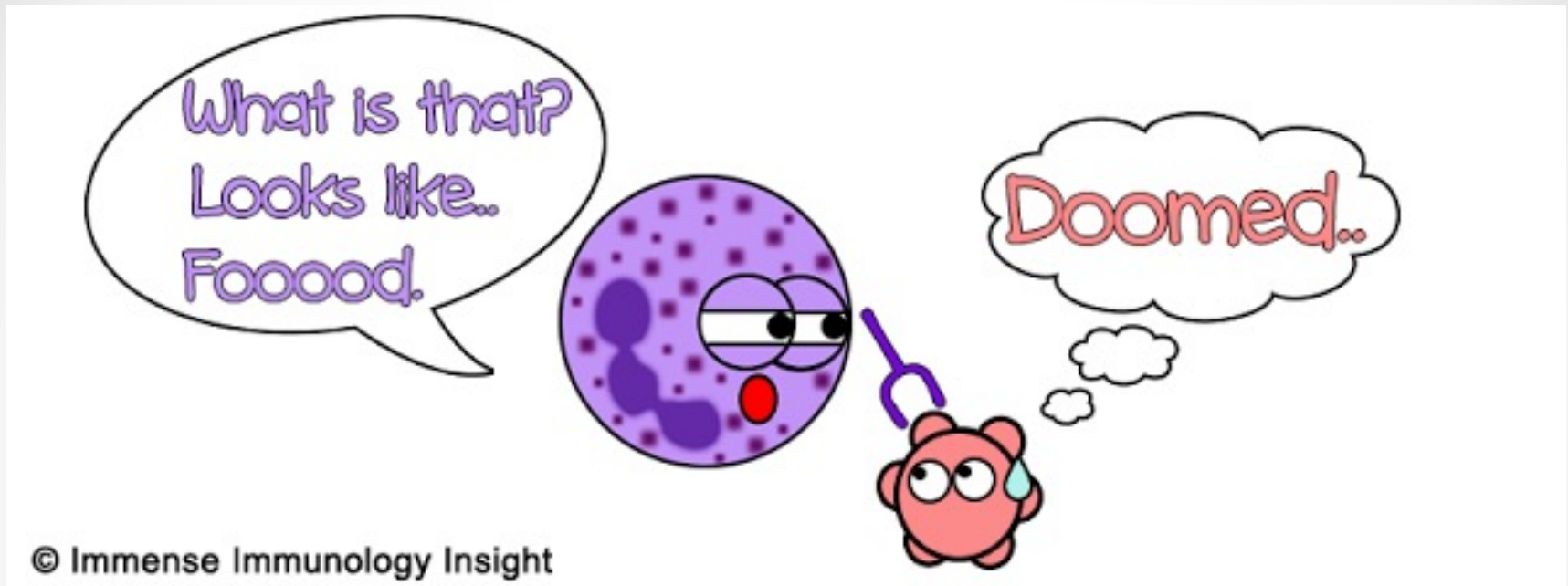


Clonal selection theory: Humoral Immunity (antibodies)



LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 18.7 Clonal Selection in B Cells
© 2004 Sinauer Associates, Inc. and W. H. Freeman & Co.

Components of adaptive immune system



Antibody binds to antigens on pathogen surfaces

Attracts phagocytic cells

Pathogen engulfed

Components of adaptive immune system

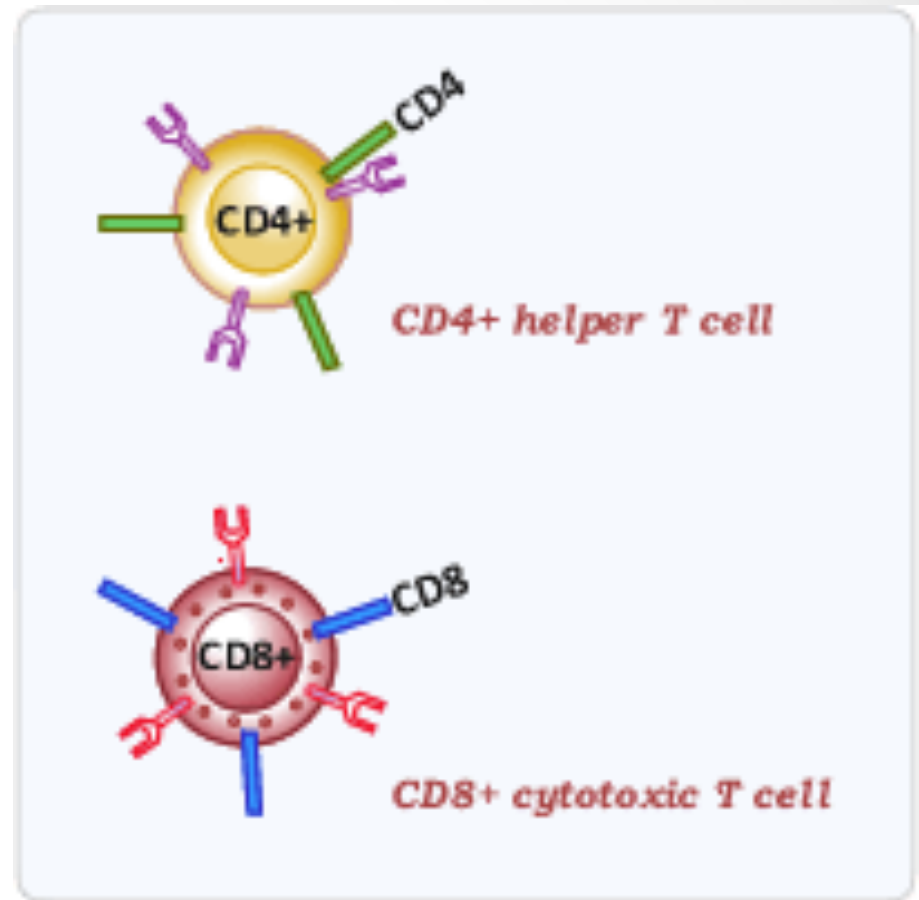
T-lymphocytes

1. CD4+/Helper T cells

Activates CD8+ cells

B-lymphocytes

Macrophages



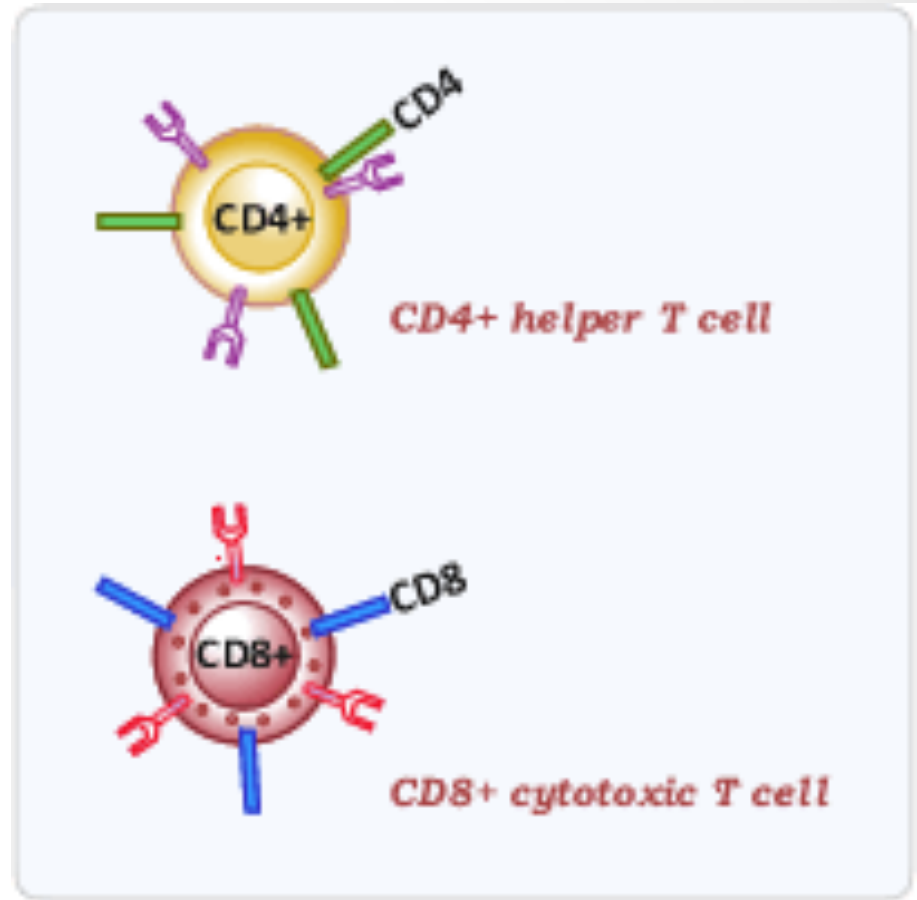
Components of adaptive immune system

T-lymphocytes

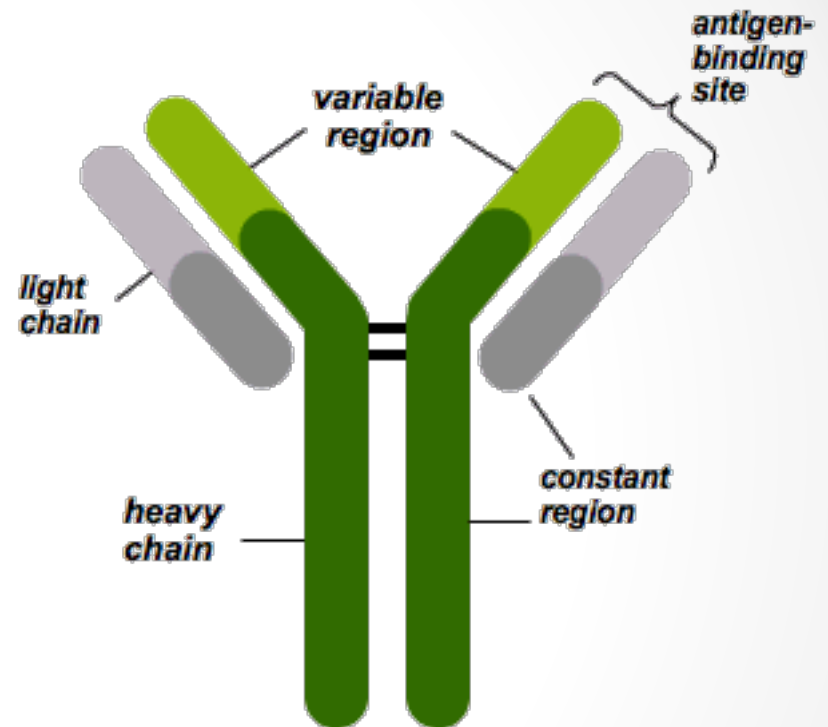
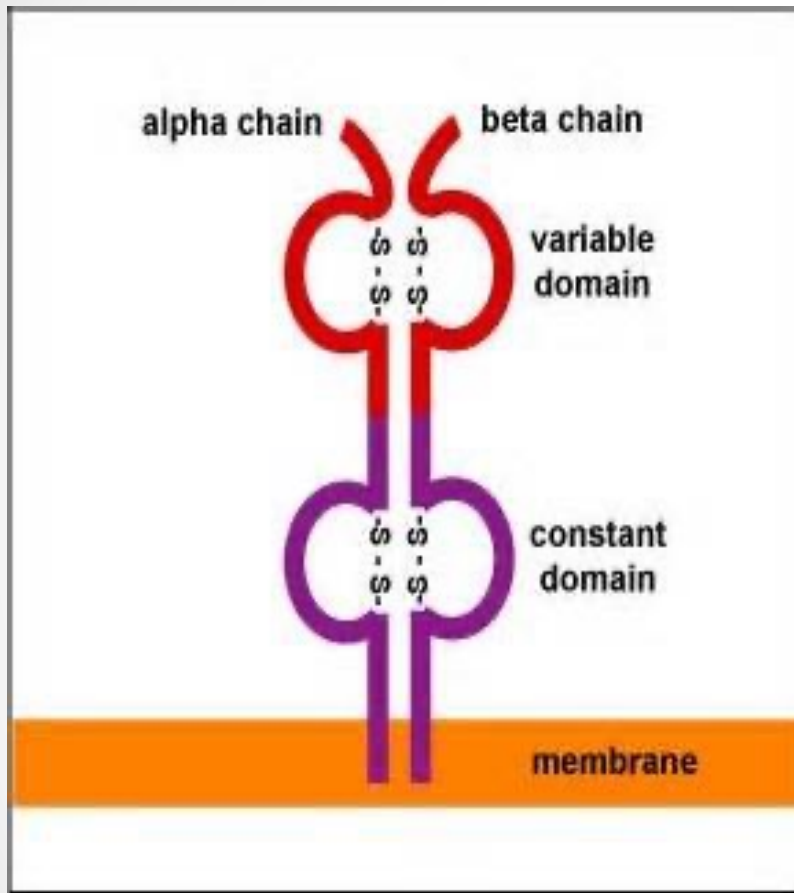
1. CD8+/Cytotoxic T cells

Kills infected cells

Major defense against viruses/
intracellular bacteria

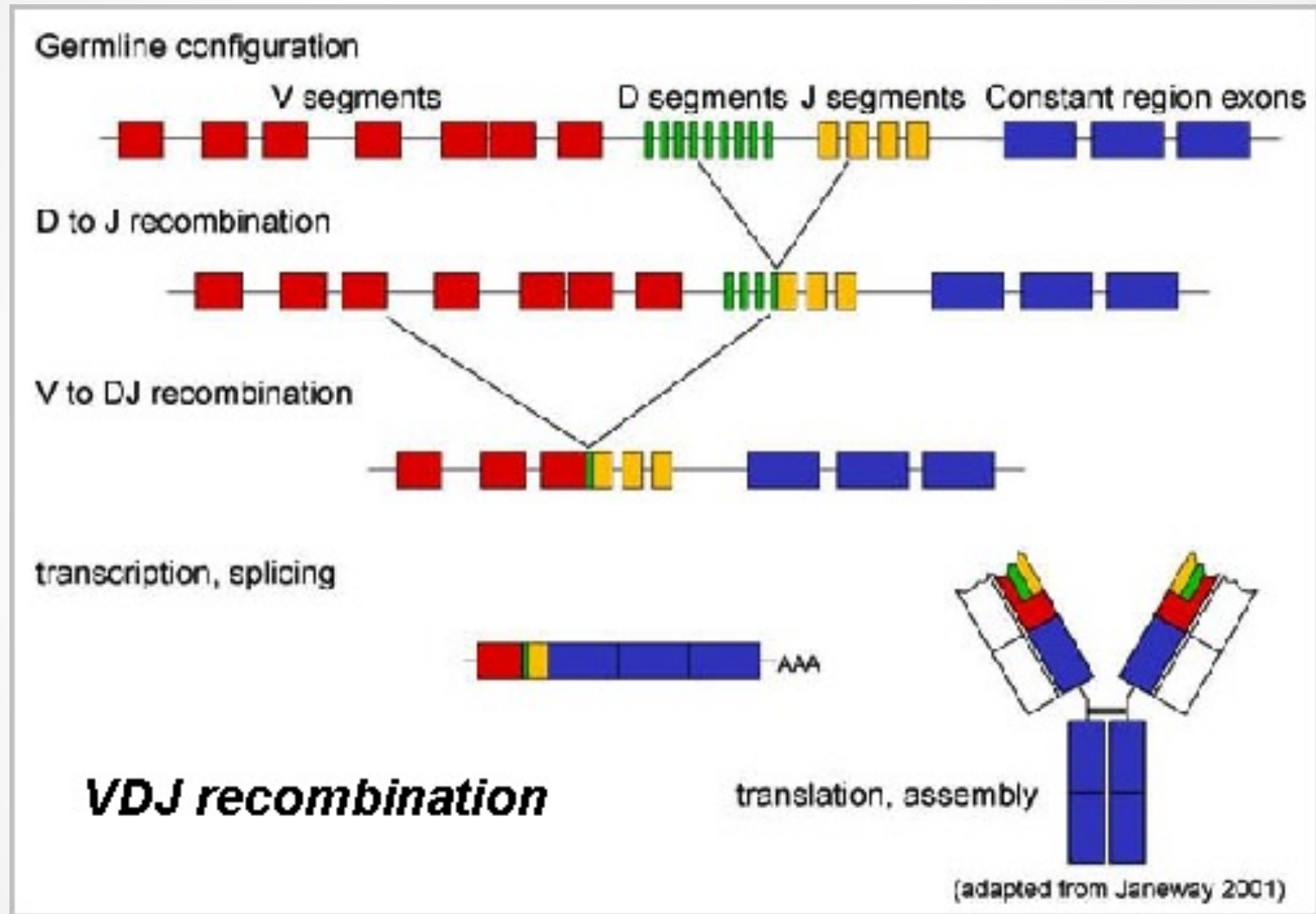


“Generation of Diversity” in B and T lymphocyte receptors



Schematic design of an Immunoglobulin (IgG)

“Generation of Diversity” in B and T lymphocyte receptors



“Generation of Diversity” in B and T lymphocyte receptors

Rearrangement and editing of genomic DNA

Happens in primary lymphoid organs (B cells - bone marrow, T cells - thymus)

Many B and T cells do not survive the recombination or quality control

Tolerance: Self-correction to ensure that “self” is not recognized as “non-self”

B and T lymphocytes are screened to ensure there is no recognition of “self”

Surviving cells move into circulation

Binding of antigen triggers clonal selection

B -cell receptors in secreted forms = Antibodies

T-cell receptors = no secreted forms

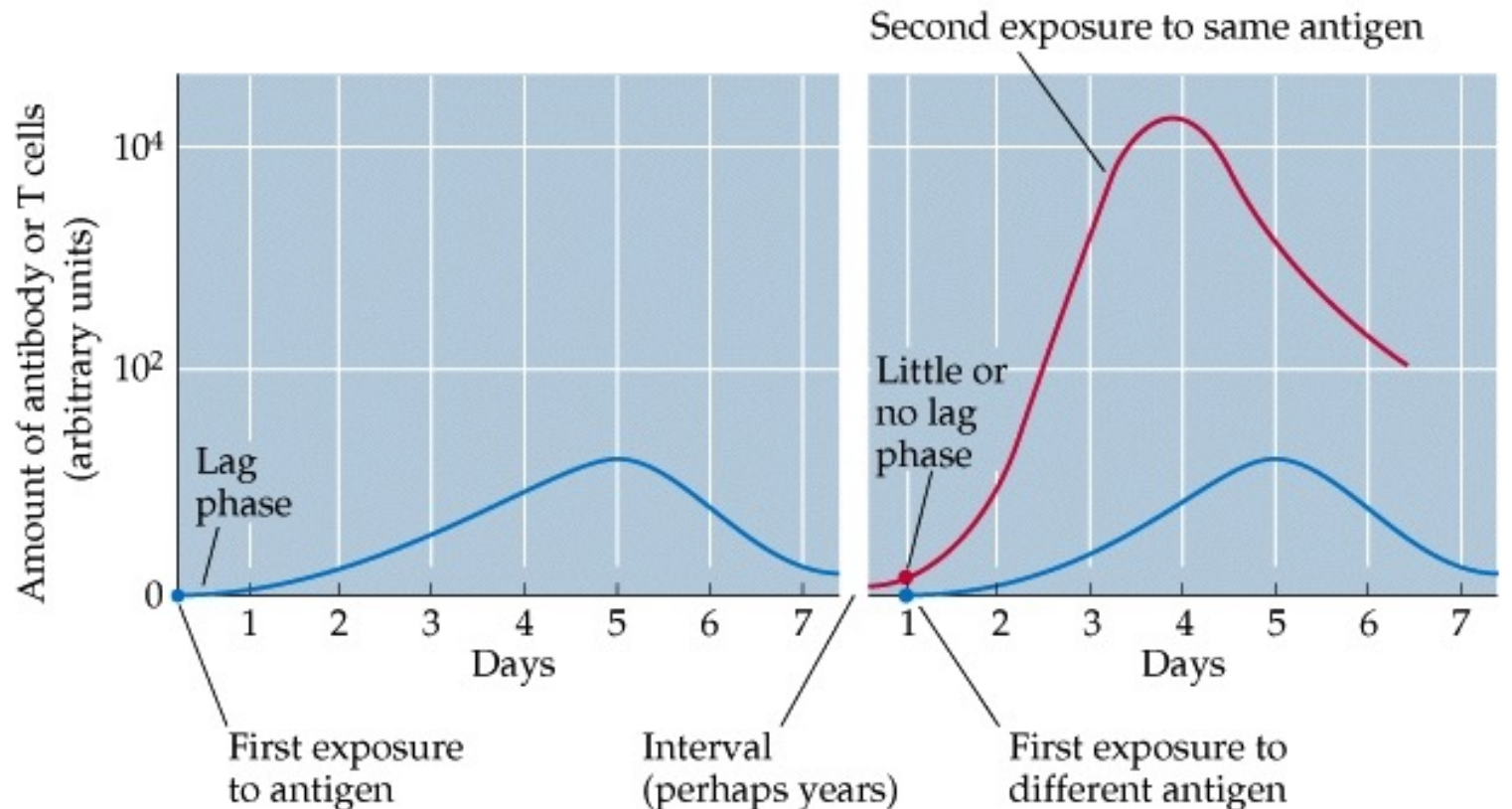
Required for recognition of “foreign” material presented by infected cells

Immunologic “memory”

Adaptive immune system generates “memory of antigen”

Can respond much more swiftly on subsequent exposures

No memory component of innate immunity



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Dysfunctional immune response

Hypersensitivity (Allergy etc.) : Attack on common, benign but foreign antigens

Autoimmune disease: Targeting of self by immune cells

Multiple sclerosis, Crohn's disease

Immune deficiency: Insufficiency of immune system to protect against pathogens

SCID, AIDS

Robust self-tolerance leads to ignorance of cancerous cells

Immune system and bacterial infections

Innate immune response

Recognition of molecular patterns

Lipopolysaccharide/lipoteichoic acid stimulate production of cytokines

Activates tissue macrophages

Innate immune cells present antigens to adaptive immune system

Extracellular bacterial infection leads to production of antibodies

Antibody-bacteria/antibody-toxin complexes phagocytosed

Cells infected with intracellular bacteria engulfed by CD8+ T-cells

Bacterial evasion of immune response

1. Alteration of surface antigens
2. Inhibition of cytokine/complement/antigen presentation
3. Blocking phagocytic cells/antibodies/T-cells

Immune system and viral infections

Barrier Immunity

Innate immunity - Involvement of Toll-like receptors

Recognition of ds RNA

Interferon generation, antiviral state

Adaptive immunity - Antibodies may bind to key viral structures

Interfere with ability of virus to enter host cells

Cell-mediated immunity is essential

T cell activity peaks after 7-10 days of infection

Eliminate sources of new virus

Viral evasion of immune response

- 1. Alteration of surface antigens**
- 2. Inhibition of cytokine/complement/antigen presentation**
- 3. Blocking phagocytic cells/antibodies/T-cells**
- 4. Immunosuppression and latency**