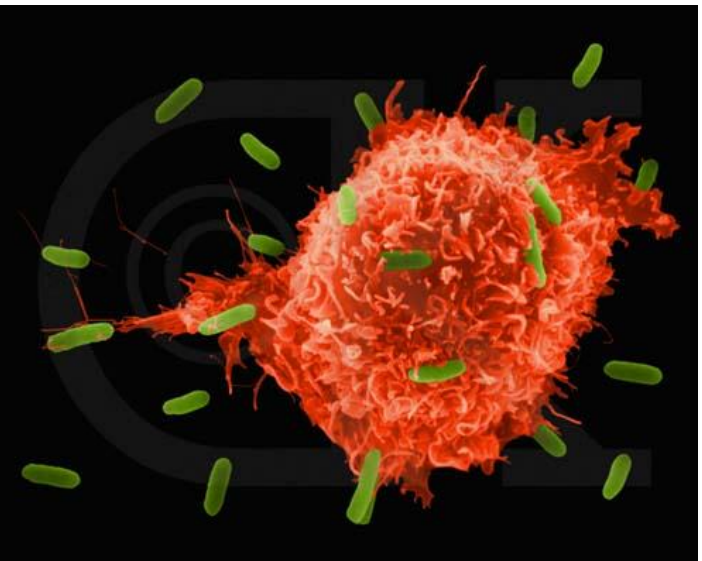
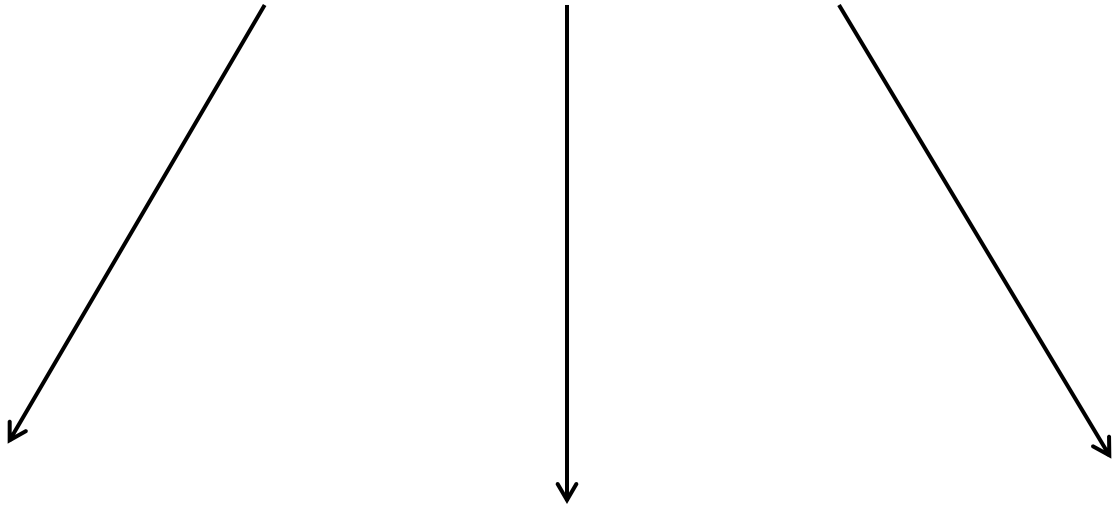
Innate Immune System



Dr. Issa Abu-Dayyeh

Why doesn’t this happen in our tissues??

Innate Immune System



Complement system

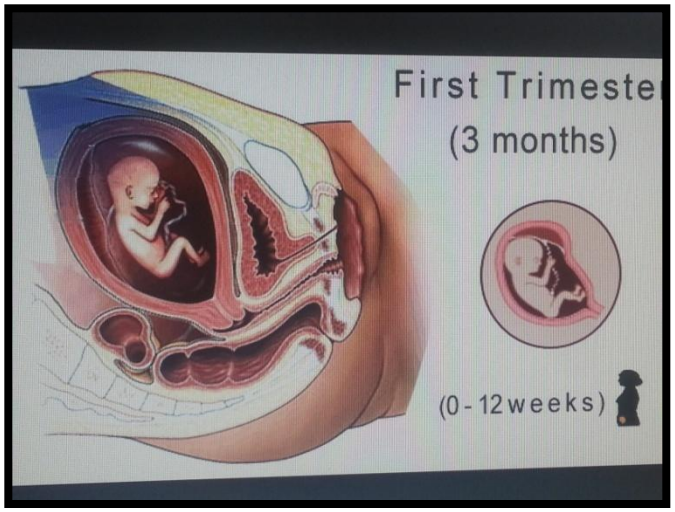
Professional Phagocytes

NK cells

Complement System

Composed of around 20 proteins that work together to destroy invaders and to signal other immune system players that the attack is ON!

Sea Urchins (Evolved around 600 Million years ago) possess a complement system



In humans, complement system develops In FIRST TRIMESTER of pregnancy.

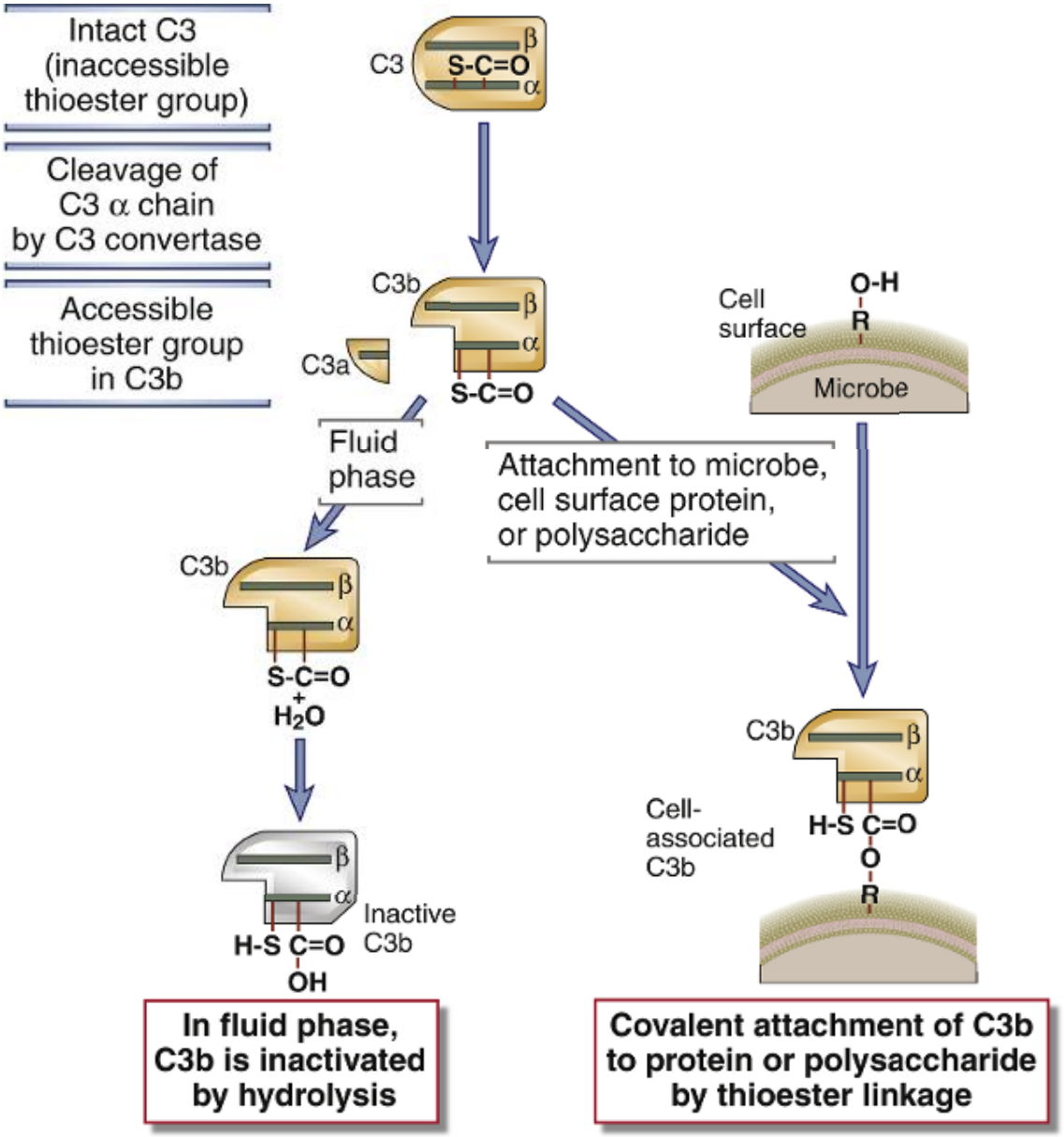
Methods of complement activation

1- Classical Pathway

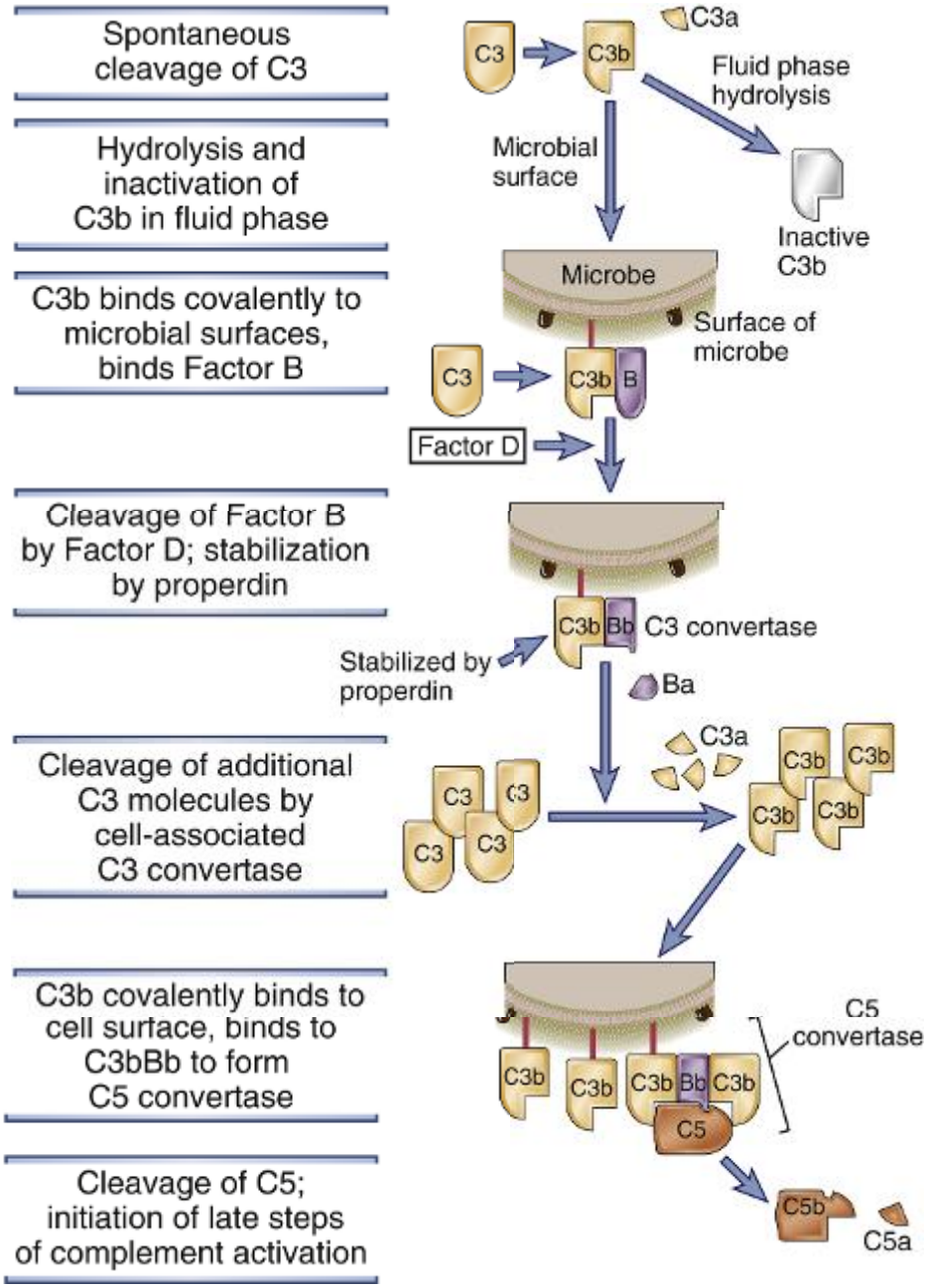
2- Alternative Pathway

3- Lectin Activation Pathway

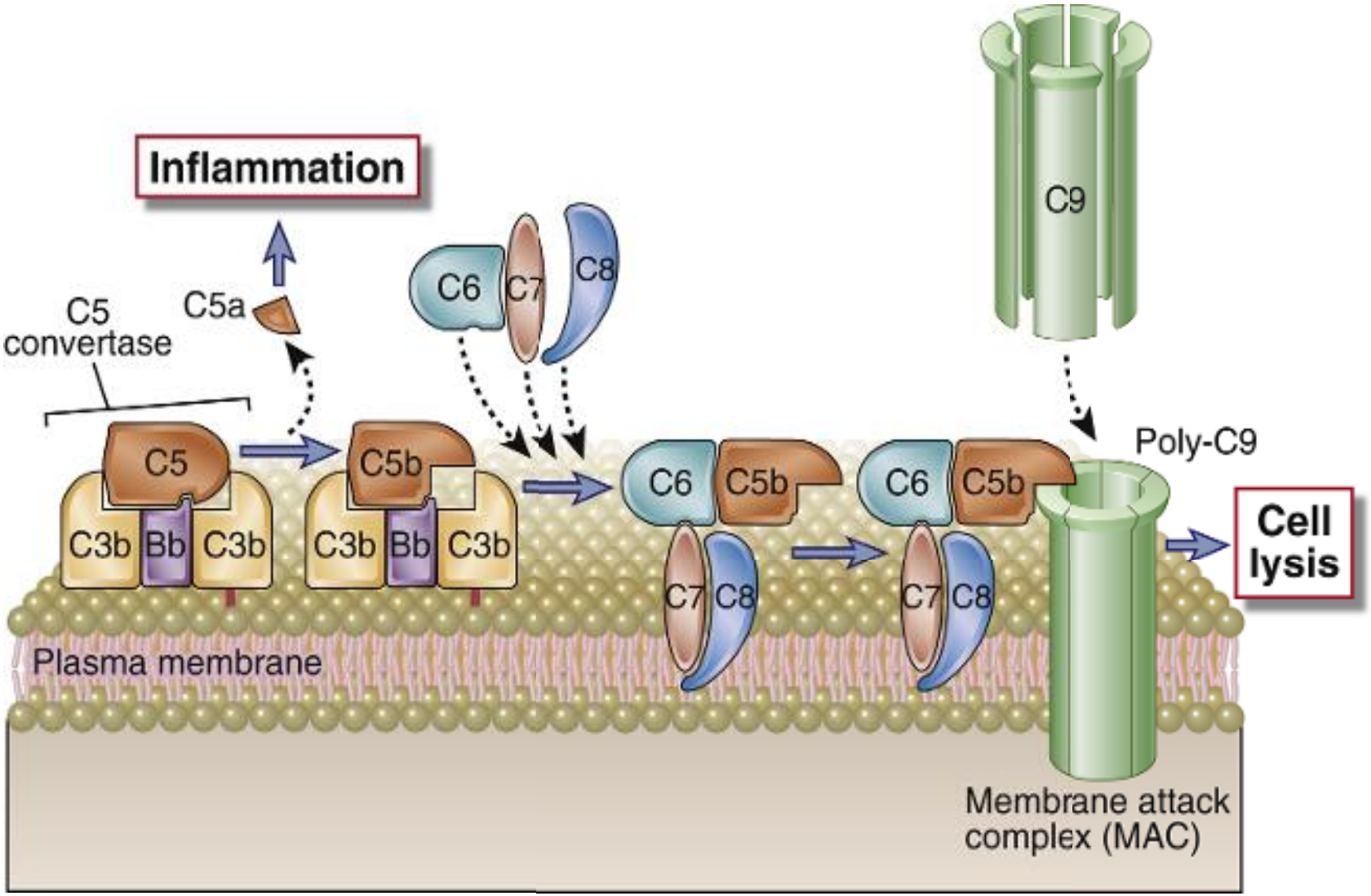
C3 Molecule


Intact C3 (inaccessible thioester group)
Cleavage of C3 α chain by C3 convertase
Accessible thioester group in C3b
C3
β
S-C=O
α
C3b
C3a
Fluid phase
Attachment to microbe, cell surface protein, or polysaccharide
Cell surface
O-H
R
Microbe
S-C=O
+
H2O
H-S C=O
OH
Inactive C3b
Cell-associated C3b
In fluid phase, C3b is inactivated by hydrolysis
Covalent attachment of C3b to protein or polysaccharide by thioester linkage

The Alternative Pathway

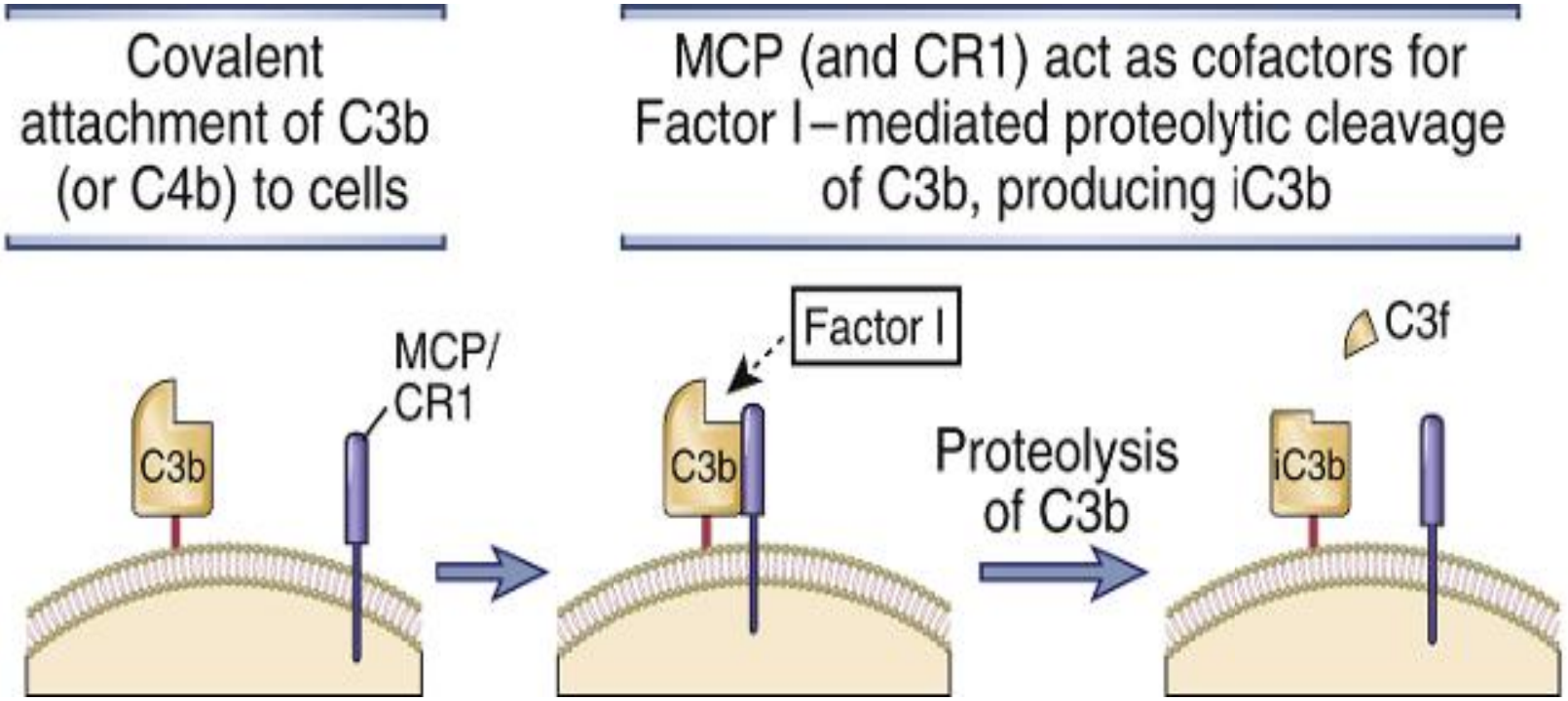


Generation of MACs

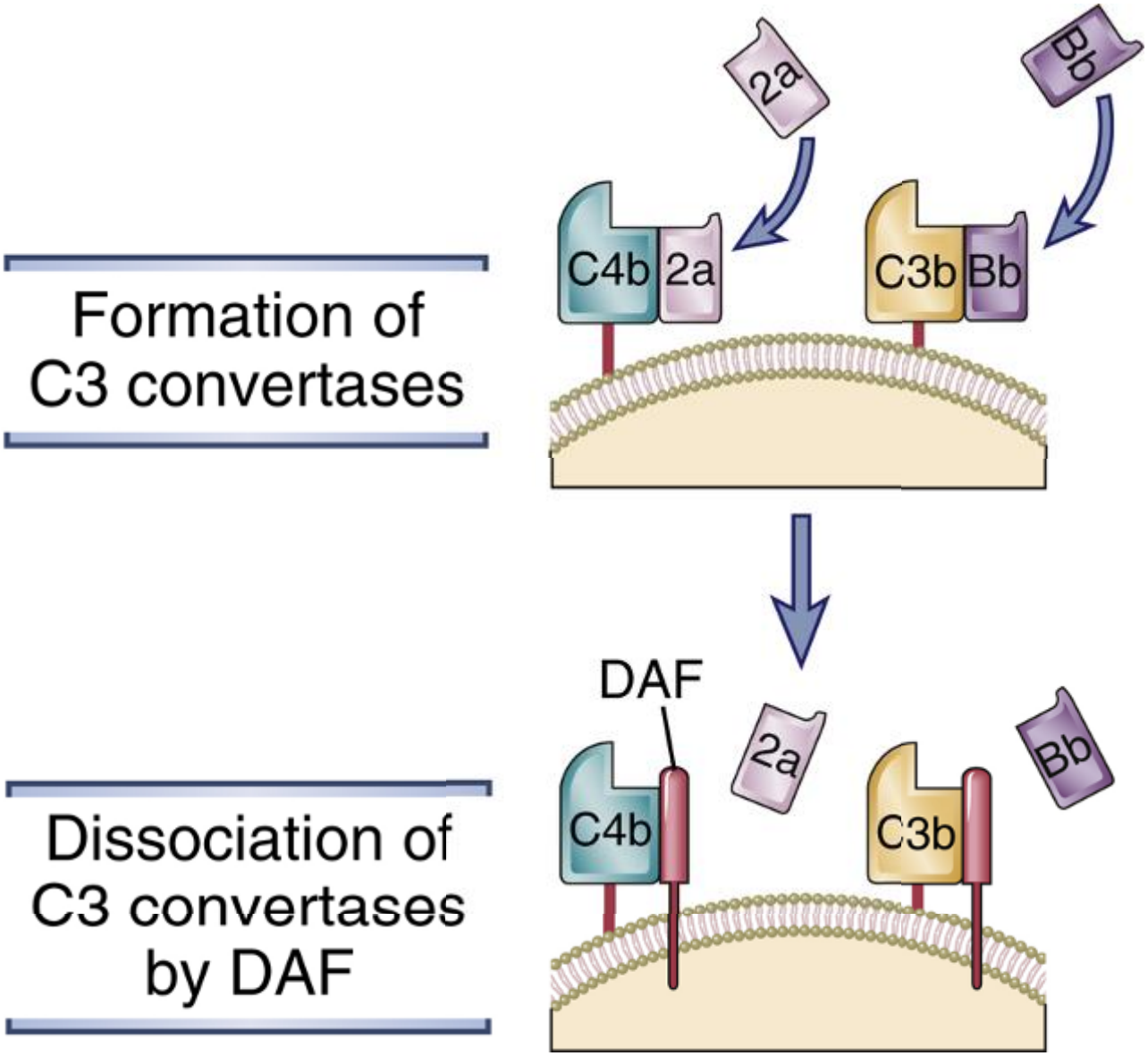


Why doesn’t complement destroy our own cells??

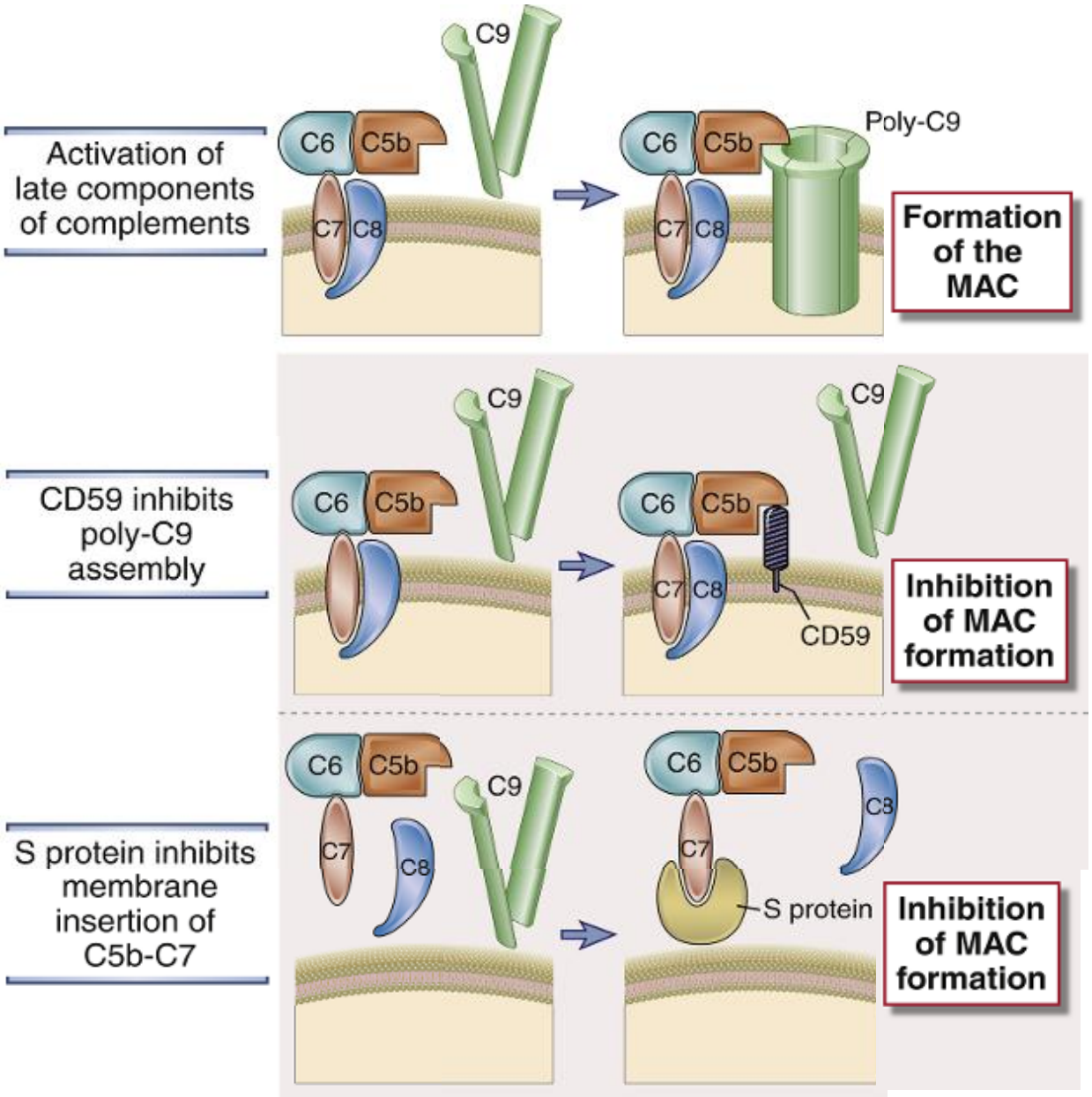
Human cells possess surface enzymes that inactivate C3b



Decay Accelerating factor DAF (CD55) destroys C3bBb



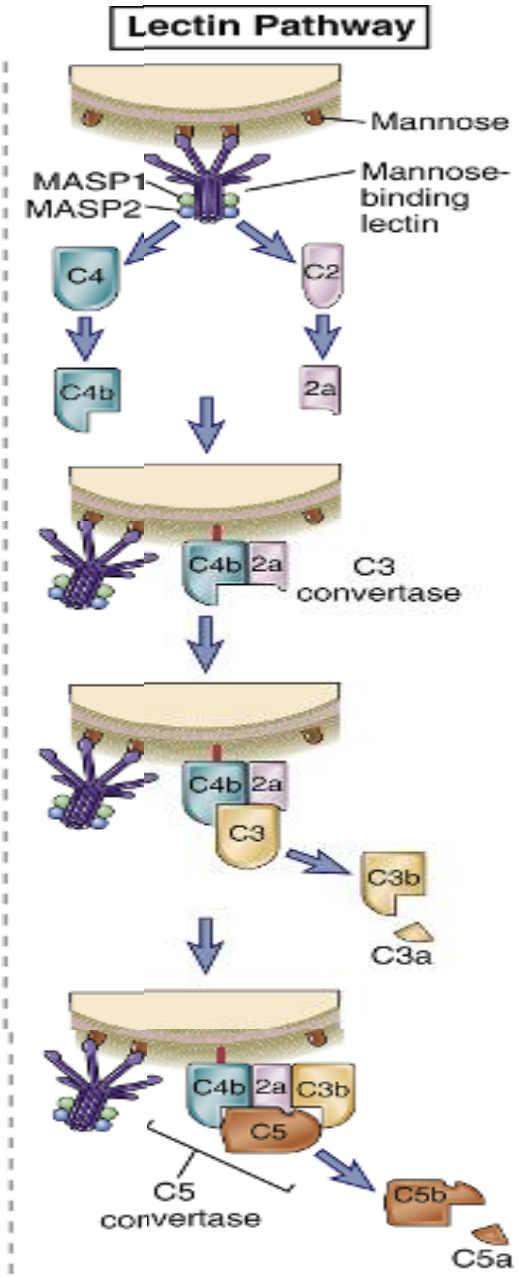
Protectin (CD59) Inhibits Poly-C9 Assembly and S Protein inhibits membrane insertion of C5b-C7



Failure of Heart Xenograft Experiments

1- Complement is fast!!

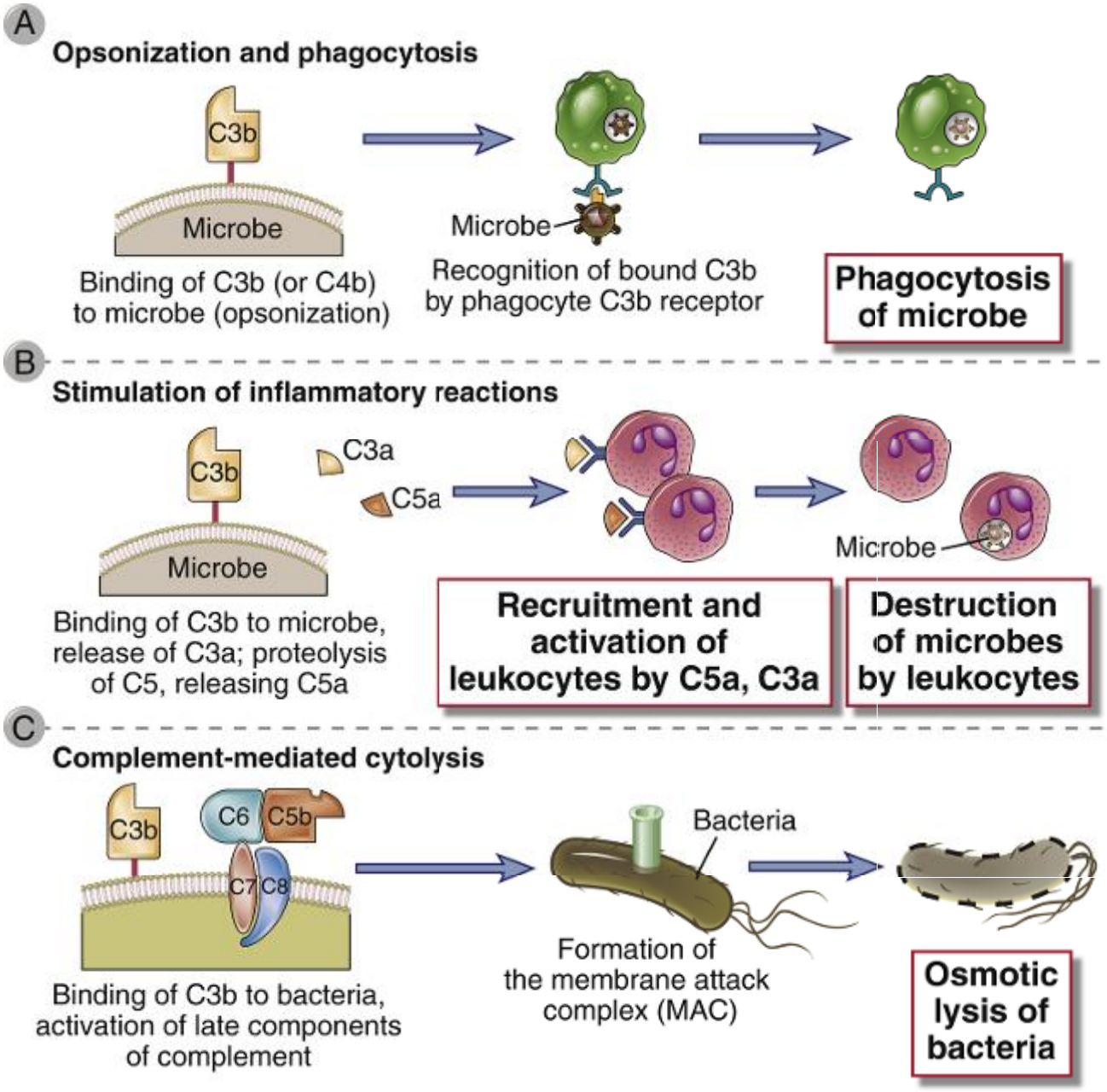
2- Complement attacks any unprotected surface.


Lectin Pathway
Mannose
MASP1
MASP2
Mannose-binding lectin
C4
C2
C4b
2a
C4b 2a
C3 convertase
C4b 2a
C3
C3b
C3a
C4b 2a C3b
C5
C5 convertase
C5b
C5a

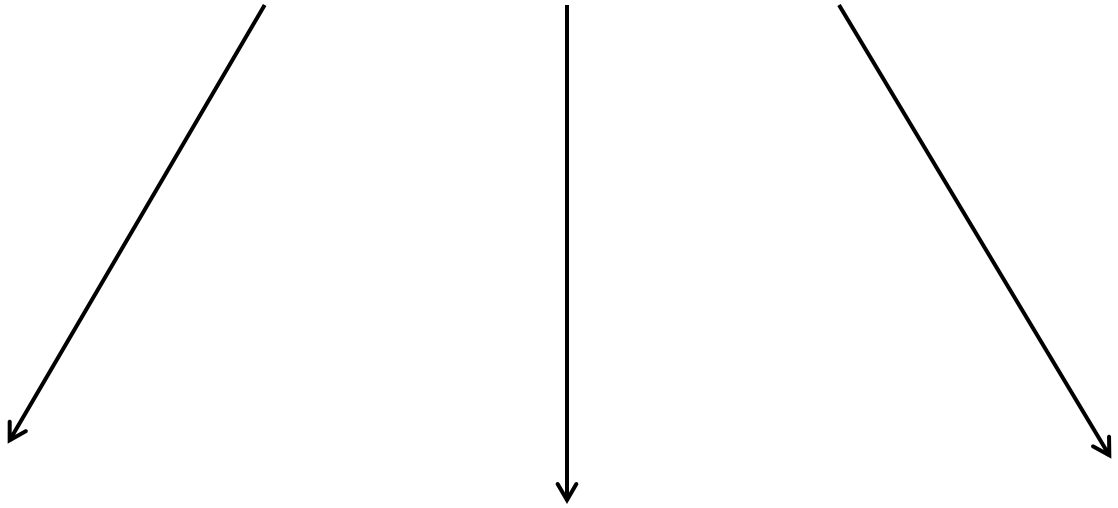
Alternative pathway: **Random Bombs**

Lectin pathway: **Smart Bombs**

Functions of the complement system



Innate Immune System



Complement system

Professional Phagocytes

NK cells

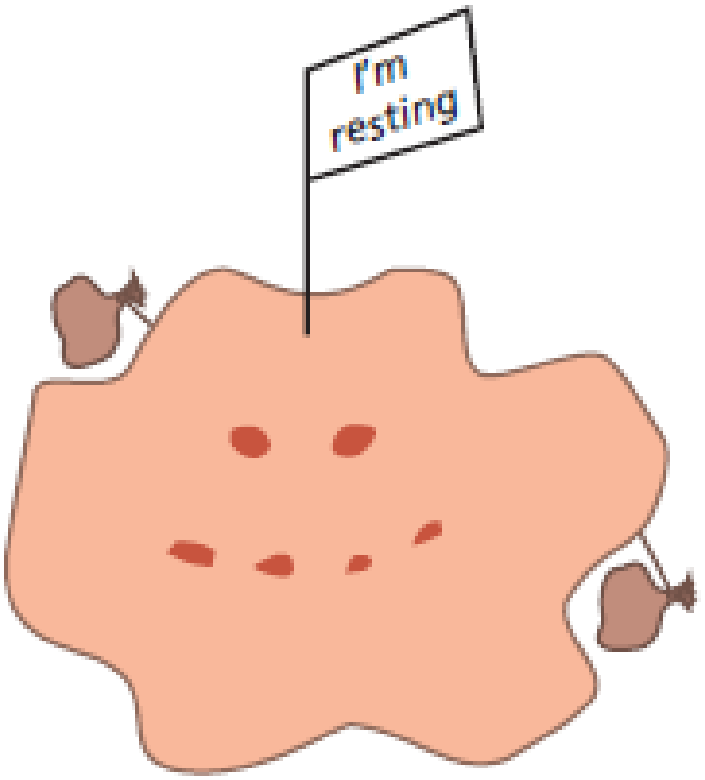
Professional Phagocytes

Macrophages (APCs found below almost all areas of the body: skin, lungs, intestines).

Dendritic Cells (APCs, found in epithelia and most tissues, most versatile sensor of PAMPs, excellent activators of adaptive immunity)

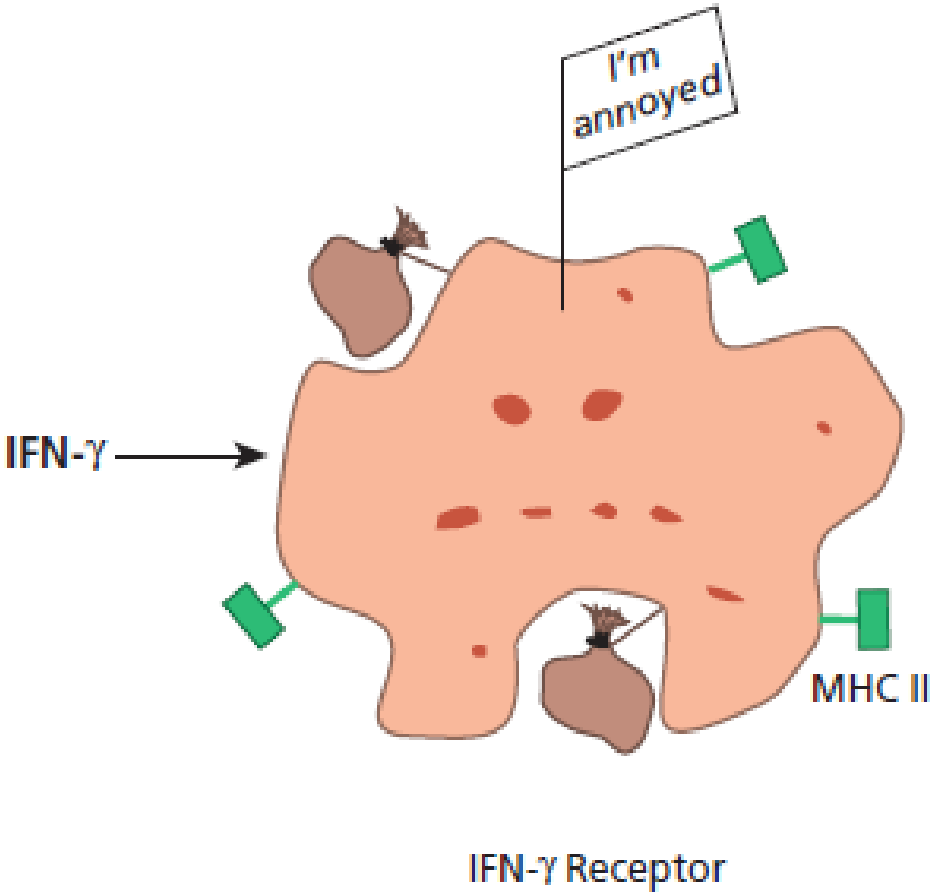
Neutrophils (NOT APCs, short-lived, and mostly involved in killing germs)

Macrophages exist in 3 states



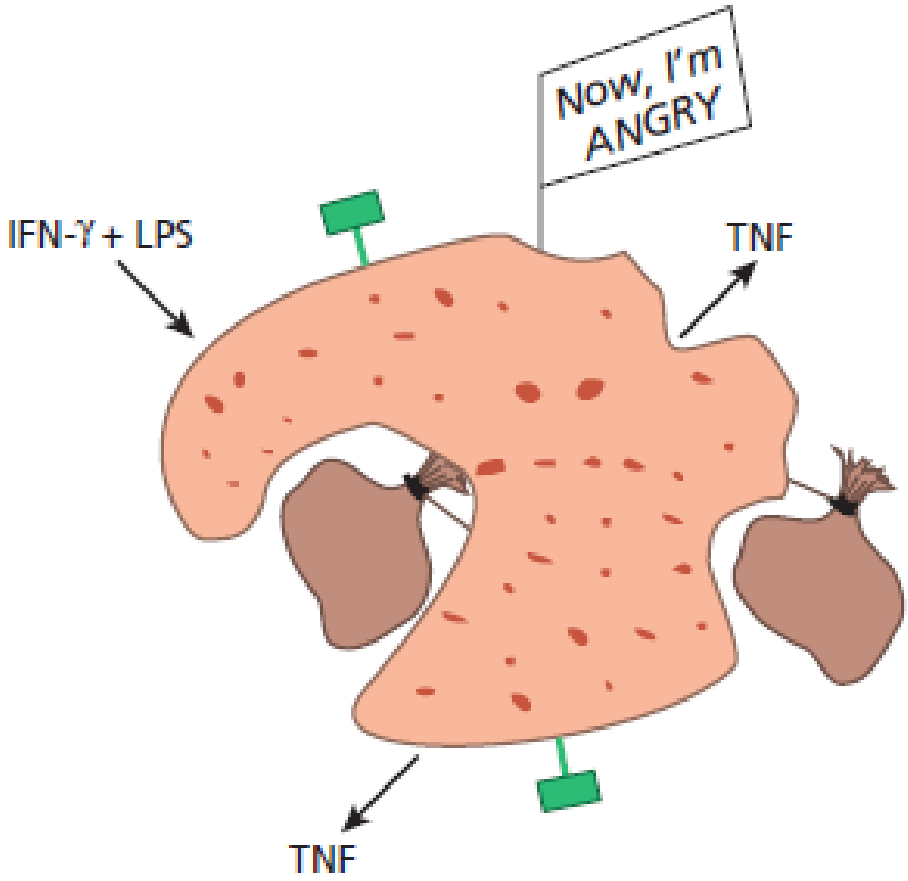
Resting Macrophage (Garbage collector)

(Low MHC II expression)



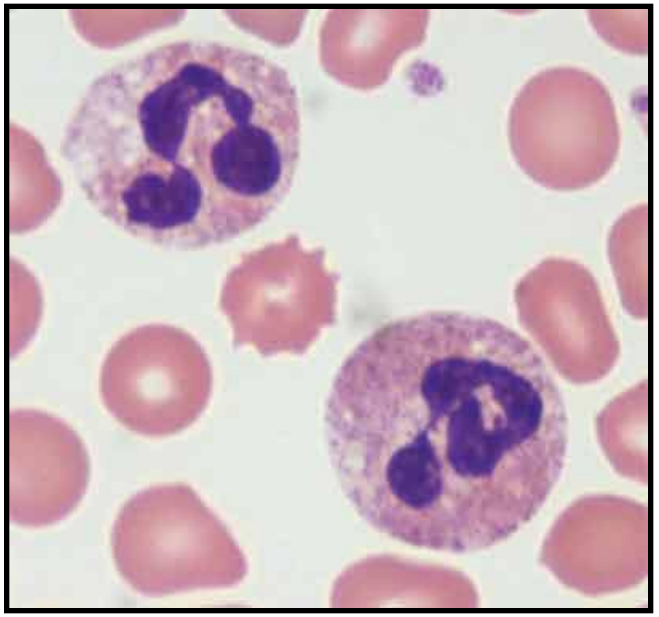
Primed Macrophage (Good APC, good killer)

(up-regulate MHC II expression)



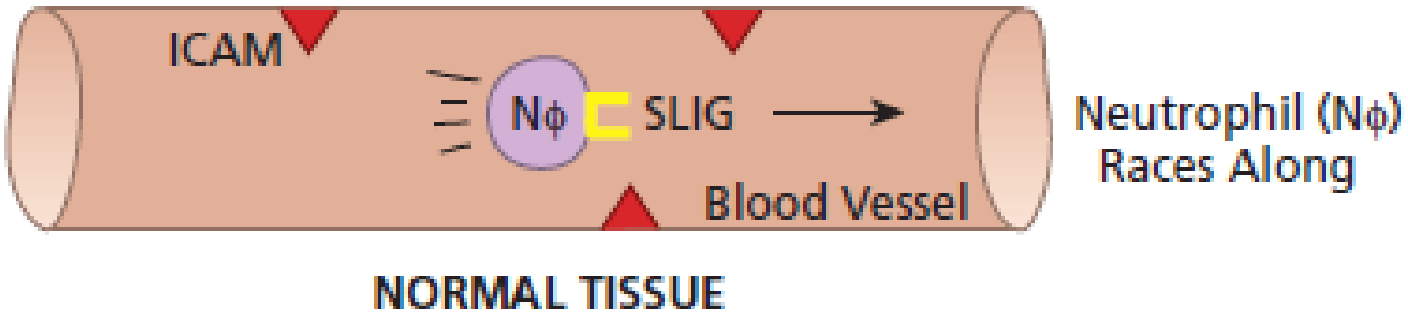
Hyperactivated Macrophage (Highly phagocytic, more lysosomes, ROI, NO)

If Macrophages are overwhelmed, who comes to the rescue??

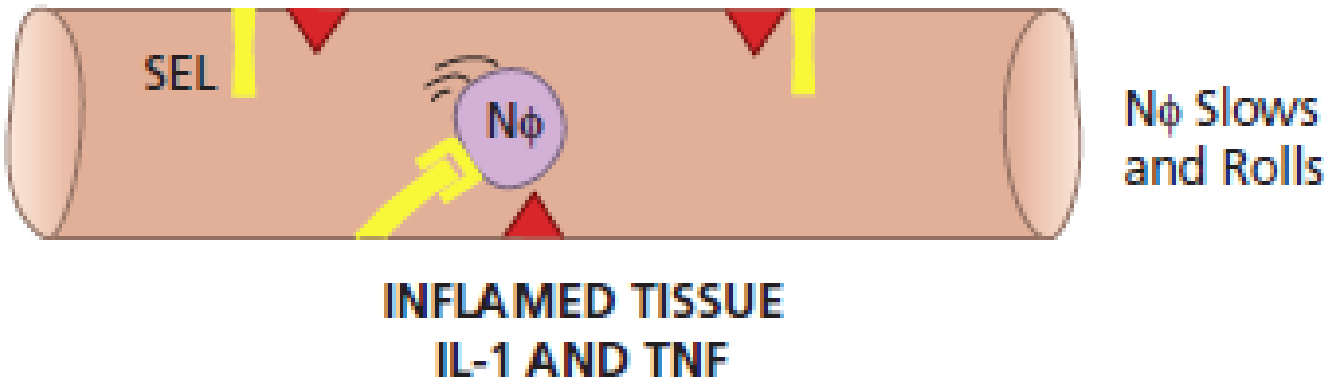


Neutrophils are NOT anitgen-presenting cells but rather professional killers

How do neutrophils know when and where to exit blood stream?

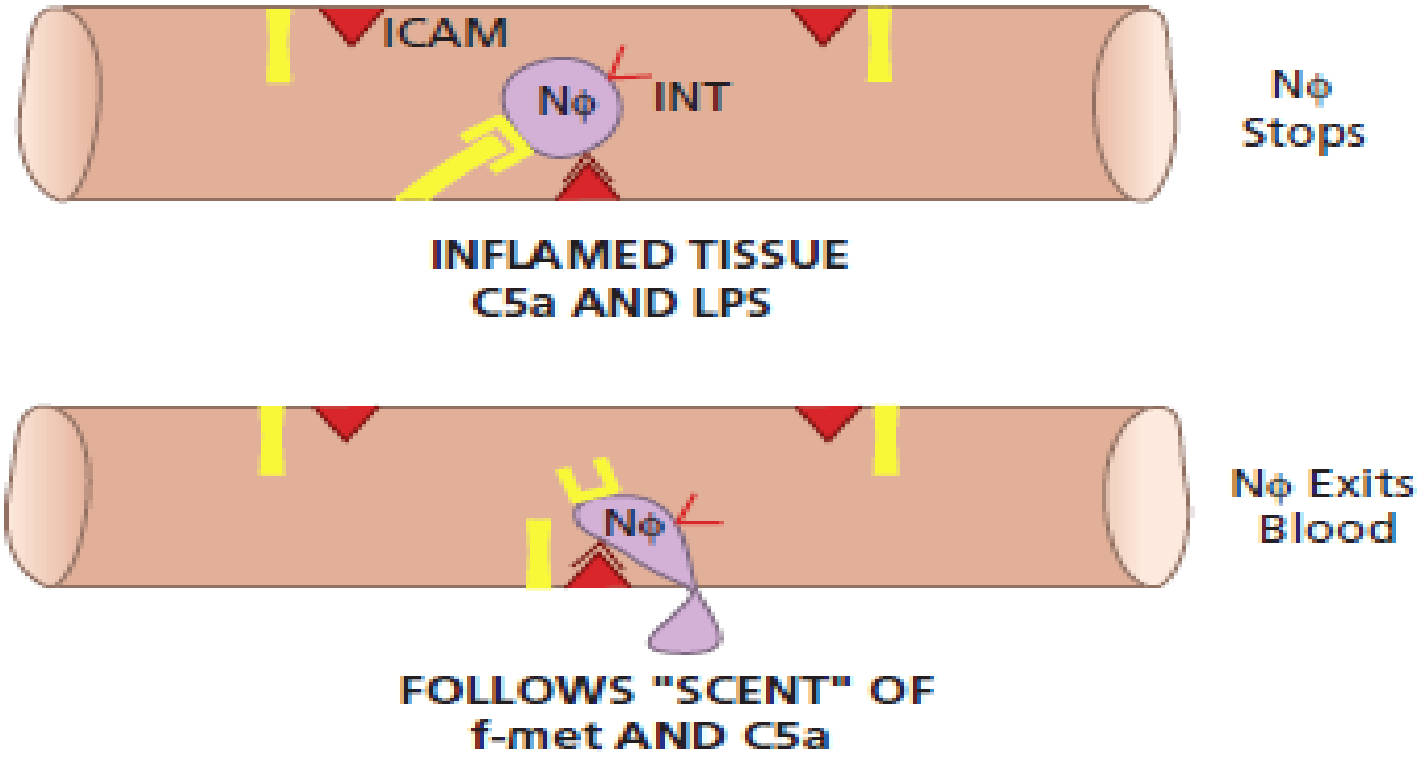


Neutrophils slow down at infection site



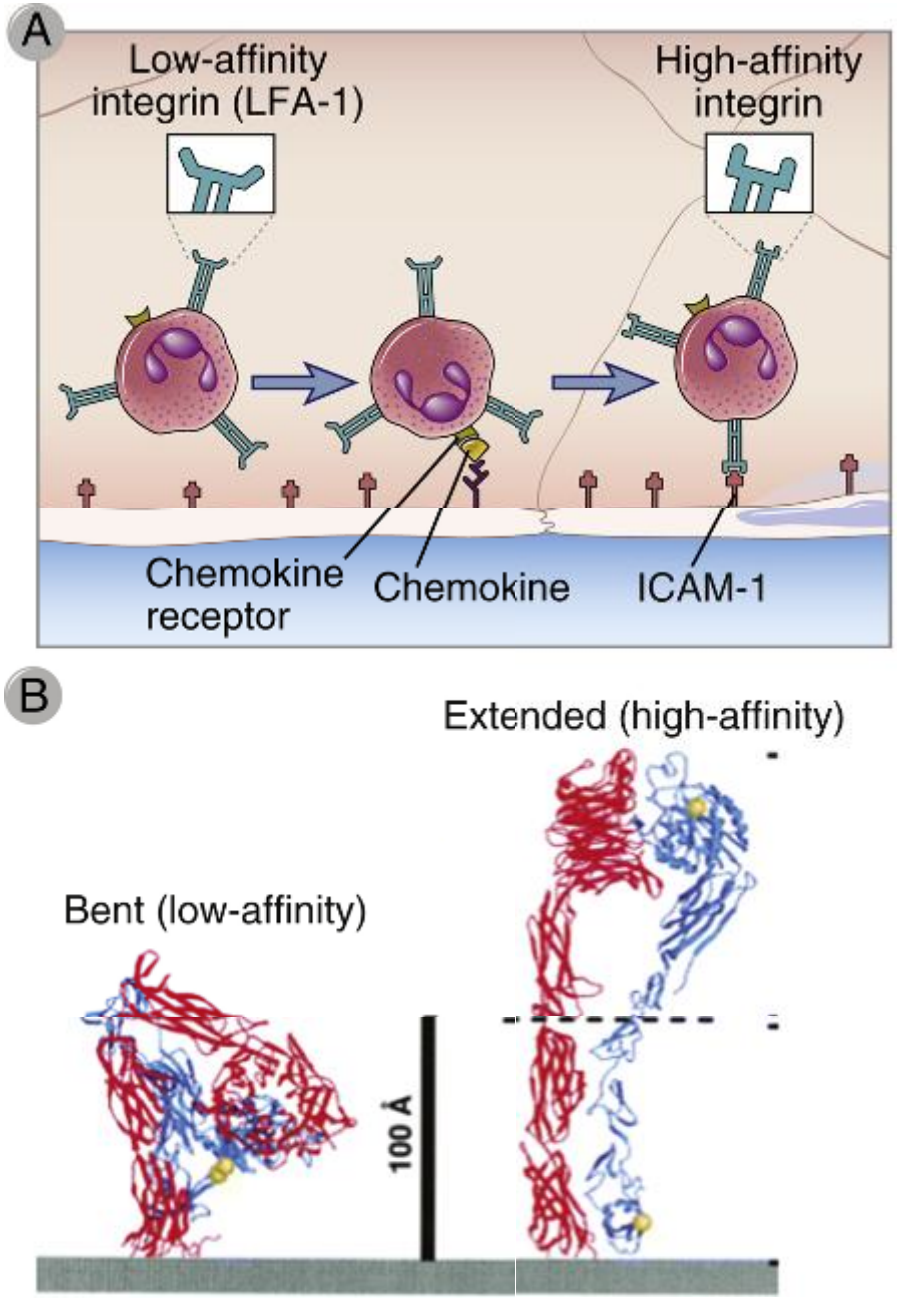
After ~6h post tissue insult, selectin is expressed on near-by endothelial cells.

Stopping and exiting circulation

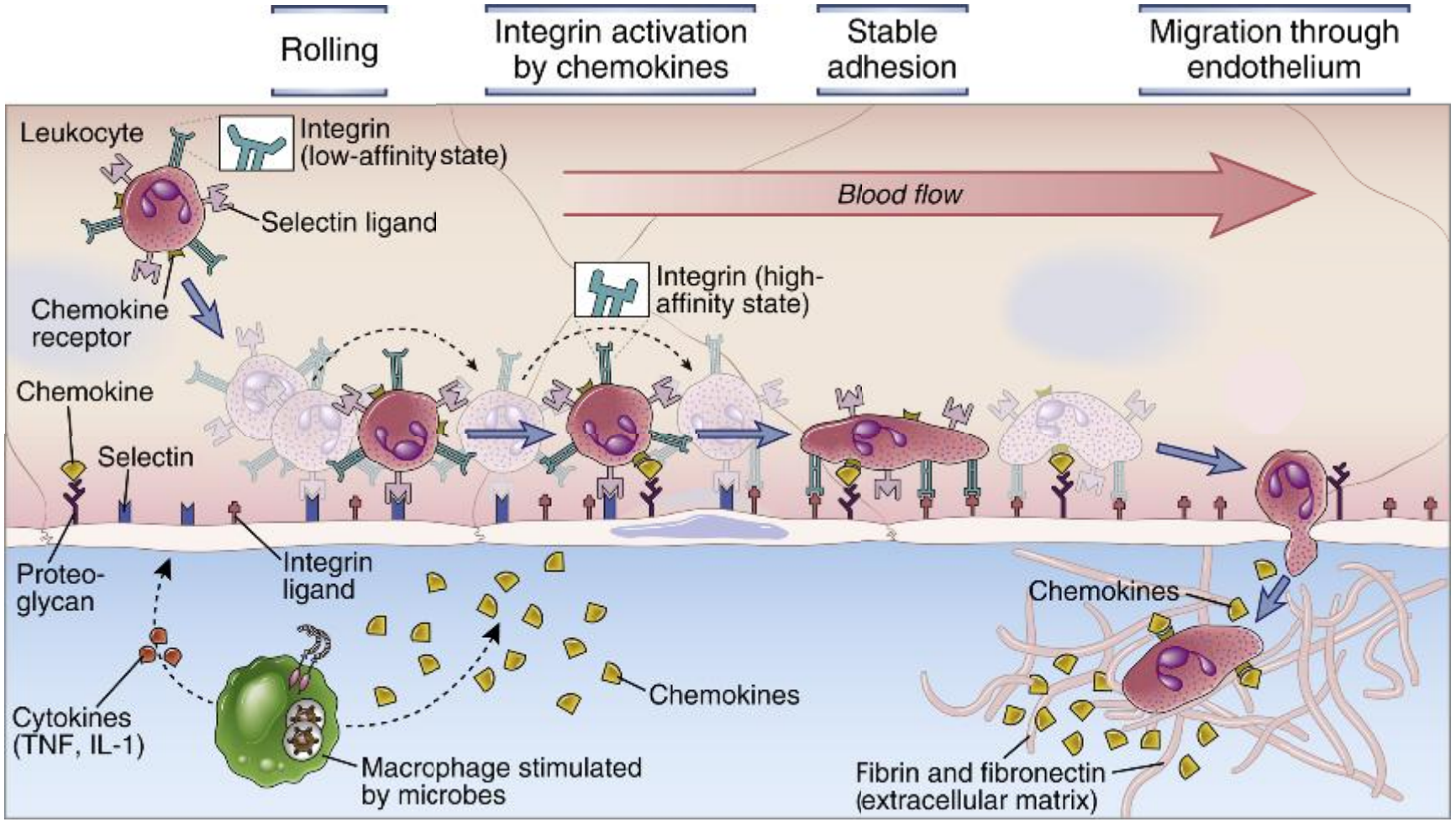


Selectins, integrins, and their ligands constitute a postal system for immune cell delivery.

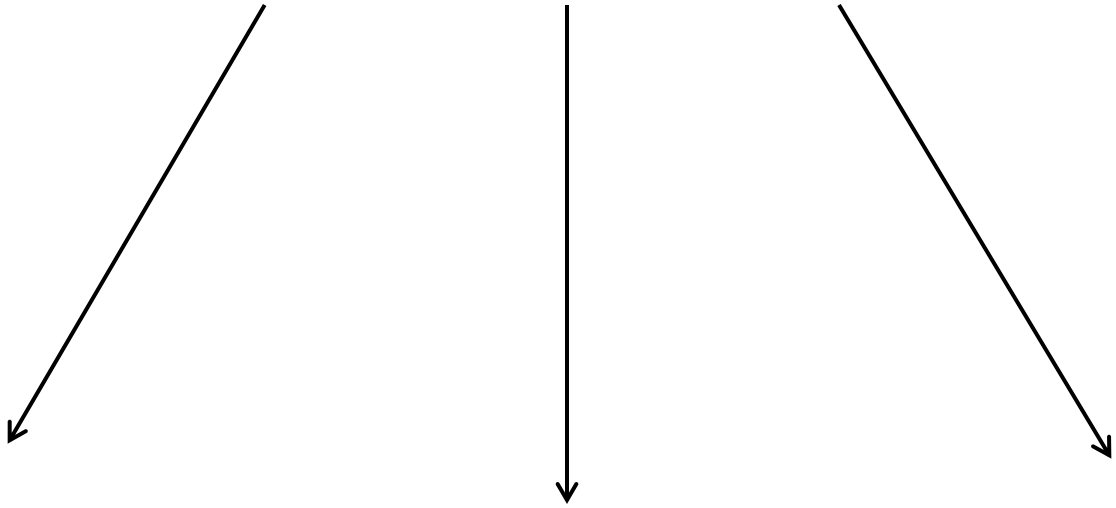
Chemokine-induced Integrin changes



Leukocyte Recruitment to Tissues



Innate Immune System



Complement system

Professional Phagocytes

NK cells

NK cells

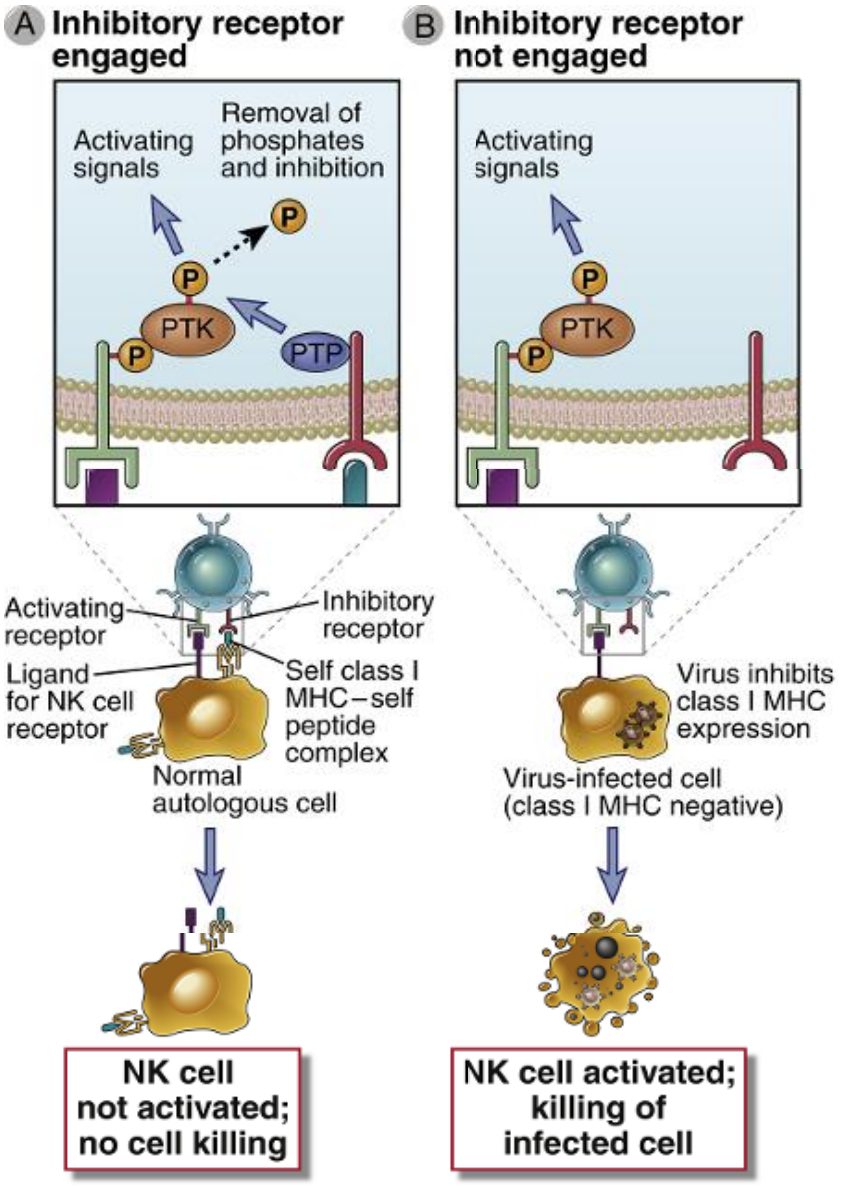
Short-lived cells (1 week), no B or T cell receptors

On call- mostly found in blood, liver, and spleen (Not in tissue)

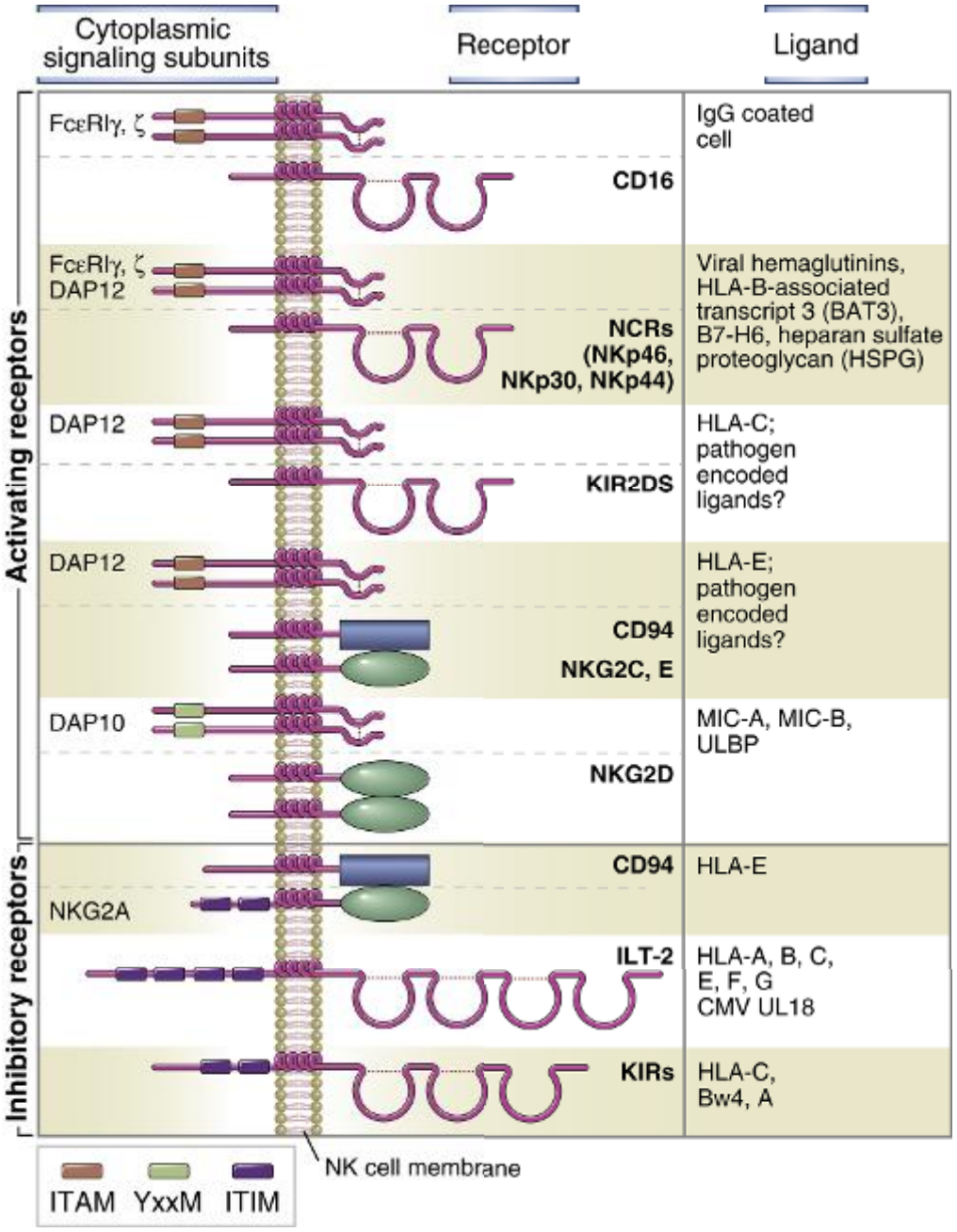
Once they enter tissue

- Produce cytokines (ex: IFN-ɣ)
- Kill Cells by forcing them to commit suicide (Injection of granzymes, FasL-Fas interactions)

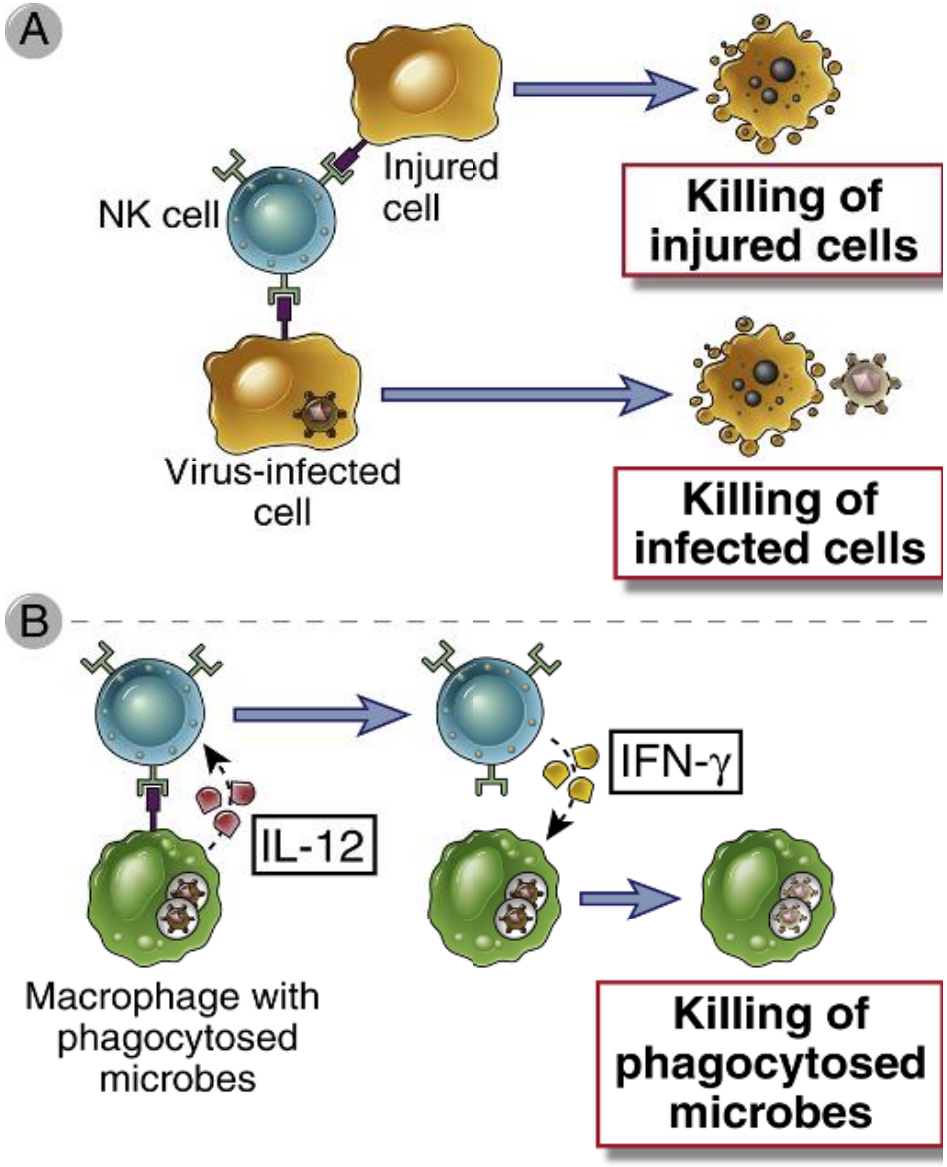
How do NK cells recognize their target??



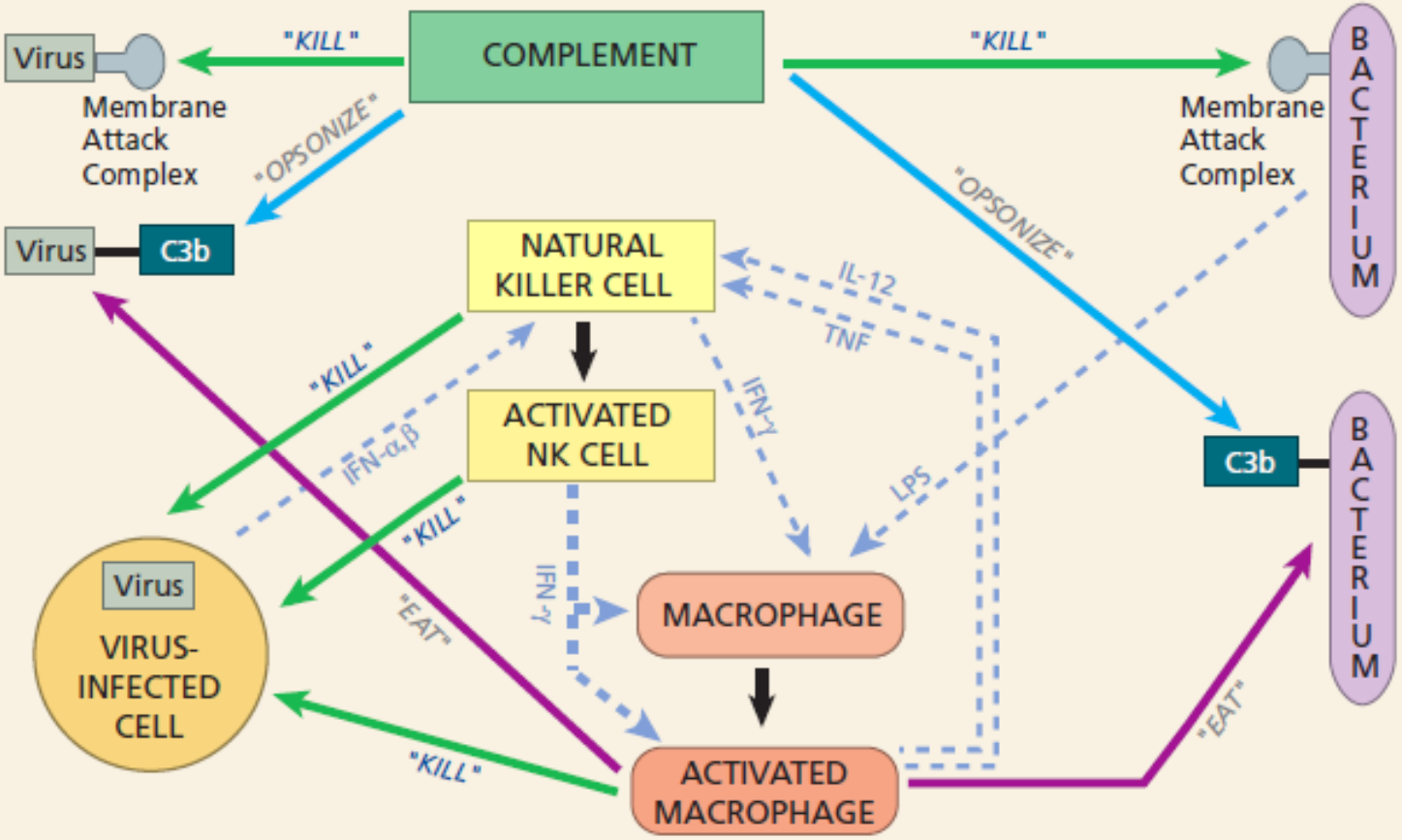
Activating and Inhibitory NK Receptors



Functions of NK cells



How the innate immune system deals with bacteria and viruses??



- Many viruses evolved defenses to protect them from the innate immune system.
- Innate system can help contain a viral infection in early stages, but more potent weapons are frequently required!

Adaptive Immune System

THANK YOU!

QUESTIONS??