Why immunology?
Innate response

DR. Nadisha Badanasinghe

Senior Lecturer

Dept. of Medical Microbiology

UNIVERSITY OF KELANIYA

Objectives

- What is the importance of learning about immune system and it's responses?
  - Functions
  - Responses
  - Imbalance
    - Diseases
    - Disorders
  - Immune modulation
- Innate immune response

Basic Immunology

- Immune system
  - Components
  - Functions
- Immune responses
  - Innate
  - Adaptive
    - Humoral
    - Cell mediated

Clinical Immunology

- Disorders and dysfunctions of immune system
  - Hypersensitivity
  - Autoimmunity
  - Immune deficiency
  - Graft rejection

- How to modulate immune response
  - Immune enhancement
  - Immune suppression

Immune system Functions

- To protect against disease or other potentially damaging foreign bodies

- Can identify a variety of threats and distinguishes them from the body's own healthy tissue

Immune system

- The immune system is a network of
  - cells (neutrophils, macrophages, lymphocytes)
  - tissues /organs (bone marrow, thymus, lymph nodes, spleen)
  - molecules (cytokines, complements)

  that work together to defend the body against attacks by "foreign" invaders

Imbalance

- Leads to many diseases and disorders
  - Autoimmunity
  - Hypersensitivity
  - Chronic inflammatory disorders
  - Cancers
  - Immune deficiency

Immune modulation

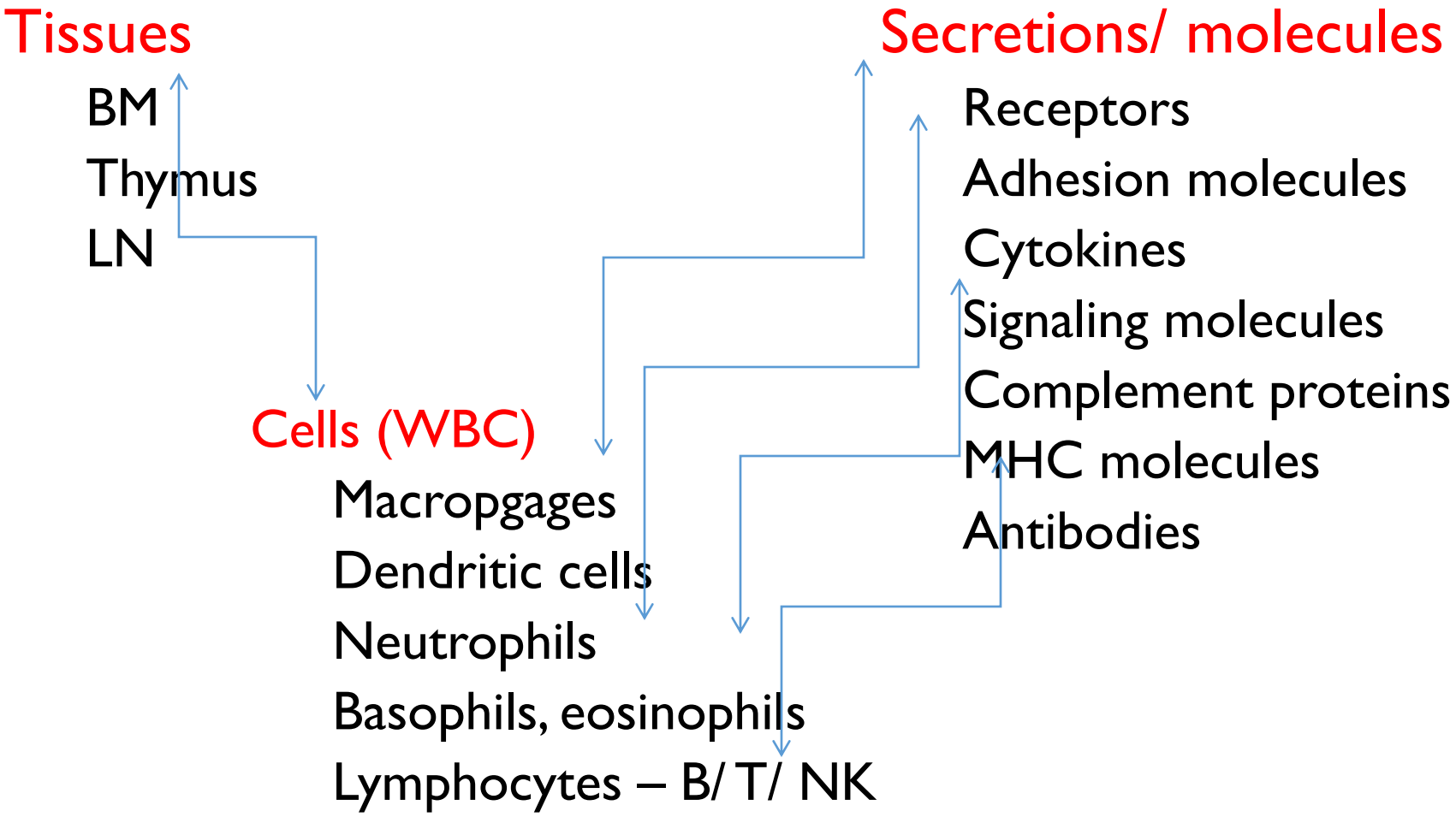
- For various diseases and disorders
  - Autoimmune diseases
  - Chronic inflammatory disorders
  - Prevention of graft rejection
  - Hypersensitivity
  - Graft Vs. host disease
  - Immune deficiency
  - Cancer Rx

Immune response

1) Innate immunity (Natural or Non specific)

2) Acquired immunity (Adaptive or Specific)

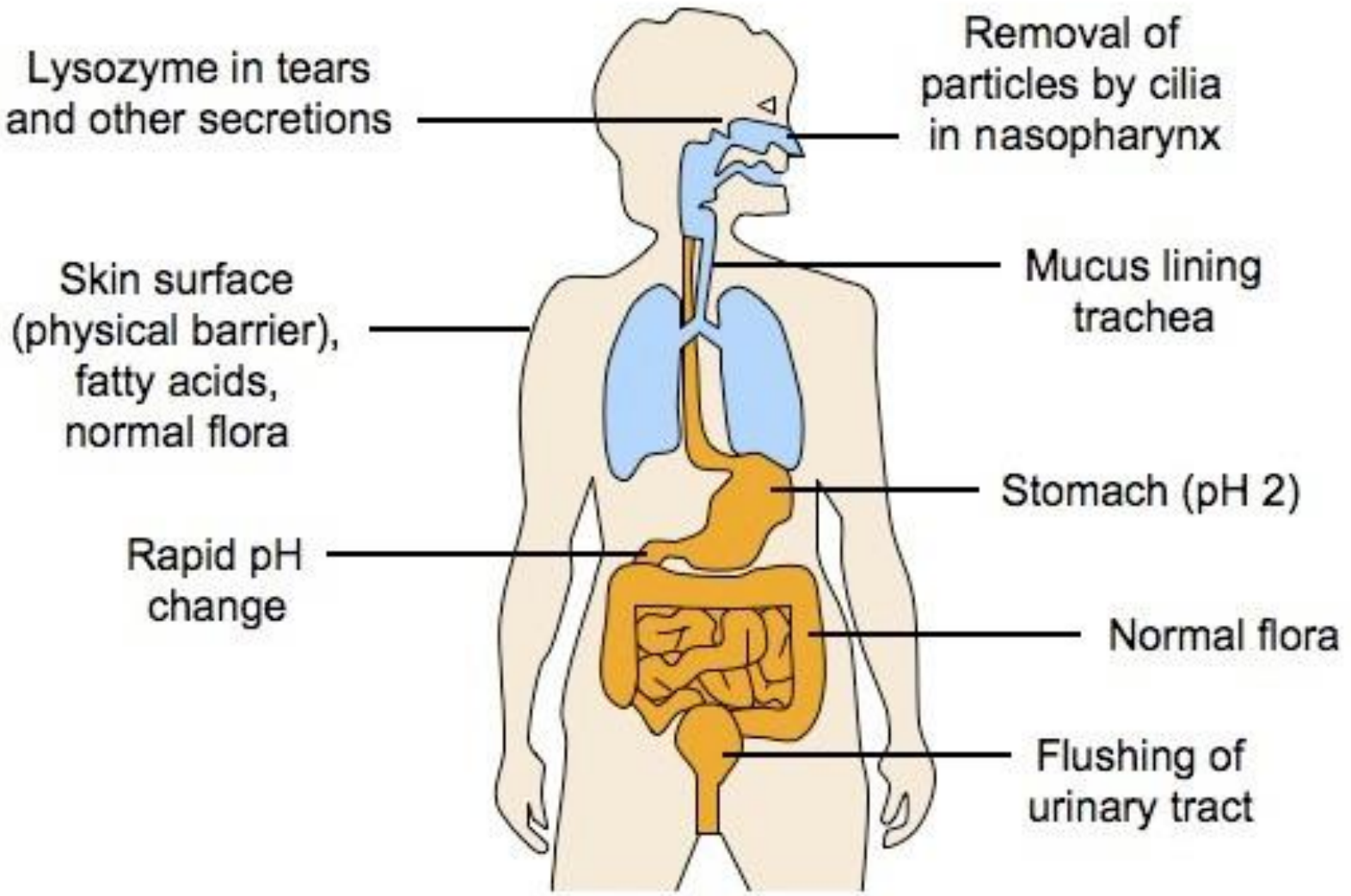
Nuts and Bolts



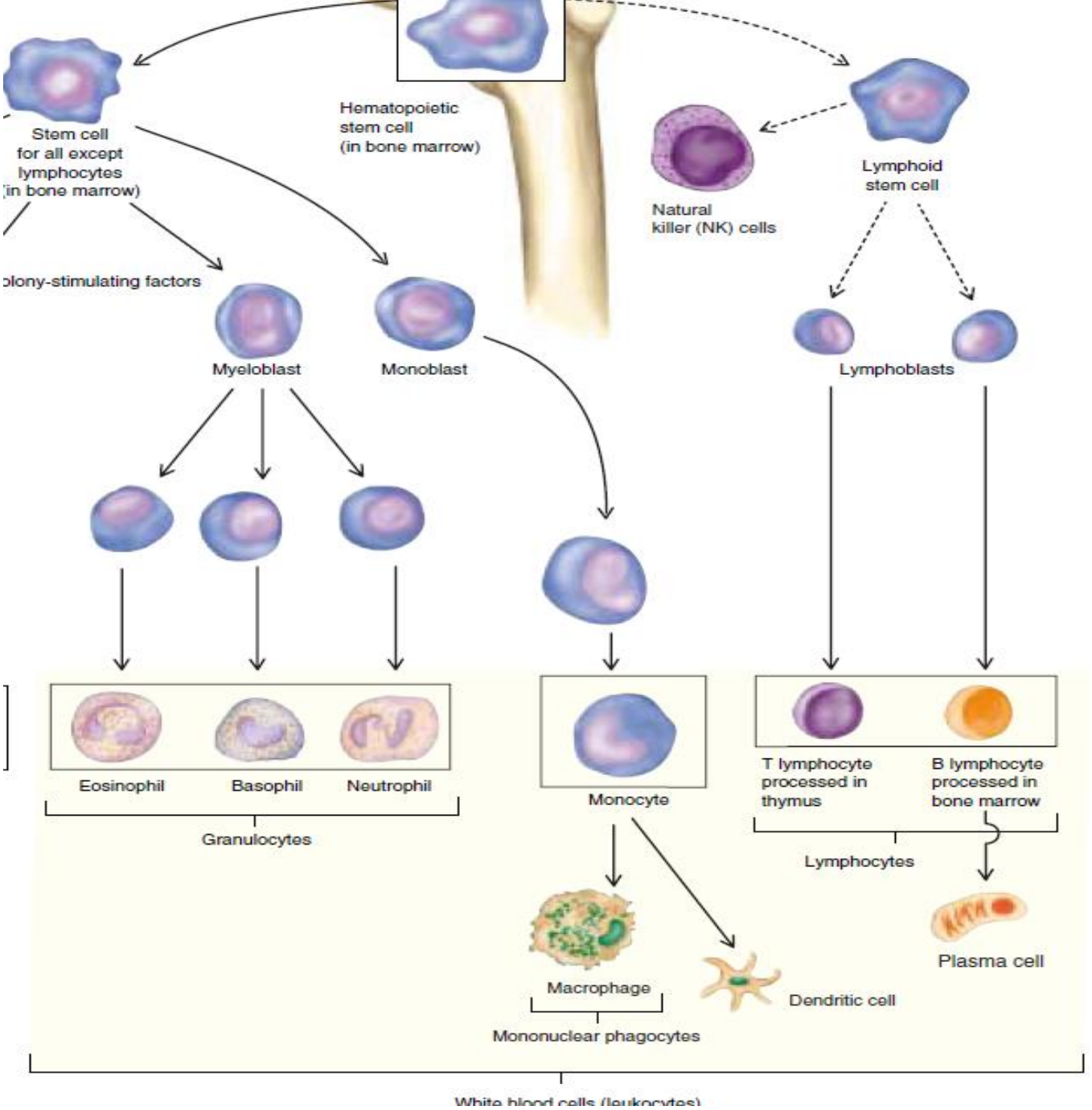
Innate Immune responses

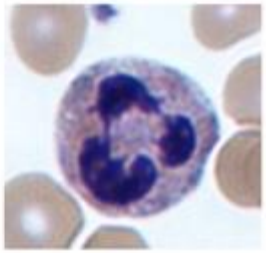
- Barriers
- Cells
- Molecules/ secretions

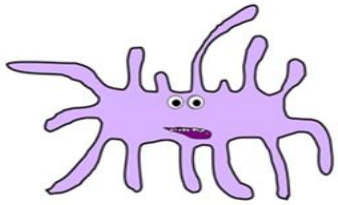
Barriers

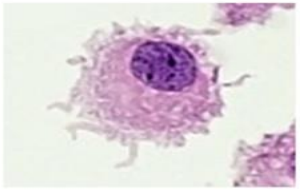

Lysozyme in tears and other secretions
Removal of particles by cilia in nasopharynx
Skin surface (physical barrier), fatty acids, normal flora
Mucus lining trachea
Stomach (pH 2)
Rapid pH change
Normal flora
Flushing of urinary tract

Cells


Hematopoietic
stem cell
(in bone marrow)
Stem cell
for all except
lymphocytes
(in bone marrow)
Natural
killer (NK) cells
Lymphoid
stem cell
olony-stimulating factors
Myeloblast
Monoblast
Lymphoblasts
Eosinophil
Basophil
Neutrophil
Granulocytes
Monocyte
T lymphocyte
processed in
thymus
B lymphocyte
processed in
bone marrow
Lymphocytes
Plasma cell
Macrophage
Dendritic cell
Mononuclear phagocytes
White blood cells (leukocytes)

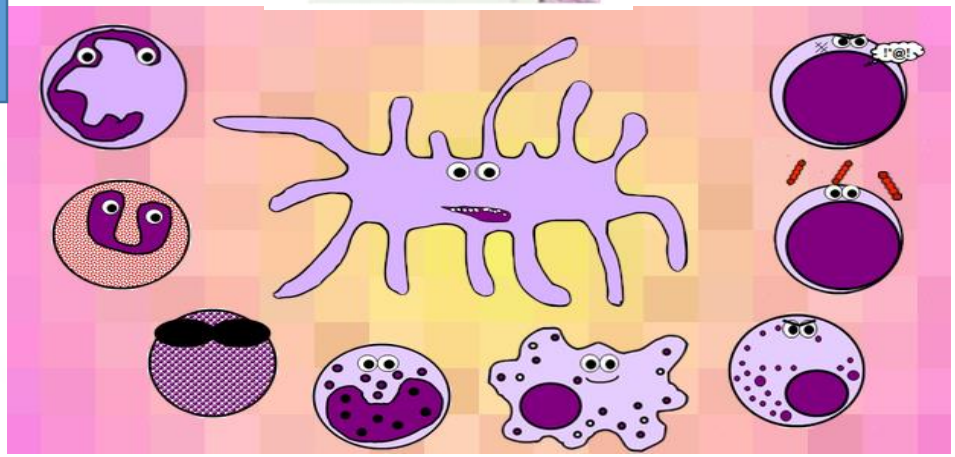


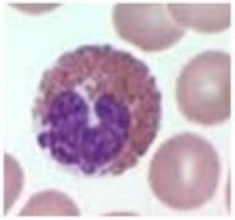


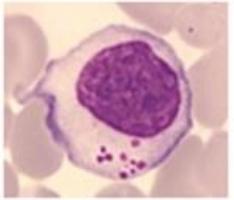


Dendritic cells

Neutrphils

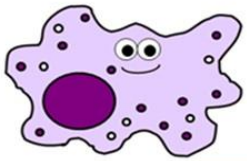


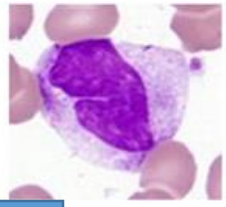


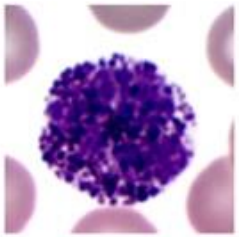


Eosinophiis

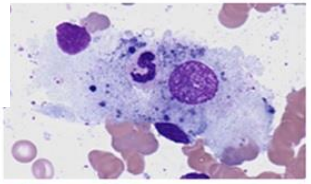
NK cells



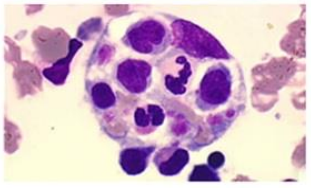




Monocyte

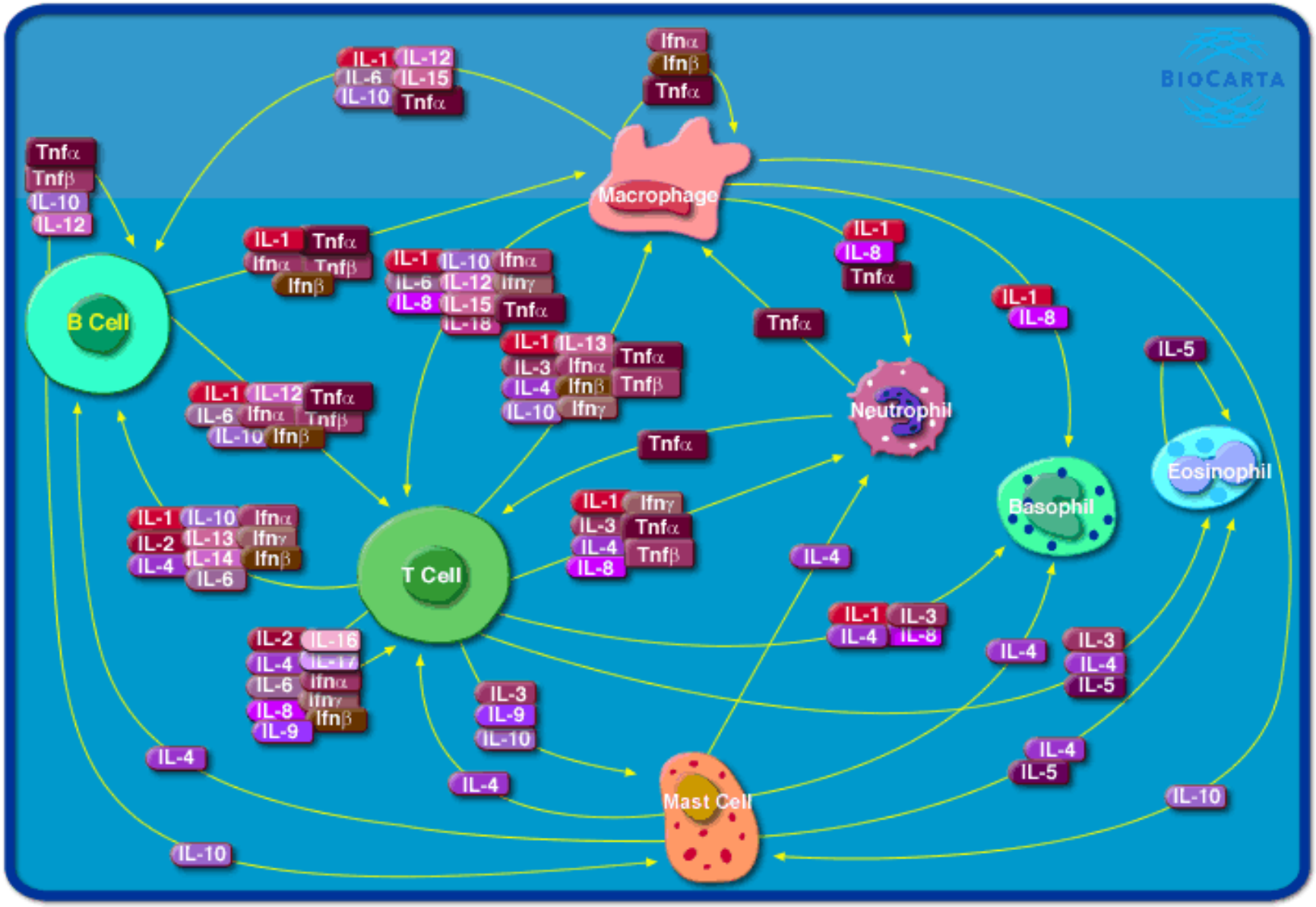


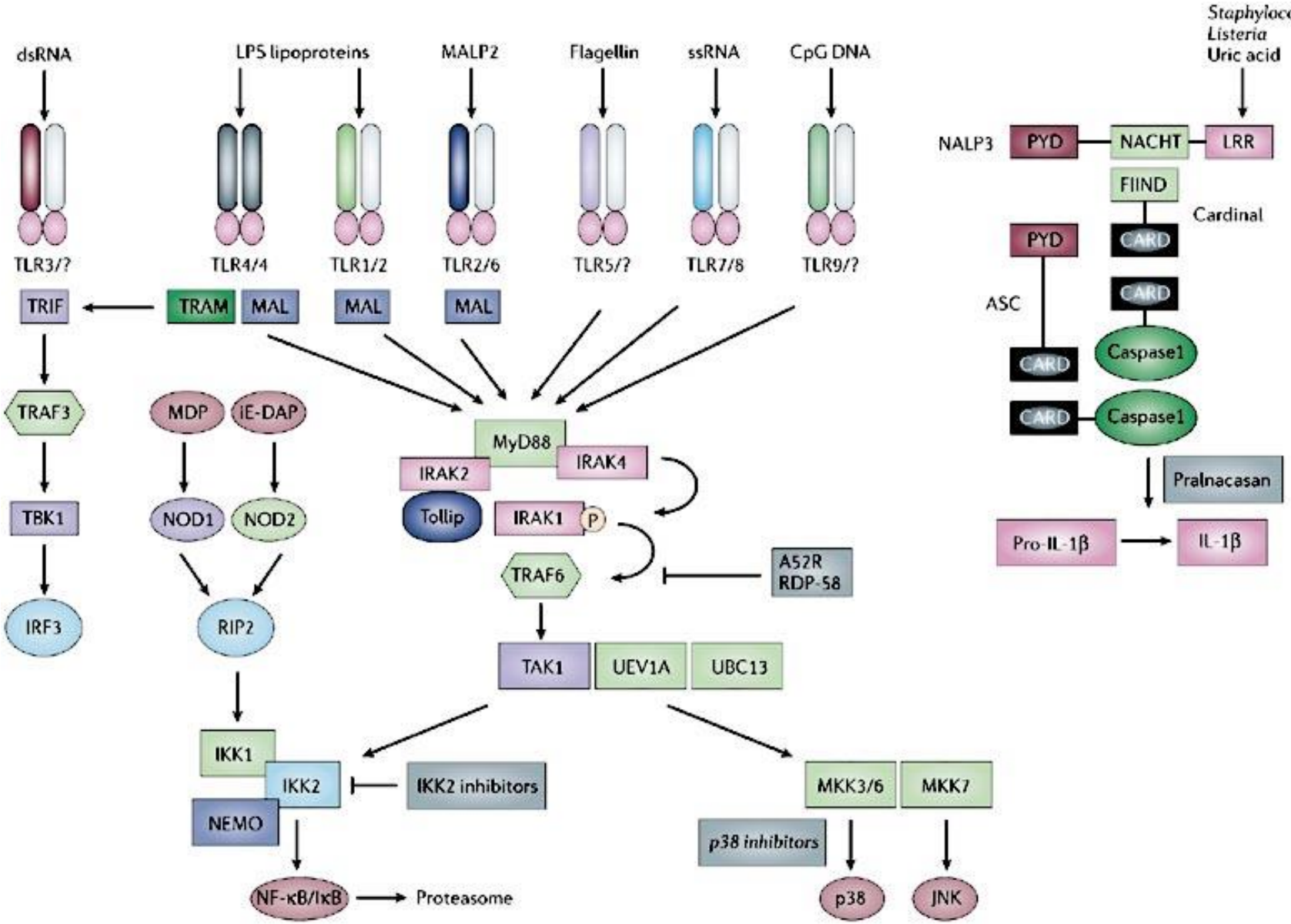
Tissue macrophages

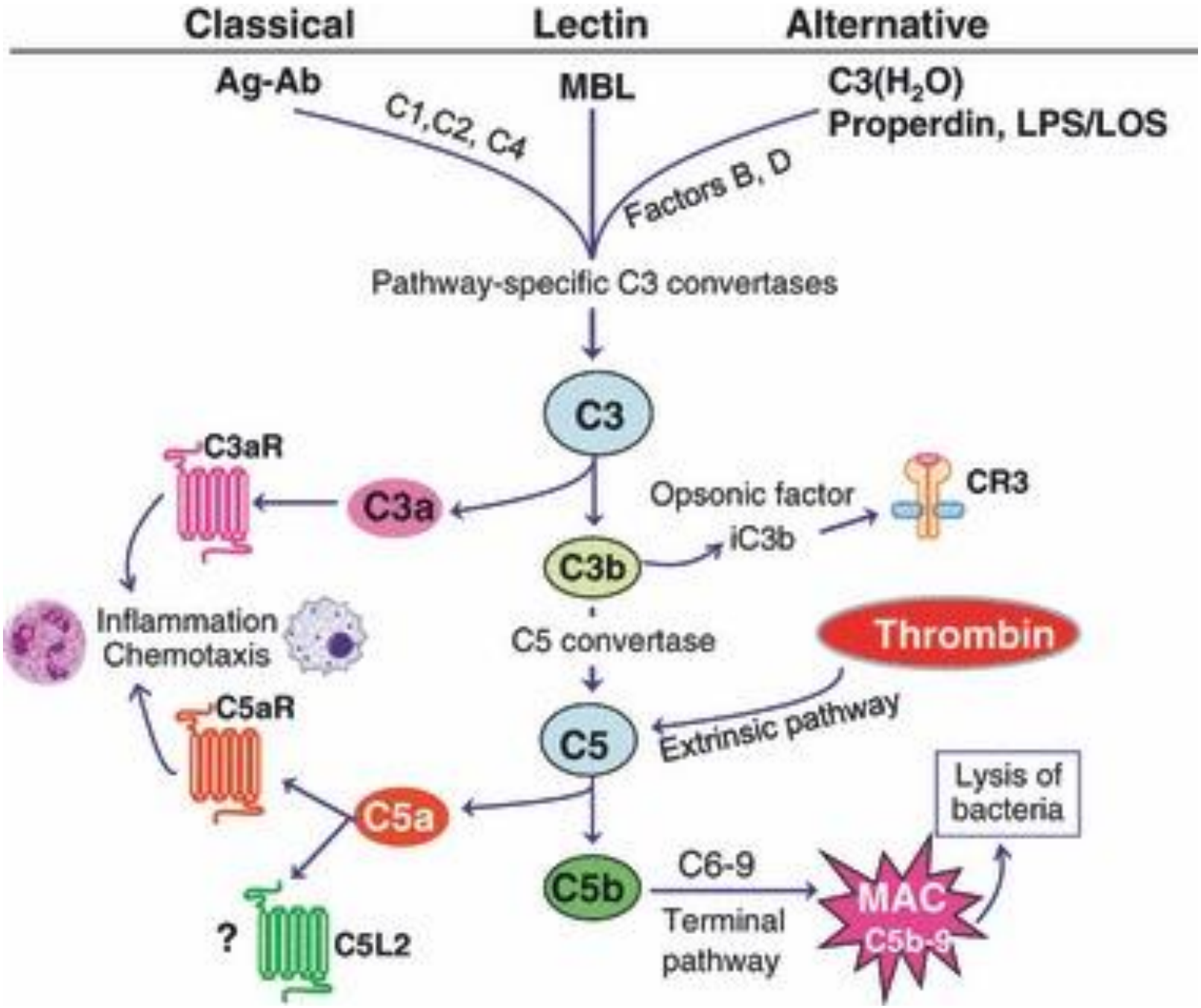


Basophils

Secretions


BioCarta
Macrophage
B Cell
T Cell
Neutrophil
Basophil
Eosinophil
Mast Cell
IL-1 IL-12 IL-6 IL-15 IL-10 Tnfα
Ifnα Ifnβ Tnfα
Tnfα Tnfβ IL-10 IL-12
IL-1 Tnfα Ifnα Tnfβ Ifnβ
IL-1 IL-10 Ifnα IL-6 IL-12 Ifnγ IL-8 IL-15 Tnfα IL-18
IL-1 IL-13 Tnfα IL-3 Ifnα IL-4 Ifnβ Tnfβ IL-10 Ifnγ
IL-1 IL-8 Tnfα
IL-1 IL-8
IL-5
Tnfα
IL-1 IL-12 Tnfα IL-6 Ifnα Tnfβ IL-10 Ifnβ
Tnfα
IL-1 Ifnγ IL-3 Tnfα IL-4 Tnfβ IL-8
IL-1 IL-10 Ifnα IL-2 IL-13 Ifnγ IL-4 IL-14 Ifnβ IL-6
IL-4
IL-1 IL-3 IL-4 IL-8
IL-2 IL-16 IL-4 IL-6 Ifnα IL-8 Ifnγ Ifnβ IL-9
IL-4
IL-3 IL-4 IL-5
IL-3 IL-9 IL-10
IL-4
IL-4 IL-5
IL-4
IL-10
IL-10

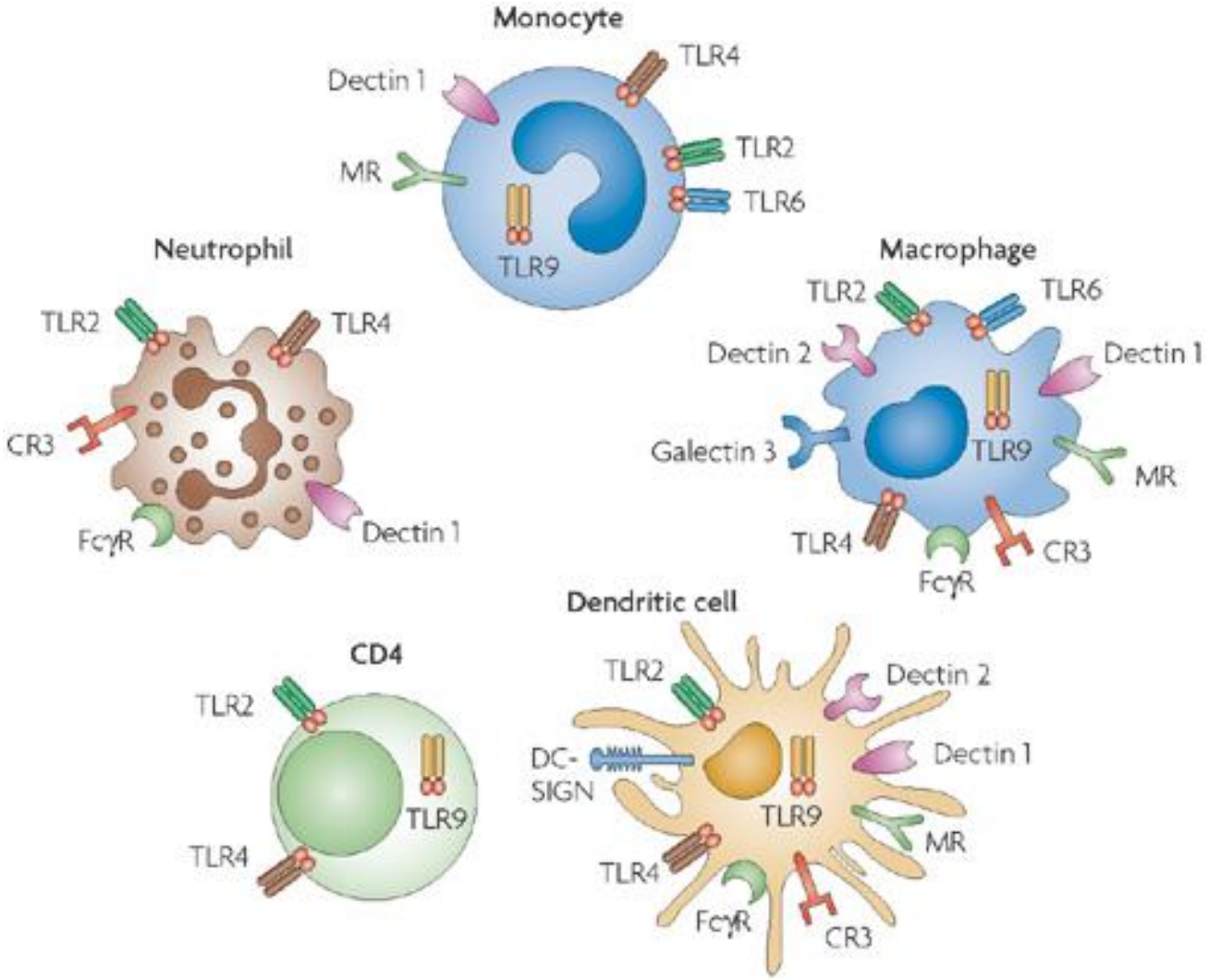



Classical
Lectin
Alternative
Ag-Ab
MBL
C3(H2O)
Properdin, LPS/LOS
C1,C2, C4
Factors B, D
Pathway-specific C3 convertases
C3
C3aR
C3a
Opsonic factor
iC3b
CR3
C3b
Inflammation
Chemotaxis
C5 convertase
Thrombin
C5aR
C5
Extrinsic pathway
Lysis of bacteria
C5a
C6-9
C5b
MAC
C5b-9
Terminal pathway
?
C5L2

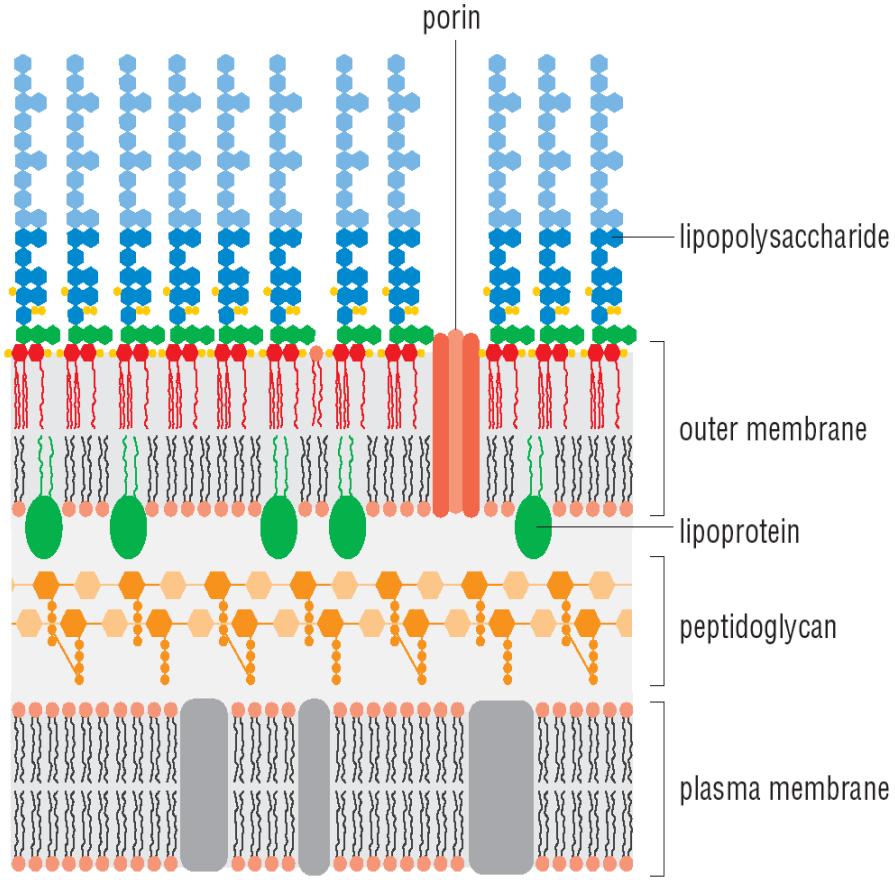
Innate immune response

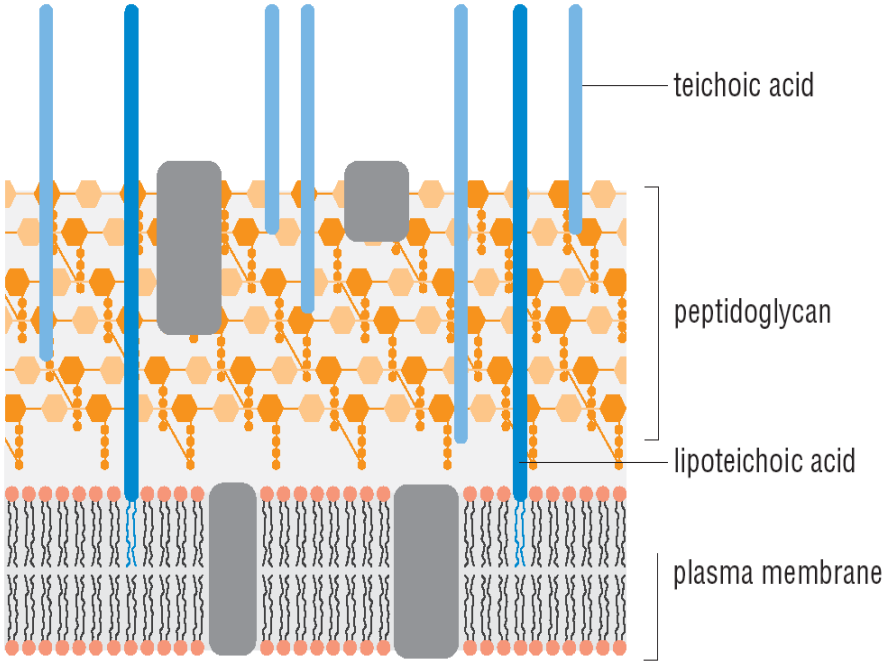
- Recognition
- Activation
- Elimination

Recognition by innate cells

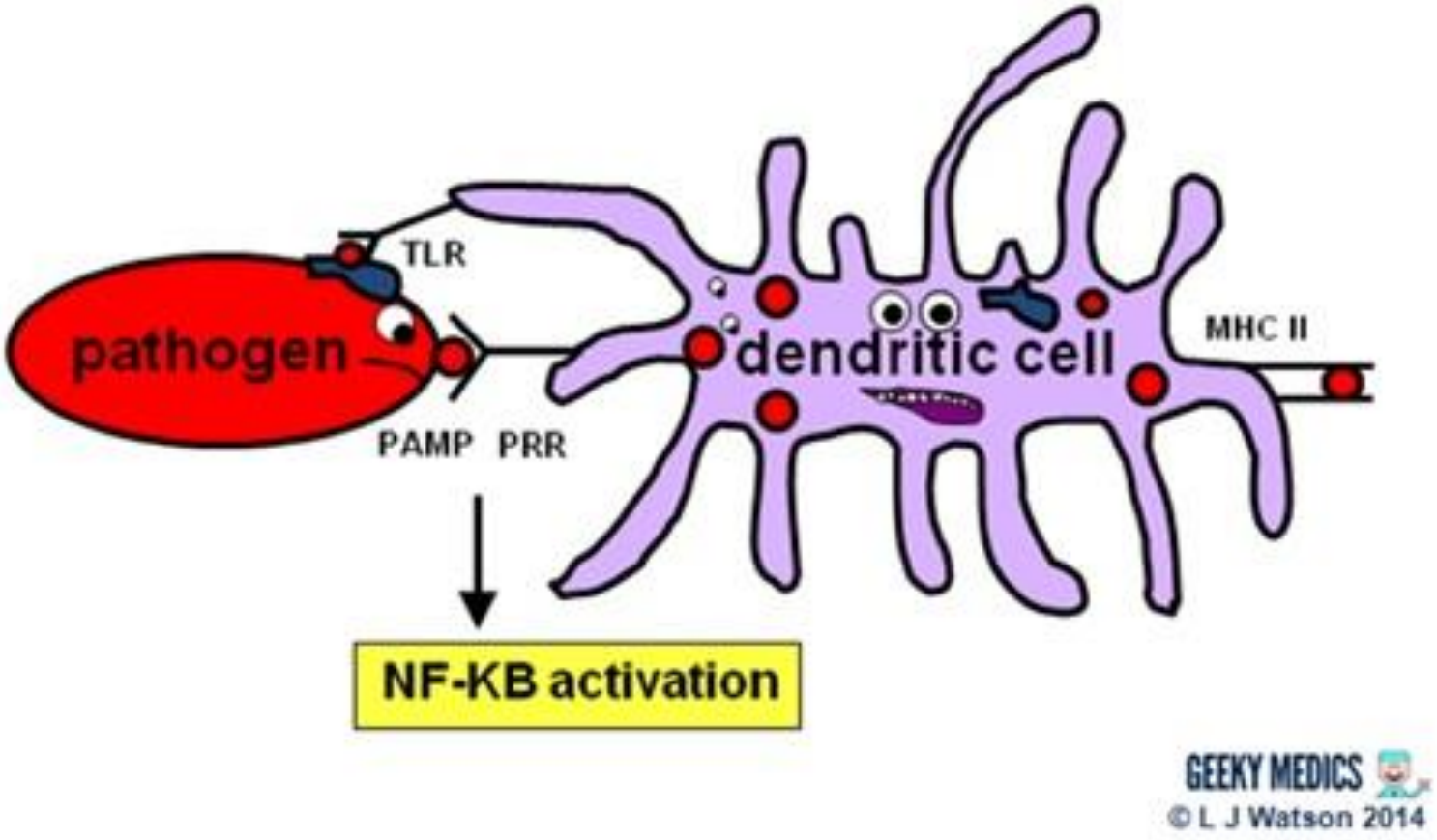


Innate immune recognition of bacterial cell wall components (PAMPS)

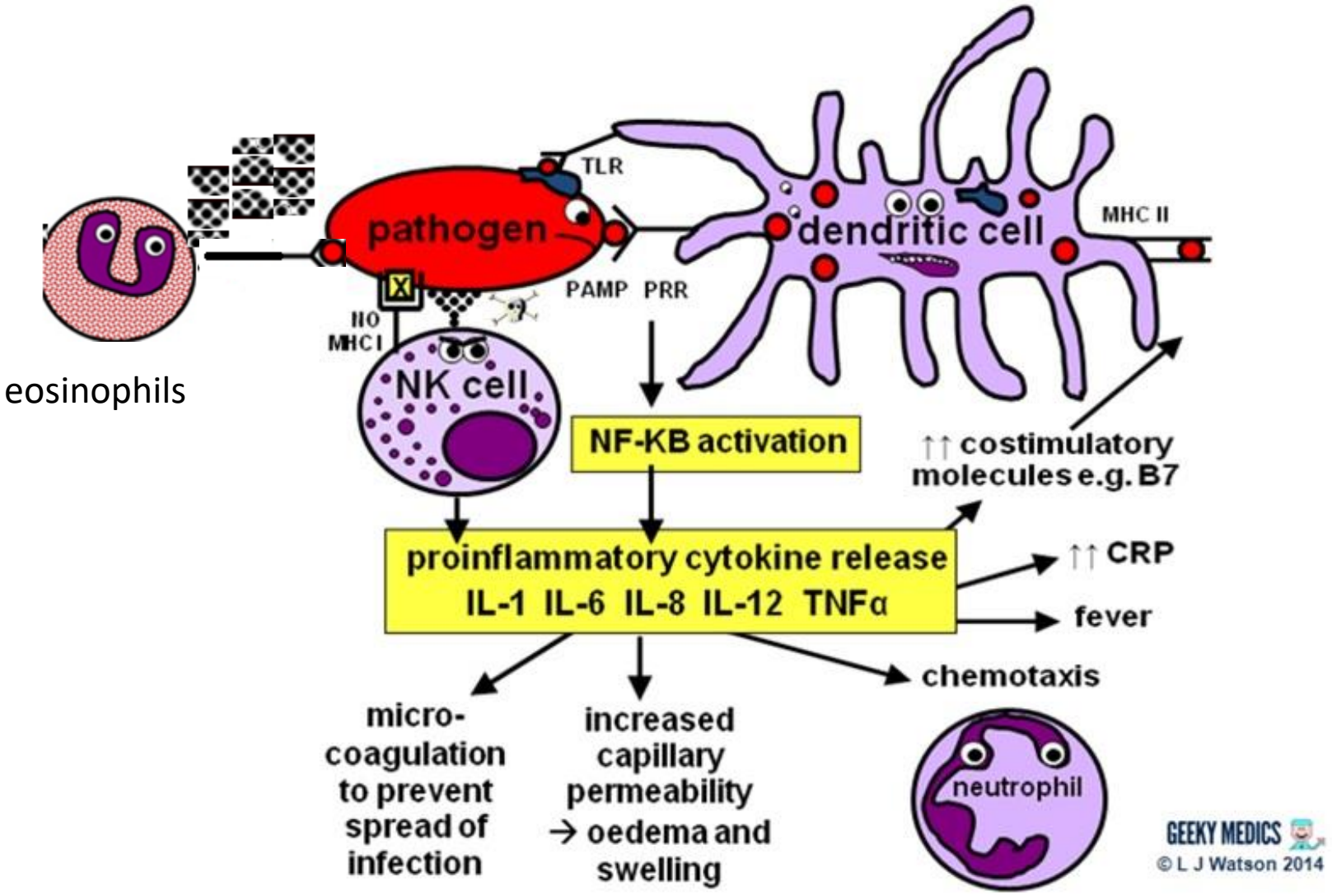




Dendritic cell



Activation


eosinophils
pathogen
TLR
PAMP
PRR
dendritic cell
MHC II
X
IIO
MHC I
NK cell
NF-KB activation
↑↑ costimulatory molecules e.g. B7
proinflammatory cytokine release
IL-1 IL-6 IL-8 IL-12 TNFα
↑↑ CRP
fever
chemotaxis
micro-coagulation to prevent spread of infection
increased capillary permeability → oedema and swelling
neutrophil
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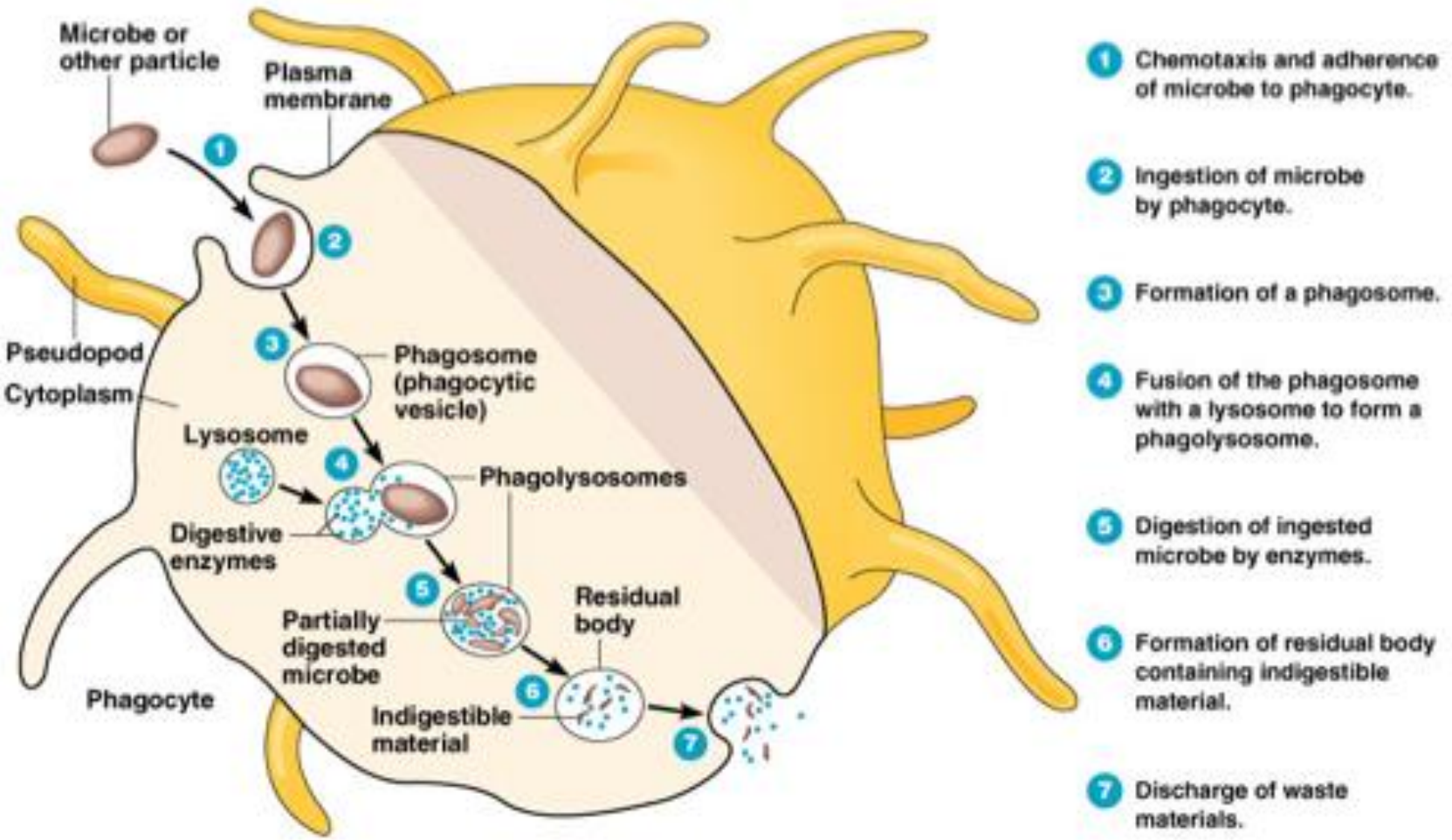
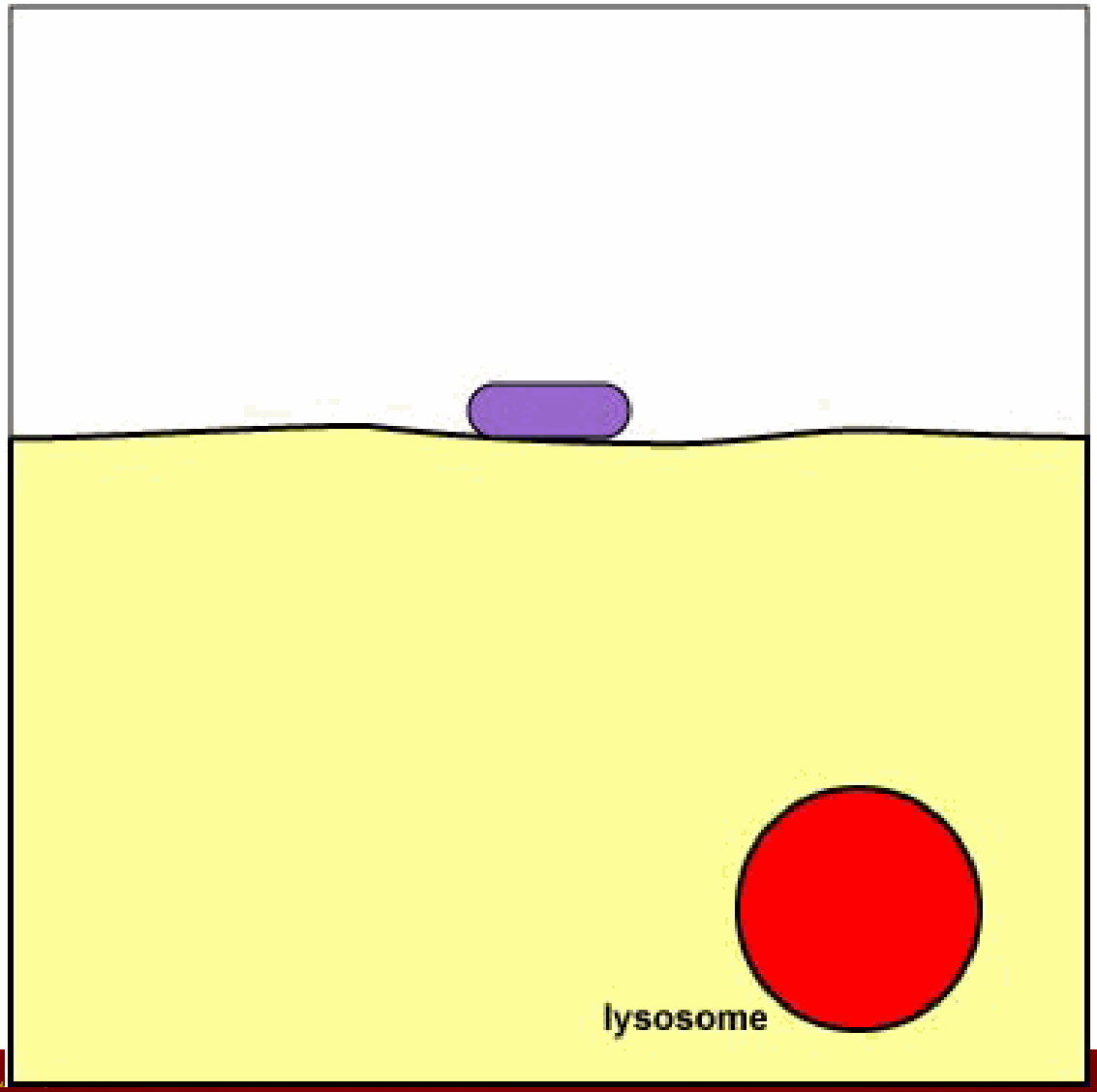
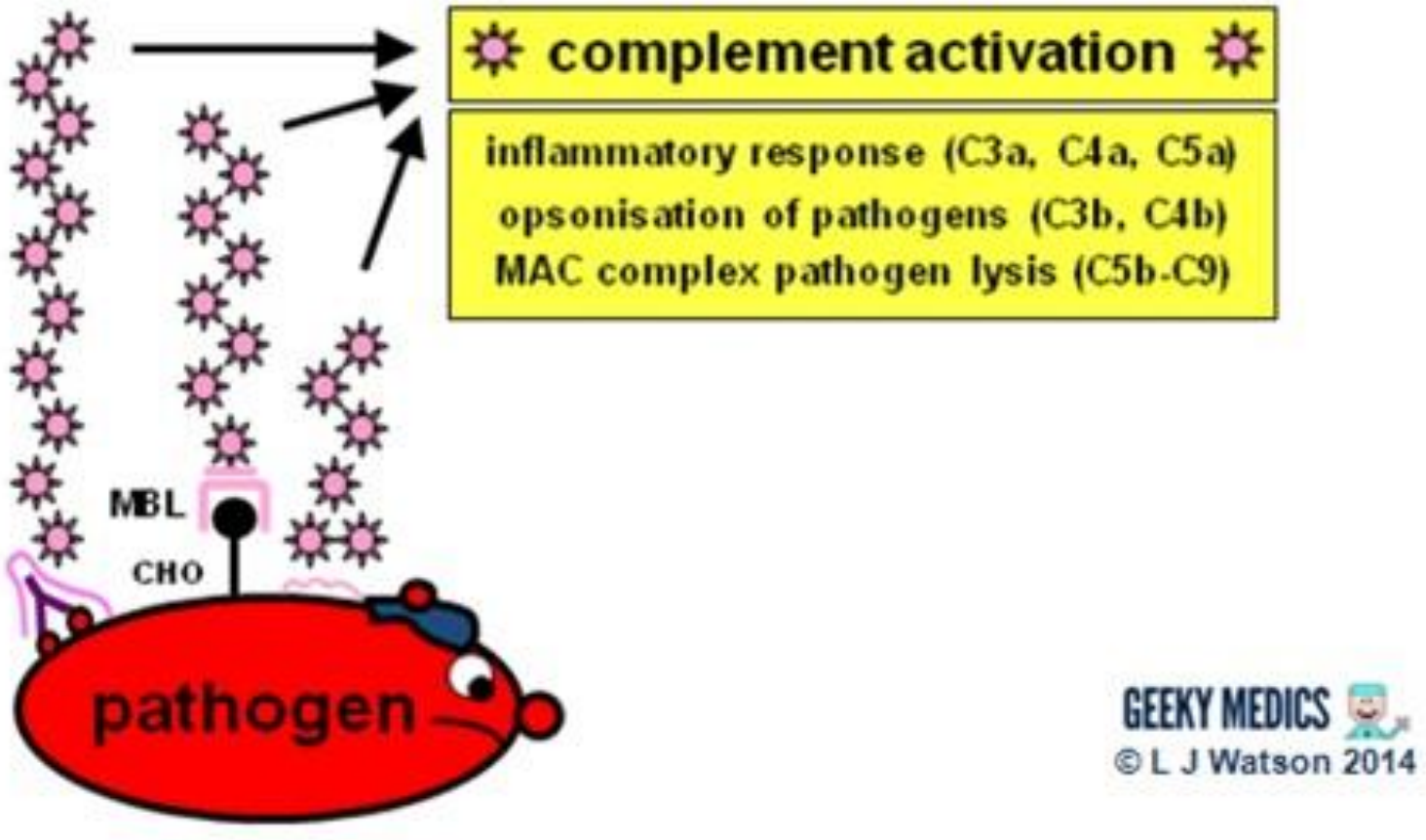
Phagocytosis by Neutrophils and Macs



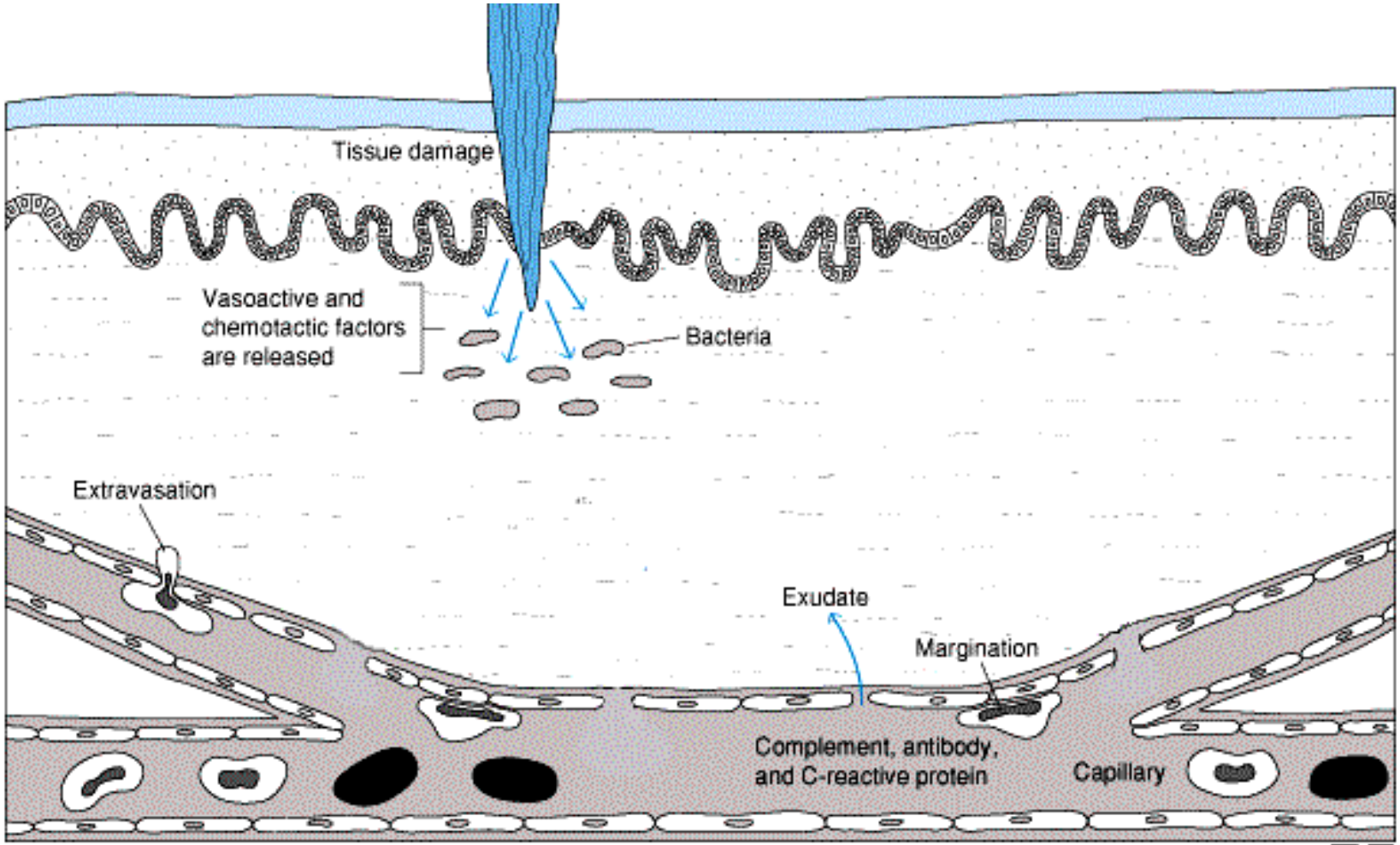
Phagocytosis



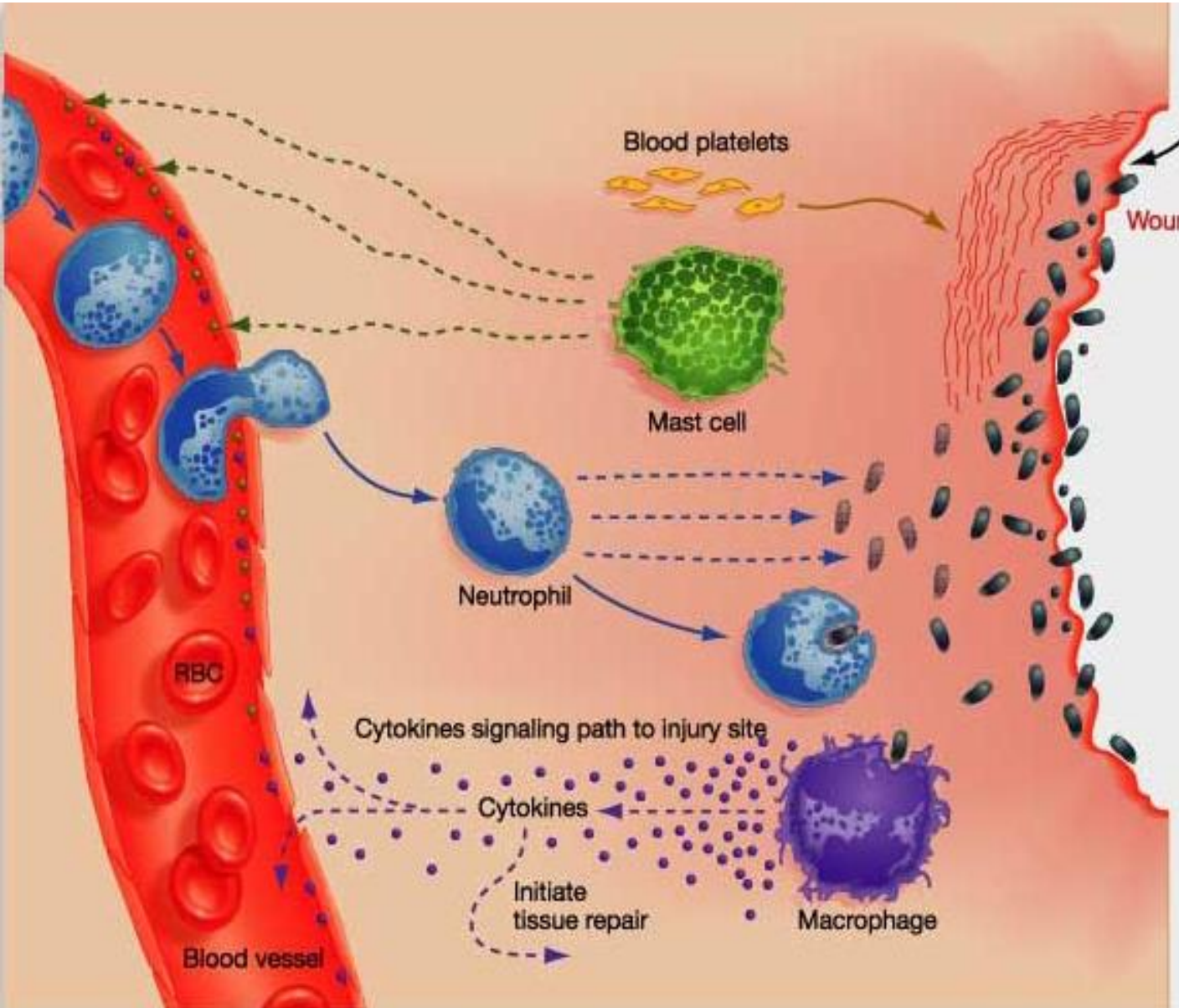
Complement activation



Inflammation



Inflammation



1. Bacteria and other pathogens enter wound.

2. Platelets from blood release blood-clotting proteins at wound site.

3. Mast cells secrete factors that mediate vasodilation and vascular constriction. Delivery of blood, plasma, and cells to injured area increases.

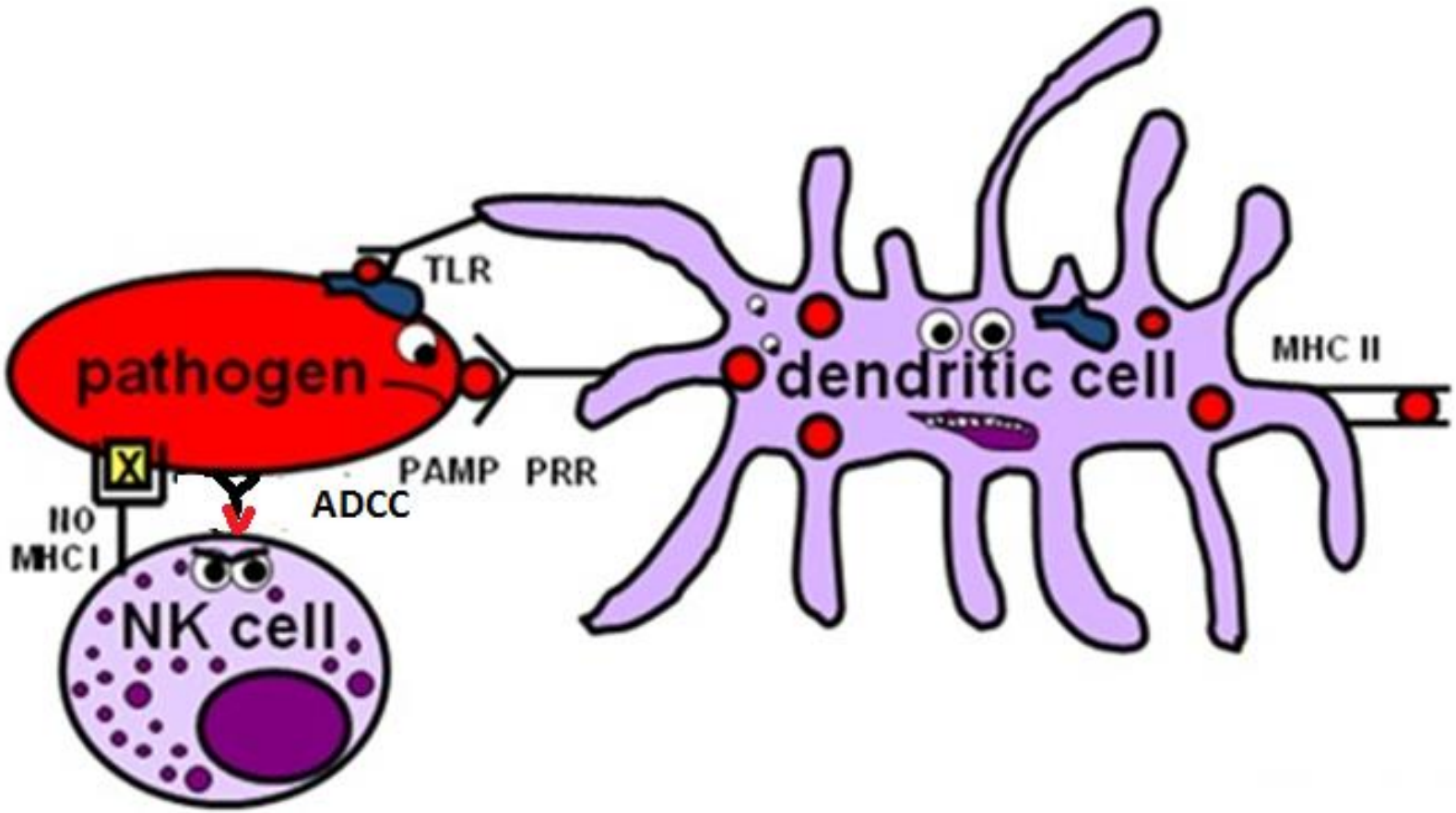
4. Neutrophils secrete factors that kill and degrade pathogens.

5. Neutrophils and macrophages remove pathogens by phagocytosis.

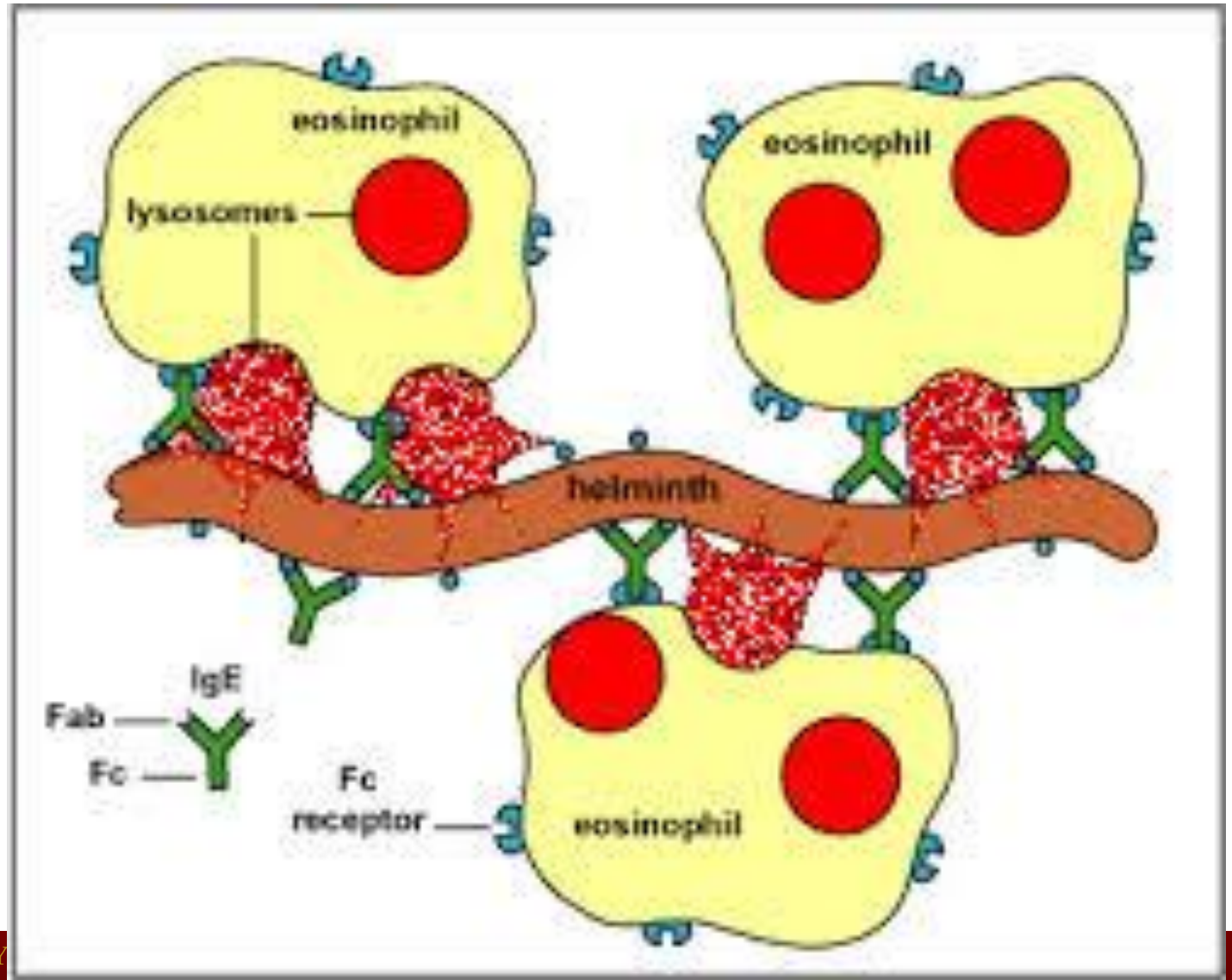
6. Macrophages secrete hormones called cytokines that attract immune system cells to the site and activate cells involved in tissue repair.

7. Inflammatory response continues until the foreign material is eliminated and the wound is repaired.

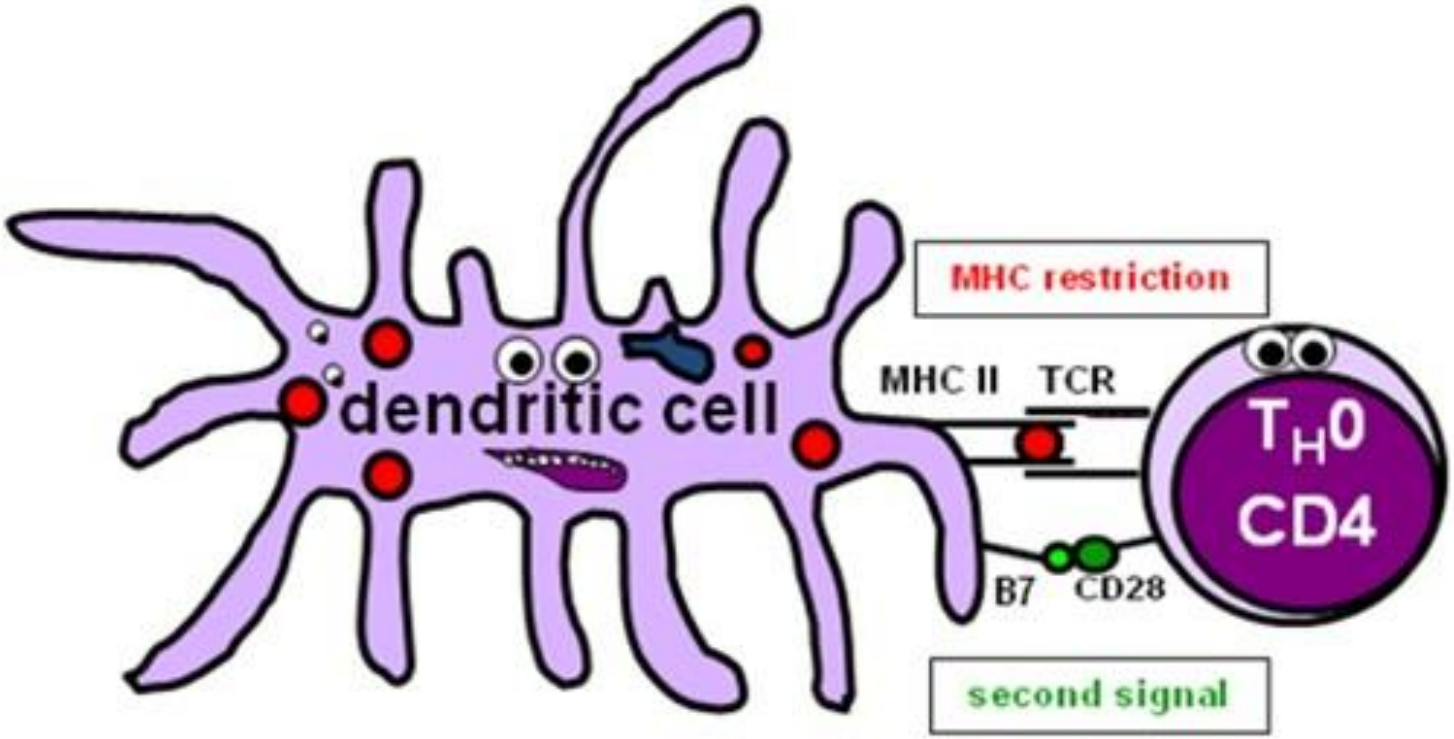
NK cell


TLR
pathogen
dendritic cell
MHC II
PAMP PRR
ADCC
MHC I
NK cell

Extracellular killing



Direct the Adaptive system



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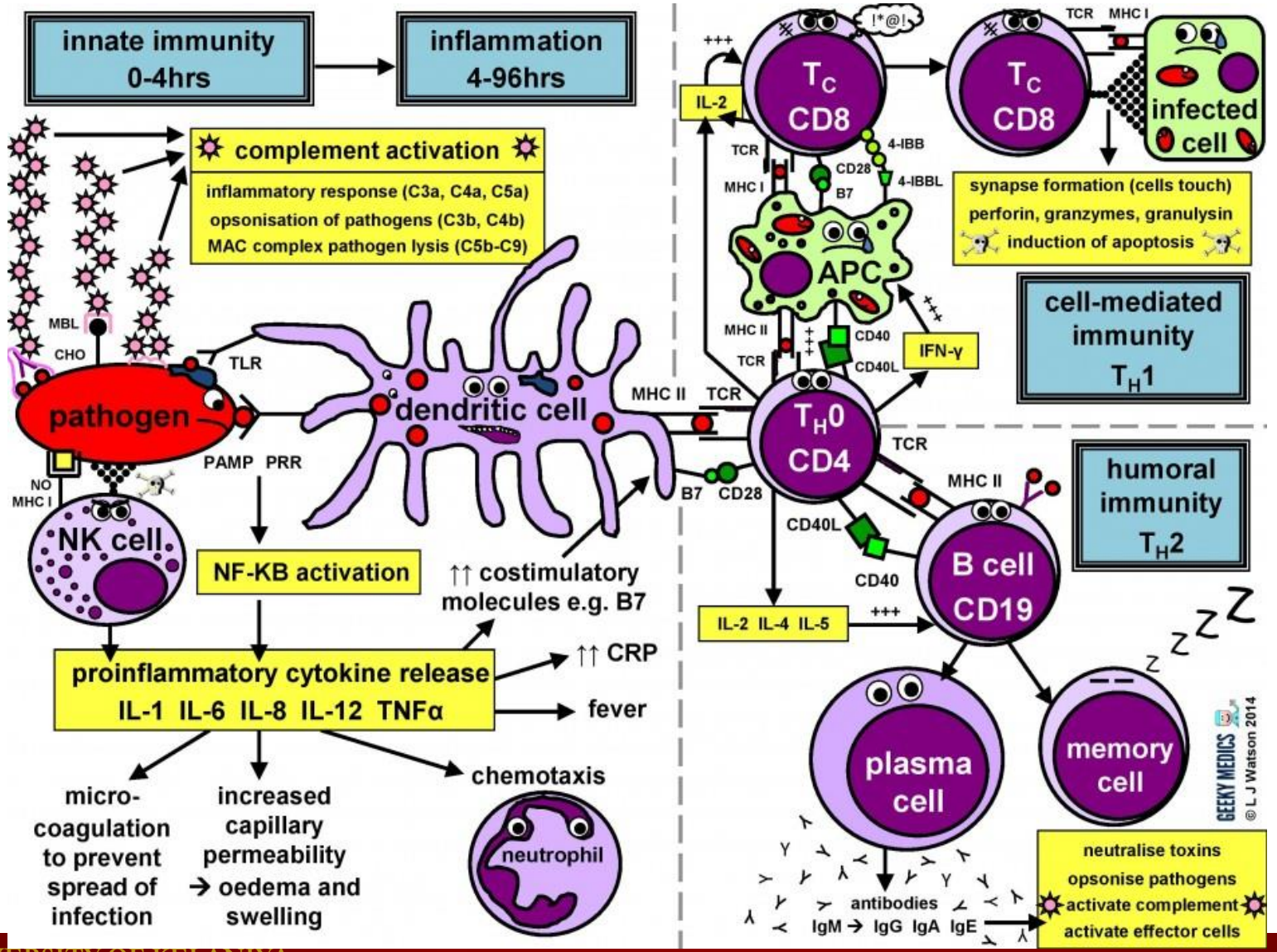
Innate responses



Innate Immune Response in specific Infections

- Viral infections
  - Barriers
  - Interferon α and β
  - NK cells
  - Cytokines
  - Dendritic cells

- Extracellular bacteria
  - Barriers
  - Phagocytes
  - Complement
  - Proinflammatory cytokines
  - Dendritic cells

- Intracellular bacteria
  - Barriers
  - Macrophages and phagocytes
  - Cytokines
  - Dendritic cells

Deficiencies and dysfunctions of innate immune response

- Neutrophil deficiency
  - Quantitative
  - Qualitative (functional)
- Alternative PW complement deficiencies
- Cytokine/ signaling PW disorders
- Deficiency in complement PW regulators
  - C1 esterase inhibitor deficiency

Summary

- Innate immune system
  - Components
    - Barriers
    - Cells
    - Secretions/ molecules
- Innate immune response
  - Inflammation
  - Phagocytosis
  - Alternative PW complement activation
  - Extracellular killing
  - Direct adaptive immune response

MCQ

1. Innate response
    1. Is specific
    2. Is quick
    3. Is activated by specific antigens of microbes
    4. Exert its activity till the adaptive responses are getting ready
    5. Directs the adaptive immunity in the correct pathway
    6. Prevents entry of organisms
    7. Act against self tissues and cells
    8. Memorize pathogens

MCQ

2. Innate response components include
   I. IFN gamma
   II. C3 complement
   III. MAC
   IV. Toll like receptors
   V. CD8 receptor
   VI. CD40 receptor
   VII. MHC I
   VIII. MHC II
   IX. TNFά

MCQ

3. Innate response components include
    - I. NK cells
    - II. Plasma cells
    - III. IgA antibodies
    - IV. Dendritic cells
    - V. Mast cells
    - VI. Histamine
    - VII. Tissue macrophages

MCQ

4. Innate responses include
    - I. Activation of Classical compliment PW
    - II. Phagocytosis
    - III. Extracellular killing
    - IV. Placental transfer to neonate
    - V. Chronic inflammation
    - VI. Memory response
    - VII. Cytotoxic response
    - VIII. Opsonization
    - IX. Humoral response
    - X. Barriers

Home Work

- Fever in infections (systemic inflammatory response)
- What are inherited disorders in innate immune system?
- What are the presentations of these disorders?