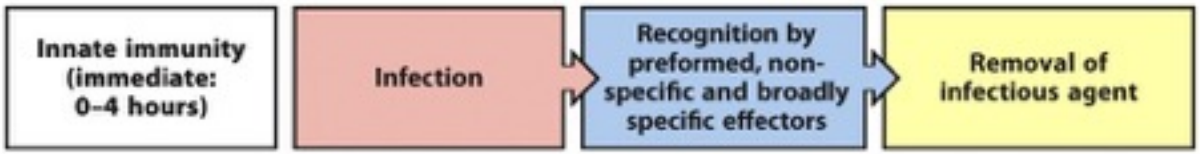
BMI296 - Aula 2

BMI296 - Aula



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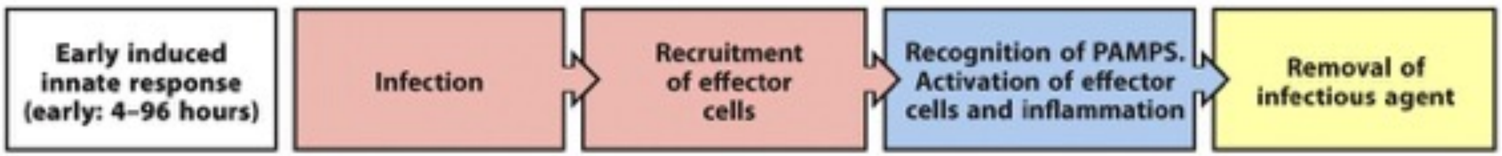

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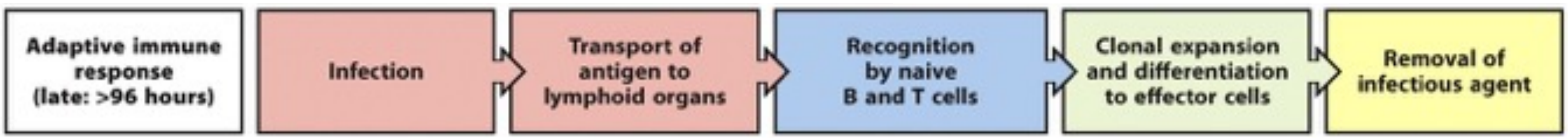

Figure 2.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

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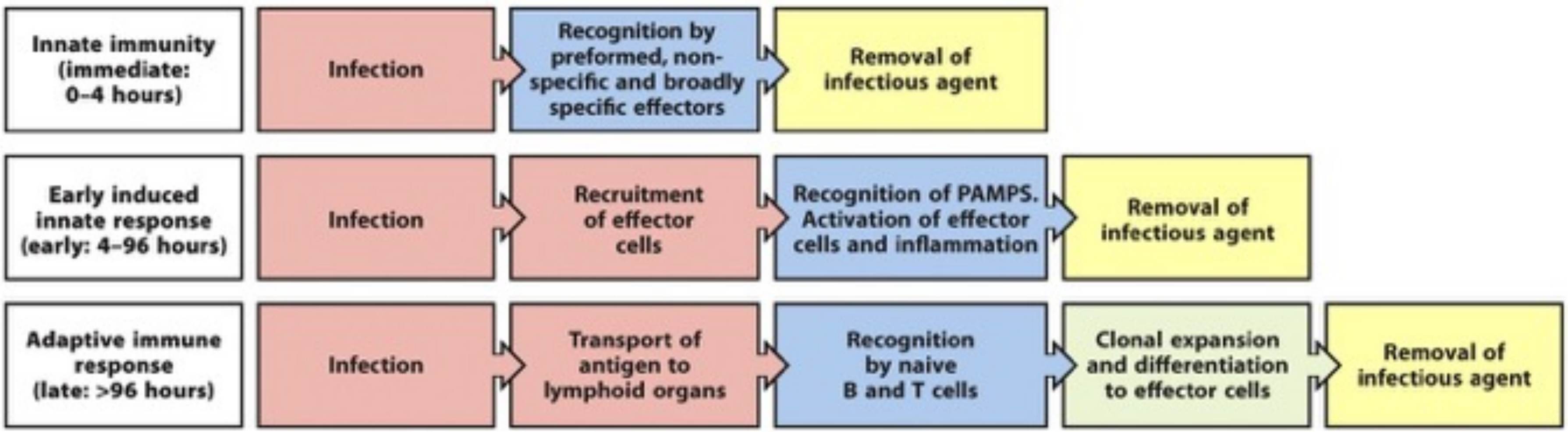

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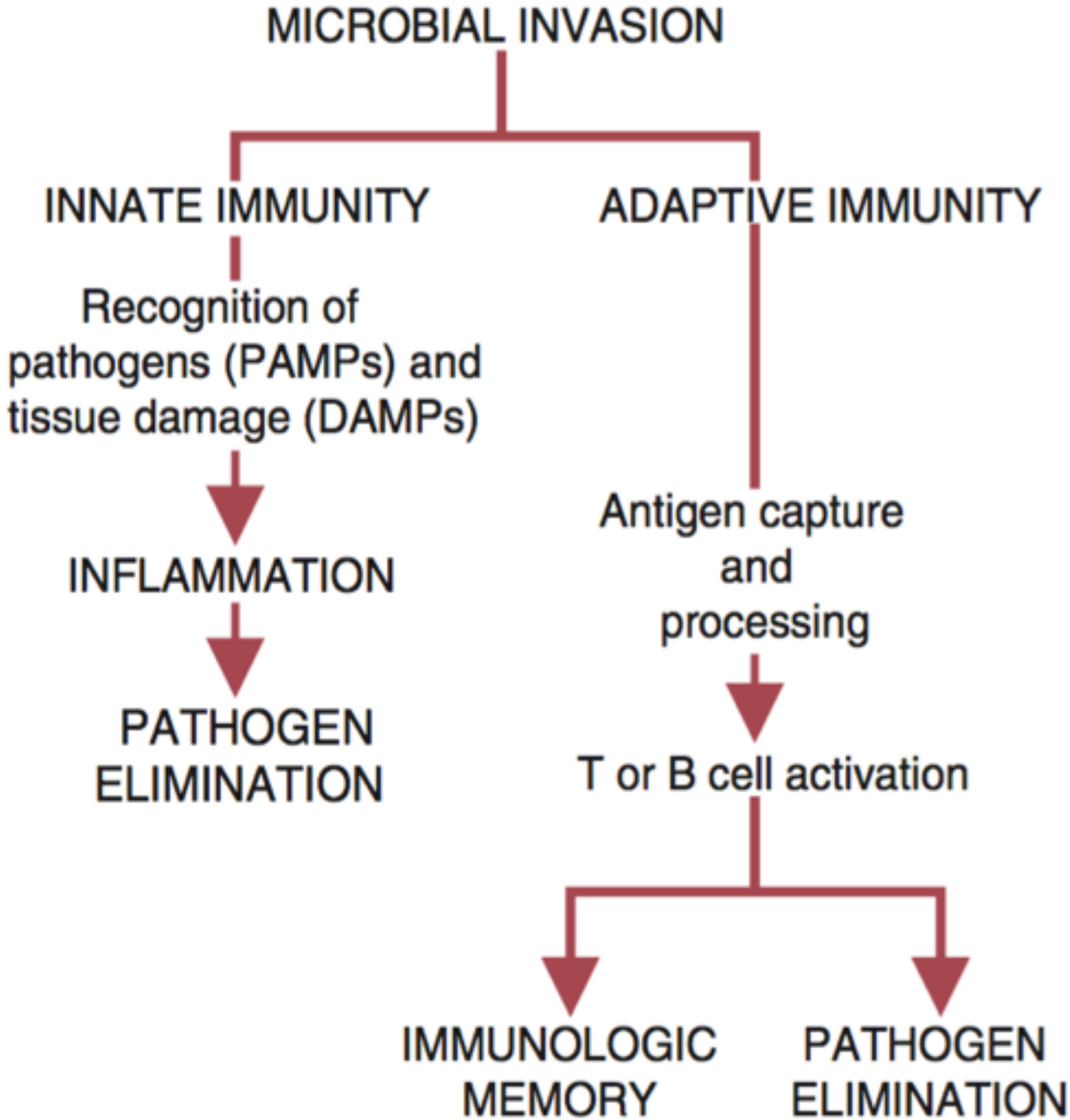
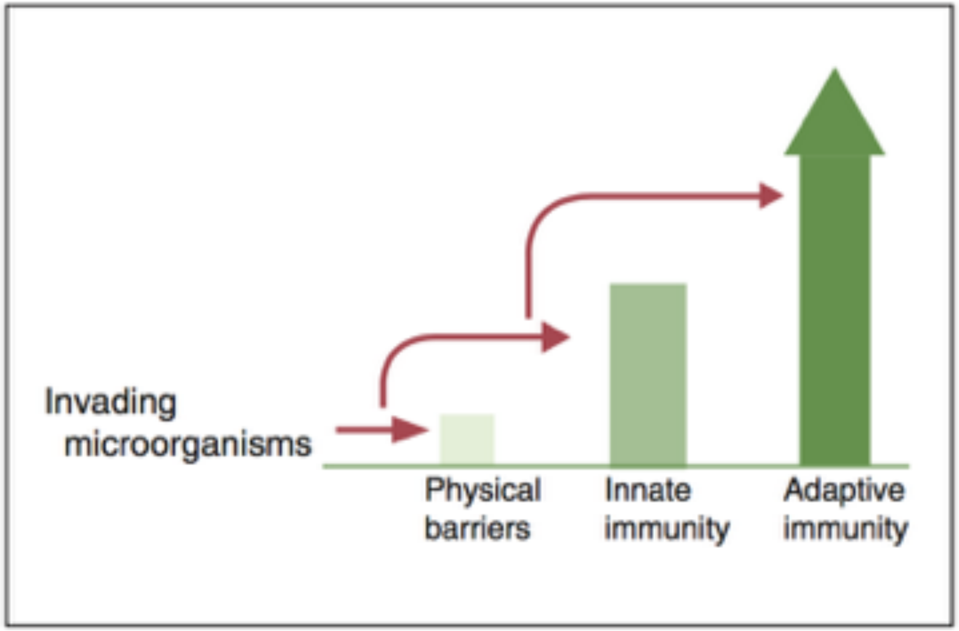
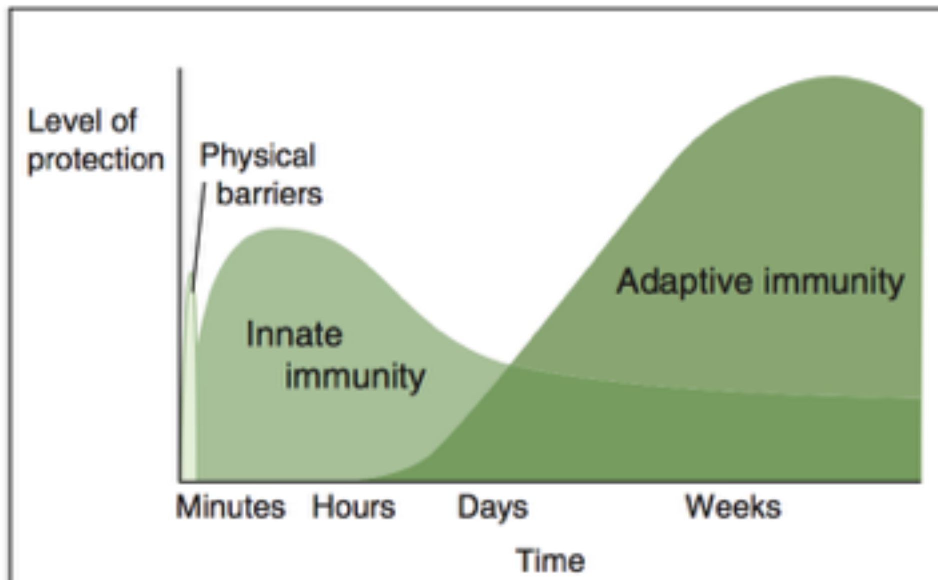
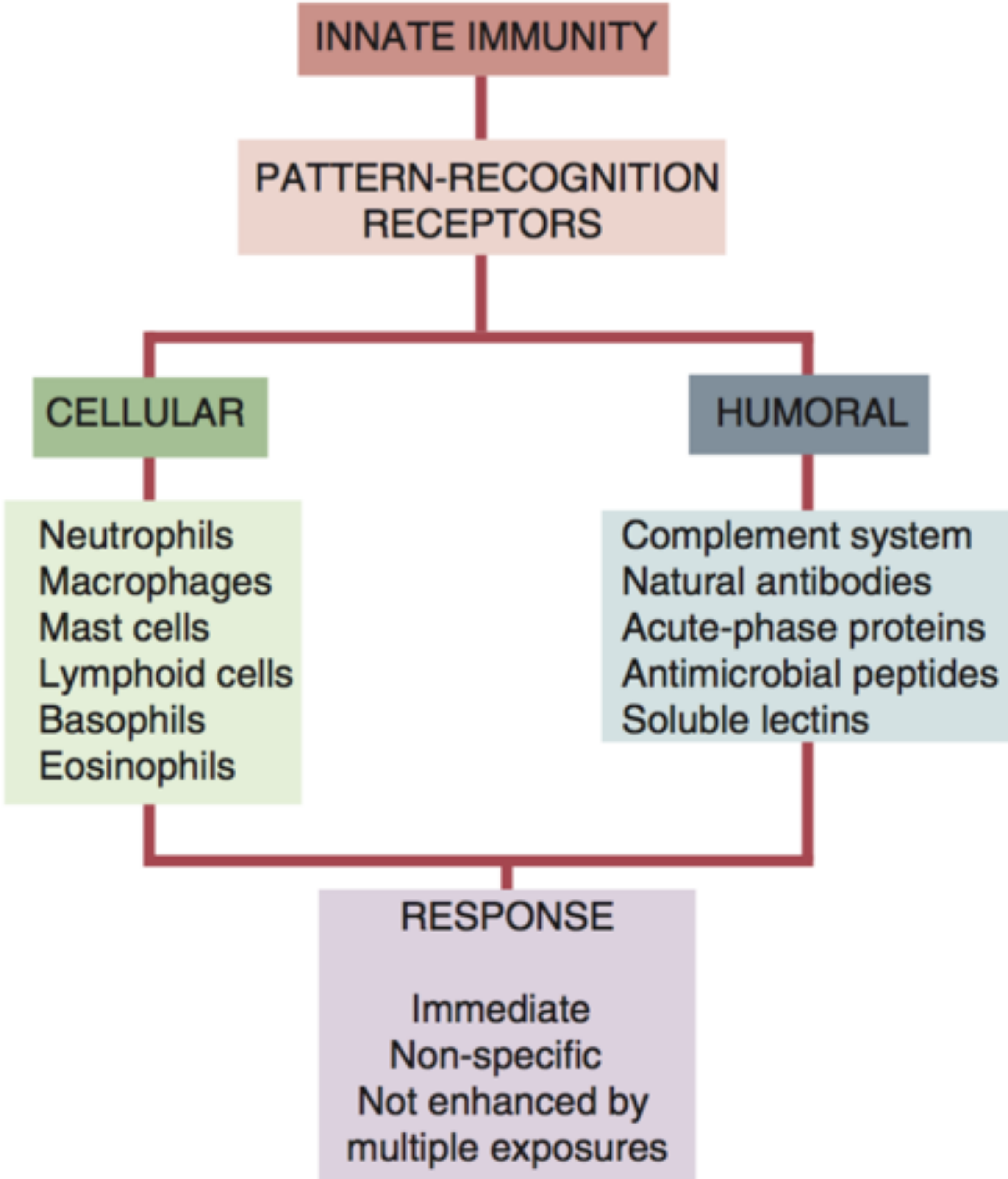

MICROBIAL INVASION
INNATE IMMUNITY
ADAPTIVE IMMUNITY
Recognition of pathogens (PAMPs) and tissue damage (DAMPs)
INFLAMMATION
PATHOGEN ELIMINATION
Antigen capture and processing
T or B cell activation
IMMUNOLOGIC MEMORY
PATHOGEN ELIMINATION


Invading
microorganisms
Physical
barriers
Innate
immunity
Adaptive
immunity


Level of
protection
Physical
barriers
Innate
immunity
Adaptive immunity
Minutes
Hours
Days
Weeks
Time


INNATE IMMUNITY
PATTERN-RECOGNITION RECEPTORS
CELLULAR
HUMORAL
Neutrophils
Macrophages
Mast cells
Lymphoid cells
Basophils
Eosinophils
Complement system
Natural antibodies
Acute-phase proteins
Antimicrobial peptides
Soluble lectins
RESPONSE
Immediate
Non-specific
Not enhanced by
multiple exposures

Routes of infection for pathogens				
Route of entry	**Mode of transmission**	**Pathogen**	**Disease**	**Type of pathogen**
Mucosal surfaces				
Mouth and respiratory tract	Inhalation or ingestion of infective material (e.g. saliva droplets)	Measles virus	Measles	Paramyxovirus
		Influenza virus	Influenza	Orthomyxovirus
		Varicella-zoster	Chickenpox	Herpesvirus
		Epstein-Barr virus	Mononucleosis	Herpesvirus
		Streptococcus pyogenes	Tonsilitis	Gram-positive bacterium
		Haemophilus influenzae	Pneumonia, meningitis	Gram-negative bacterium
	Spores	*Neisseria meningitidis*	Meningococcal meningitis	Gram-negative bacterium
		Bacillus anthracis	Inhalation anthrax	Gram-positive bacterium
Gastrointestinal tract	Contaminated water or food	Rotavirus	Diarrhea	Rotavirus
		Hepatitis A	Jaundice	Picornavirus
		Salmonella enteritidis, S. typhimurium	Food poisoning	Gram-negative bacterium
		Vibrio cholerae	Cholera	Gram-negative bacterium
		Salmonella typhi	Typhoid fever	Gram-negative bacterium
Reproductive tract and other routes	Sexual transmission/ infected blood	Hepatitis B virus	Hepatitis B	Hepadnavirus
		Human immunodeficiency virus (HIV)	Acquired immunodeficiency syndrome (AIDS)	Retrovirus
	Sexual transmission	*Neisseria gonorrhoeae*	Gonorrhea	Gram-negative bacterium
		Treponema pallidum	Syphilis	Bacterium (spirochete)
Opportunistic pathogens				
	Resident microbiota	*Candida albicans*	Candidiasis, thrush	Fungus
	Resident lung microbiota	*Pneumocystis jirovecii*	Pneumonia	Fungus
External epithelia				
External surface	Physical contact	*Trichophyton*	Athlete's foot	Fungus
Wounds and abrasions	Minor skin abrasions	*Bacillus anthracis*	Cutaneous anthrax	Gram-positive bacterium
	Puncture wounds	*Clostridium tetani*	Tetanus	Gram-positive bacterium
	Handling infected animals	*Francisella tularensis*	Tularemia	Gram-negative bacterium
Insect bites	Mosquito bites (*Aedes aegypti*)	Flavivirus	Yellow fever	Virus
	Deer tick bites	*Borrelia burgdorferi*	Lyme disease	Bacterium (spirochete)
	Mosquito bites (*Anopheles*)	*Plasmodium* spp.	Malaria	Protozoan

Figure 2.2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

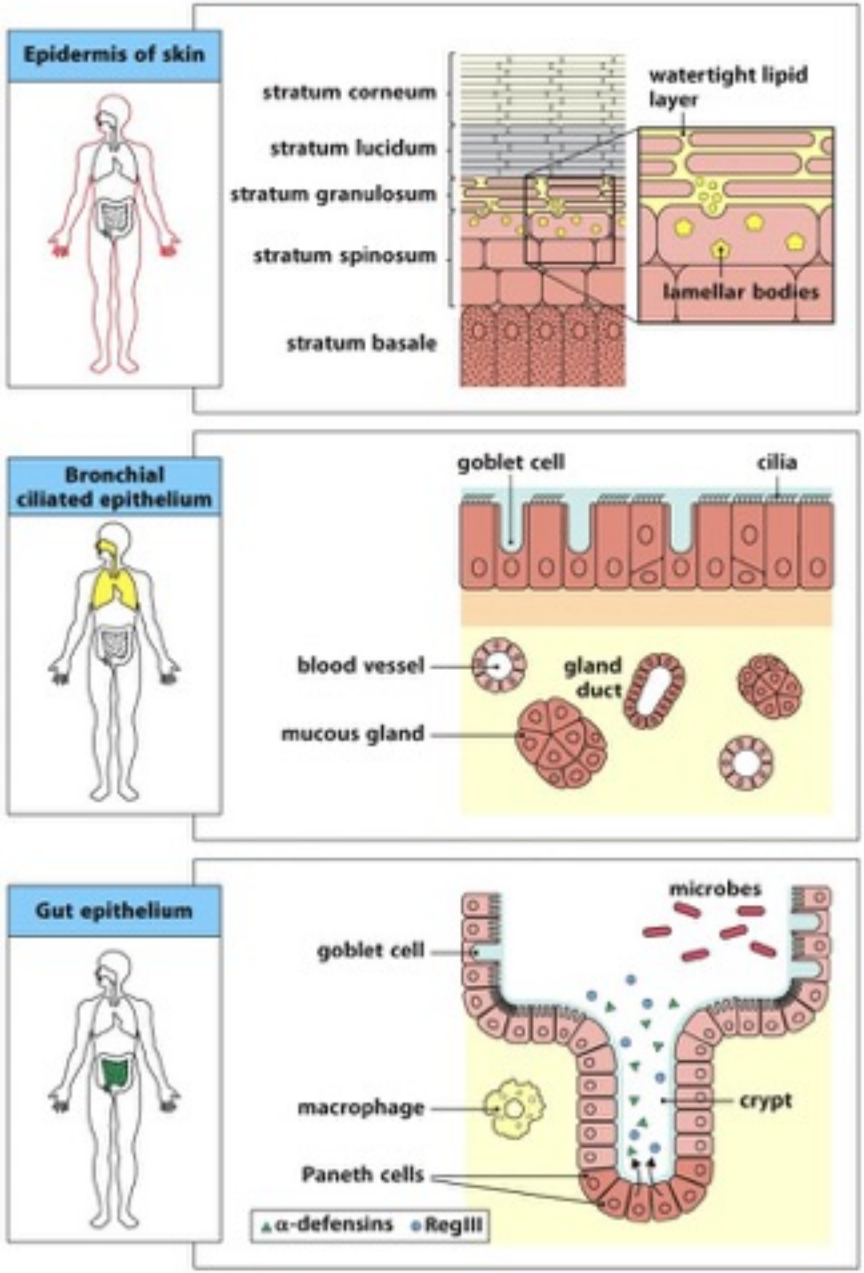


Figure 2.10 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

1.5 - 2 m^2

30 - 100 m^2

~ 1/2 quadra de tênis

30 - 40 m^2

~ studio

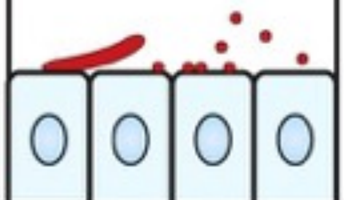
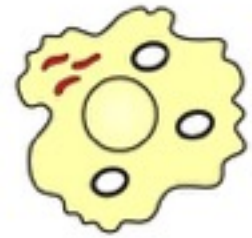
	Extracellular		Intracellular	
	Interstitial spaces, blood, lymph	**Epithelial surfaces**	**Cytoplasmic**	**Vesicular**
Site of infection				
Organisms	Viruses Bacteria Protozoa Fungi Worms	*Neisseria gonorrhoeae* *Streptococcus pneumoniae* *Vibrio cholerae* *Helicobacter pylori* *Candida albicans* Worms	Viruses *Chlamydia* spp. *Rickettsia* spp. Protozoa	*Mycobacterium* spp. *Yersinia pestis* *Legionella pneumophila* *Cryptococcus neoformans* *Leishmania* spp.
Protective immunity	Complement Phagocytosis Antibodies	Antimicrobial peptides Antibodies, especially IgA	NK cells Cytotoxic T cells	T-cell and NK-cell dependent macrophage activation

Figure 2.3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

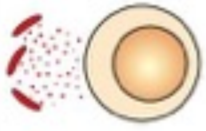
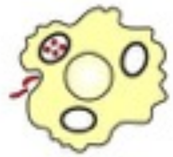
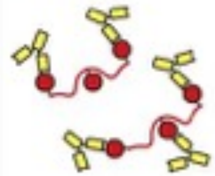
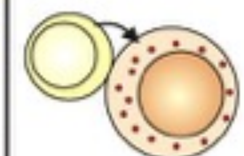
	Direct mechanisms of tissue damage by pathogens			Indirect mechanisms of tissue damage by pathogens		
	Exotoxin production	**Endotoxin**	**Direct cytopathic effect**	**Immune complexes**	**Anti-host antibody**	**Cell-mediated immunity**
Pathogenic mechanism						
Infectious agent	*Streptococcus pyogenes* *Staphylococcus aureus* *Corynebacterium diphtheriae* *Clostridium tetani* *Vibrio cholerae*	*Escherichia coli* *Haemophilus influenzae* *Salmonella typhi* *Shigella* *Pseudomonas aeruginosa* *Yersinia pestis*	Variola Varicella-zoster Hepatitis B virus Polio virus Measles virus Influenza virus Herpes simplex virus Human herpes virus 8 (HHV8)	Hepatitis B virus Malaria *Streptococcus pyogenes* *Treponema pallidum* Most acute infections	*Streptococcus pyogenes* *Mycoplasma pneumoniae*	Lymphocytic choriomeningitis virus Herpes simplex virus *Mycobacterium tuberculosis* *Mycobacterium leprae* *Borrelia burgdorferi* *Schistosoma mansoni*
Disease	Tonsilitis, scarlet fever Boils, toxic shock syndrome, food poisoning Diphtheria Tetanus Cholera	Gram-negative sepsis Meningitis, pneumonia Typhoid fever Bacillary dysentery Wound infection Plague	Smallpox Chickenpox, shingles Hepatitis Poliomyelitis Measles,subacute sclerosing panencephalitis Influenza Cold sores Kaposi's sarcoma	Kidney disease Vascular deposits Glomerulonephritis Kidney damage in secondary syphilis Transient renal deposits	Rheumatic fever Hemolytic anemia	Aseptic meningitis Herpes stromal keratitis Tuberculosis Tuberculoid leprosy Lyme arthritis Schistosomiasis

Figure 2.4 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Barreiras não-imunológicas

	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			

Figure 2.6 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

conceito importante!

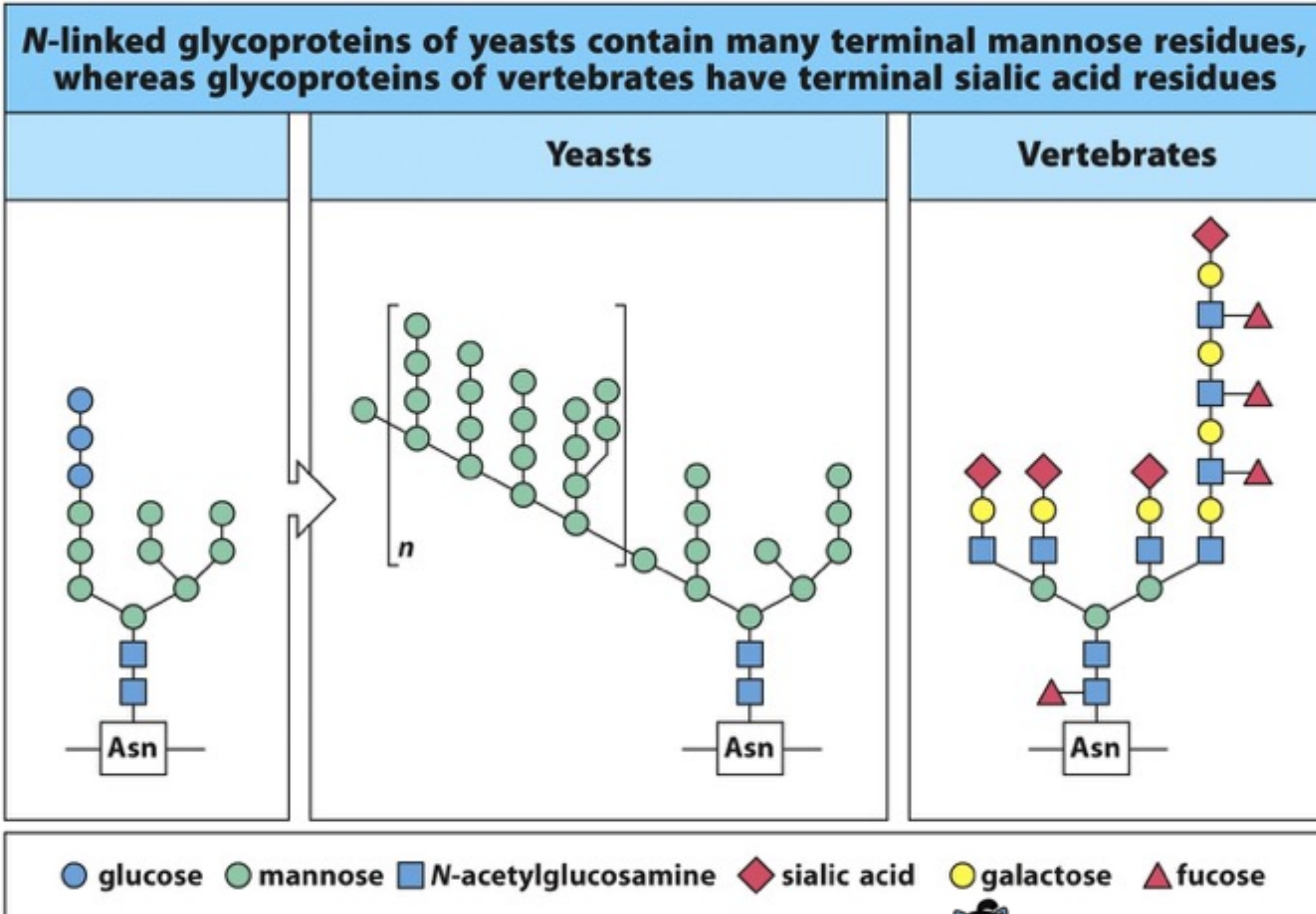


Figure 2.14 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

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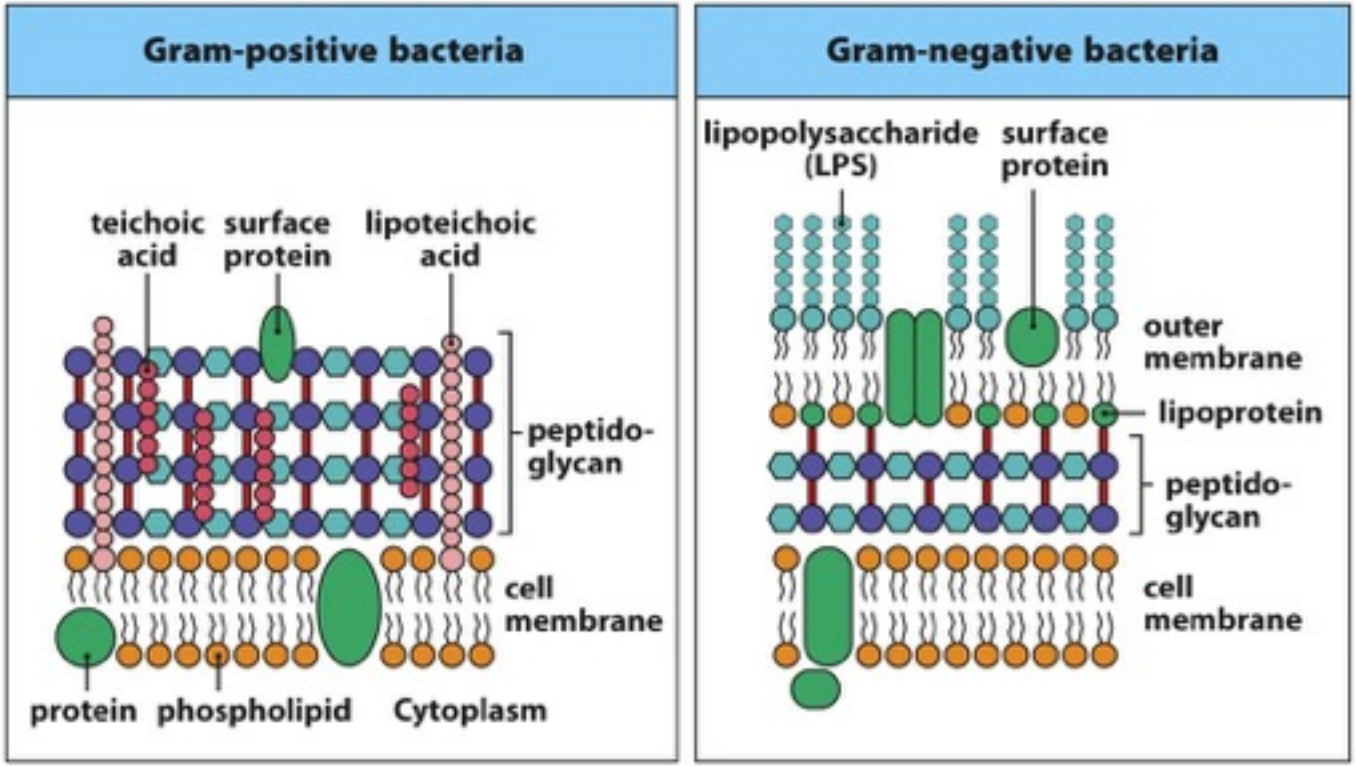

PAMPS

conceito importante!

Receptor characteristic	Innate immunity	Adaptive immunity
Specificity inherited in the genome	Yes	No
Expressed by all cells of a particular type (e.g. macrophages)	Yes	No
Triggers immediate response	Yes	No
Recognizes broad classes of pathogens	Yes	No
Interacts with a range of molecular structures of a given type	Yes	No
Encoded in multiple gene segments	No	Yes
Requires gene rearrangement	No	Yes
Clonal distribution	No	Yes
Able to discriminate between even closely related molecular structures	No	Yes

Figure 3.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

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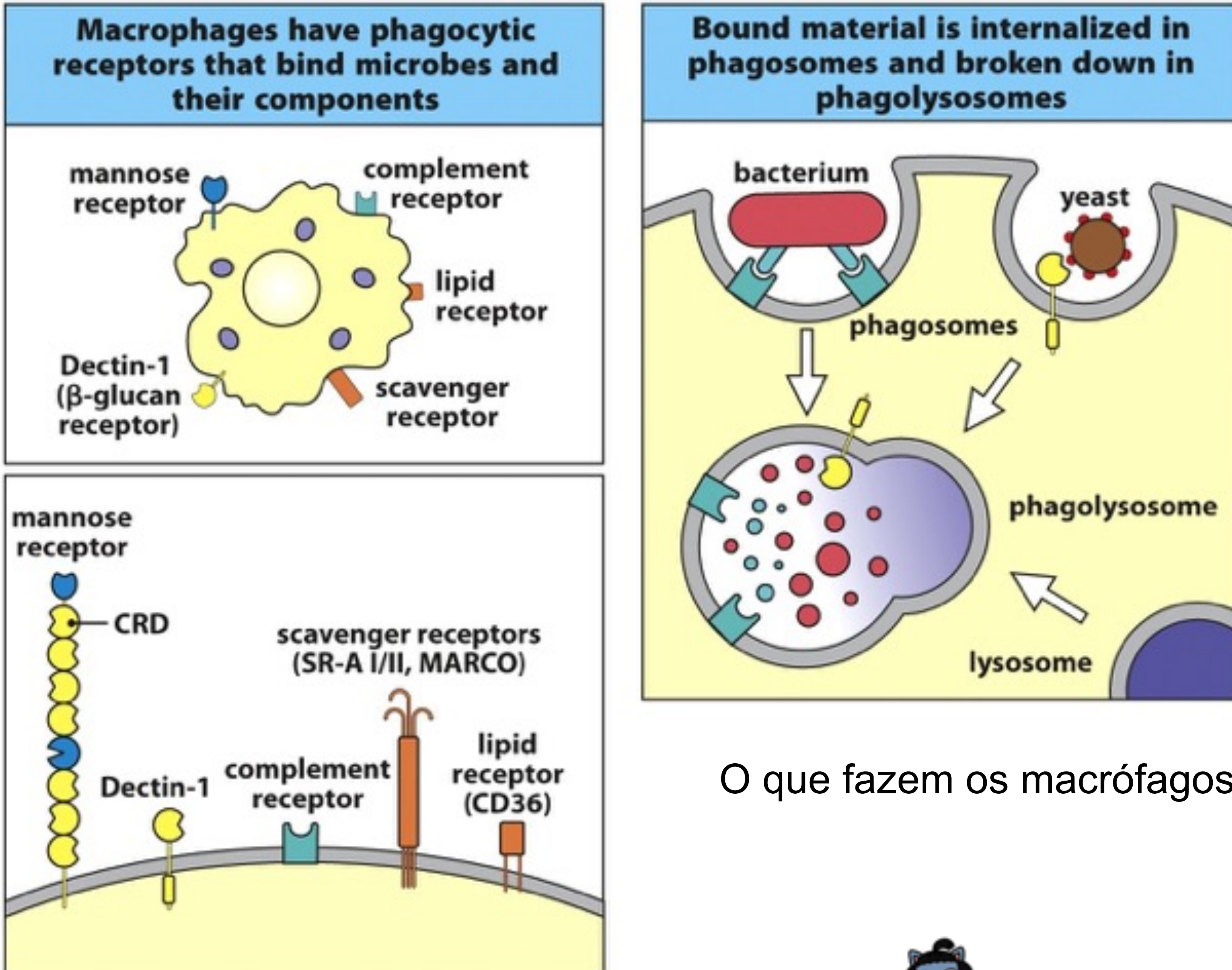


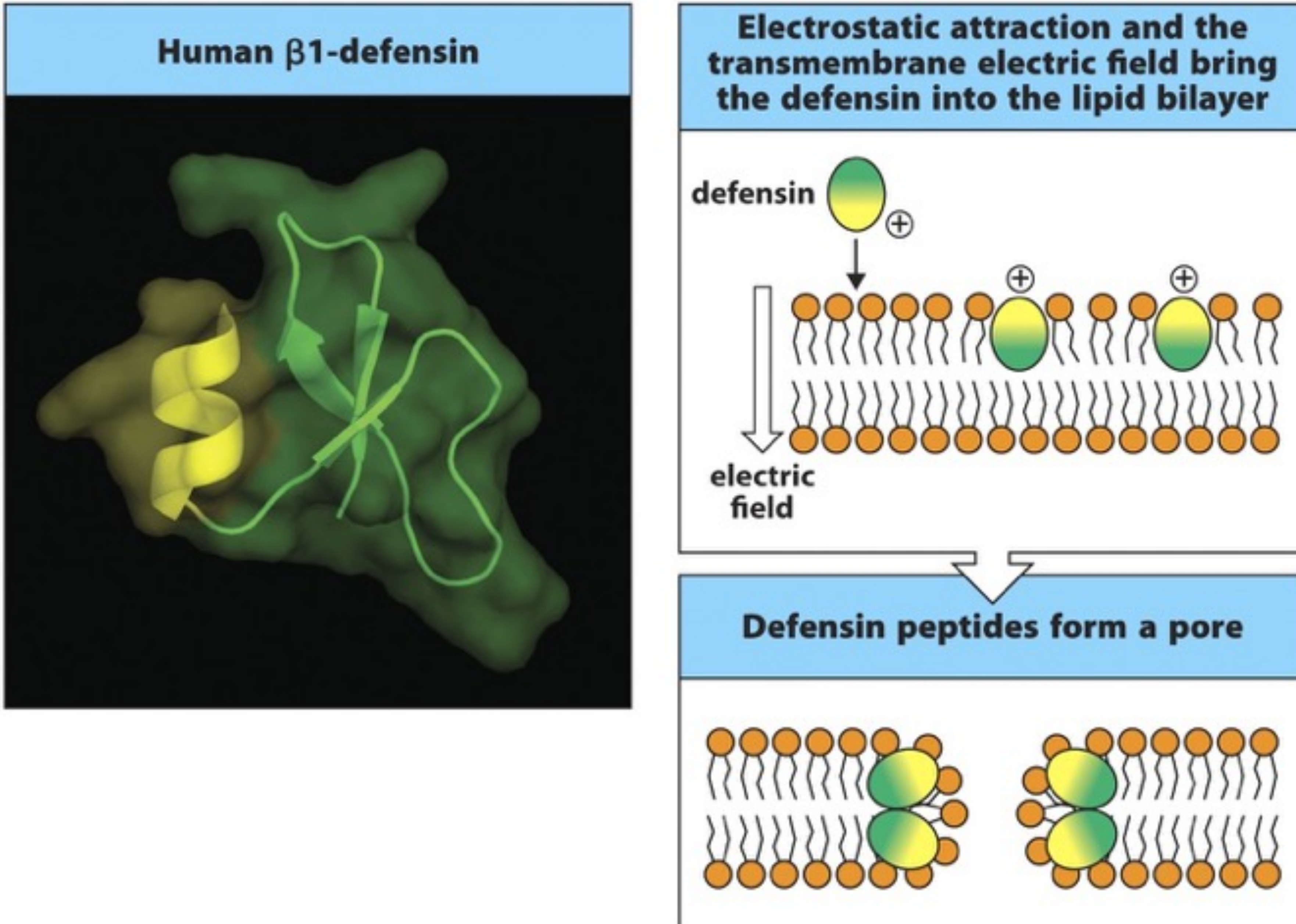
Figure 3.2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

O que fazem os macrófagos?

conceito importante!

Antimicrobial mechanisms of phagocytes		
Class of mechanism	**Macrophage products**	**Neutrophil products**
Acidification	pH=~3.5–4.0, bacteriostatic or bactericidal	
Toxic oxygen-derived products	Superoxide O_2^-, hydrogen peroxide H_2O_2, singlet oxygen $^1O_2^{\cdot}$, hydroxyl radical $^{\cdot}OH$, hypohalite OCl^-	
Toxic nitrogen oxides	Nitric oxide NO	
Antimicrobial peptides	Cathelicidin, macrophage elastase-derived peptide	α-Defensins (HNP1–4), β-defensin HBD4, cathelicidin, azurocidin, bacterial permeability inducing protein (BPI), lactoferricin
Enzymes	Lysozyme: digests cell walls of some Gram-positive bacteria Acid hydrolases (e.g. elastase and other proteases): break down ingested microbes	
Competitors		Lactoferrin (sequesters Fe^{2+}), vitamin B_{12}-binding protein

Figure 3.4 Janeway's Immunobiology, 8ed. (© Garland Science 2012)



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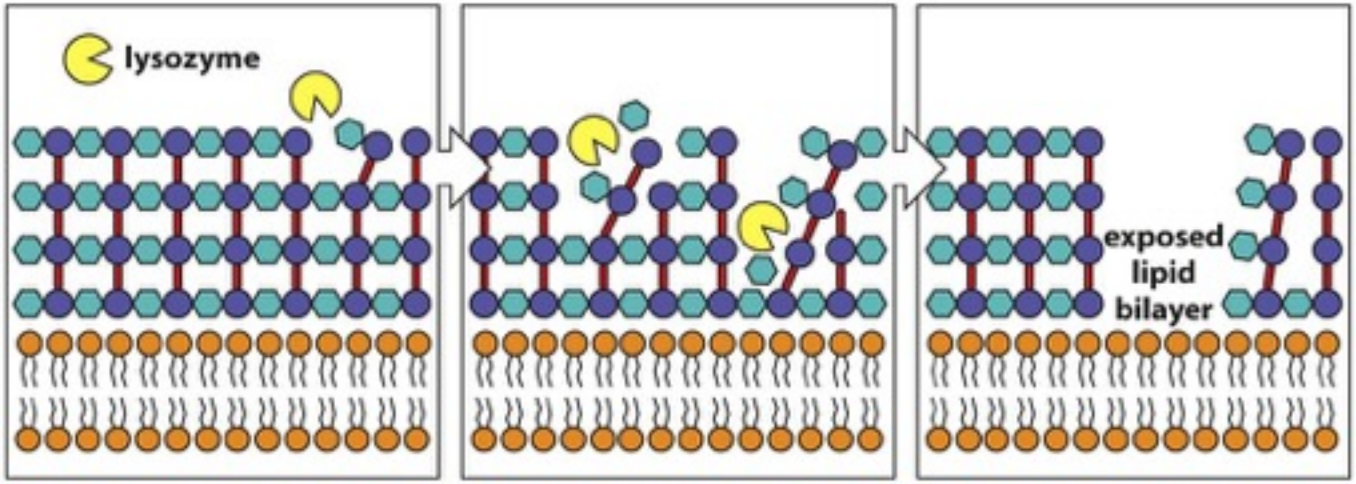


Figure 2.7 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Atenção aos Macrófagos: diferentes nomes em diferentes tecidos

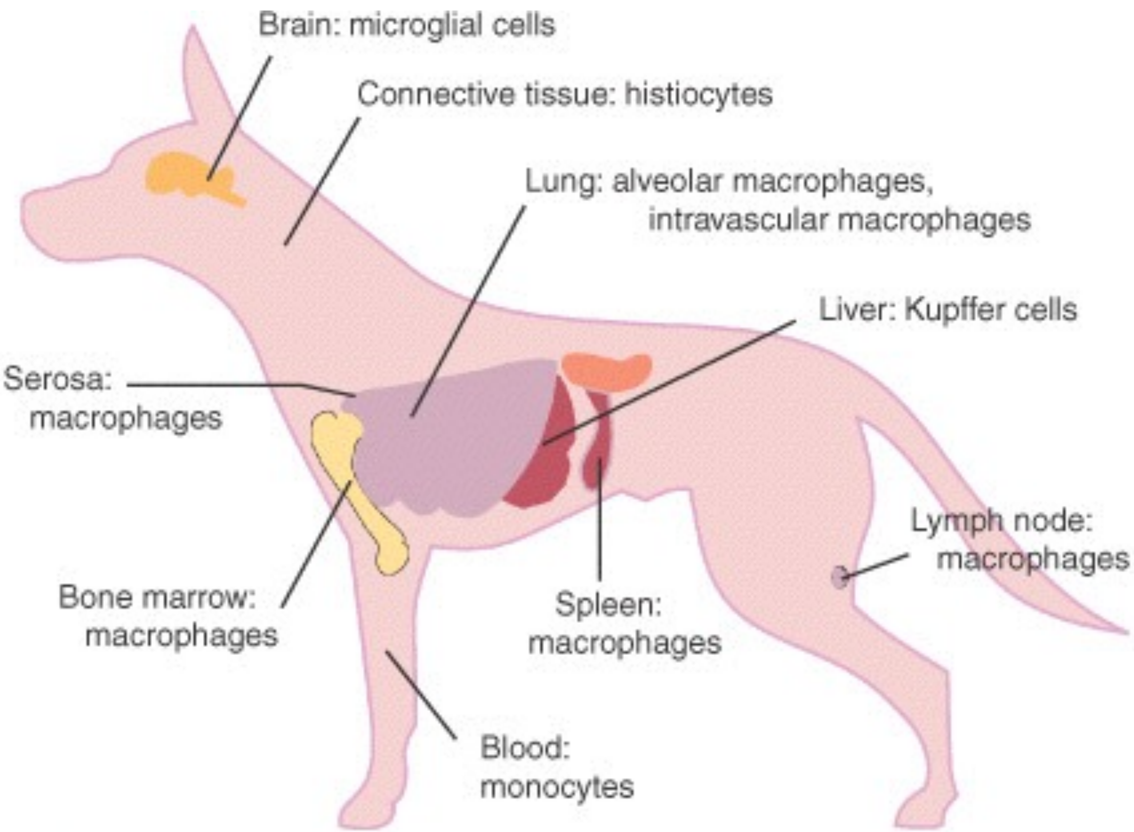


FIGURE 2-5 The location of the cells of the mononuclear phagocyte system.

O que fazem os neutrófilos?

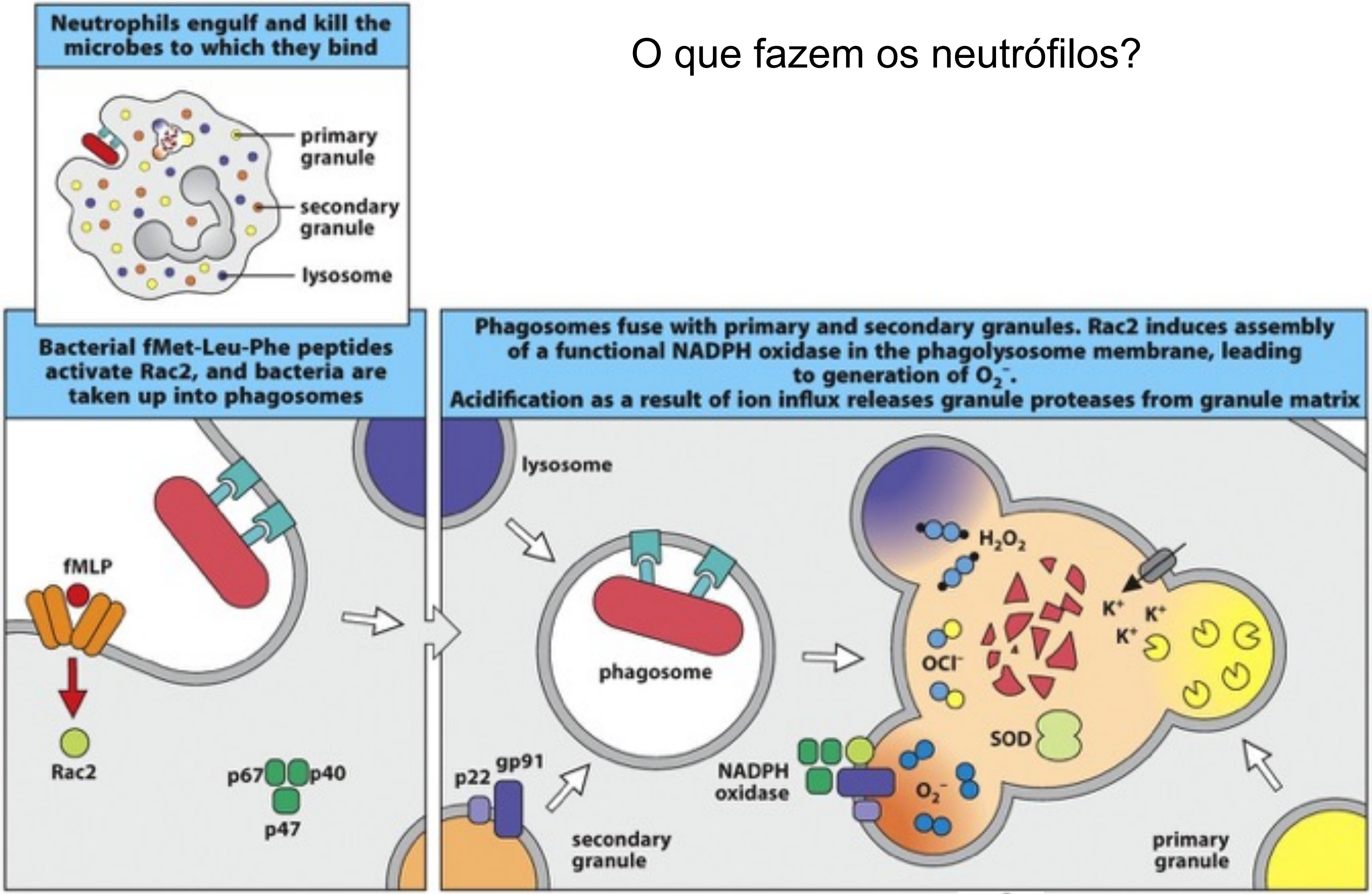
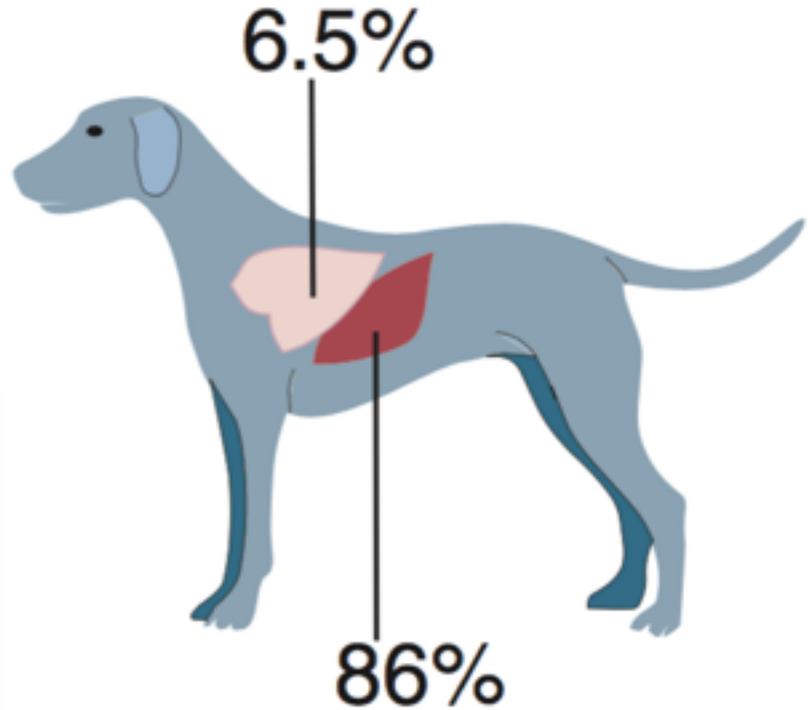


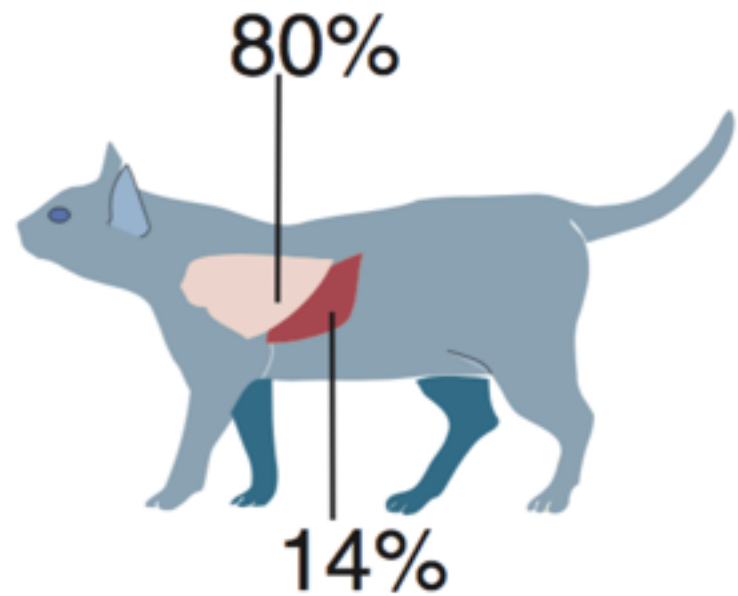
Figure 3.5 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

conceito importante!

TABLE 6.1 Sites of Clearance of Particles From the Blood in Domestic Mammals

	LOCALIZATION (%)	
Species	**Lung**	**Liver/Spleen**
Calf	93	6
Sheep	94	6
Dog	6.5	80
Cat	86	14
Rabbit	0.6	83
Guinea pig	1.5	82
Rat	0.5	97
Mouse	1.0	94





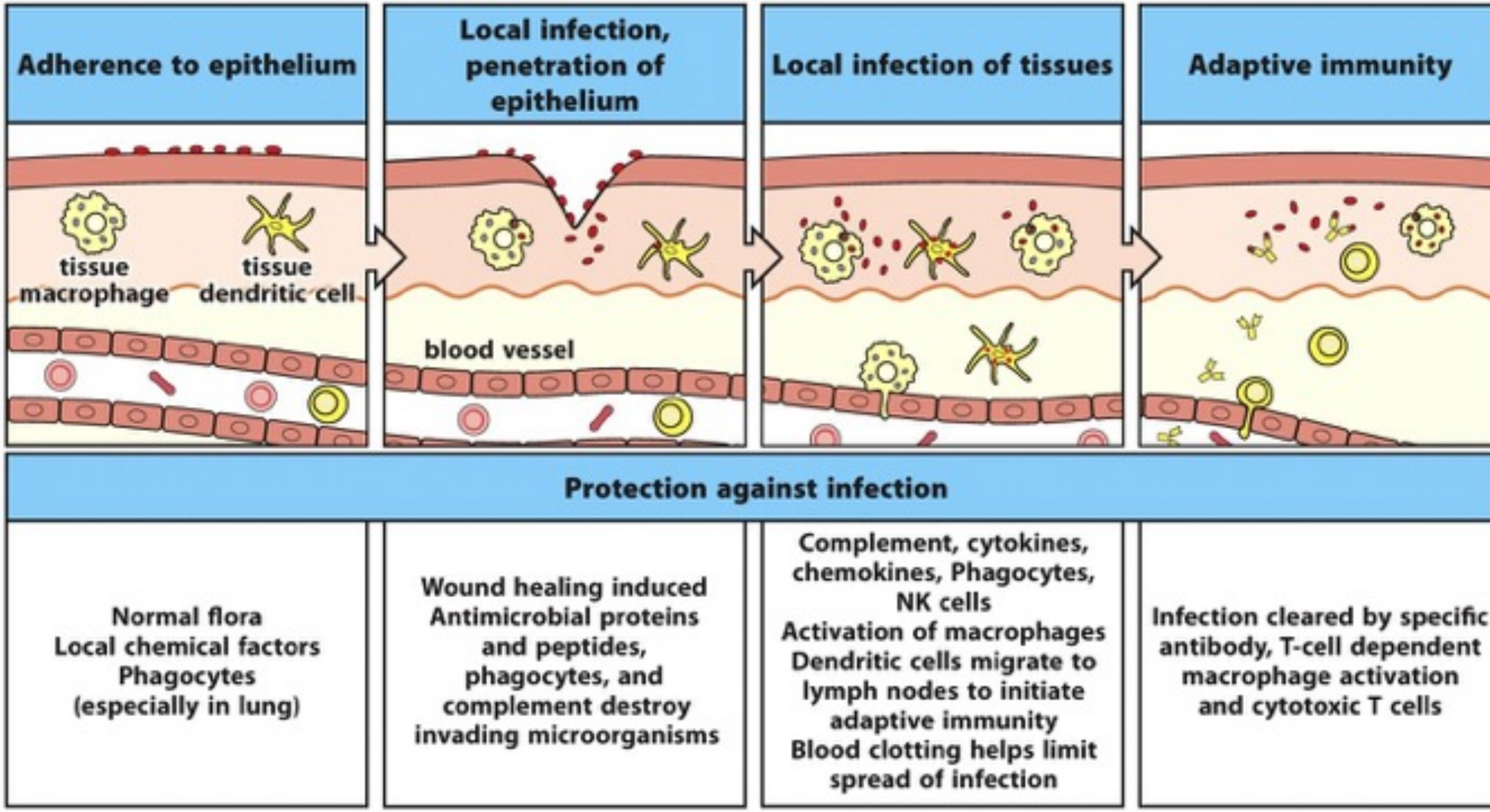


Figure 2.5 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

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Como os leucócitos chegam na lesão?

QUIMIOTAXIA

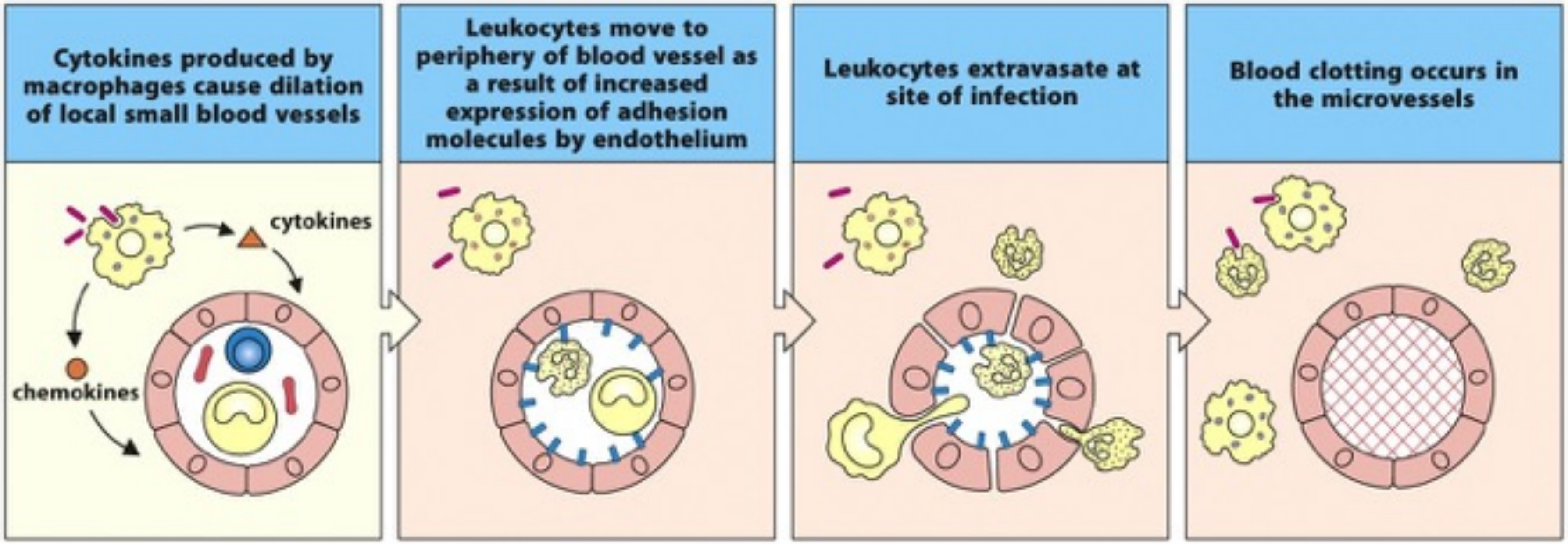

Figure 3.6 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

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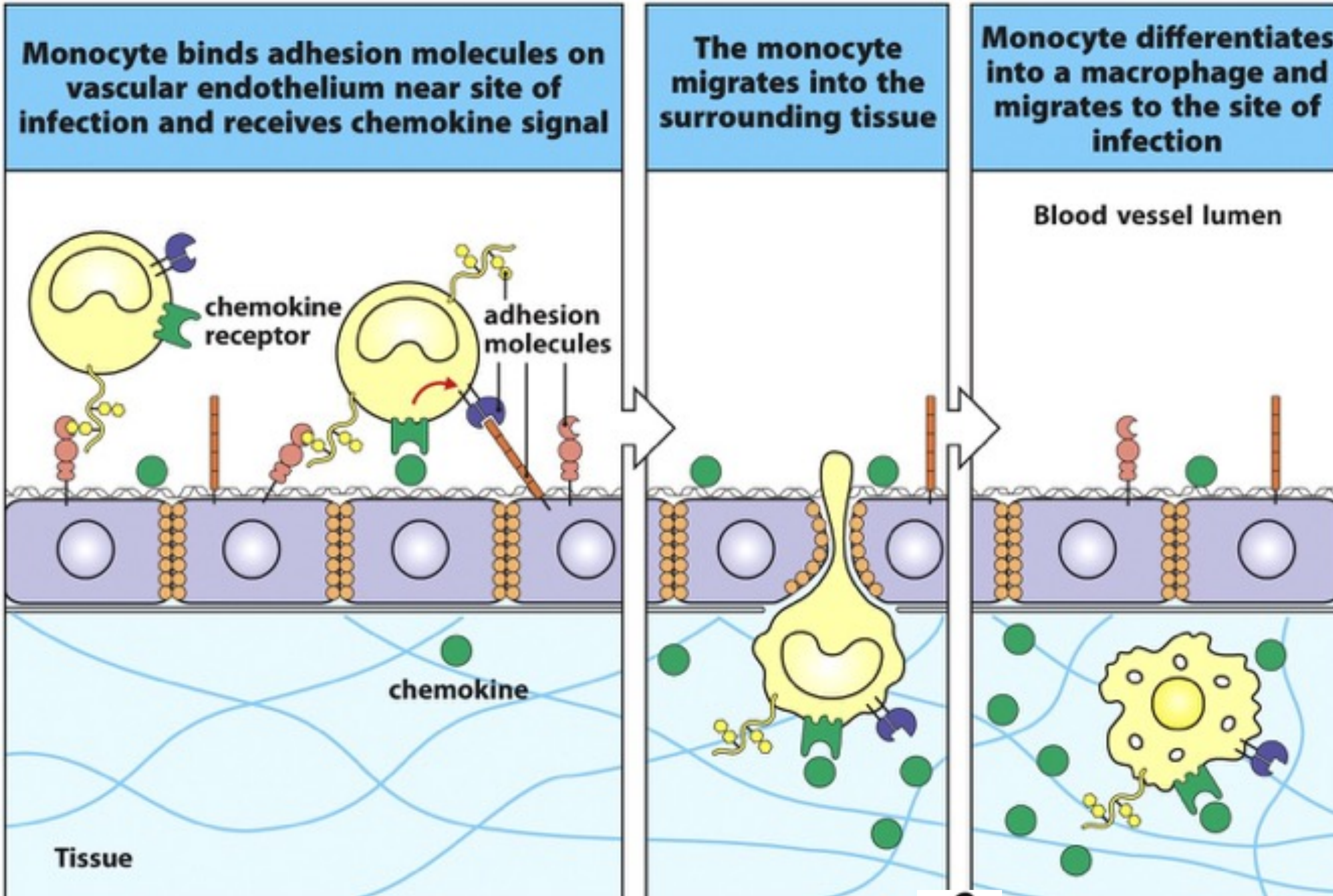

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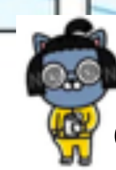

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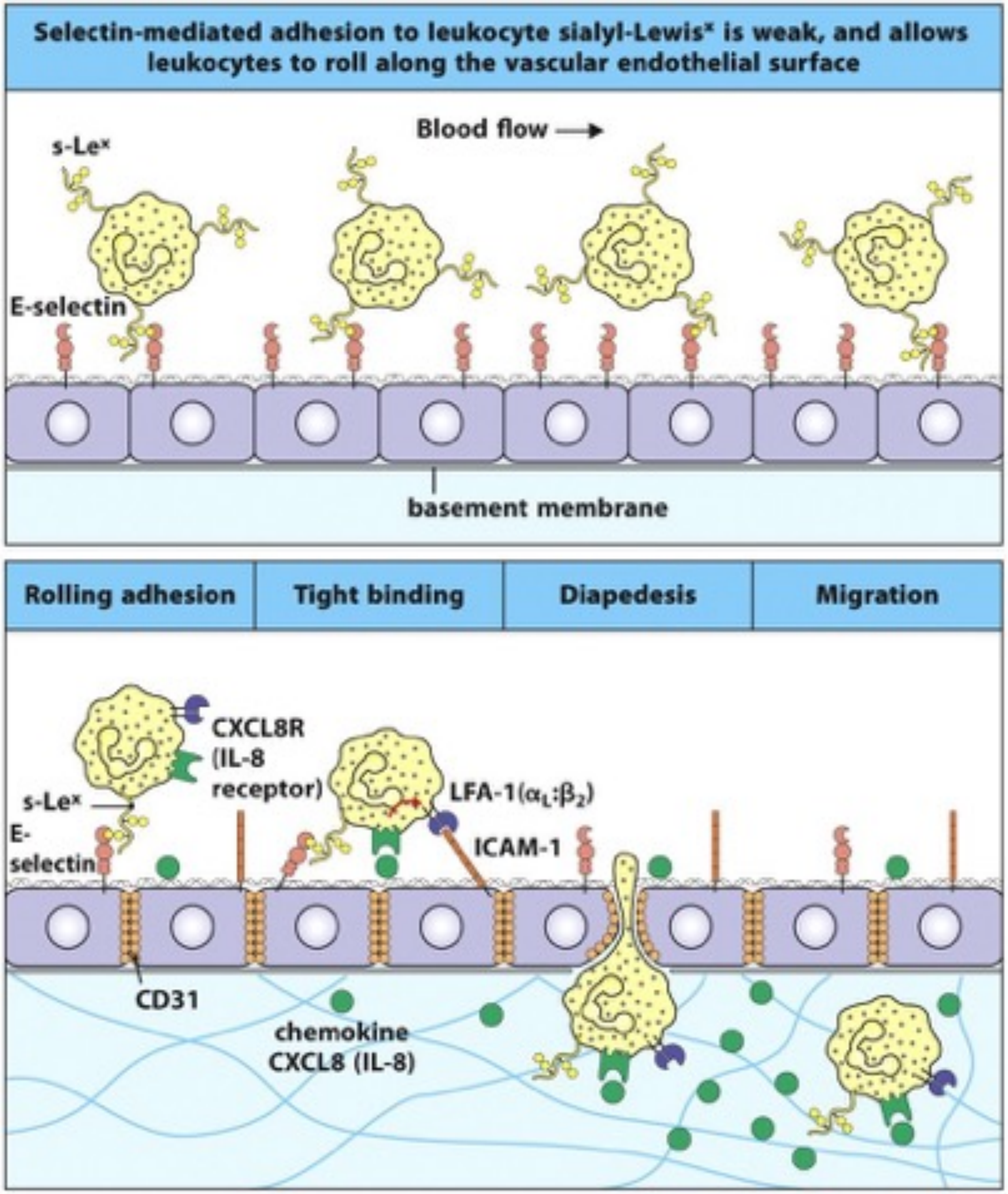


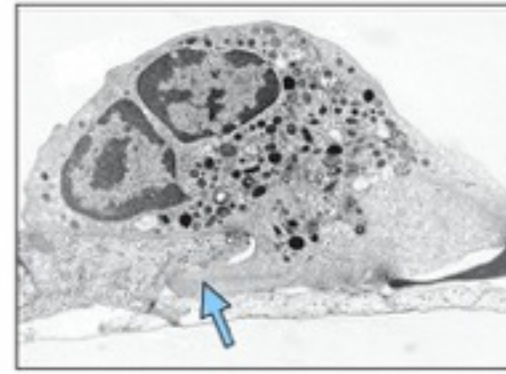


Figure 3.25 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Class	Chemokine	Produced by	Receptors	Cells attracted	Major effects
CXC	CXCL8 (IL-8)	Monocytes Macrophages Fibroblasts Epithelial cells Endothelial cells	CXCR1 CXCR2	Neutrophils Naive T cells	Mobilizes, activates and degranulates neutrophils Angiogenesis
	CXCL7 (PBP, β-TG, NAP-2)	Platelets	CXCR2	Neutrophils	Activates neutrophils Clot resorption Angiogenesis
	CXCL1 (GROα) CXCL2 (GROβ) CXCL3 (GROγ)	Monocytes Fibroblasts Endothelium	CXCR2	Neutrophils Naive T cells Fibroblasts	Activates neutrophils Fibroplasia Angiogenesis
CC	CCL3 (MIP-1α)	Monocytes T cells Mast cells Fibroblasts	CCR1, 3, 5	Monocytes NK and T cells Basophils Dendritic cells	Competes with HIV-1 Antiviral defense Promotes T_H1 immunity
	CCL4 (MIP-1β)	Monocytes Macrophages Neutrophils Endothelium	CCR1, 3, 5	Monocytes NK and T cells Dendritic cells	Competes with HIV-1
	CCL2 (MCP-1)	Monocytes Macrophages Fibroblasts Keratinocytes	CCR2B	Monocytes NK and T cells Basophils Dendritic cells	Activates macrophages Basophil histamine release Promotes T_H2 immunity
	CCL5 (RANTES)	T cells Endothelium Platelets	CCR1, 3, 5	Monocytes NK and T cells Basophils Eosinophils Dendritic cells	Degranulates basophils Activates T cells Chronic inflammation
CXXXC (CX_3C)	CX3CL1 (Fractalkine)	Monocytes Endothelium Microglial cells	CX_3CR1	Monocytes T cells	Leukocyte–endothelial adhesion Brain inflammation

Figure 3.22 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

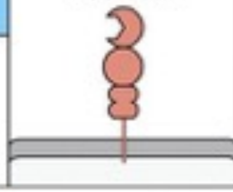
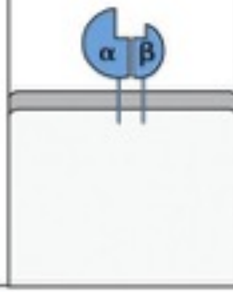
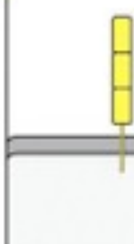
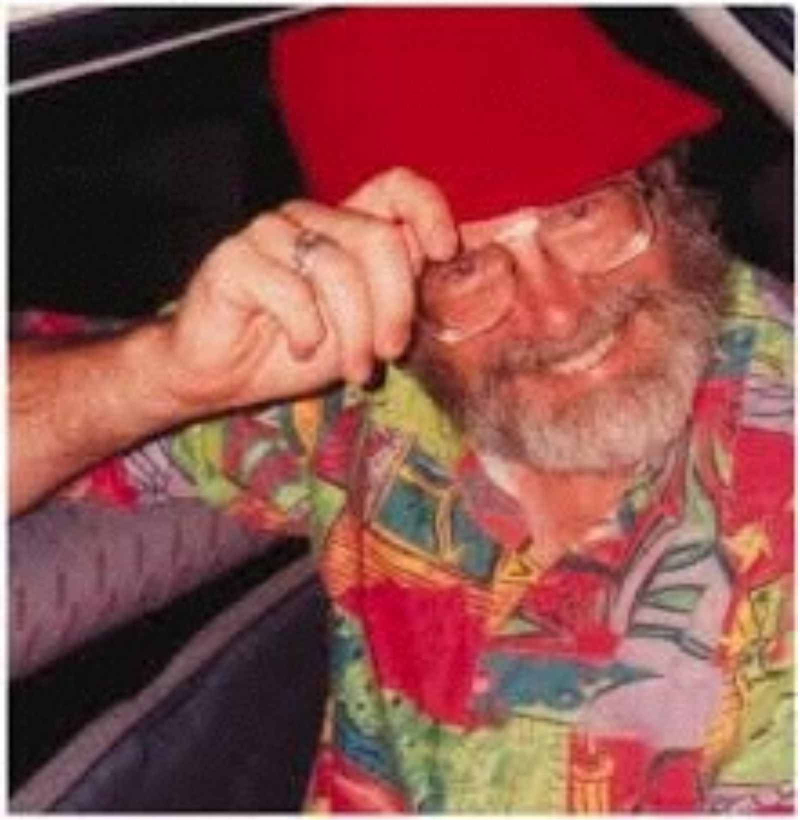
		Name	Tissue distribution	Ligand
Selectins Bind carbohydrates. Initiate leukocyte–endothelial interaction	P-selectin 	P-selectin (PADGEM, CD62P)	Activated endothelium and platelets	PSGL-1, sialyl-Lewis^x
		E-selectin (ELAM-1, CD62E)	Activated endothelium	Sialyl-Lewis^x
Integrins Bind to cell-adhesion molecules and extracellular matrix. Strong adhesion	LFA-1 	α_L:β_2 (LFA-1, CD11a:CD18)	Monocytes, T cells, macrophages, neutrophils, dendritic cells, NK cells	ICAMs
		α_M:β_2 (CR3, Mac-1, CD11b:CD18)	Neutrophils, monocytes, macrophages, NK cells	ICAM-1, iC3b, fibrinogen
		α_X:β_2 (CR4, p150.95, CD11c:CD18)	Dendritic cells, macrophages, neutrophils, NK cells	iC3b
		α_5:β_1 (VLA-5, CD49d:CD29)	Monocytes, macrophages	Fibronectin
Immunoglobulin superfamily Various roles in cell adhesion. Ligand for integrins	 ICAM-1	ICAM-1 (CD54)	Activated endothelium, activated leukocytes	LFA-1, Mac1
		ICAM-2 (CD102)	Resting endothelium, dendritic cells	LFA-1
		VCAM-1 (CD106)	Activated endothelium	VLA-4
		PECAM (CD31)	Activated leukocytes, endothelial cell–cell junctions	CD31

Figure 3.23 Janeway's Immunobiology, 8ed. (© Garland Science 2012)



Charles Janeway Jr.
1943 - 2003

Predição teórica da existência de receptores que reconhecessem padrões moleculares para ativação do sistema inato

Christiane Nüsslein-Volhard

Envolvimento dos receptores Toll no **desenvolvimento** de invertebrados

The Nobel Prize in Physiology or Medicine 1995

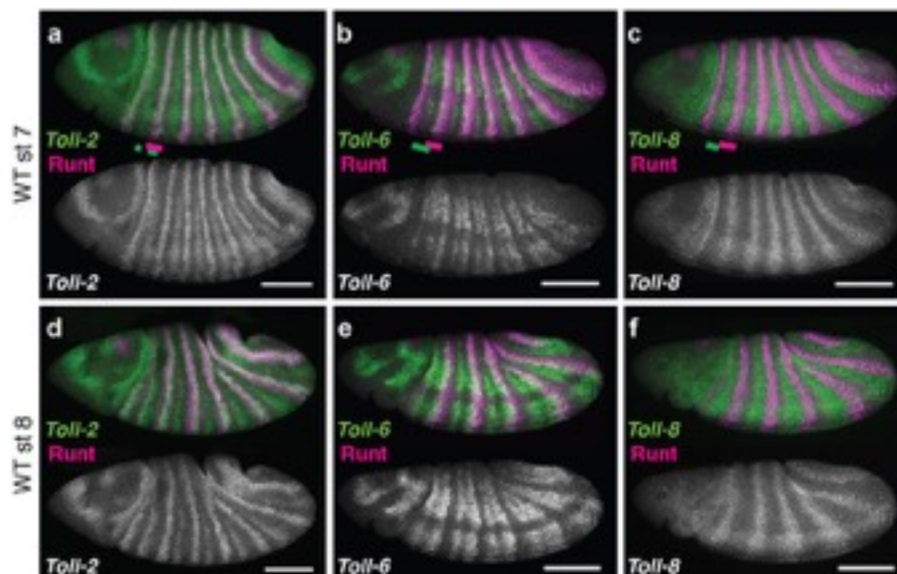
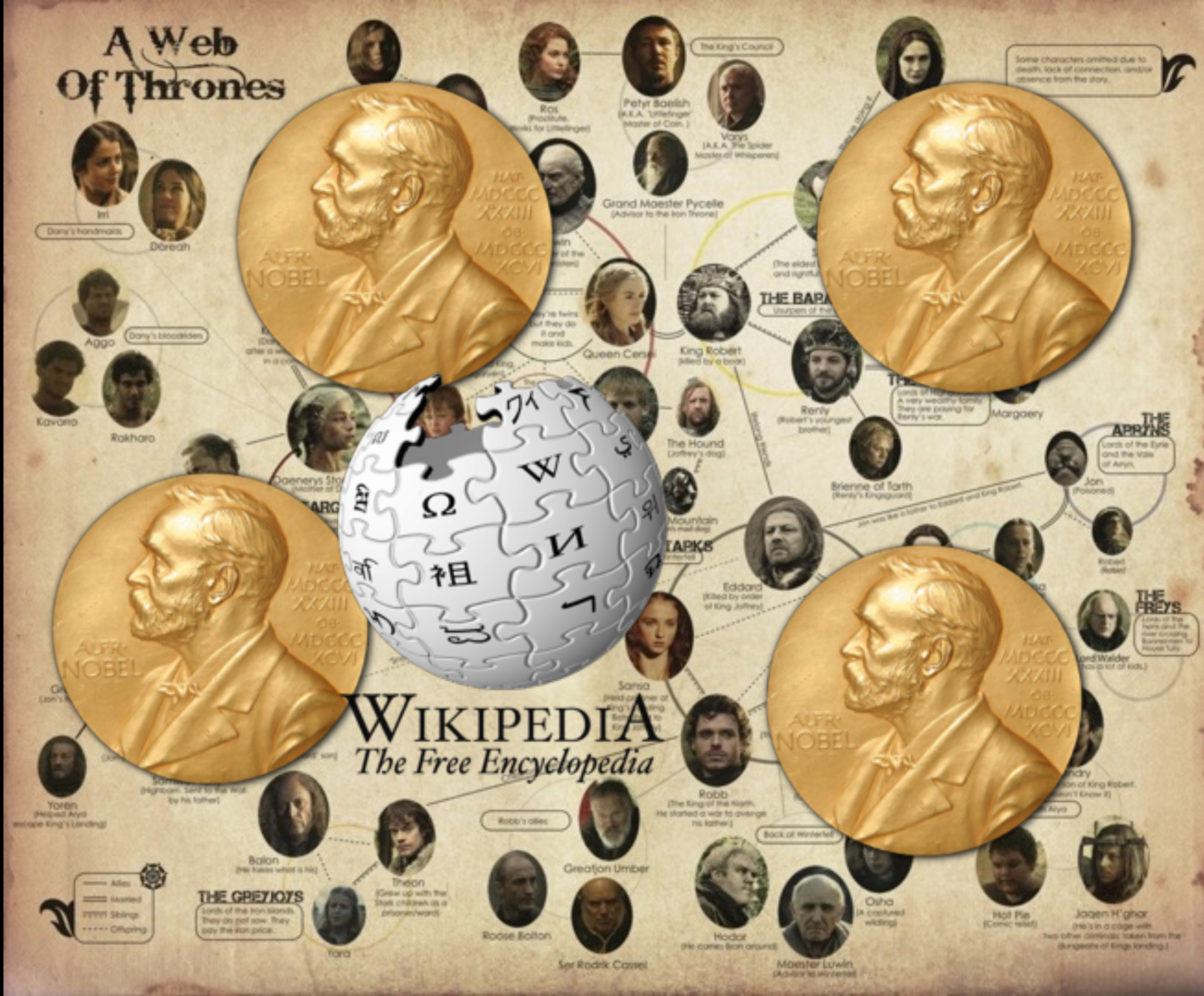


Figure 3.8 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Jules Hoffmann

Envolvimento dos receptores Toll na **imunidade** de invertebrados



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Varys
Grand Maester Pycelle
Ros
Irri
Doreah
Dany's handmaids
Aggo
Dany's bloodriders
Kovarro
Rakharo
Queen Cersei
King Robert
Renly
Margaery
Brienne of Tarth
The Hound
Eddard
Sansa
Robb
Robb's allies
Greatjon Umber
Roose Bolton
Ser Rodrik Cassel
Hodor
Maester Luwin
Osha
Hot Pie
Jaqen H'ghar
Back at Winterfell
Theon
Balon
Yara
THE GREYJOYS
Yoren
Jon
Lord Walder
THE FREYS
Allies
Married
Siblings
Offspring

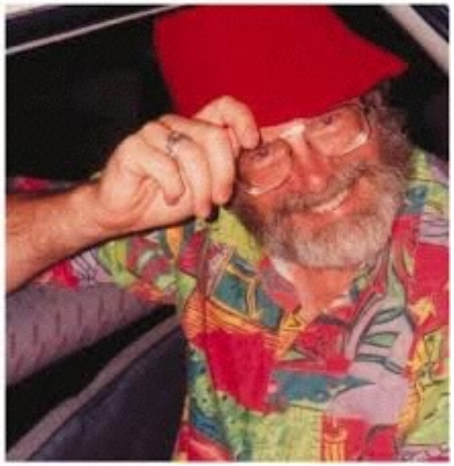
The Nobel Prize in Physiology or Medicine 2011

Bruce A. Beutler

Prize share: 1/4

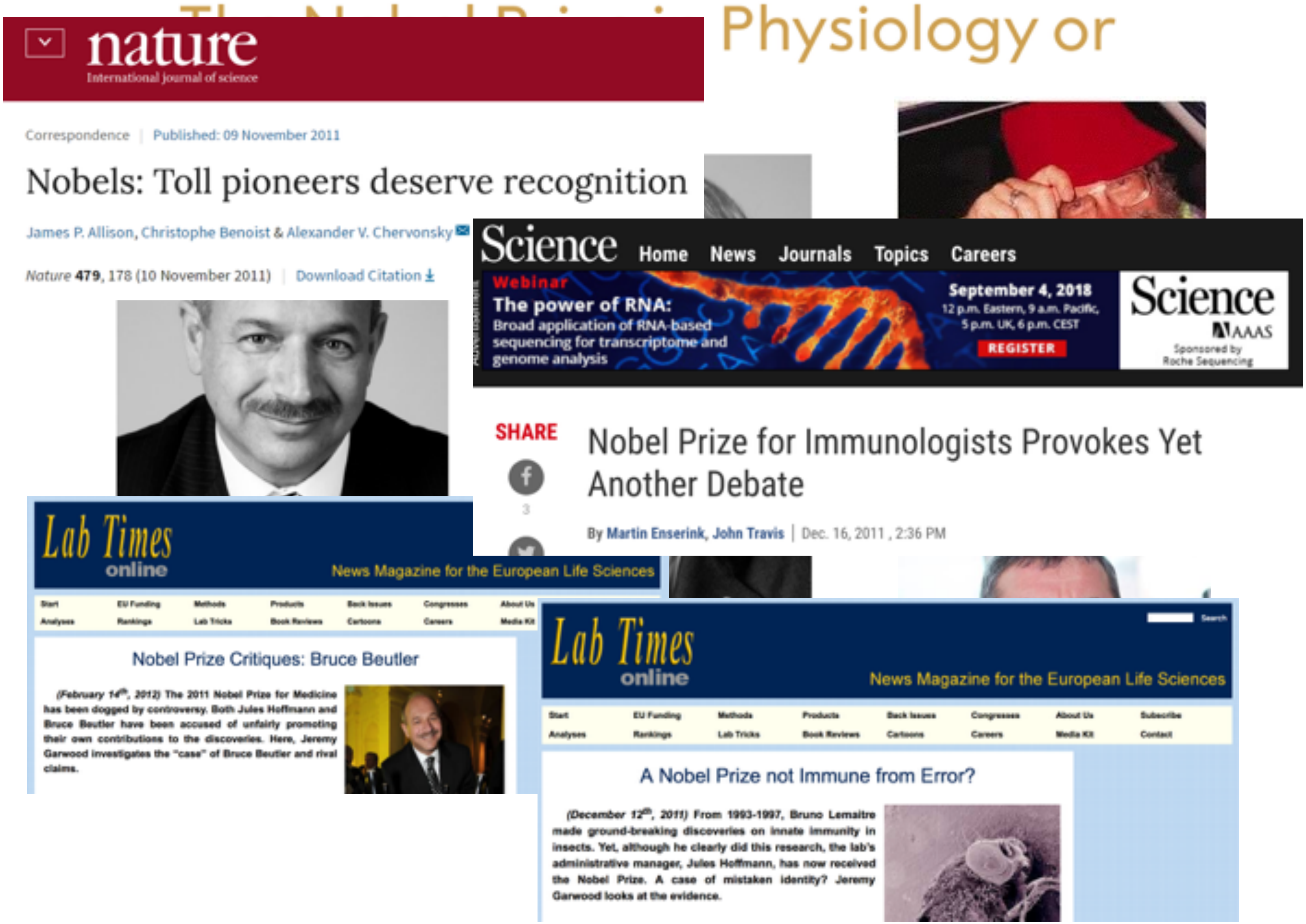
Jules A. Hoffmann

Prize share: 1/4



Charles Janeway Jr.
1943 - 2003

Ruslan Medzhitov


Physiology or
nature
International journal of science
Correspondence | Published: 09 November 2011
Nobels: Toll pioneers deserve recognition
James P. Allison, Christophe Benoist & Alexander V. Chervonsky
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Nobel Prize for Immunologists Provokes Yet Another Debate
By Martin Enserink, John Travis | Dec. 16, 2011 , 2:36 PM
Lab Times online
News Magazine for the European Life Sciences
Nobel Prize Critiques: Bruce Beutler
(February 14th, 2012) The 2011 Nobel Prize for Medicine has been dogged by controversy. Both Jules Hoffmann and Bruce Beutler have been accused of unfairly promoting their own contributions to the discoveries. Here, Jeremy Garwood investigates the "case" of Bruce Beutler and rival claims.
Lab Times online
News Magazine for the European Life Sciences
A Nobel Prize not Immune from Error?
(December 12th, 2011) From 1993-1997, Bruno Lemaitre made ground-breaking discoveries on innate immunity in insects. Yet, although he clearly did this research, the lab's administrative manager, Jules Hoffmann, has now received the Nobel Prize. A case of mistaken identity? Jeremy Garwood looks at the evidence.

The Nobel Prize in Physiology or Medicine 2011

Bruce A. Beutler

Prize share: 1/4

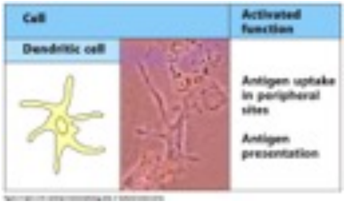
Jules A. Hoffmann

Prize share: 1/4

Photo: The Rockefeller University

Ralph M. Steinman

Prize share: 1/2



The Nobel Prize in Physiology or Medicine 2011

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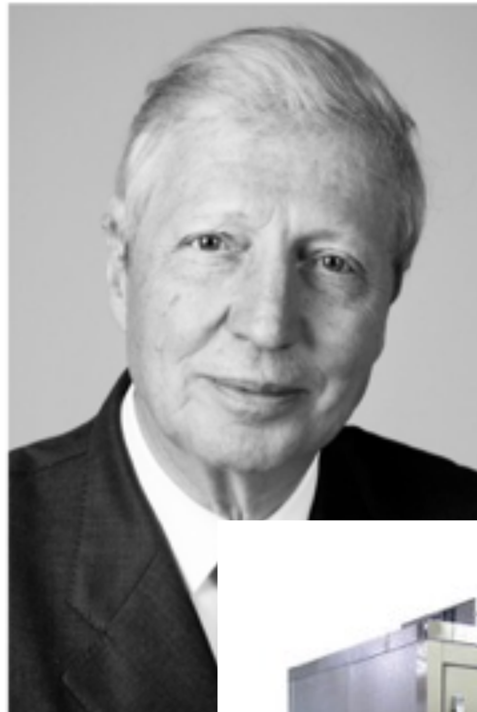
Bruce A. Beutler

Prize share: 1/4



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Jules A. H

Prize share: 1

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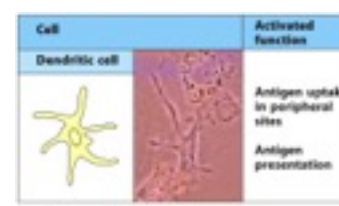



I had no problem getting my medal. Losers...

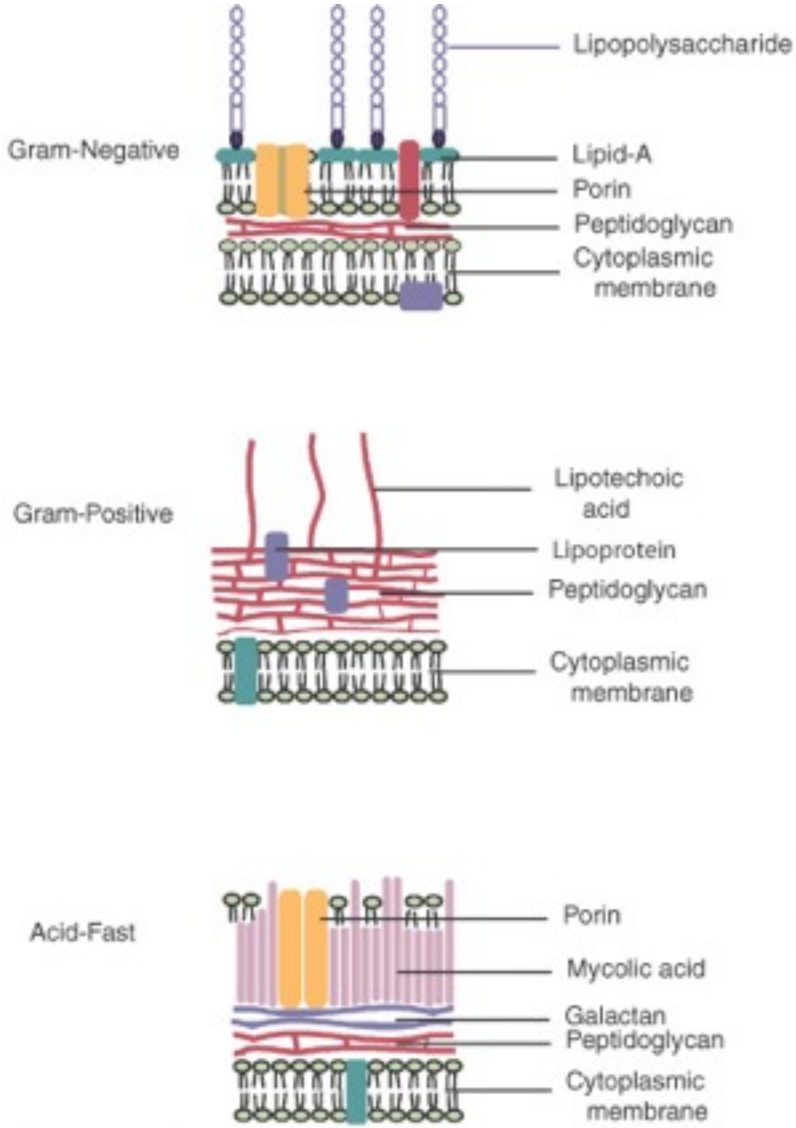
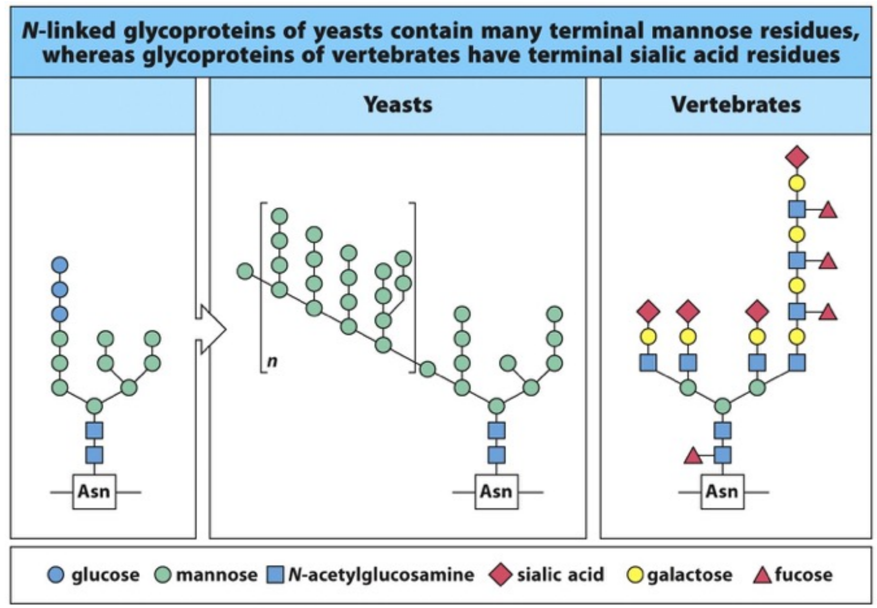
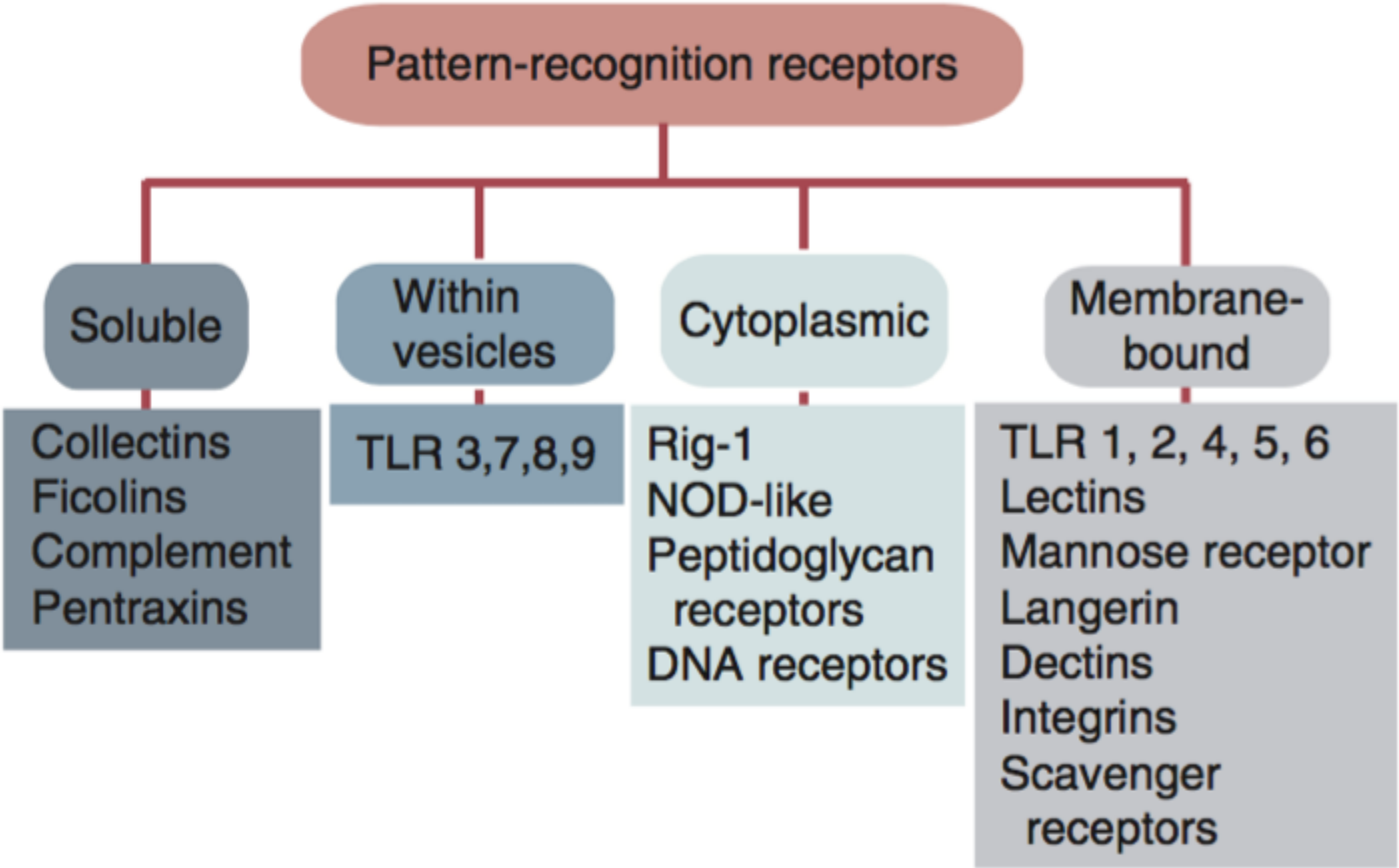


FIGURE 2-2 The major structural features of the cell walls of Gram-negative, Gram-positive, and acid-fast bacteria. These conserved structural molecules serve as pathogen-associated molecular patterns and can bind to pattern-recognition receptors such as the toll-like receptors.



Receptores de reconhecimento de padrão (PRR)



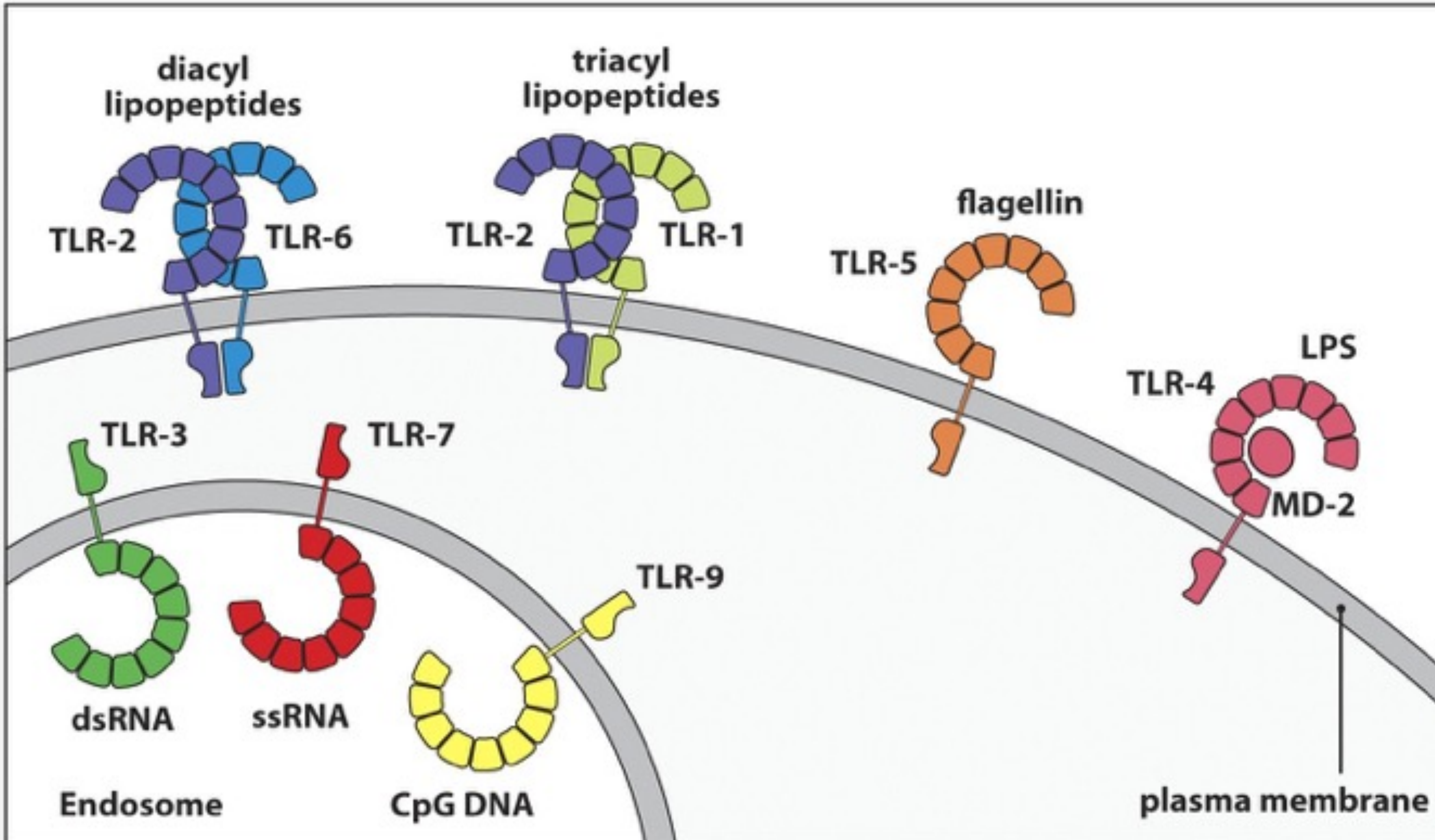


Figure 3.10 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

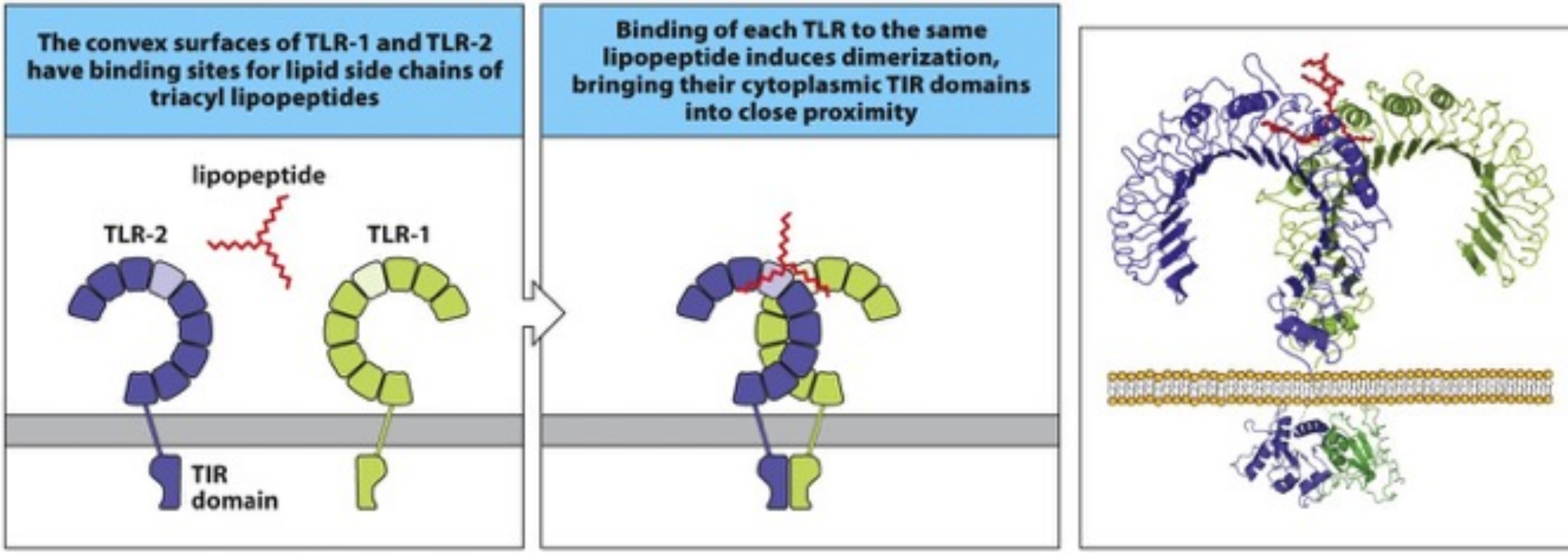


Figure 3.11 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Innate immune recognition by mammalian Toll-like receptors		
Toll-like receptor	**Ligand**	**Cellular distribution**
TLR-1:TLR-2 heterodimer	Lipomannans (mycobacteria) Lipoproteins (diacyl lipopeptides; triacyl lipopeptides) Lipoteichoic acids (Gram-positive bacteria) Cell-wall β-glucans (bacteria and fungi) Zymosan (fungi)	Monocytes, dendritic cells, mast cells, eosinophils, basophils
TLR-2:TLR-6 heterodimer		
TLR-3	Double-stranded RNA (viruses)	NK cells
TLR-4 (plus MD-2 and CD14)	LPS (Gram-negative bacteria) Lipoteichoic acids (Gram-positive bacteria)	Macrophages, dendritic cells, mast cells, eosinophils
TLR-5	Flagellin (bacteria)	Intestinal epithelium
TLR-7	Single-stranded RNA (viruses)	Plasmacytoid dendritic cells, NK cells, eosinophils, B cells
TLR-8	Single-stranded RNA (viruses)	NK cells
TLR-9	DNA with unmethylated CpG (bacteria and herpesviruses)	Plasmacytoid dendritic cells, eosinophils, B cells, basophils
TLR-10	Unknown	Plasmacytoid dendritic cells, eosinophils, B cells, basophils
TLR-11 (mouse only)	Profilin and profilin-like proteins (*Toxoplasma gondii*, uropathogenic bacteria)	Macrophages, dendritic cells, liver, kidney, and bladder epithelial cells

Figure 3.9 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

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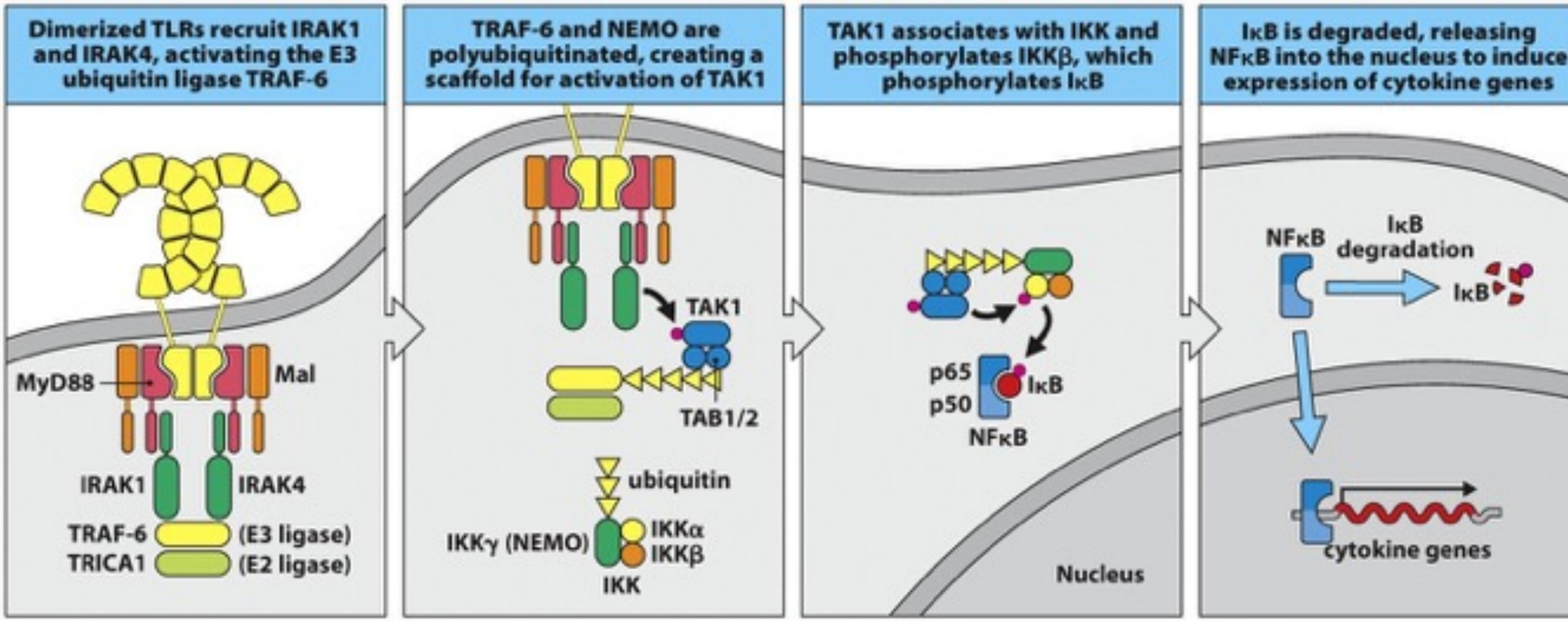

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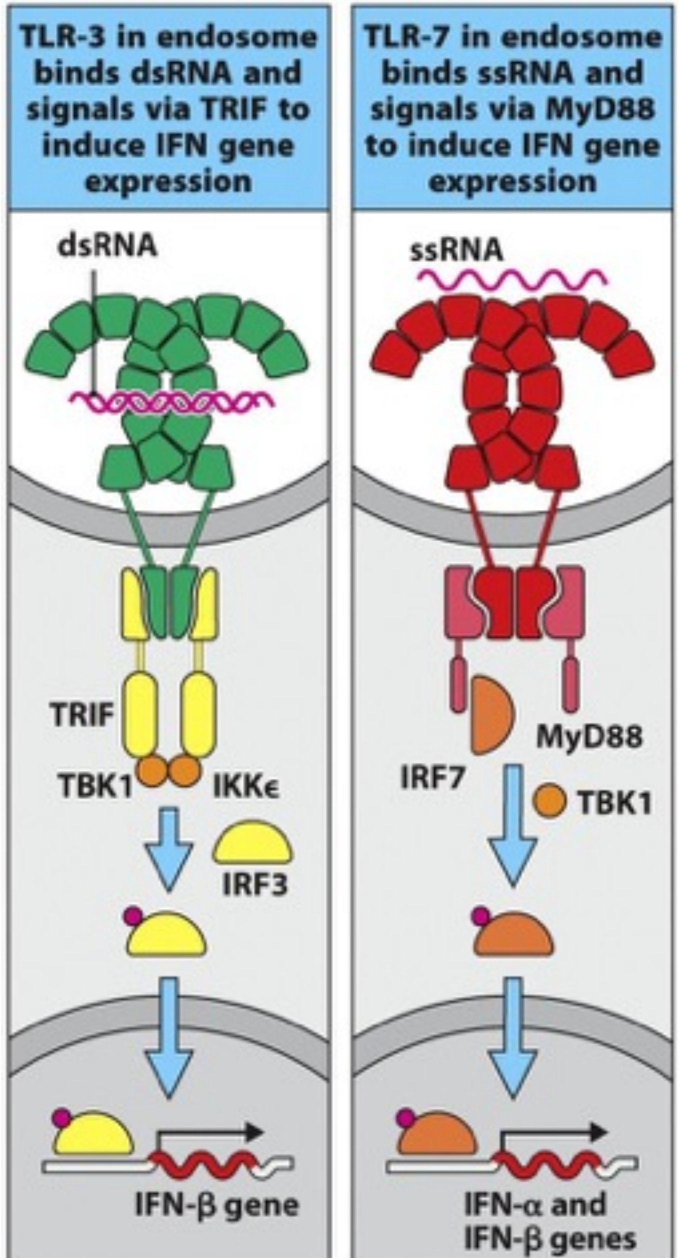

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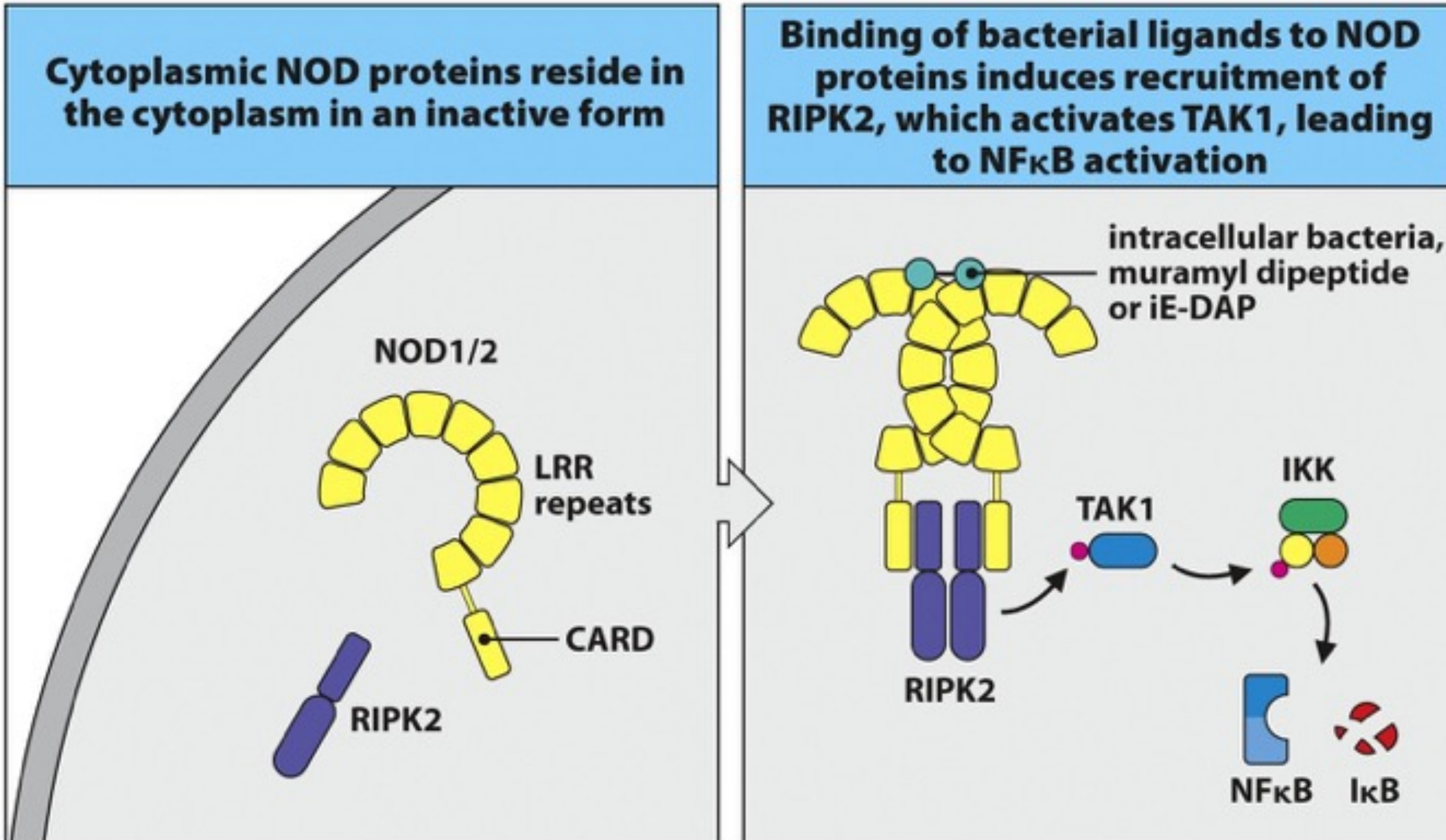

Figure 3.15 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

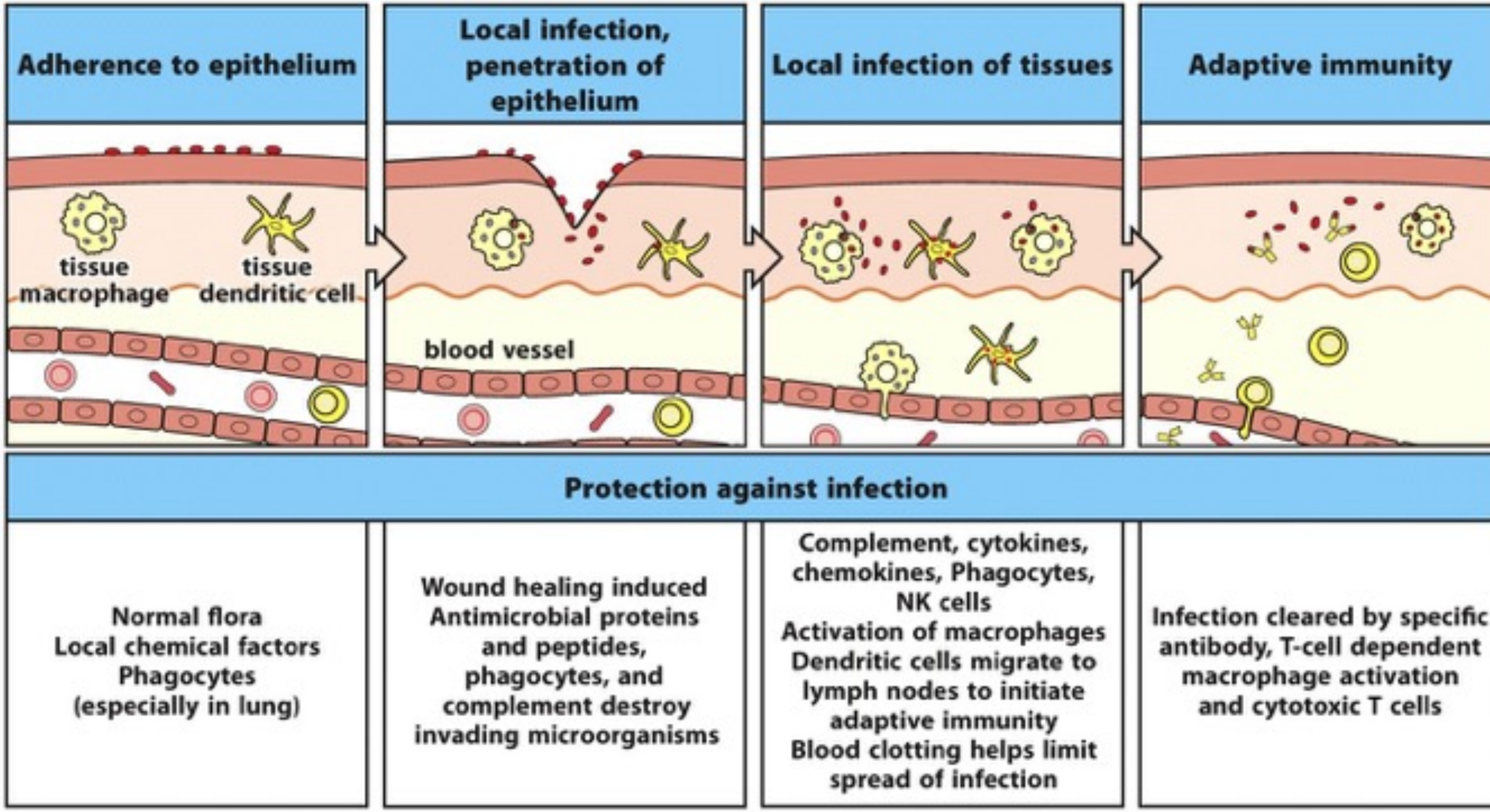

Figure 2.5 Janeway's Immunobiology, 8ed. (© Garland Science 2012)


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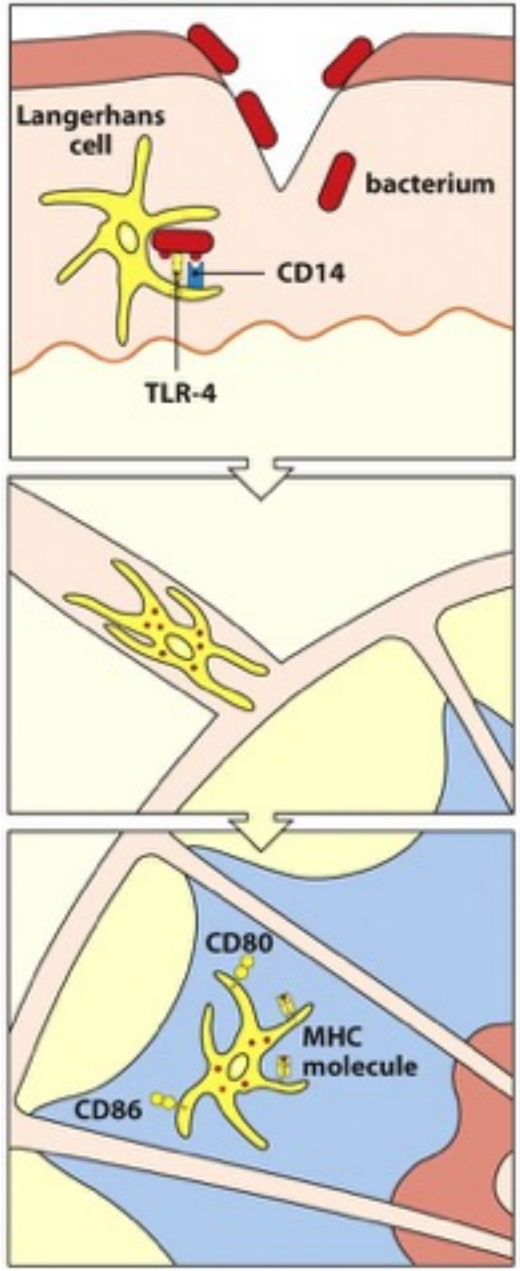

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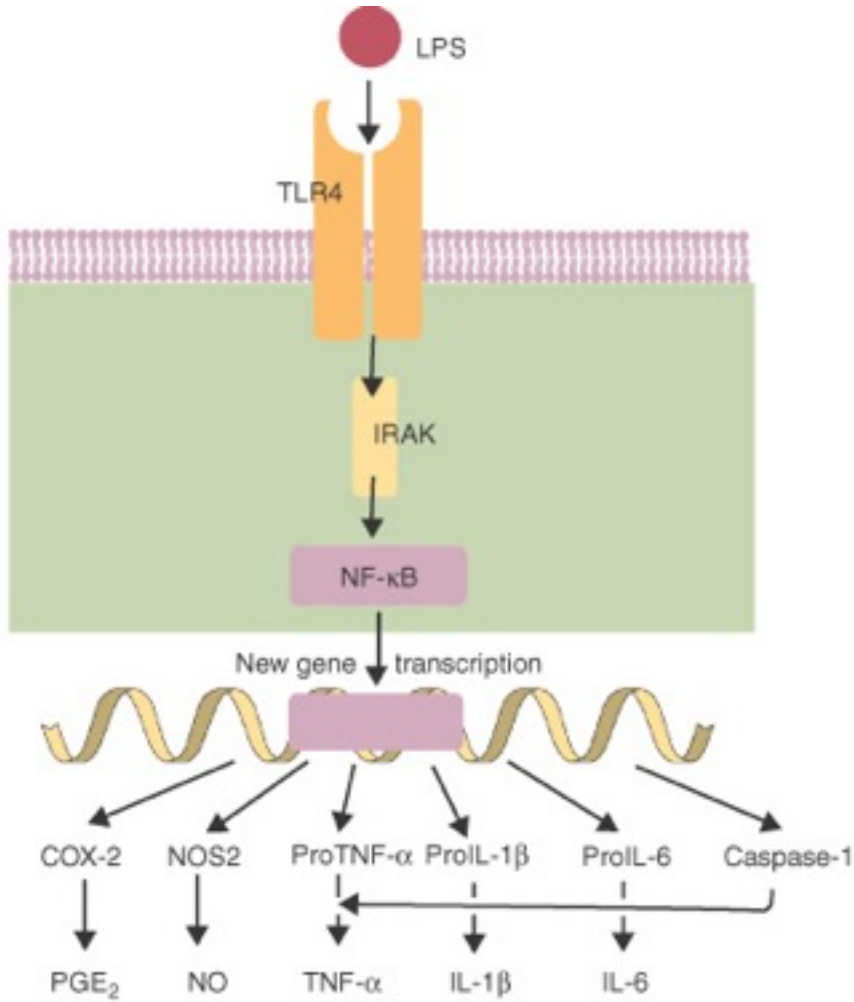

FIGURE 2-3 Binding of a pathogen-associated molecular pattern such as lipopolysaccharide to a toll-like receptor *(TLR)* leads to generation of a transcription factor called nuclear factor kappa-B *(NF-κB)*. NF-κB turns on the genes for three major cytokines, interleukin-1 *(IL-1)*, IL-6, and tumor necrosis factor-α *(TNF-α)*. It also turns on the genes for nitric oxide synthase 2 *(NOS2)* and cyclooxygenase-2 *(COX-2)*. These two enzymes generate nitric oxide and prostaglandins and leukotrienes, respectively.

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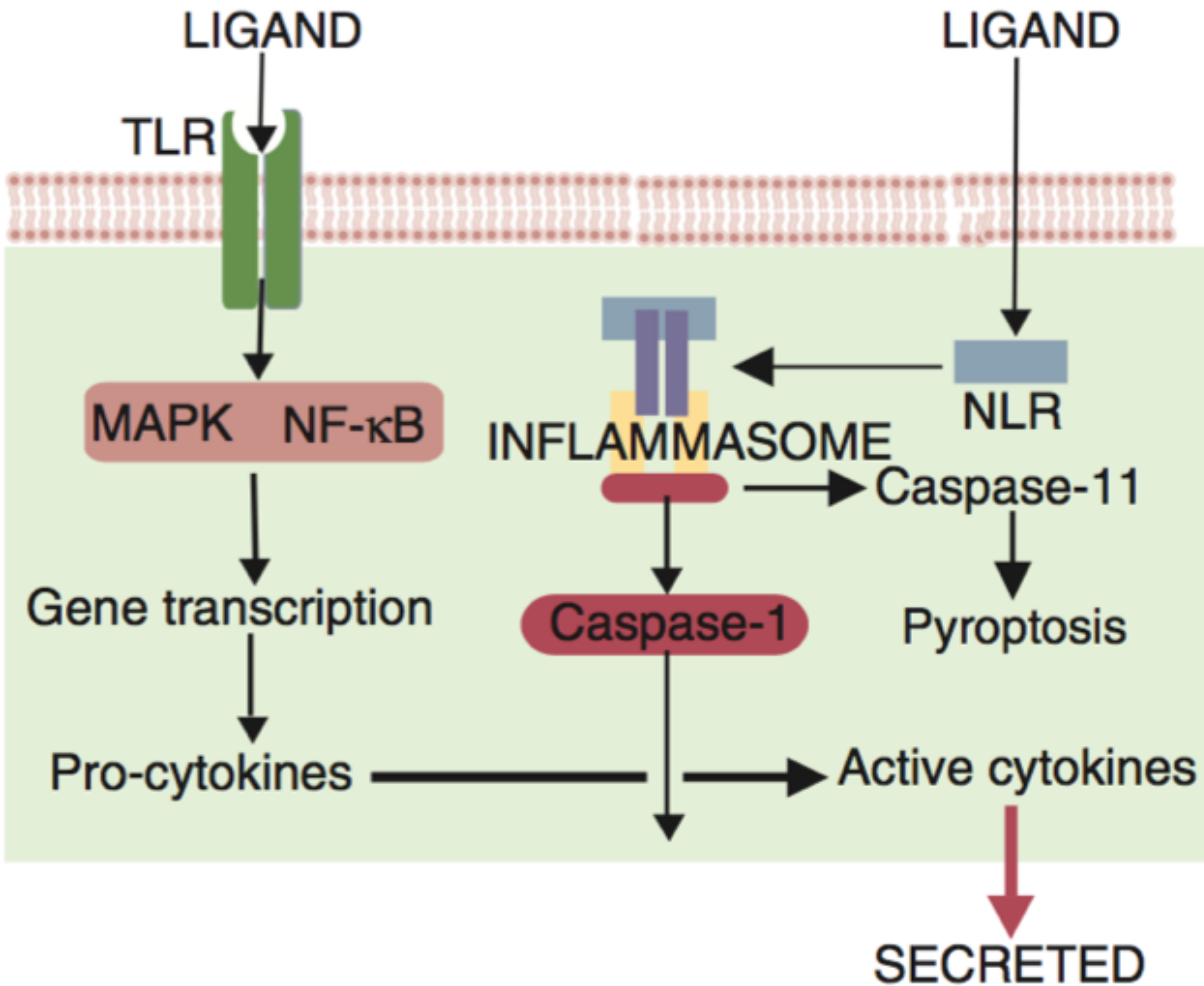
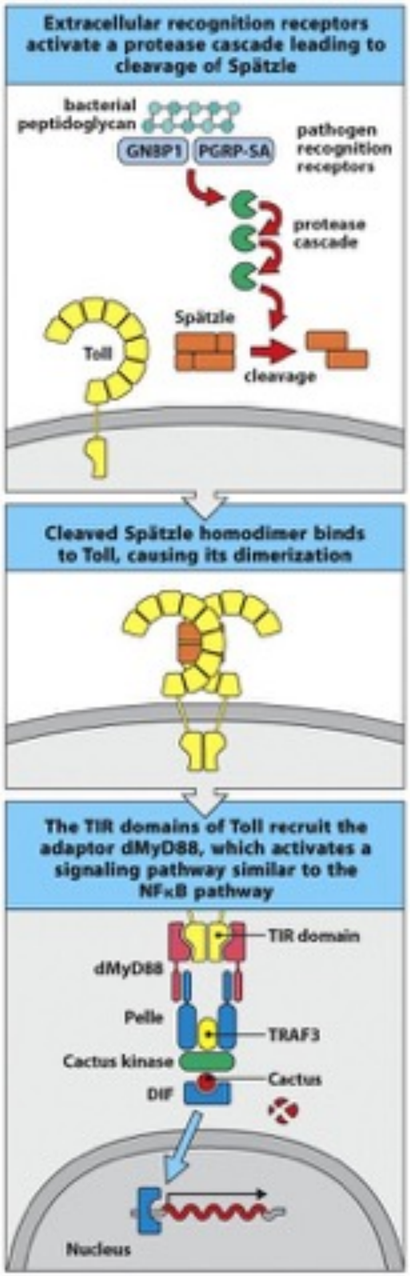


LIGAND
LIGAND
TLR
MAPK
NF-κB
INFLAMMASOME
NLR
Caspase-11
Gene transcription
Caspase-1
Pyroptosis
Pro-cytokines
Active cytokines
SECRETED



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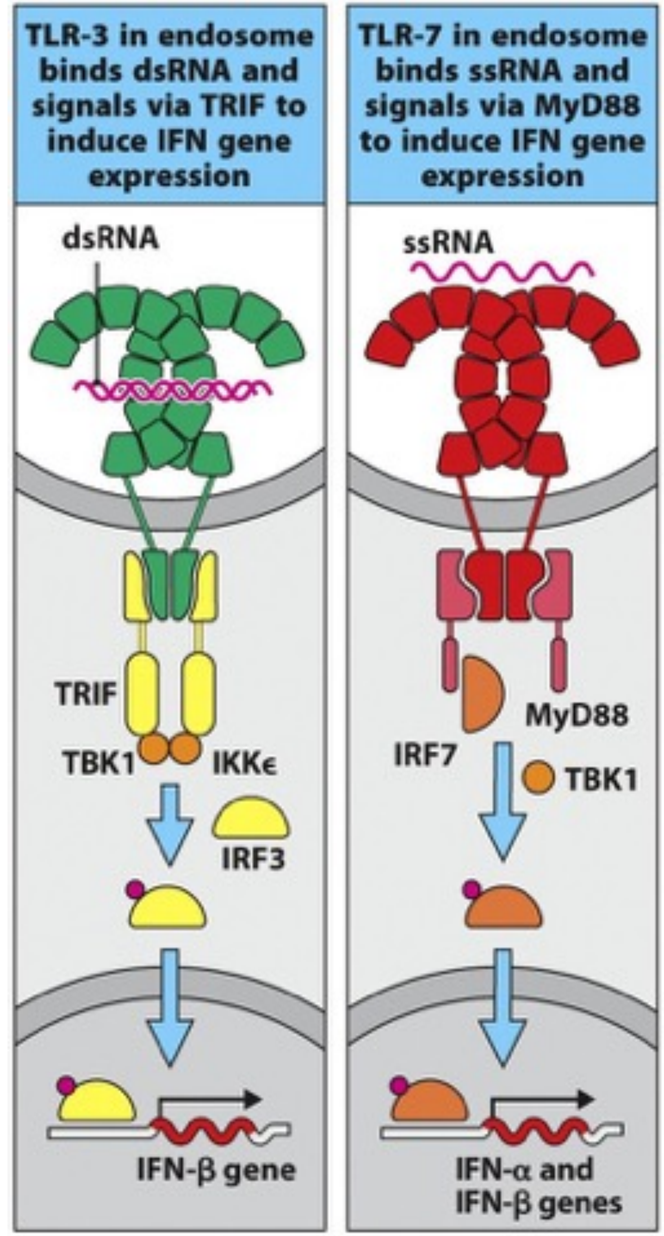


Figure 3.14 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Momento Veterinário

Polymorphisms in the Tlr4 and Tlr5 Gene Are Significantly Associated with Inflammatory Bowel Disease in German Shepherd Dogs

Aarti Kathrani, Arthur House, Brian Catchpole, Angela Murphy, Alex German, Dirk Werling, Karin Allenspach

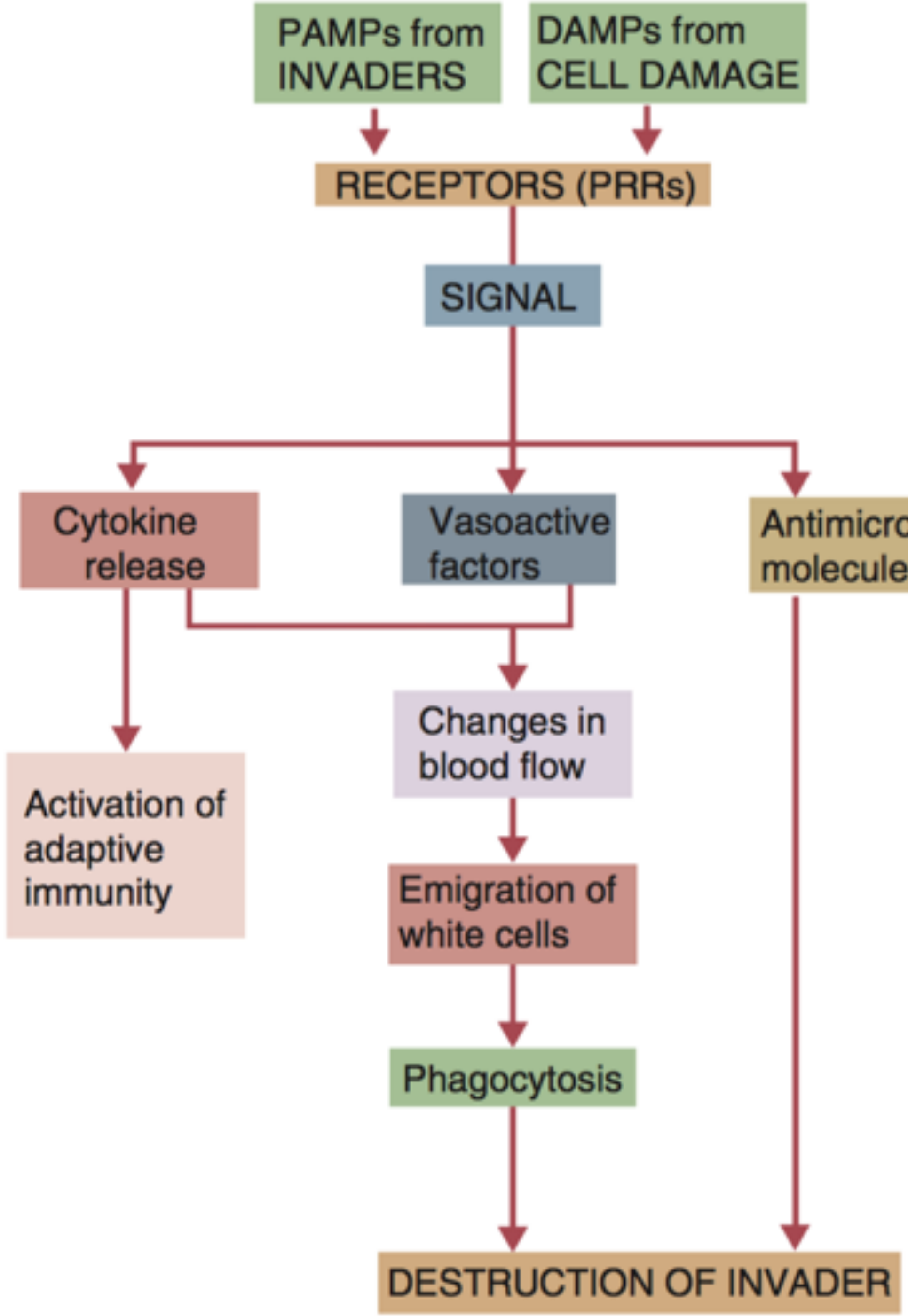
Published: December 23, 2010 • https://doi.org/10.1371/journal.pone.0015740

	SNP	Amino-acid wild-type	Amino-acid change associated with SNP
TLR4	T23C	Valine	Alanine
	G1039A	Alanine	Threonine
	A1571T	Valine	Glutamic acid
	G1807A	Lysine	Glutamic acid
TLR5	G22A	Alanine	Threonine
	C100T	Arginine	Cystiene
	T1844C	Leucine	Serine

Amino-acid change coded by the non-synonymous single nucleotide polymorphisms (SNPs) identified in the TLR4 and TLR5 gene by mutational analysis of ten German shepherd dogs with inflammatory bowel disease (non-polar amino acids-valine, alanine and leucine, basic amino-acids-lysine and arginine, acidic amino-acid-glutamic acid and polar amino-acids-threonine, cystiene and serine).
doi:10.1371/journal.pone.0015740.t001

SNP	Associated allele	Minor allele freq.	P-value
TLR5 G22A	A	**0.112**	**5.5414e^{-5}**
TLR5 C100T	C	**0.44**	**4.7128E^{-5}**
TLR5 T1844C	C	**0.466**	**0.0071**
TLR4 T23C	T	0.274	0.1013
TLR4 G1039A	G	0.316	0.0926
TLR4 A1571T	A	**0.149**	**0.0282**
TLR4 G1807A	G	**0.149**	**0.0282**

Association of TLR4 and TLR5 single nucleotide polymorphism (SNP) alleles in a case-control association study of inflammatory bowel disease in German shepherd dogs (GSDs) carried out using a SNaPSHOT multiplex reaction (case = 55 unrelated GSDs, control = 61 GSDs; 47 GSDs with non-inflammatory disease and 14 healthy GSDs).


PAMPs from INVADERS
DAMPs from CELL DAMAGE
RECEPTORS (PRRs)
SIGNAL
Cytokine release
Vasoactive factors
Antimicrobial molecules
Changes in blood flow
Activation of adaptive immunity
Emigration of white cells
Phagocytosis
DESTRUCTION OF INVADER

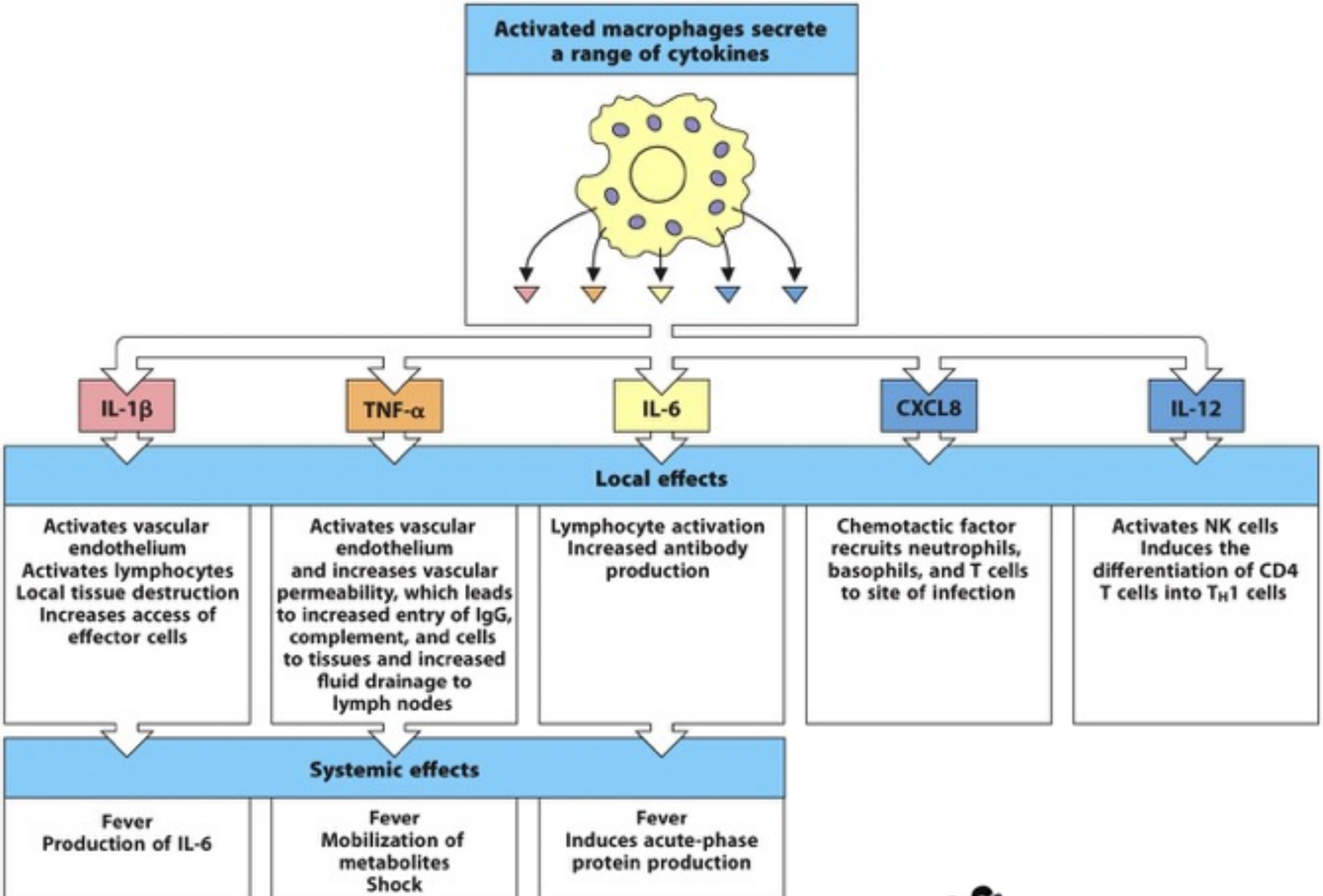


Figure 3.21 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

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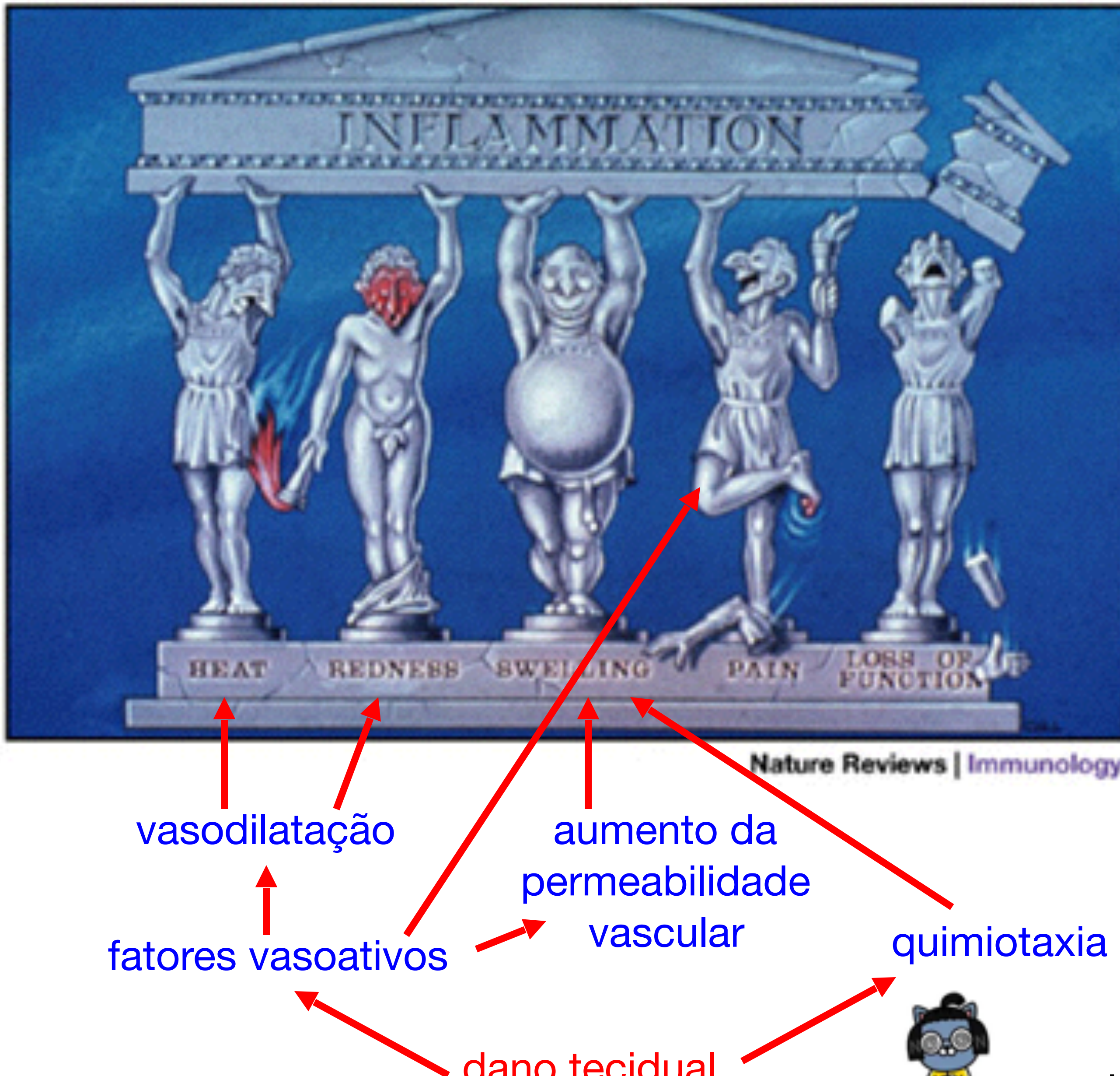

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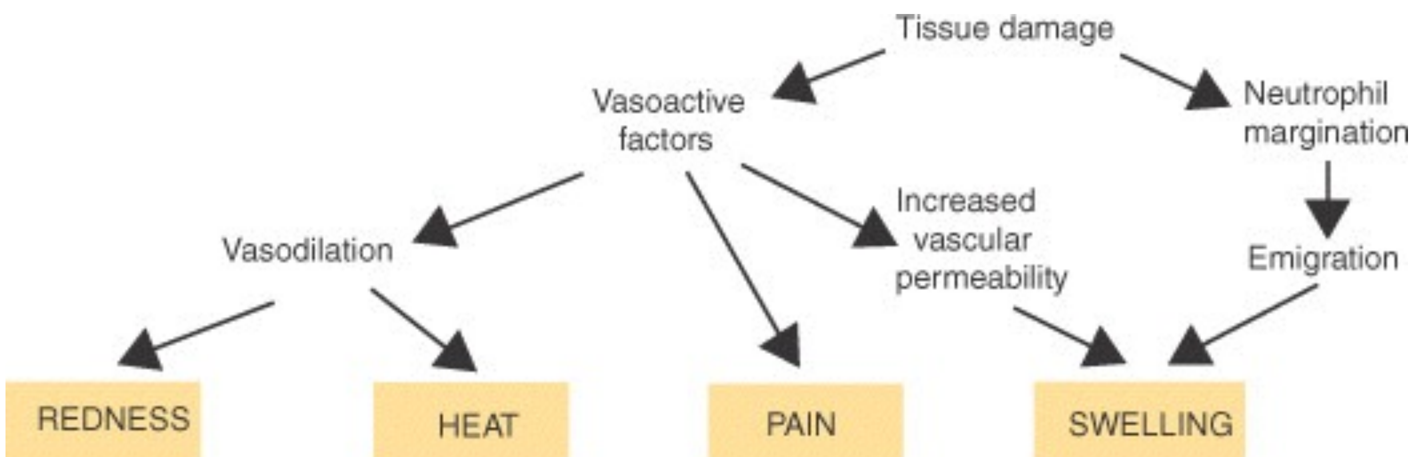

FIGURE 2-17 The cardinal signs of acute inflammation and how they are generated.

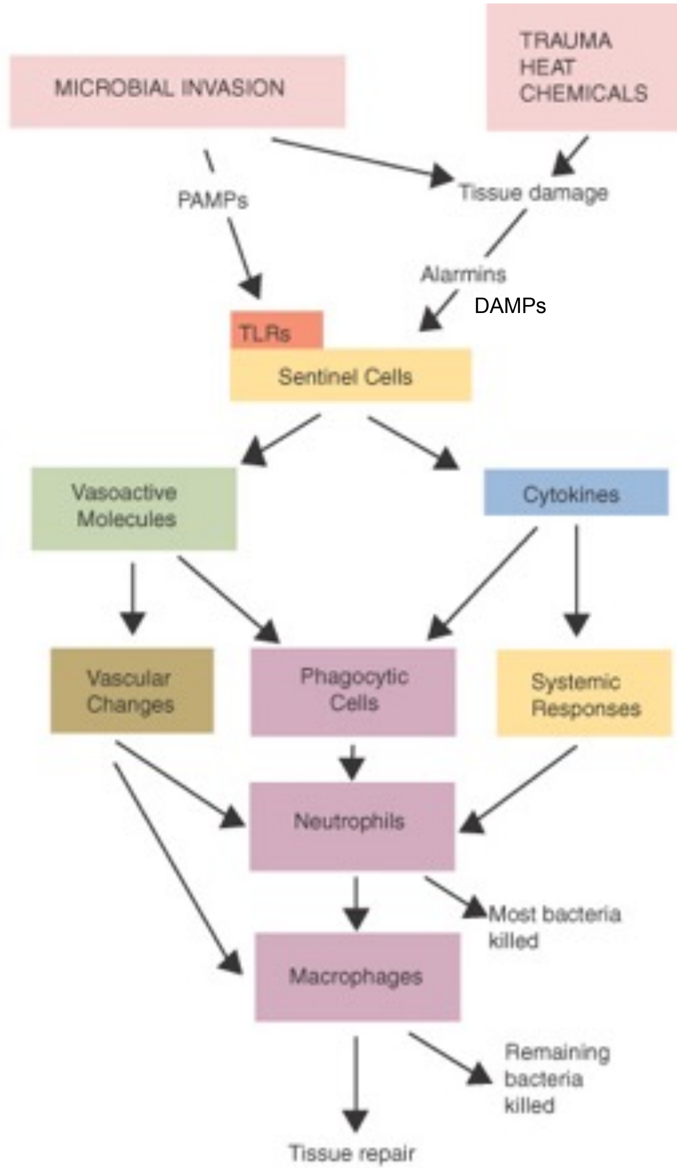

FIGURE 2-1 An overview of the essential features of acute inflammation, an innate mechanism for focusing cells and other defensive mechanisms. It is triggered by microbial invasion and tissue damage.

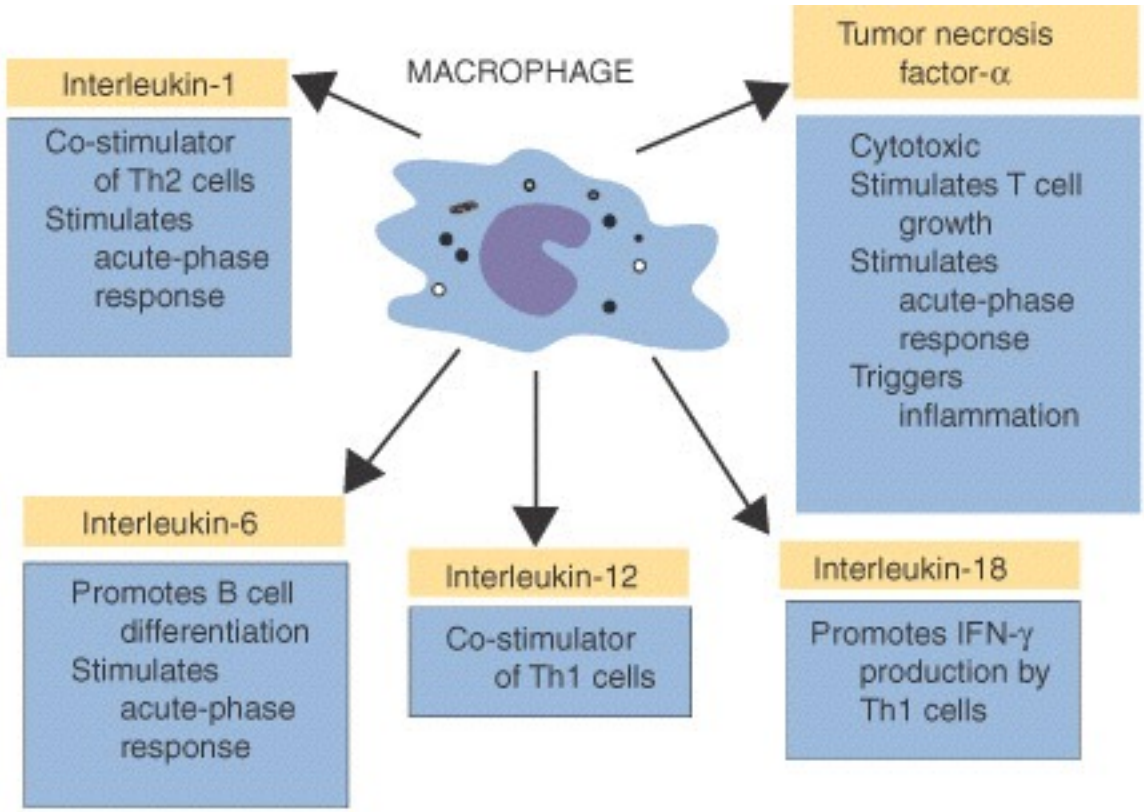

FIGURE 4-1 The cytokines secreted by macrophages and their functions.

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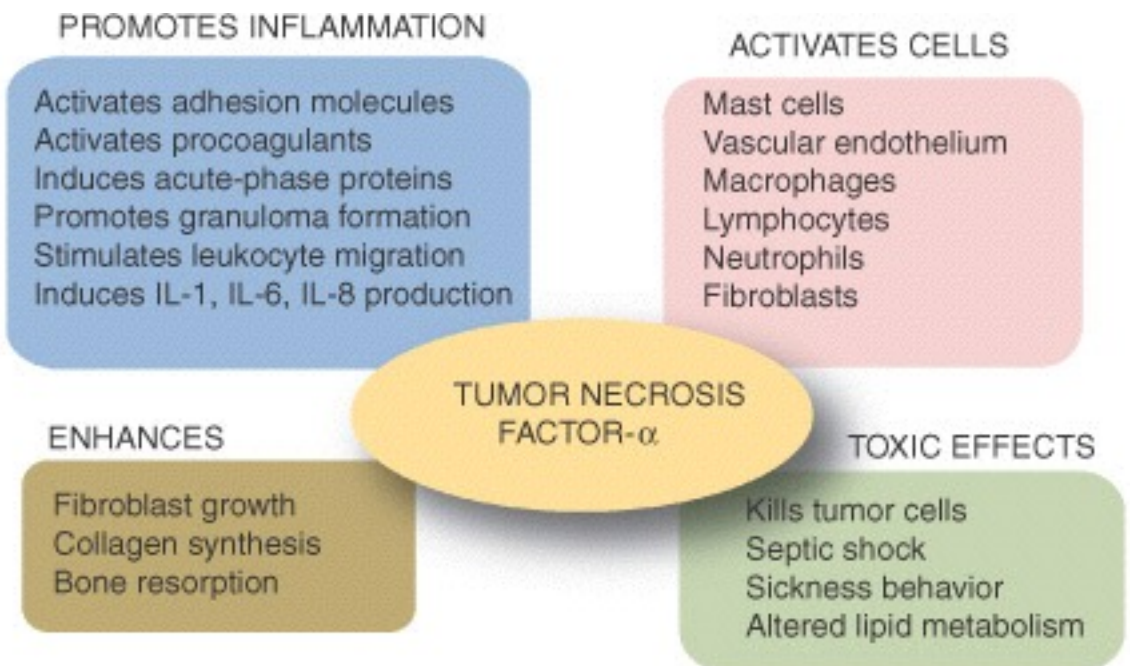

FIGURE 2-13 Some of the properties of tumor necrosis factor-α.

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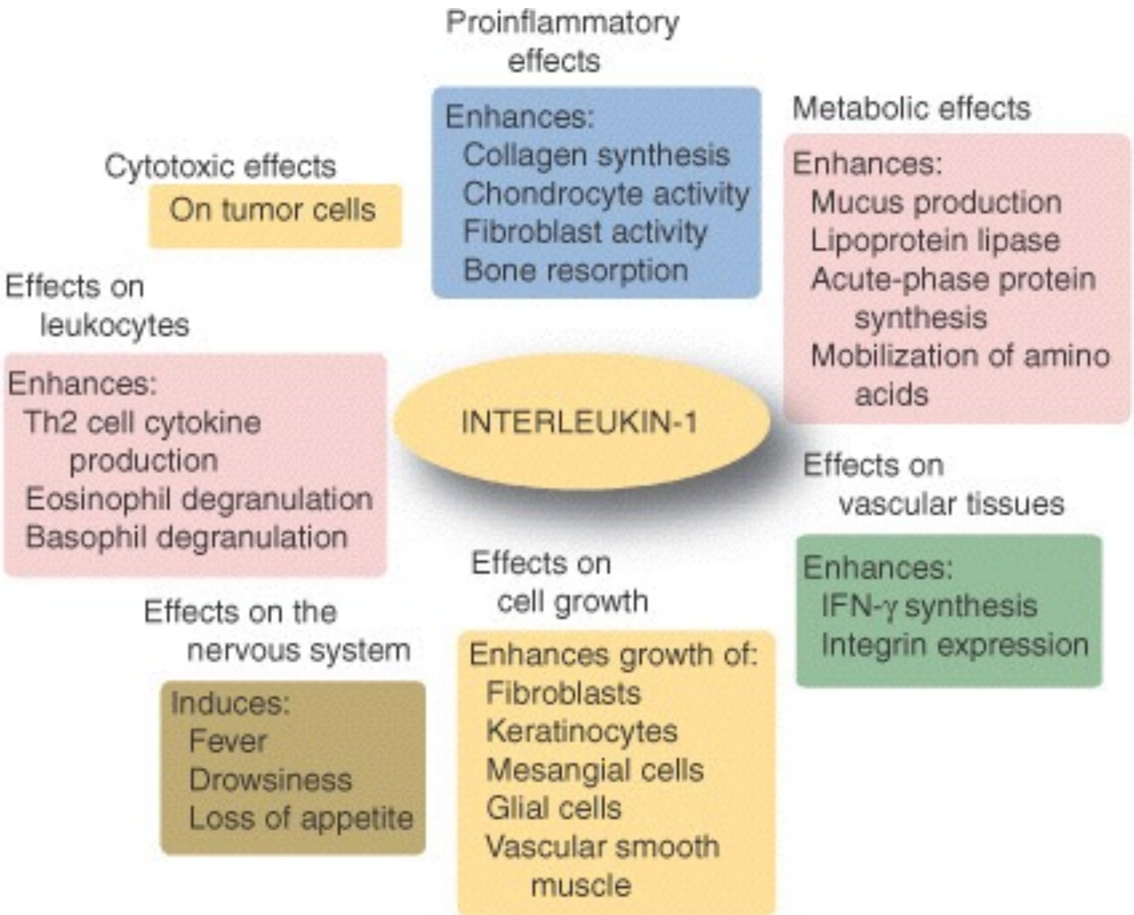

FIGURE 2-15 Some of the effects of interleukin-1 on the cells of the body.

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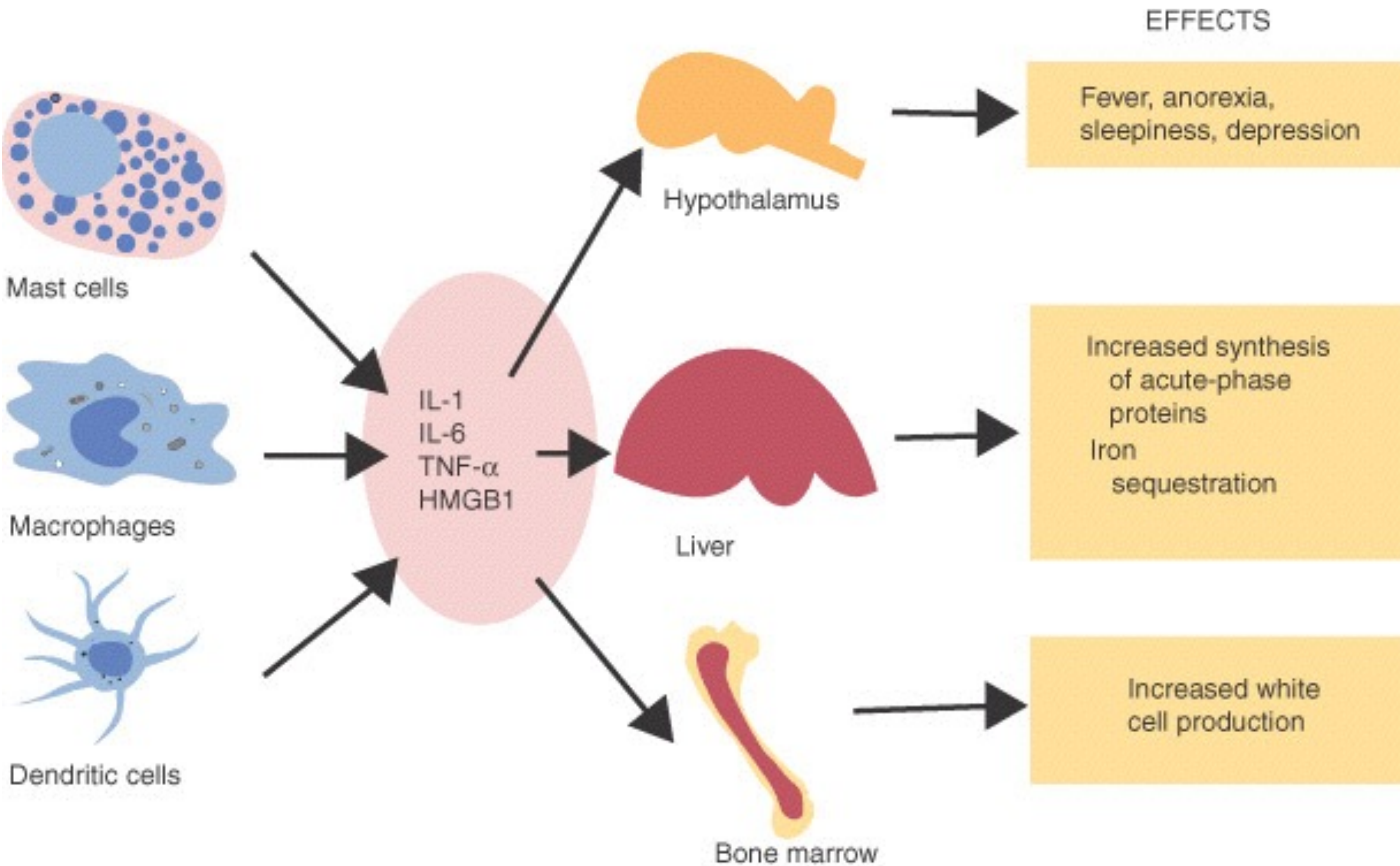

FIGURE 4-13 Sickness behavior is part of the response of the body to inflammatory stimuli. Multiple systemic effects are due to the four major cytokines secreted by sentinel cells, mast cells, macrophages, and dendritic cells. The major sickness-inducing cytokines are interleukin-1 *(IL-1)*, IL-6, tumor necrosis factor-α *(TNF-α)*, and high mobility group box protein-1 *(HMGB1)*.

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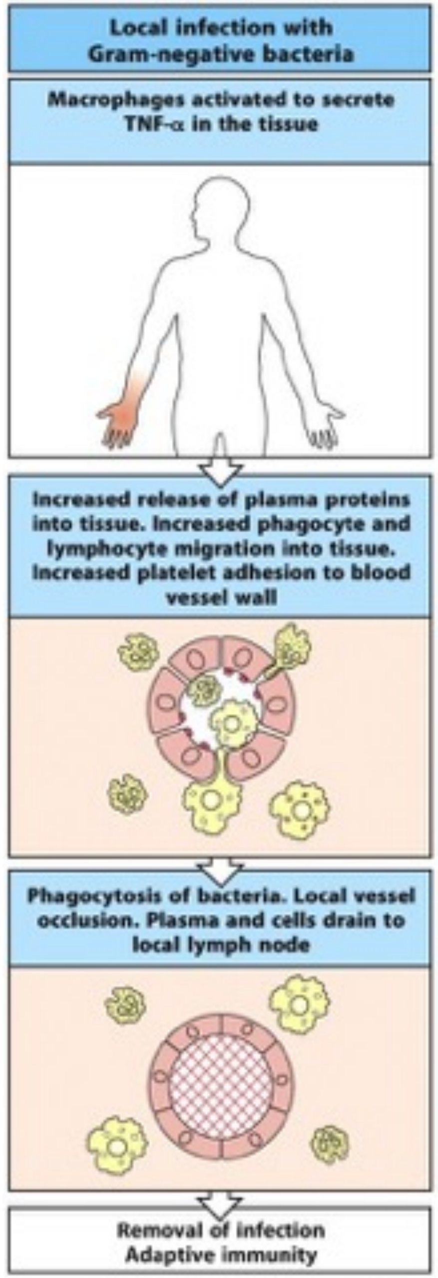
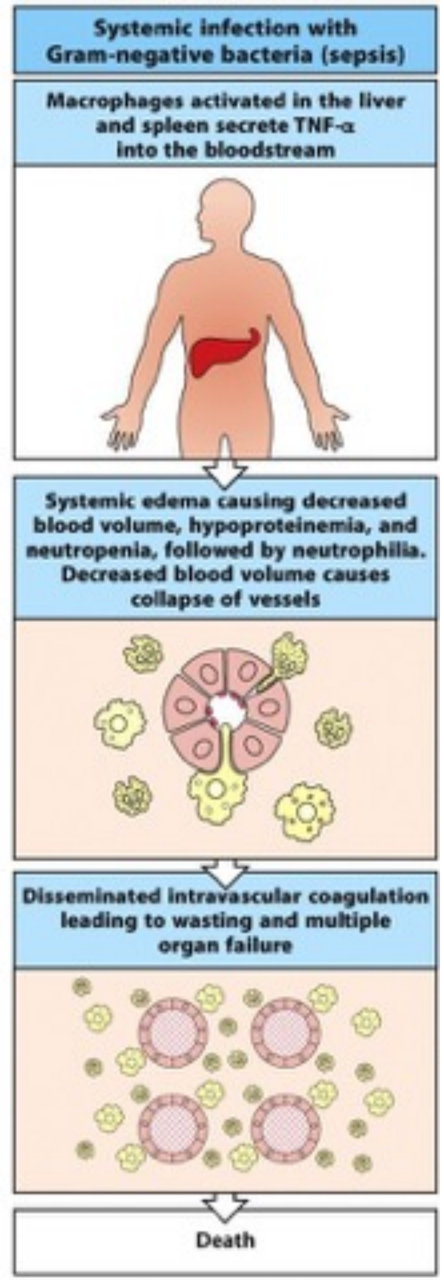


Figure 3.26 Janeway's Immunobiology, 8



Bed. (© Garland Science 2012)

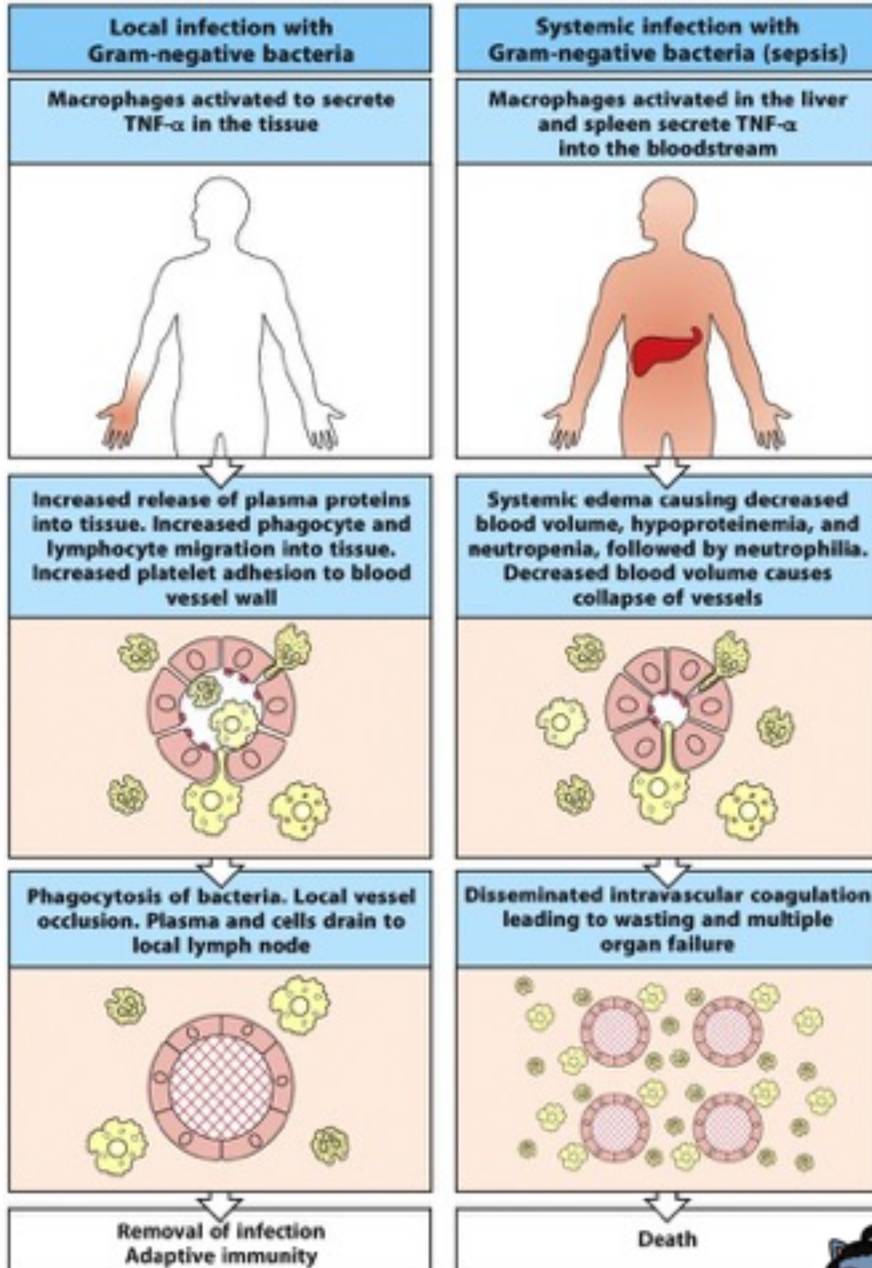


Figure 3.26 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

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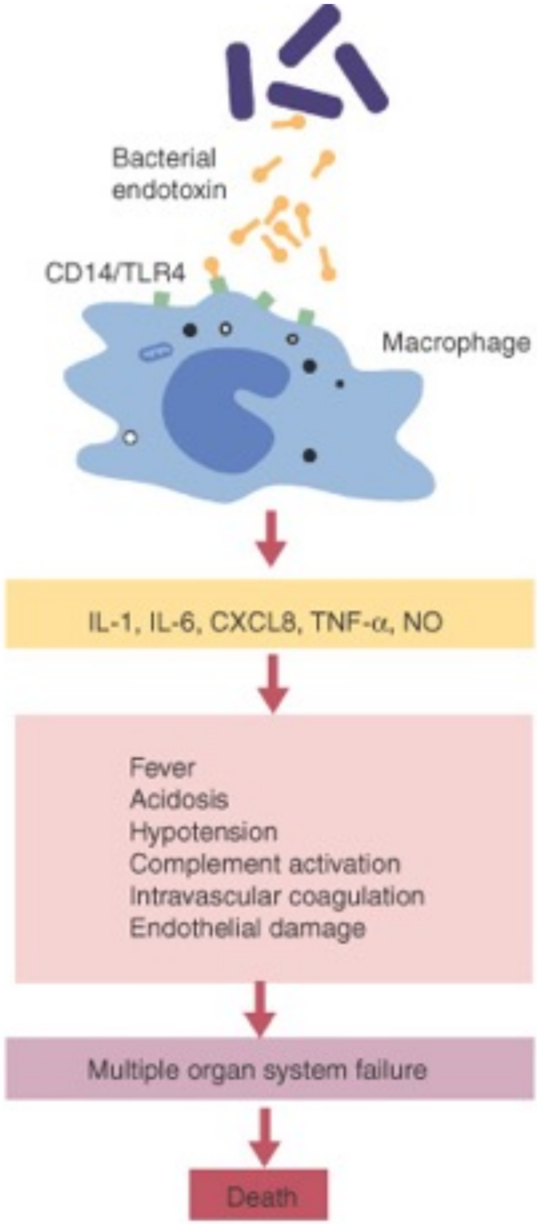
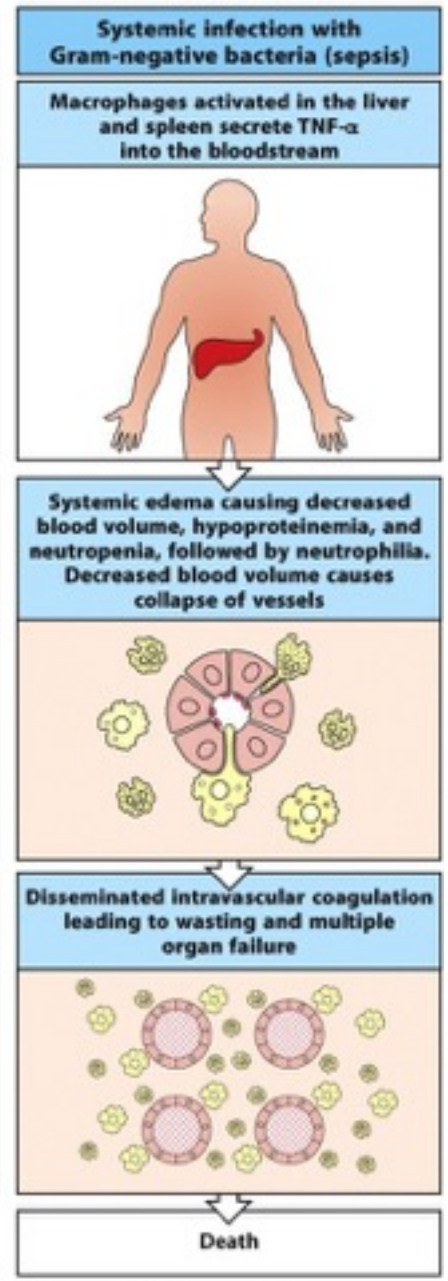


FIGURE 4-16 The pathogenesis of the systemic inflammatory response syndrome.



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1st description of clinical manifestations of sepsis by Hippocrates (460-377 BC)