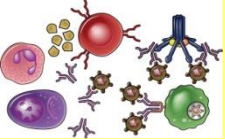


Basic immunology

Lecture 6.

Innate immunity, inflammatory reaction

Timea Berki



Innate and Adaptive Immunity

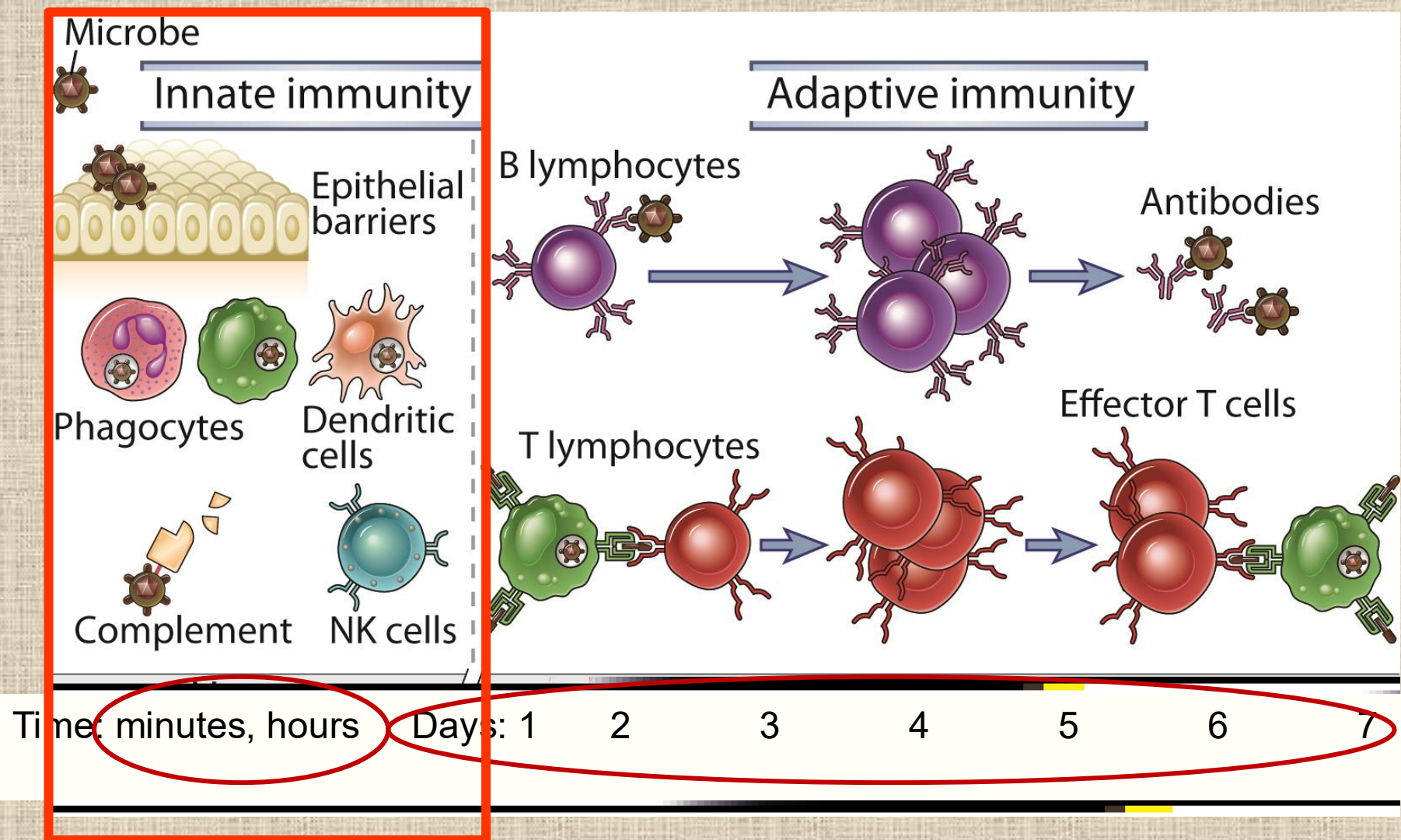
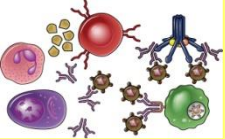


Fig. 1-1 **Inflammatory reaction**



Routes of Antigen Entry

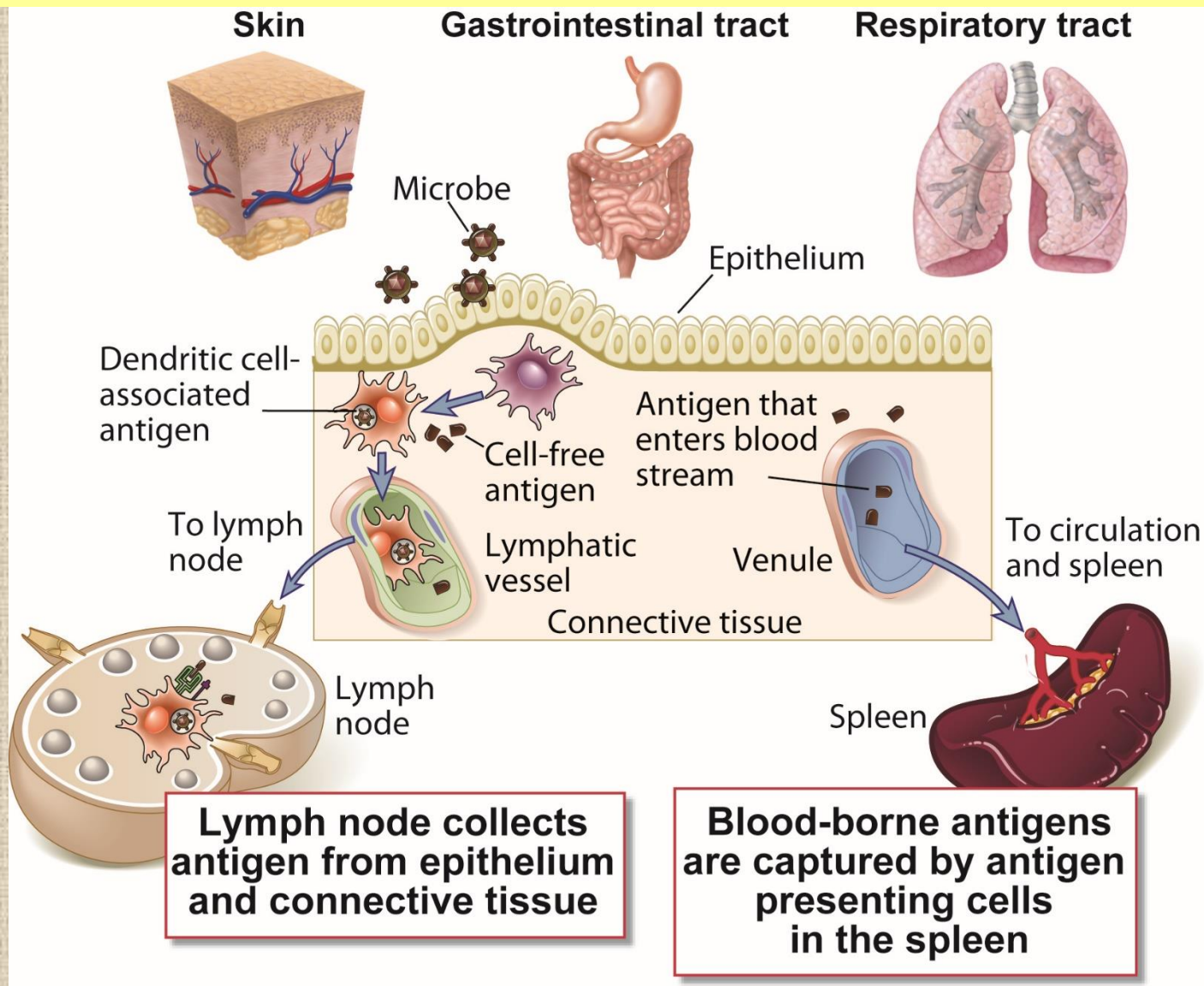
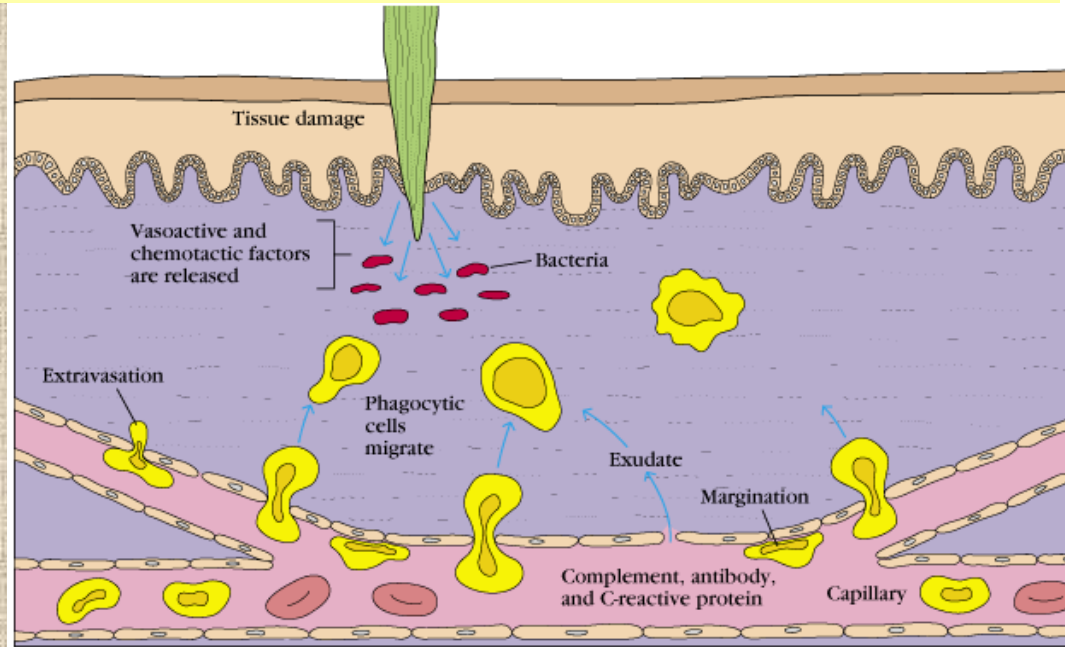


Fig. 6-3

- **Local acute inflammation**

Acute, local inflammation:

- Infection or tissue-injury initiate the cascade of non-specific reactions
- Immediate reaction
- Its role is to inhibit the spreading of infection and tissue injury



Celsus: 4 signs of inflammation: - rubor (red), calor (hot), dolor (painfull), tumor (swelling) + functio laesa (loss of function)

3 main events:

- Vasodilation – minutes
- Increased capillary permeability, fluid efflux, oedema
- Phagocytes migration: - hours

Molecular mediators of inflammation

Plasma enzyme mediators:

- kinin kallikrein system
- Fibrinolytic system
- **Complement cascade**
- Clotting cascade

Lipid mediators:

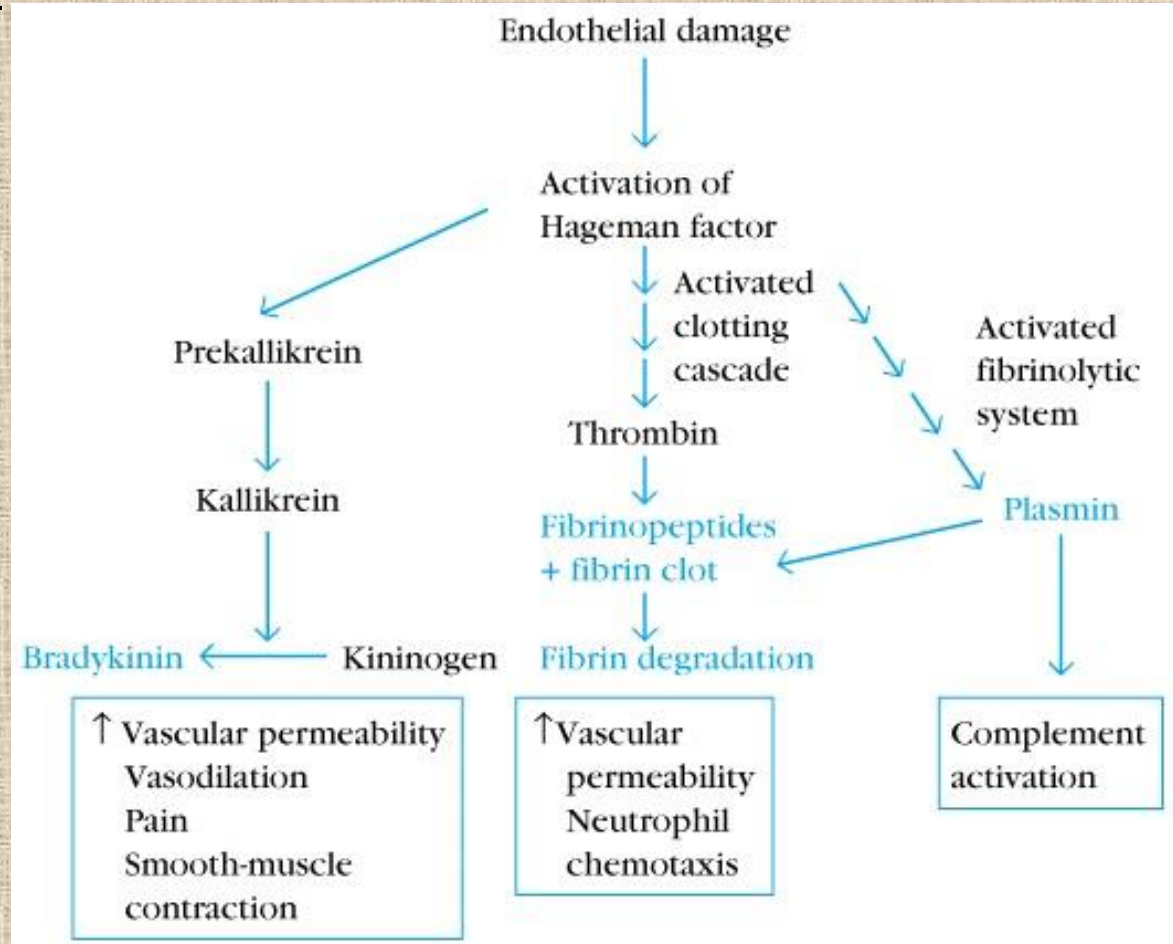
leukotrienes,
prostaglandins (PGE)

Chemoattractants:

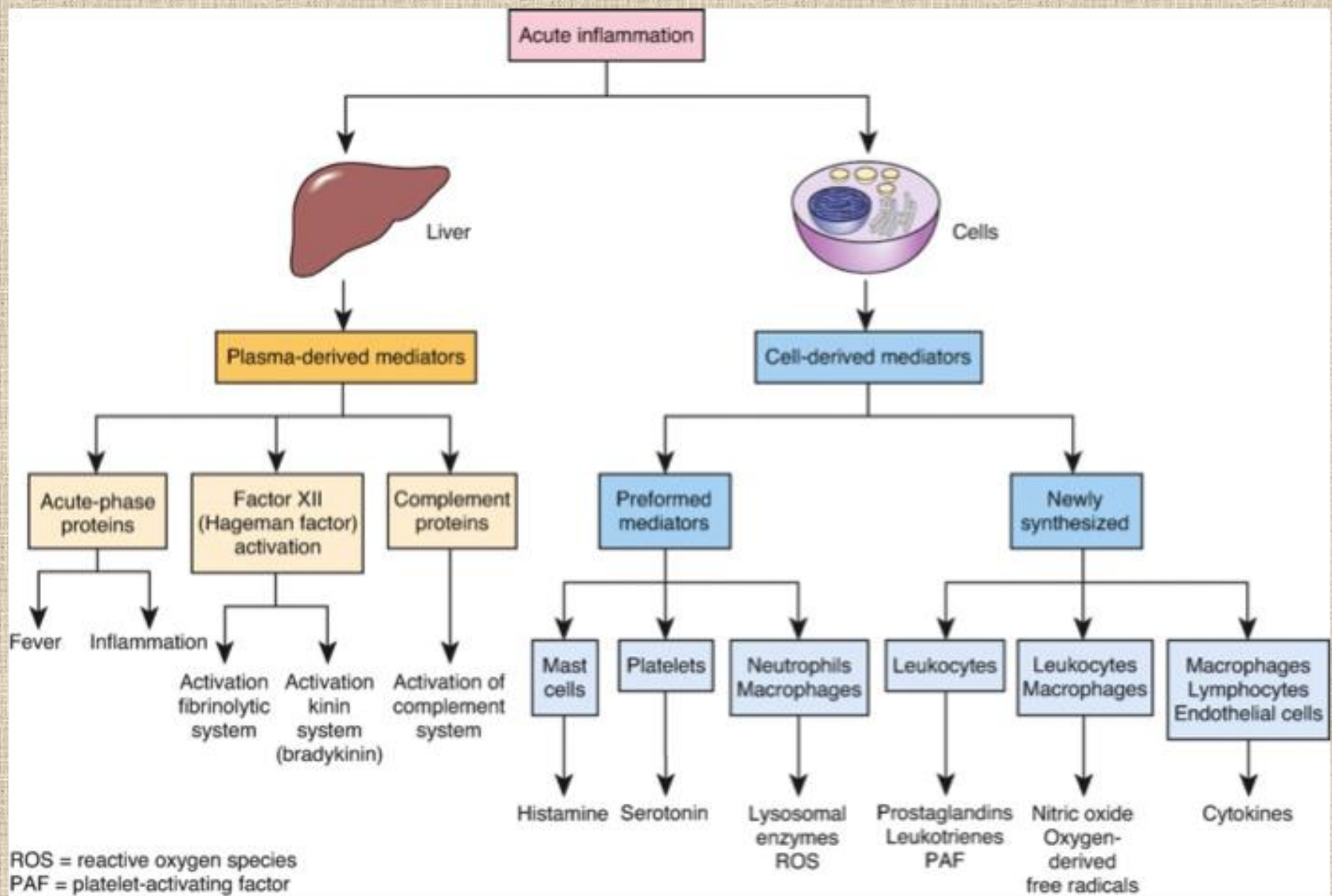
- Chemokines: IL-8
- Complement components
- PAF (platelet activating factor)

Inflammatory cytokines:

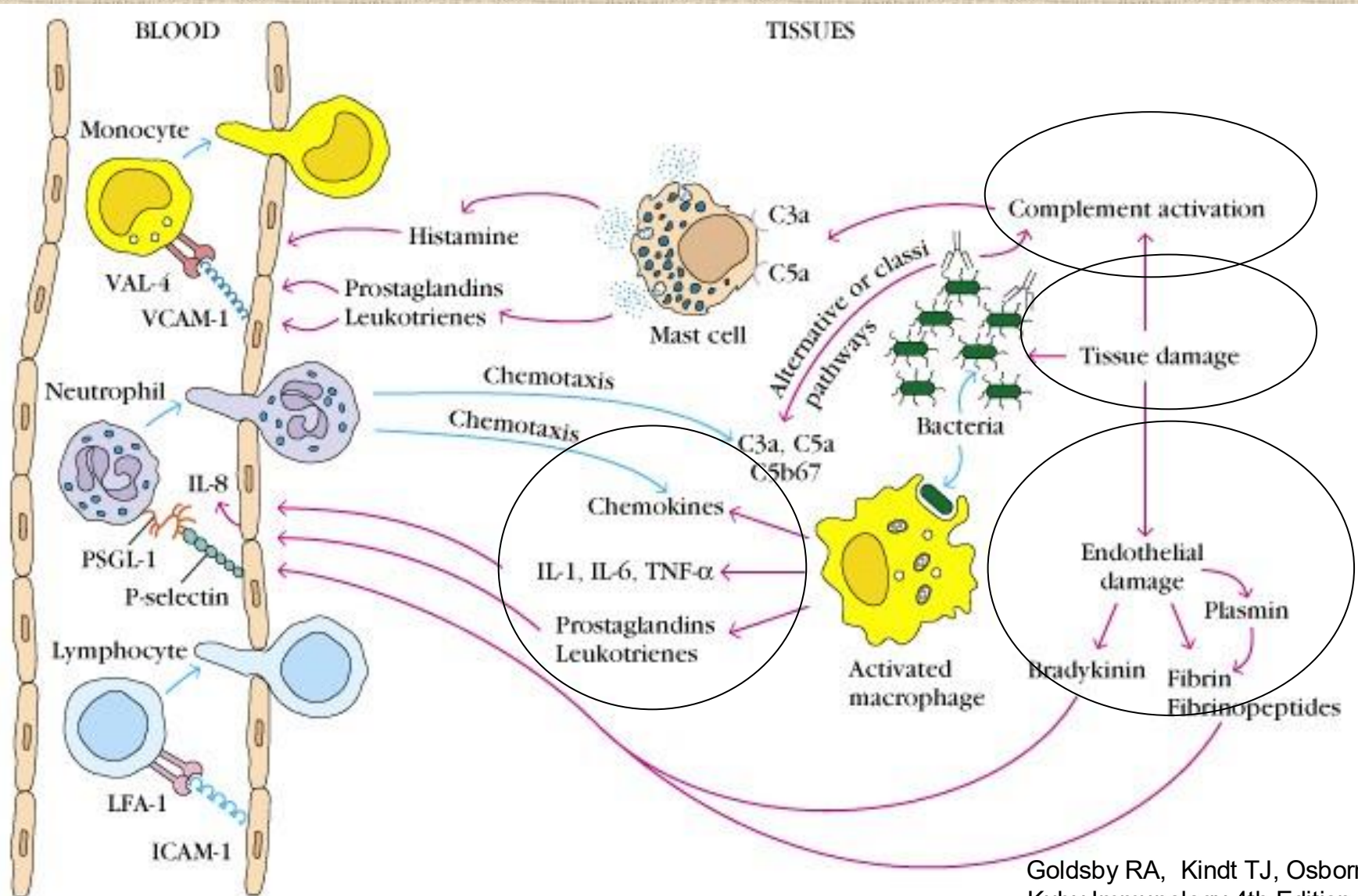
IL-1, IL-6, TNF α



Mediators of inflammation



Initiation of acute inflammation

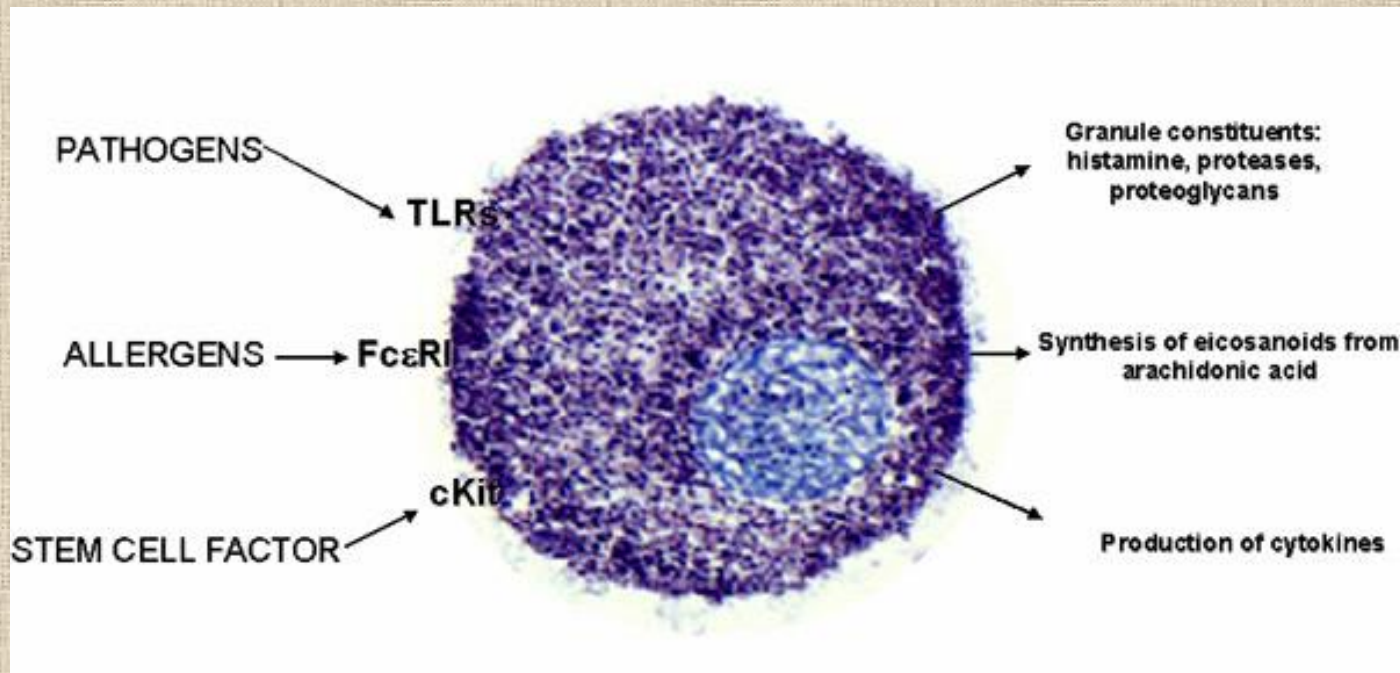


Mast cells and their activation

TLR4 – LPS → IL-1 β , TNF- α , IL-6 and IL-13, without mast cell degranulation

TLR2 – peptidoglycan → mast cell degranulation and production of IL-4 and IL-5, IL-6, IL-13

TLR3,7,9 – Poly (I:C), CpG oligonucleotid → release of pro-inflammatory cytokines and chemokines



they express several hundred thousand high affinity receptors for IgE (Fc ϵ R1) and thus respond to IgE-directed antigens

express the pathogen-recognizing Toll-like receptors (TLRs) which probably account for the ability of mast cells to mount an effective innate immune response



Maturation of Macrophages and DCs

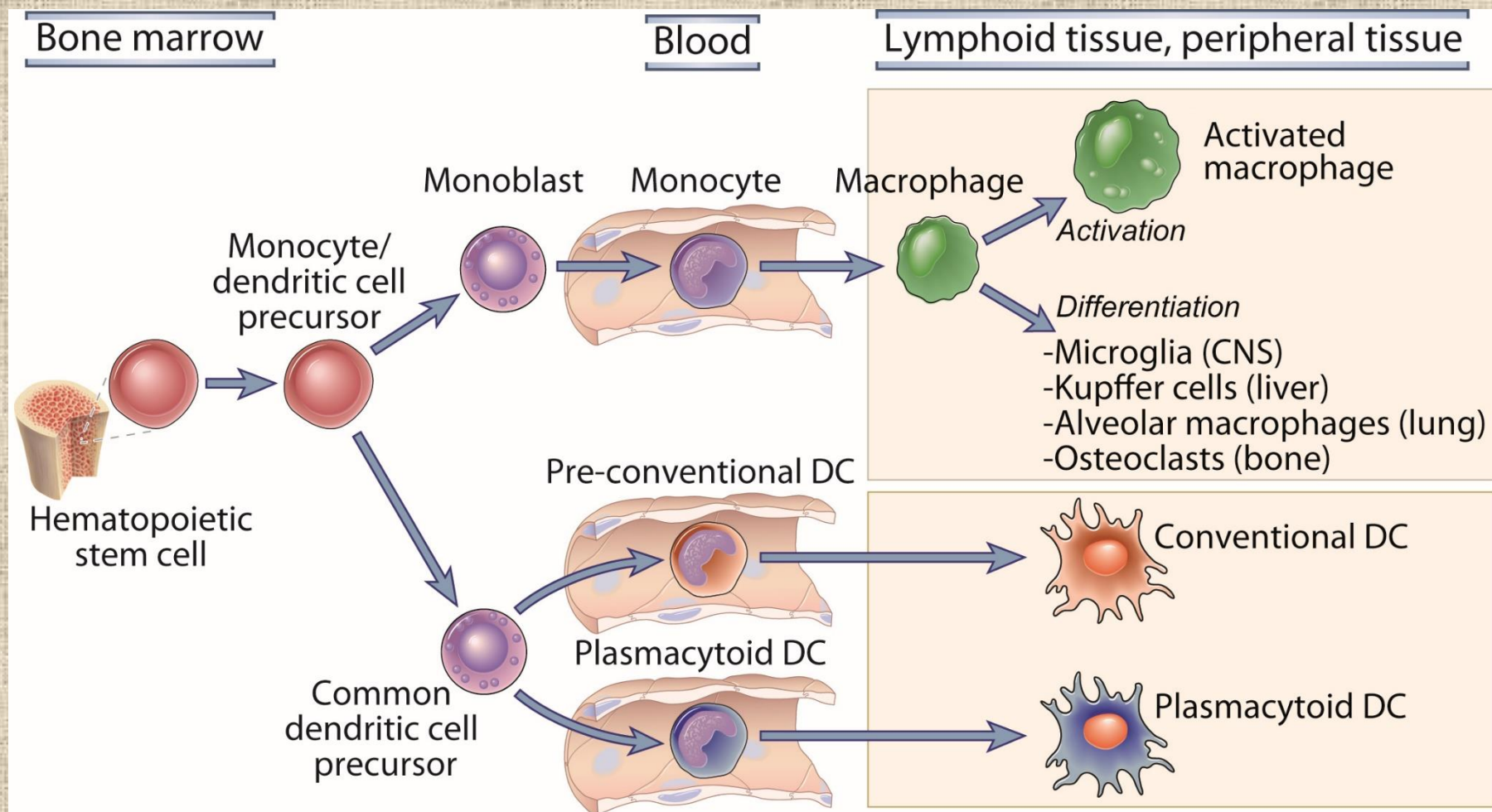
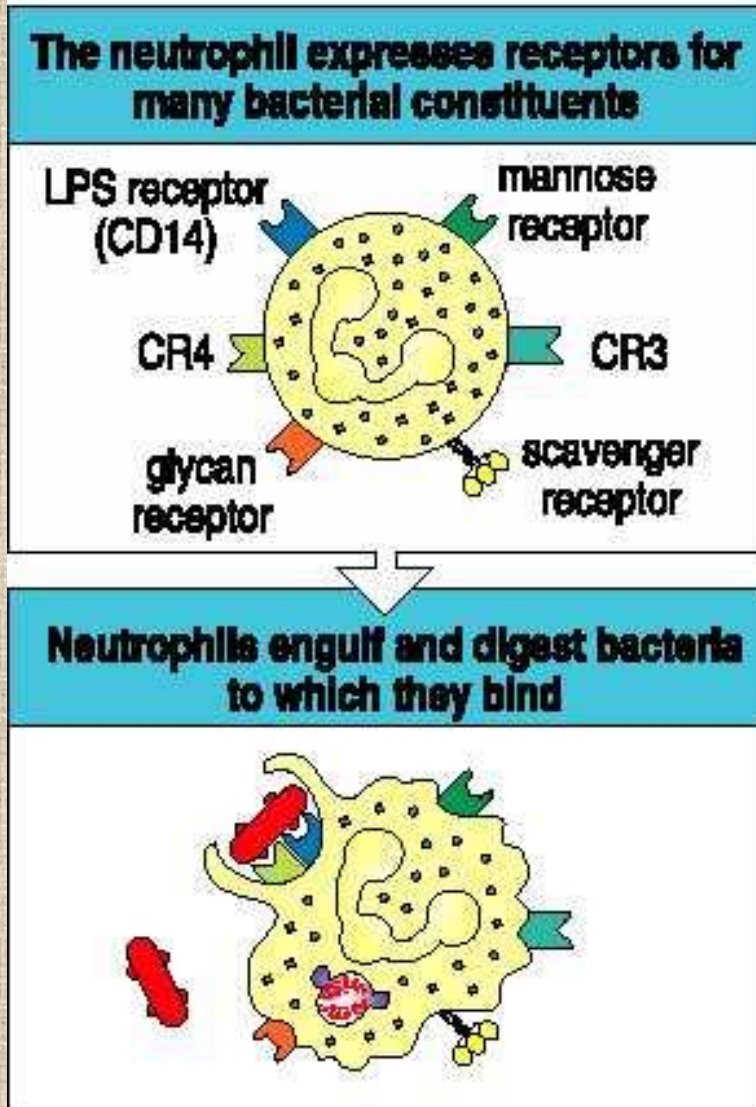


Fig. 2-2

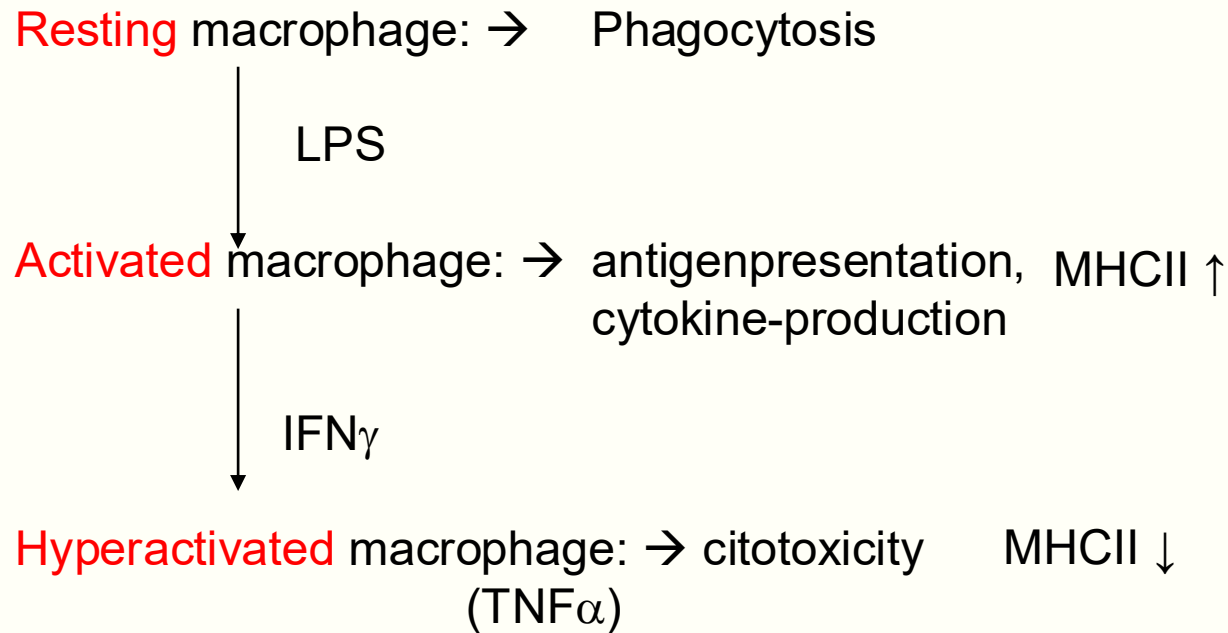
Role of Neutrophils

Figure 8.8



1. Phagocytosis / Receptor mediated endocytosis
2. Degranulation
3. NET formation

Role of macrophages in acute inflammation: classical activation

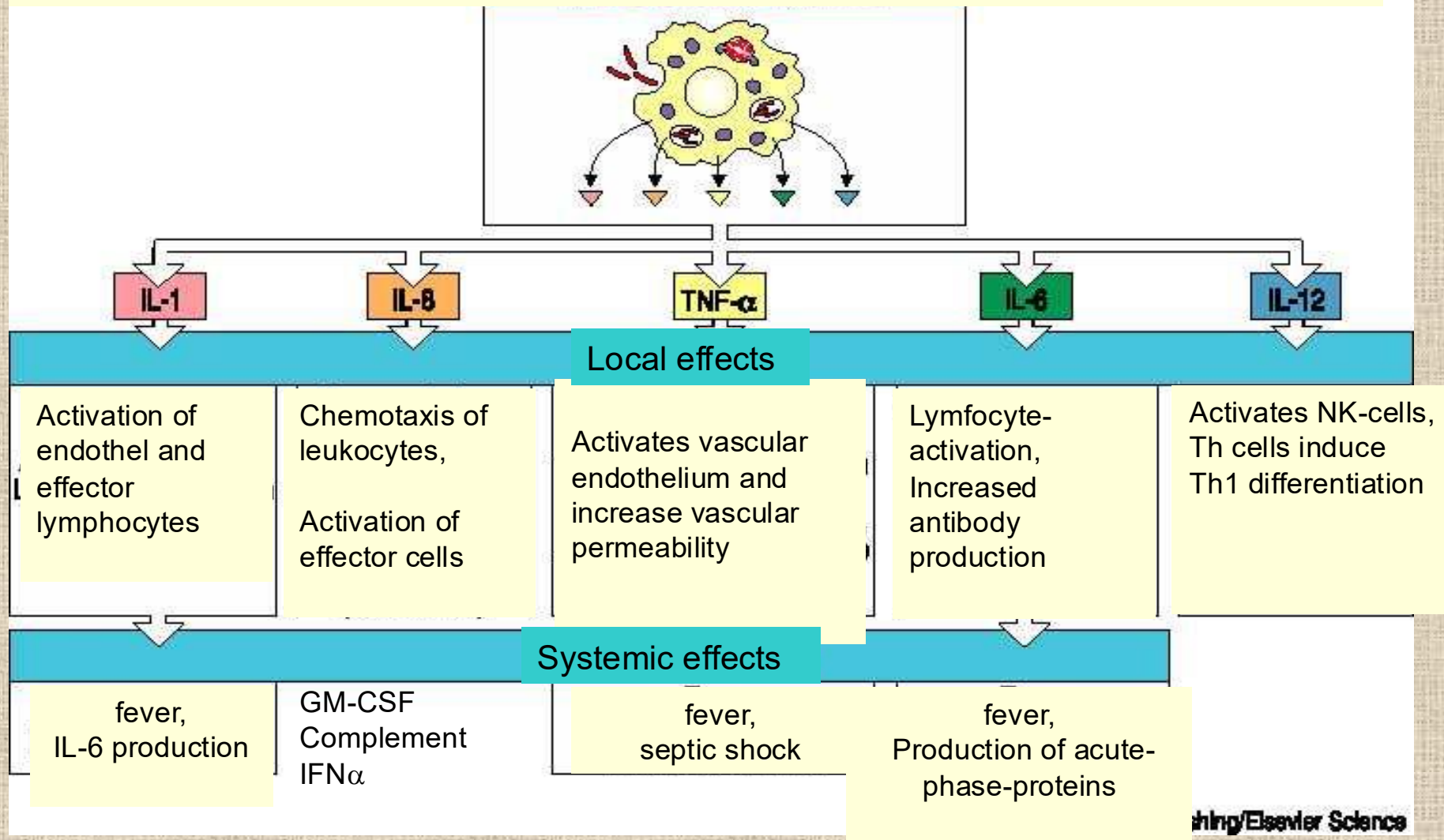


Functional groups of cytokines

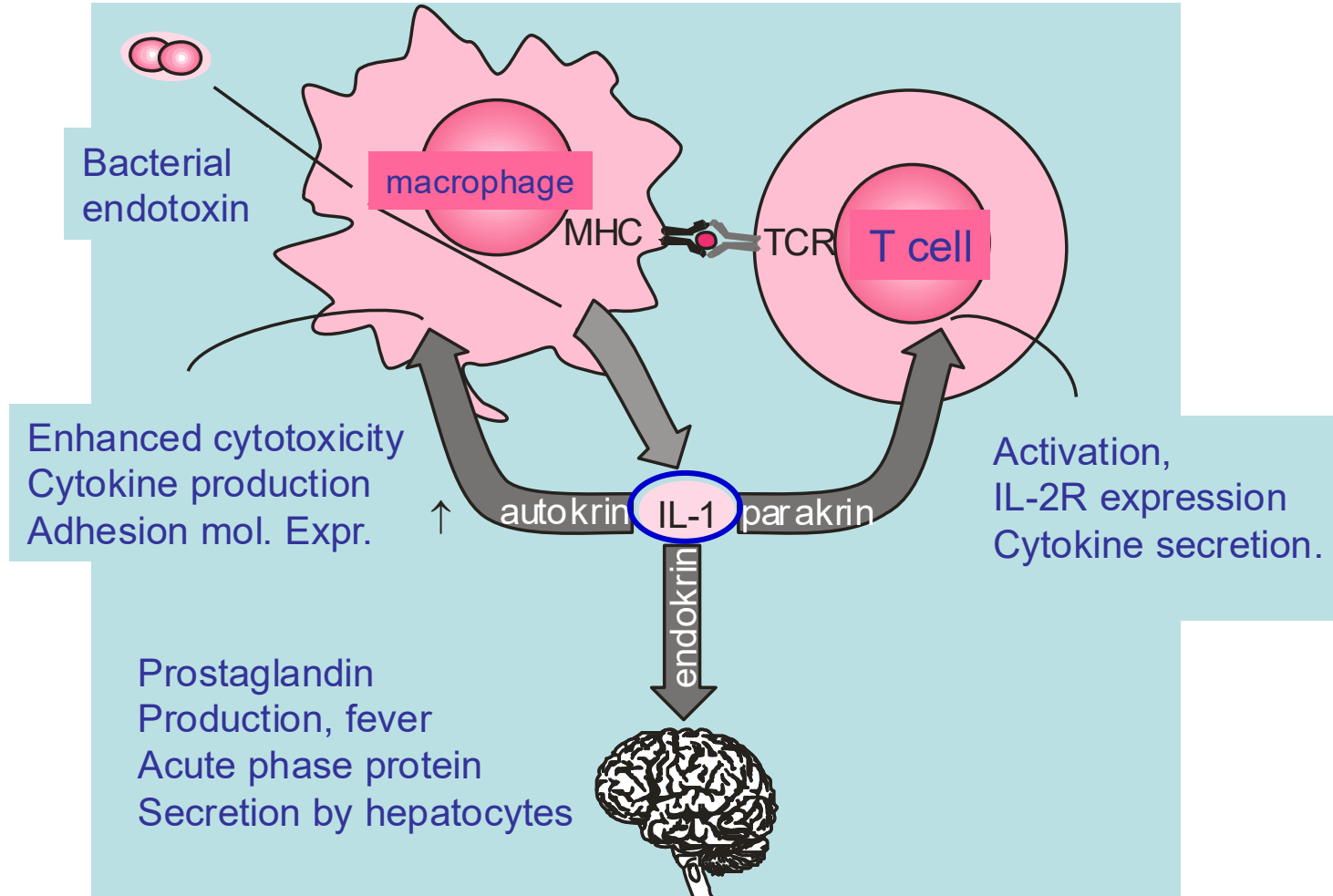
I. Regulators of natural immunity and inflammation	IFN α , IFN β , IL-1 α , IL-1 β , IL-6, TNF α IL-12, Chemokines: CXCL8 (IL-8), CCL3,4 (MCP, MIP-1)
II. Regulators of lymphocyte activation and differentiation	TH1: IL-2, INF γ , TNF β (LT) TH2: , IL-4, IL-5, IL-6, IL-13, IL-15 Treg: IL-10 and TGF β
III. Regulators of haematopoiesis	IL-3, IL-7, GM-CSF, SCF

Activated macrophages produce inflammatory cytokines

LPS originated from Gram – bacterium LPS activates the macrophages, those produce various cytokines

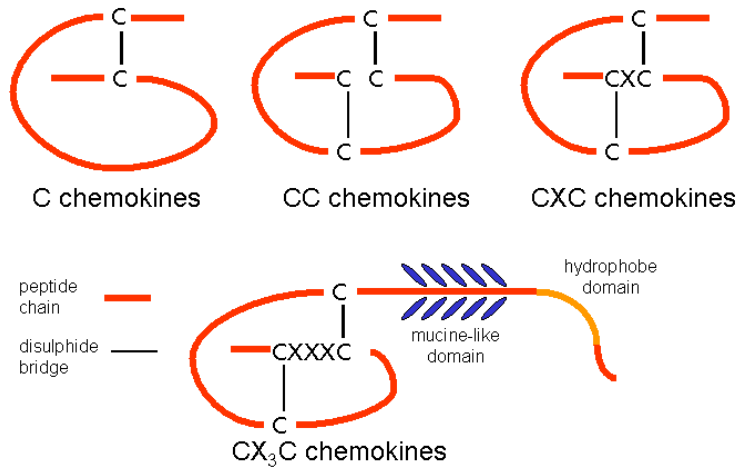


Autocrine, paracrine and endocrine action of IL-1

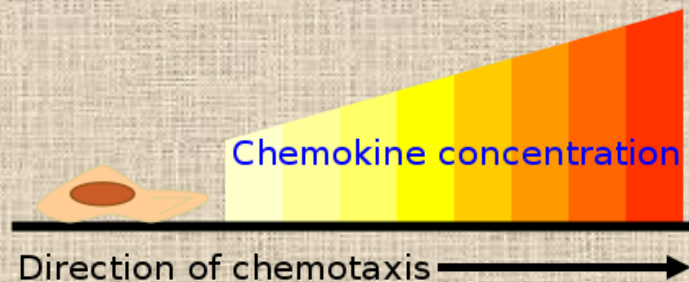
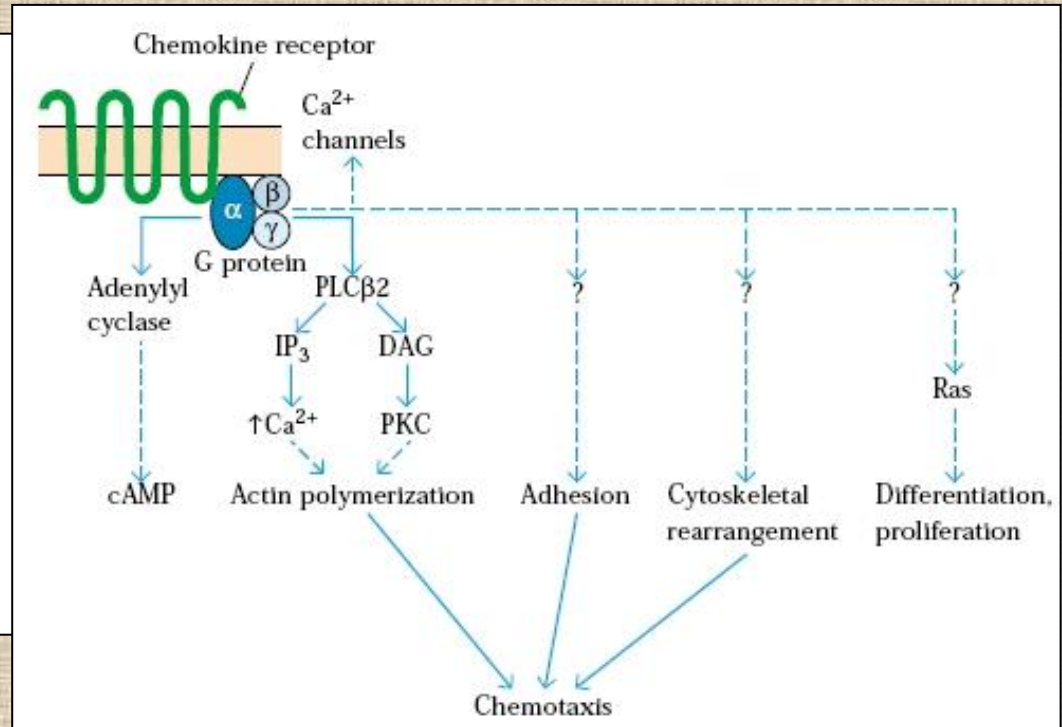


Chemokine action

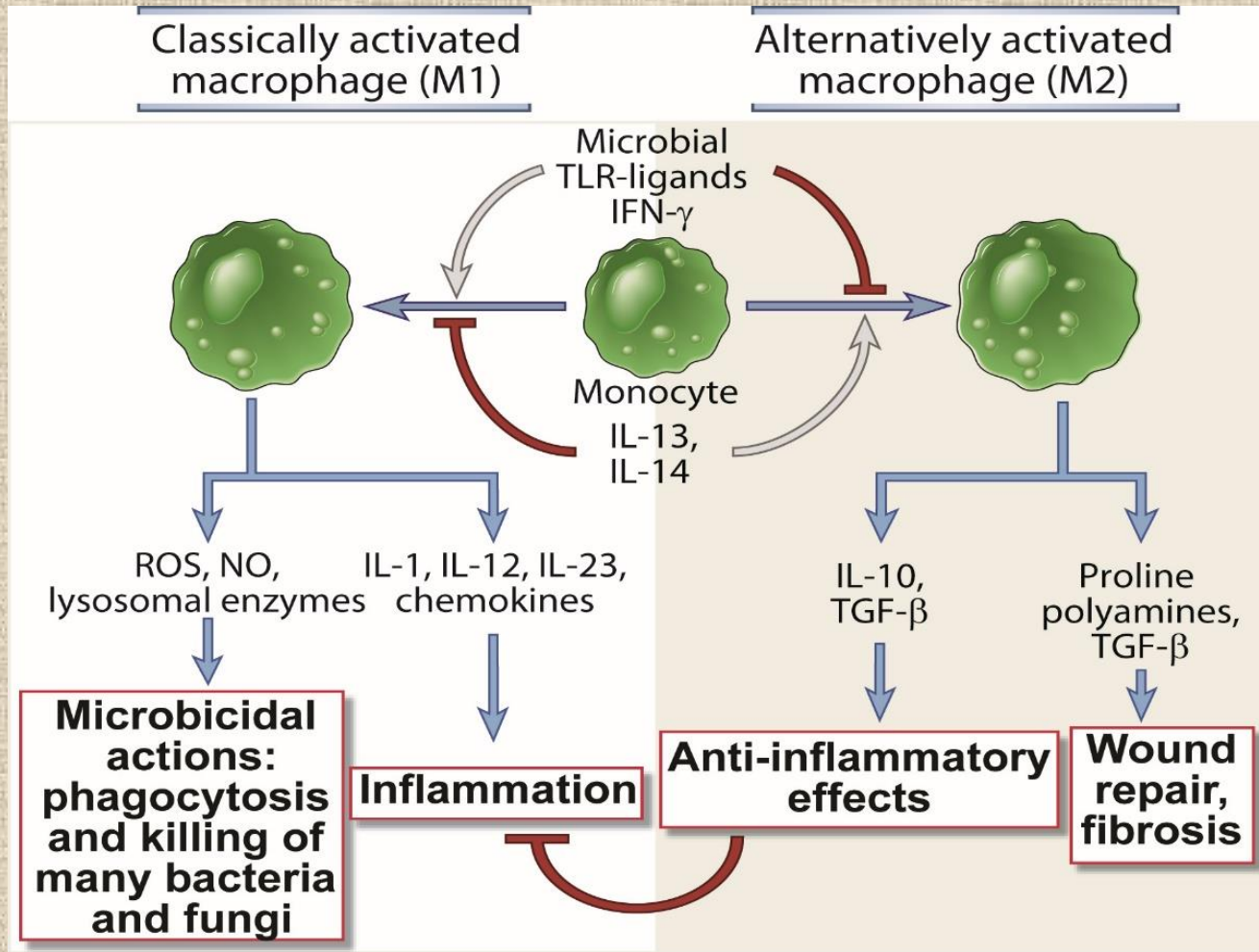
Structure of chemokine classes



© Kohidai, L.



Polarization of macrophages



Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

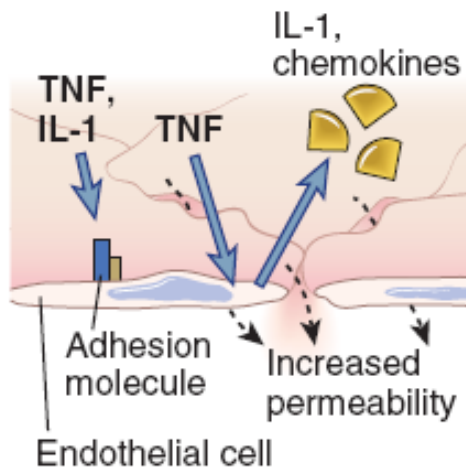
Janeway CA Jr, Travers P, Walport M, Shlomchik MJ. Immunobiology, 2005.

- **Systemic inflammation**

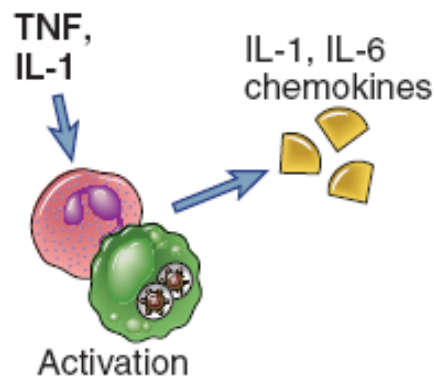
Local and systemic effects of TNF

Local inflammation

Endothelial cells

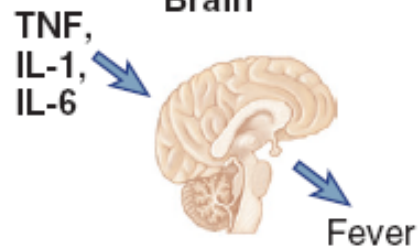


Leukocytes

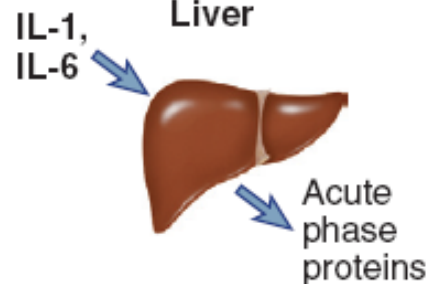


Systemic protective effects

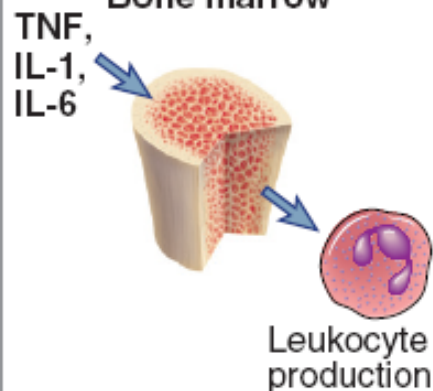
Brain



Liver

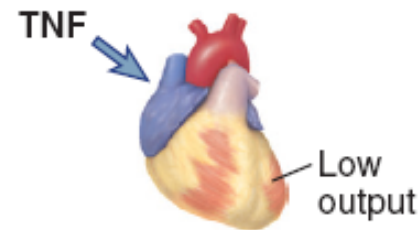


Bone marrow

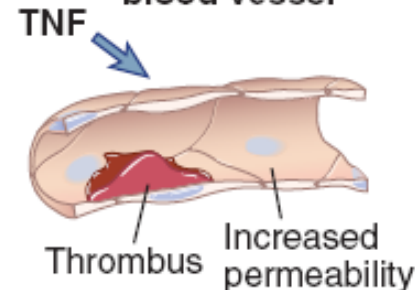


Systemic pathological effects

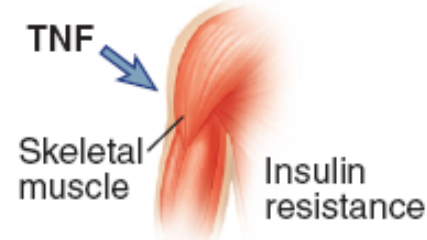
Heart



Endothelial cells/ blood vessel

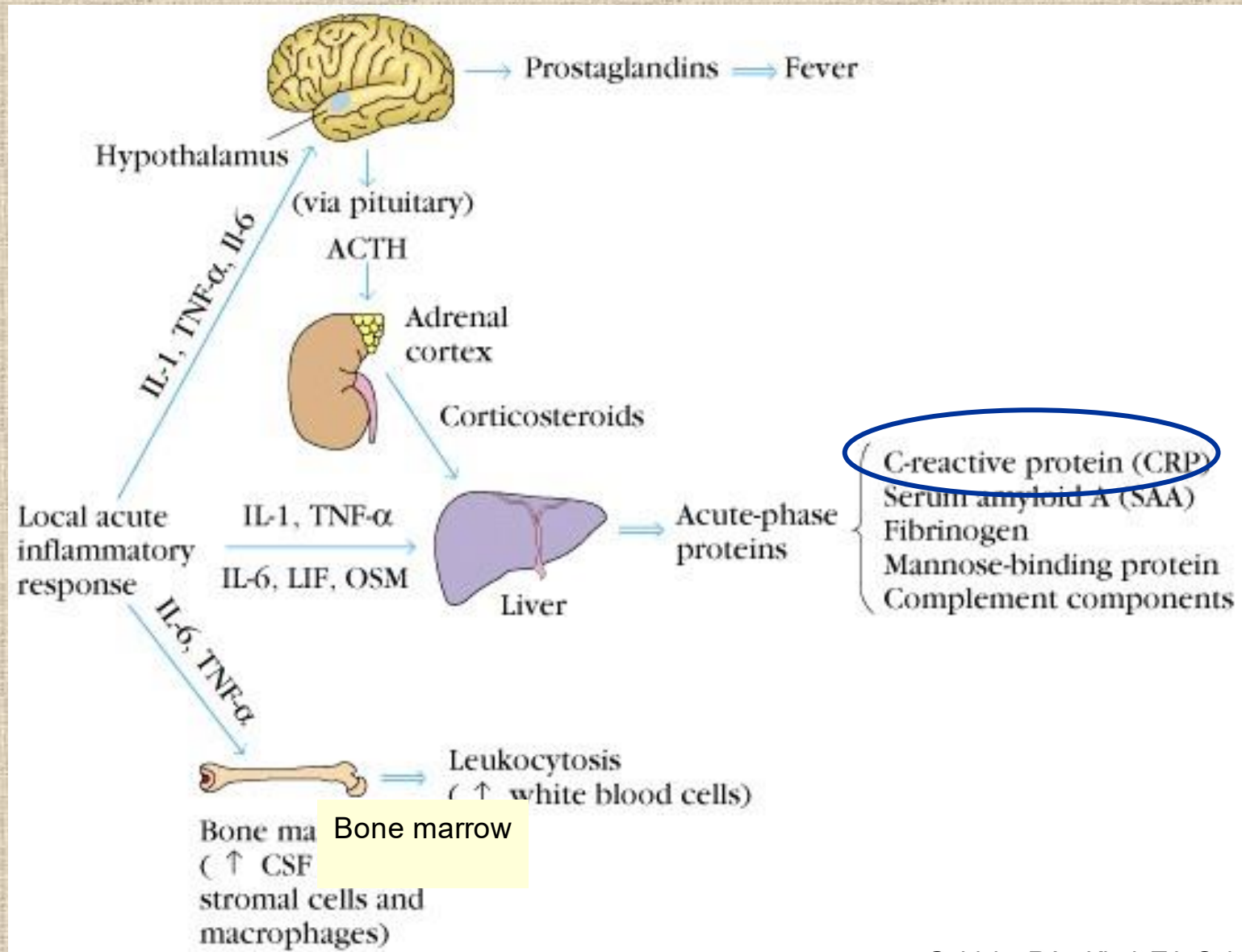


Multiple tissues

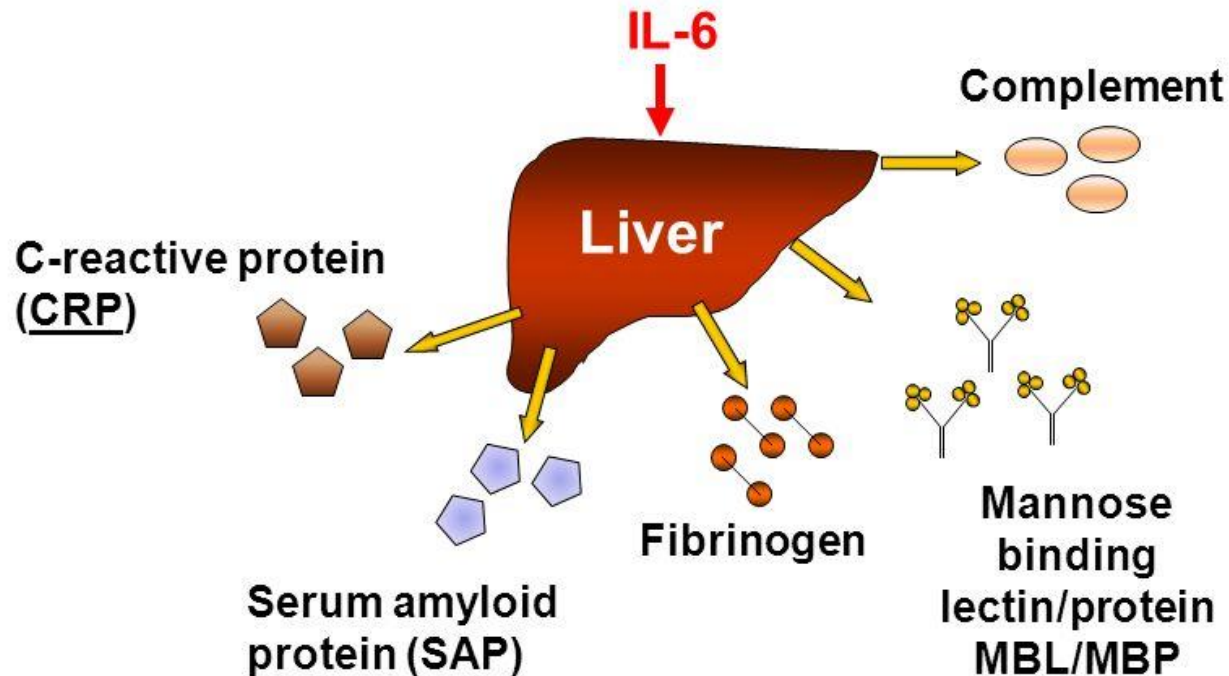


TNF inhibitors,
Steroids

Systemic acute inflammation = acute phase reaction



ACUTE PHASE REACTION

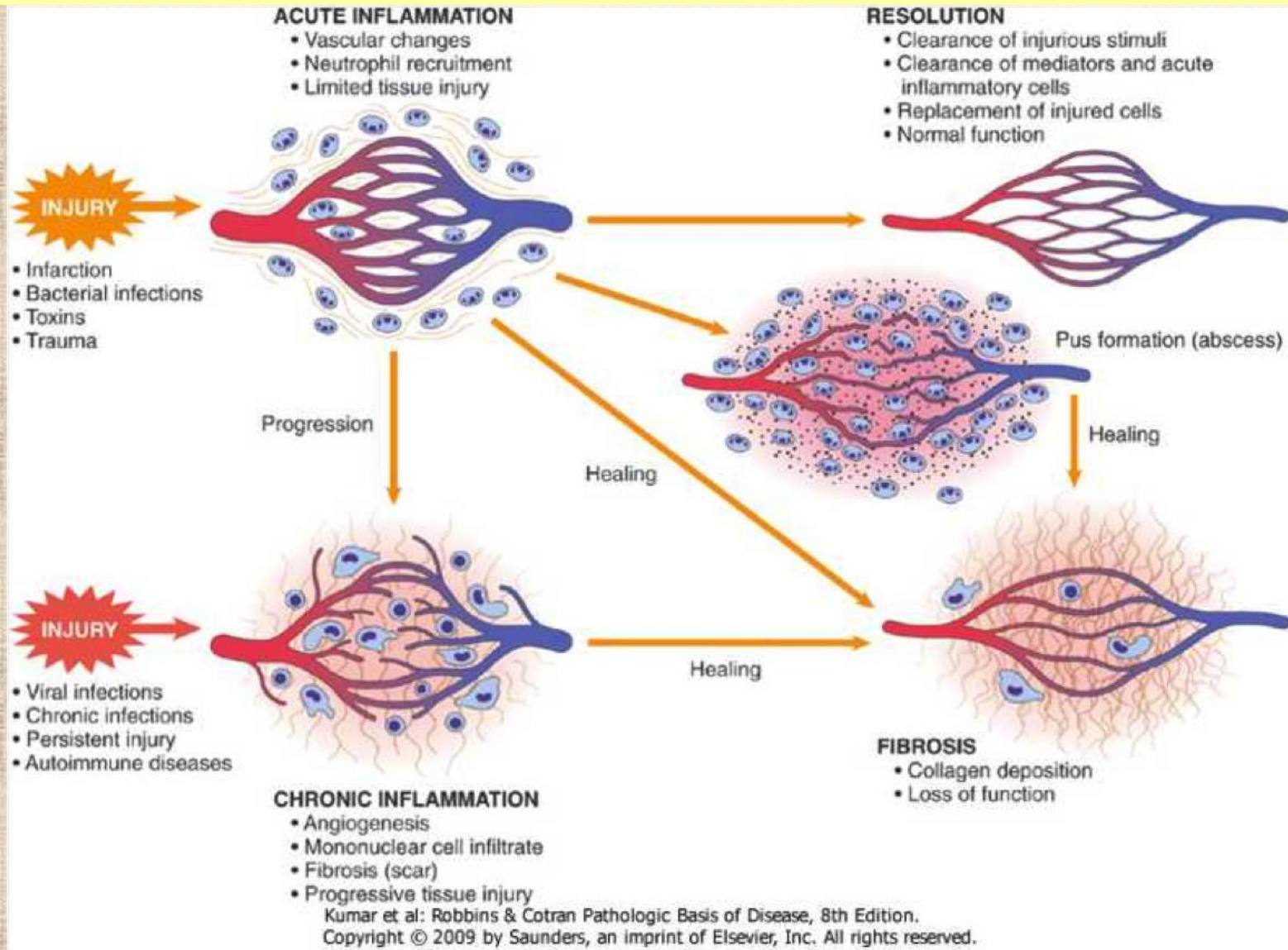


UNDER THE INFLUENCE OF IL-6 THE LIVER PRODUCES A BUNCH OF ACUTE-PHASE PROTEINS

Systemic effects of acute inflammation *acute phase response*

- Fever (temperature $> 37.8^{\circ}\text{C}$ or $>100\text{ F}$)
 - Increased pulse, blood pressure
 - Chills
 - Anorexia
- Leukocytosis
 - neutrophilia and left shift of neutrophils points to bacterial infection
 - Lymphocytosis points to viral infection
 - Eosinophilia point to allergy or parasitic infection
- Acute phase protein production in liver
 - fibrinogen, CRP, SAA leads to increased ESR

Outcomes of acute inflammation



Causes of Chronic Inflammation

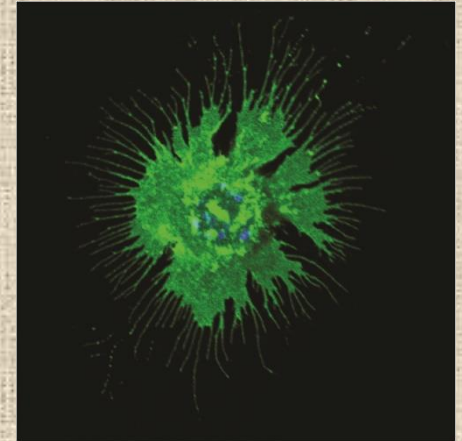
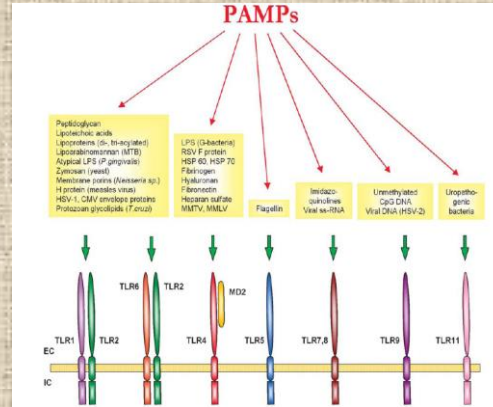
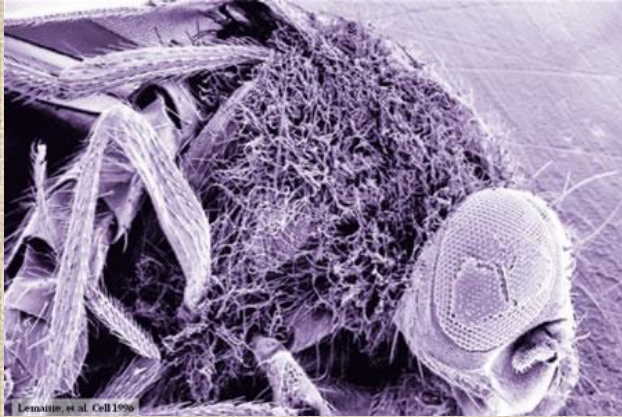
Unlike acute inflammation showing redness, swelling and pain, chronic inflammation can be invisible

Causes

- Autoimmune diseases e.g. such as rheumatoid arthritis, lupus
- Infectious agents e.g. H. pylori, viruses
- Atherosclerosis
- Environmental e.g. smoking
- Allergens
- Central adiposity: more macrophages localised in fat will thus produce more inflammatory mediators

<https://create.kahoot.it/my-library/kahoots/4bbb2f64-93ca-41fb-a8b6-a0343ee8575d>

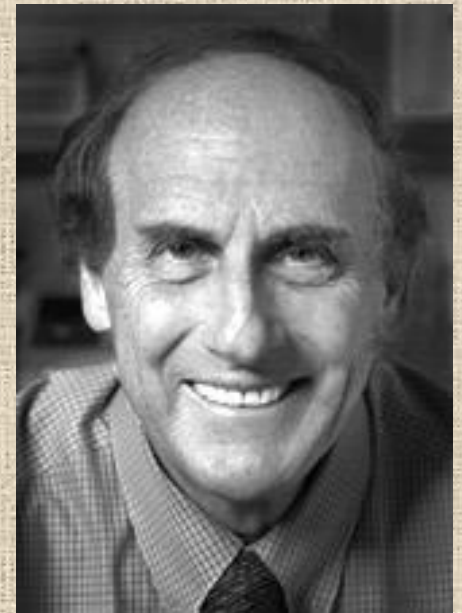
Nobel Laureates in 2011 for medicine and physiology



Jules A. Hoffmann



Bruce A. Beutler



Ralph M. Steinmann