Basic immunology

Lecture 5.

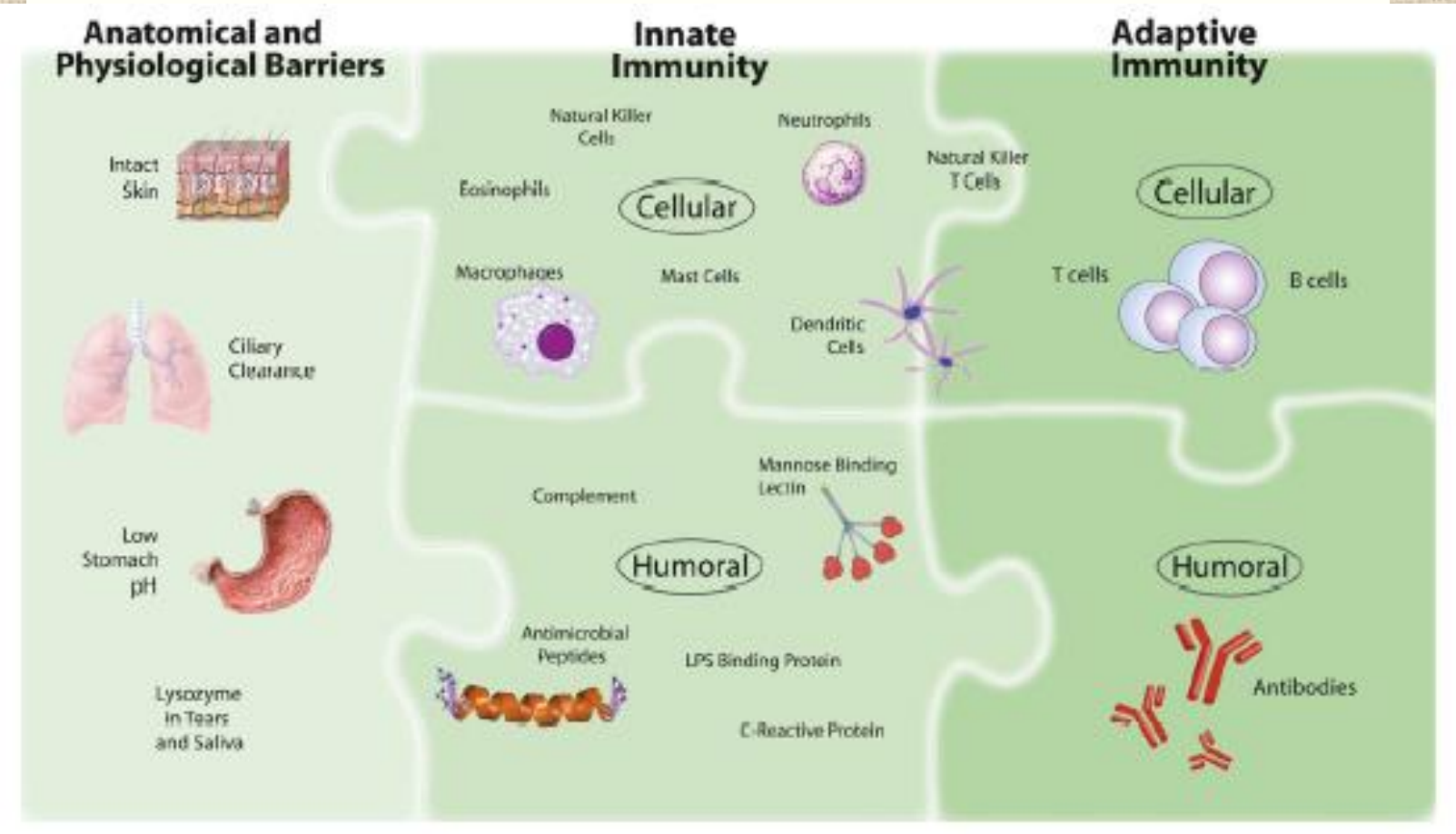
Innate immunity, cell adhesion

Péter Engelmann

- Different levels of the immune response
- Recognition molecules of the innate immunity
- Adhesion molecules, extravasation („homing”)

The levels of host defense

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



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

The levels of host defense

- Anatomic „barriers”
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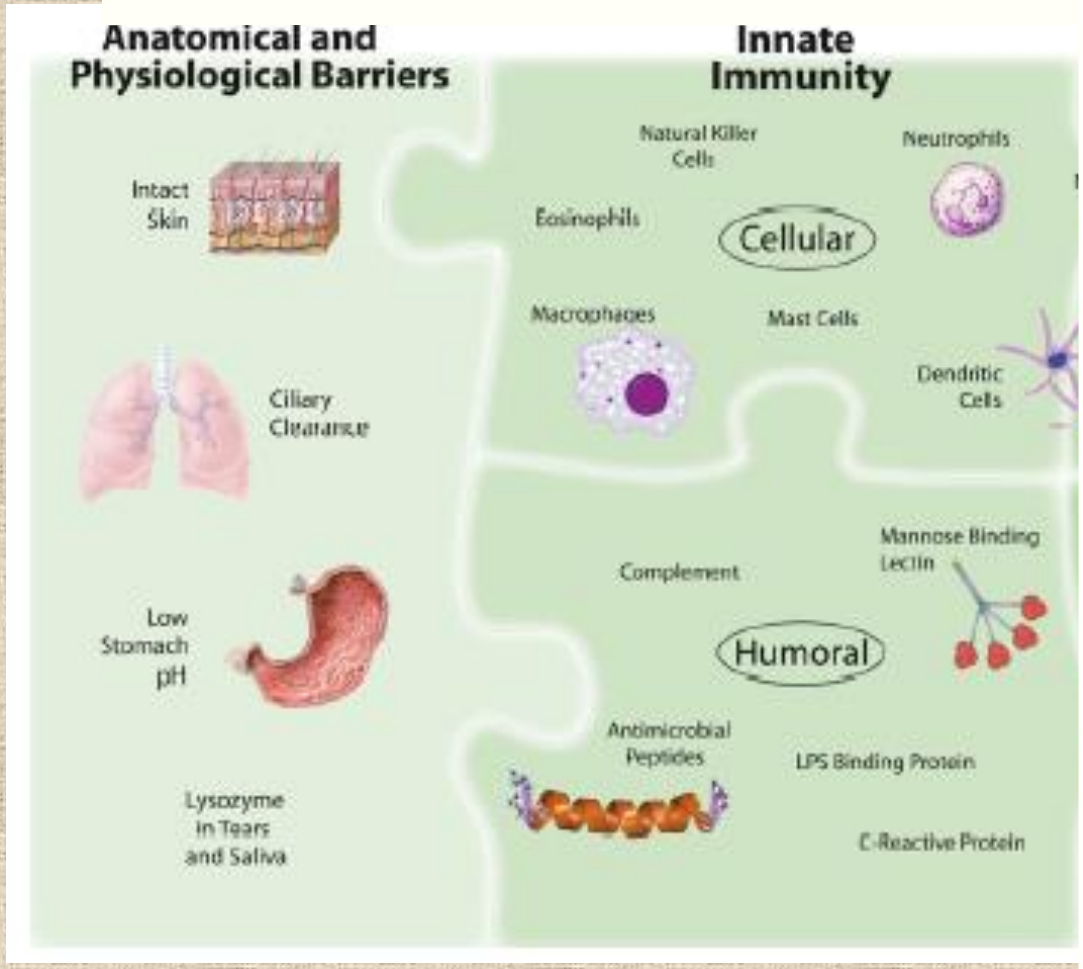


I. First line of defense: anatomic „barriers”

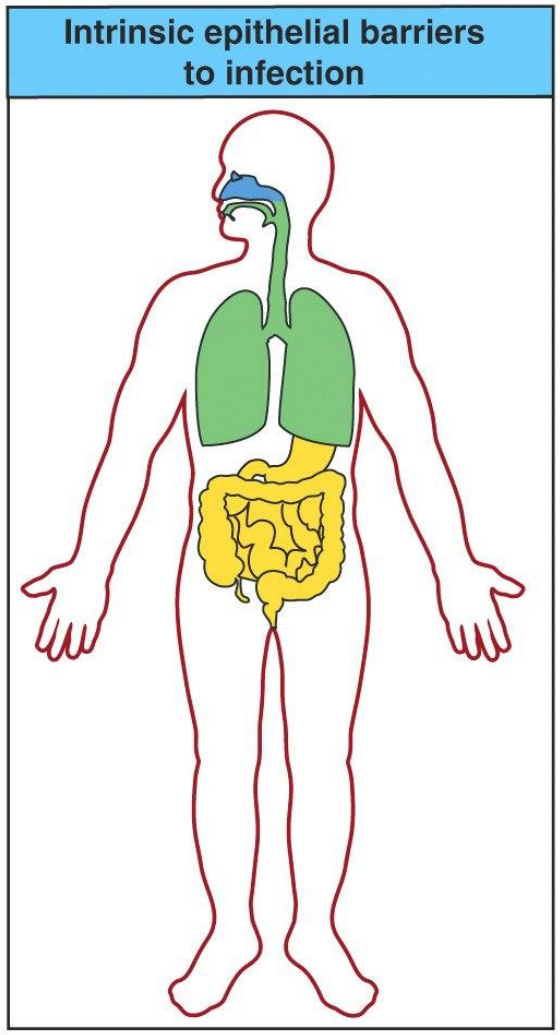


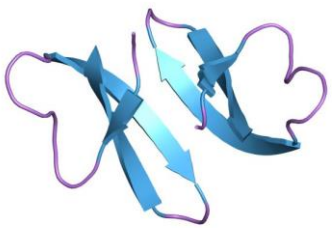
Figure 2-4 Immunobiology, 6/e. (© Garland Science 2005)

	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			

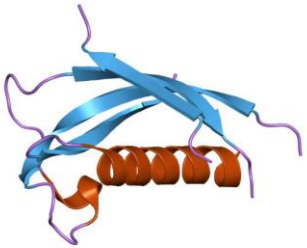
1. Mechanical defense
2. Slightly acidic environment
3. Normal (commensal) microorganisms
4. Antimicrobial factors in the body fluids, on the skin.
5. Cilia

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

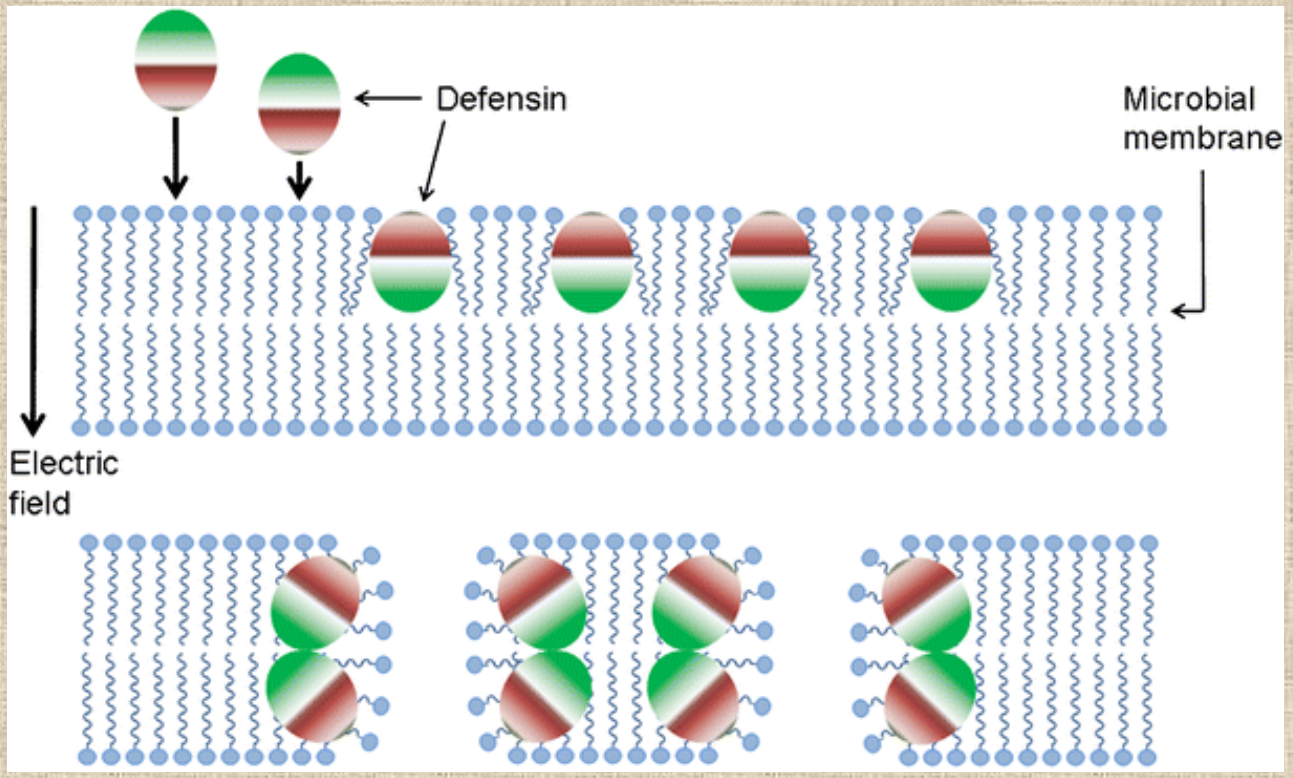
Antimicrobial peptides

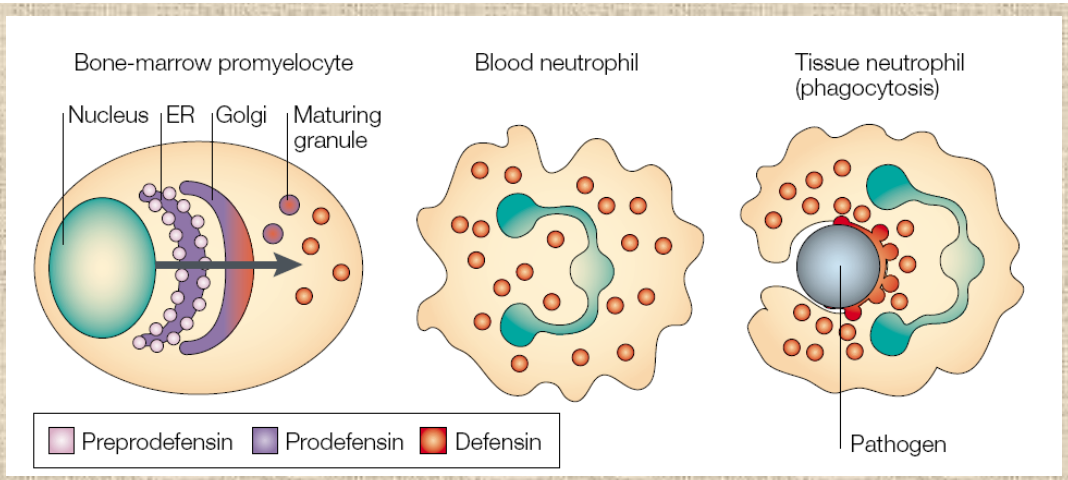


Defensin



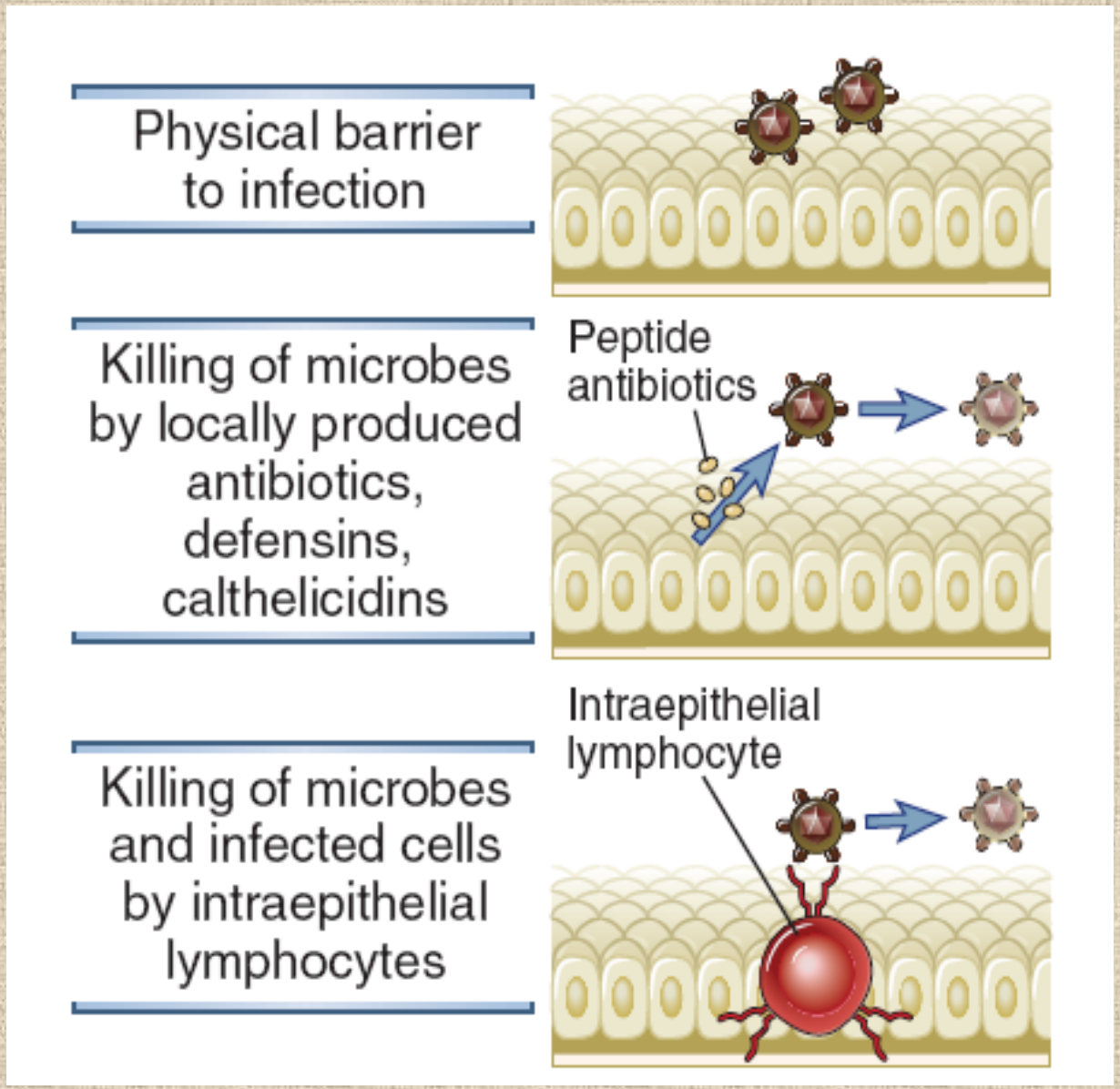
Cathelicidin





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

The role of epithelial barriers

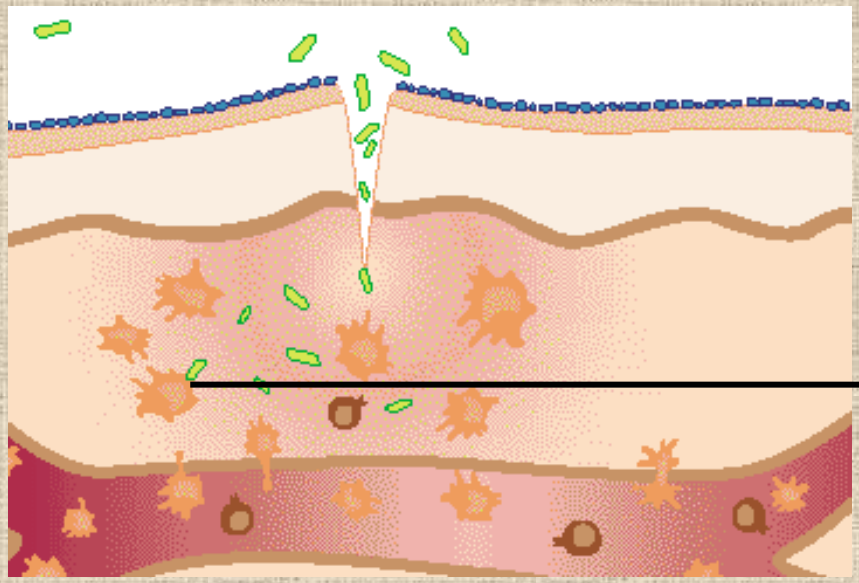


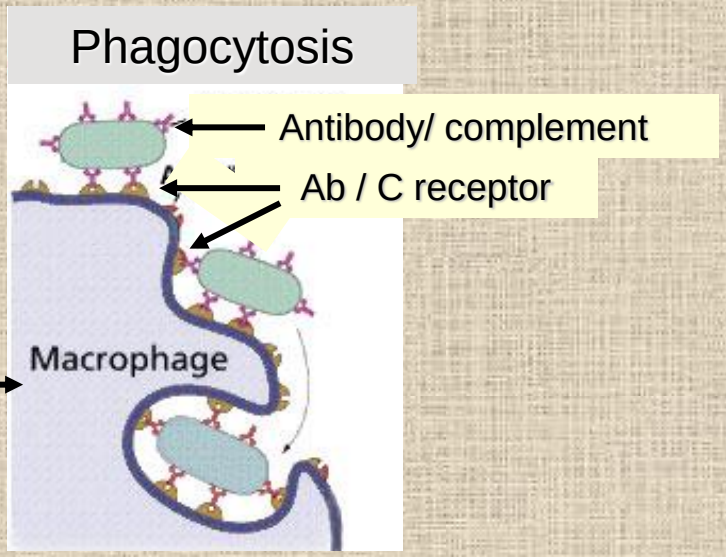
Defensins, cathelicidins

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



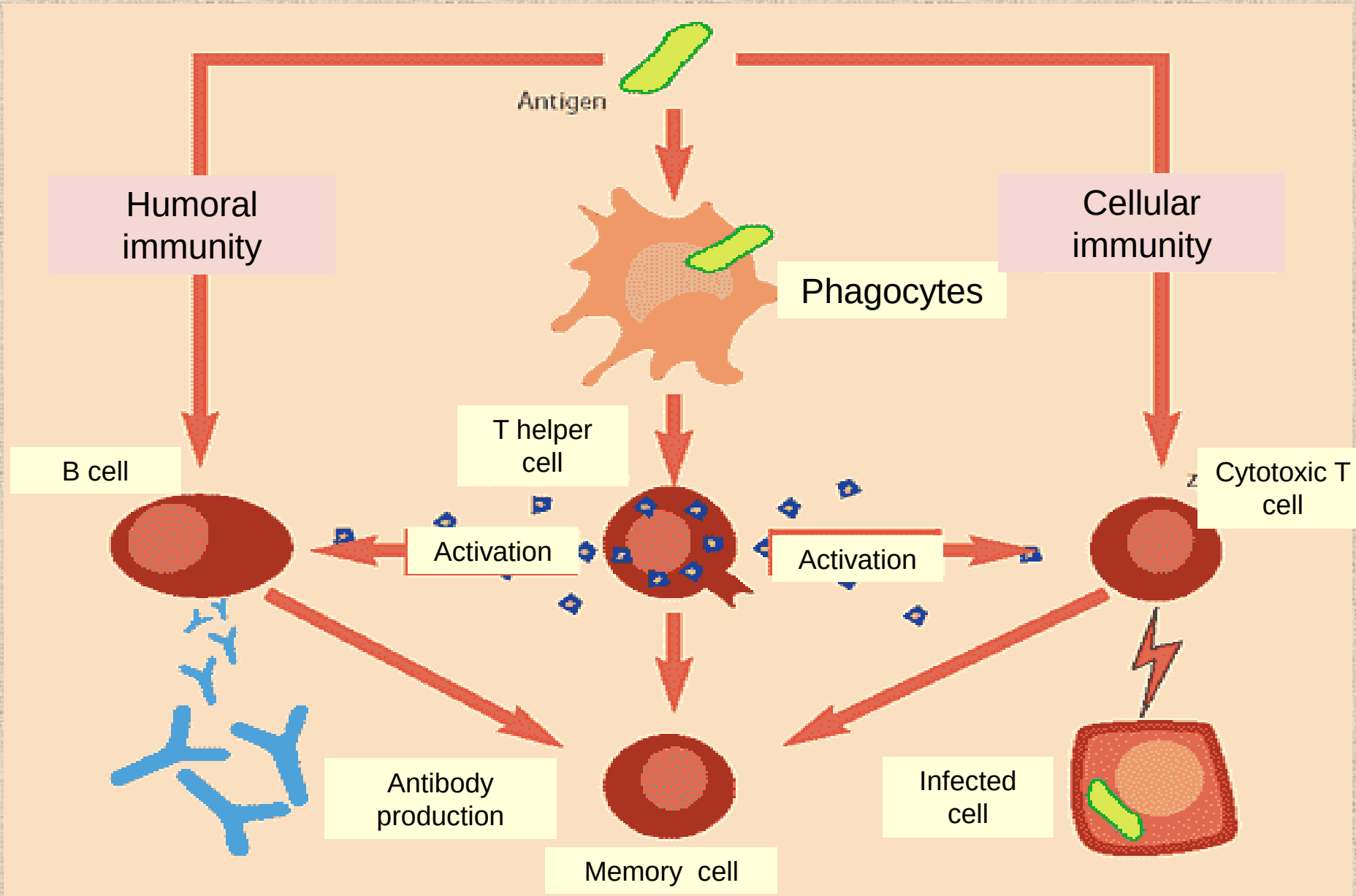


1. Phagocytes in the blood and tissues.
2. Soluble proteins (immunglobulin and complement, C-reactive protein), bind to microbe surface (opsonisation) to enhace the phagocytosis.

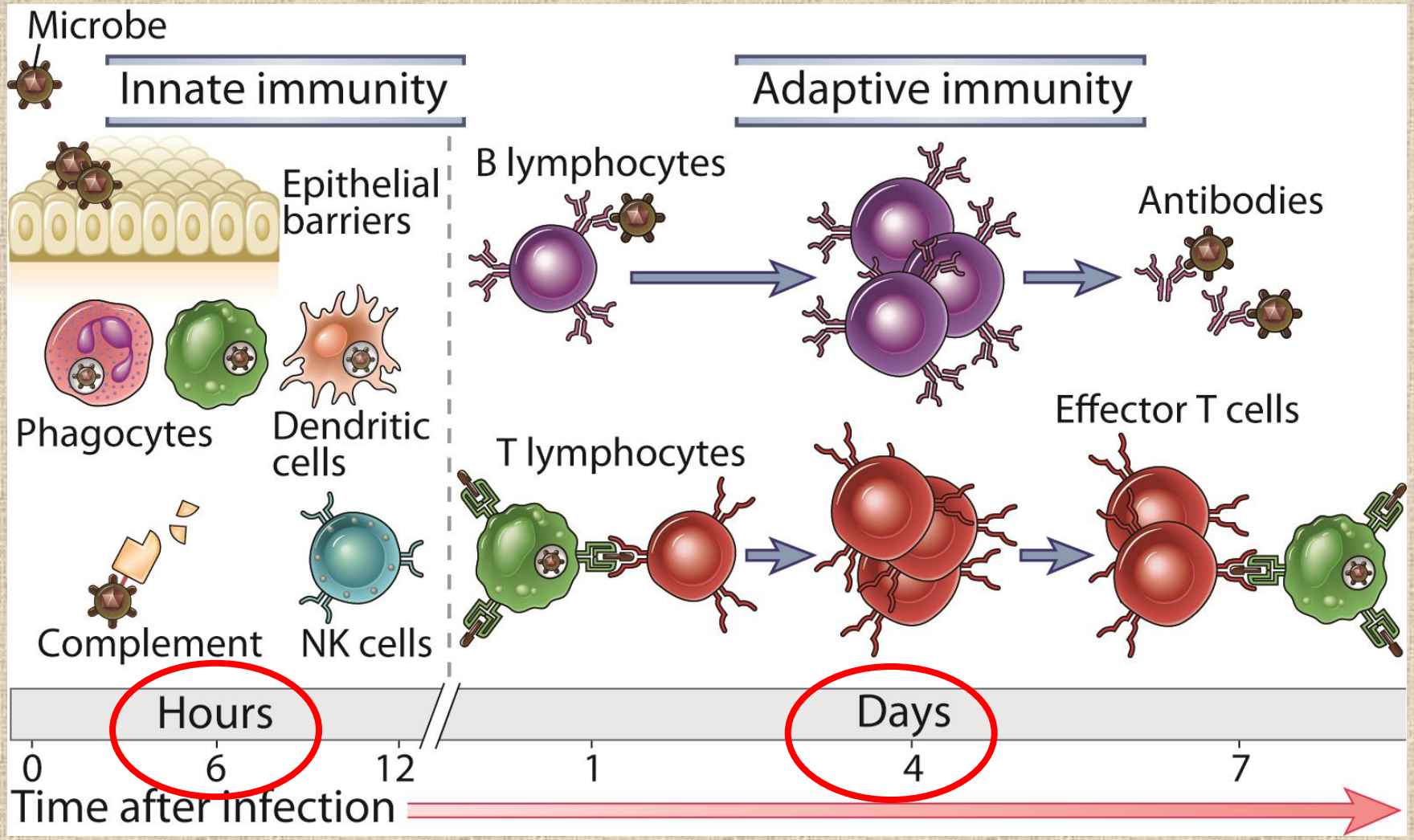
Functions of innate immunity

- 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



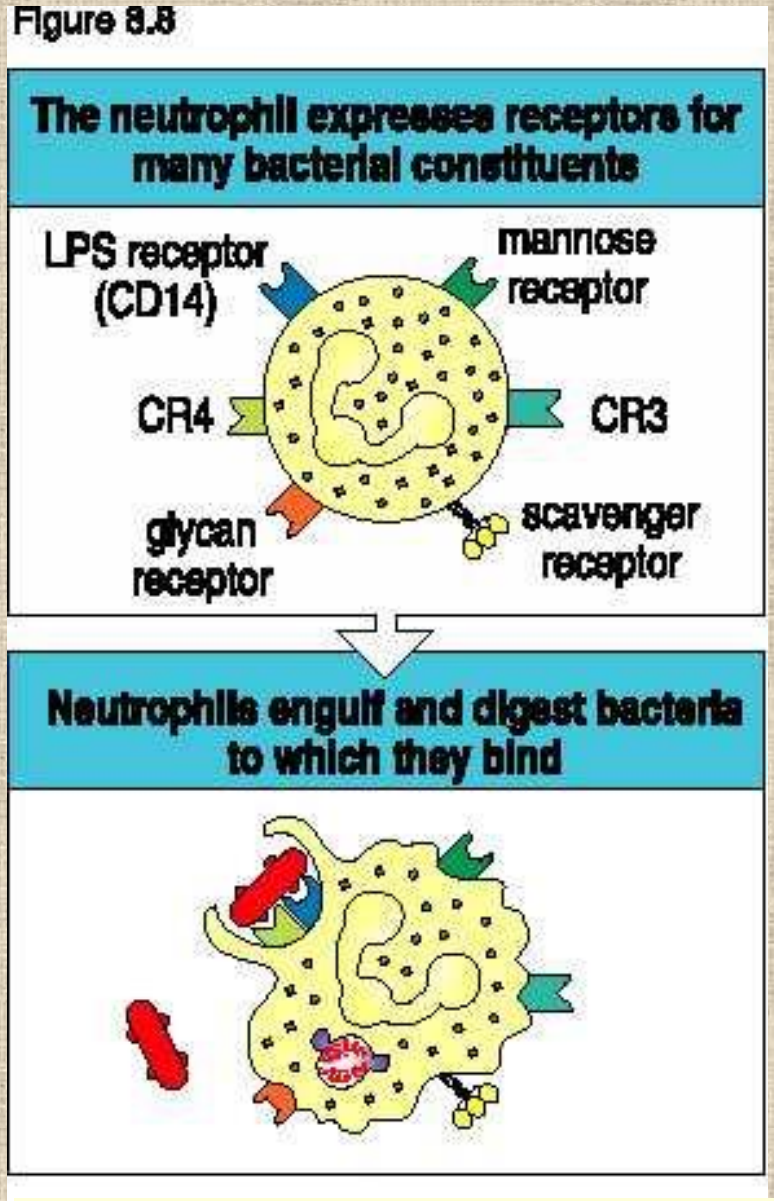
The kinetics of innate and adaptive immune response



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

- Different levels of the immune response
- Recognition molecules of innate immunity
- Adhesion molecules, extravasation („homing”)

Recognition of pathogens, phagocytosis



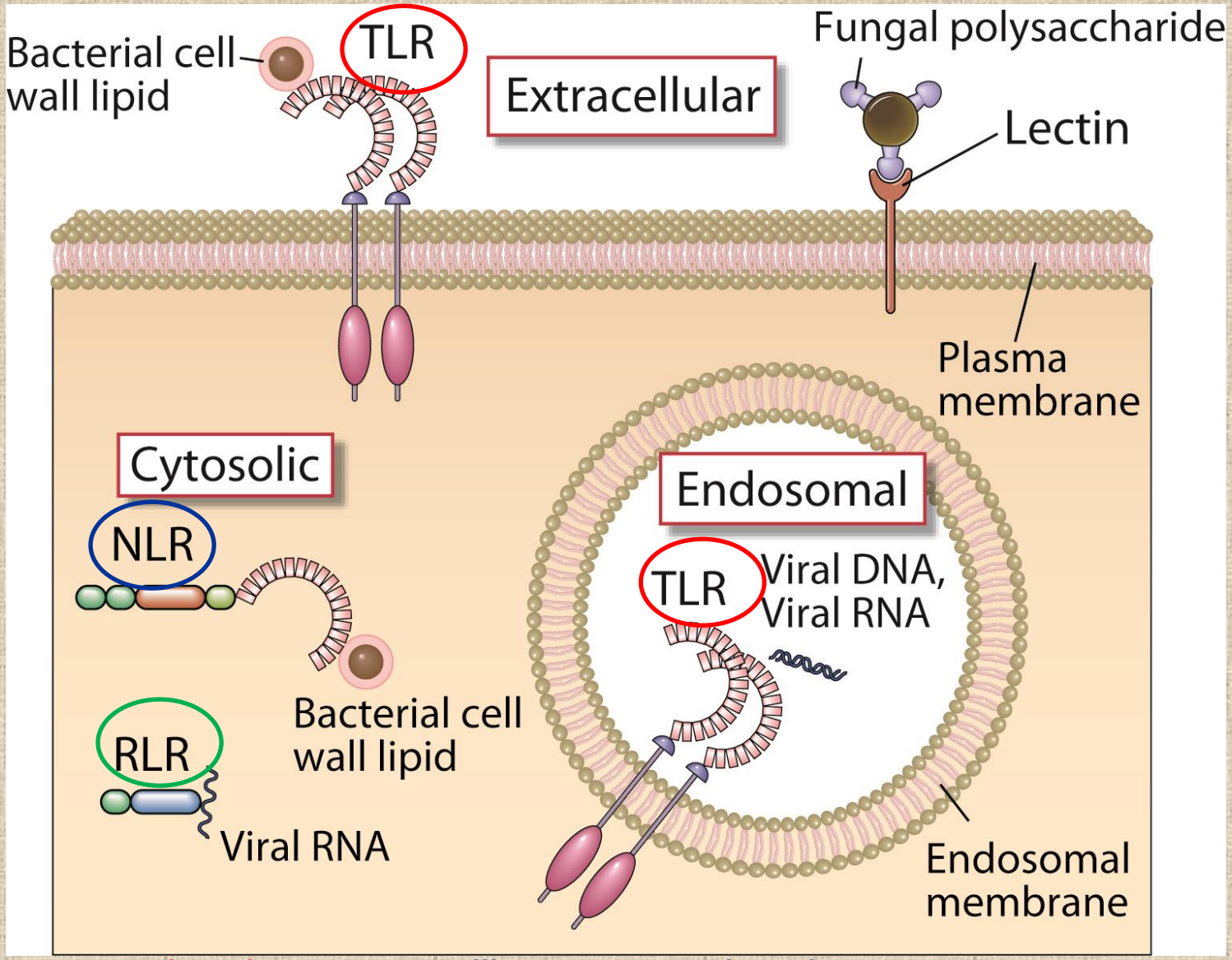
PRR= „Pattern Recognition Receptors”

→Binding to the PAMPS of microbes

PAMP=„Pathogen Associated Molecular Patterns

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

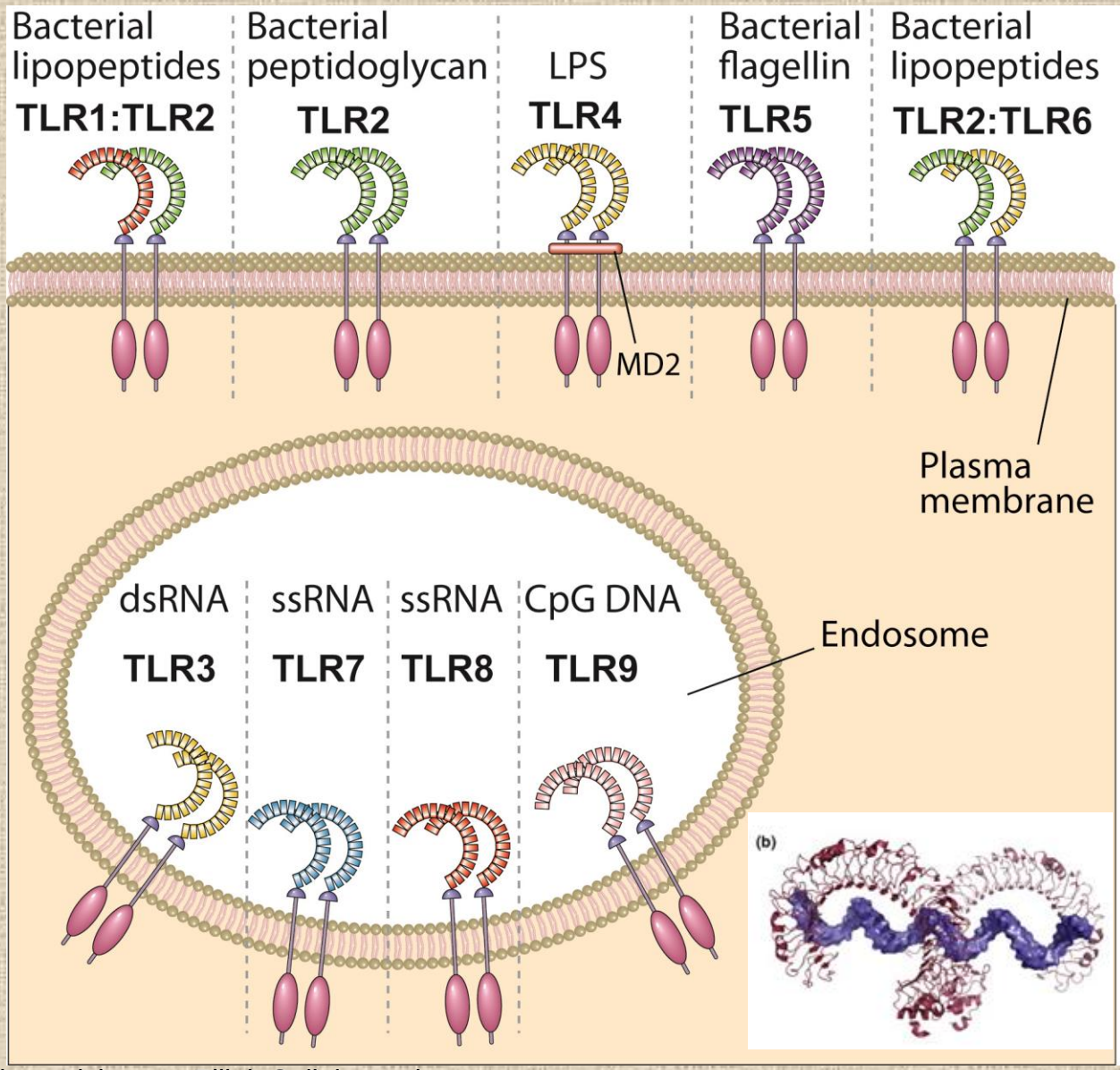
Pattern recognition receptors

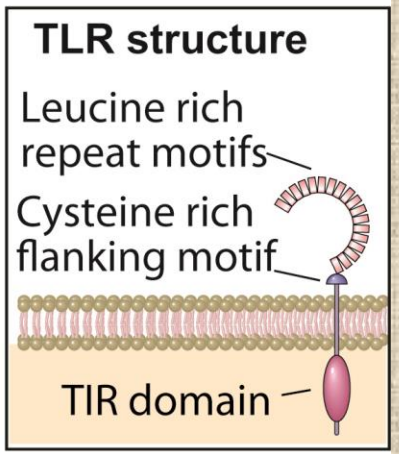


Toll-like receptors (TLR) NOD-like receptors (NLR) RIG-like receptors (RLR)

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

Pattern recognition receptors: Toll-like receptors (TLR)

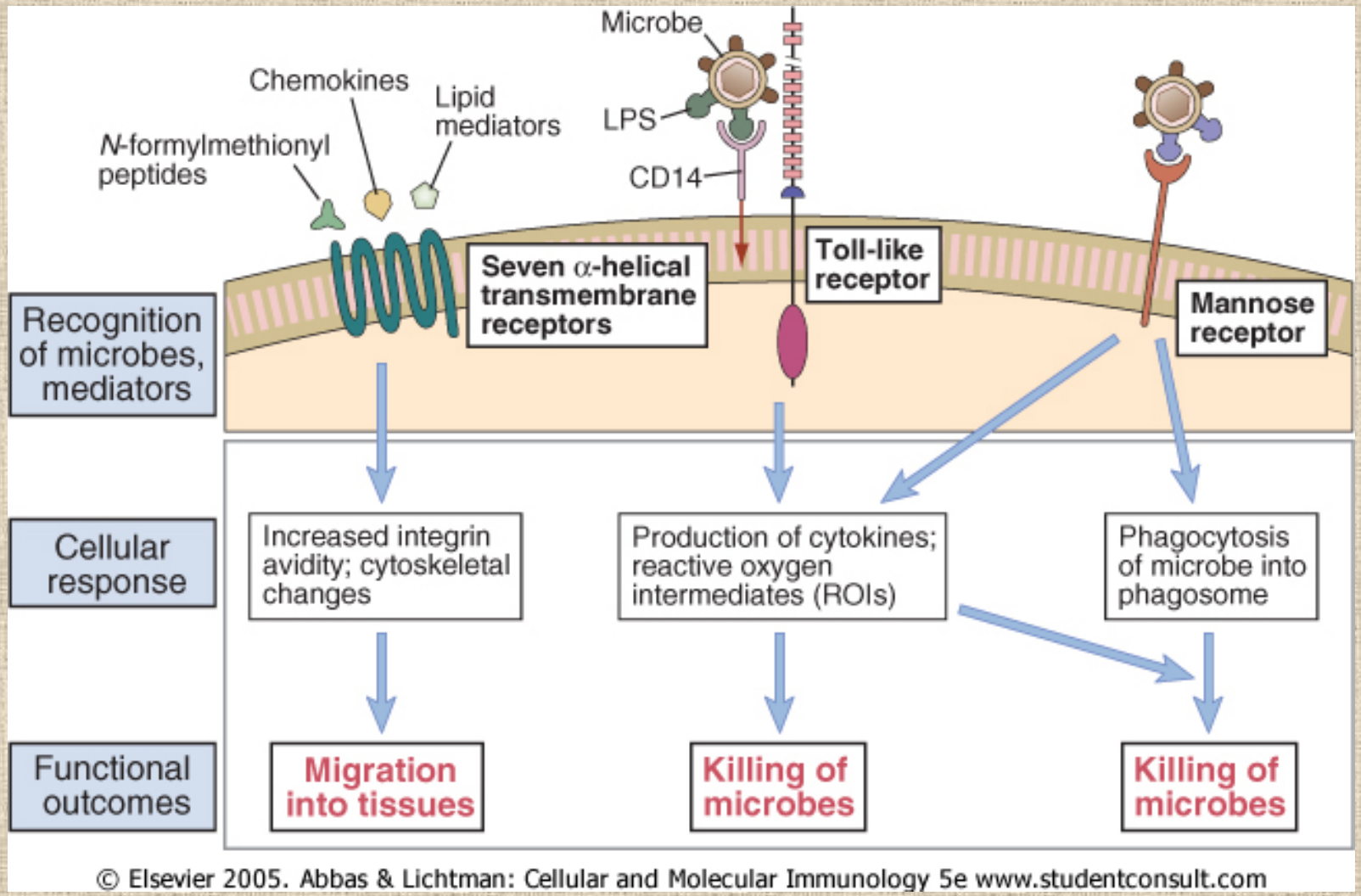




Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

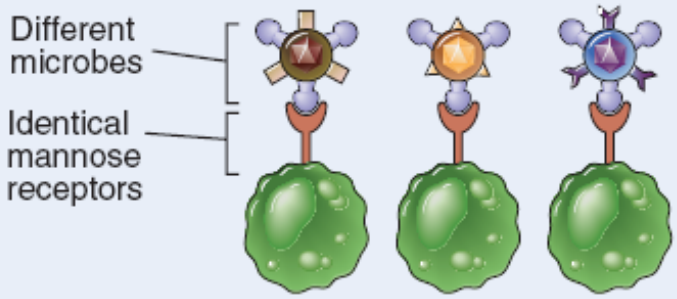
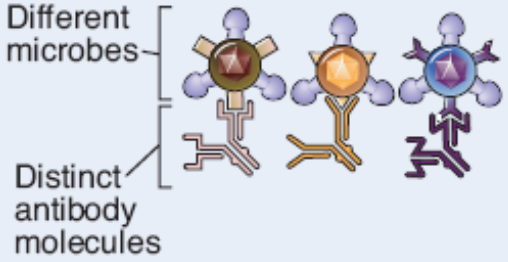
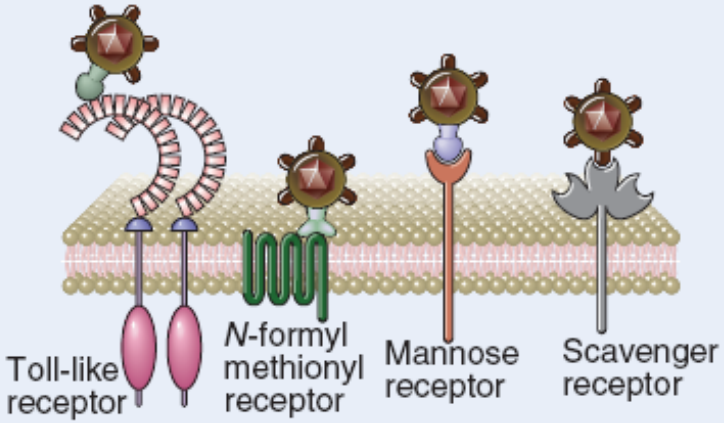
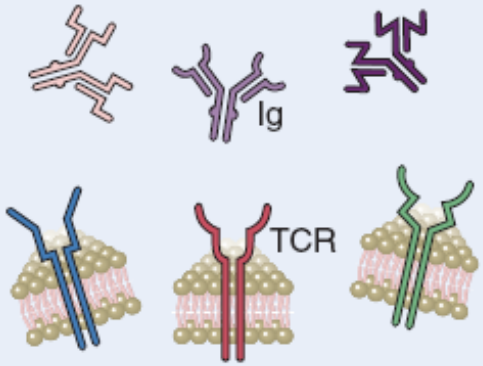
Trends in Biochemical Sciences 2009; 34: 553-561.

Phagocyte receptors



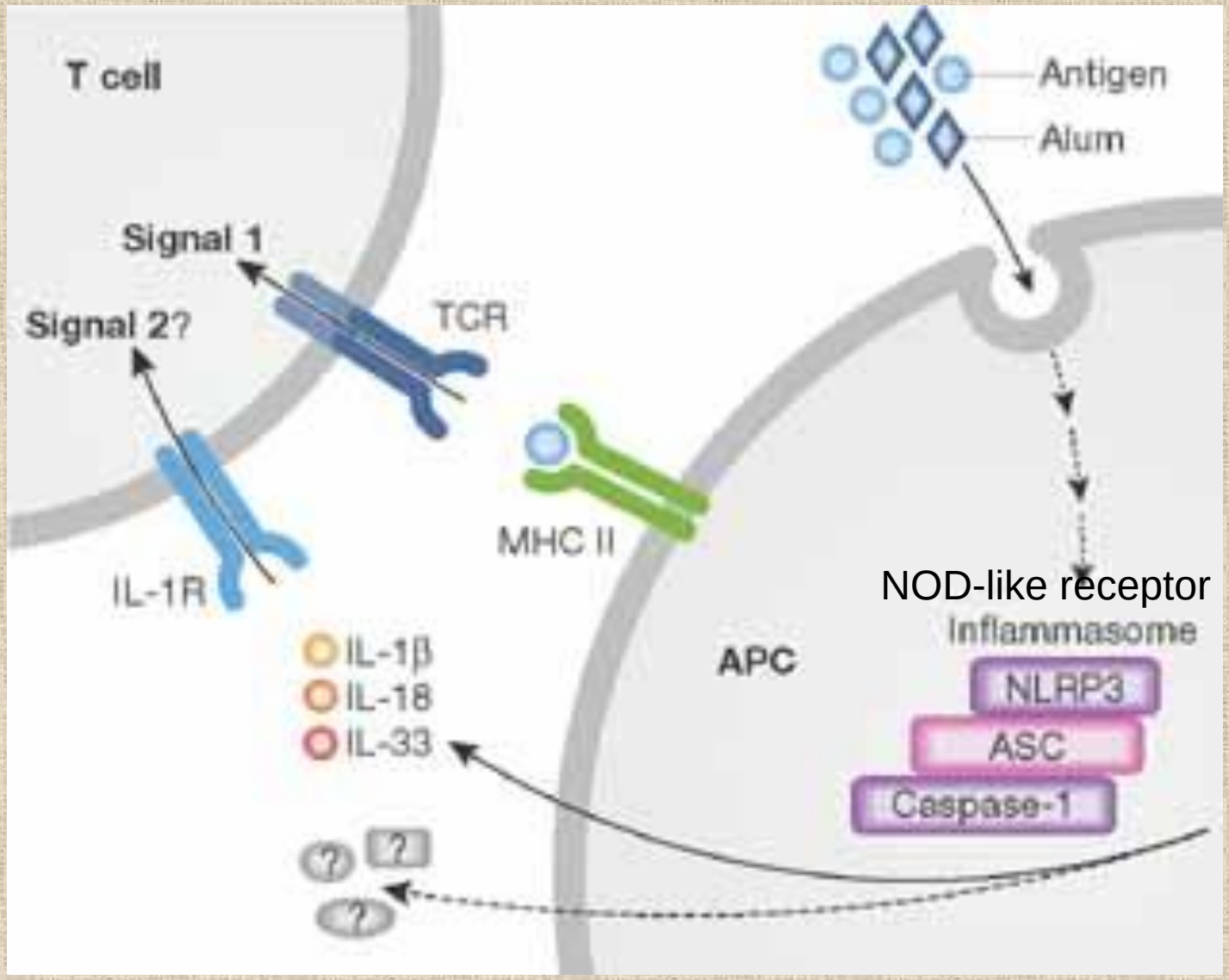
Abbas, Lichtman: Cellular and Molecular Immunology 5th Edition, 2005.

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.

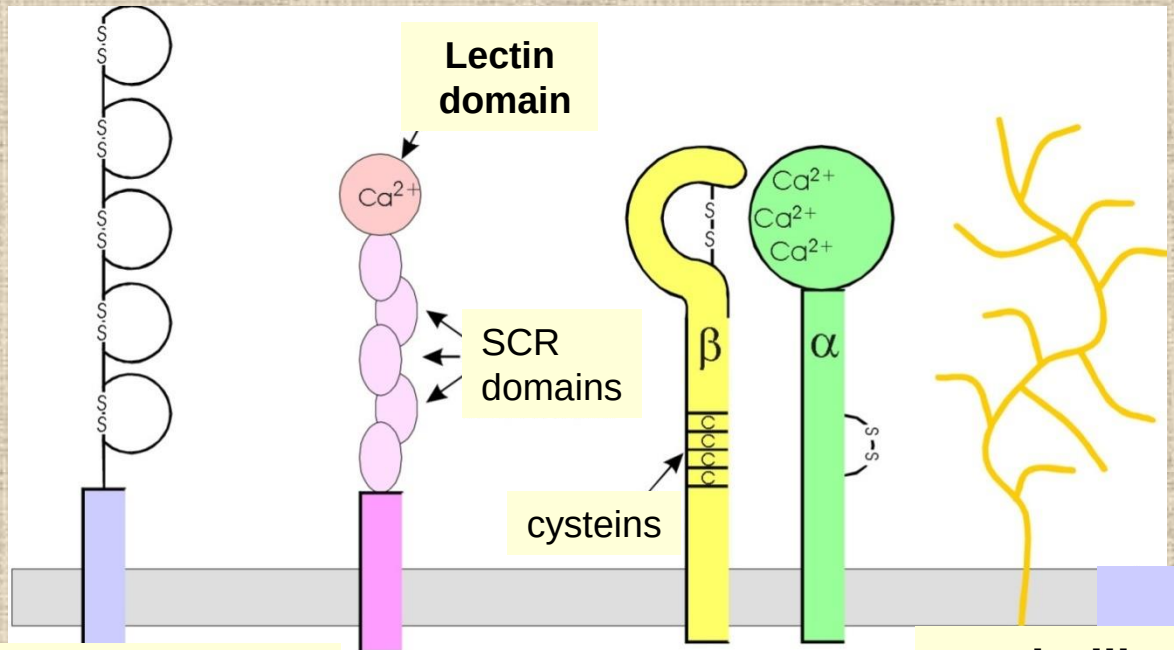
Vaccination and the role of adjuvants



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

- Different levels of the immune system
- Recognition molecules of the innate immunity
- Adhesion molecules, extravasation („homing”)

Families of adhesion molecules



Ig-superfamily members

Selectins

Integrins

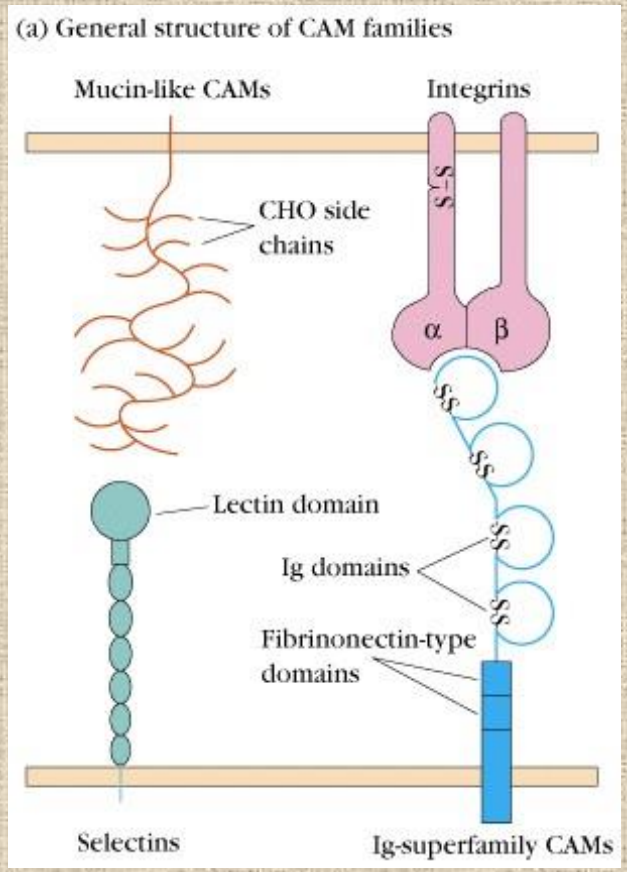
Mucin-like molecules

„other" accessory molecules

CD2 CD4 CD8 B7 CD28 CTLA 4 ICAM	L selectin E selectin P selectin	VLA LFA Mac1	„vascular addressins"

CD45
CD44
CD40, CD40L
CD19/CD21/CD81
CD22

Adhesion molecules build receptor – ligand interactions

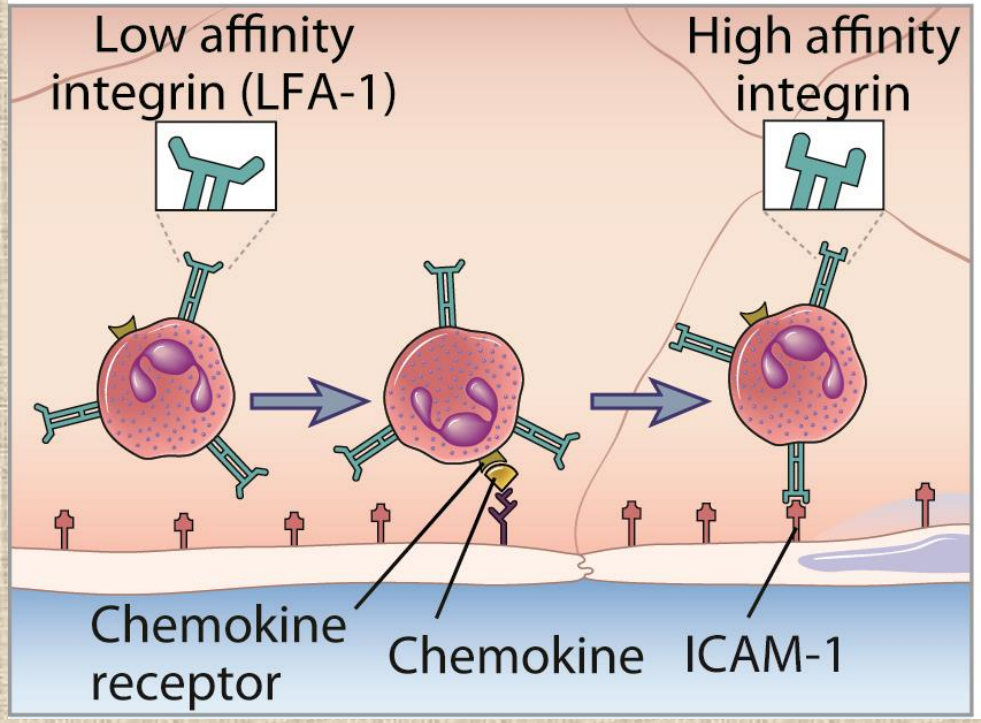


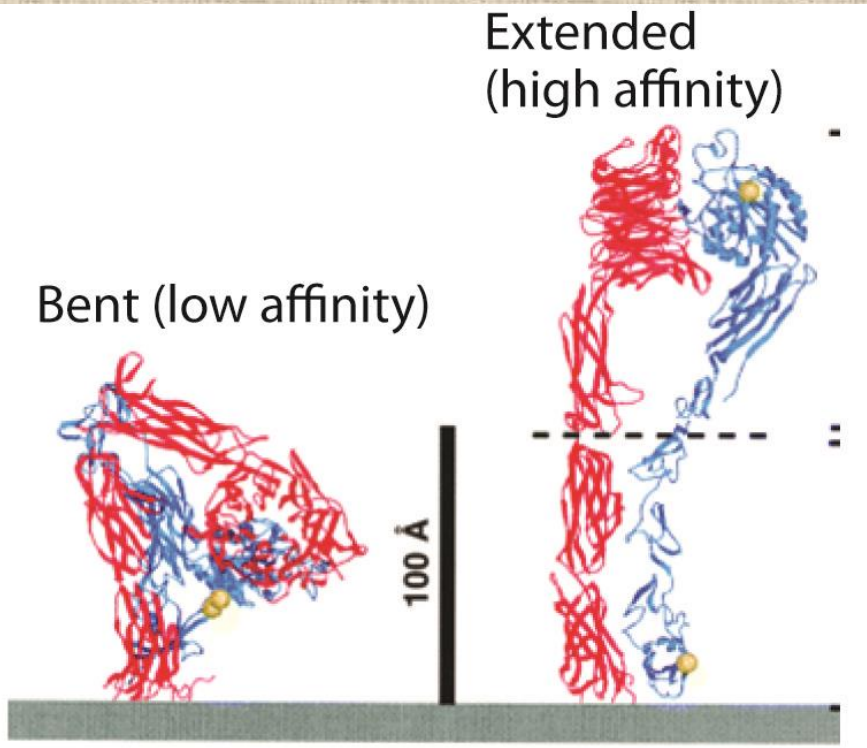
(b) Selected CAMs belonging to each family

Mucin-like CAMs:		Selectins:
GlyCAM-1	⇄	L-selectin
CD34		P-selectin
PSGL-1		E-selectin
MAdCAM-1		

Ig-superfamily CAMs:		Integrins:
ICAM-1, -2, -3	⇄	α4β1 (VLA-4, LPAM-2)
VCAM-1		α4β7 (LPAM-1)
LFA-2 (CD2)		α6β1 (VLA-6)
LFA-3 (CD58)		αLβ2 (LFA-1)
MAdCAM-1		αMβ2 (Mac-1)
		αXβ2 (CR4, p150/95)

Chemokines accelerate conformational changes in integrins





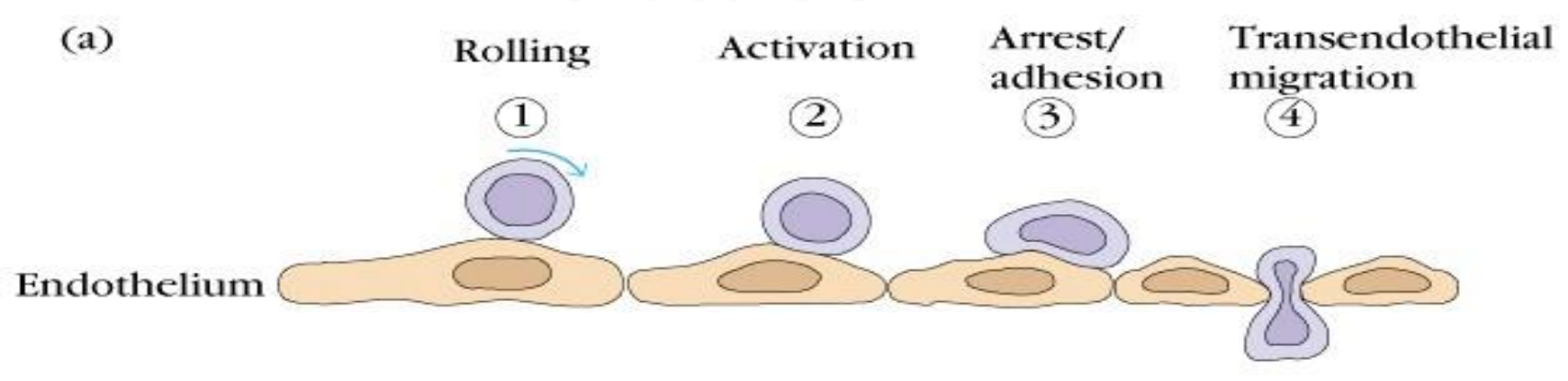
Leukocyte functional antigen 1 (LFA-1)

↕

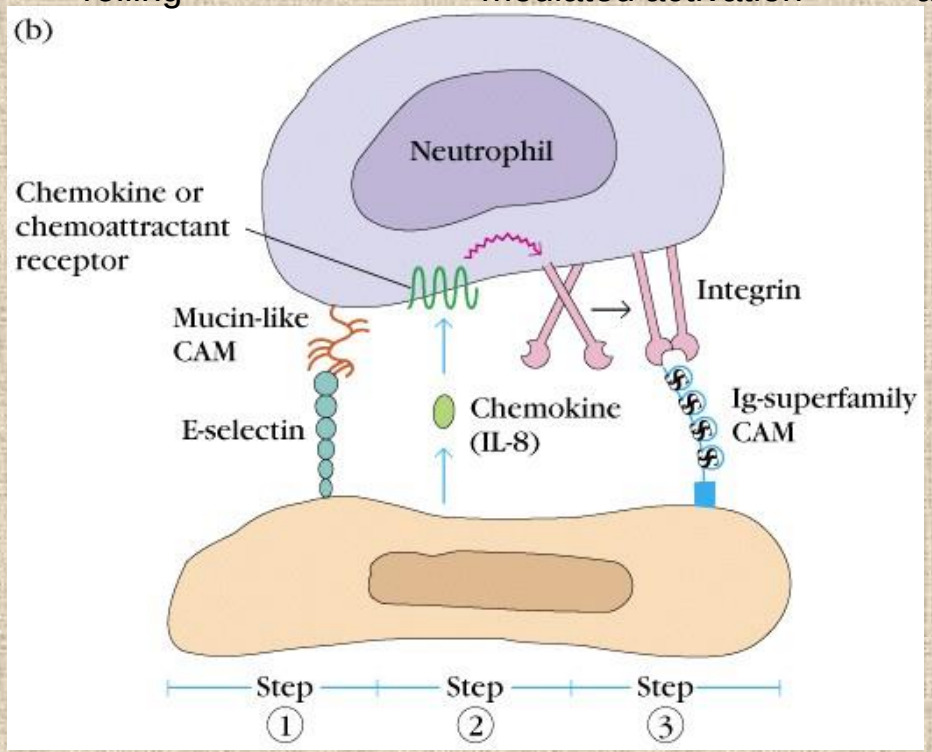
Intercellular adhesion molecule 1 (ICAM-1)

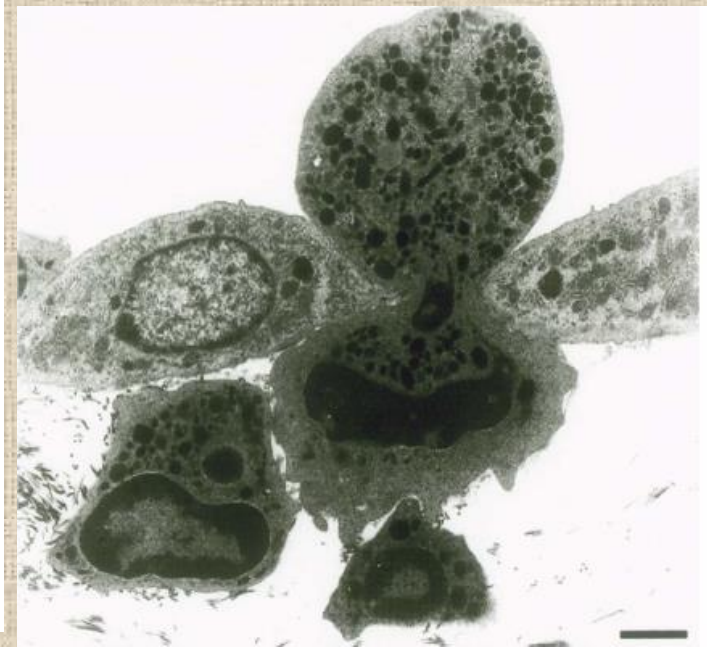
Abbas, Lichtman, Pillai: Cellular and Molecular Immunology 7th Edition, 2012.

Neutrophils extravasation through the inflamed endothels



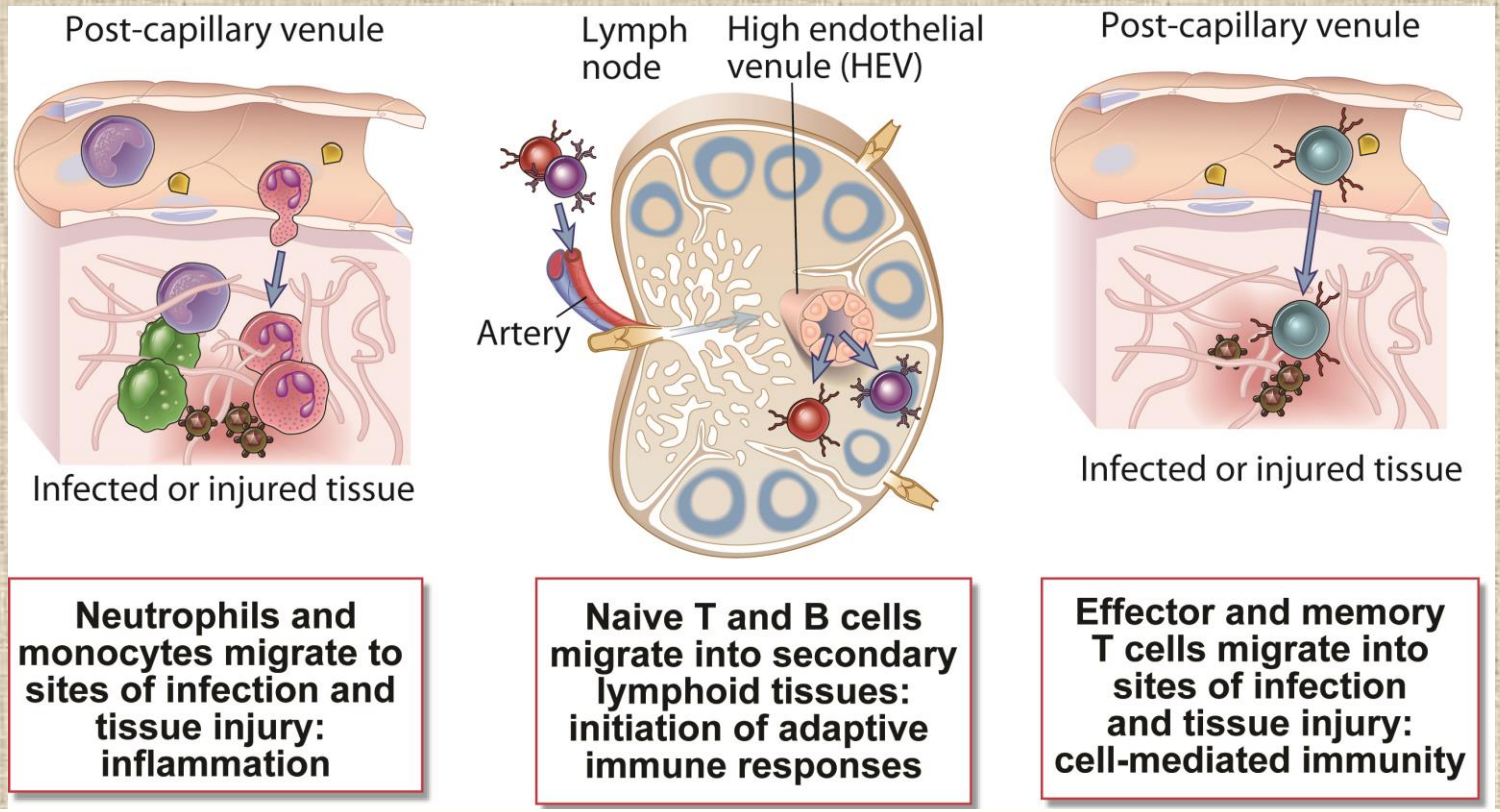
1. Selectin-mediated rolling
2. Chemoattractant mediated activation
3. Integrin-mediated adhesion
4. Transendothelial migration





Goldsby RA, Kindt TJ, Osborne BA: Kuby Immunology 4th Edition, 2000.

Lymphocyte recirculation: continous migration of cells from the blood and lymph into the lymphoid and inflamed tissues = HOMING



Role:

- Promotes the encounter with antigen
-Promotes the initiation of inflammatory response

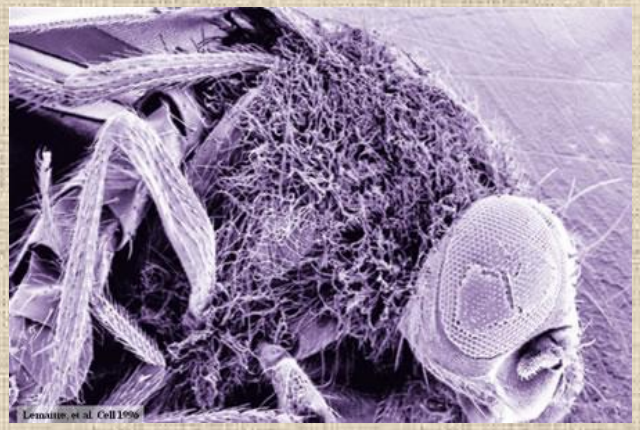
Mechanisms:

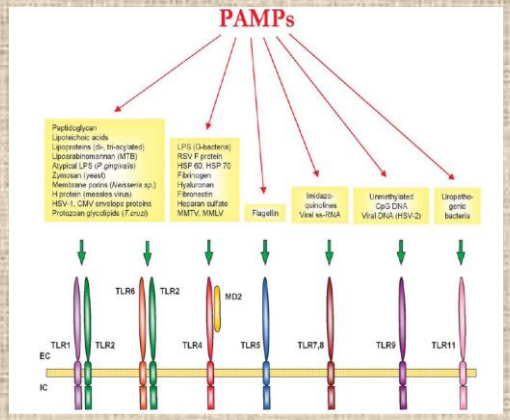
-Extravasation: adhesion then transmigration of leukocytes through the endothel from the bloodgflow into the tissue.

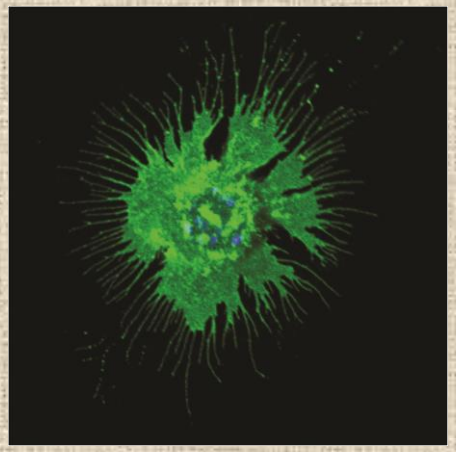
All lymphocyte circulates approx. 1-2 times per day.

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

Nobel Laureates in 2011 for medicine and physiology

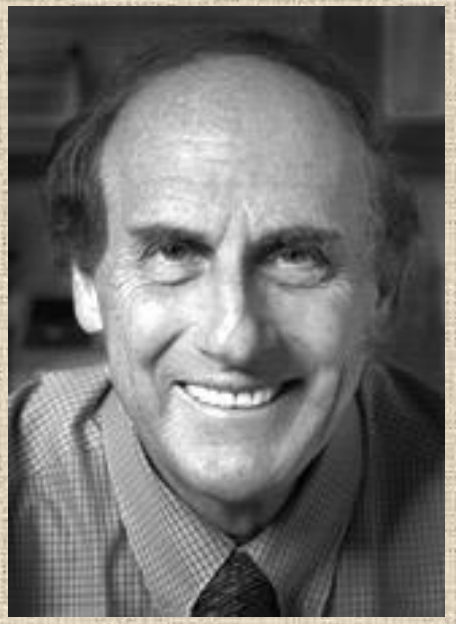






Jules A. Hoffmann

Bruce A. Beutler



Ralph M. Steinmann