

# Johns Hopkins Engineering

## Immunoengineering

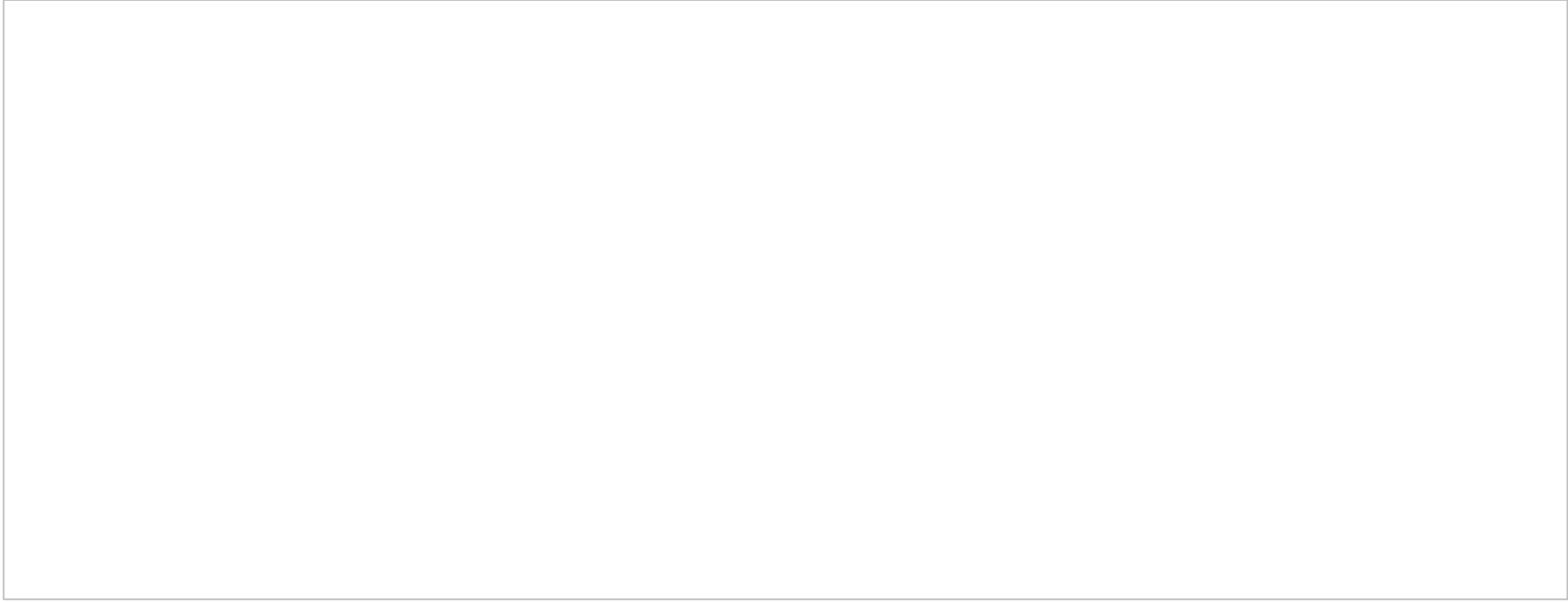
Module 2/Lecture 2C

**Immune Response to Pathogens: Cells of the Innate Immune System**

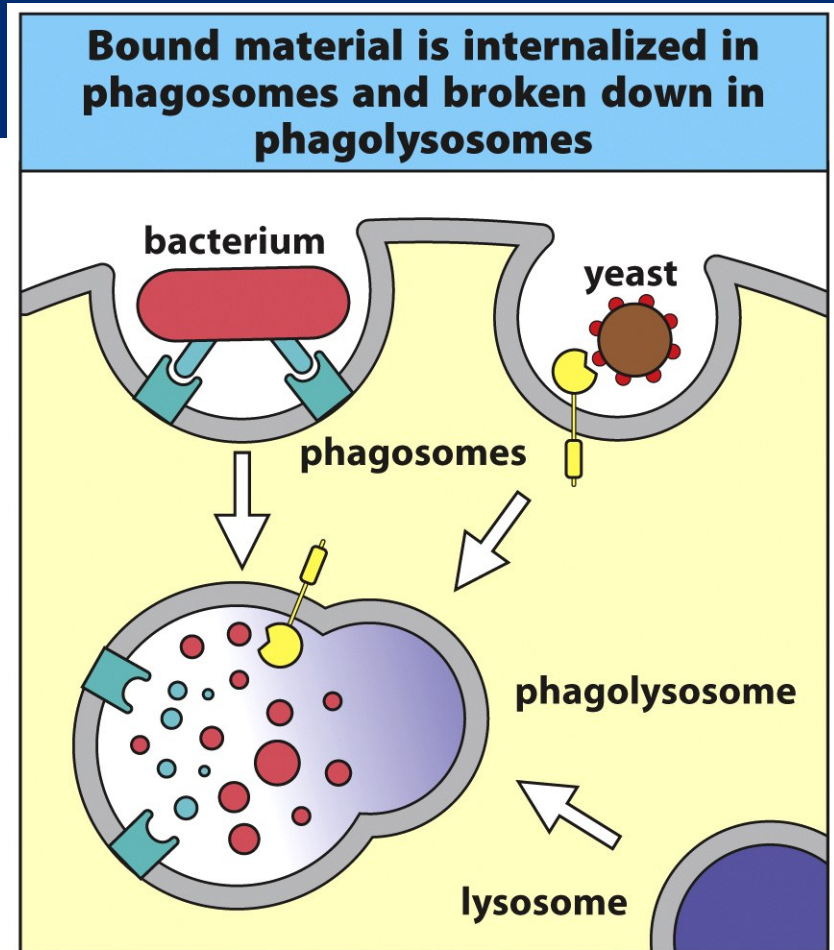


JOHNS HOPKINS  
WHITING SCHOOL  
of ENGINEERING

# This is war!



# Phagocytosis



# Video of Chemotaxis and Phagocytosis

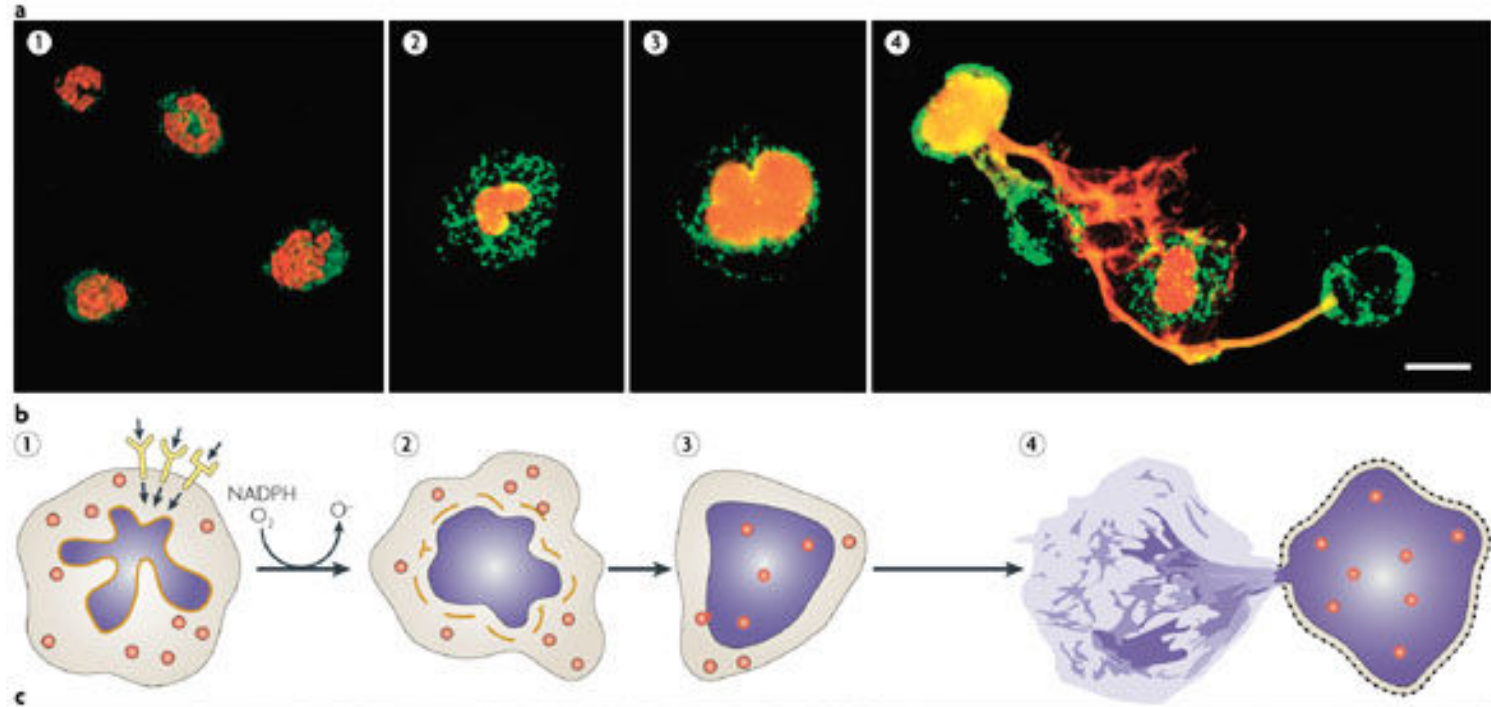
<https://www.youtube.com/watch?v=JnIULOjUhSQ>

# Degranulation

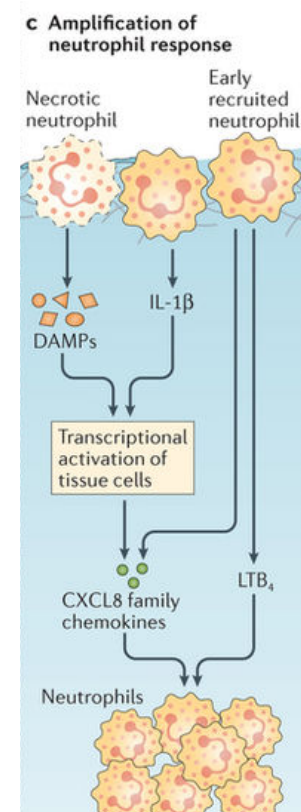
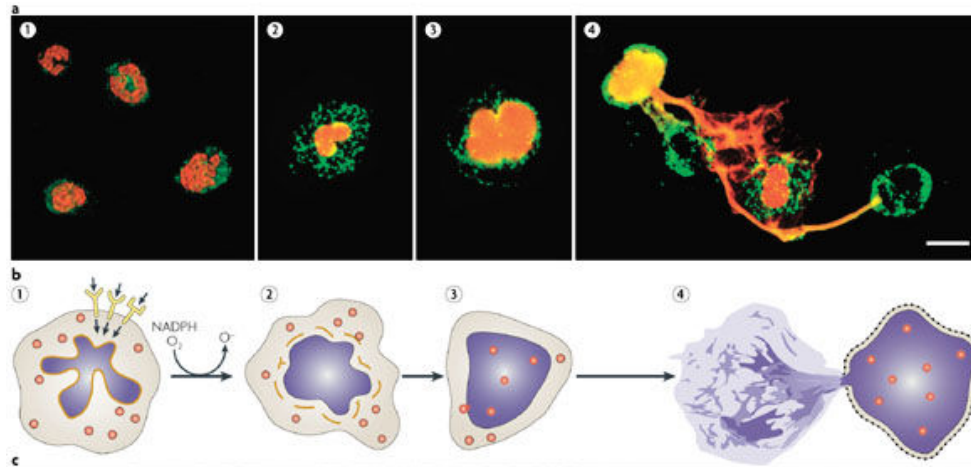
Antimicrobial mechanisms of phagocytes		
Class of mechanism	Macrophage products	Neutrophil products
Acidification	pH $\approx$ 3.5–4.0, bacteriostatic or bactericidal	
Toxic oxygen-derived products	Superoxide O <sub>2</sub> <sup>-</sup> , hydrogen peroxide H <sub>2</sub> O <sub>2</sub> , singlet oxygen <sup>1</sup> O <sub>2</sub> <sup>*</sup> , hydroxyl radical <sup>*</sup> OH, hypohalite OCl <sup>-</sup>	
Toxic nitrogen oxides	Nitric oxide NO	
Antimicrobial peptides	Cathelicidin, macrophage elastase-derived peptide	$\alpha$ -Defensins (HNP1–4), $\beta$ -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 <sup>2+</sup> ), vitamin B <sub>12</sub> -binding protein

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

# Neutrophil Extracellular Traps



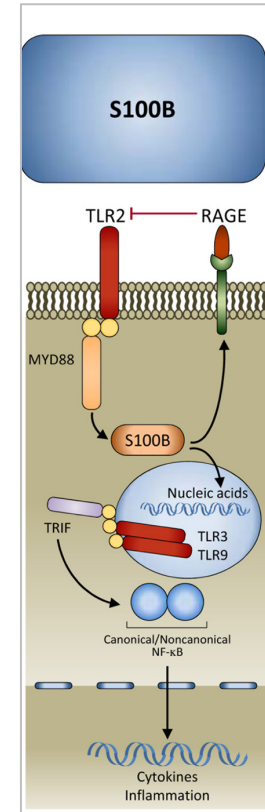
# Danger-associated Molecular Patterns—DAMPs



# Danger-associated Molecular Patterns—DAMPs

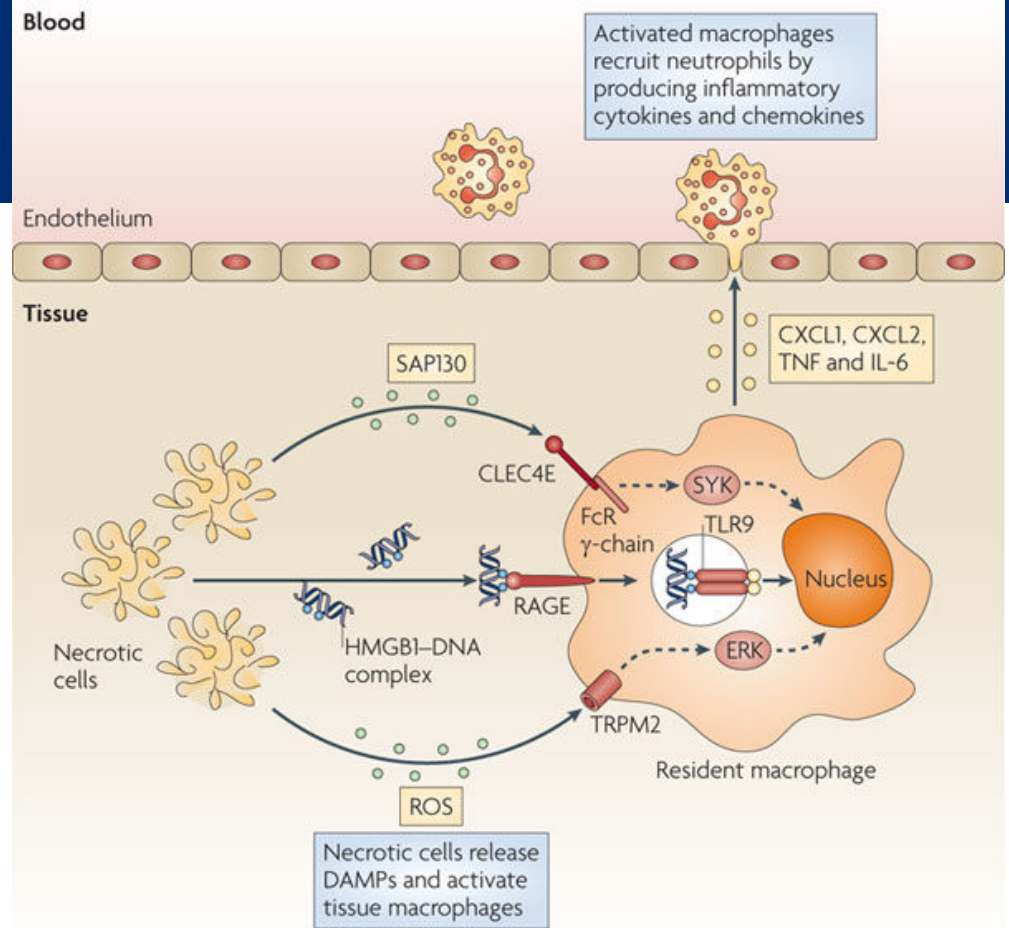
**Table 1** List of recognized DAMPs

Intracellular location	DAMPs	Receptors
Nucleus	Histones	TLR 2, 4, 9
	Genomic DNA	TLR 9
	HMGB 1	TLR 2, 4, RAGE, TIM3
	IL-1 $\alpha$	IL-1R
	IL-33	ST2
Cytosol	ATP	P2Y2, P2X7
	F-actin	DNGR 1
	Cyclophilin A	CD147
	HSPs	CD91, TLR 2, 4, SREC 1, FEEL 1
	Uric acid crystals	NLRP3
	S100s	TLR 2, 4, RAGE
Mitochondria	Mitochondrial DNA	TLR 9
	Mitochondrial transcriptional factor A	RAGE, TLR 9
Endoplasmic reticulum	Calreticulin	CD91

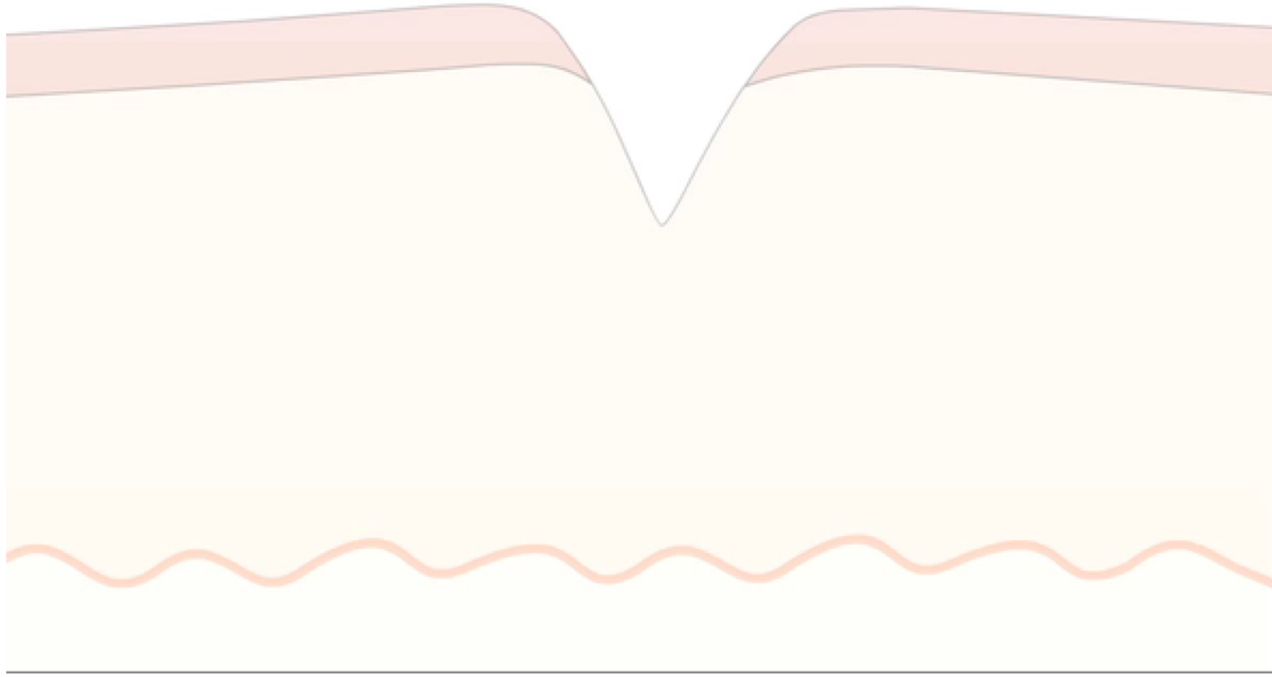




# Macrophages



# Pathogen-associated Molecular Patterns—PAMPs



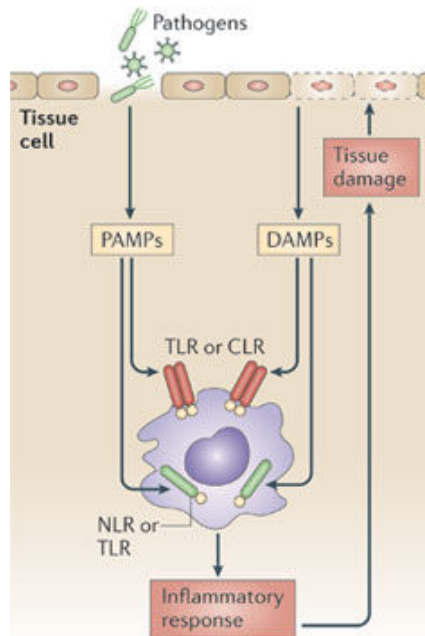
# TLRs & PAMPs

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 $\beta$ -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 ( <i>Toxoplasma gondii</i> , uropathogenic bacteria)	Macrophages, dendritic cells, liver, kidney, and bladder epithelial cells

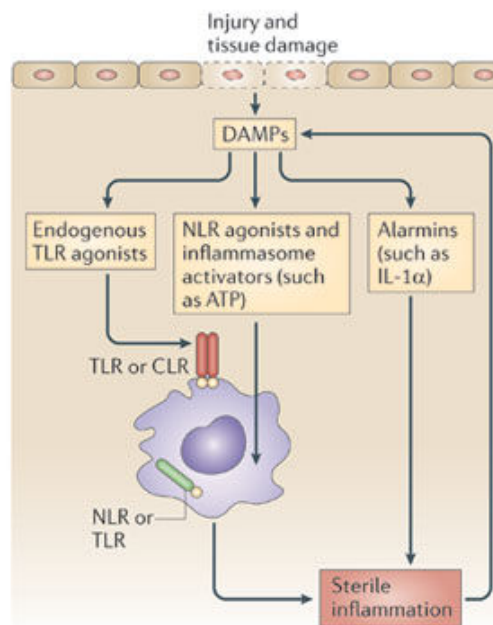
Figure 3.9 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# Innate Immunity

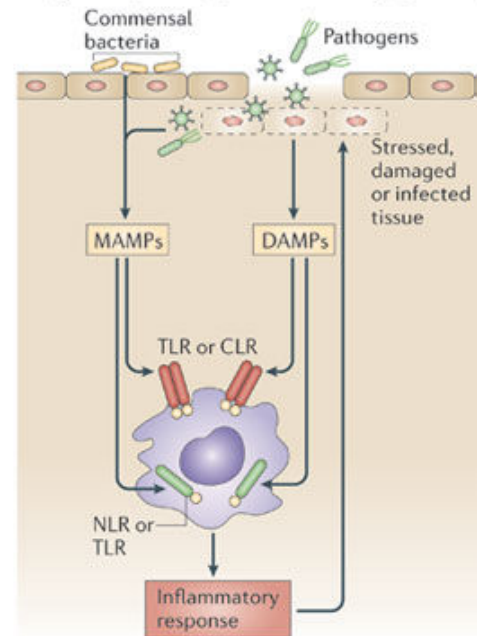
**a Infection (PAMPs)**



**b Tissue damage (DAMPs)**



**c Pathogenic and non-pathogenic micro-organisms (MAMPs) and tissue damage (DAMPs)**





JOHNS HOPKINS

WHITING SCHOOL  
*of* ENGINEERING