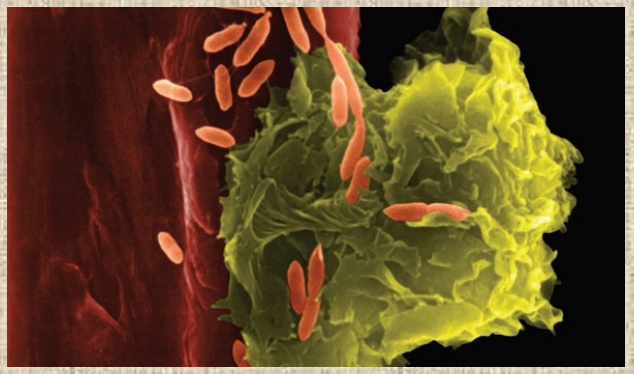
Az immunológia alapjai

3. előadás

Az immunválasz kezdeti lépései: veleszületett immunválasz, mintázatfelismerés

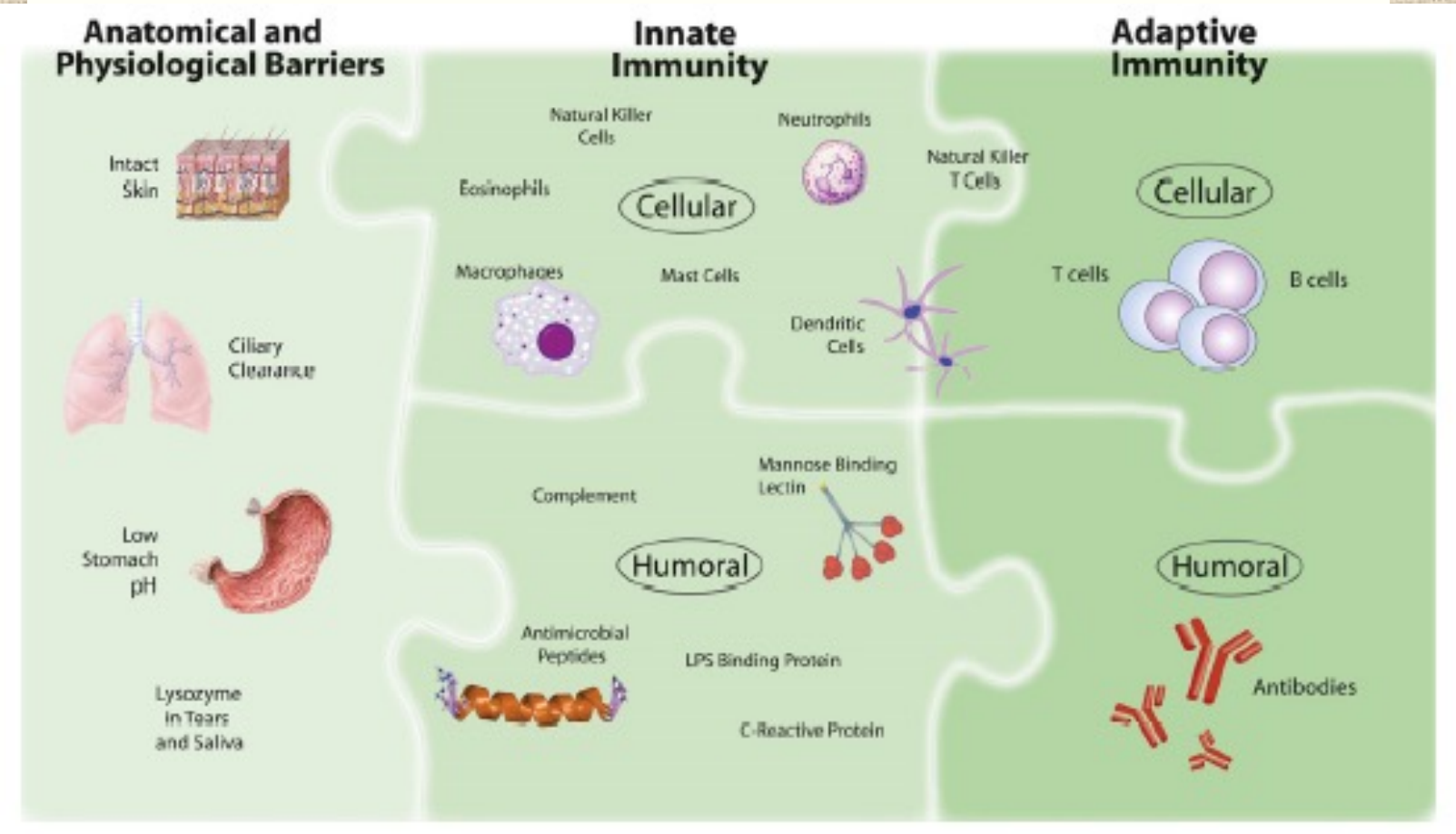


Engelmann Péter

- Az immunvédekezés különböző szintjei
- A veleszületett immunitás felismerő receptorai

Az immunvédekezés különböző szintjei

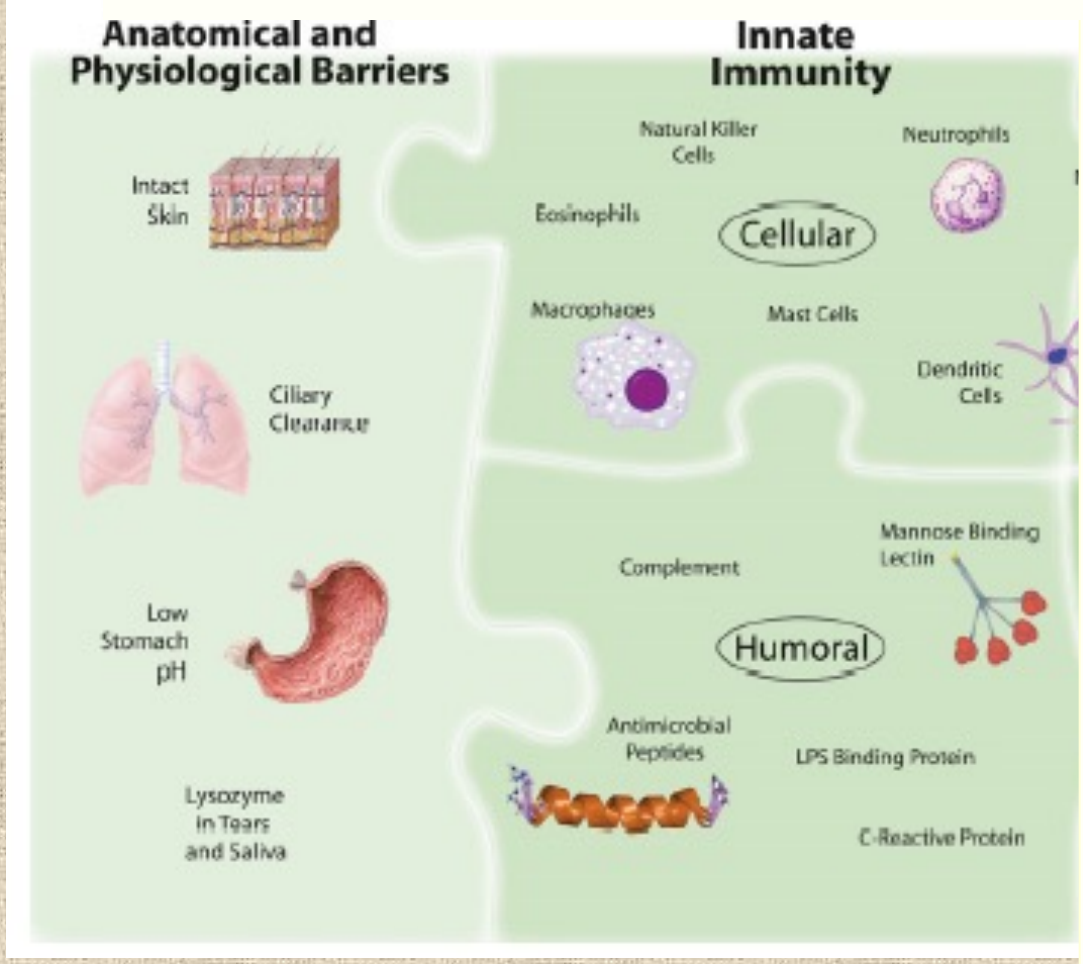
- Anatómiai „barrierek”
- Veleszületett immunválasz, gyulladás
- Adaptív immunválasz



J Allergy Clin Immunol. 2010;125:S24–S32.

Az immunvédekezés különböző szintjei

- Anatómiai „barrierek”
- Veleszületett immunválasz, gyulladás
- Adaptív immunválasz



J Allergy Clin Immunol. 2010;125:S24–S32.

I. Az első védelmi vonal: anatómiai „barrierek”

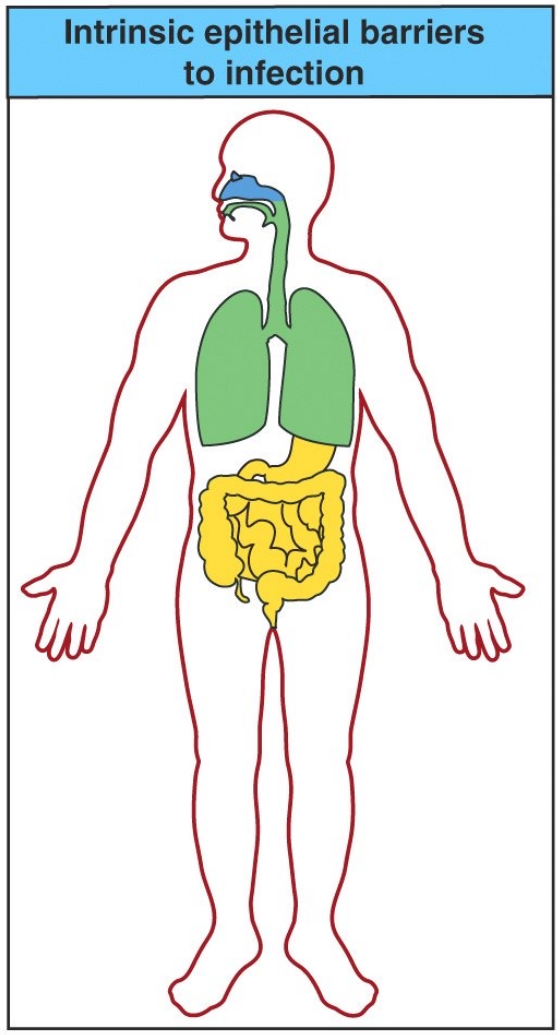


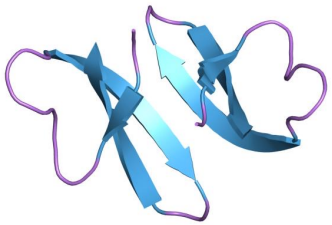
Figure 2-4 Immunobiology, 6/e. (© Garland Science 2005

	Skin	Gut	Lungs	Eyes/nose/oral cavity
Mechanical	Epithelial cells joined by tight junctions			
	Longitudinal flow of air or fluid		Movement of mucus by cilia	Tears Nasal cilia
Chemical	Fatty acids	Low pH	Pulmonary surfactant	Enzymes in tears and saliva (lysozyme)
		Enzymes (pepsin)		
	β-defensins Lamellar bodies Cathelicidin	α-defensins (cryptdins) RegIII (lecticidins) Cathelicidin	α-defensins Cathelicidin	Histatins β-defensins
Microbiological	Normal microbiota			

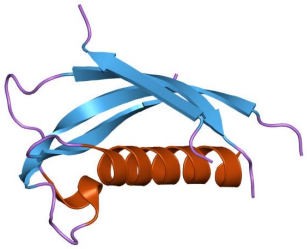
1. Mechanikai védelem
2. Enyhén savas környezet
3. Normál mikroorganizmus-flóra: az ártalmatlan baktériumok és gombák kiszorítják az kórokozó mikroorganizmusokat.
4. Antimikrobiális faktorok lizozim (nyál, könny) defenzin (bőr, bél), cryptidine (bél).
5. Cilia – a légutak megtisztítása a belélegzett partikulumoktól.

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

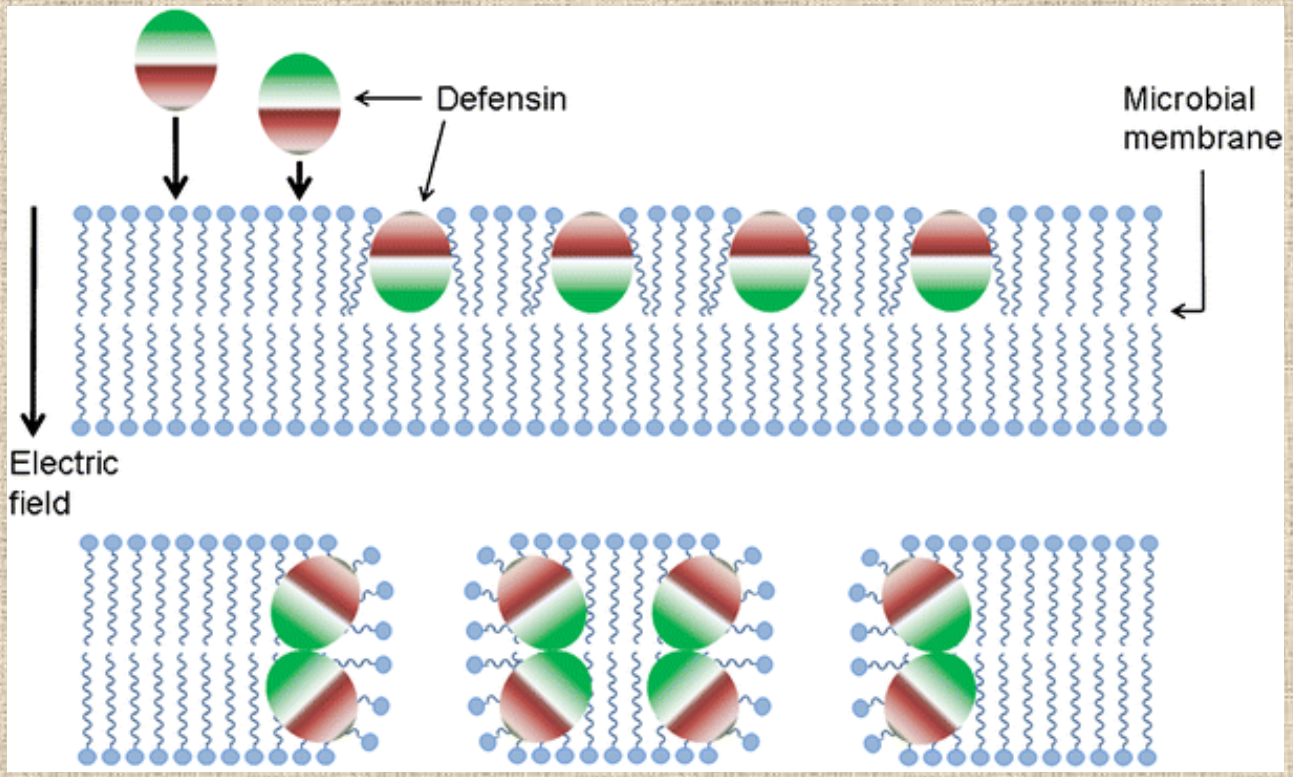
Antimikrobiális fehérjék I

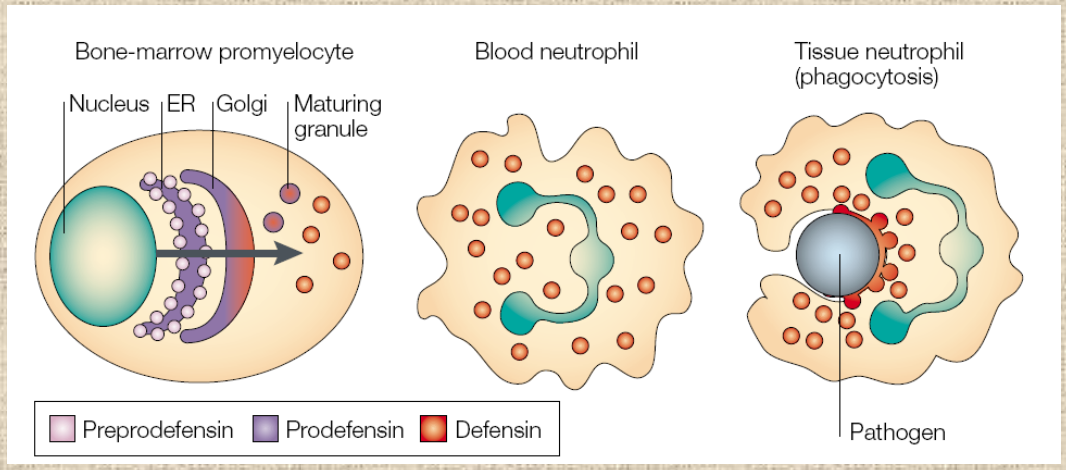


Defenzin



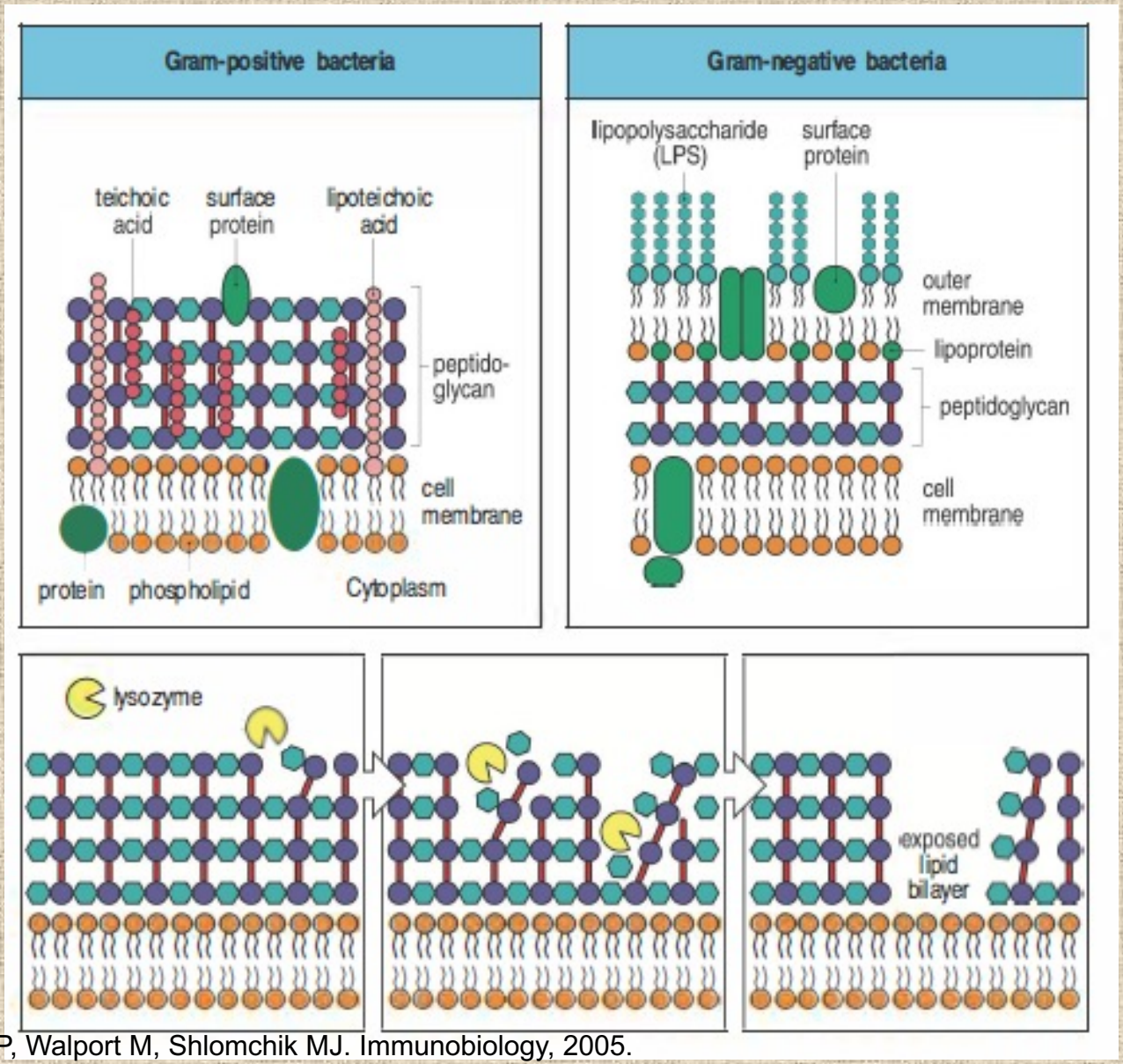
Cathelicidin





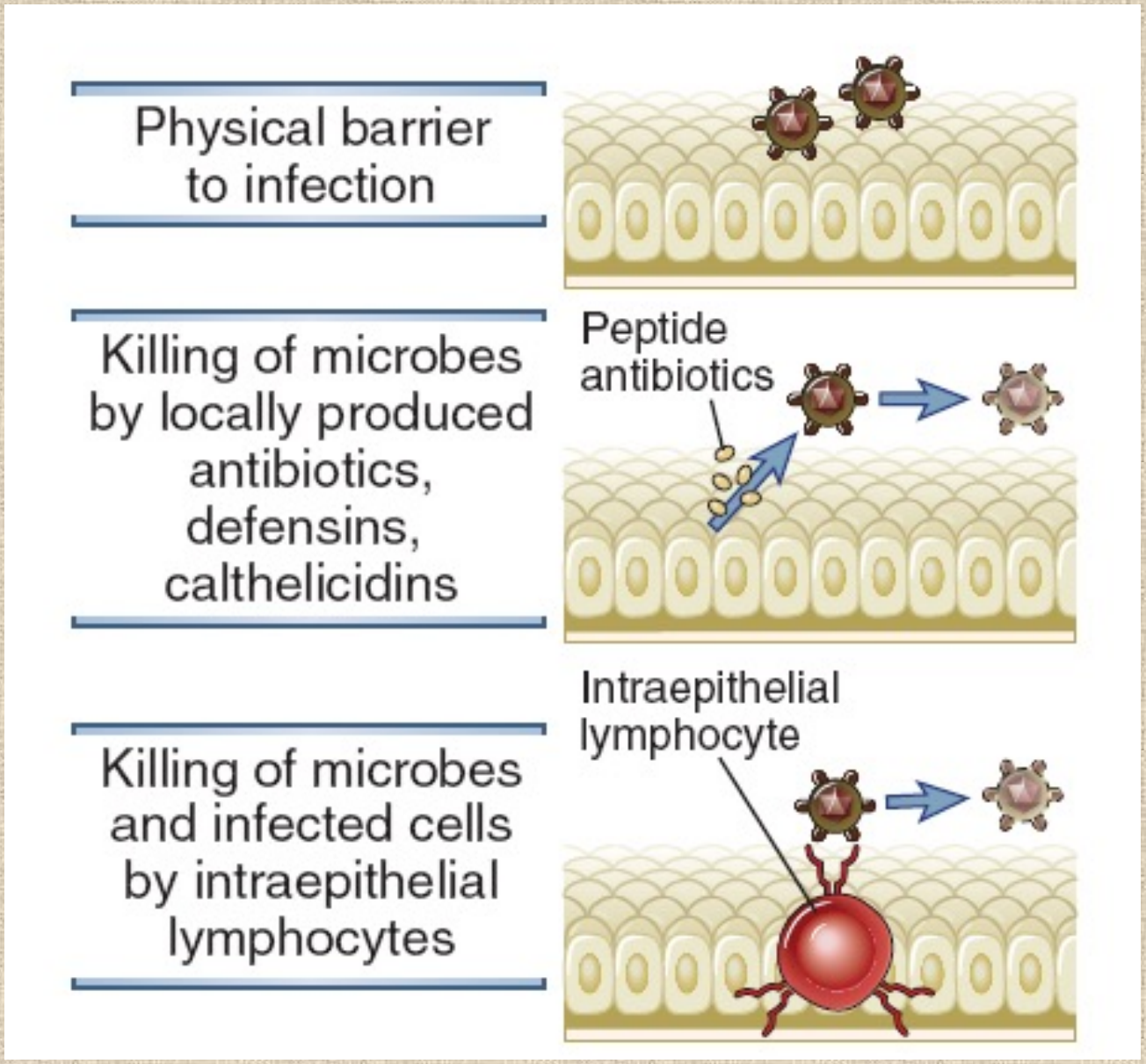
Nat Rev Immunol. 2003 ;3:710-720. Cell Tissue Res. 2011 ;343:175-88.

Antimikrobiális fehérjék II



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

Az epitheliális „barrierek” feladatai

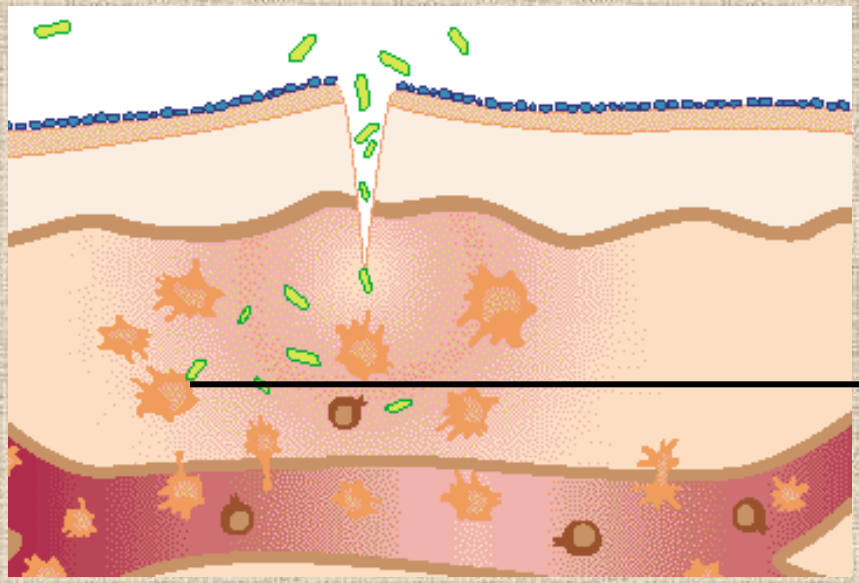


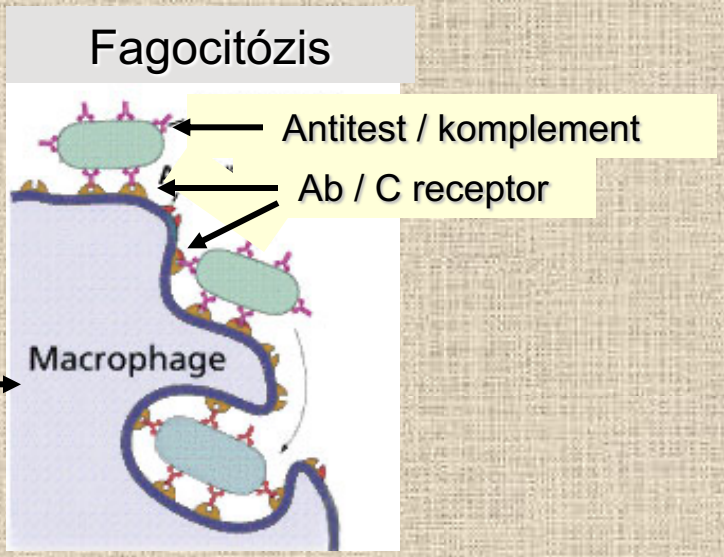
Defenzinek, cathelicidinek

Hízósejtek, IEL: γδ T-sejtek

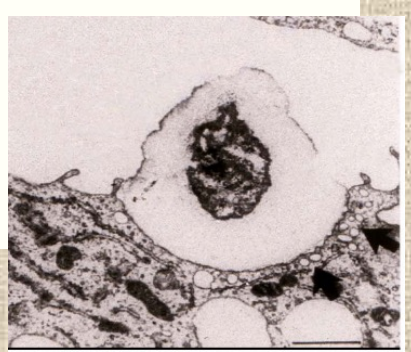
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition , 2012.

II. A második védelmi vonal: veleszületett immunitás, fagocita sejtek, gyulladás





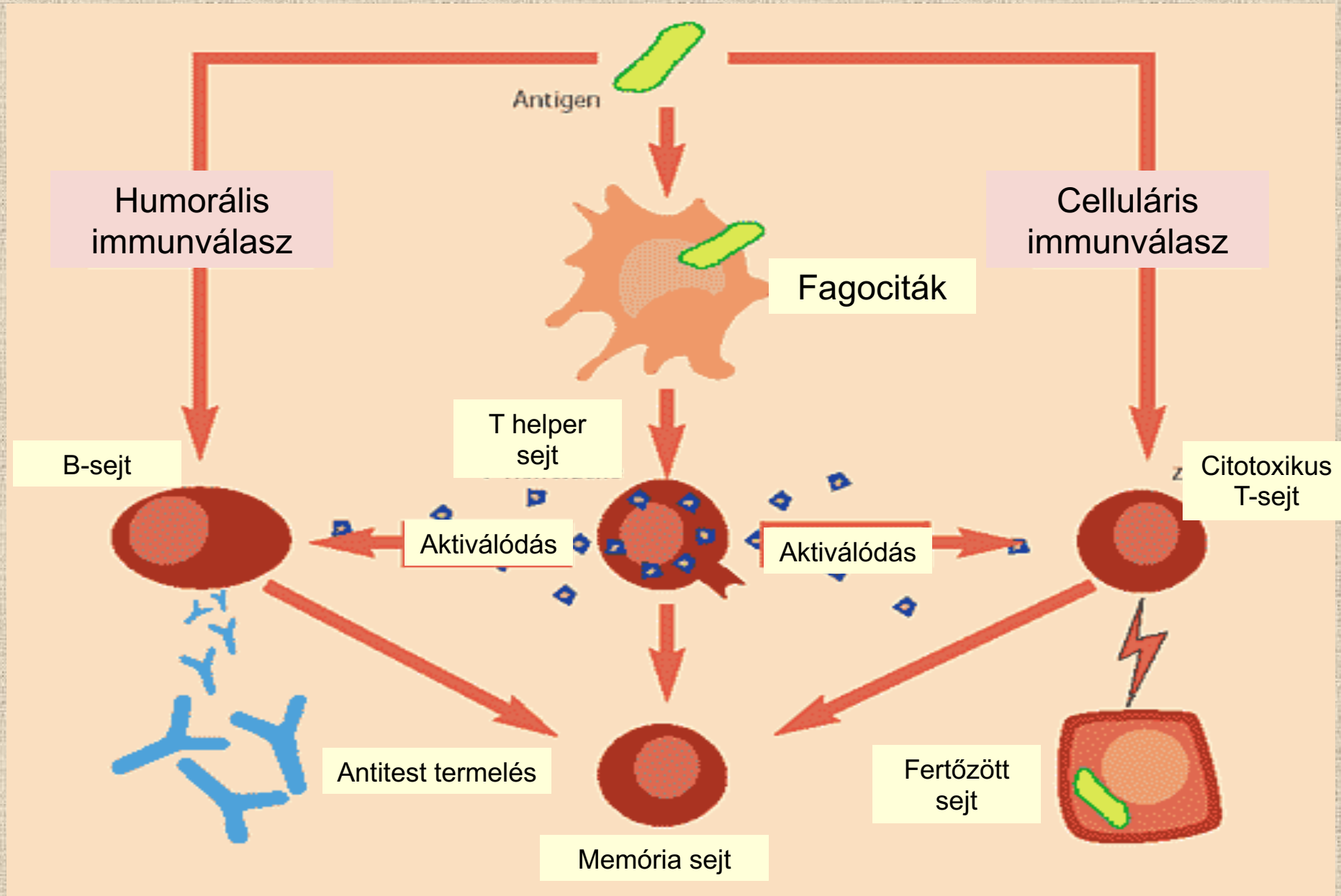
1. Fagocita sejtek a vérben és a szövetekben.
2. A szolubilis fehérjék (immunglobulin és komplement), bevonják a mikróba felszínét (opszonizálás) ezáltal megkönnyítik a fagocitózist.



A veleszületett immunválasz funkciói

- A fertőzések elleni első aktív védekezési vonal
- Lokalizálja és megakadályozza a mikróbák szétterjedését
- A veleszületett immunválasz effektor mechanizmusai segítik az adaptív immunválaszt a kórokozók eltávolításában
- Aktiválja és befolyásolja az adaptív immunválasz lefolyását

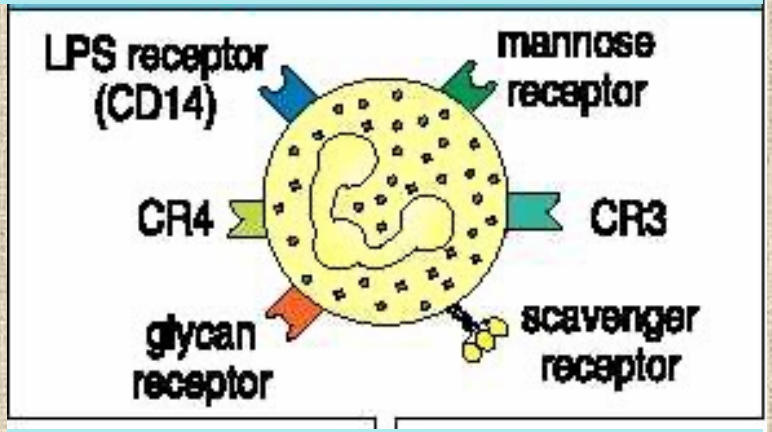
III. A harmadik védelmi vonal: adaptív immunitás



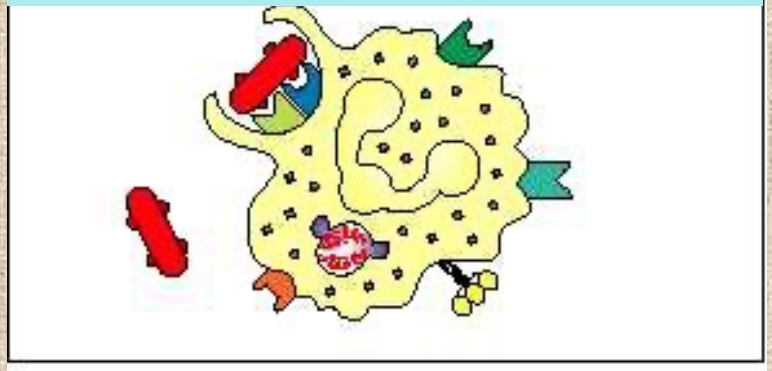
- Az immunvédekezés különböző szintjei
- A veleszületett immunitás felismerő receptorai

A patogének felismerése, fagocitózis

A neutrofil granulociták a bakteriális sejtfalkomponenseket felismerő receptorokat expresszálnak



A neutrofil sejtek felveszik és megemésztik a megkötött baktériumokat



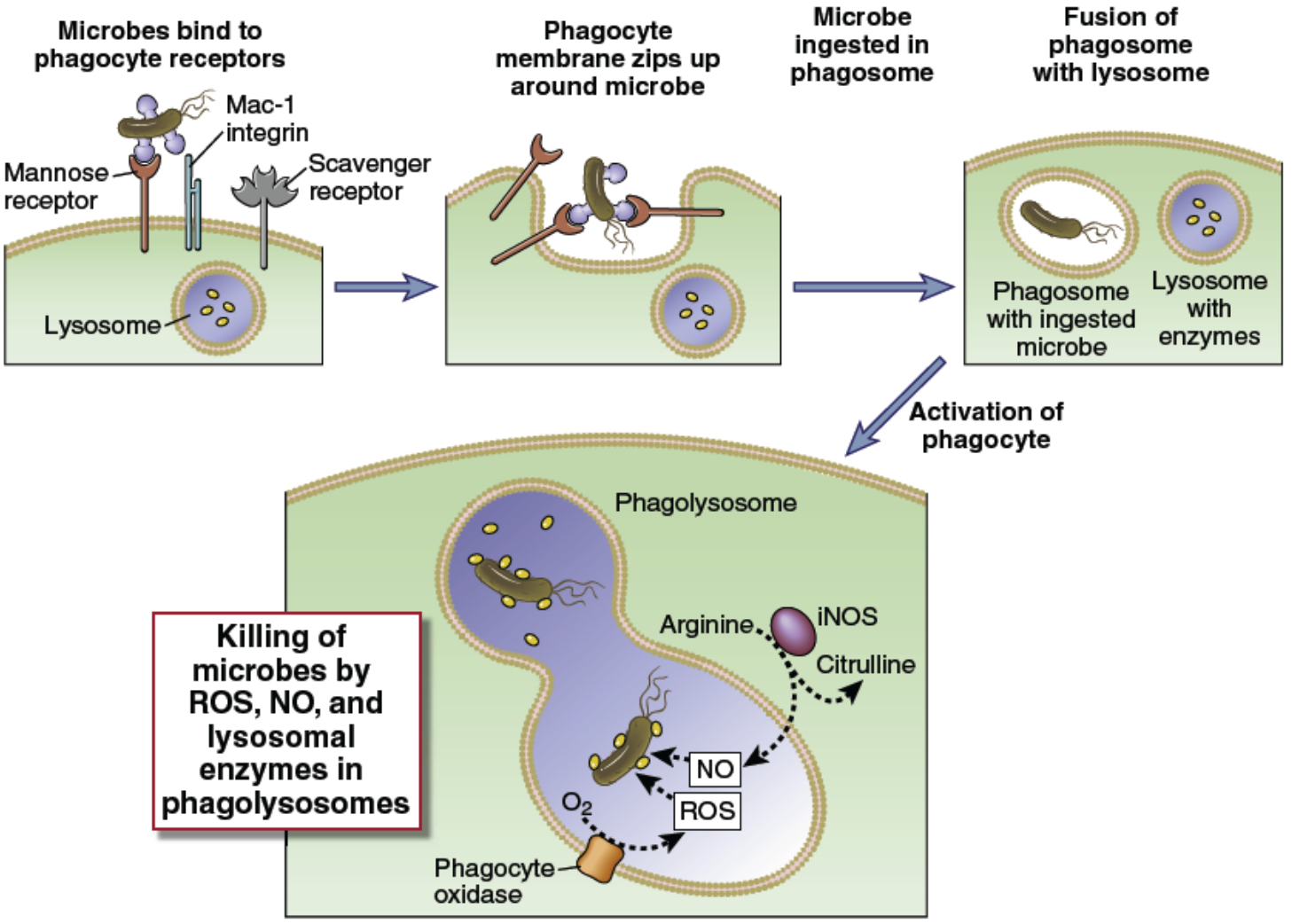
PRR= „Pattern Recognition Receptors”
Mintázatfelismerő receptorok

→A mikróbák megkötése PAMP-hoz kapcsolódva

„Pathogen Associated Molecular Patterns”
Patogén-asszociált molekuláris mintázatok

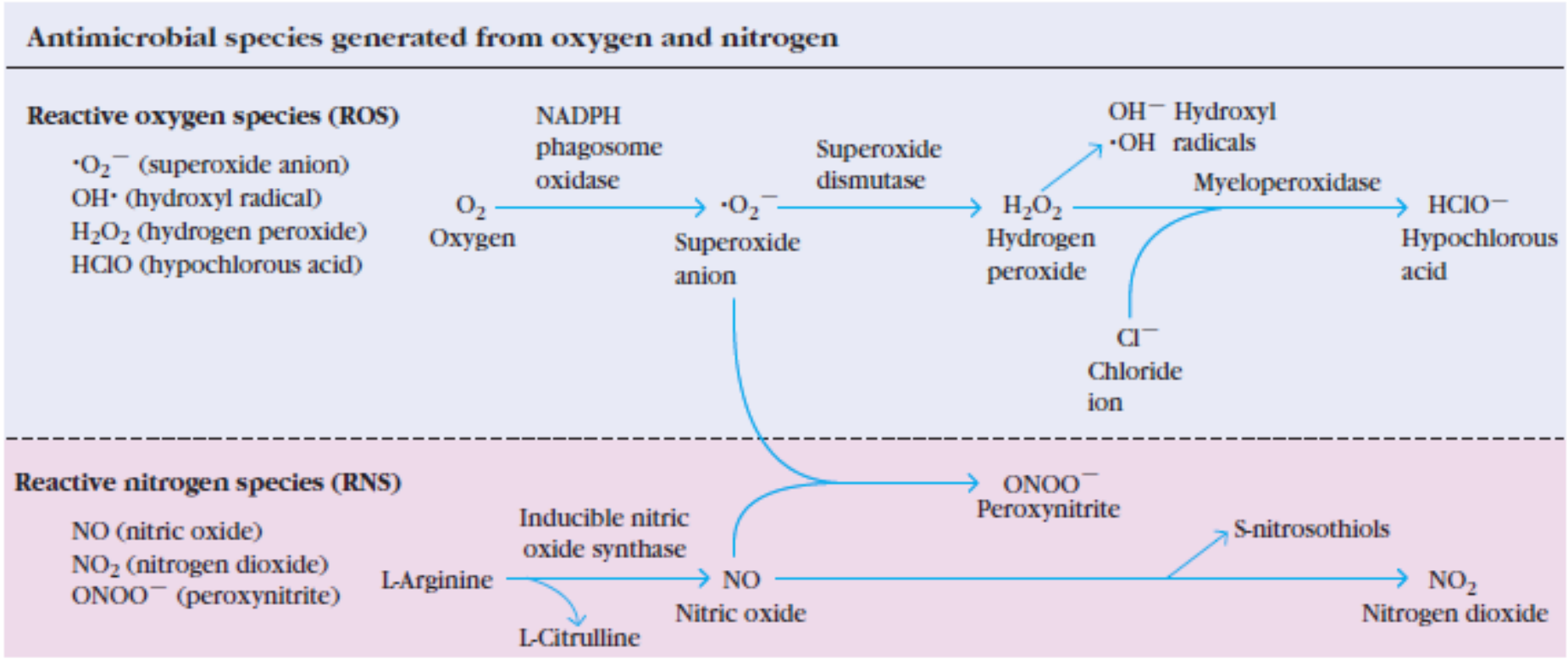
Janeway CA Jr, Travers P, Walport M, Shlomchik MJ. Immunobiology, 2005.

A fagocitózis folyamata



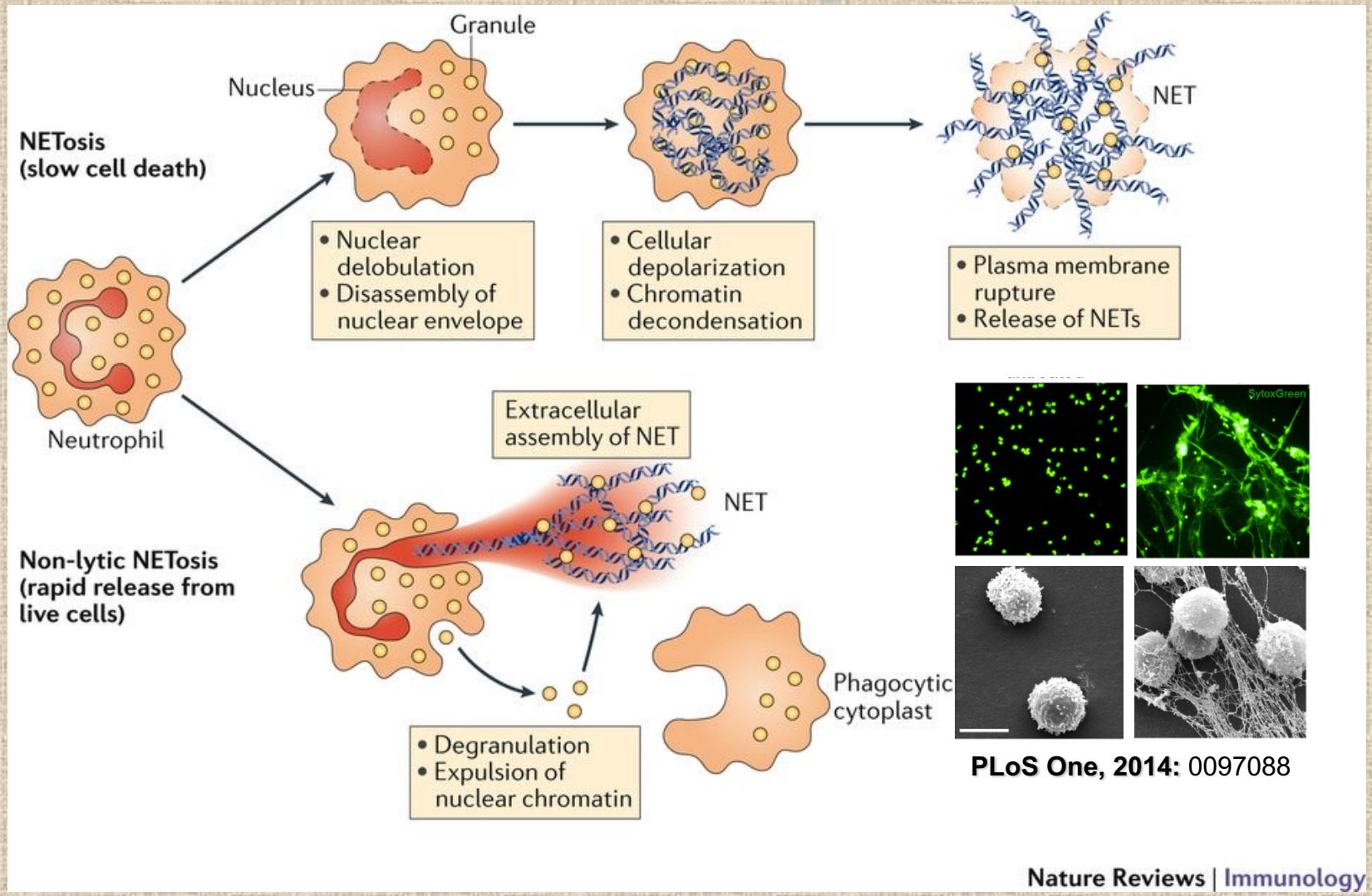
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012 .

Reaktív oxigén/nitrogén intermedierek



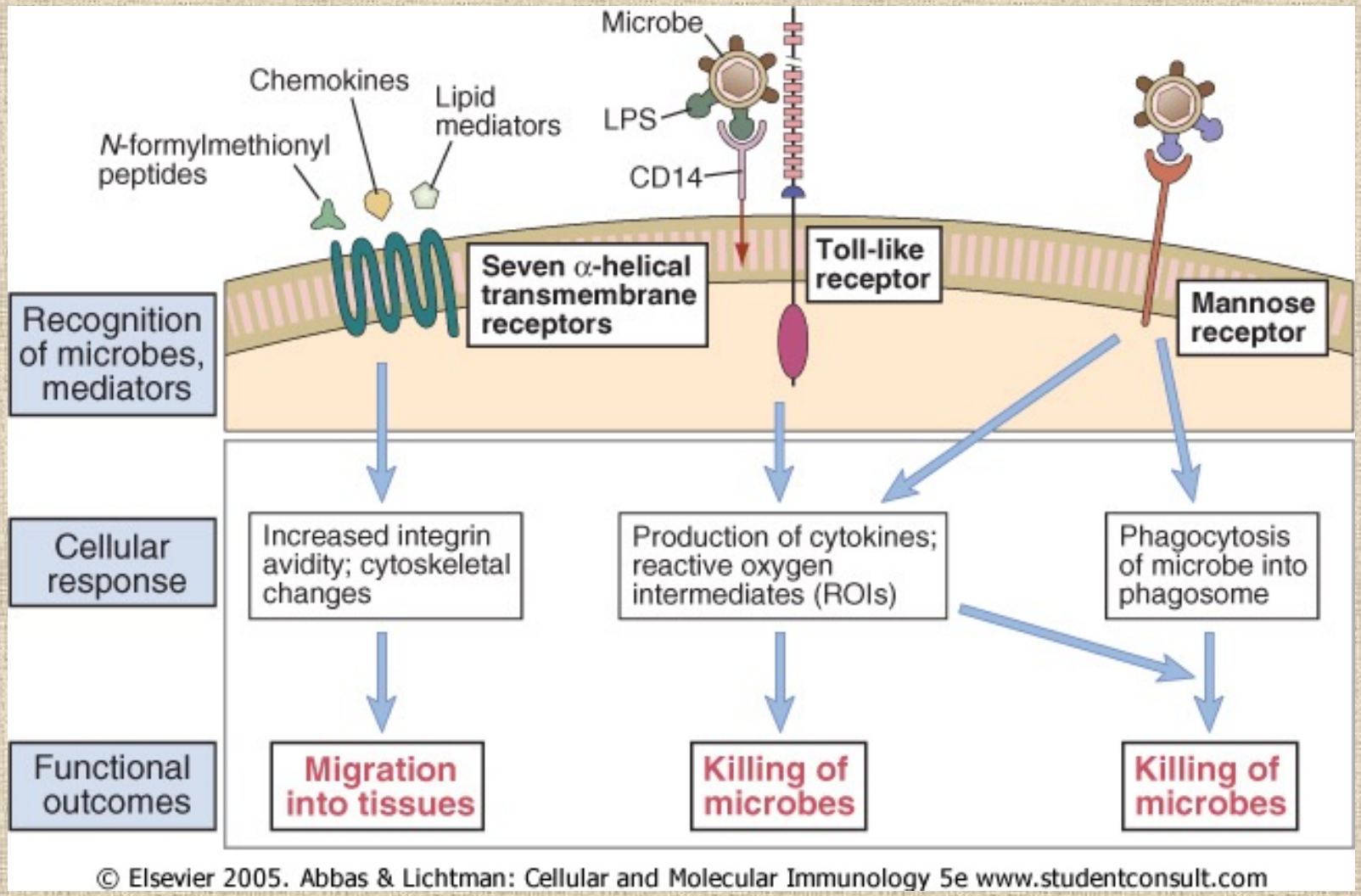
Owen, Punt, Stranford : Kuby Immunology
7th Edition, 2013.

A NETózis folyamata



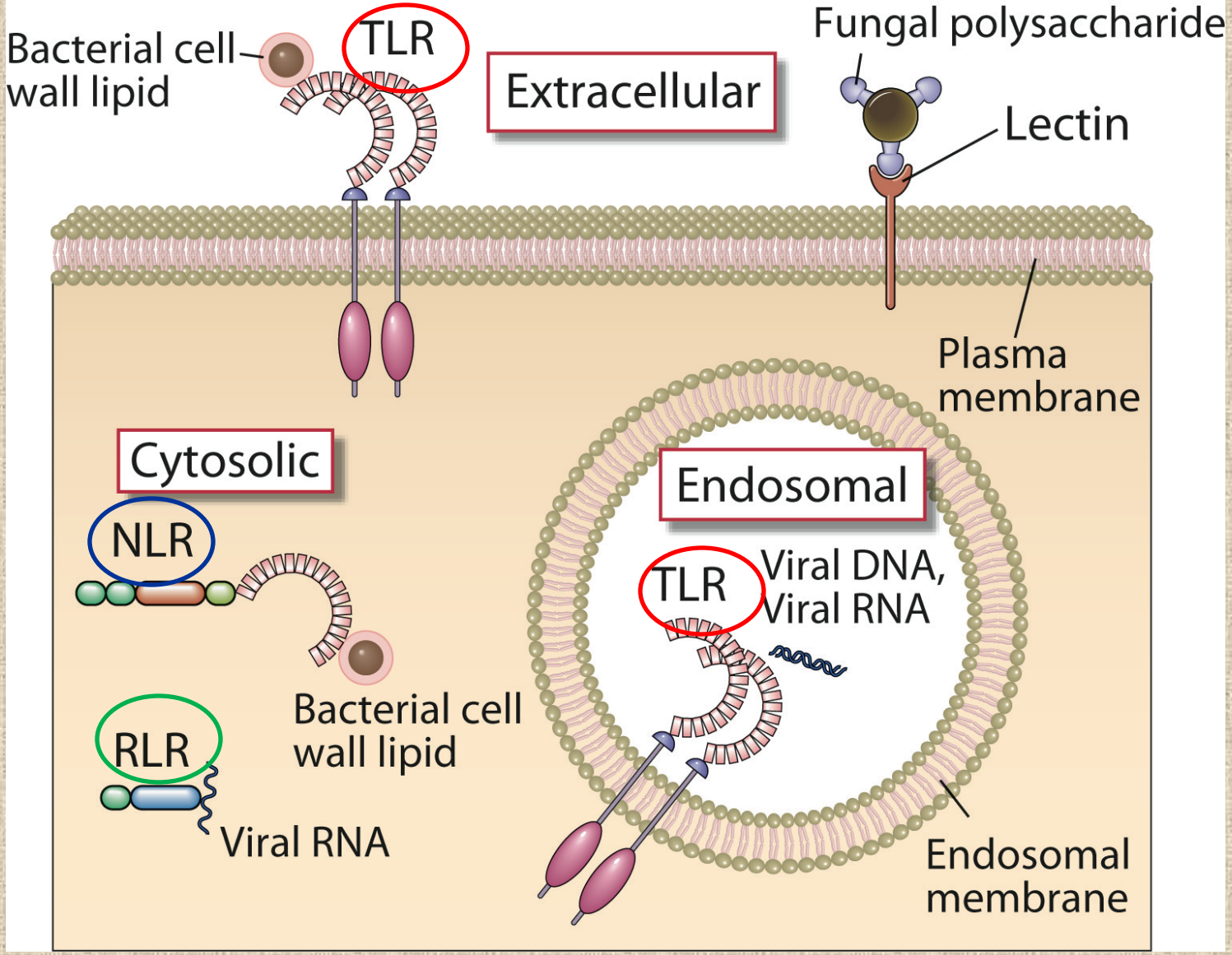
NET: neutrophyl extracellular trap

Fagocita receptorok



Abbas, Lichtman: Cellular and Molecular Immunology 5th Edition, 2005.

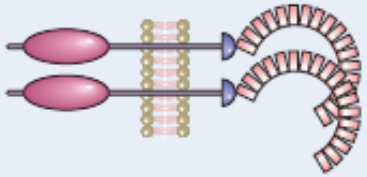
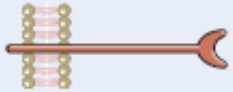
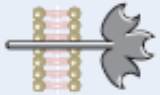
Mintázatfelismerő receptorok



Toll-like receptorok (TLR) NOD-like receptorok (NLR) RIG-like receptorok (RLR)

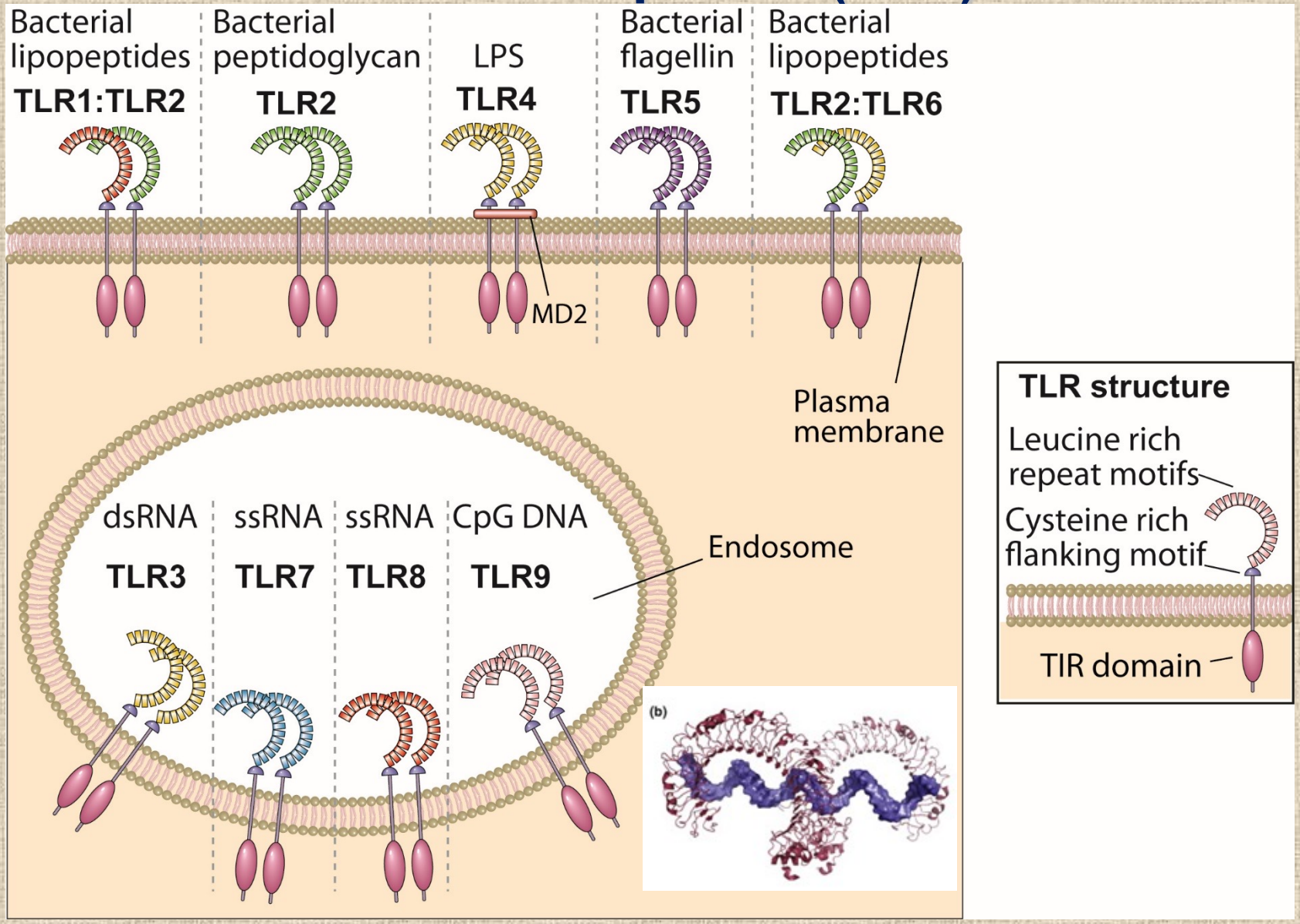
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

Mintázatfelismerő receptorok csoportjai

Toll-like receptors (TLRs) 	Plasma membrane and endosomal membranes of dendritic cells, phagocytes, B cells endothelial cells, and many other cell types	TLRs 1-9	Various microbial molecules including bacterial LPS and peptidoglycans, viral nucleic acids
NOD-like receptors (NLRs) 	Cytoplasm of phagocytes epithelial cells, and other cells	NOD1/2 NALP family (inflammasomes)	Bacterial cell wall peptidoglycans Flagellin, muramyl dipeptide, LPS; urate crystals; products of damaged cells
RIG-like receptors (RLRs) 	Cytoplasm of phagocytes and other cells	RIG-1, MDA-5	Viral RNA
C-type lectin–like receptors 	Plasma membranes of phagocytes	Mannose receptor Dectin	Microbial surface carbohydrates with terminal mannose and fructose Glucans present in fungal cell walls
Scavenger receptors 	Plasma membranes of phagocytes	CD36	Microbial diacylglycerides
N-Formyl met-leu-phe receptors 	Plasma membranes of phagocytes	FPR and FPRL1	Peptides containing *N*-formylmethionyl residues

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

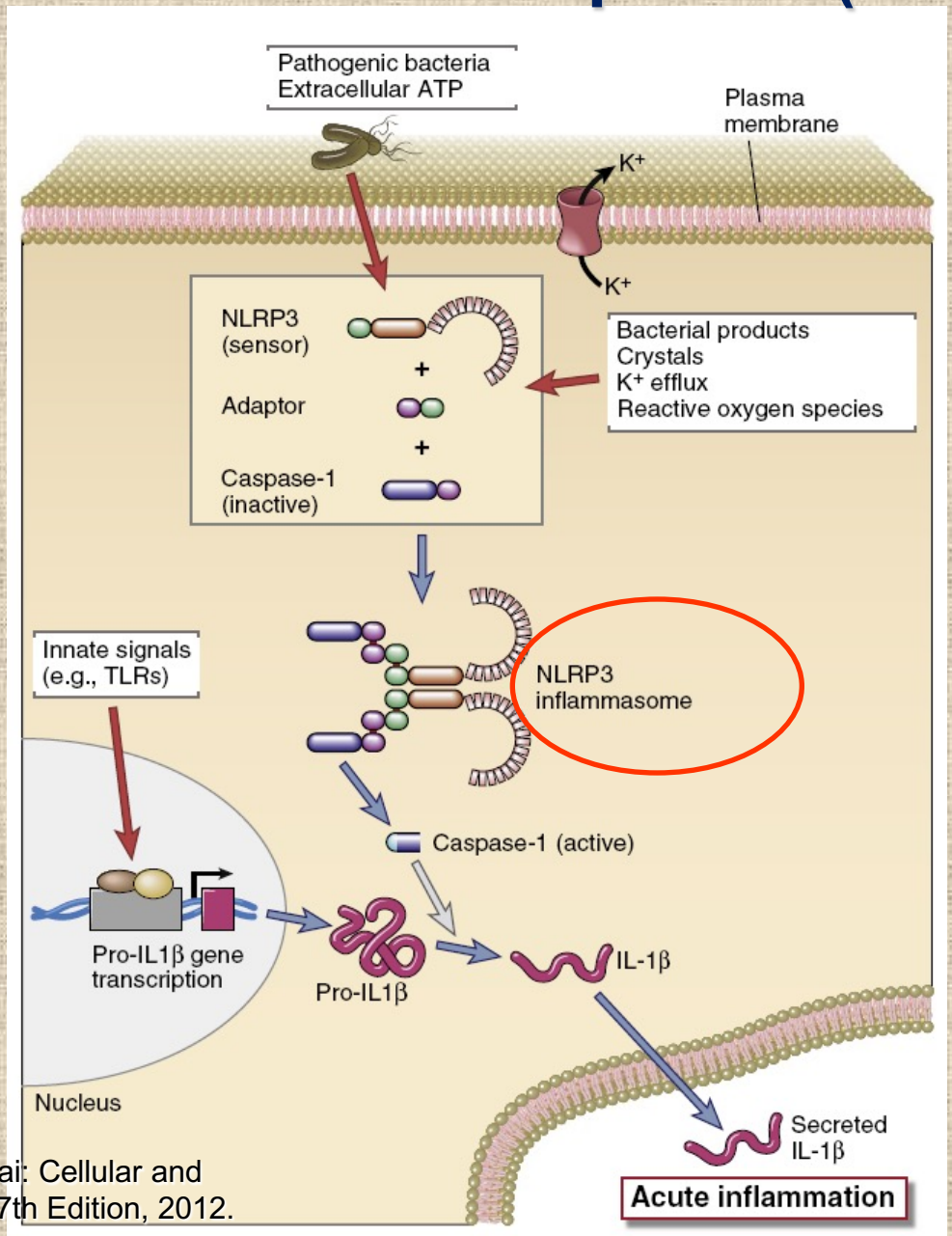
Mintázatfelismerő receptorok: Toll-like receptorok (TLR)



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

Trends in Biochemical Sciences 2009; 34: 553-561.

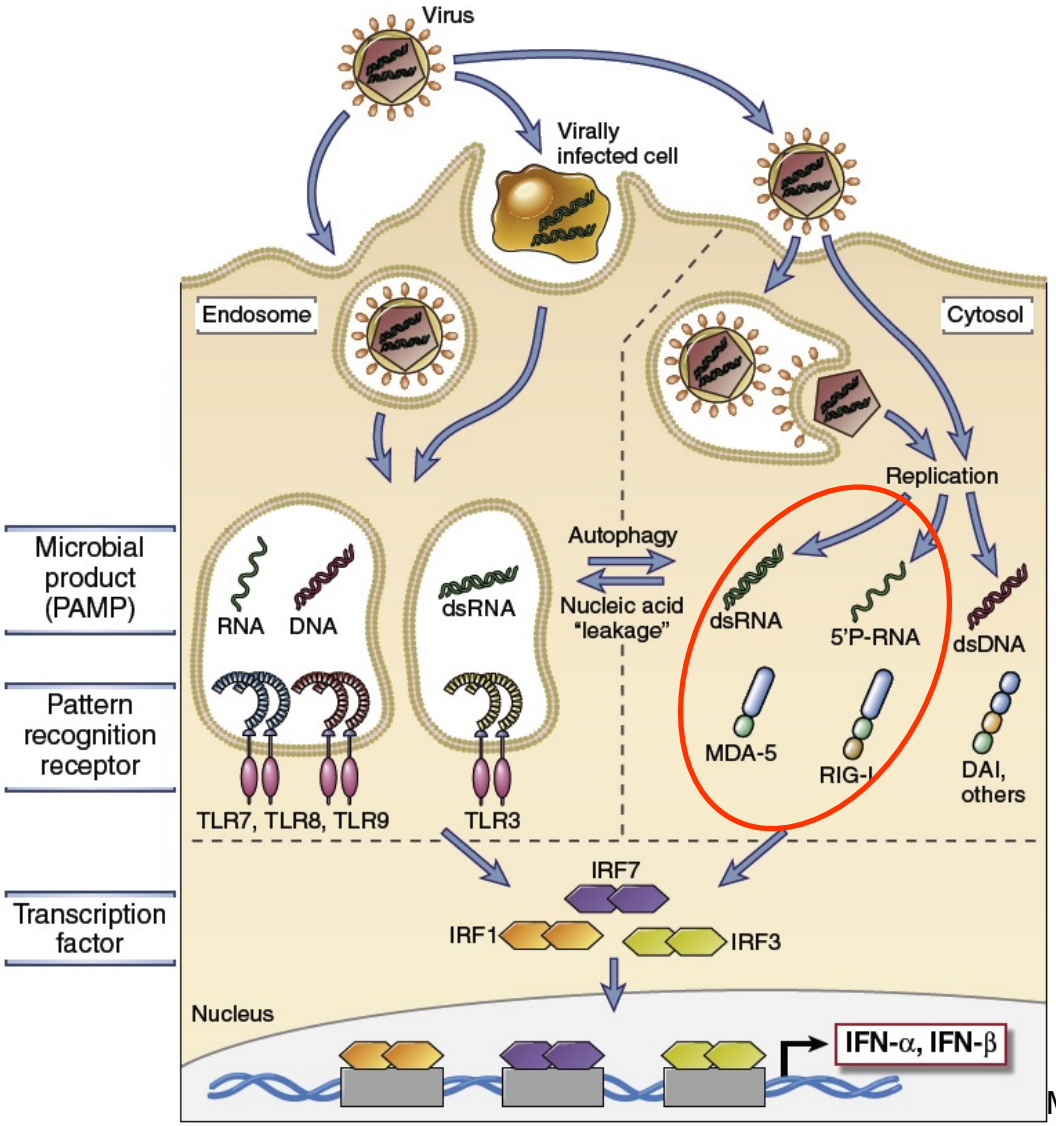
Mintázatfelismerő receptorok: NOD-like receptorok (NLR)



NOD: Nucleotide oligomerization domain

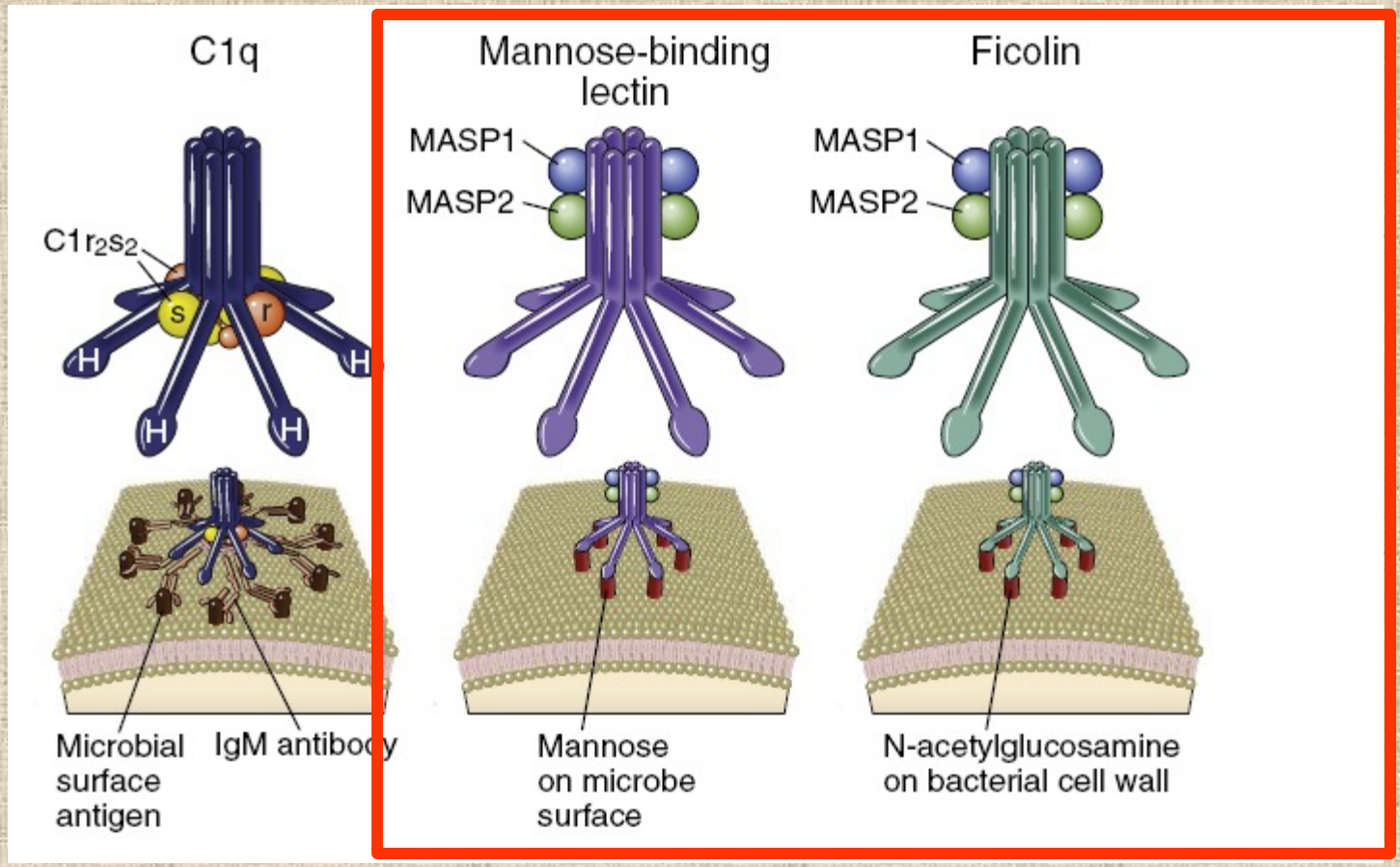
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

Mintázatfelismerő receptorok: RIG-like receptorok (RLR)



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

Szolúbilis mintázatfelismerő molekulák I

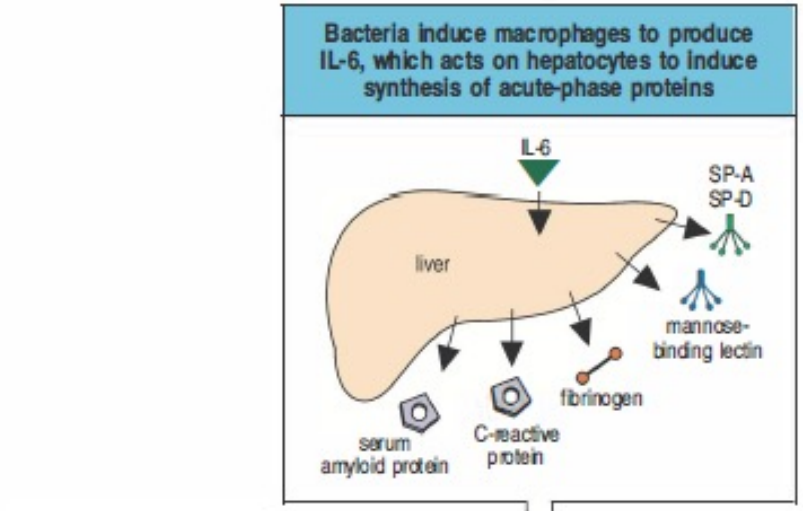


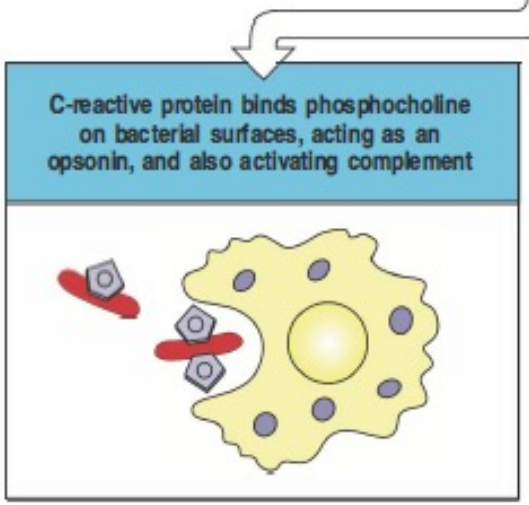
Collectin (MBL, SP-A, SP-D): C-type lectin domain

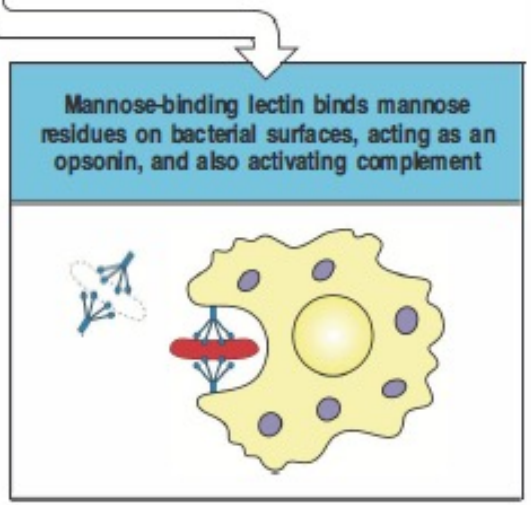
Ficolin: Fibrinogen domain

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

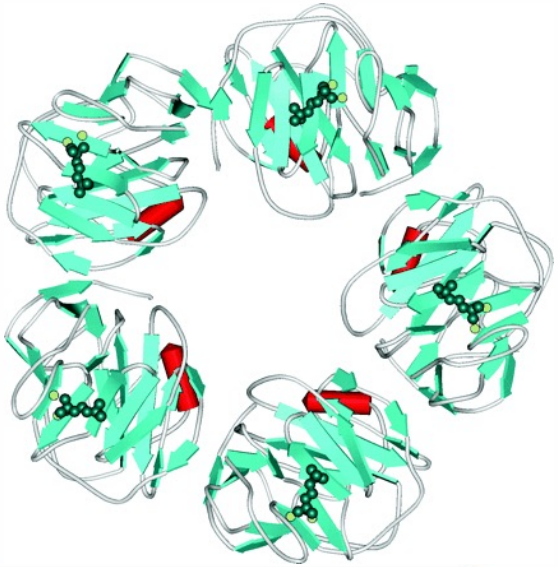
Szolúbilis mintázatfelismerő molekulák II: pentraxinok

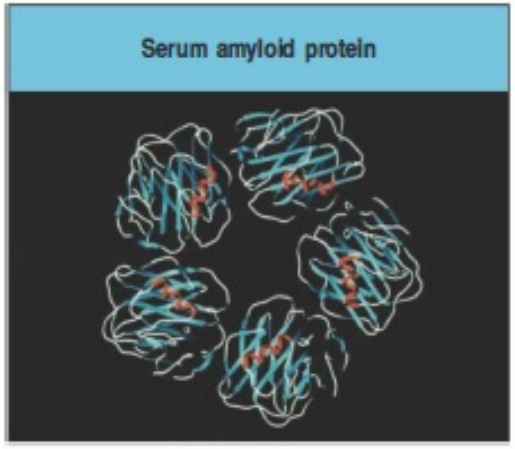






C-reaktív protein-CRP





Murphy. Janeway's Immunobiology, 8th Edition ,2012.

J Biol Chem. 2004 Nov 19;279(47):48487-90.

C-reaktív protein klinikai jelentősége

Infekció, szepszis gyanúja

↓

CRP levétele, teljes vérkép, hemokultúra után
Antibiotikus kezelés

↓ CRP 48 hr →

CRP <10 mg/L & hemokultúra negatív →

Antibiotikus kezelés leállítása

CRP >10 mg/L, antibiotikum terápia folytatása

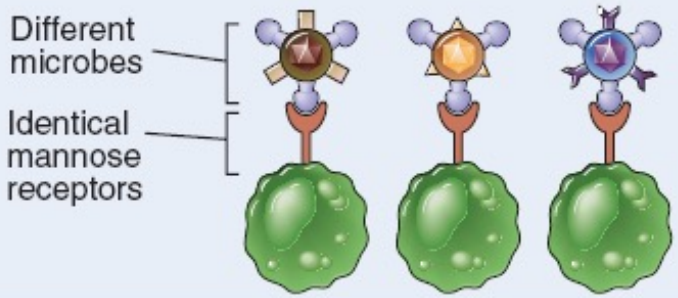
↓ CRP 7 nap

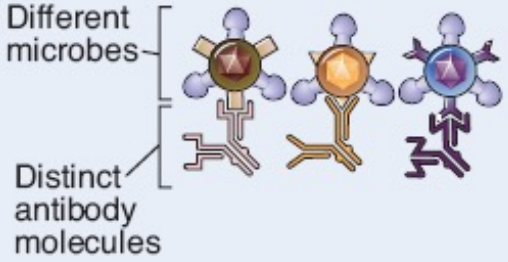
CRP <10 mg/L: antibiotikus kezelés leállítása

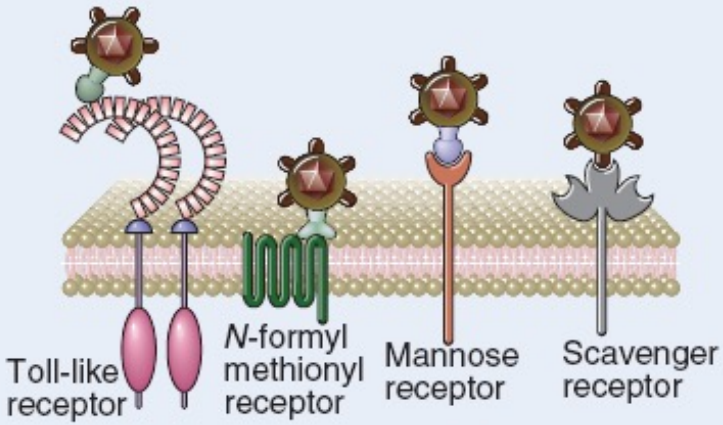
CRP >10 mg/L: klinikai adatok újraértékelése (új vérkép, más antibiotikum)

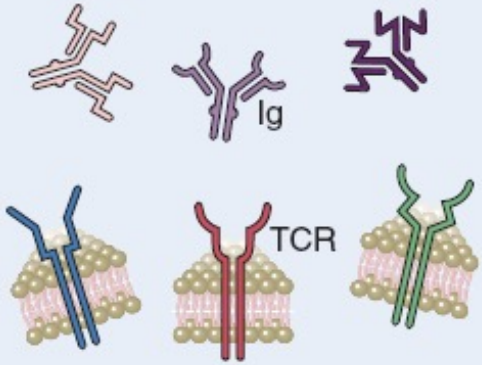
A veleszületett és adaptív immunitás jellemzői

	Innate Immunity	Adaptive Immunity
Specificity	For structures shared by classes of microbes (pathogen-associated molecular patterns)	For structural detail of microbial molecules (antigens); may recognize nonmicrobial antigens
Receptors	Encoded in germline; limited diversity (pattern recognition receptors)	Encoded by genes produced by somatic recombination of gene segments; greater diversity
Distribution of receptors	Nonclonal: identical receptors on all cells of the same lineage	Clonal: clones of lymphocytes with distinct specificities express different receptors
Discrimination of self and non-self	Yes; healthy host cells are not recognized or they may express molecules that prevent innate immune reactions	Yes; based on elimination or inactivation of self-reactive lymphocytes; may be imperfect (giving rise to autoimmunity)



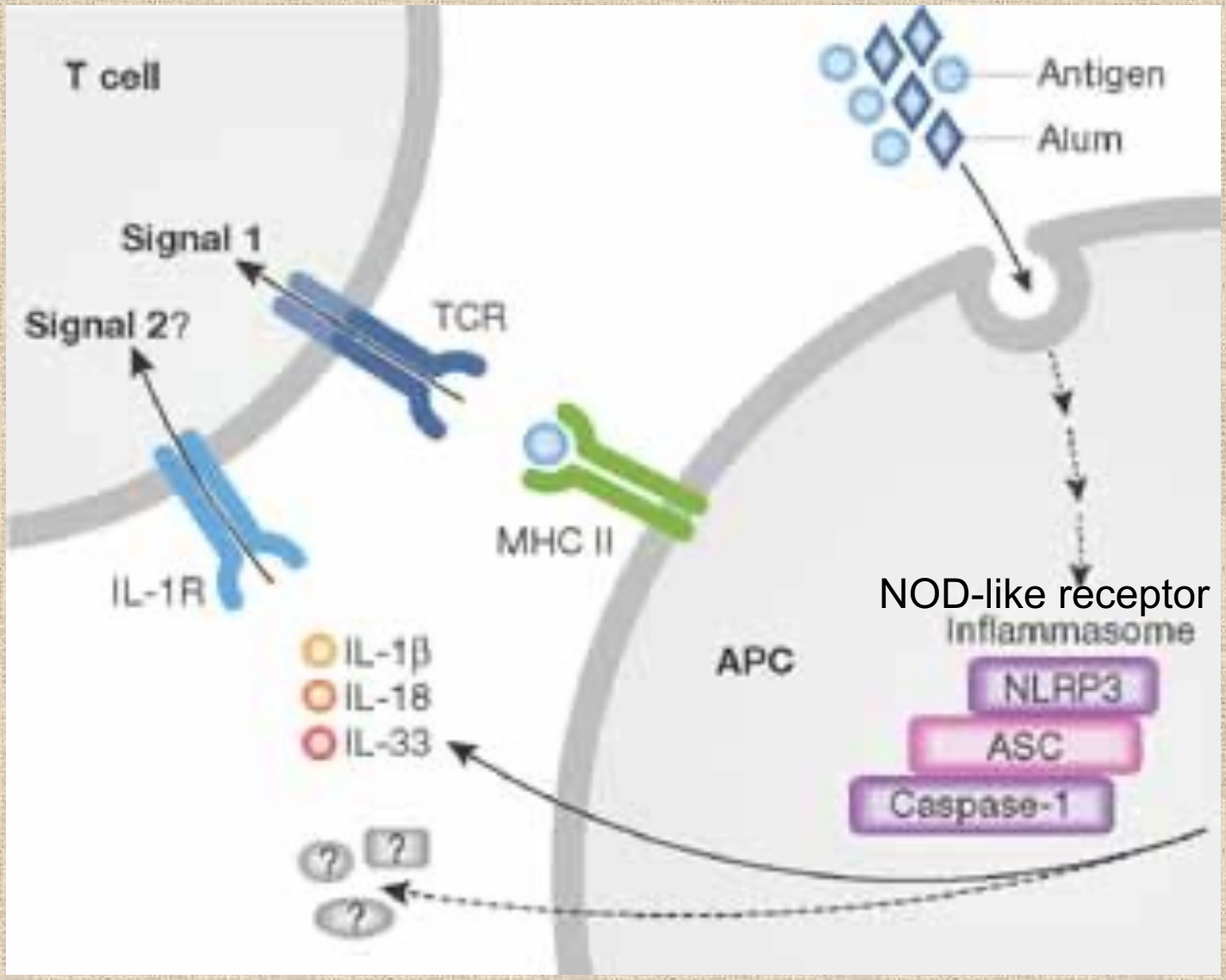






Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

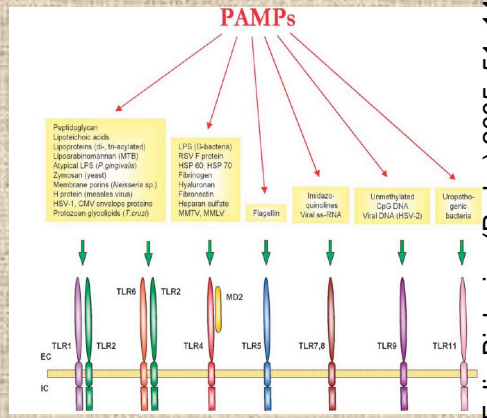
Vakcináció és az adjuvánsok szerepe



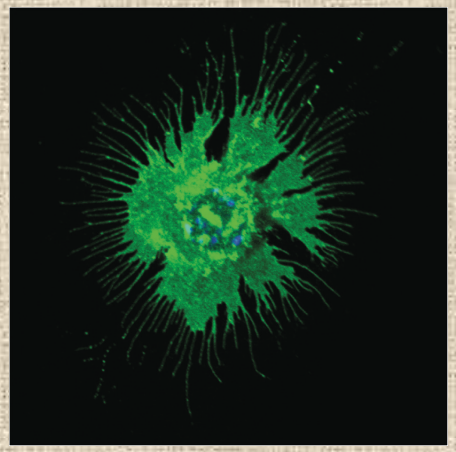
EMBO Mol Med. 2009;1: 92-8.

Orvostudományi-fiziológiai Nobel-díj 2011

Lemaitre et al., 1996, Cell ***86:973***

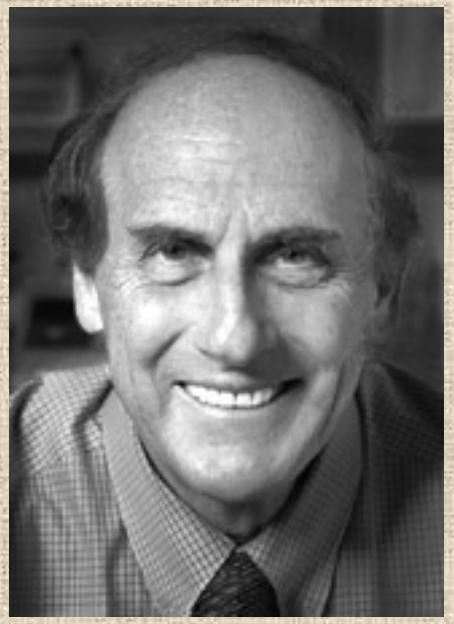


Folia Biologica (Praha) 2005; 51: 148-156



Jules A. Hoffmann

Bruce A. Beutler



Ralph M. Steinmann