

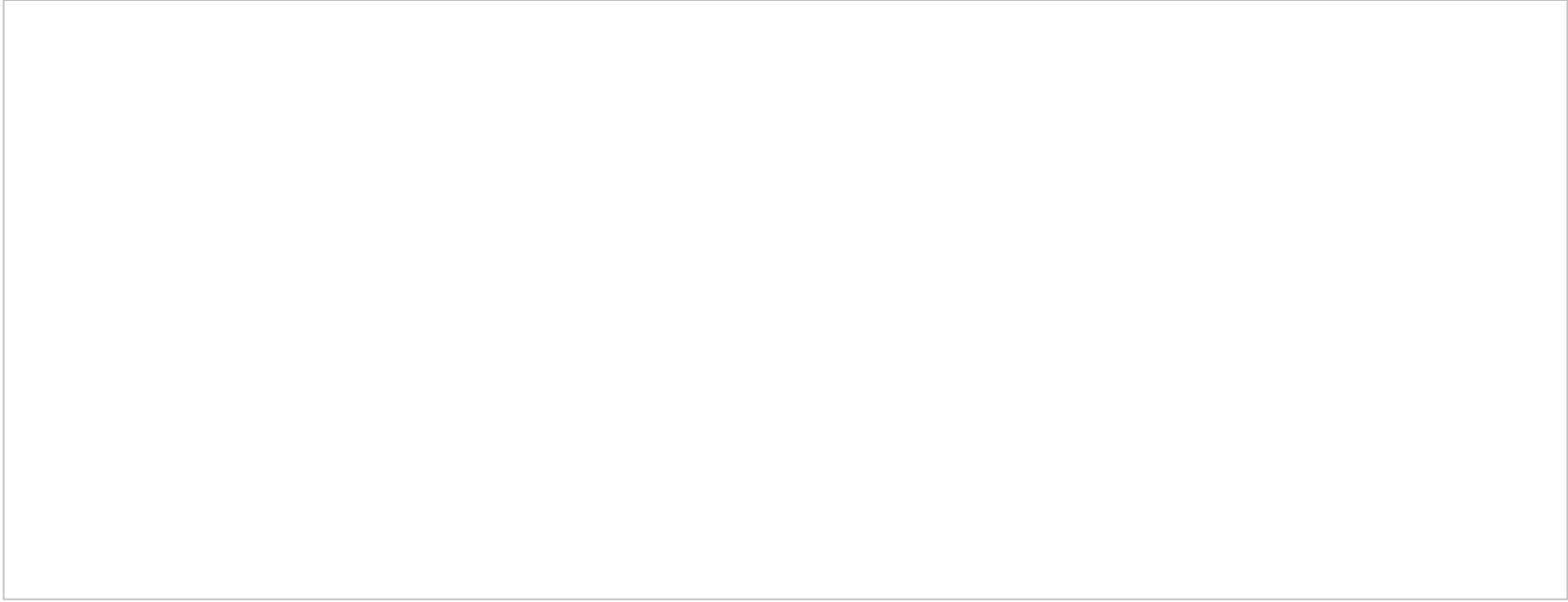
# Johns Hopkins Engineering

## Immunoengineering

Module 2/Lecture 2B

**Immune Response to Pathogens: Protein Components of the Innate  
Immune System**

# This is war!



# Complement

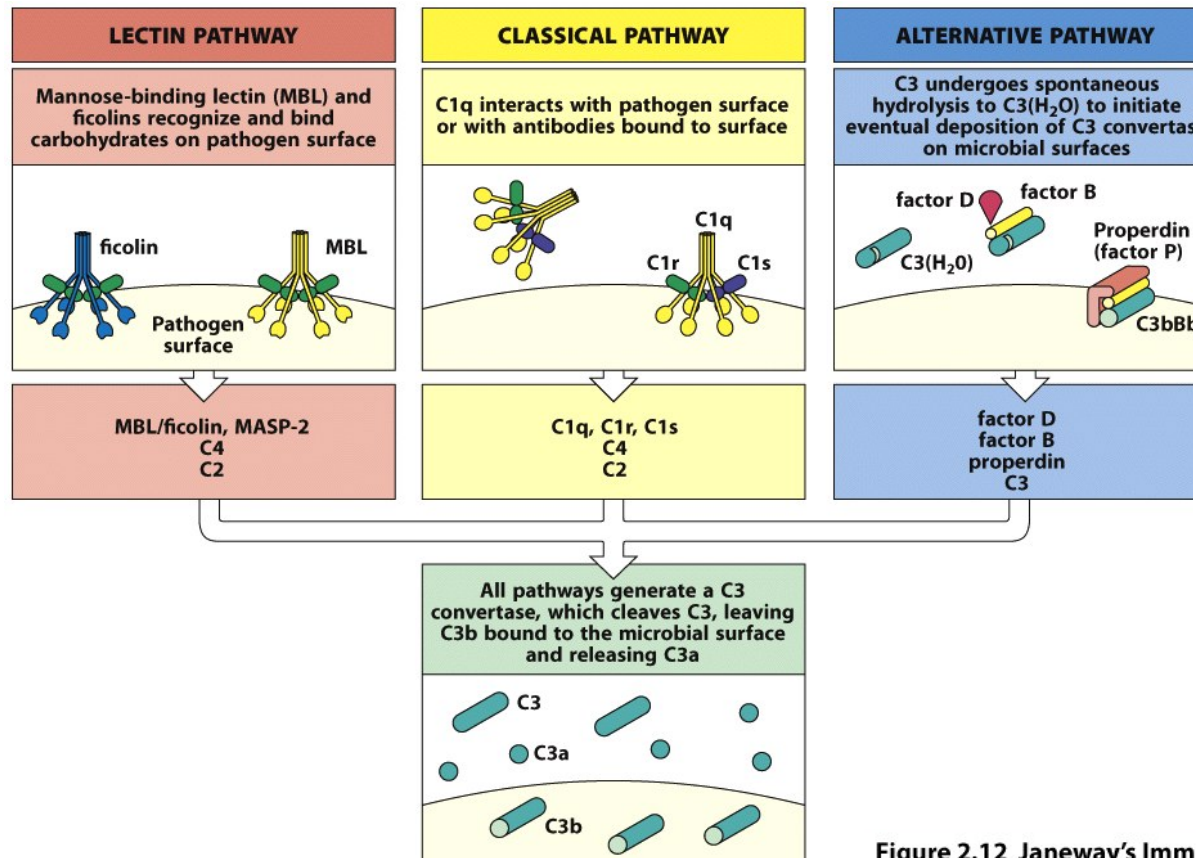


Figure 2.12 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# Complement

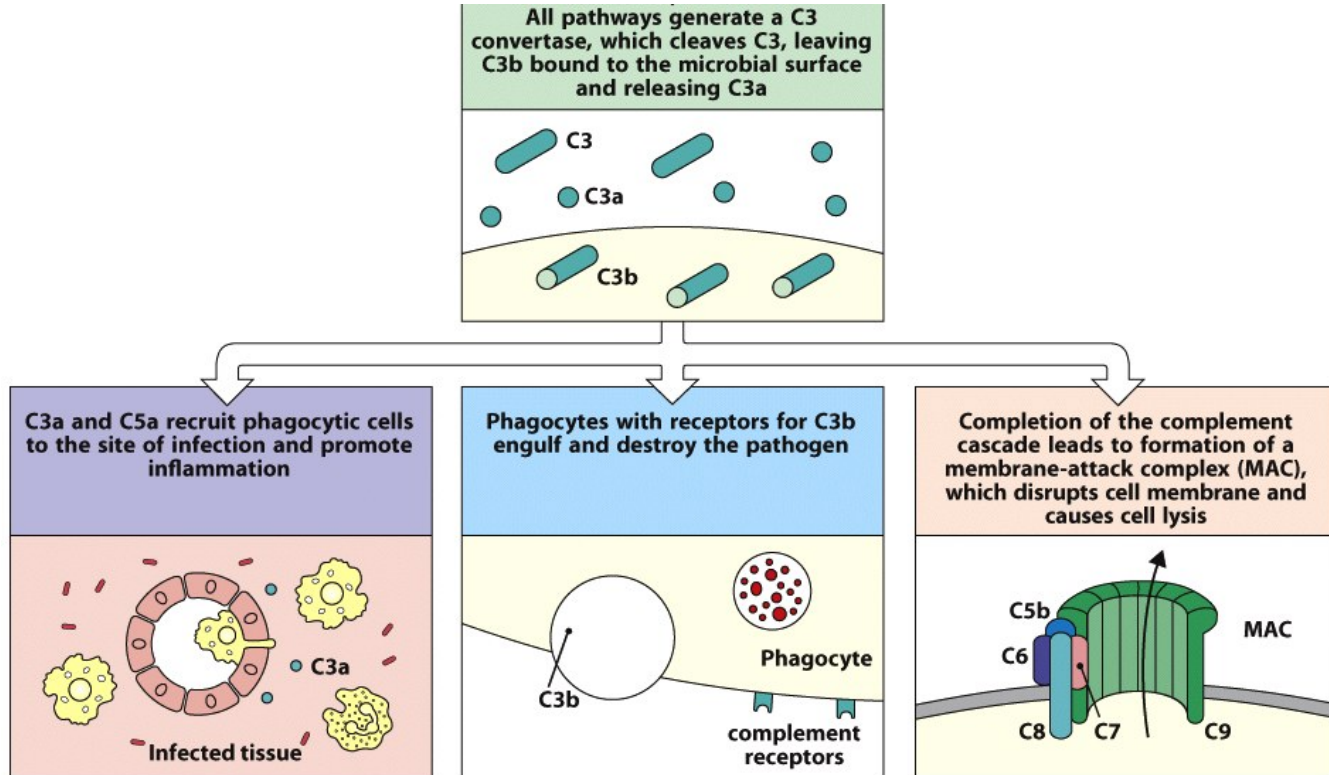


Figure 2.12 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# Question:

- What is analogous in war to the function of complement?

# Cytokines

Small proteins which provide signaling to cells and influences cell behavior

# Cytokines

Cytokine	T-cell source	Effects on					Effect of gene knockout
		B cells	T cells	Macrophages	Hemato-poietic cells	Other tissue cells	
Interleukin-2 (IL-2)	Naive, T <sub>H</sub> 1, some CD8	Stimulates growth and J-chain synthesis	Growth	–	Stimulates NK cell growth	–	↓ T-cell responses IBD
Interferon-γ (IFN-γ)	T <sub>H</sub> 1, CTL	Differentiation IgG2a synthesis (mouse)	Inhibits T <sub>H</sub> 2 cell growth	Activation, ↑ MHC class I and class II	Activates NK cells	Antiviral ↑ MHC class I and class II	Susceptible to mycobacteria, some viruses
Lymphotoxin-α (LT-α, TNF-β)	T <sub>H</sub> 1, some CTL	Inhibits	Kills	Activates, induces NO production	Activates neutrophils	Kills fibroblasts and tumor cells	Absence of lymph nodes Disorganized spleen
Interleukin-4 (IL-4)	T <sub>H</sub> 2	Activation, growth IgG1, IgE ↑ MHC class II induction	Growth, survival	Inhibits macrophage activation	↑ Growth of mast cells	–	No T <sub>H</sub> 2
Interleukin-5 (IL-5)	T <sub>H</sub> 2	Mouse: Differentiation IgA synthesis	–	–	↑ Eosinophil growth and differentiation	–	Reduced eosinophilia
Interleukin-10 (IL-10)	T <sub>H</sub> 2 (human: some T <sub>H</sub> 1), T <sub>reg</sub>	↑ MHC class II	Inhibits T <sub>H</sub> 1	Inhibits cytokine release	Co-stimulates mast cell growth	–	IBD
Interleukin-3 (IL-3)	T <sub>H</sub> 1, T <sub>H</sub> 2 some CTL	–	–	–	Growth factor for progenitor hematopoietic cells (multi-CSF)	–	–
Tumor necrosis factor-α (TNF-α)	T <sub>H</sub> 1, some T <sub>H</sub> 2 some CTL	–	–	Activates, induces NO production	–	Activates microvascular endothelium	Susceptibility to Gram –ve sepsis
Granulocyte-macrophage colony-stimulating factor (GM-CSF)	T <sub>H</sub> 1, some T <sub>H</sub> 2 some CTL	Differentiation	Inhibits growth?	Activation Differentiation to dendritic cells	↑ Production of granulocytes and macrophages (myelopoiesis) and dendritic cells	–	–
Transforming growth factor-β (TGF-β)	CD4 T cells (T <sub>reg</sub> )	Inhibits growth IgA switch factor	Inhibits growth, promotes survival	Inhibits activation	Activates neutrophils	Inhibits/ stimulates cell growth	Death at ~10 weeks
Interleukin-17 (IL-17)	CD4 T cells (T <sub>H</sub> 17) macrophages	–	–	–	Stimulates neutrophil recruitment	Stimulates fibroblasts and epithelial cells to secrete chemokines	–

Figure 9.34 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# Example of Cytokine Function

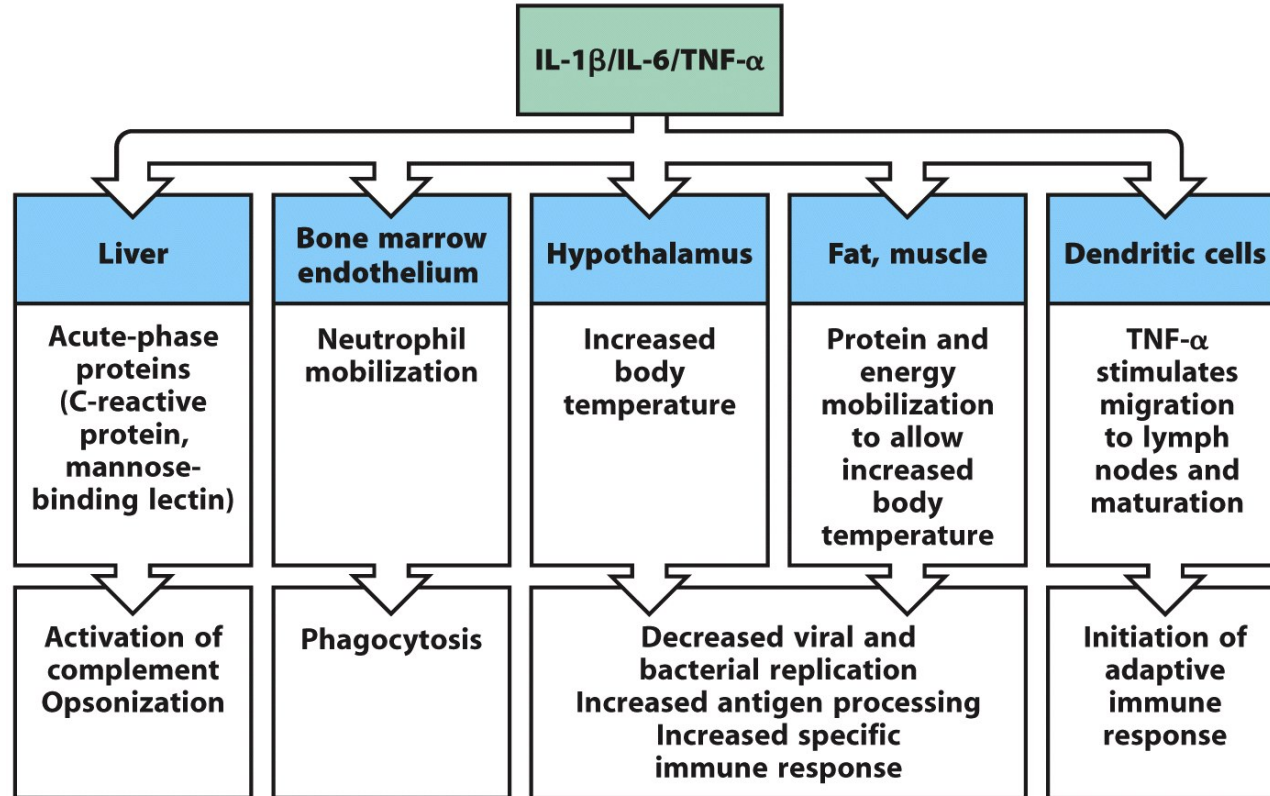


Figure 3.27 Janeway's Immunobiology, 8ed. (© Garland Science 2012)



# Chemokines

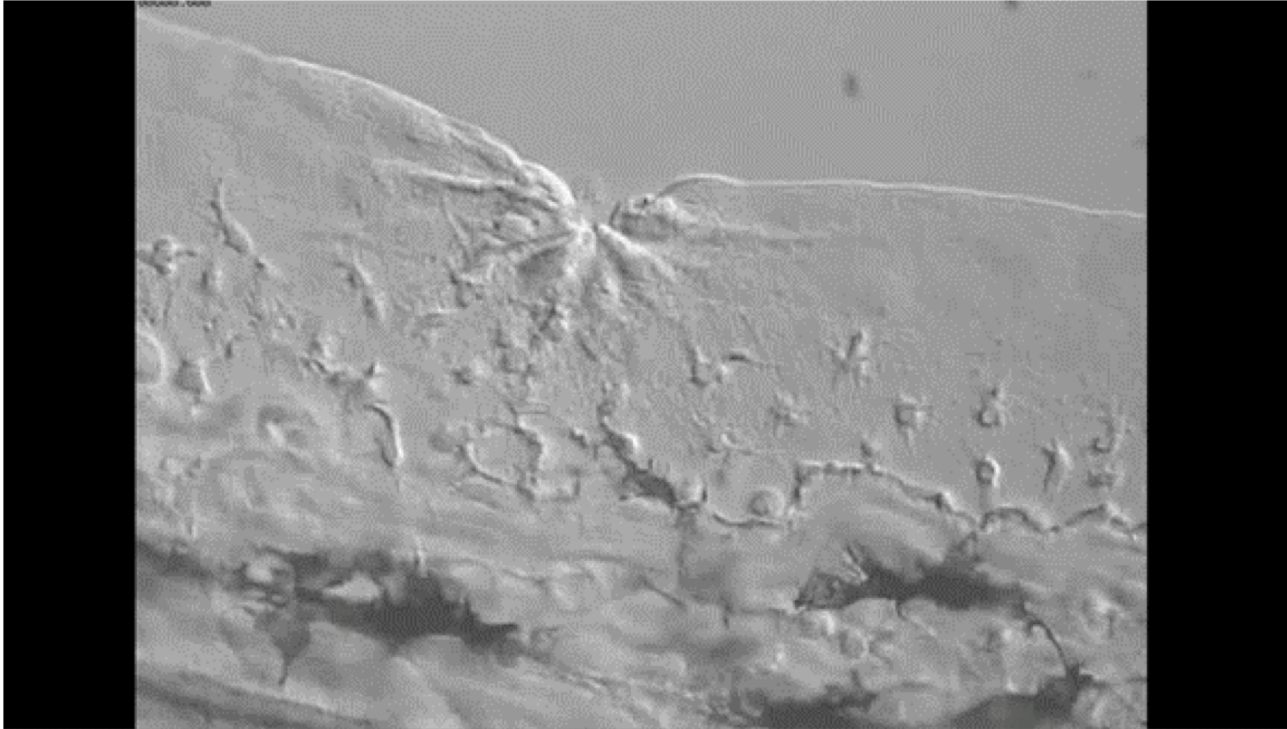
Subset of cytokines responsible for inducing cell migration

# Chemokines

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, $\beta$ -TG, NAP-2)	Platelets	CXCR2	Neutrophils	Activates neutrophils Clot resorption Angiogenesis
	CXCL1 (GRO $\alpha$ ) CXCL2 (GRO $\beta$ ) CXCL3 (GRO $\gamma$ )	Monocytes Fibroblasts Endothelium	CXCR2	Neutrophils Naive T cells Fibroblasts	Activates neutrophils Fibroplasia Angiogenesis
CC	CCL3 (MIP-1 $\alpha$ )	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 <sub>H</sub> 1 immunity
	CCL4 (MIP-1 $\beta$ )	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 <sub>H</sub> 2 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 <sub>3</sub> C)	CX3CL1 (Fractalkine)	Monocytes Endothelium Microglial cells	CX <sub>3</sub> CR1	Monocytes T cells	Leukocyte-endothelial adhesion Brain inflammation

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

# Leukocyte Homing



# 12 Summary of First Responders – Important protein components of the immune system

- Complement
- Cytokines
- Chemokines



JOHNS HOPKINS  
WHITING SCHOOL  
*of* ENGINEERING