

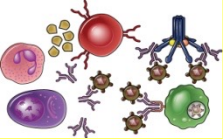
# **Az immunológia alapjai**

## *5. előadás*

Az immunválasz áttekintése

A veleszületett immunválasz, gyulladás

**Berki Tímea**



# A veleszületett és szerzett immunitás kinetikája

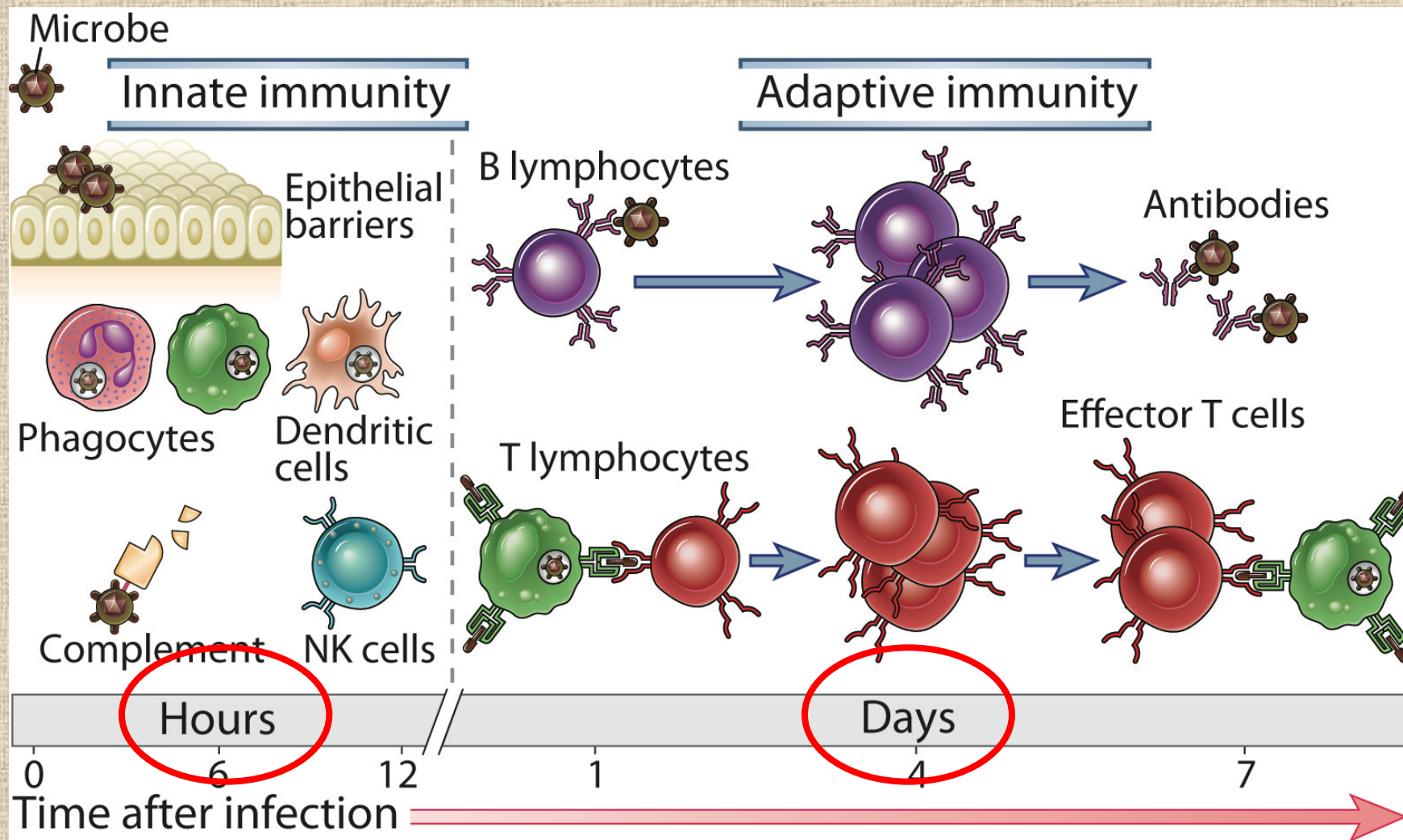


Fig. 1-1

# Az antigén bejutás helye

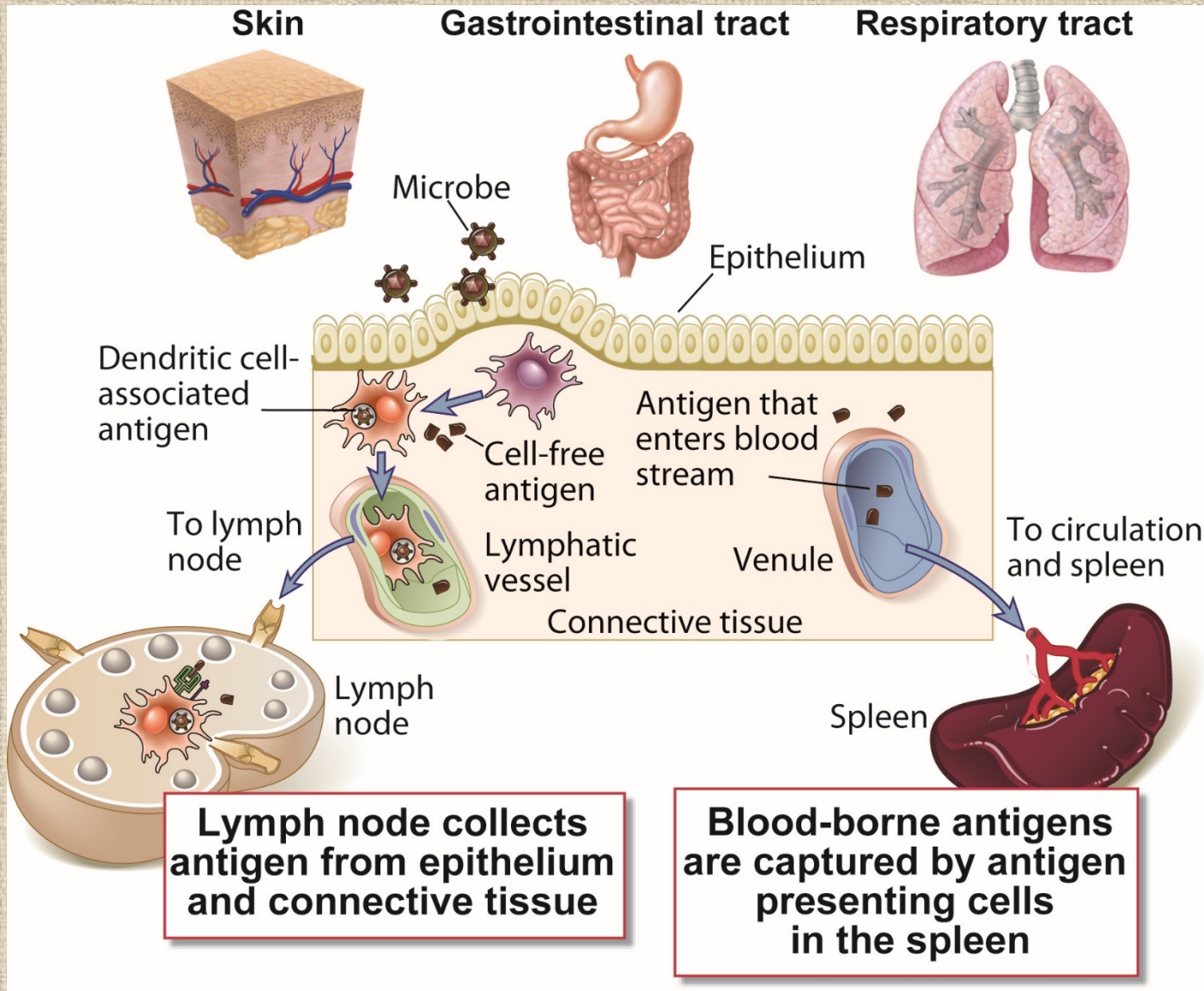
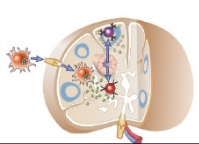


Fig. 6-3



# Az immunválasz aktivációja

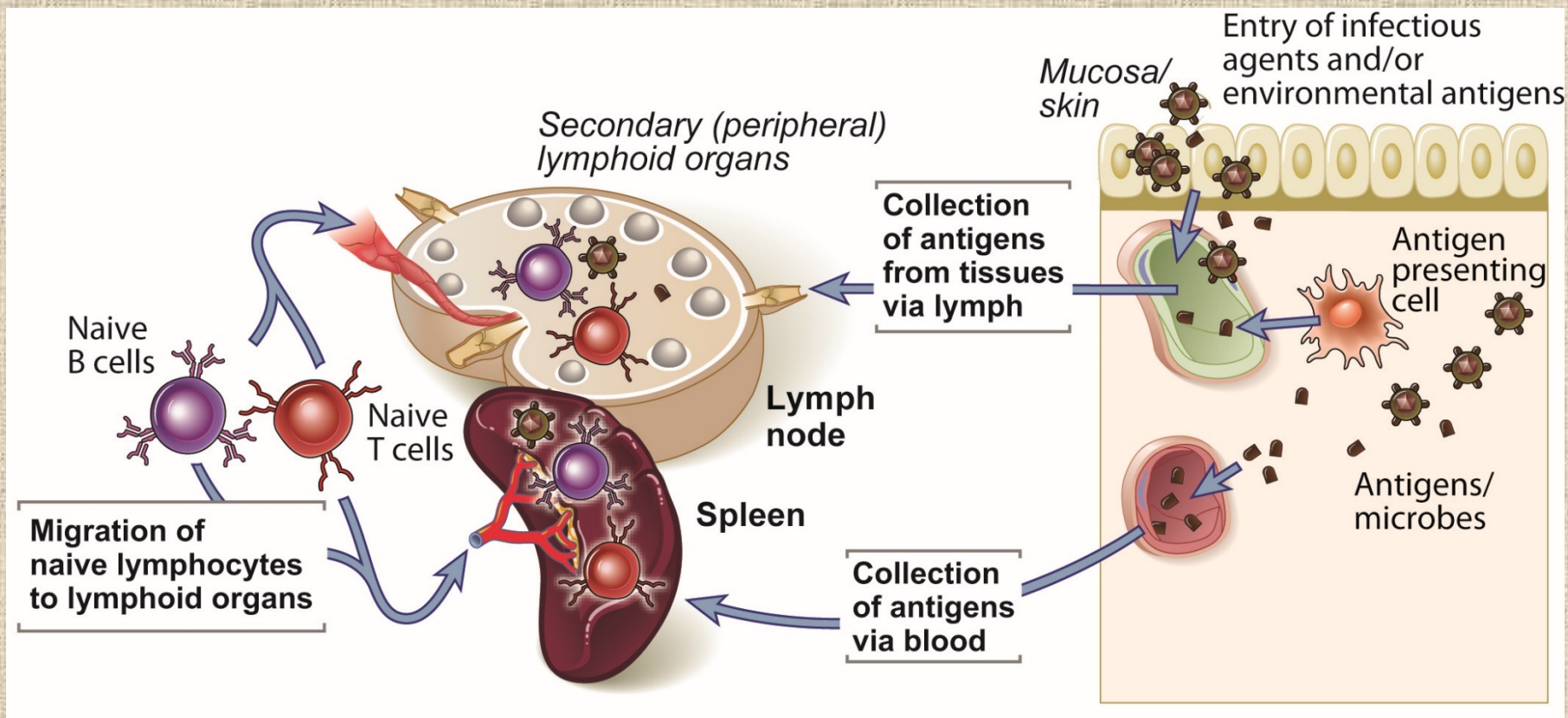


Fig. 2-6

# Effektor fázis: sejtek és ellenanyagok jutnak a fertőzés helyére

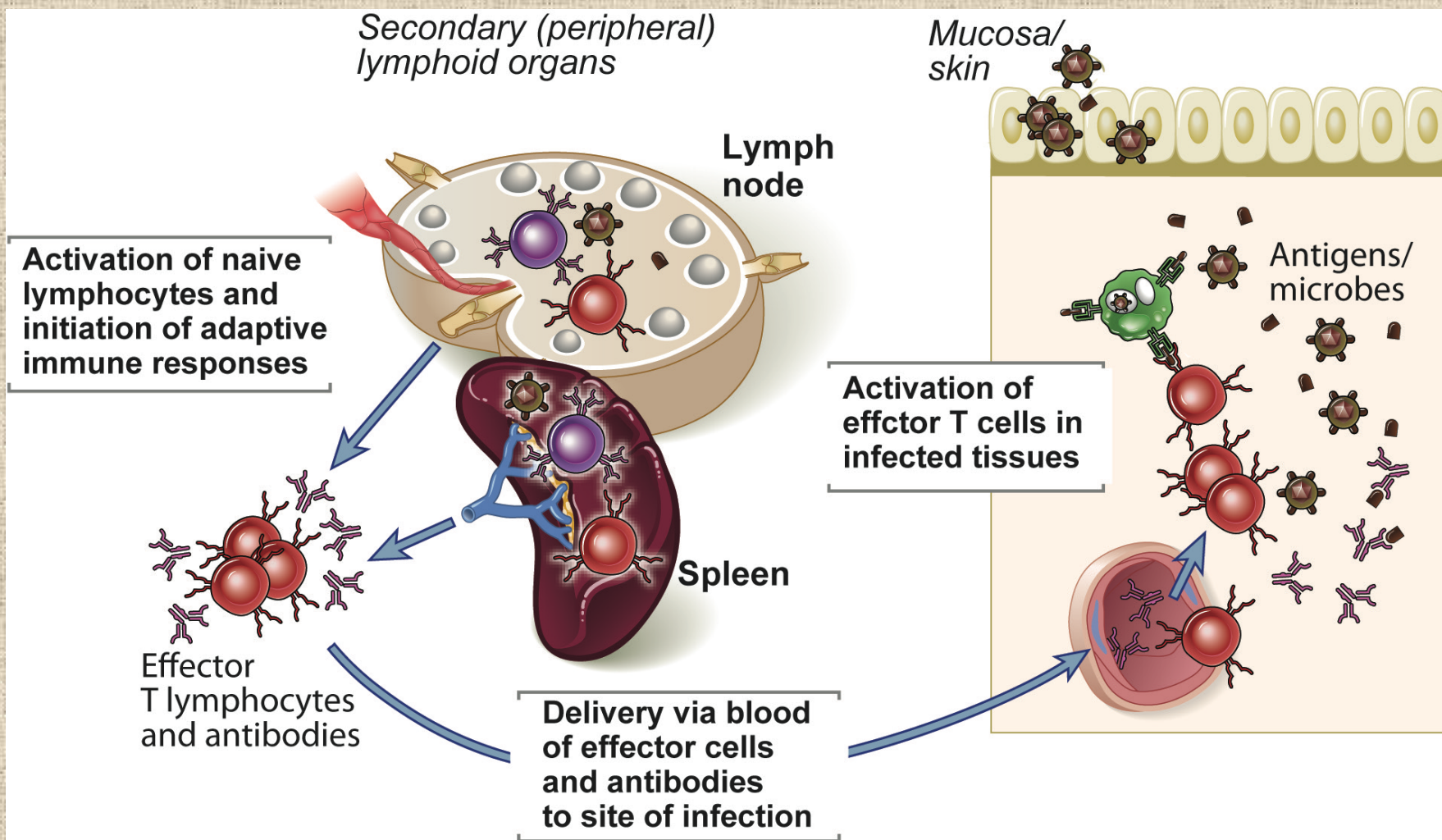
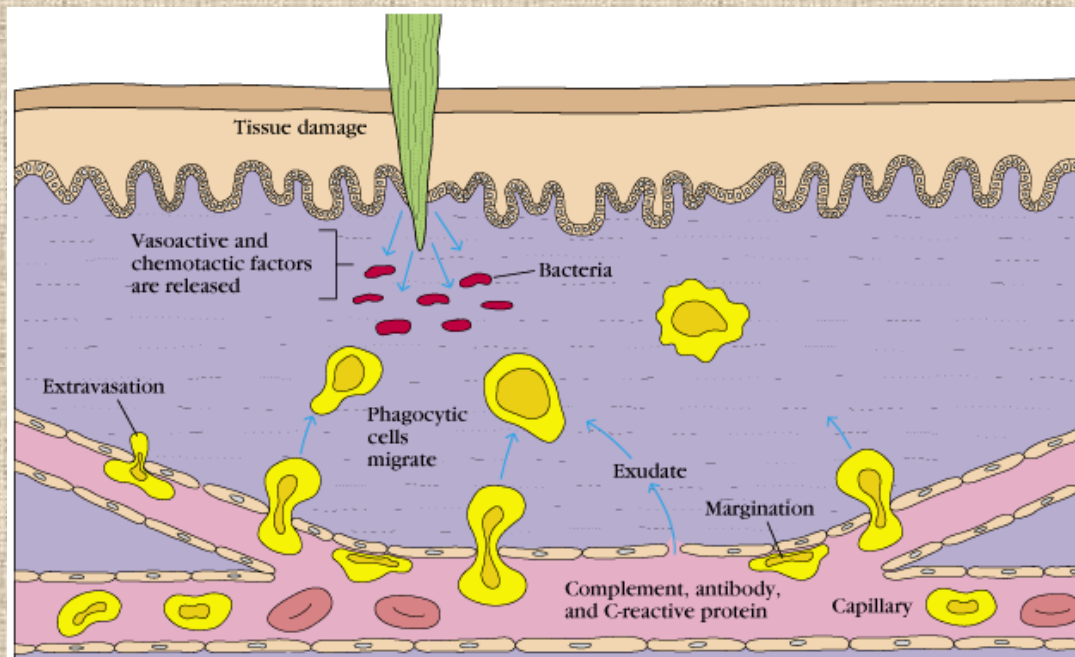


Fig. 2-6

- **Lokális, akut gyulladás kialakulása**

# Akut gyulladás:

- Fertőzés vagy szövetkárosodás nem-specifikus reakciók kaszkádját indítja el
- Azonnali válasz
- szerepe, hogy megakadályozza a fertőzés és szövetkárosodás tovaterjedését



**Celsus:** a gyulladás 4 jele: - rubor (piros), calor (meleg), dolor (fájdalmas), tumor (duzzadt) + functio laesa (csökkent funkció)

Kialakulásának

- 3 fő szakasza:
- Értágulat (vazodilatáció) – percek
  - A kapilláris permeabilitás nő, folyadék kiáramlás, ödéma
  - A fagocita sejtek kiáramlása: - órák

# A gyulladás molekuláris mediátorai

## Plazma enzim mediátorok:

Kinin-kallikrein rendszer

Fibrinolitikus rendszer

**Komplement rendszer**

Véralvadási kaszkád

## Lipid mediátorok:

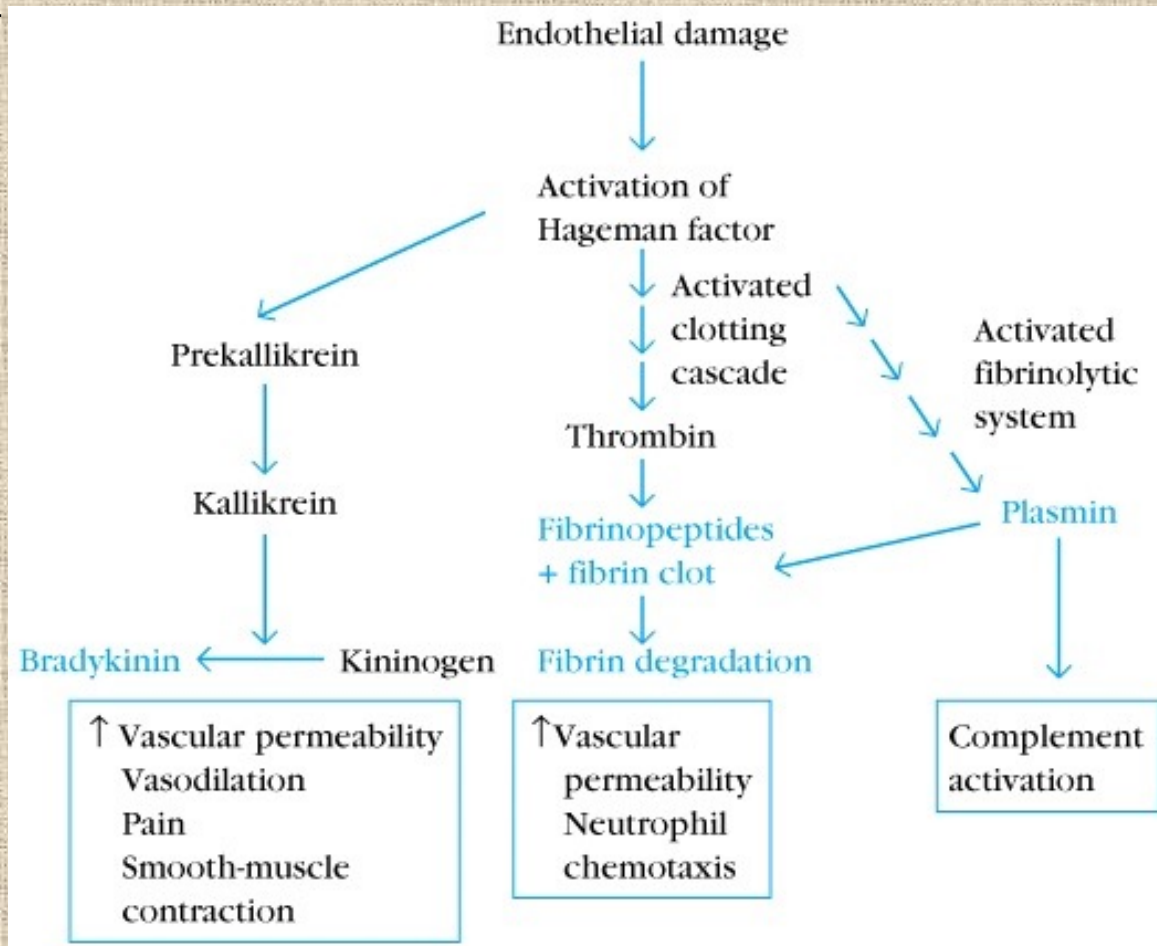
leukotriének,  
prostaglandinok (PGE)

## Kemoattraktánsok:

- kemokinek (IL-8)
- komplement alegységek
- PAF (platelet activating factor)

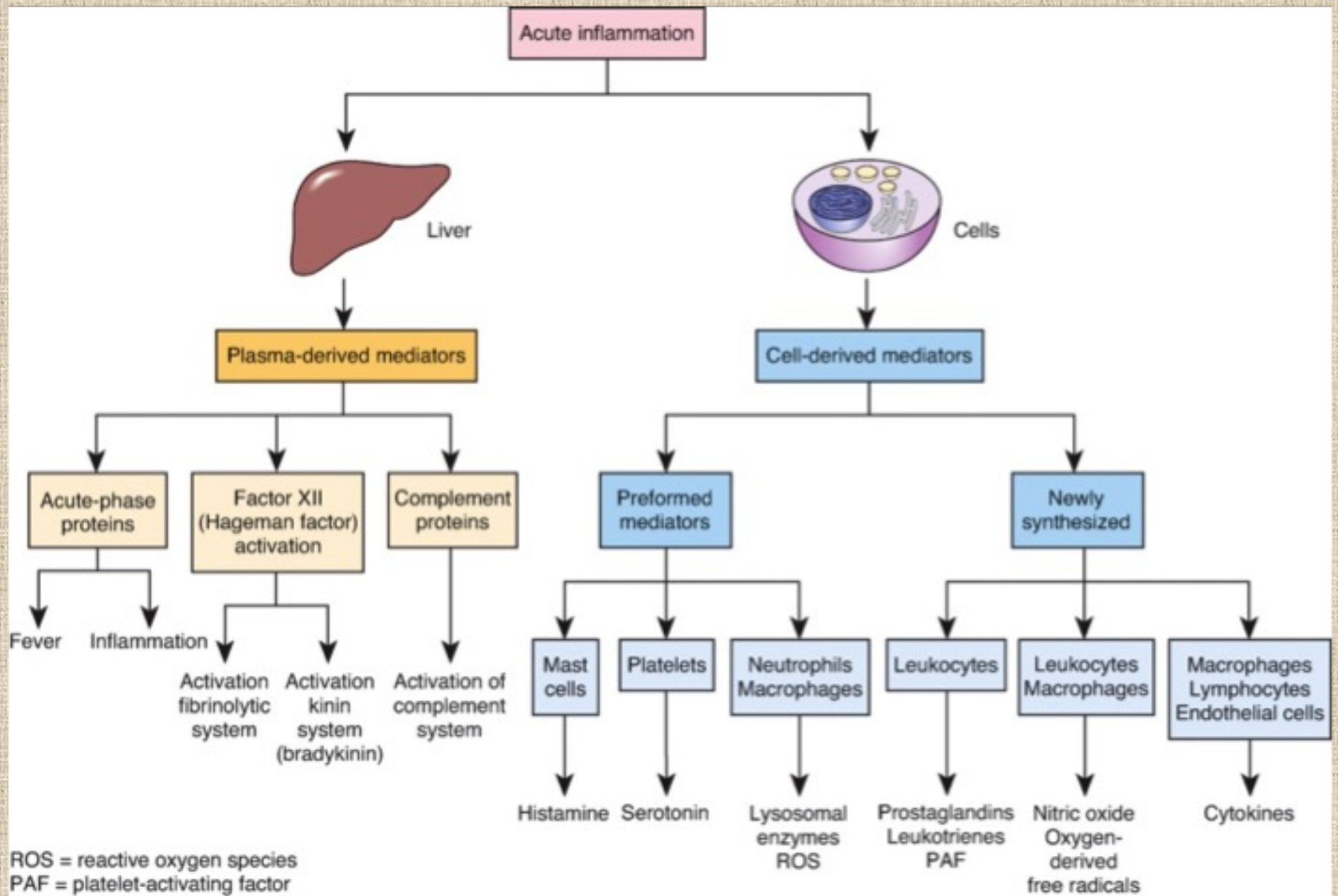
## Gyulladásos citokinek:

IL-1, IL-6, TNFalpha

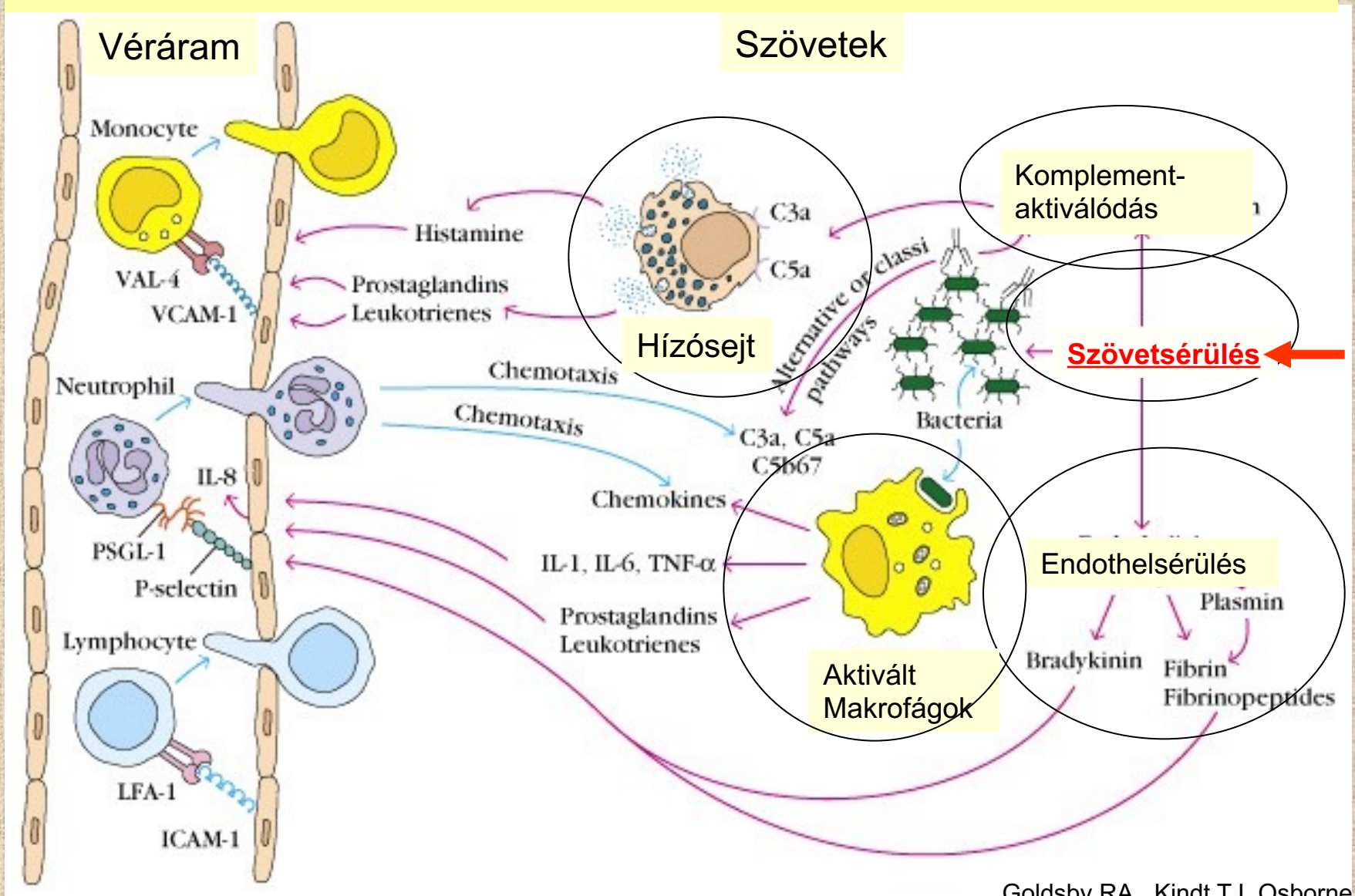




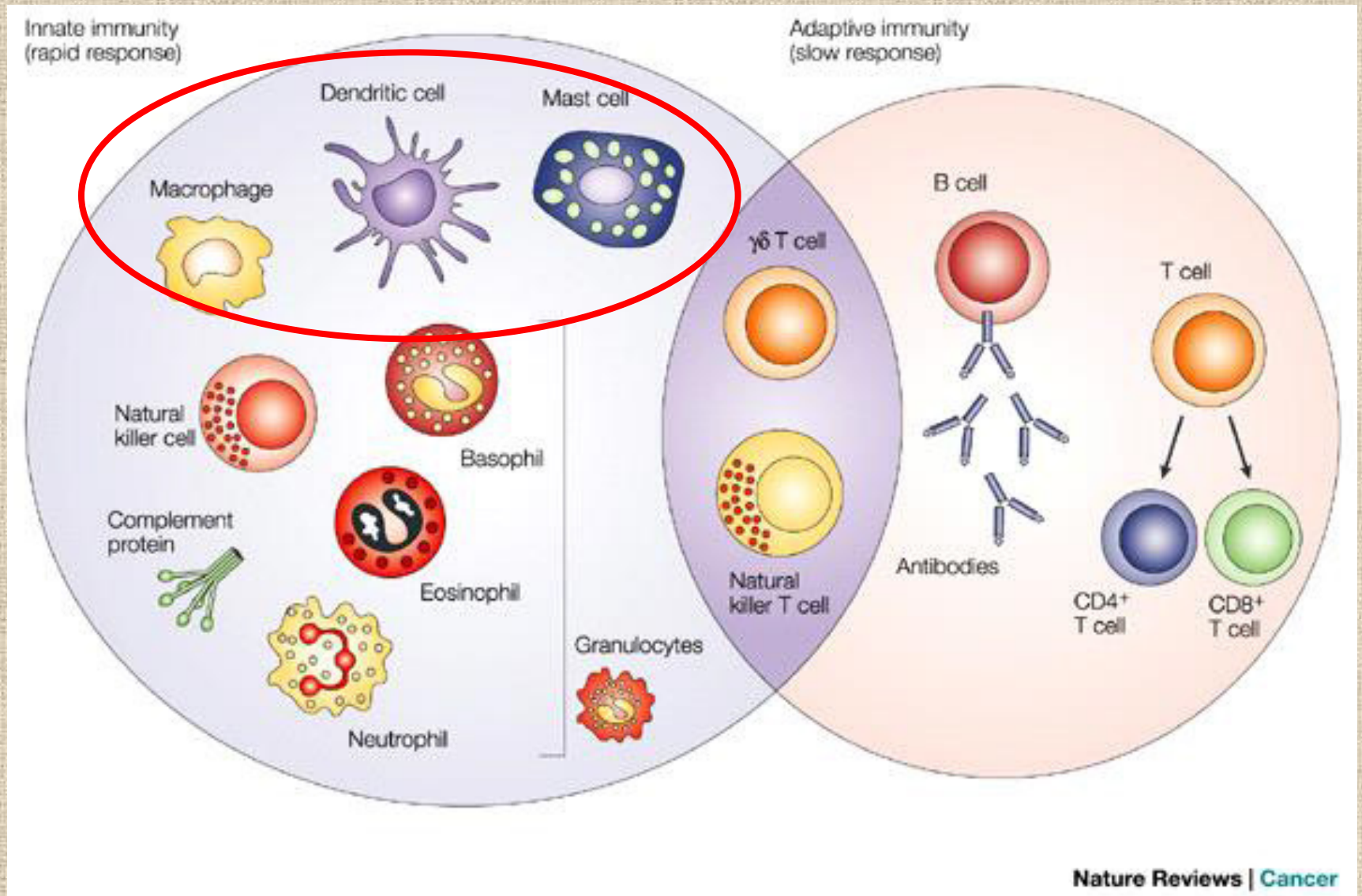
# A gyulladás molekuláris mediátorai



# Az akut gyulladás kialakulása



# Sejtes elemek



# Leukocita toborzás a szövetekbe

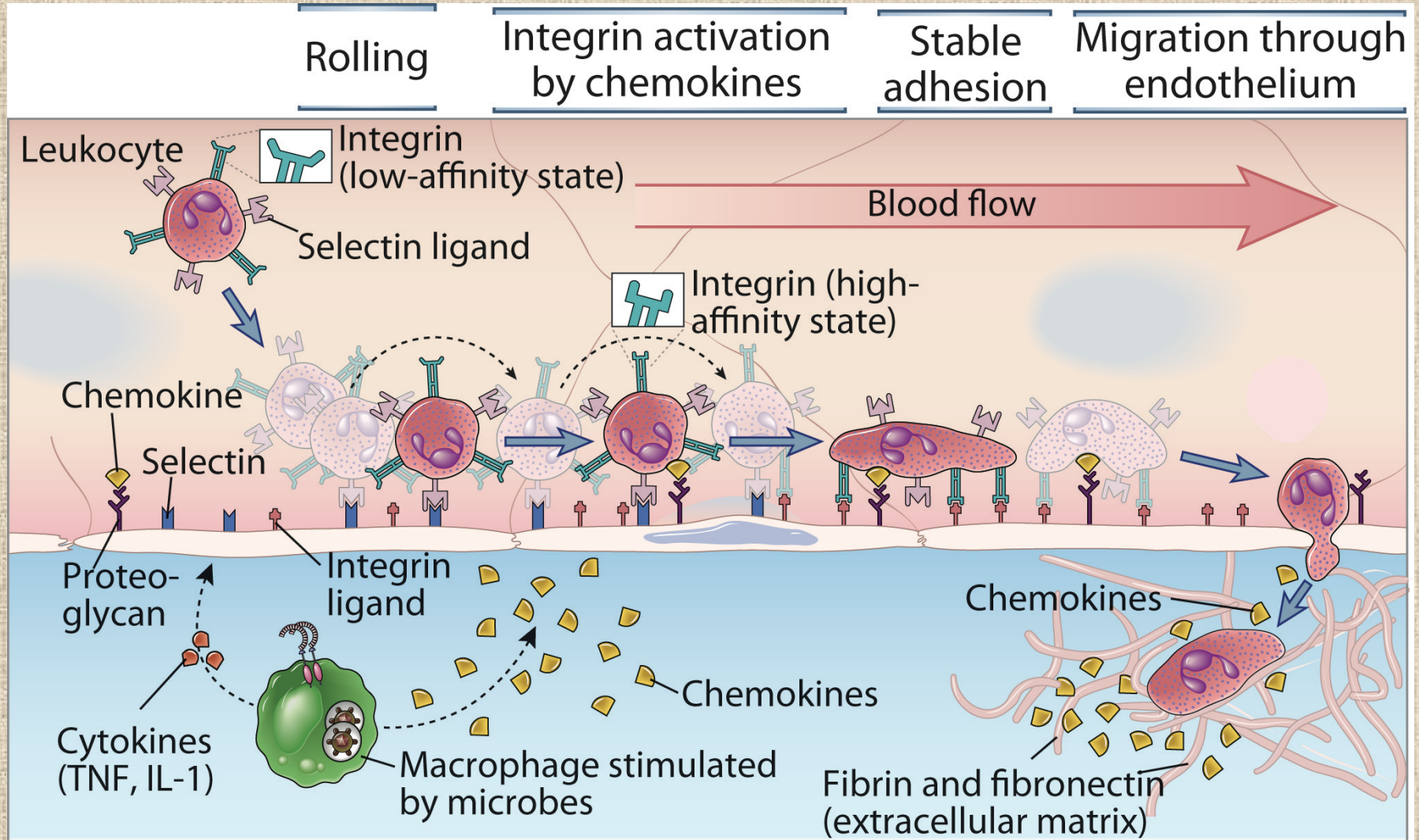
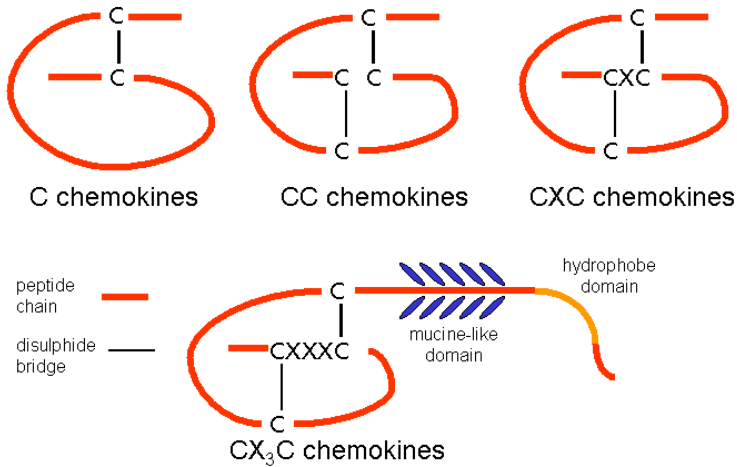


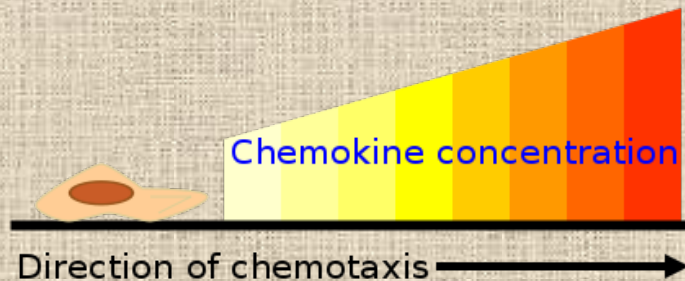
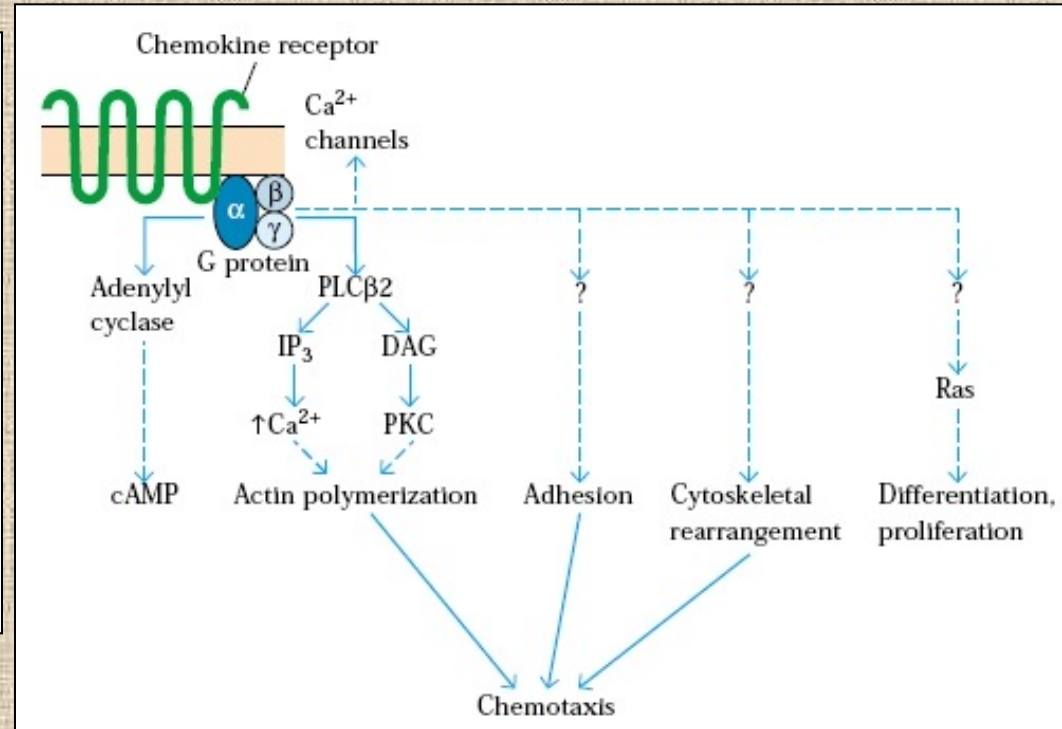
Fig. 3-3

# Kemokinek hatásmódja

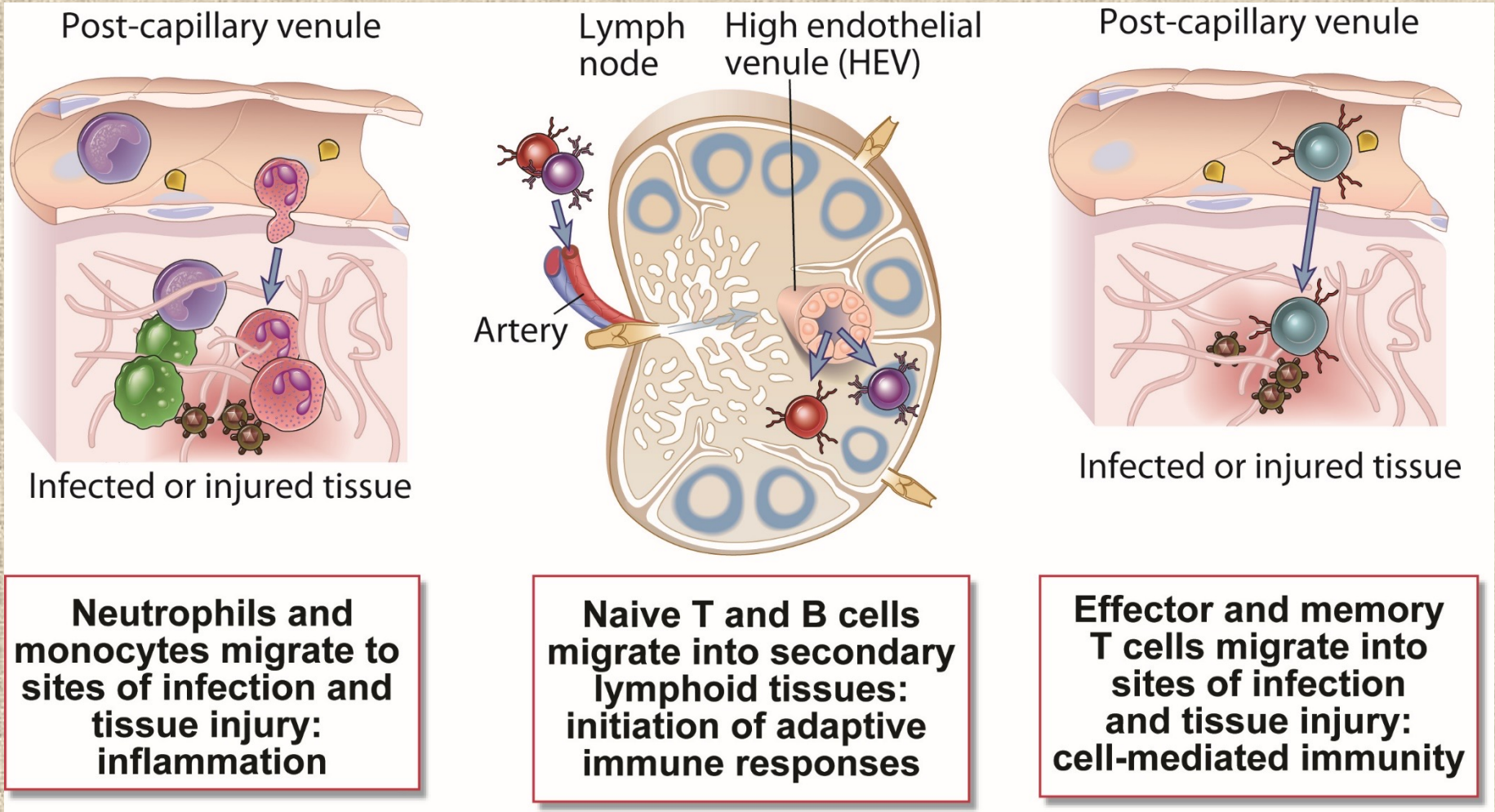
Structure of chemokine classes



© Kohidai, L.



# Leukocita migráció által biztosított folyamatok

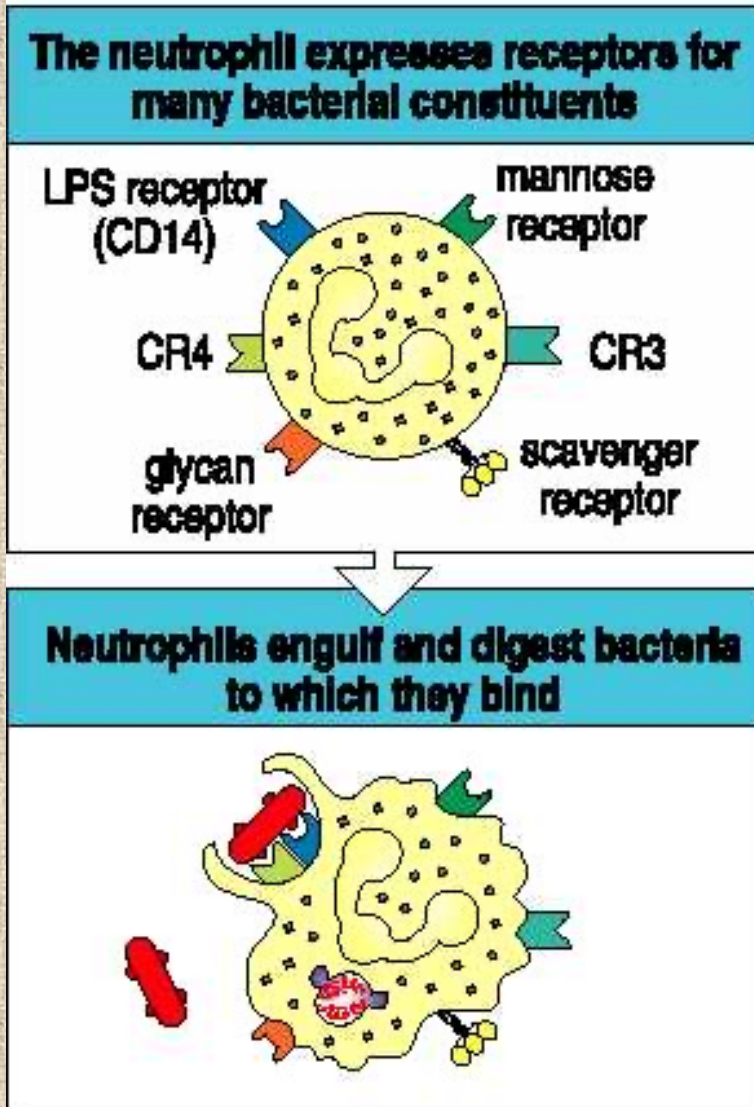


**All lymphocyte circulates approx. 1-2 times per day.**

Fig. 3-1

# Mikroba felismerés, fagocitózis

Figure 8.8

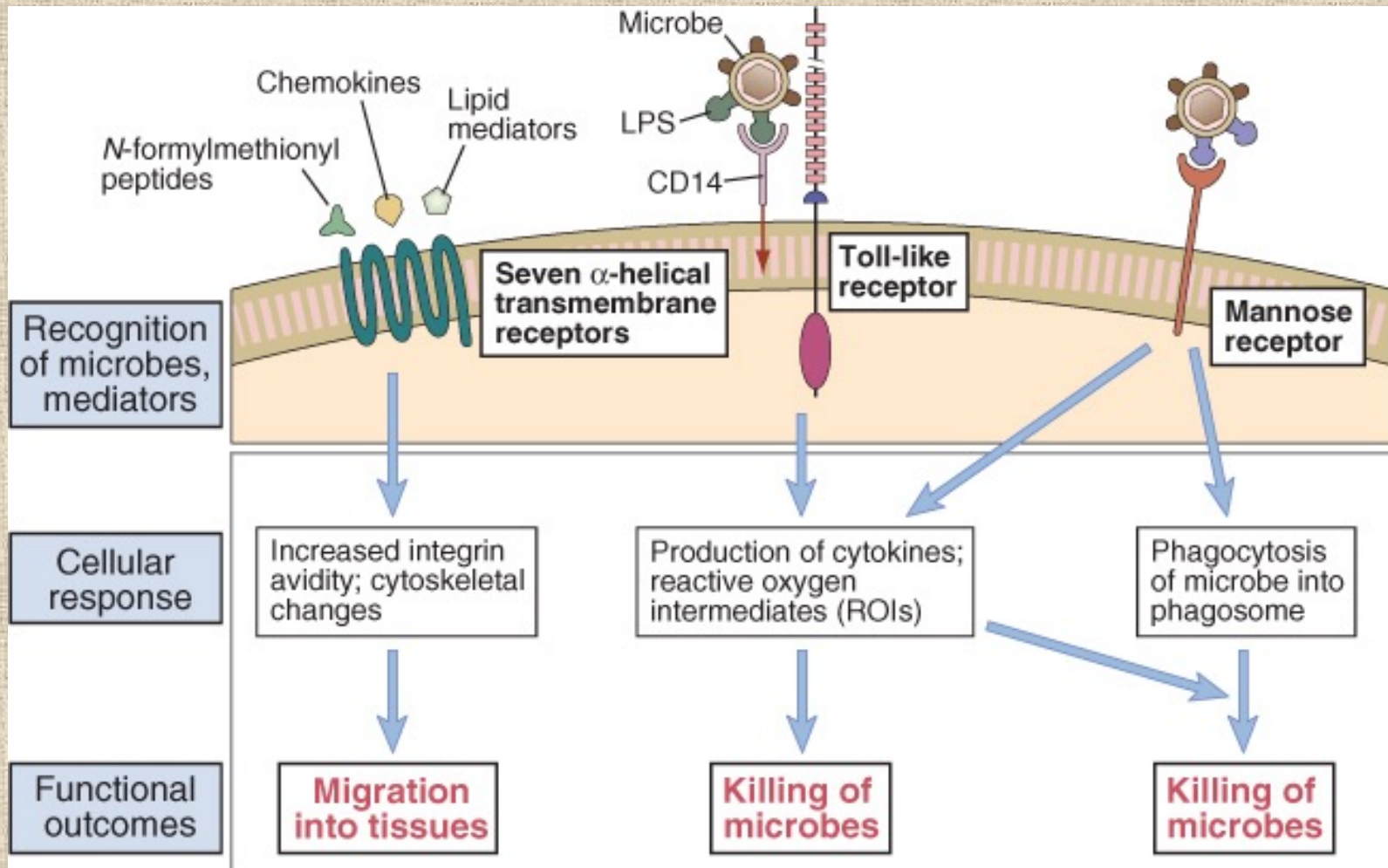


**PRR** = „Pattern Recognition Receptors”

→ Binding to the PAMPS of microbes

**PAMP** = „Pathogen Associated Molecular Patterns

# Phagocyte receptors

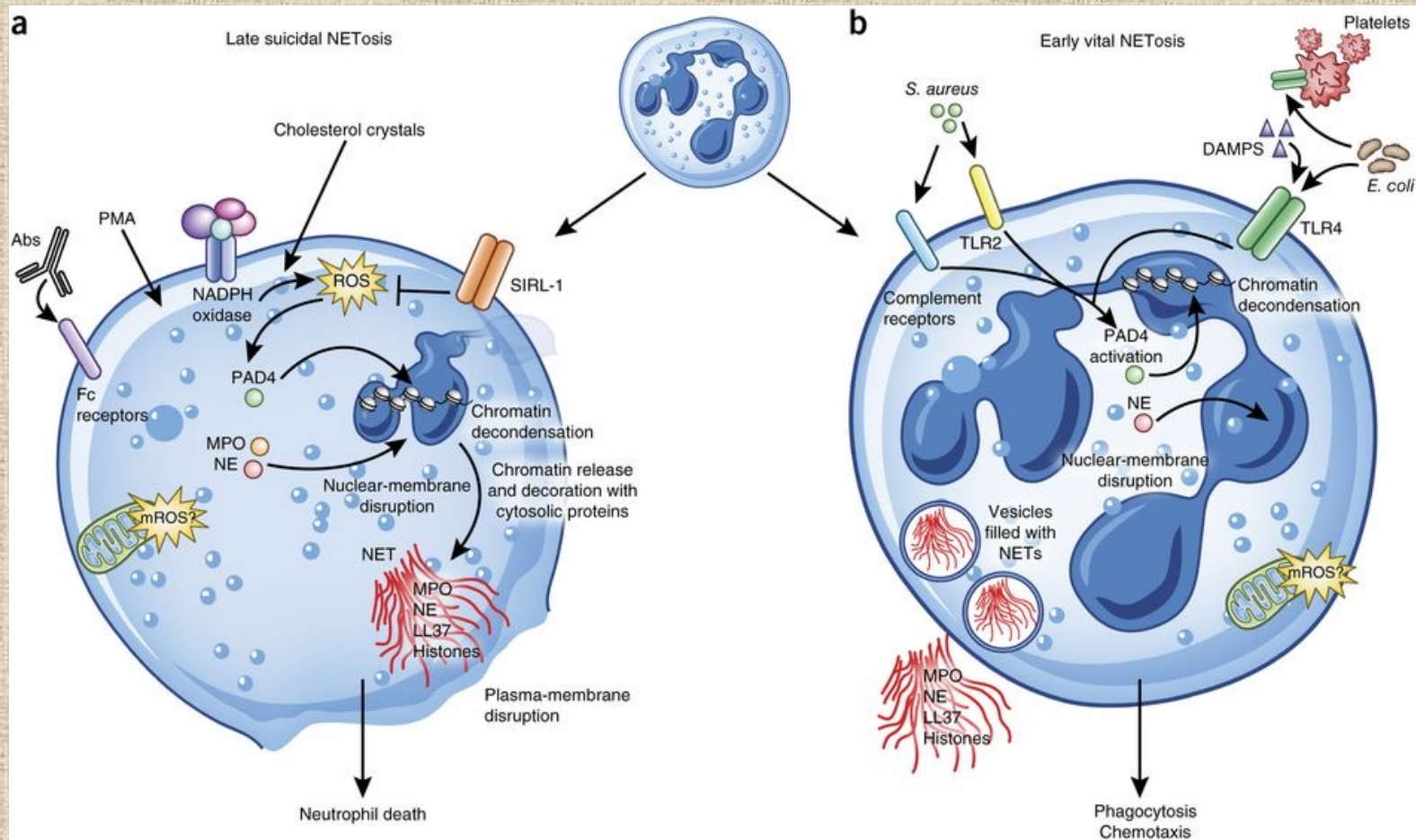


© Elsevier 2005. Abbas & Lichtman: Cellular and Molecular Immunology 5e [www.studentconsult.com](http://www.studentconsult.com)



# Neutrophil extracellular traps (NETs)

Networks of extracellular fibers, primarily composed of DNA and granule content from neutrophils, which bind pathogens.

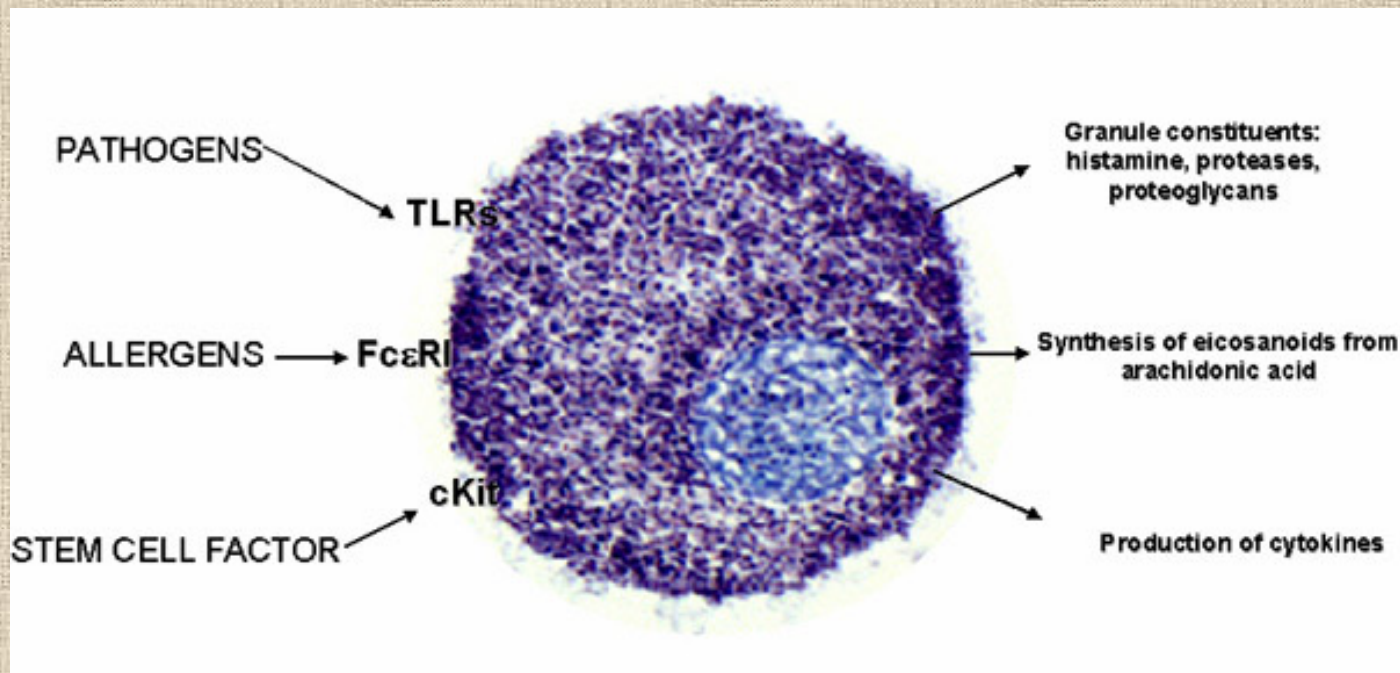


# Hízósejtek aktivációja

**TLR4** – LPS → IL-1 $\beta$ , TNF- $\alpha$ , IL-6 and IL-13, without mast cell degranulation

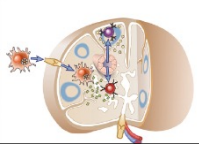
**TLR2** – peptidoglycan → mast cell degranulation and production of IL-4 and IL-5, IL-6, IL-13

**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 $\epsilon$ 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



# Makrofág és dendritikus sejt érés

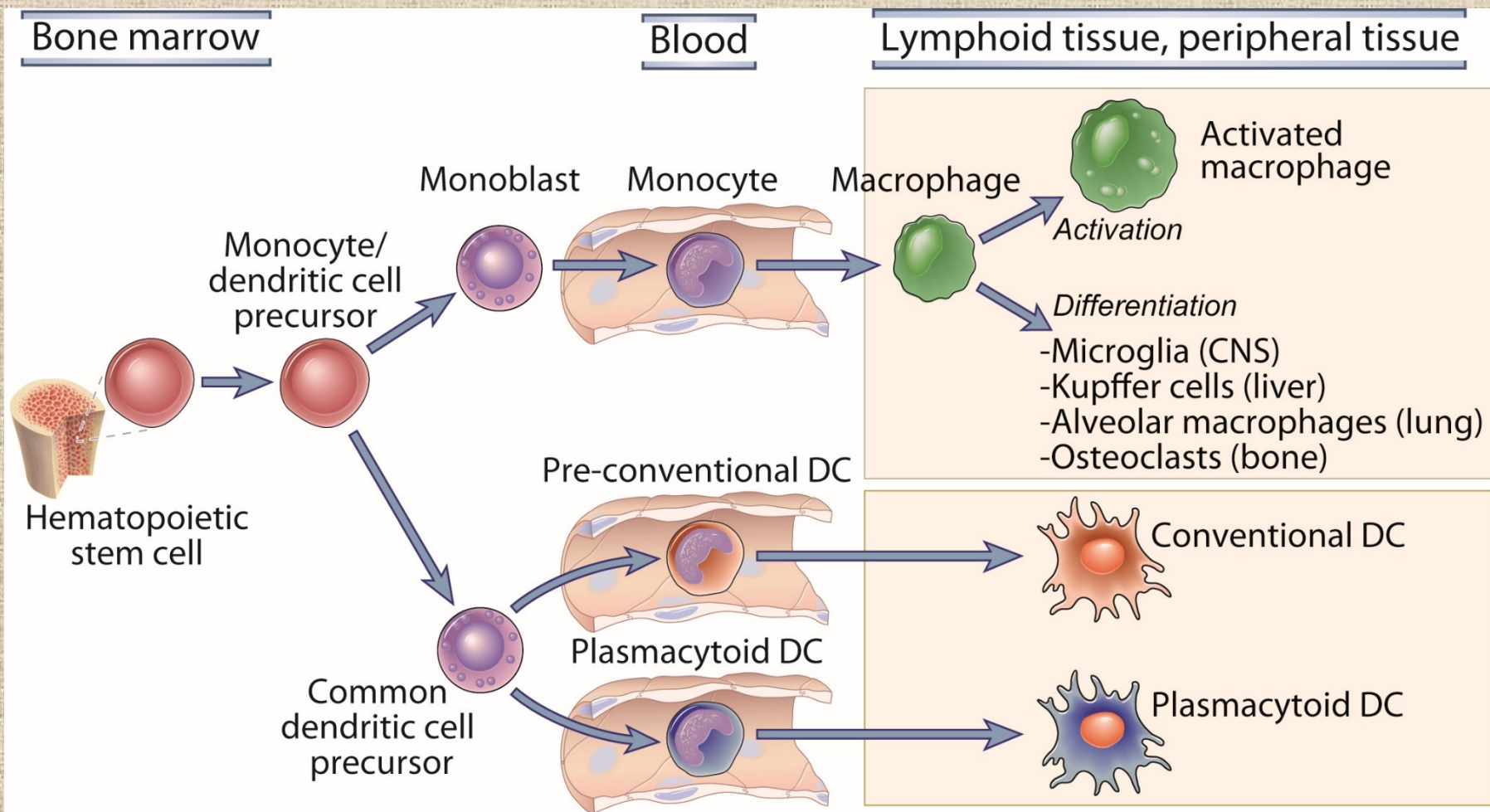
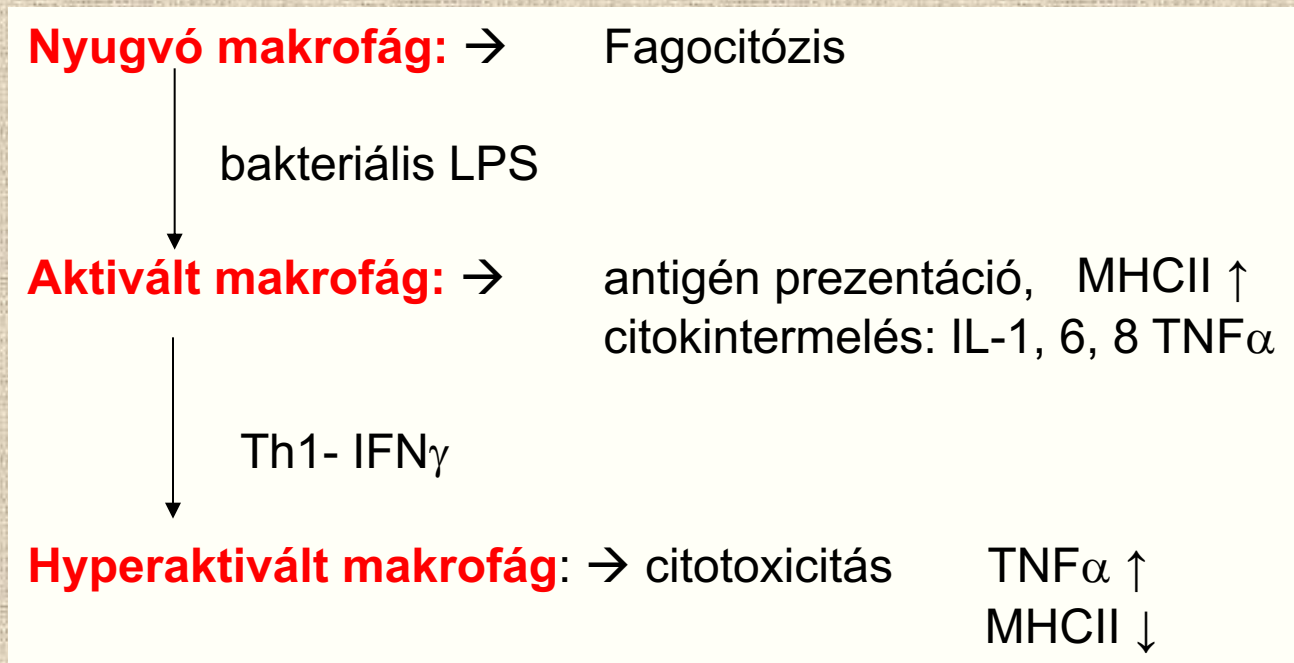


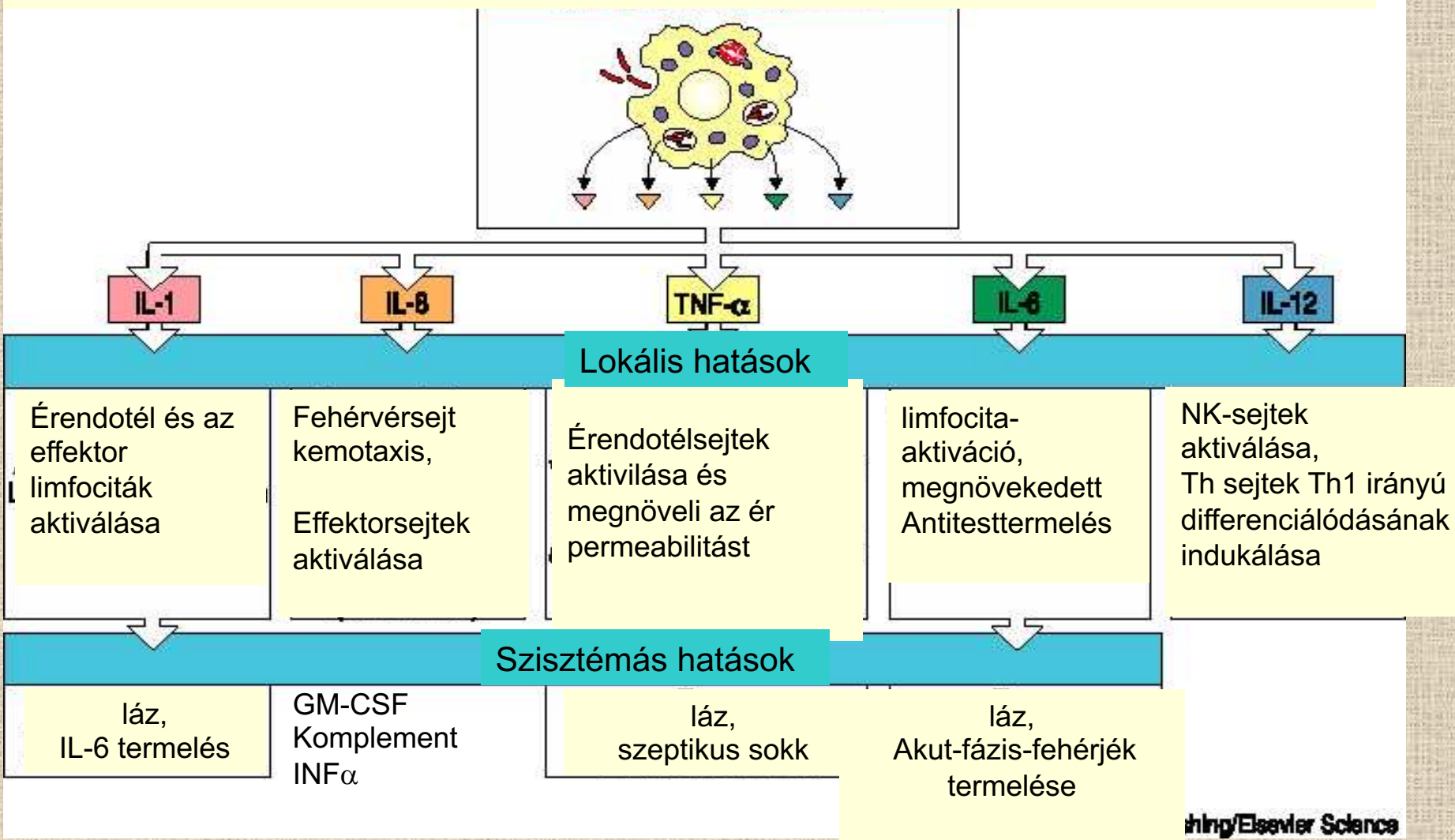
Fig. 2-2

# Makrofág aktiváció és funkció

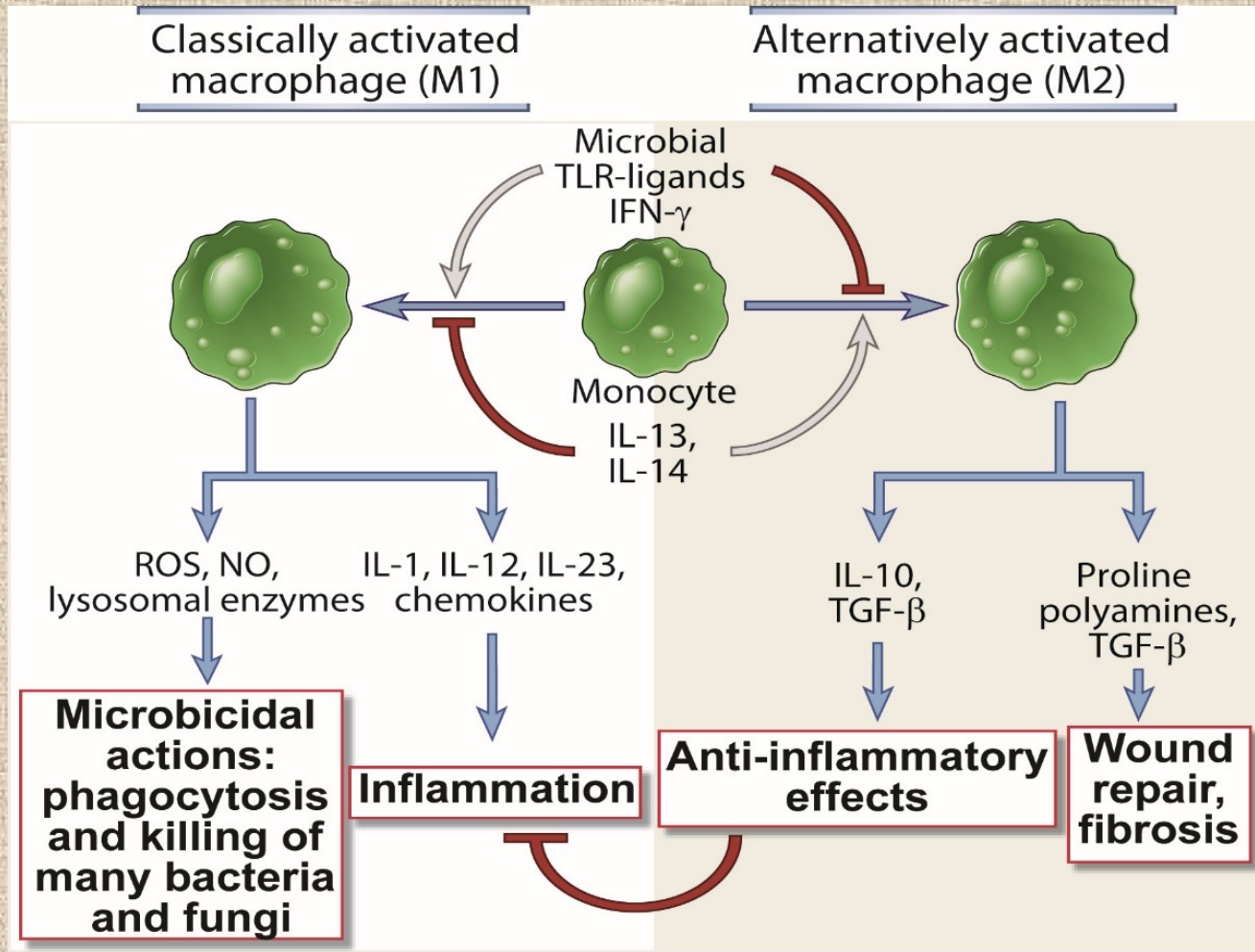


# A makrofágok szerepe az akut gyulladásban:

A Gram- baktérium eredetű LPS aktiválja a makrofágokat, melyek különböző **citokineket termelnek**



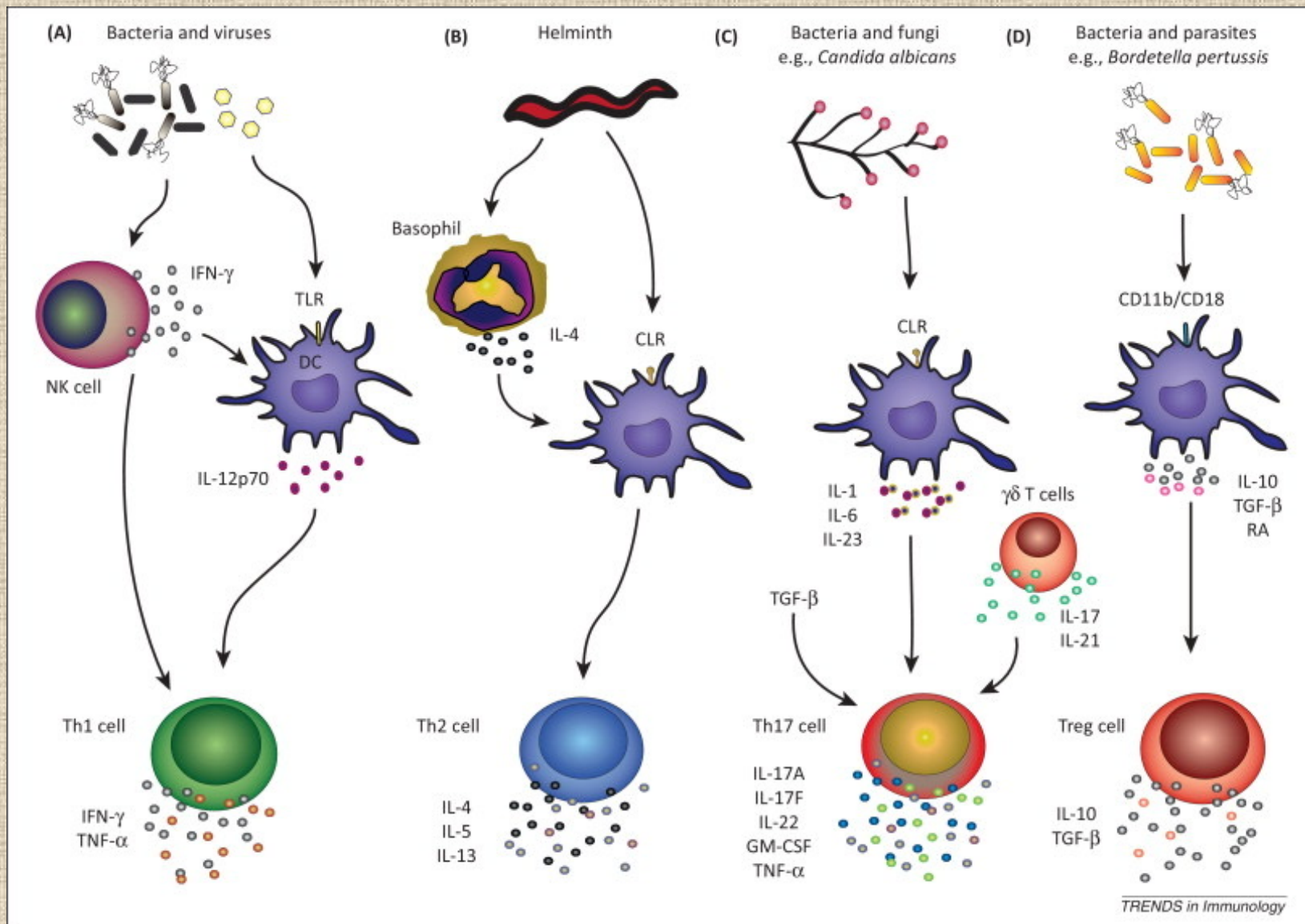
# Makrofág polarizáció a gyulladásban



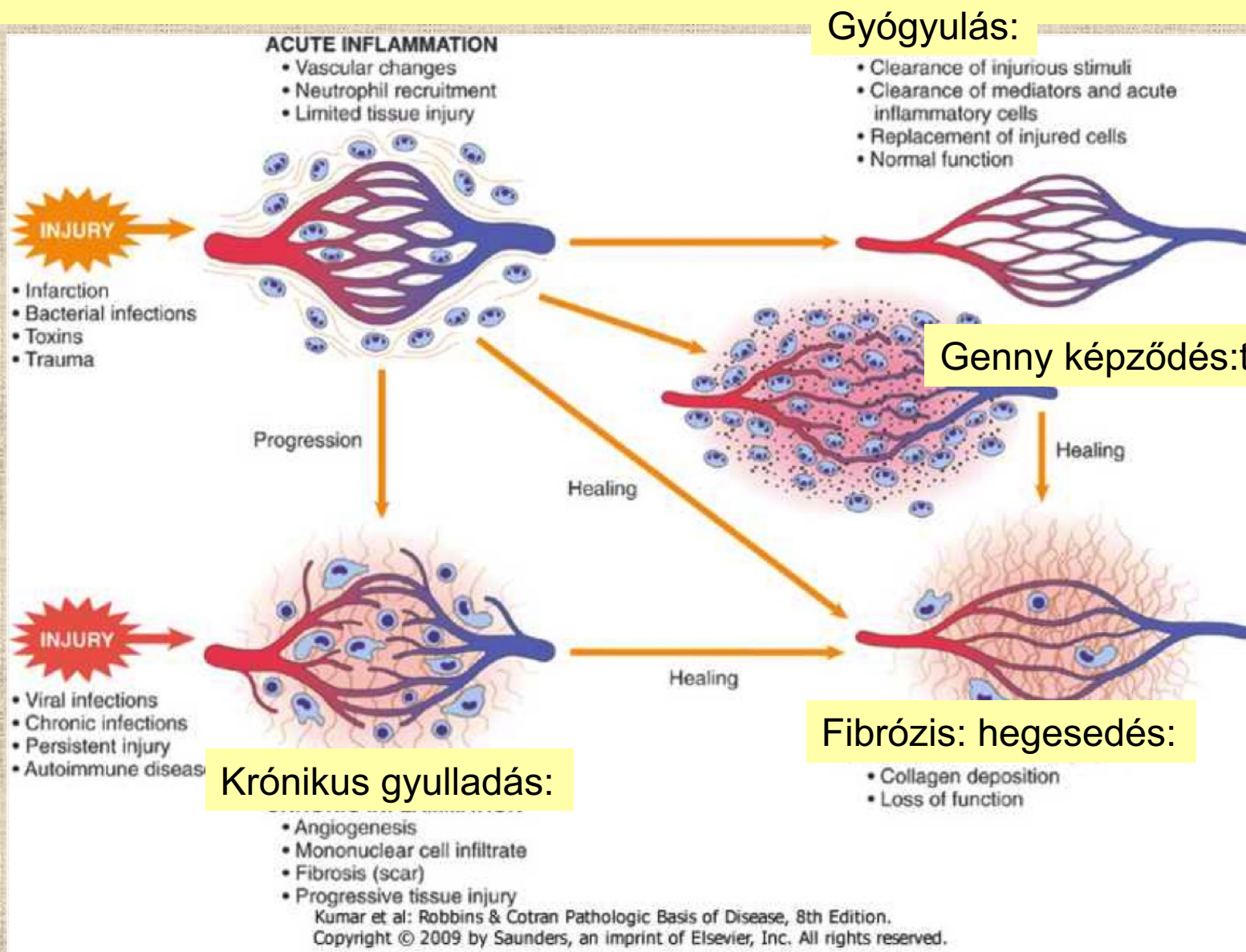
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

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

# Dendritikus sejt polarizáció



# Az akut gyulladás kimenetele





# A krónikus gyulladás kiváltó tényezői

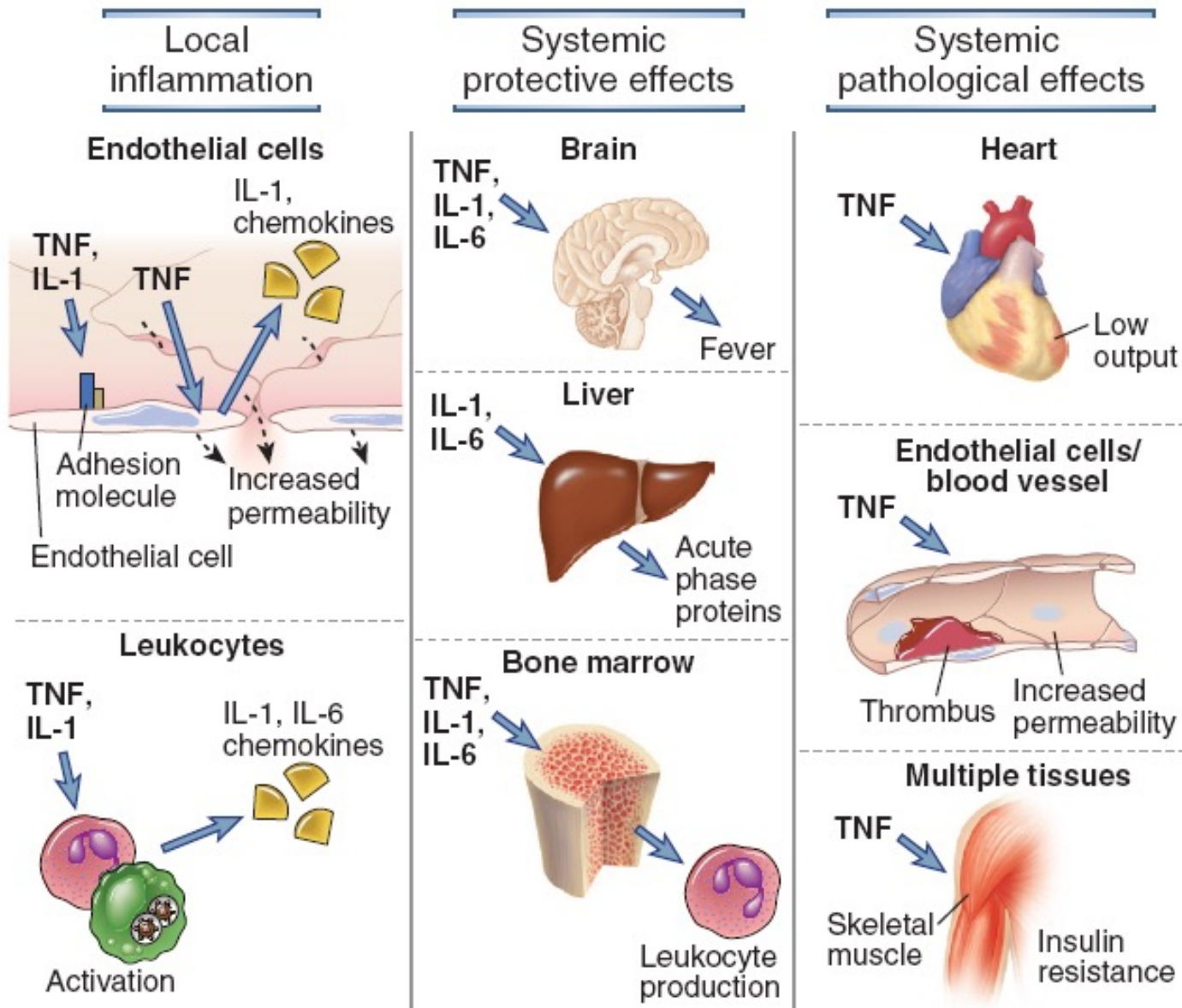
Unlike acute inflammation showing redness, swelling and pain, chronic inflammation can be invisible

## 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

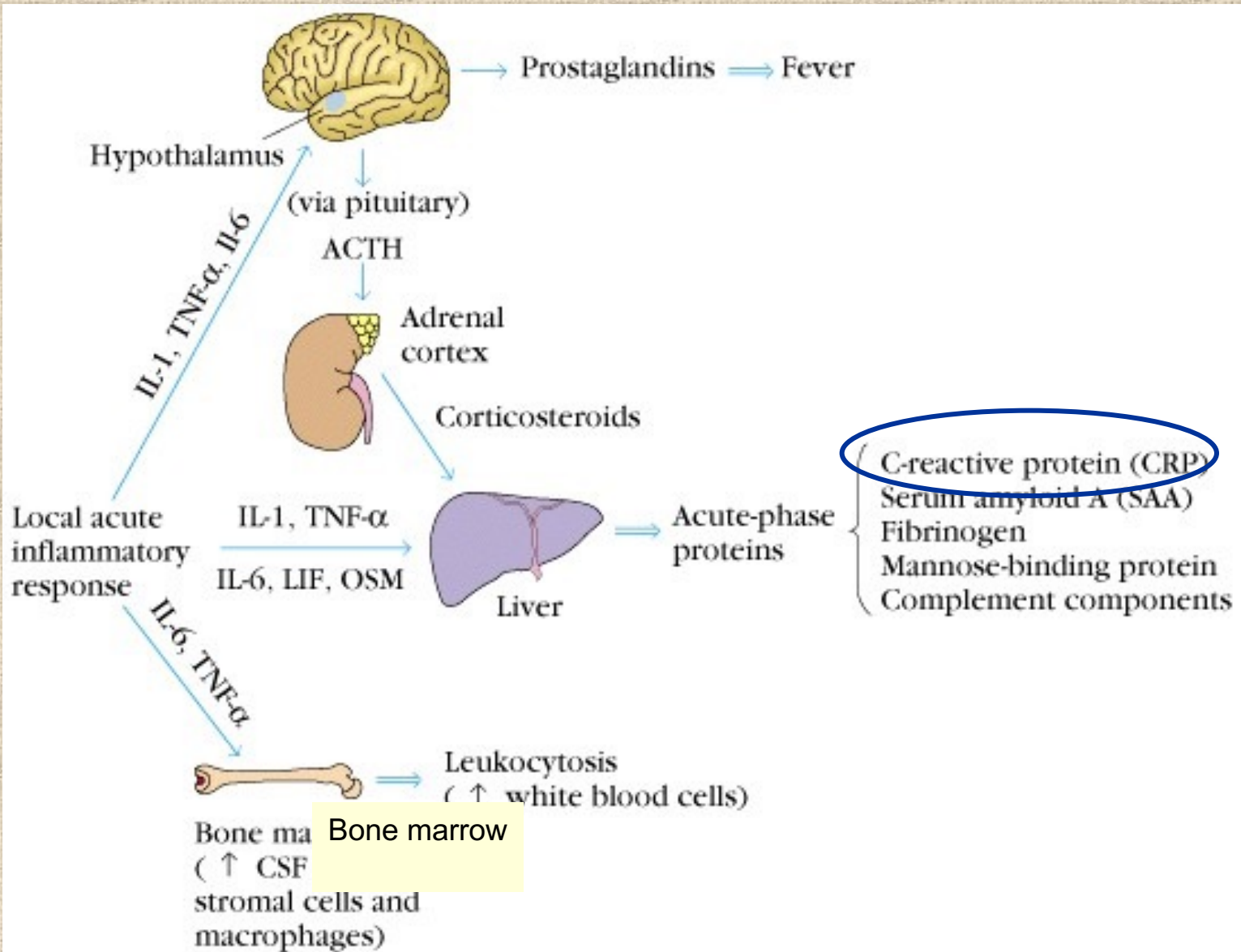
- **Szisztémás gyulladás**

# A TNF $\alpha$ koncentráció-függő hatásai

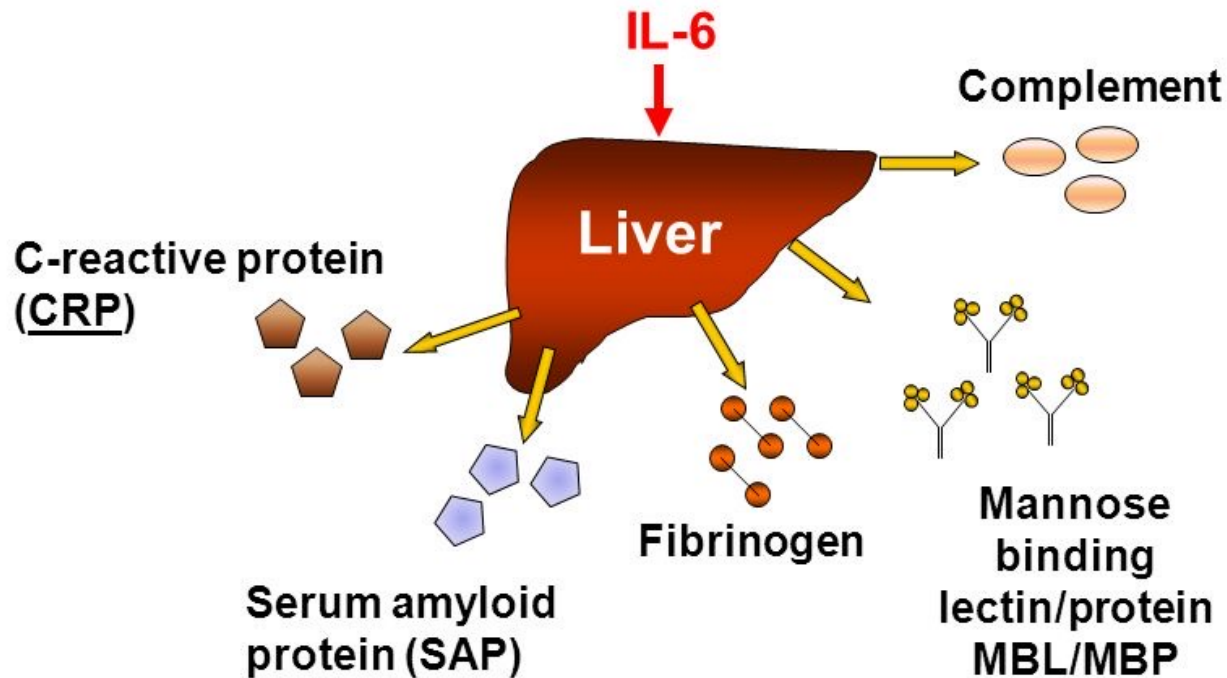


TNF inhibitors,  
Steroids

# Szisztémás gyulladás = akut fázis reakció



# ACUTE PHASE REACTION



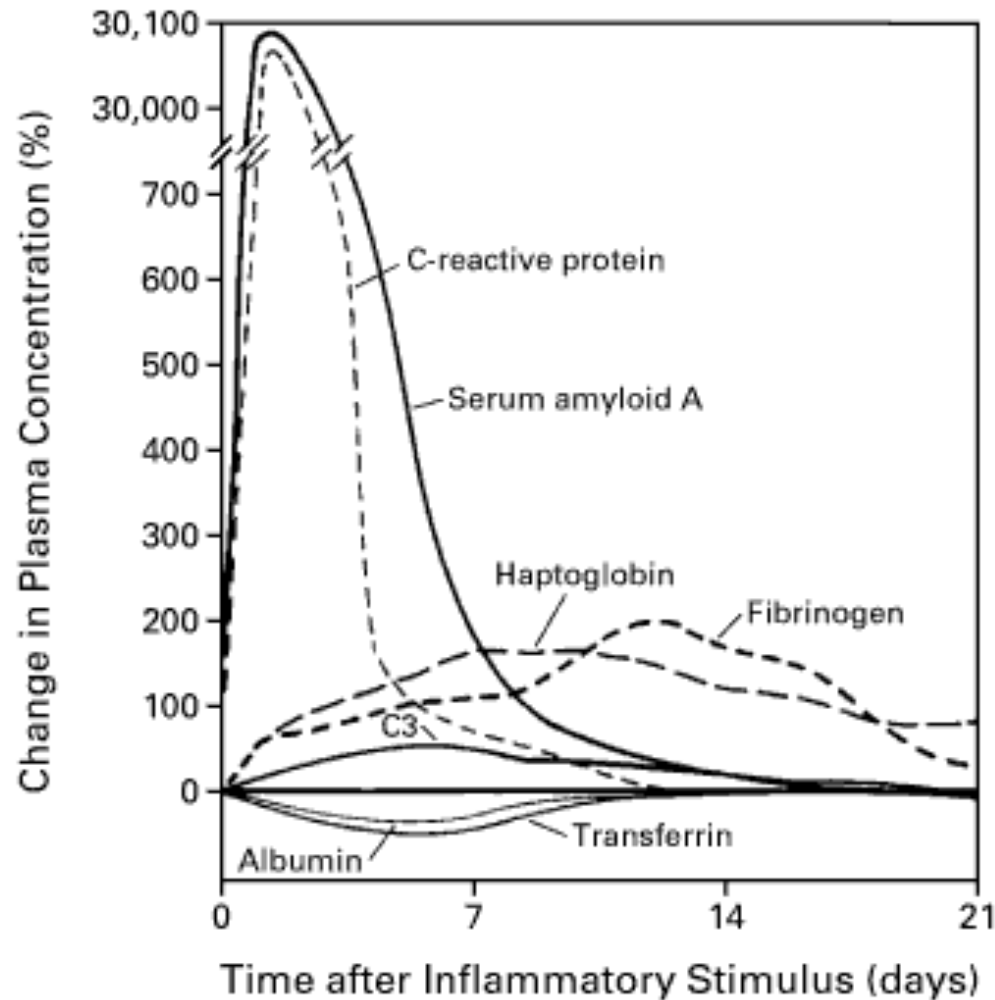
**UNDER THE INFLUENCE OF IL-6 THE LIVER PRODUCES A BUNCH OF ACUTE-PHASE PROTEINS**

## Systemic effects of acute inflammation *acute phase response*

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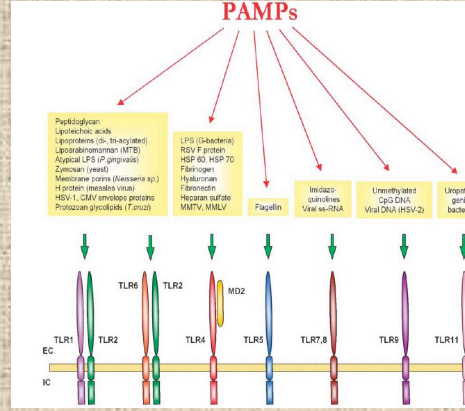
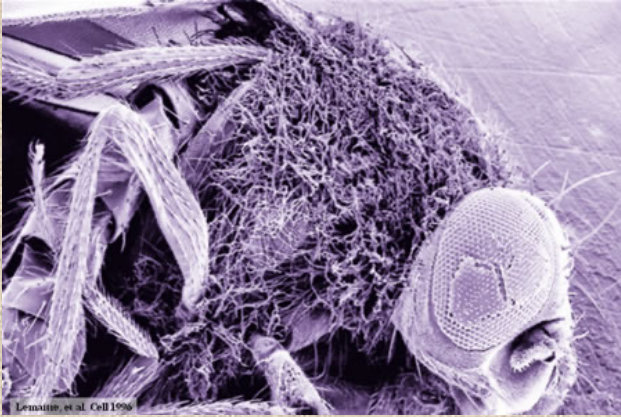
- Fever (temperature  $> 37.8^{\circ}\text{C}$  or  $>100\text{ F}$ )
  - Increased pulse, blood pressure
  - Chills
  - Anorexia
- Leukocytosis
  - neutrophilia and left shift of neutrophils points to bacterial infection
  - Lymphocytosis points to viral infection
  - Eosinophilia point to allergy or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

# Akut fázis fehérjék megjelenése a szérumban

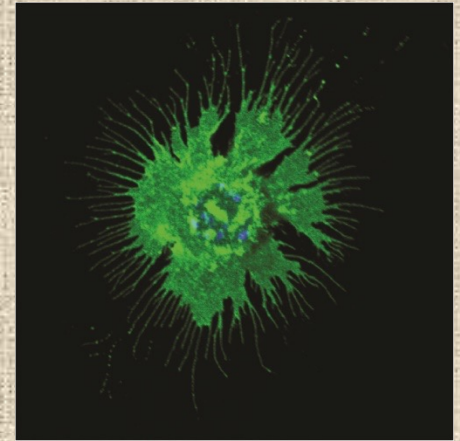


# Orvostudományi-fiziológiai Nobel-díj 2011

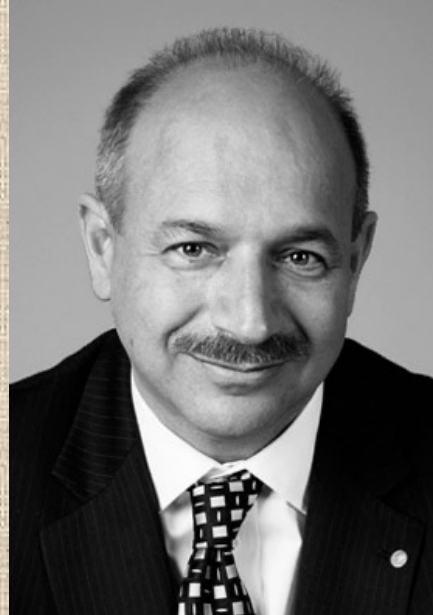
Lemaitre et al., 1996, Cell 86:973



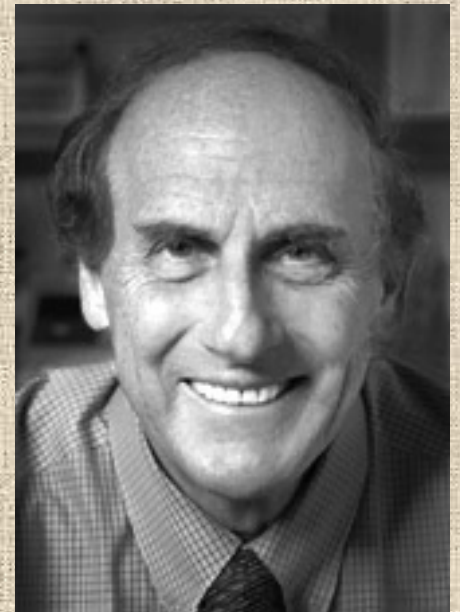
Folia Biologica (Praha) 2005; 51: 148-156



Jules A. Hoffmann



Bruce A. Beutler



Ralph M. Steinmann