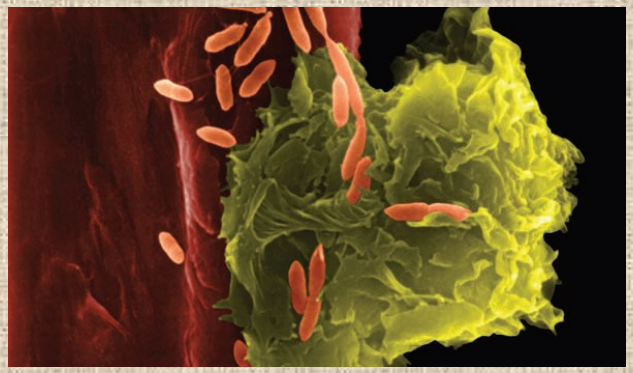
Basic immunology

Lecture 3.

Innate immunity, pattern recognition

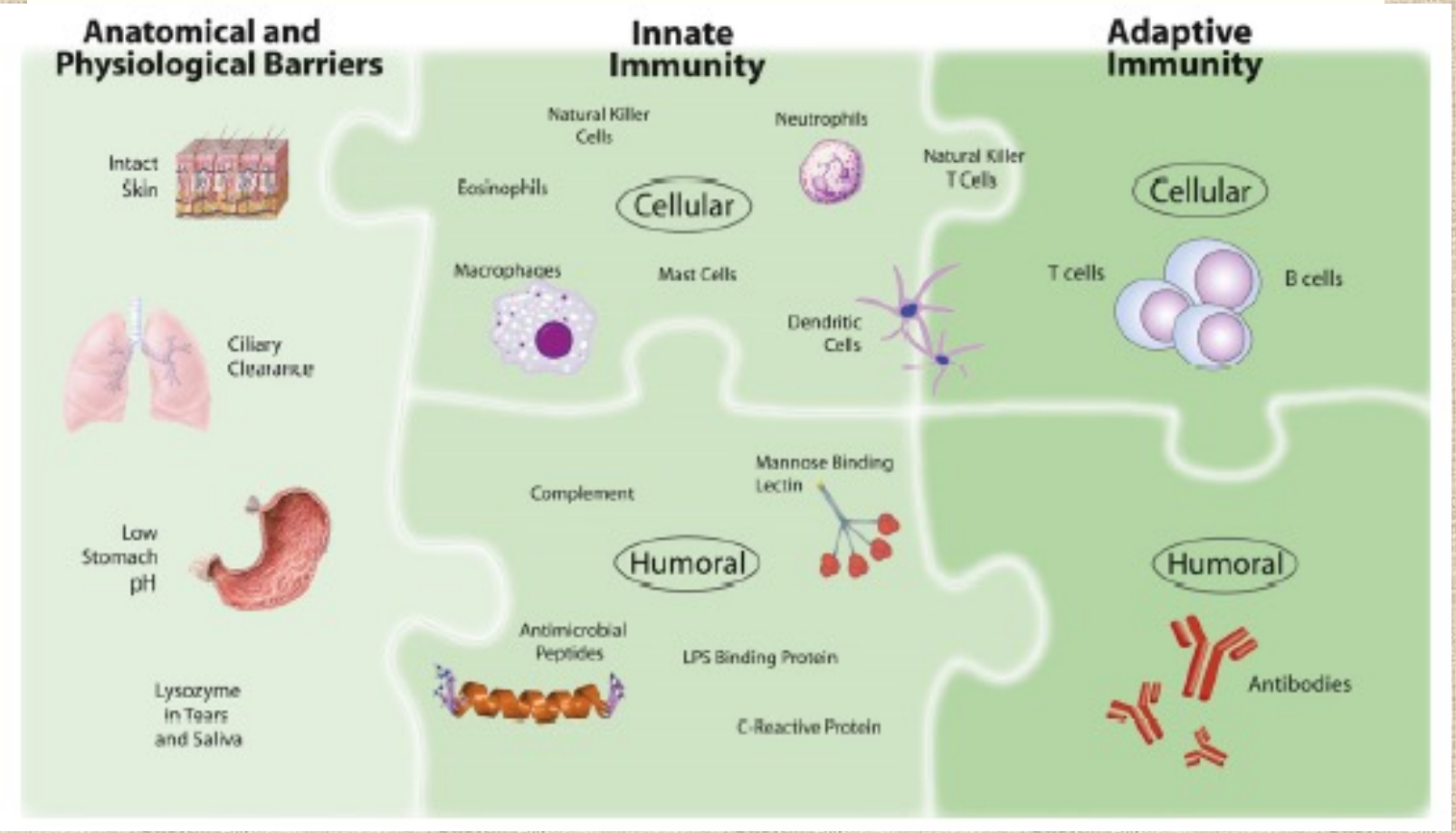


Péter Engelmann

- Different levels of the immune response
- Recognition molecules of the innate immunity

The levels of host defense

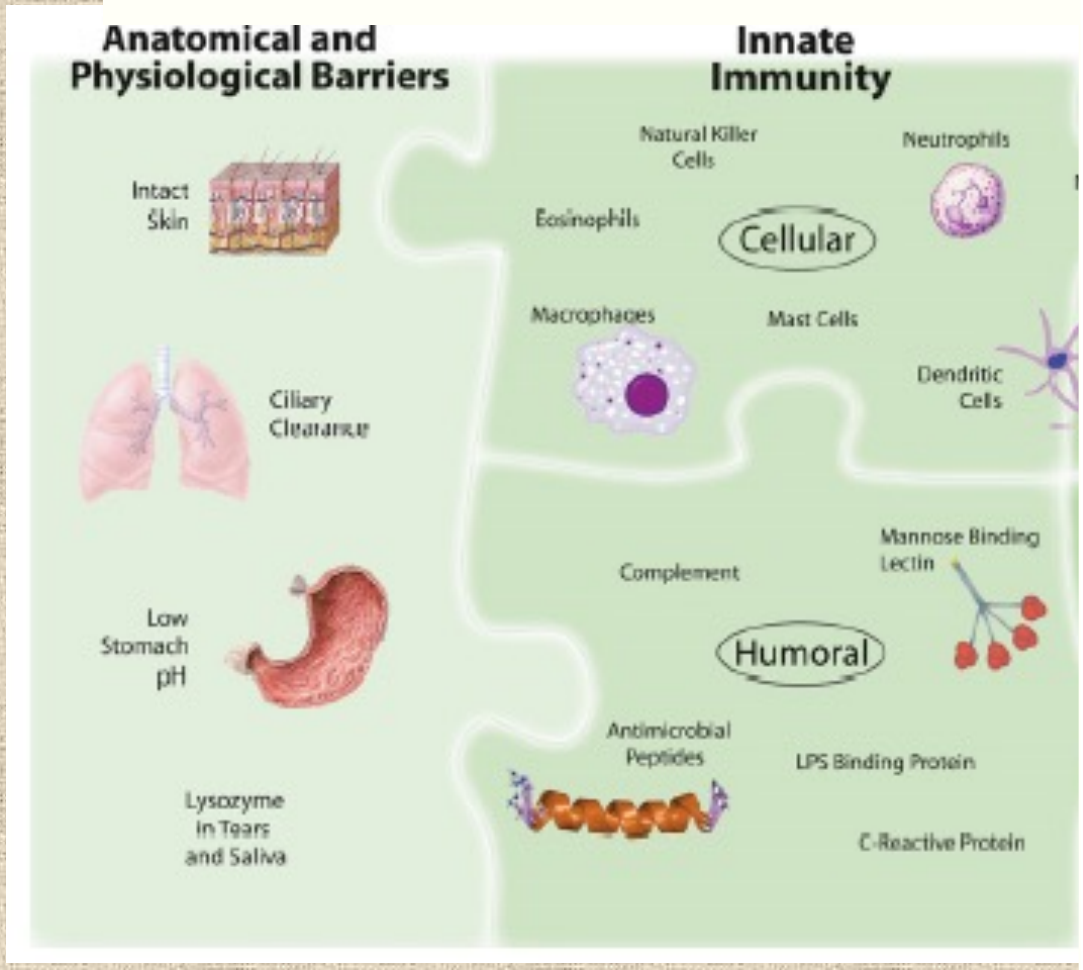
- Anatomical „barriers”
- Innate immunity, inflammation
- Adaptive immunity



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

The levels of host defense

- Anatomical „barriers”
- Innate immunity, inflammation
- Adaptive immunity



I. First line of defense: anatomic „barriers”

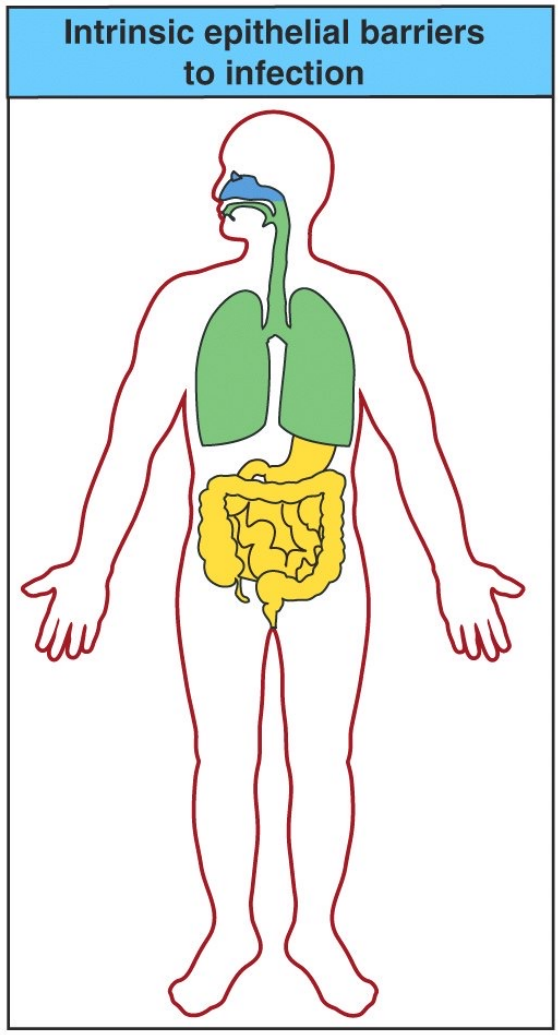


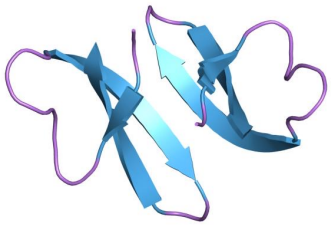
Figure 2-4 Immunobiology, 6/e. (© Garland Science 2005)

	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 Enzymes (pepsin)	Pulmonary surfactant	Enzymes in tears and saliva (lysozyme)
	β-defensins Lamellar bodies Cathelicidin	α-defensins (cryptdins) RegIII (lecticidins) Cathelicidin	α-defensins Cathelicidin	Histatins β-defensins
Microbiological	Normal microbiota			

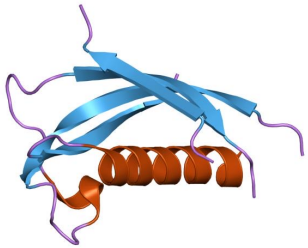
1. Mechanical defense
2. Slightly acidic environment
3. Normal (commensal) microorganisms
4. Antimicrobial factors in the body fluids, on the skin / in the gut.
5. Cilia

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

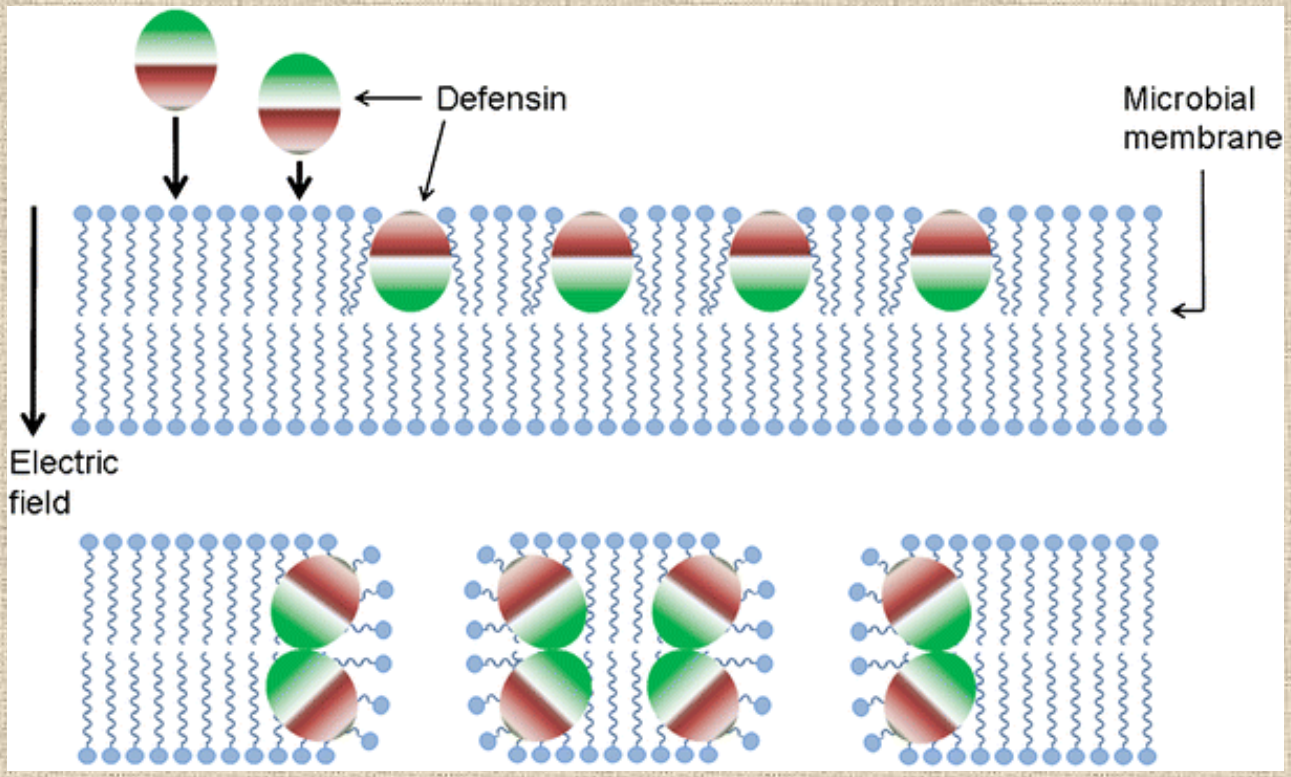
Antimicrobial peptides I

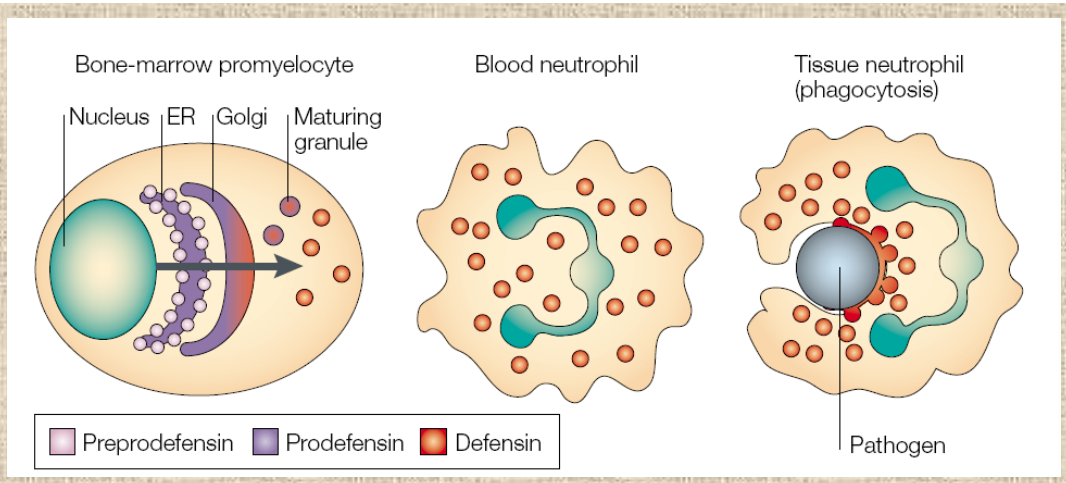


Defensin



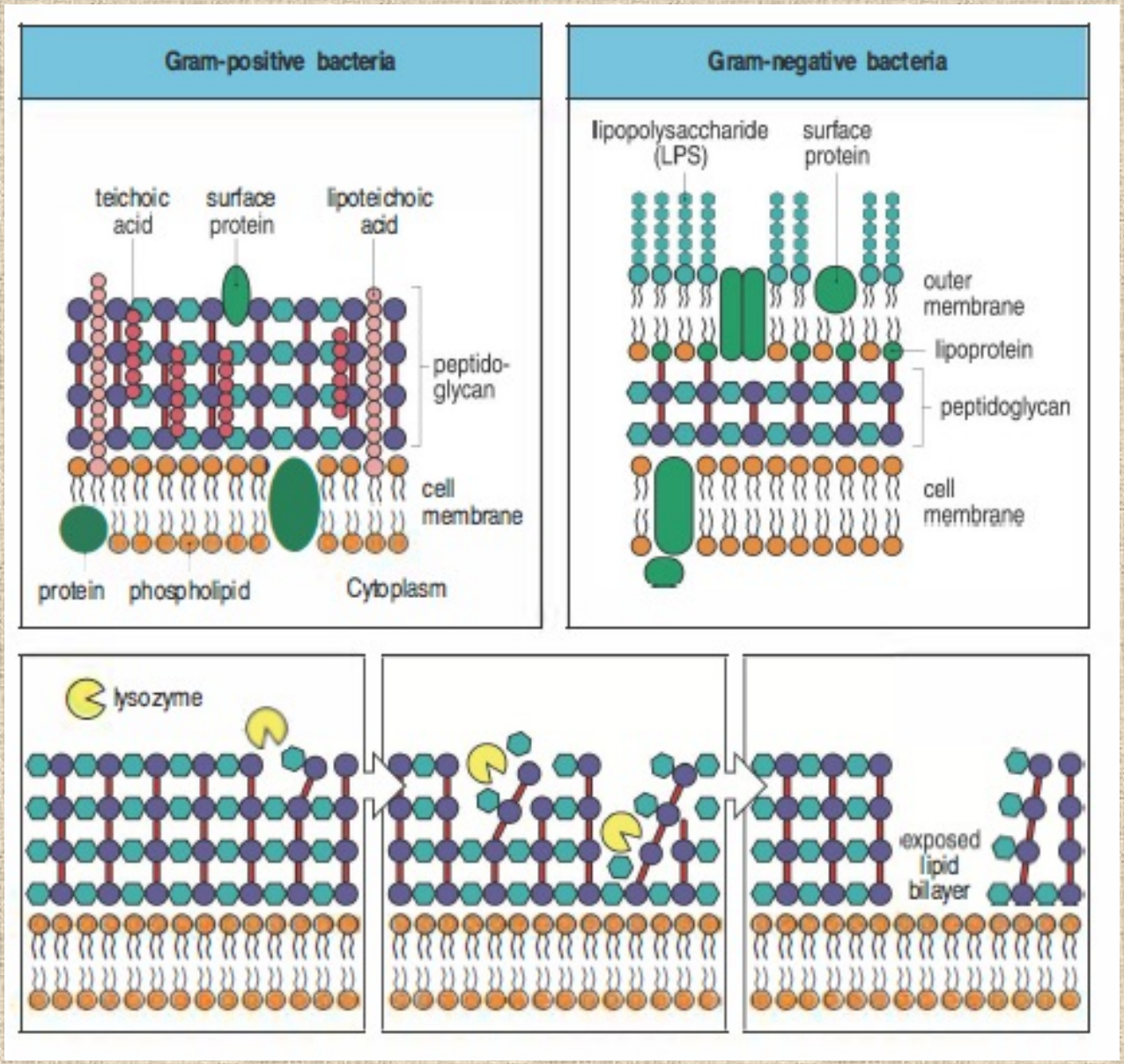
Cathelicidin



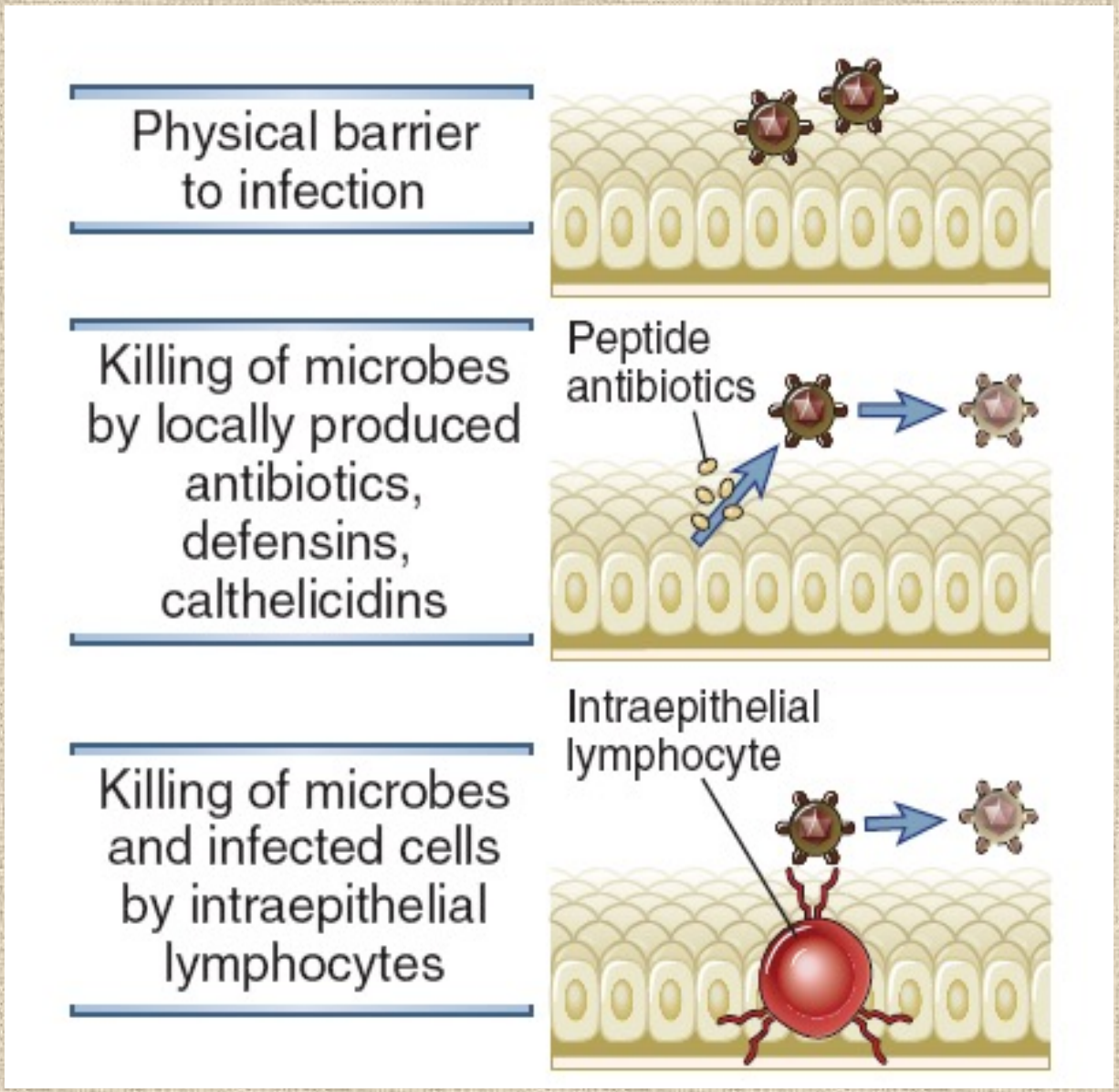


Nat Rev Immunol. 2003 ;3:710-720. Cell Tissue Res. 2011 ;343:175-88.

Antimicrobial peptides II



The role of epithelial barriers

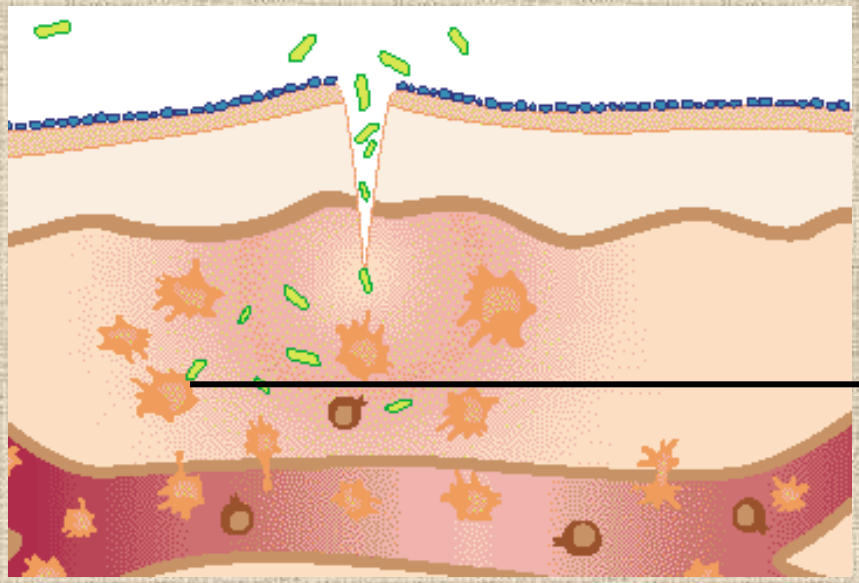


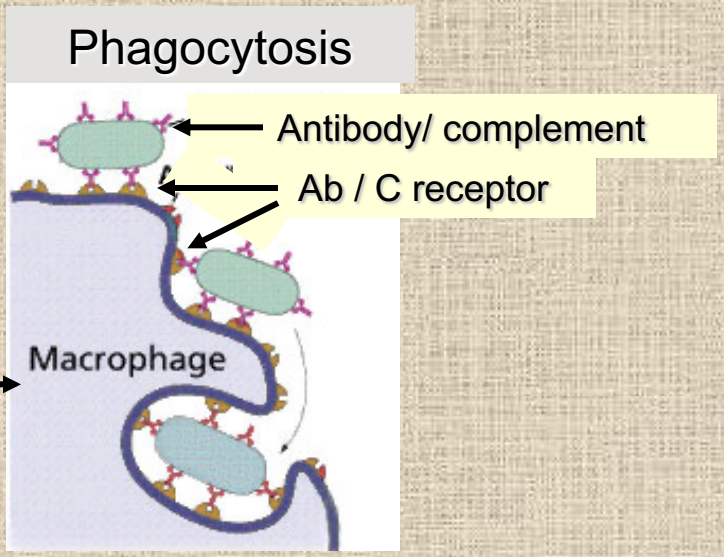
Defensins, cathelicidins

Mast cells, IEL: γδ T cells

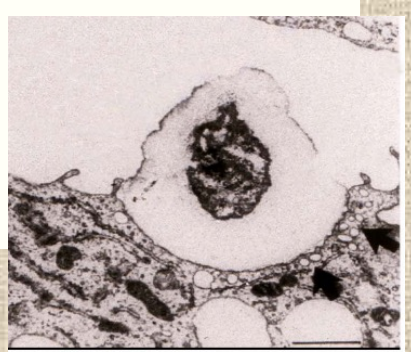
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition , 2012.

II. Second line of defense: innate immunity, phagocytes, inflammation





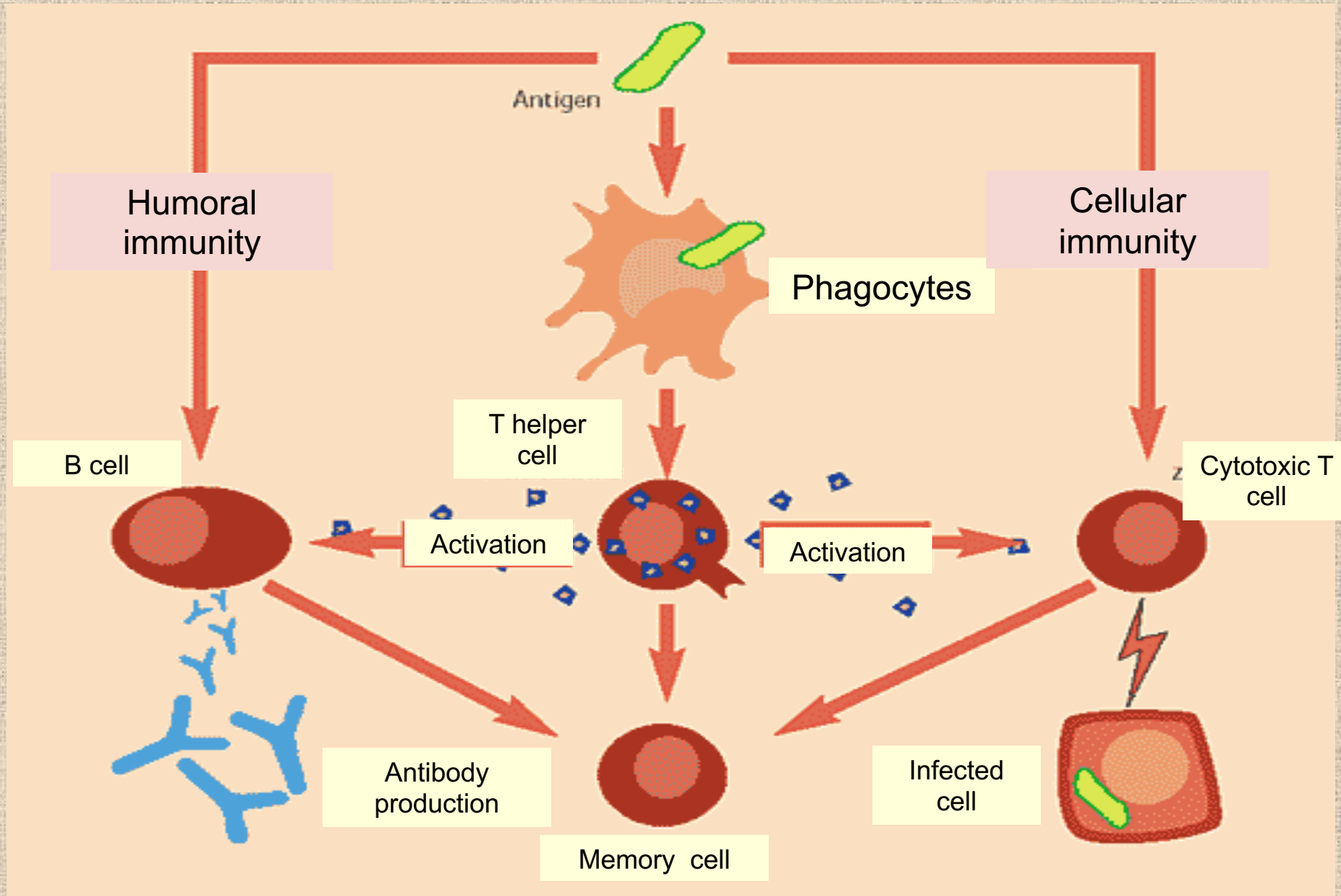
1. Phagocytes in the blood and tissues.
2. Soluble proteins (immunglobulin and complement), bind to microbe surface (opsonisation) to enhance the phagocytosis.



Functions of innate immunity

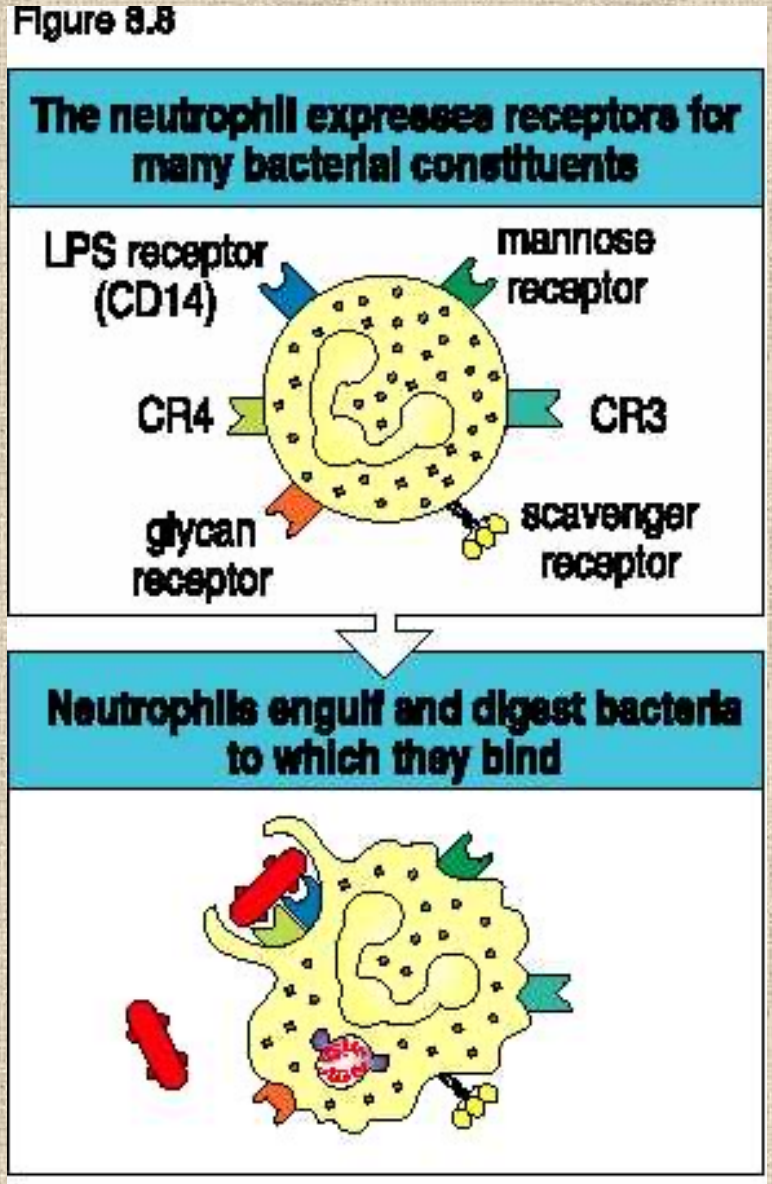
- The first line of defense against infections-local
- Localisation of microbes and inhibits their spreading
- The effector mechanisms of innate immunity aid the adaptive immunity to eliminate the pathogens
- Activate and influence the adaptive immunity

III. The third line of defense: adaptive immunity



- Different levels of the immune response
- Recognition molecules of innate immunity

Recognition of pathogens, phagocytosis



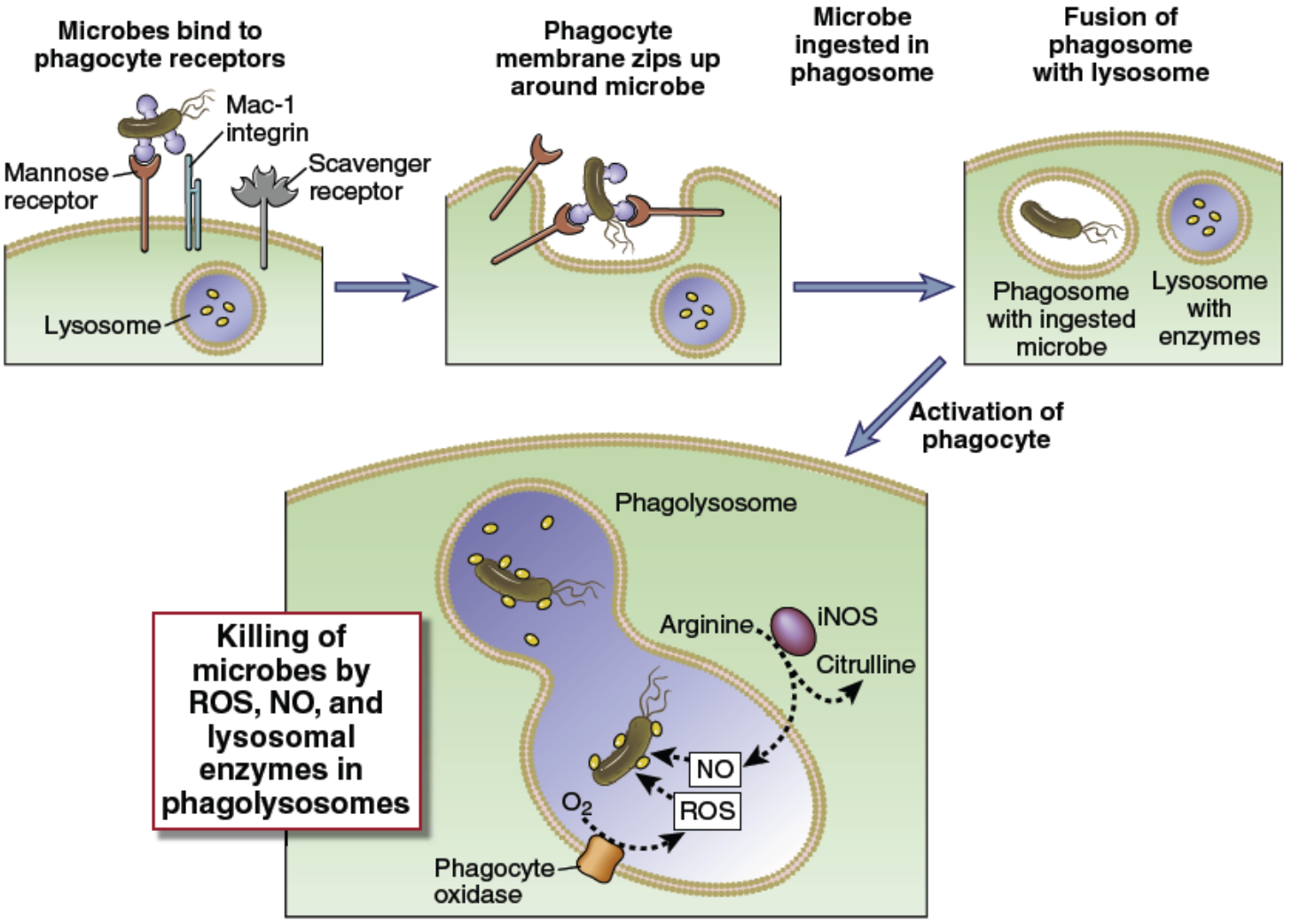
PRR= „Pattern Recognition Receptors”

→Binding to the PAMPS of microbes

PAMP=„Pathogen Associated Molecular Patterns

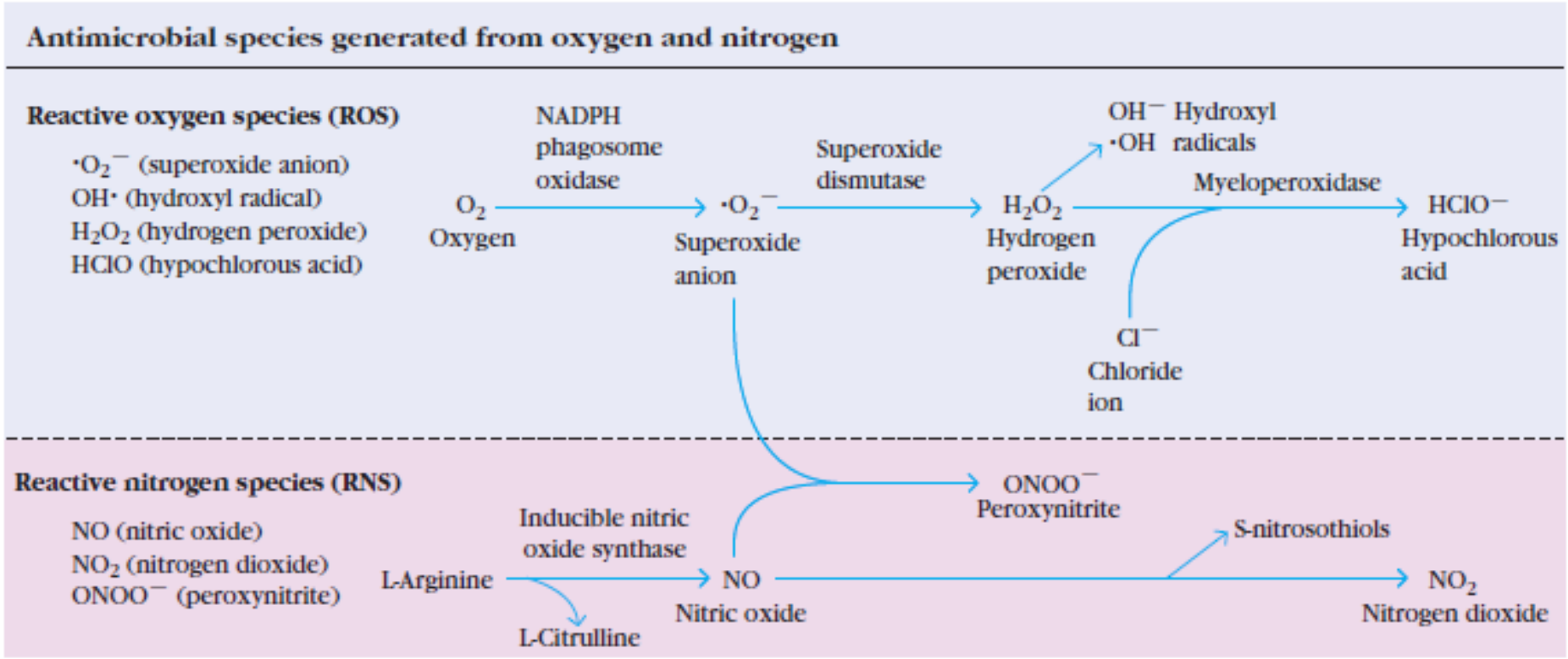
Janeway CA Jr, Travers P, Walport M, Shlomchik MJ. Immunobiology, 2005.

Process of phagocytosis



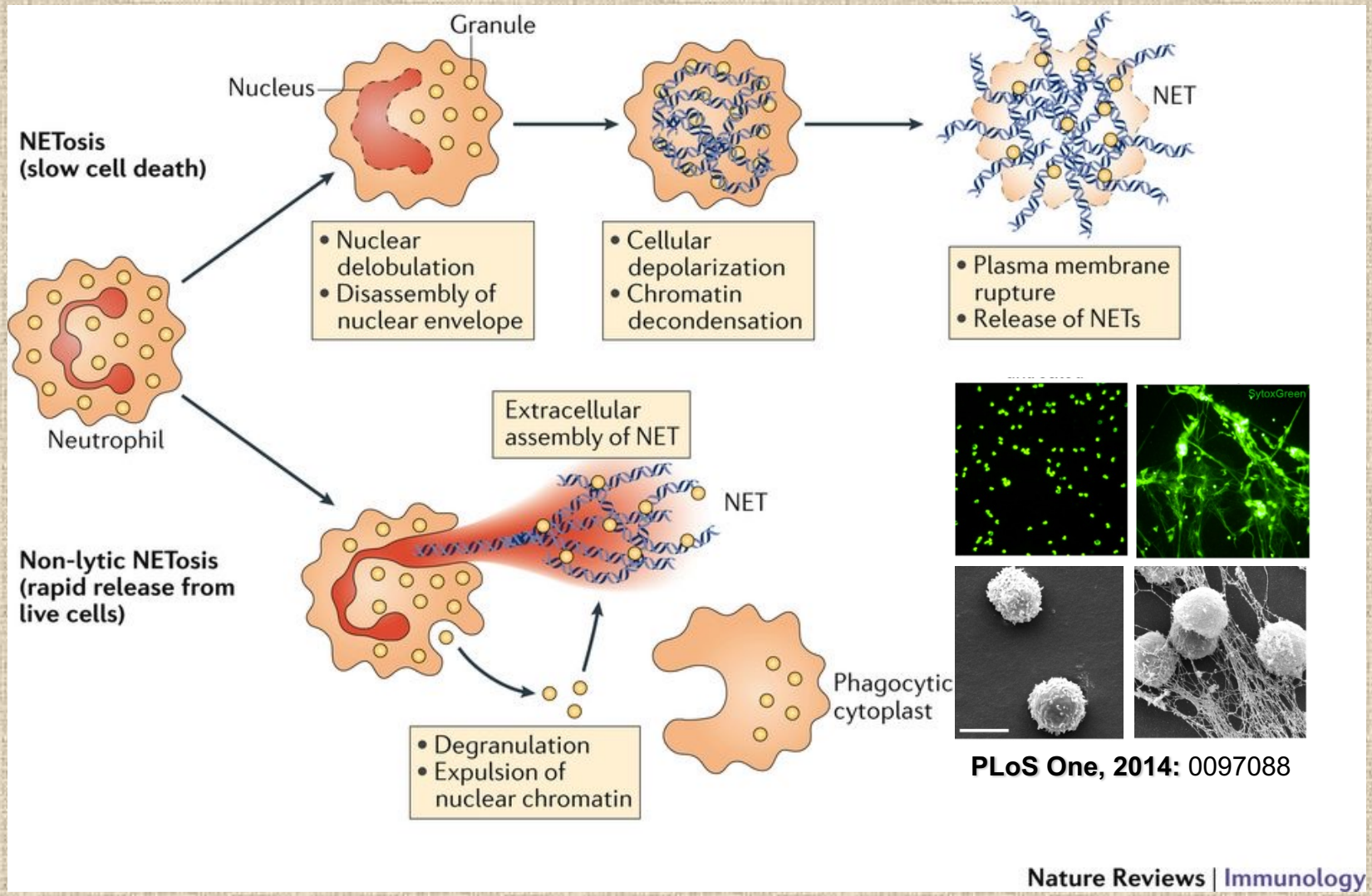
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012 .

Reactive oxygen/nitrogen intermediers



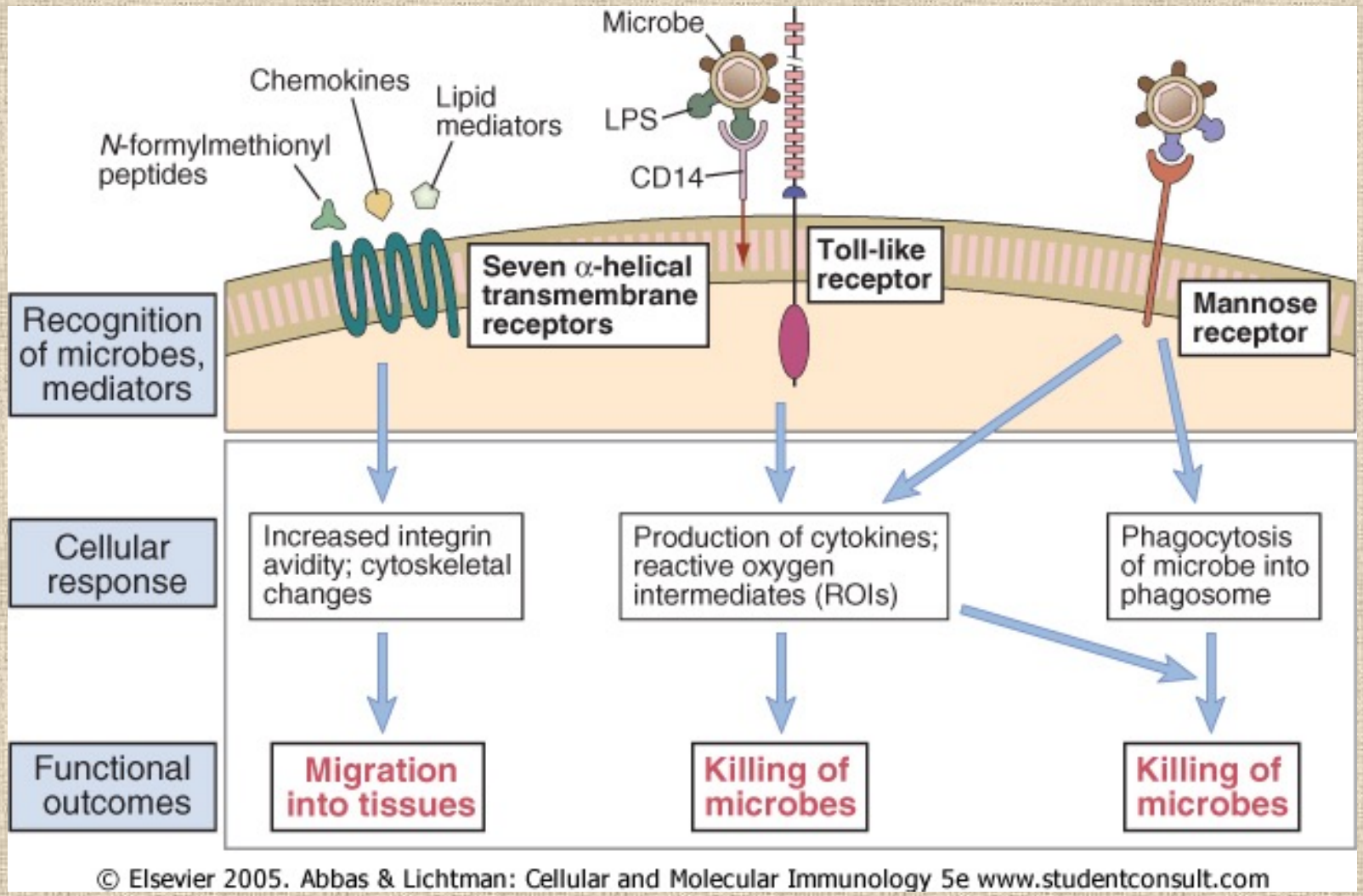
Owen, Punt, Stranford : Kuby Immunology 7th Edition, 2013.

Process of NETosis



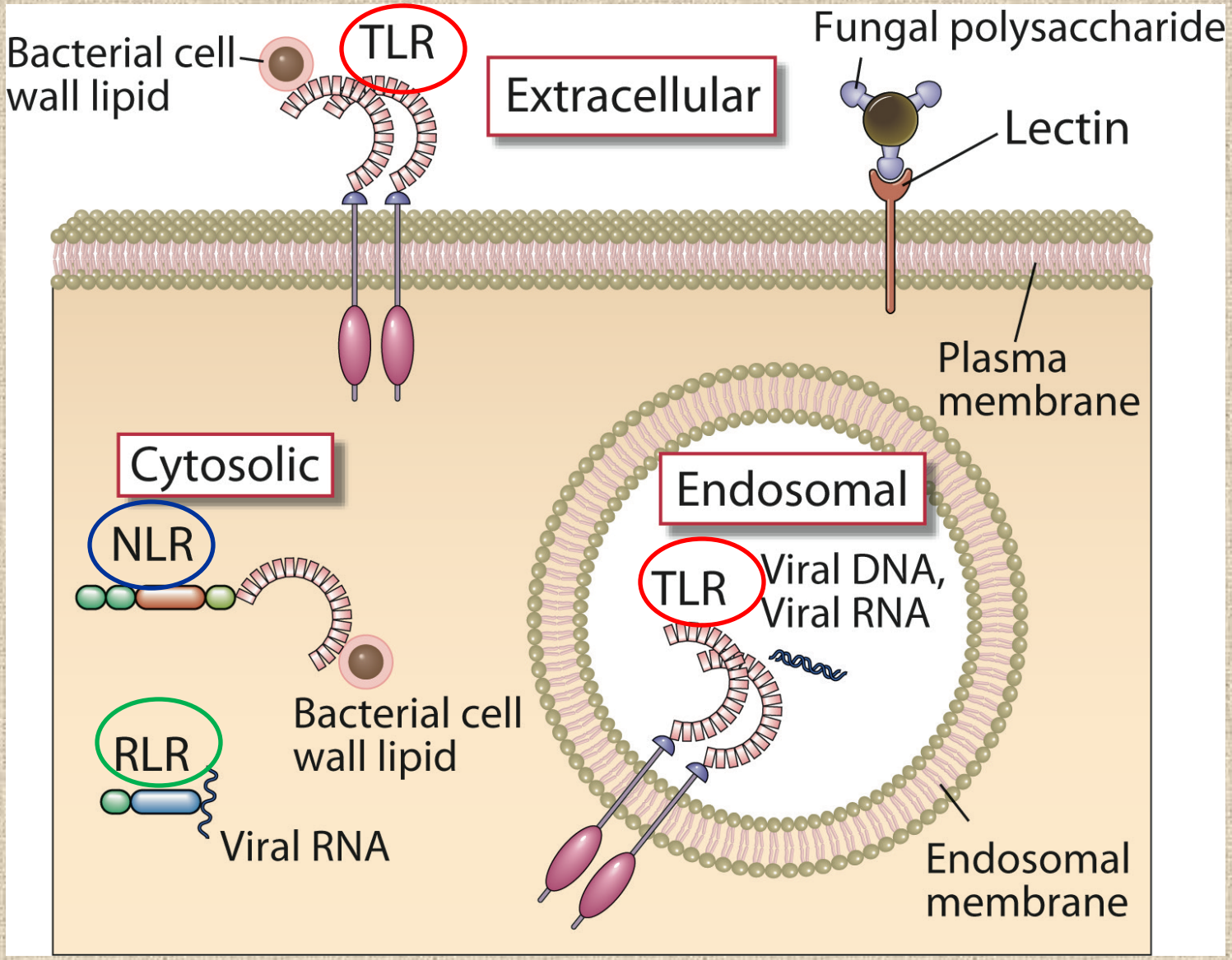
NET: neutrophyl extracellular trap

Phagocyte receptors



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

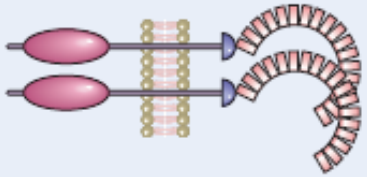
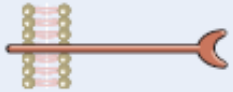
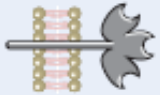
Pattern recognition receptors



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

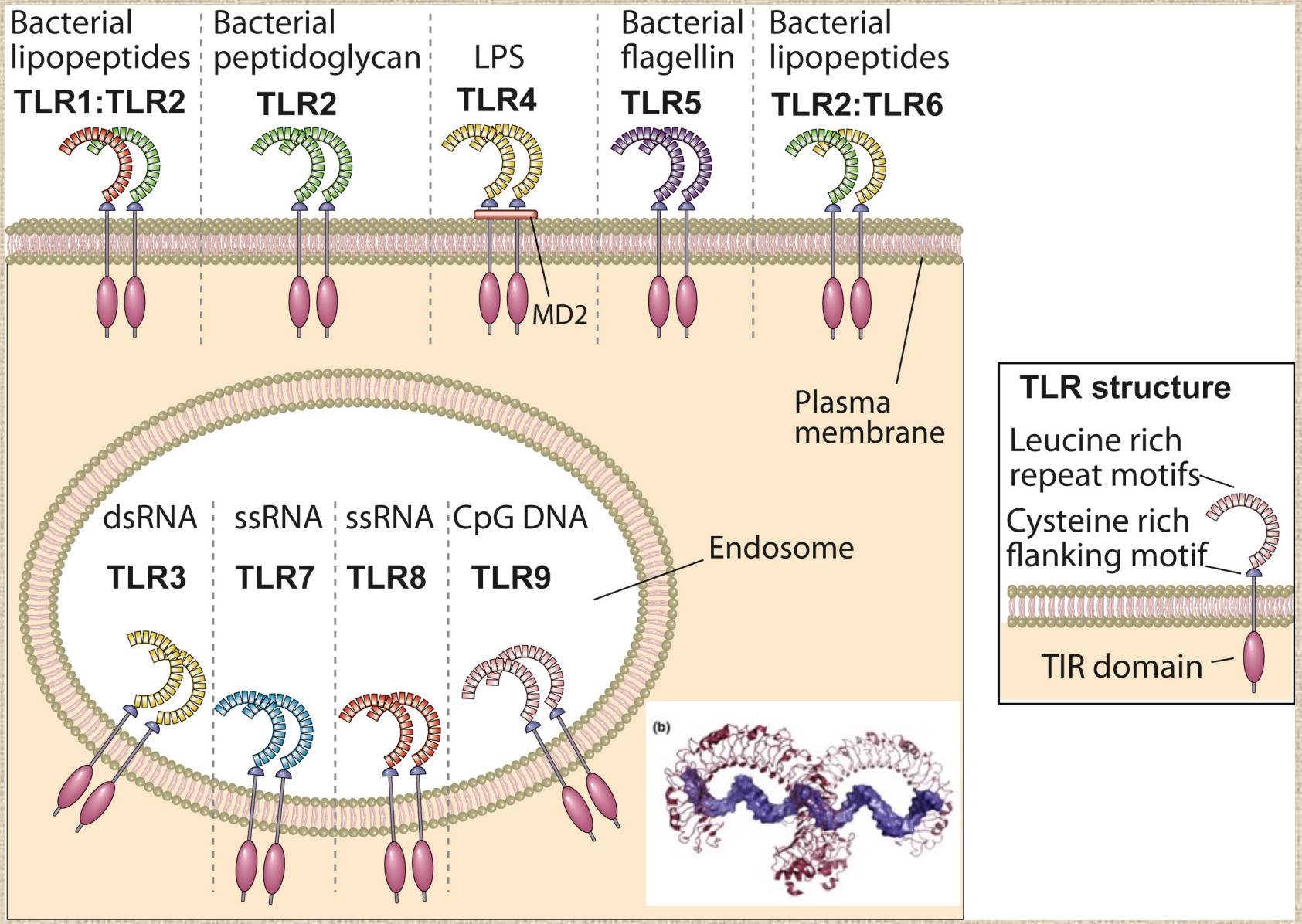
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

Main groups of pattern recognition receptors

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.

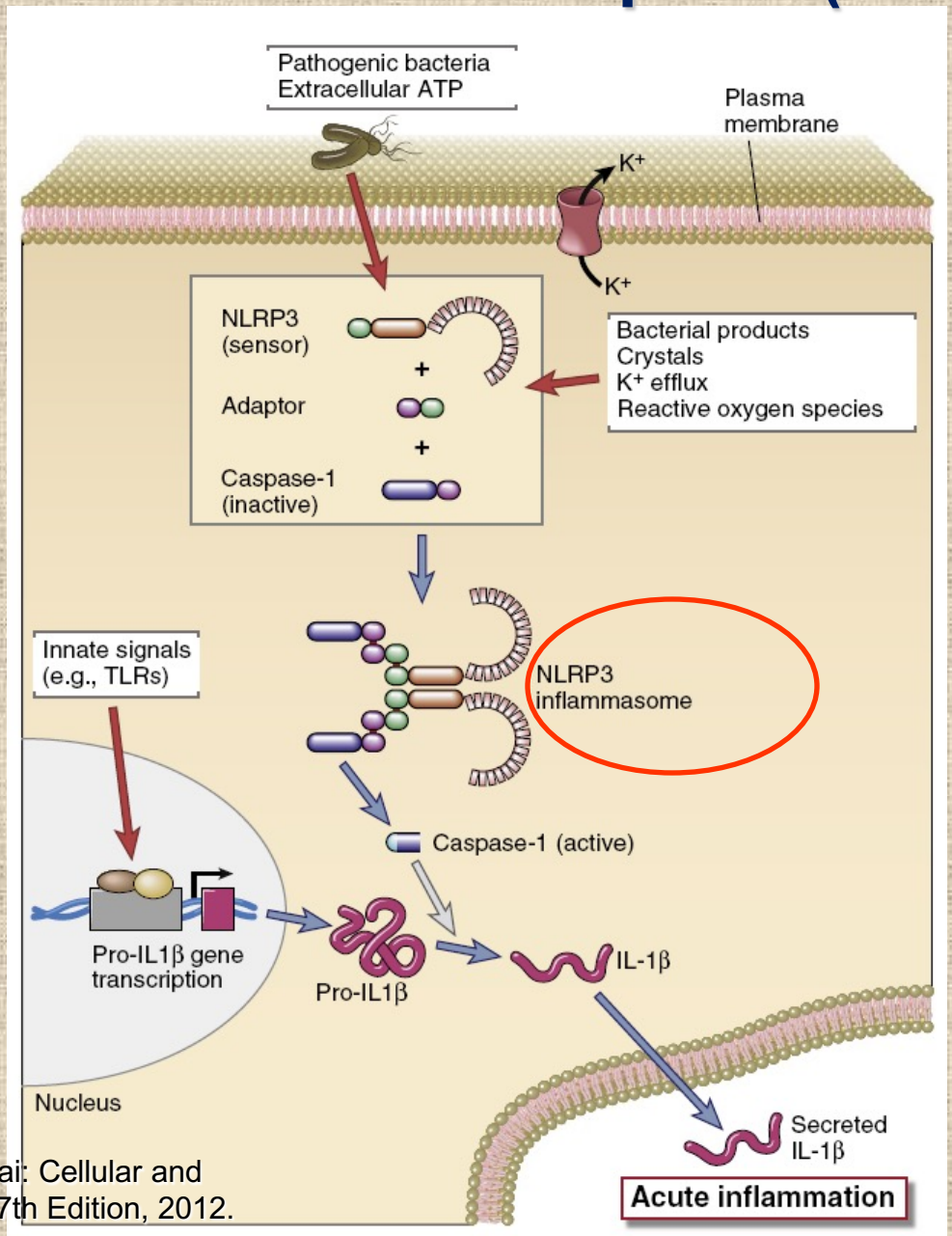
Pattern recognition receptors: Toll-like receptors (TLR)



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

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

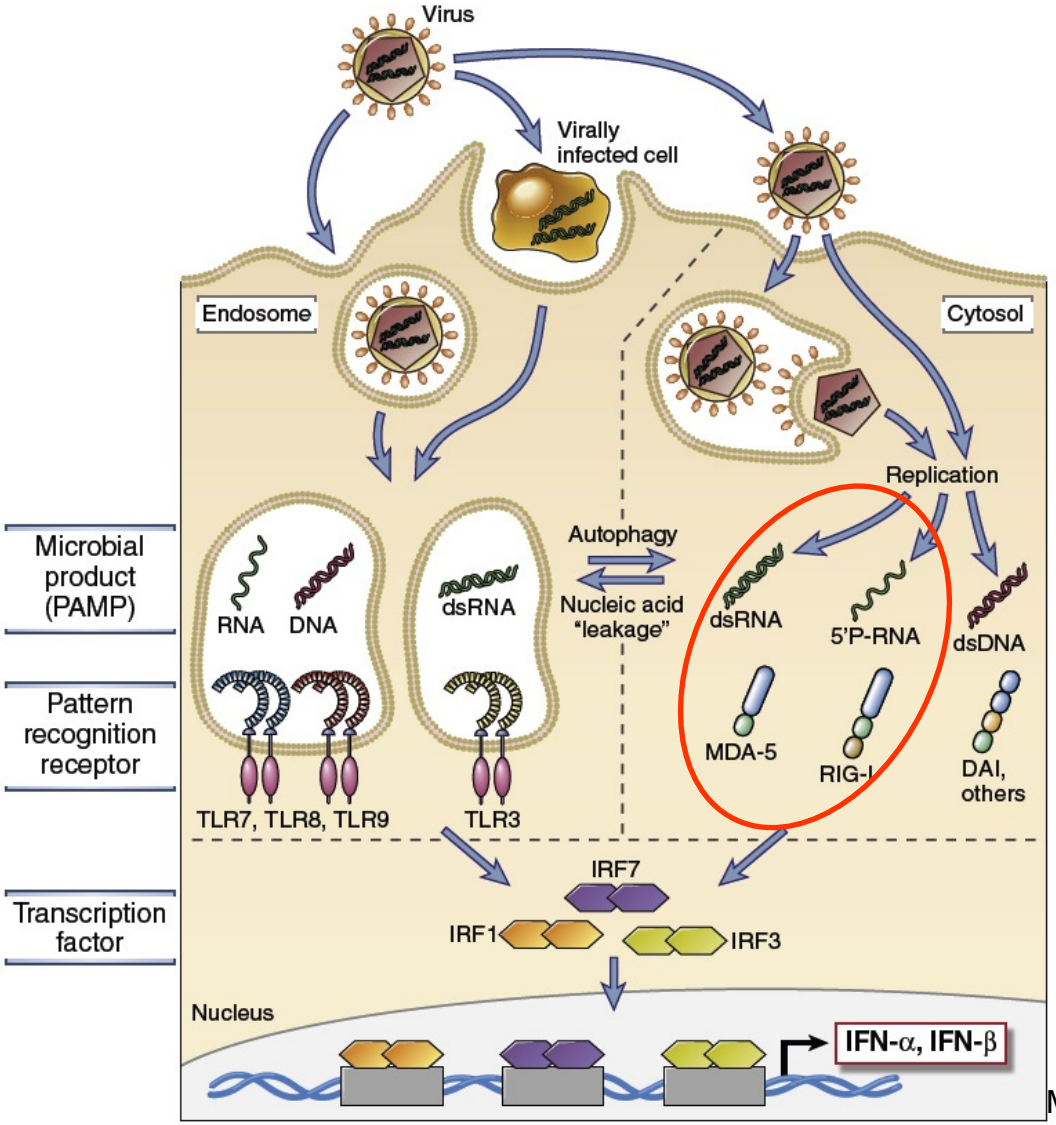
Pattern recognition receptors: NOD-like receptors (NLR)



NOD: Nucleotide oligomerization domain

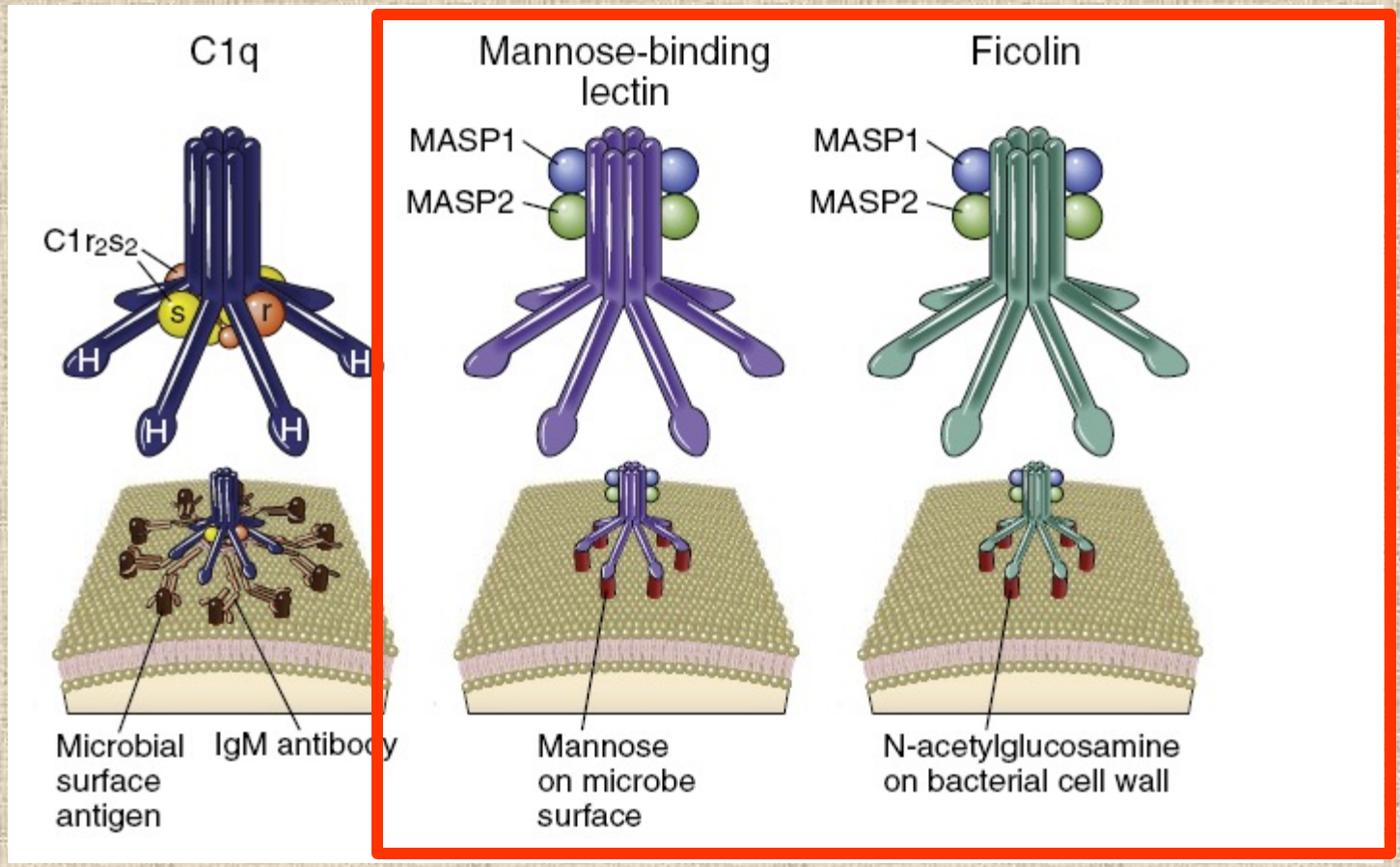
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

Pattern recognition receptors: RIG-like receptors (RLR)



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

Soluble pattern recognition molecules I

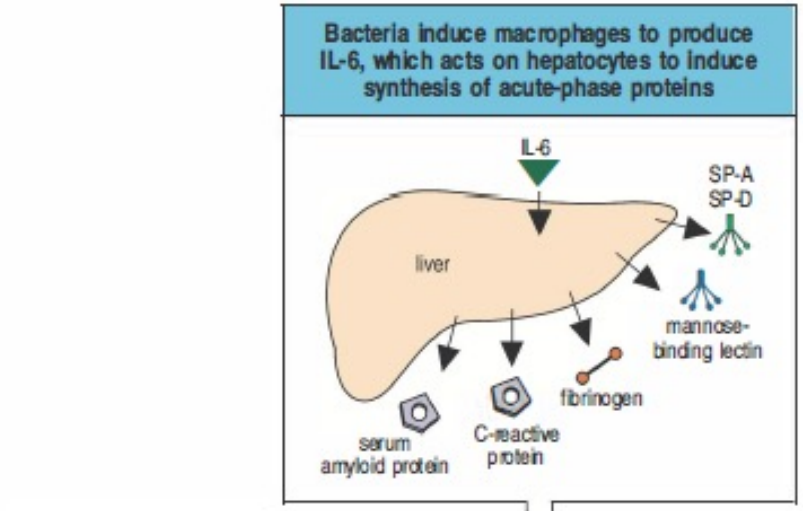


Collectin (MBL, SP-A, SP-D): C-type lectin domain

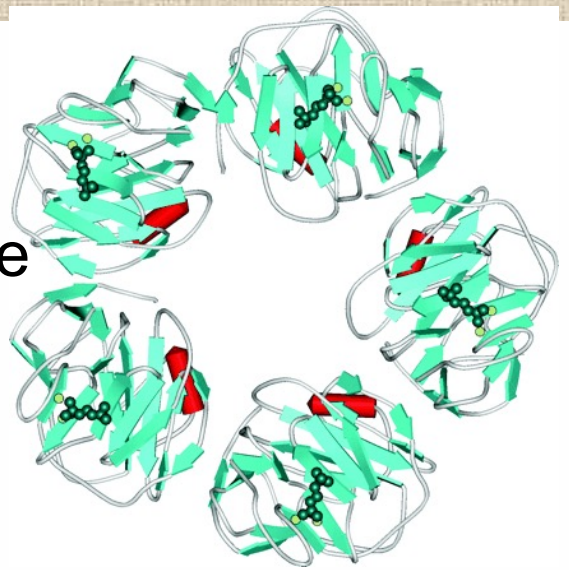
Ficolin: Fibrinogen domain

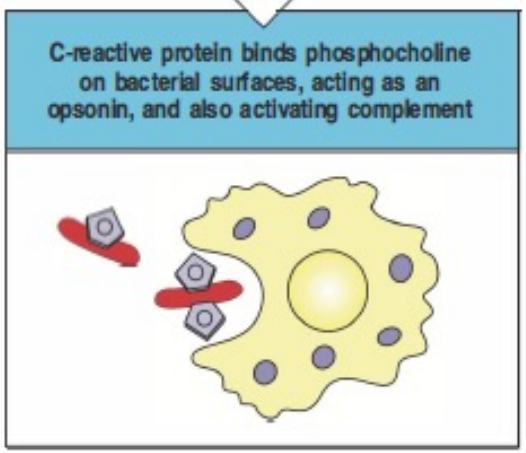
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012 .

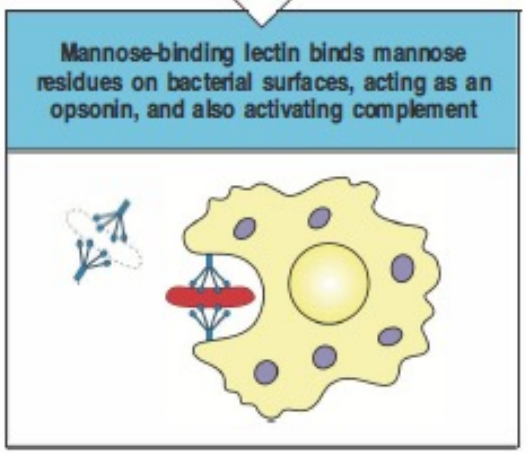
Soluble pattern recognition molecules II: pentraxins

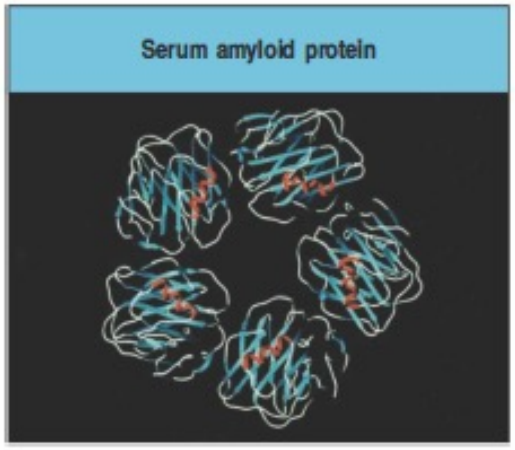


C-reactive protein-CRP









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

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

Clinical significance of C-reactive protein level

Risk of infection, sepsis

↓

CRP test, complete blood count, blood culture
Then start Antibiotics treatment

↓

CRP 48 hr → CRP <10 mg/L & blood culture negative → Discontinue antibiotic treatment

↓

CRP >10 mg/L, Continue antibiotics therapy

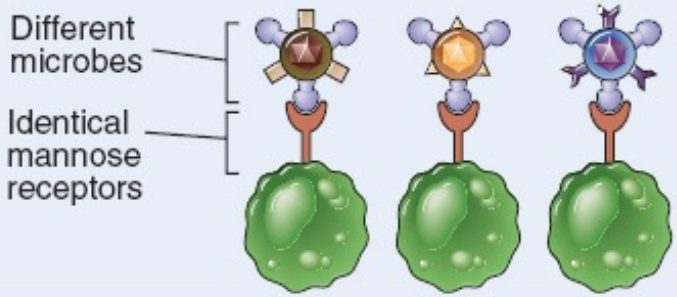
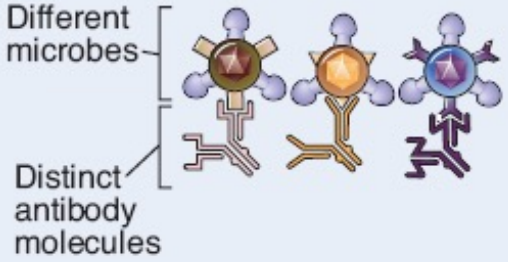
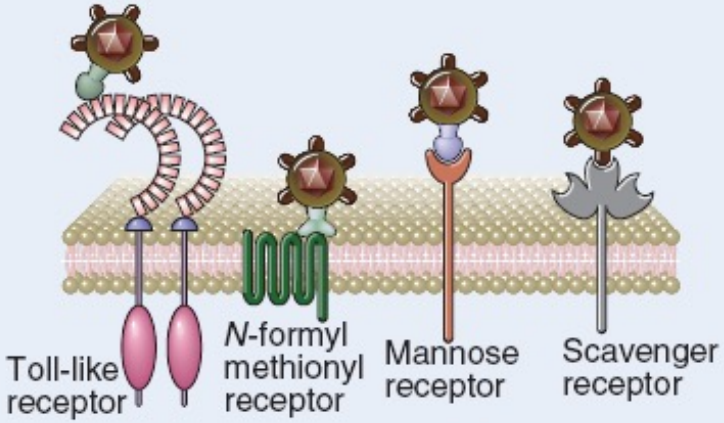
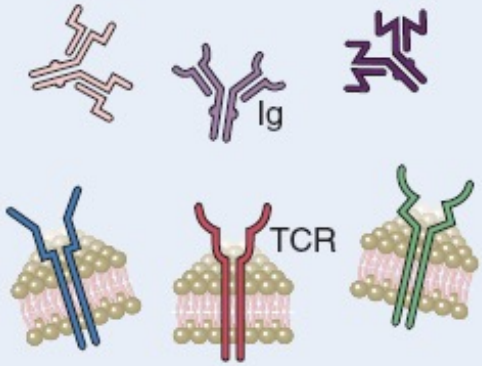
↓

CRP at 7 days

CRP <10 mg/L: discontinue antibiotic treatment

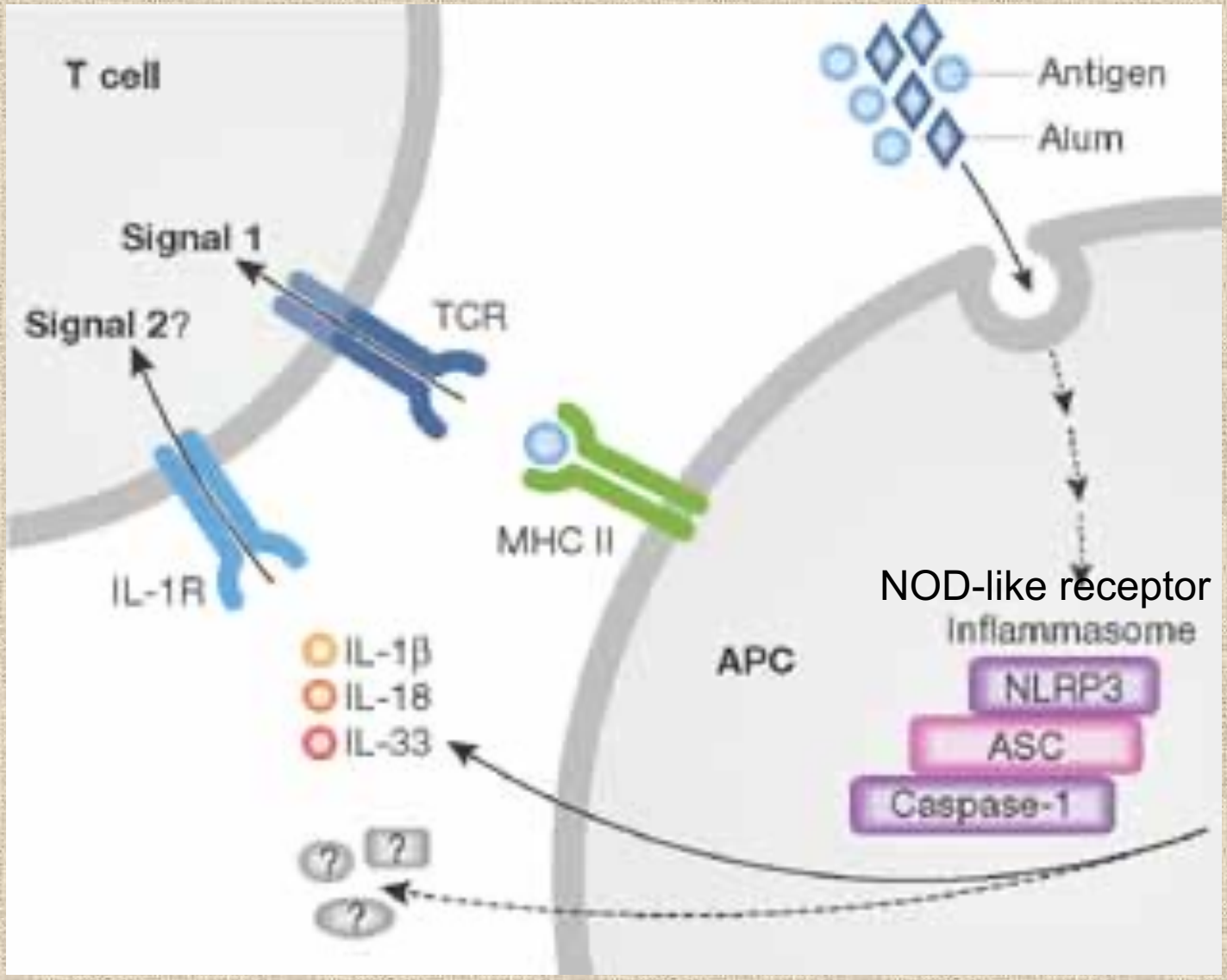
CRP >10 mg/L: reevaluate (new blood count, change antibiotics)

Specificity of innate and adaptive immunity

	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)

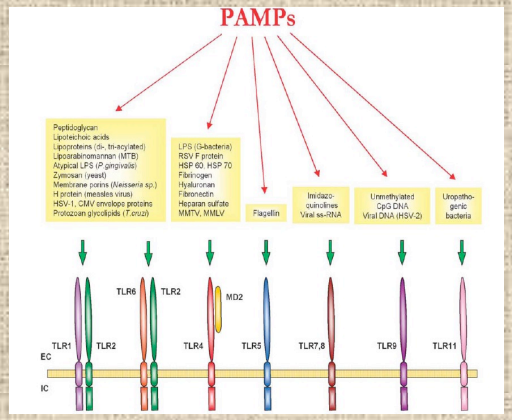
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

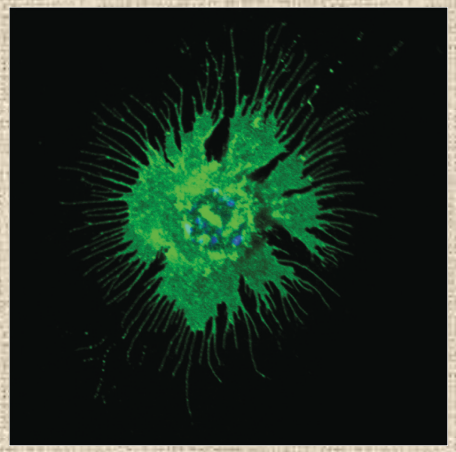
Vaccination and the role of adjuvants



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

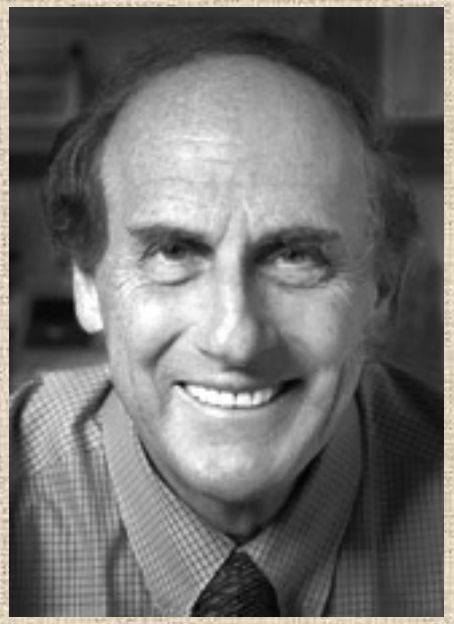
Nobel Laureates in 2011 for medicine and physiology





Jules A. Hoffmann

Bruce A. Beutler



Ralph M. Steinmann