Processes in Innate Immunity

[1] Recognize the presence of infection and sound the alarm.

[2] Recruitment effector functions to kill pathogen, prevent its replication.

[3] Recruit the adaptive immune response if needed.

Pathogen damage human cells in different ways

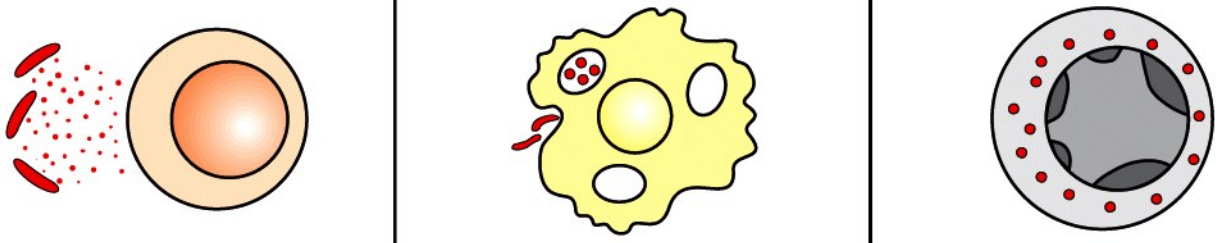
	Mechanisms of tissue damage by pathogens		
	Exotoxin release	**Endotoxin release**	**Direct cytopathic effect**
Pathogenic mechanism			
Infectious agent	***Vibrio cholerae***	***Yersinia pestis***	**Influenza virus**
Disease	**Cholera**	**Plague**	**Influenza**

Figure 2.1 The Immune System, 3ed. (© Garland Science 2009)

Pathogens exploit different cellular and tissue environments

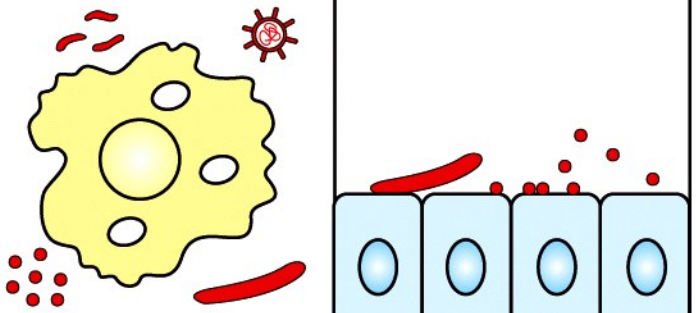
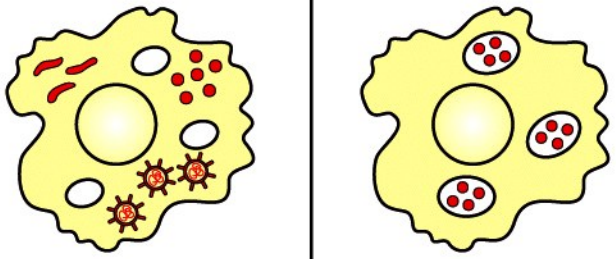
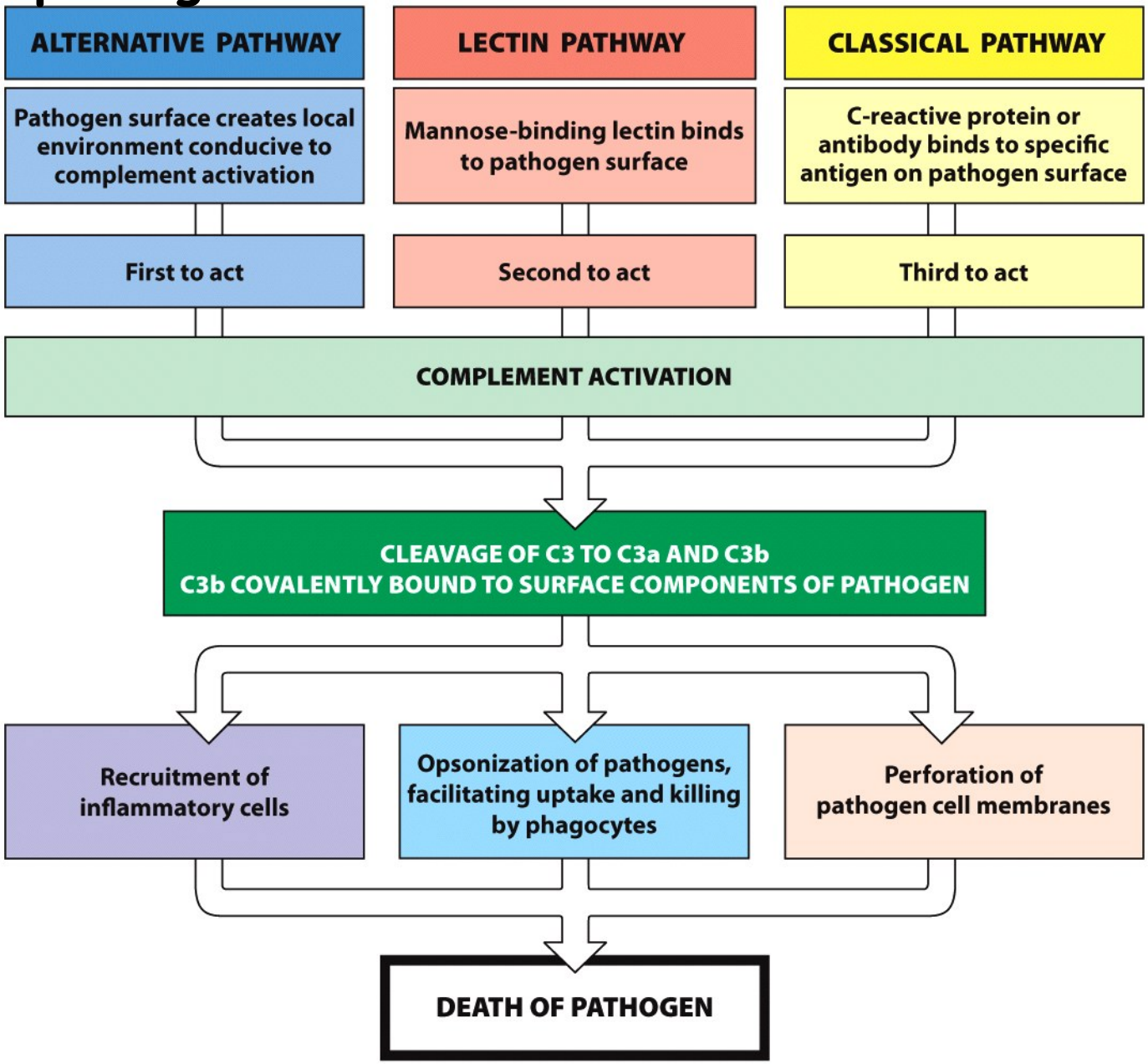
	Extracellular		Intracellular	
	Interstitial spaces, blood, lymph	Epithelial surfaces	Cytoplasmic	Vesicular
Site of infection				
Organisms	Viruses Bacteria Protozoa Fungi Worms	*Neisseria gonorrhoeae* *Candida albicans* Worms	Viruses *Listeria* Protozoa	Mycobacteria Trypanosomes *Cryptococcus neoformans*
Defense mechanism	Complement Macrophages Neutrophils	Antimicrobial peptides	NK cells	Activated macrophages

Figure 2.2 The Immune System, 3ed. (© Garland Science 2009)

Complement: a system of serum proteins that tags pathogens to facilitate their destruction.



Phagocytosis of bacteria by macrophages

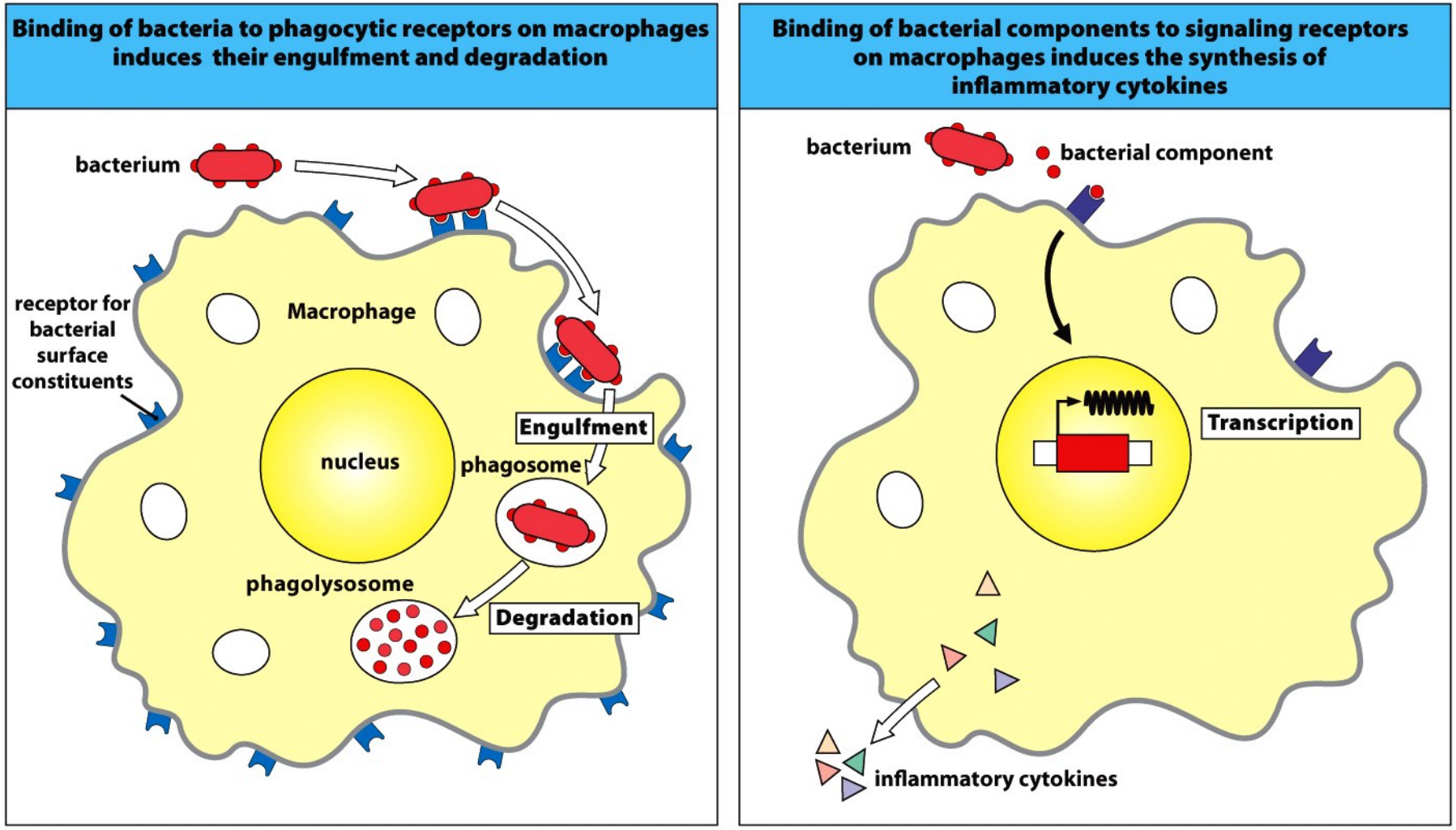


Figure 1.17 The Immune System, 3ed. (© Garland Science 2009)

Toll-like receptors recognize microbe-specific macromolecules

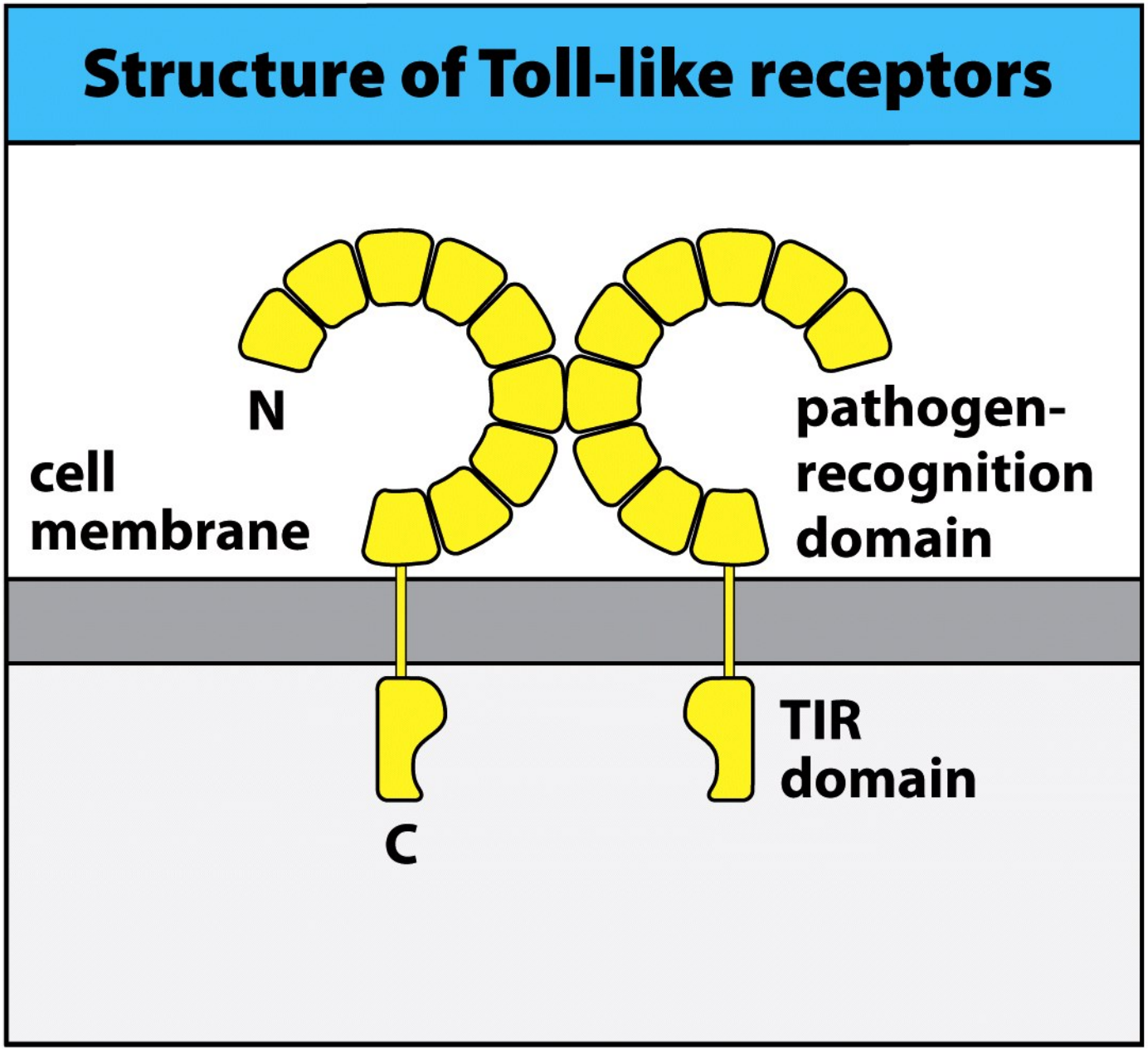


Figure 2.20 The Immune System, 3ed. (© Garland Science 2009)

Specificities of Toll-like receptors

Recognition of microbial products through Toll-like receptors				
Receptor	**Ligands**	**Microorganisms recognized**	**Cells carrying receptor**	**Cellular location of receptor**
TLR1:TLR2 heterodimer	Lipopeptides	Bacteria	Monocytes, dendritic cells, eosinophils, basophils, mast cells	Plasma membrane
	GPI	Parasites e.g., trypanosomes		
TLR2:TLR6 heterodimer	Lipoteichoic acid	Gram-positive bacteria		Plasma membrane
	Zymosan	Yeasts (fungi)		
TLR3	Double-stranded viral RNA	Viruses e.g., West Nile virus	NK cells	Endosomes
TLR4:TLR4 homodimer	Lipopolysaccharide	Gram-negative bacteria	Macrophages, dendritic cells, mast cells, eosinophils	Plasma membrane
TLR5	Flagellin	Motile bacteria having a flagellum	Intestinal epithelium	Plasma membrane
TLR7	Single-stranded viral RNAs	Viruses e.g., human immunodeficiency virus (HIV)	Plasmacytoid dendritic cells, NK cells, eosinophils, B cells	Endosomes
TLR8	Single-stranded viral RNAs	Viruses e.g., influenza	NK cells	Endosomes
TLR9	Unmethylated CpG-rich DNA	Bacteria Viruses e.g., herpes viruses	Plasmacytoid dendritic cells, B cells, eosinophils, basophils	Endosomes
TLR10 homodimer and heterodimers with TLR1 and 2	Unknown		Plasmacytoid dendritic cells, basophils, eosinophils, B cells	Unknown

Figure 2.21 The Immune System, 3ed. (© Garland Science 2009)

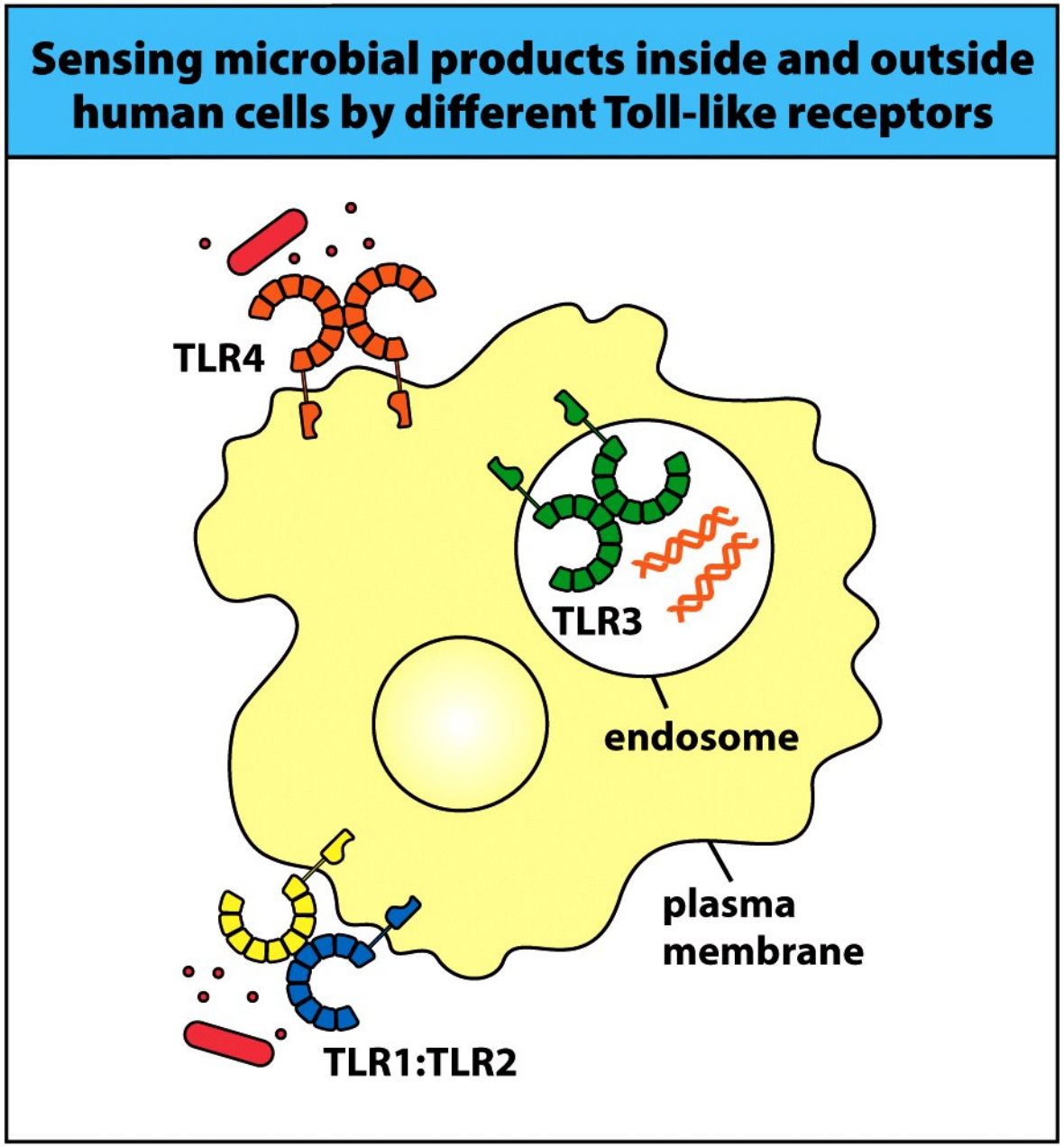


Figure 2.22 The Immune System, 3ed. (© Garland Science 2009)

On detecting infection macrophages orchaestrate a state of inflammation

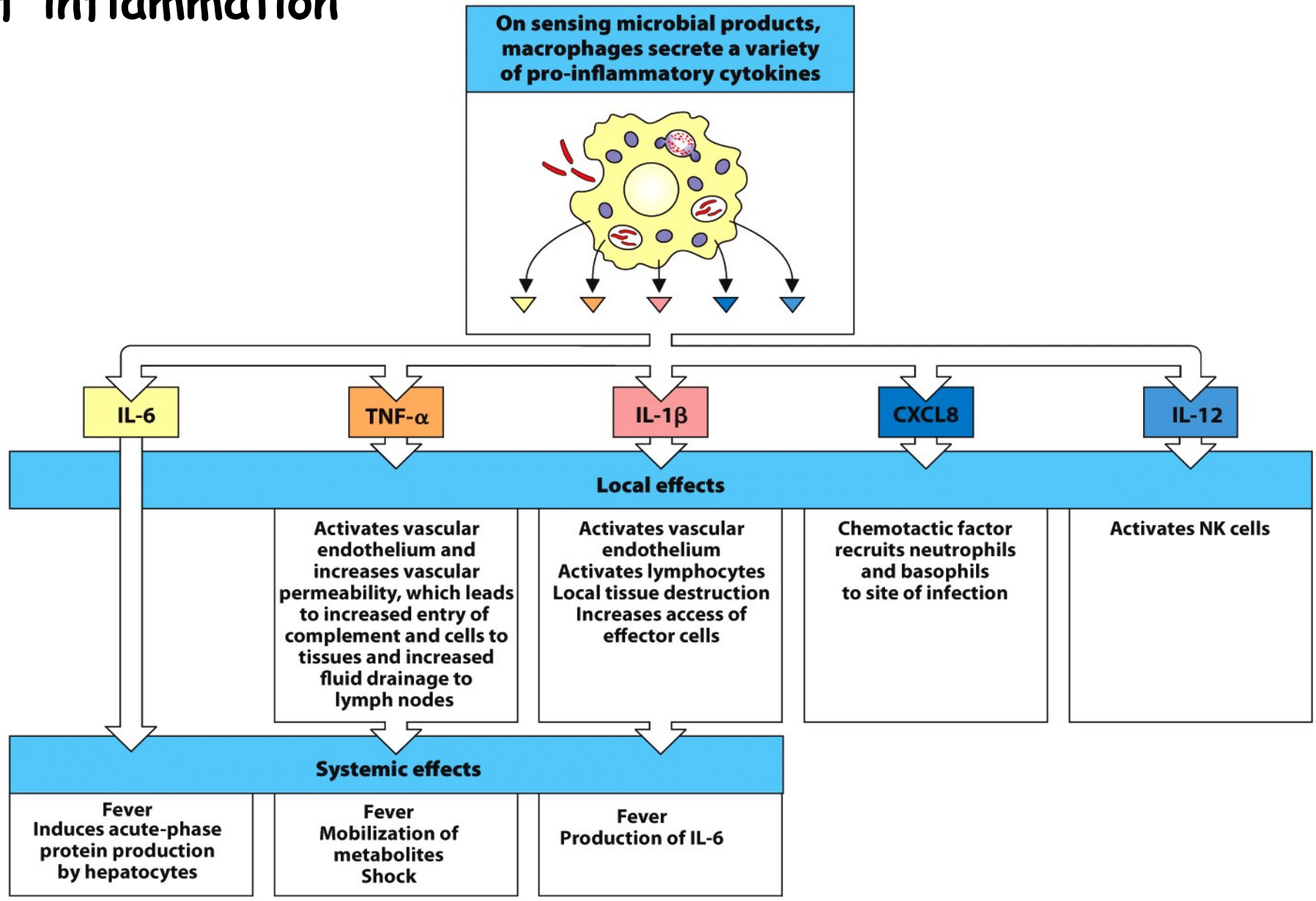


Figure 2.27 The Immune System, 3ed. (© Garland Science 2009)

Neutrophils are stock-piled in the bone marrow awaiting the call for inflammation

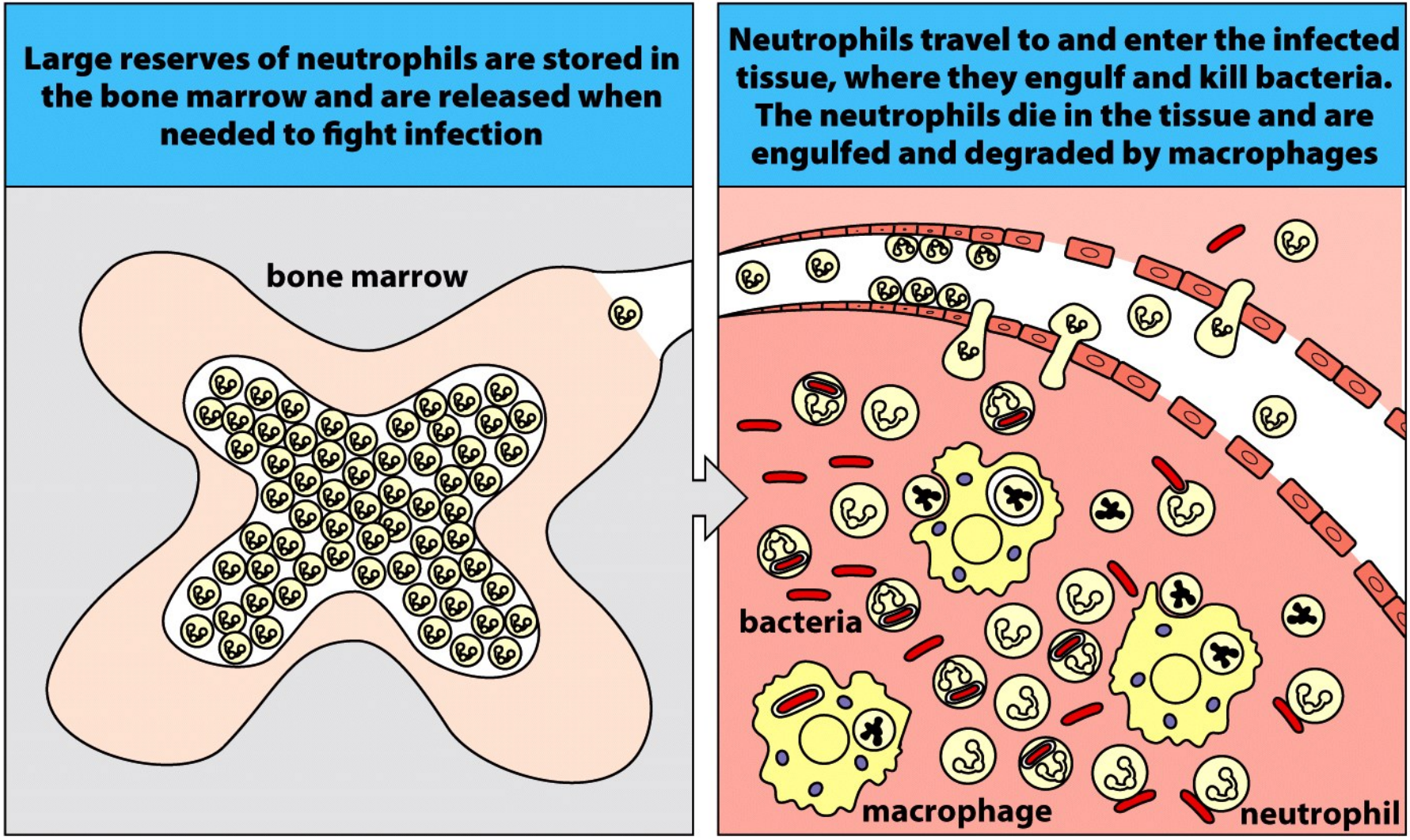


Figure 1.16 The Immune System, 3ed. (© Garland Science 2009)

Recruitment of neutrophils from blood to the infected tissue

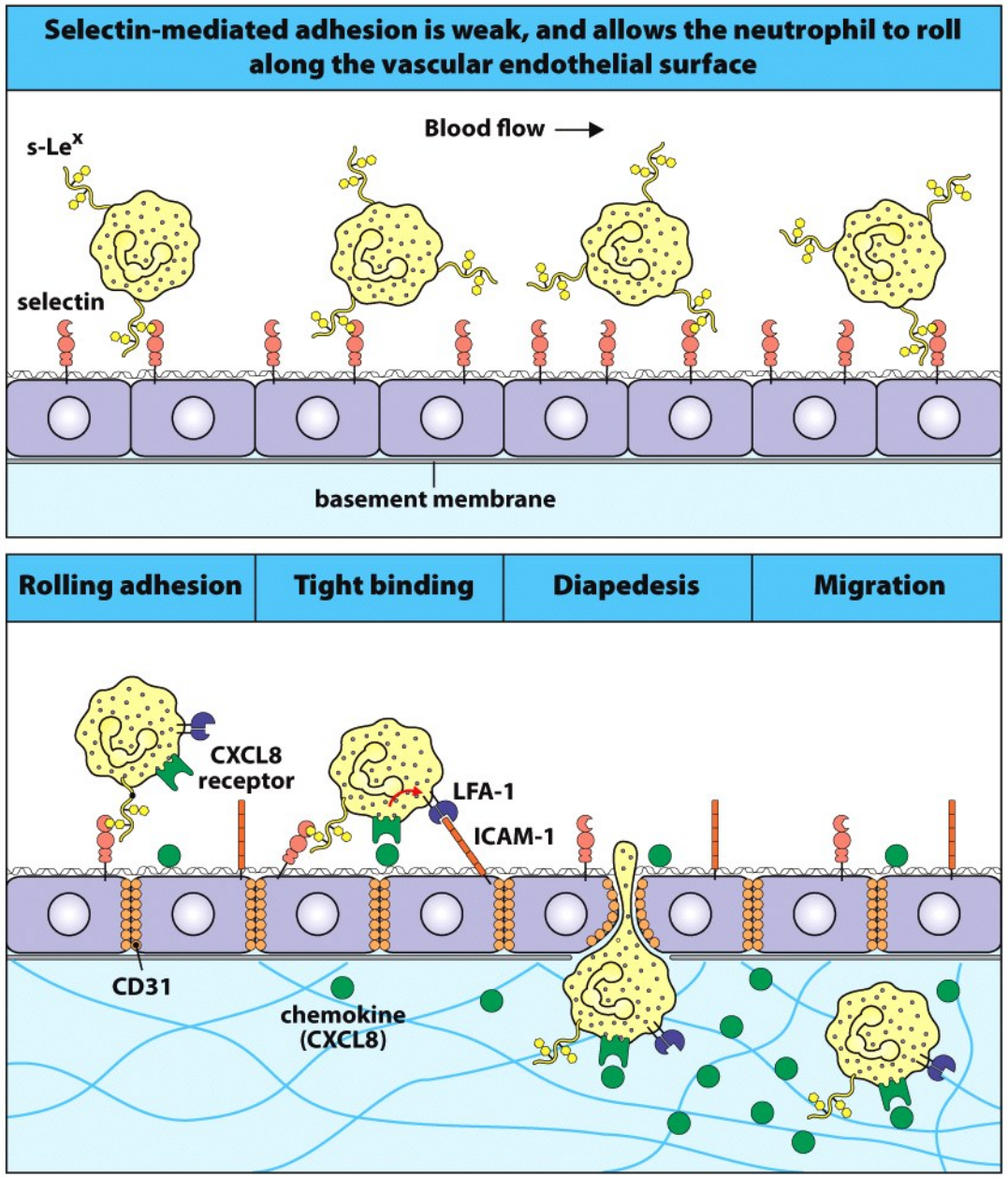
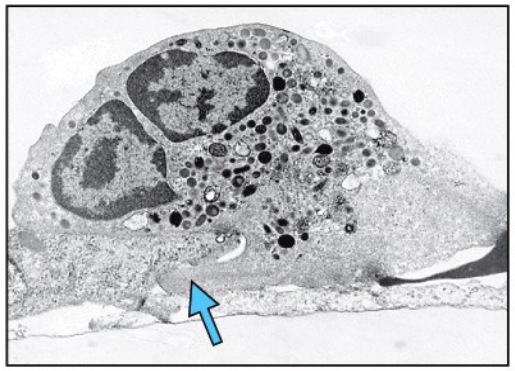


Figure 2.31 The Immune System, 3ed. (© Garland Science 2009)



Recognition, endocytosis and destruction of bacteria by neutrophils

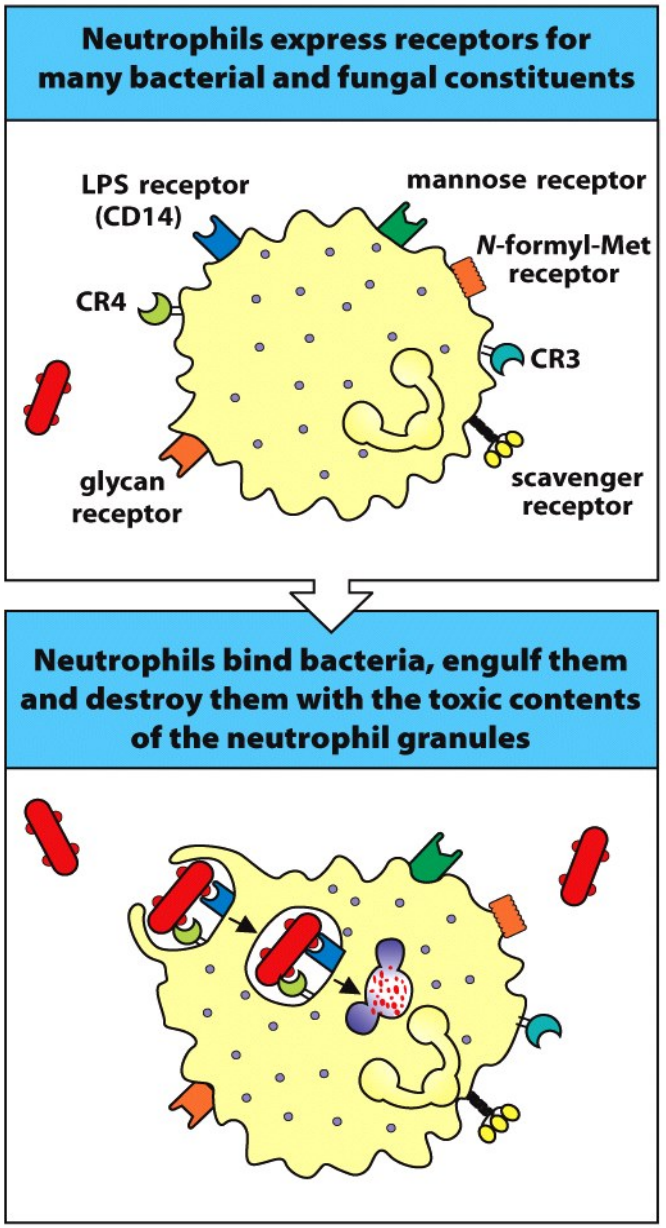


Figure 2.32 The Immune System, 3ed. (© Garland Science 2009)

Neutrophils are potent, short lived and die on the battlefield

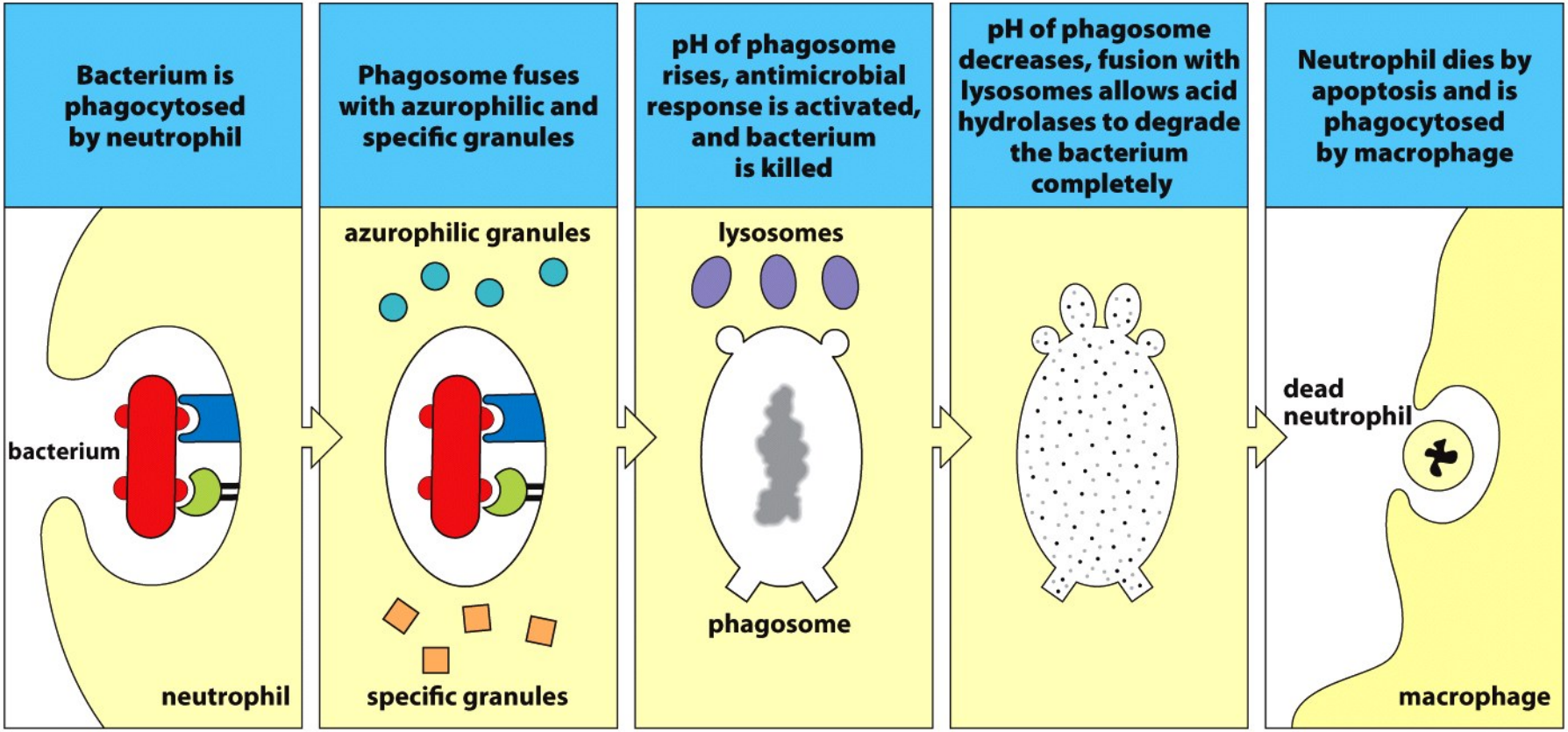


Figure 2.33 The Immune System, 3ed. (© Garland Science 2009)

Recruitment of natural killer (NK) cells to sites of infection

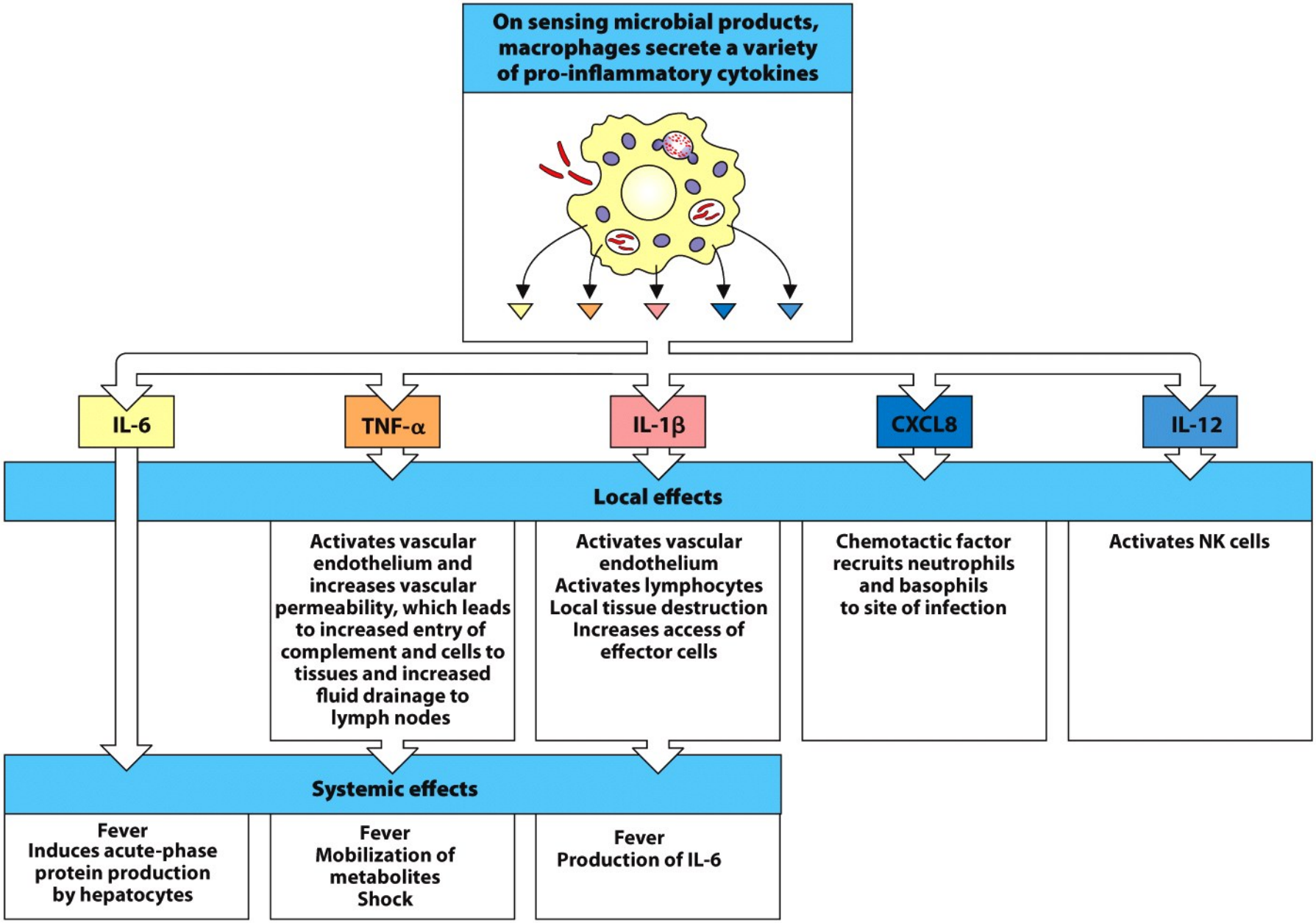


Figure 2.27 The Immune System, 3ed. (© Garland Science 2009)

NK cells are active in defense against virus infection

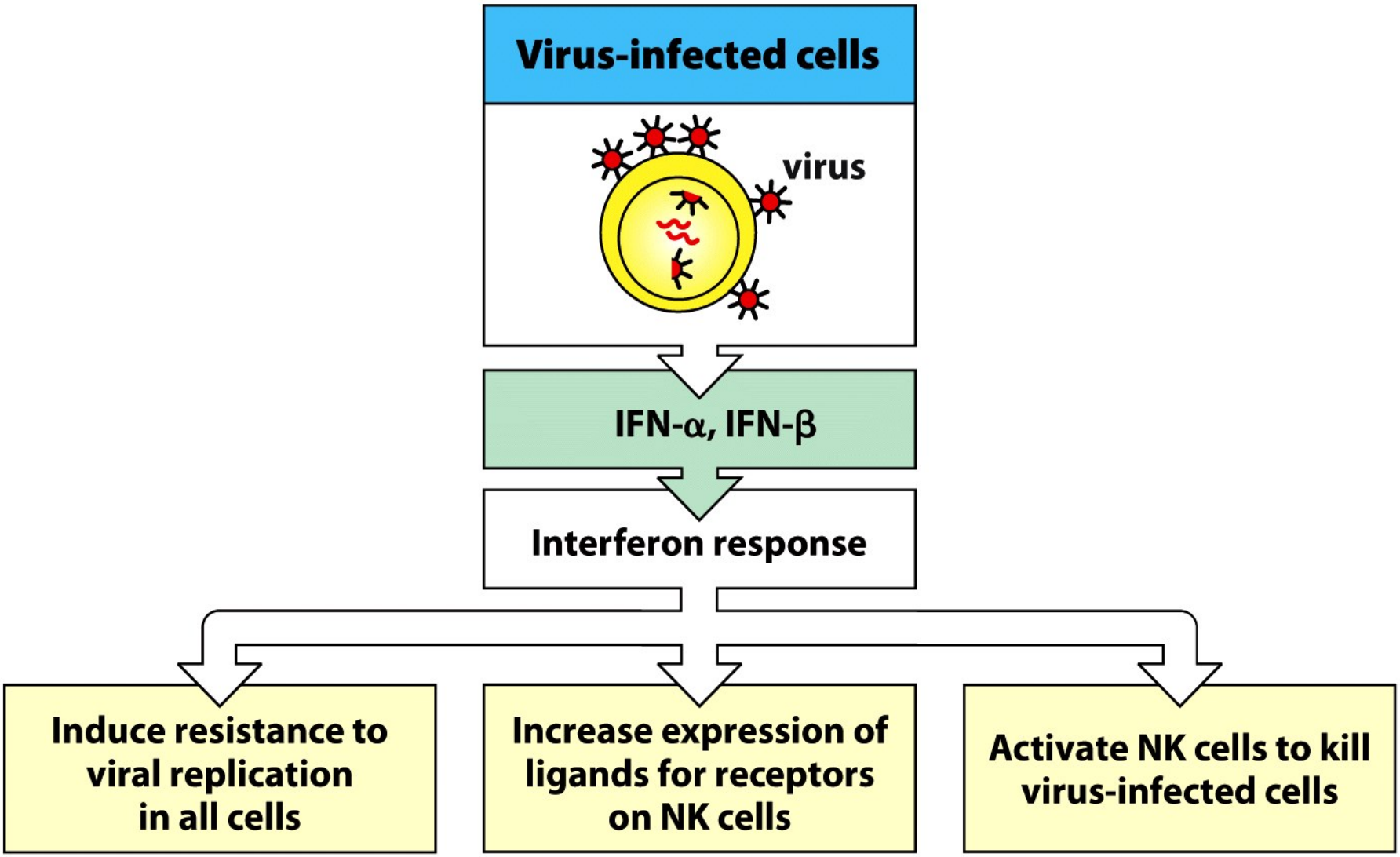


Figure 2.45 The Immune System, 3ed. (© Garland Science 2009)

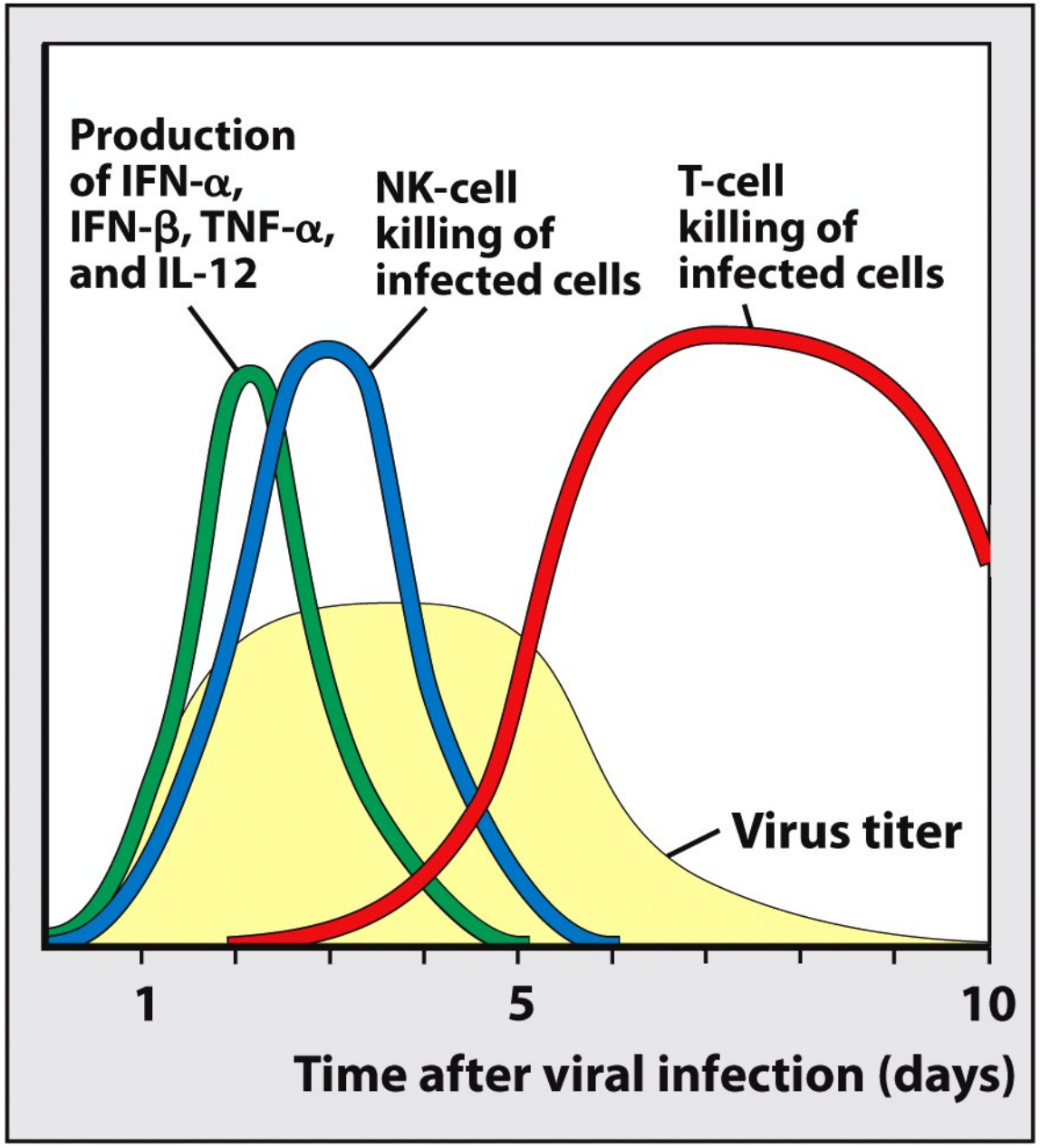


Figure 2.47 The Immune System, 3ed. (© Garland Science 2009)

NK cells recognize perturbation in HLA class I

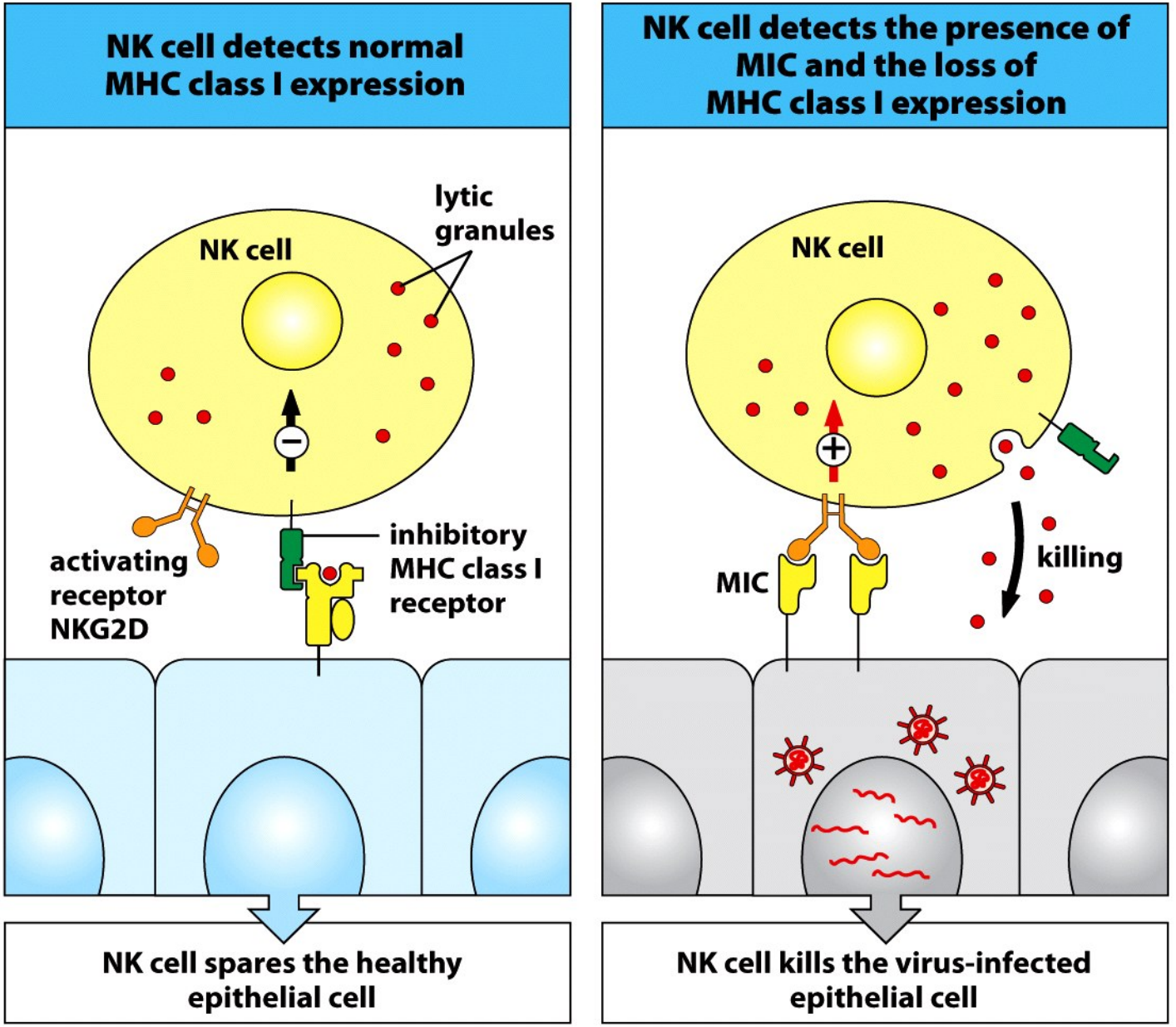


Figure 10.34 The Immune System, 3ed. (© Garland Science 2009)

NK cell receptors for HLA class I are encoded in two genomic complexes

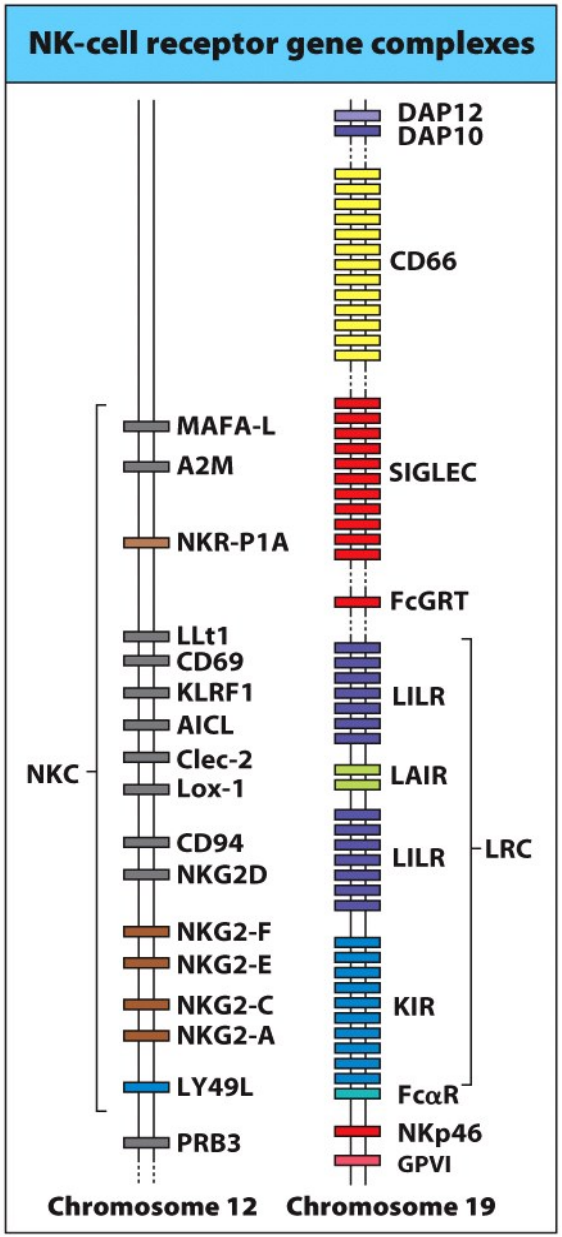


Figure 10.33 The Immune System, 3ed. (© Garland Science 2009)

Inhibitory NK-cell receptors for MHC class I	
Receptor	**Ligand**
CD94:NKG2A	Complexes of HLA-E with peptides derived from the leader peptides of HLA-A, -B, and -C
KIR2DL1	HLA-C allotypes having lysine at position 80
KIR2DL2/3	HLA-C allotypes having asparagine at position 80
KIR3DL1	HLA-A and HLA-B allotypes having the Bw4 serological epitope determined by sequence motifs at positions 77–83
KIR3DL2	Complexes of HLA-A3 and HLA-A11 with a specific peptide from Epstein–Barr virus
LILRB1	All HLA class I

Figure 10.37 The Immune System, 3ed. (© Garland Science 2009)

Killer cell immunoglobulin-like receptors (KIR)

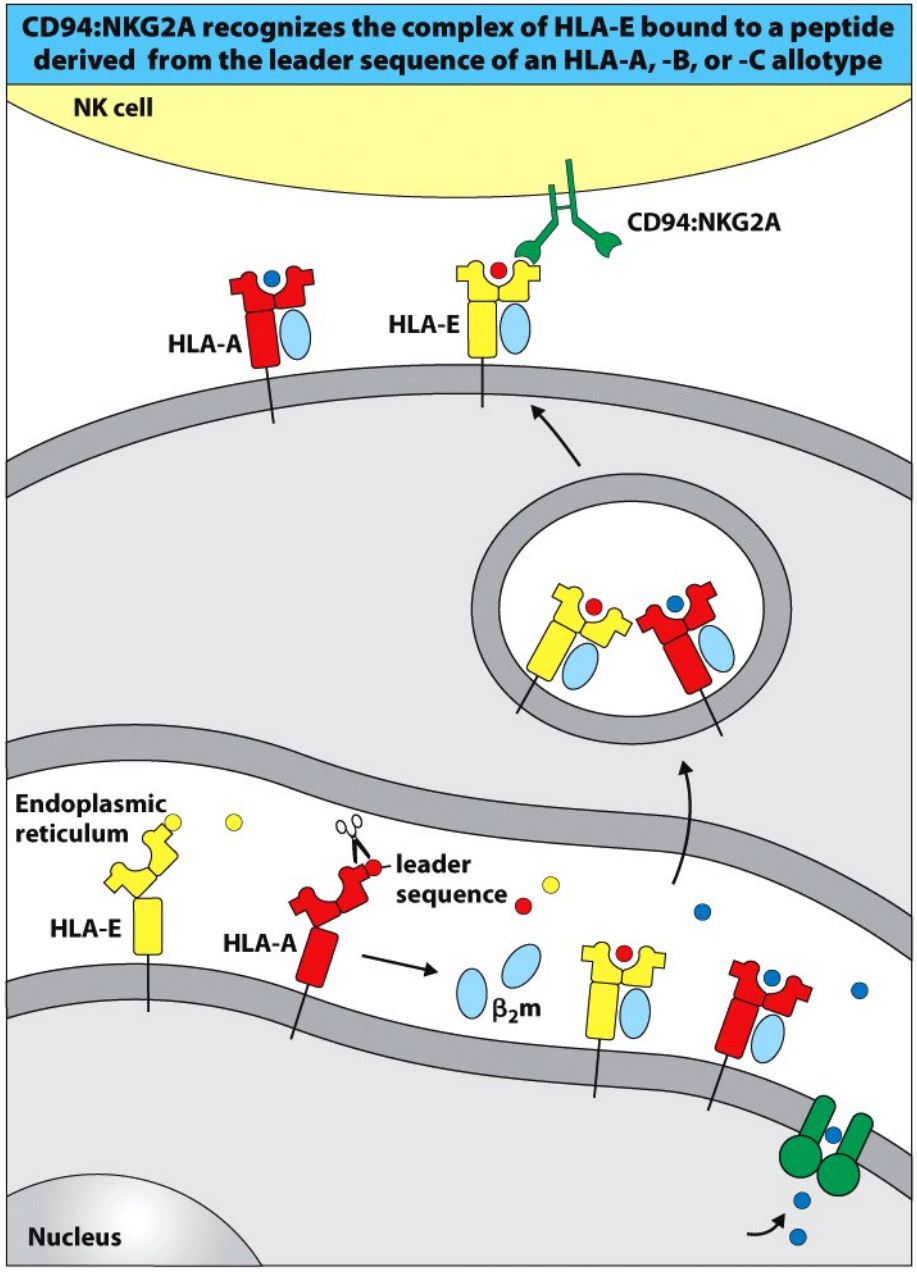
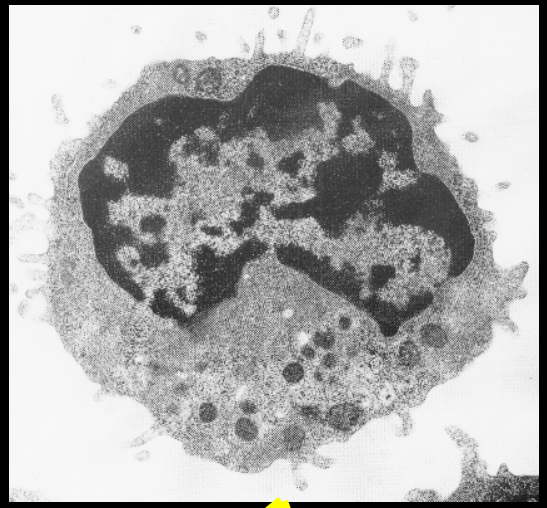


Figure 10.35 The Immune System, 3ed. (© Garland Science 2009)

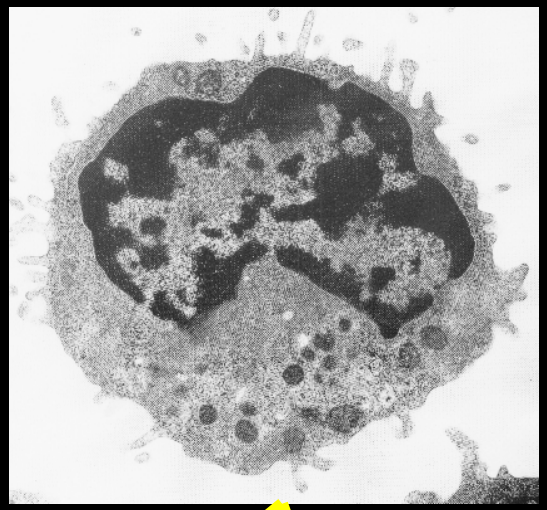
Functions of Natural Killer (NK) cells



Immune system

Reproductive system

Functions of Natural Killer (NK) cells



Immune system

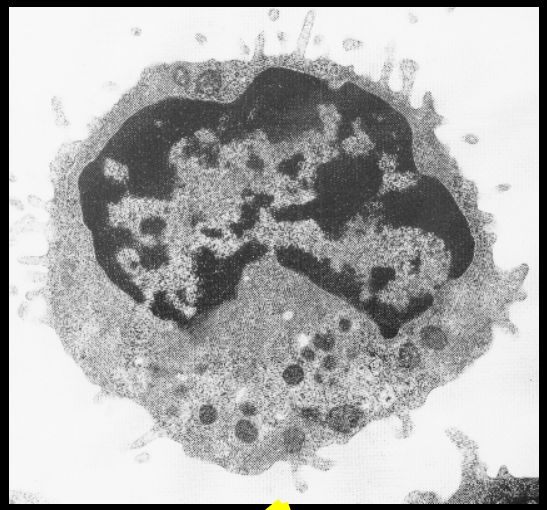
Kill virus-infected cells

and cancerous cells.

Co-operate with dendritic cells

Reproductive system

Functions of Natural Killer (NK) cells



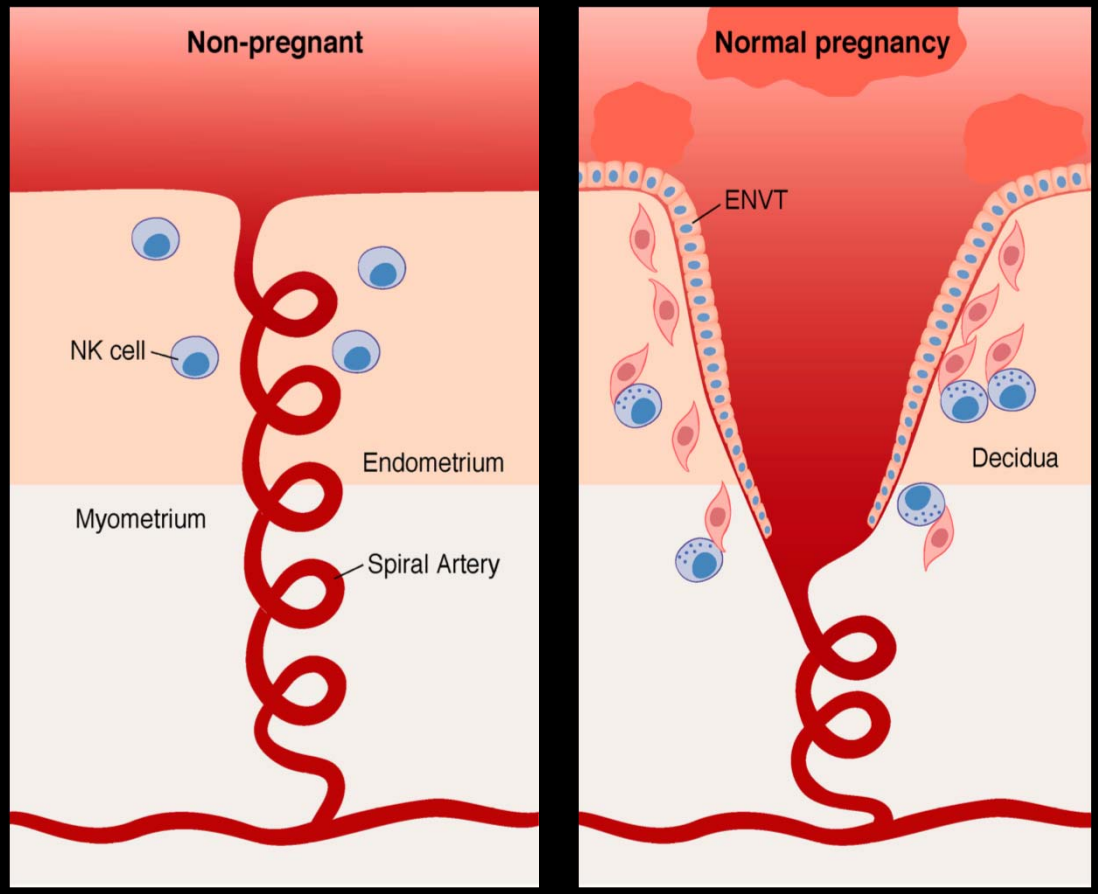
Immune system

Kill virus-infected cells
and cancerous cells.
Co-operate with dendritic cells

Reproductive system

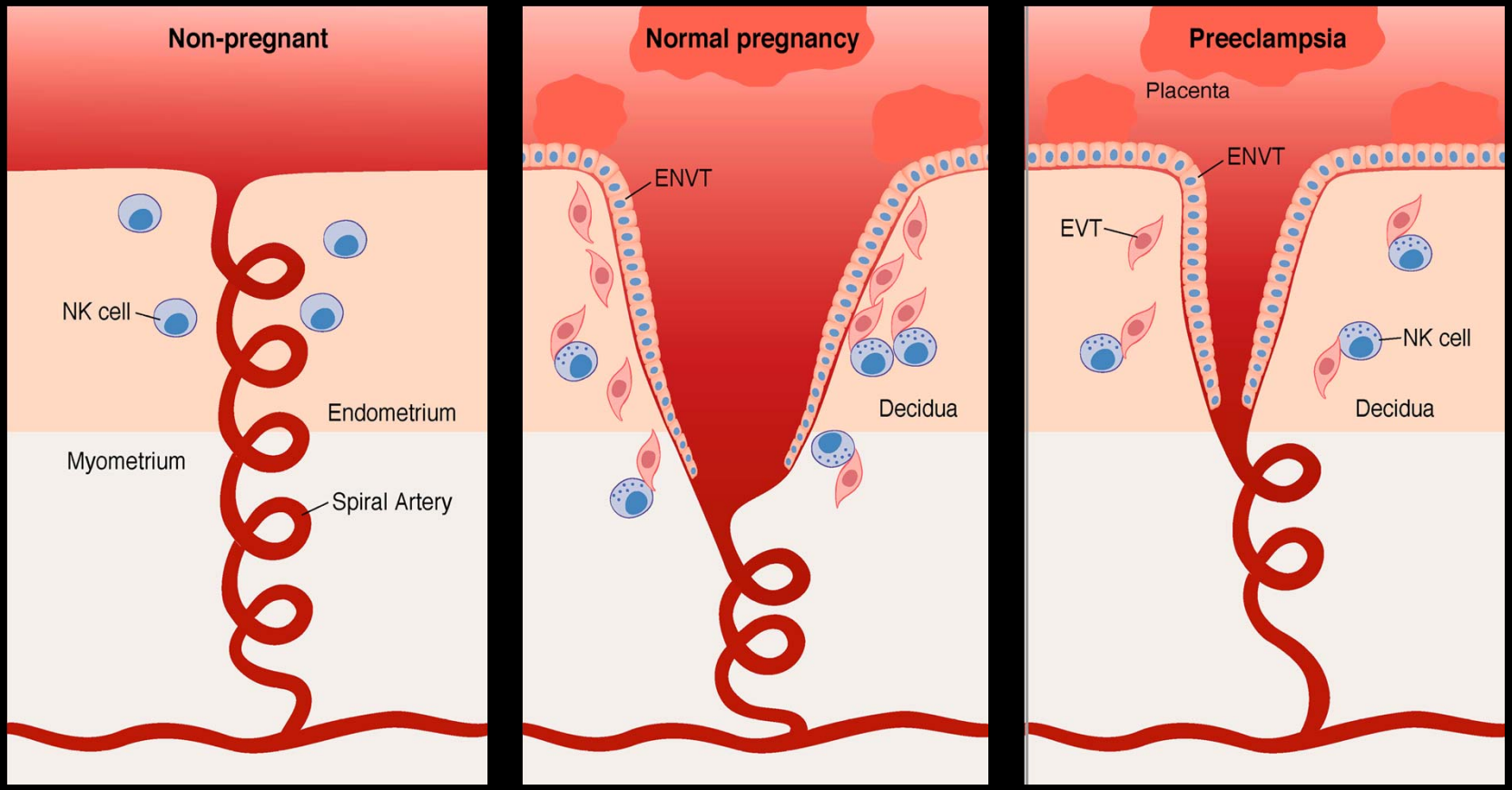
Maternal uterine NK cells co-operate with fetal extra-villous trophoblast to widen maternal arteries supplying blood to the placenta.

Interactions between fetal trophoblast and maternal uterine NK cells remodel the spiral arteries



after Ashley Moffett

Preeclampsia and other disorders of pregnancy are associated with insufficient remodeling of the spiral arteries



What happens when a person lacks NK cells?