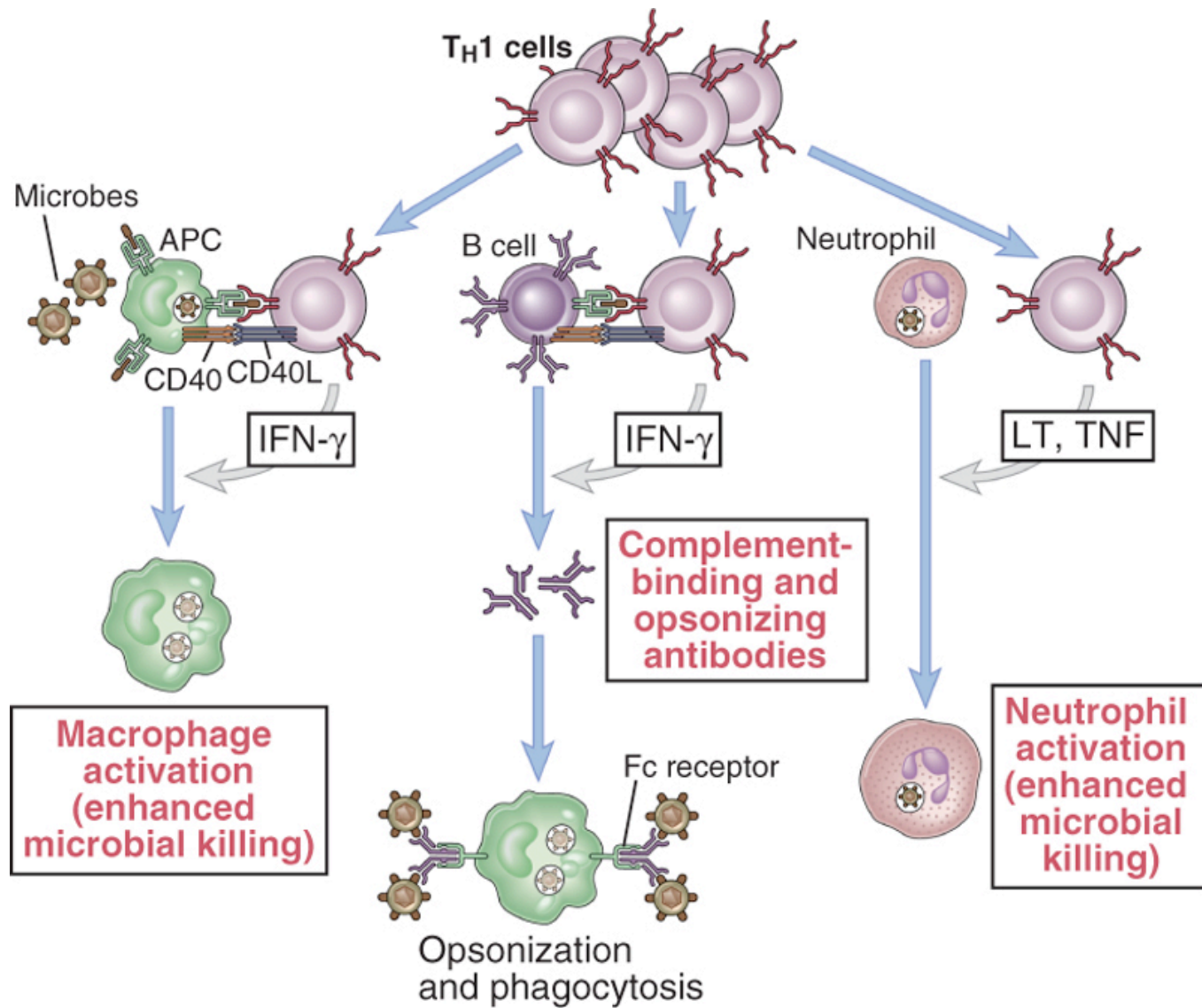


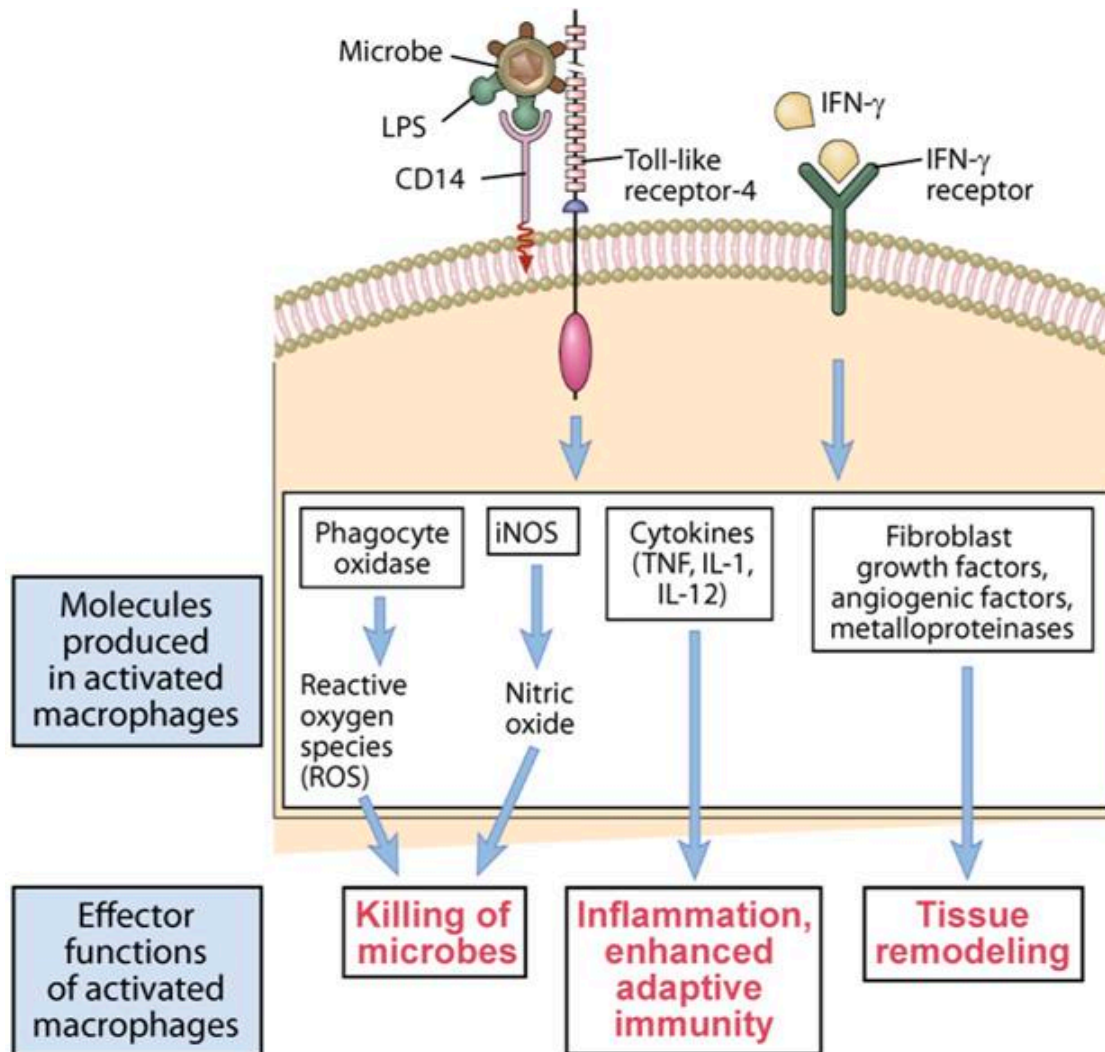
Effector mechanisms

T lymphocytes

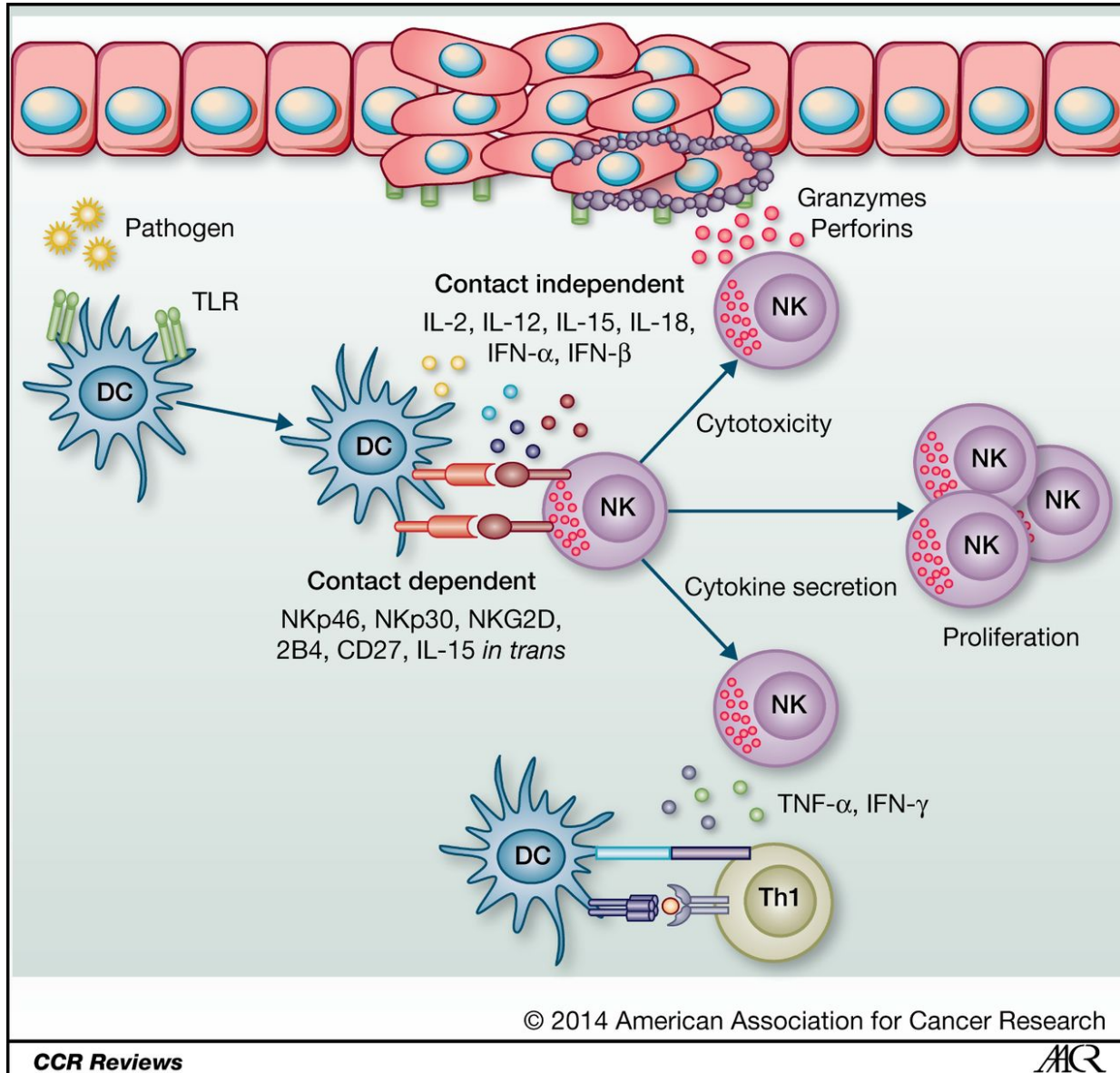
T cells – Th1 response



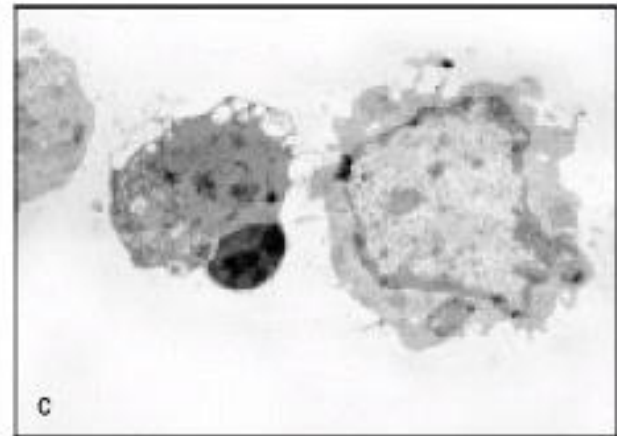
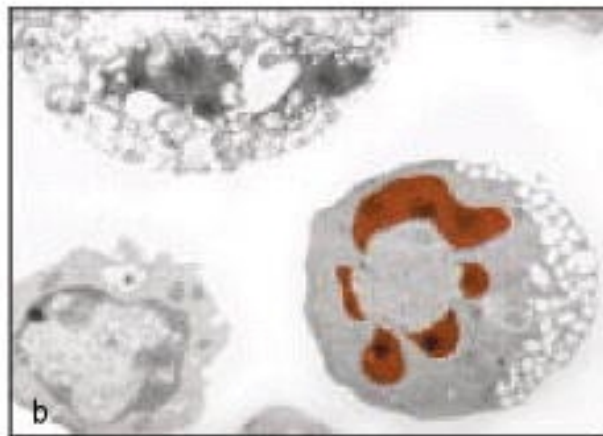
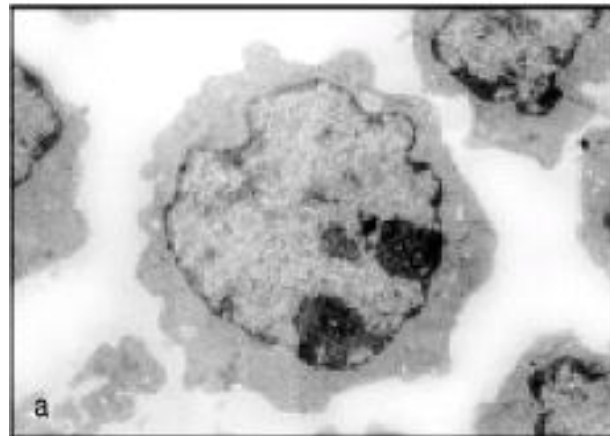
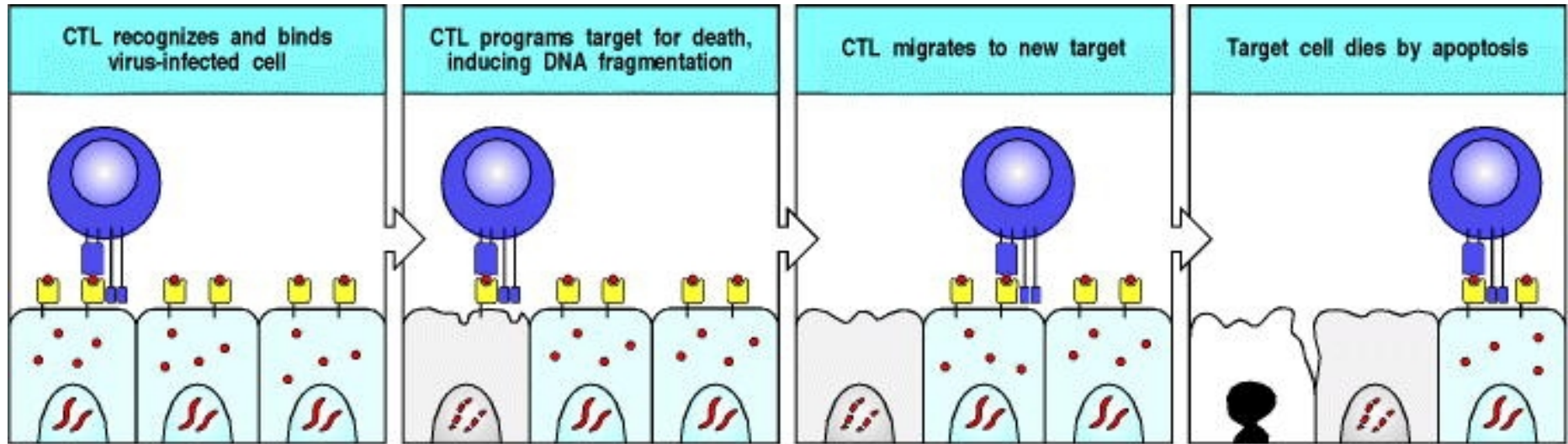
IFN gamma activates macrophages



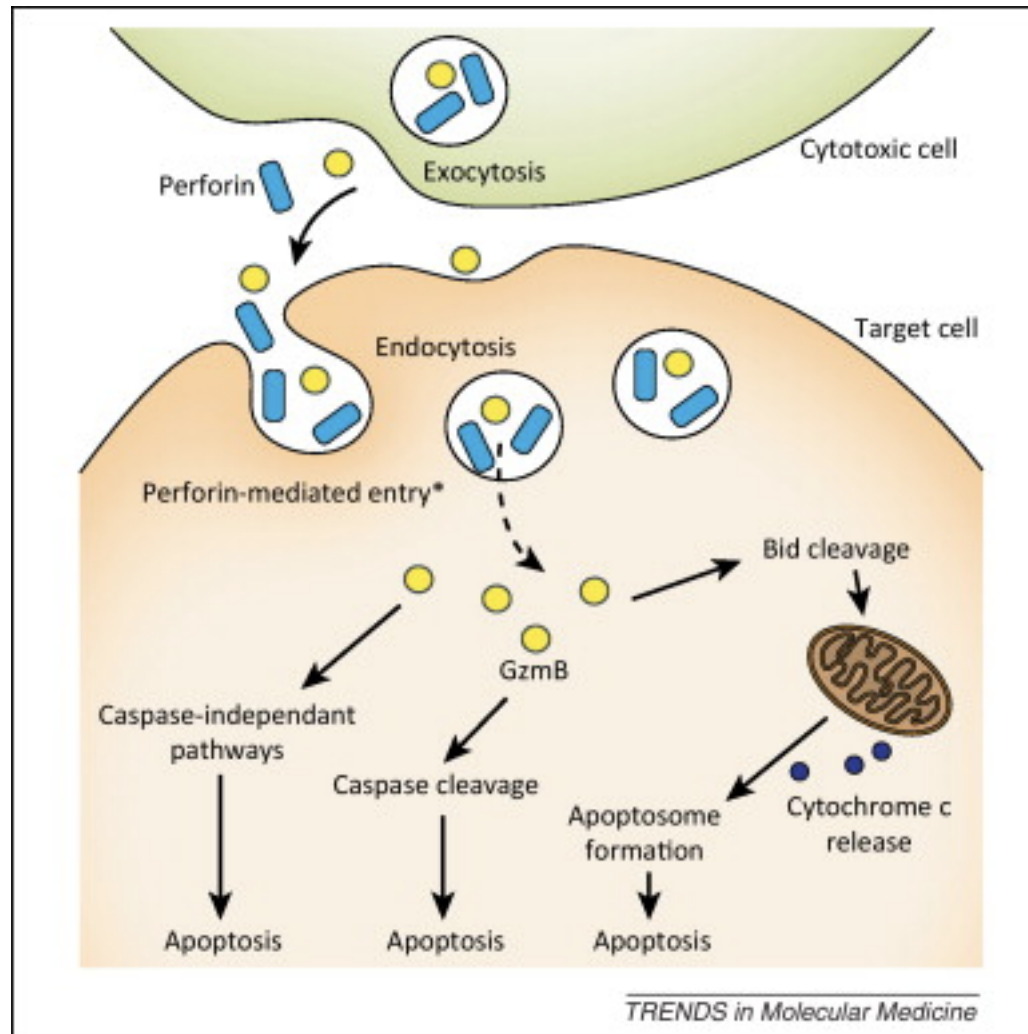
IFN gamma activates NK cells



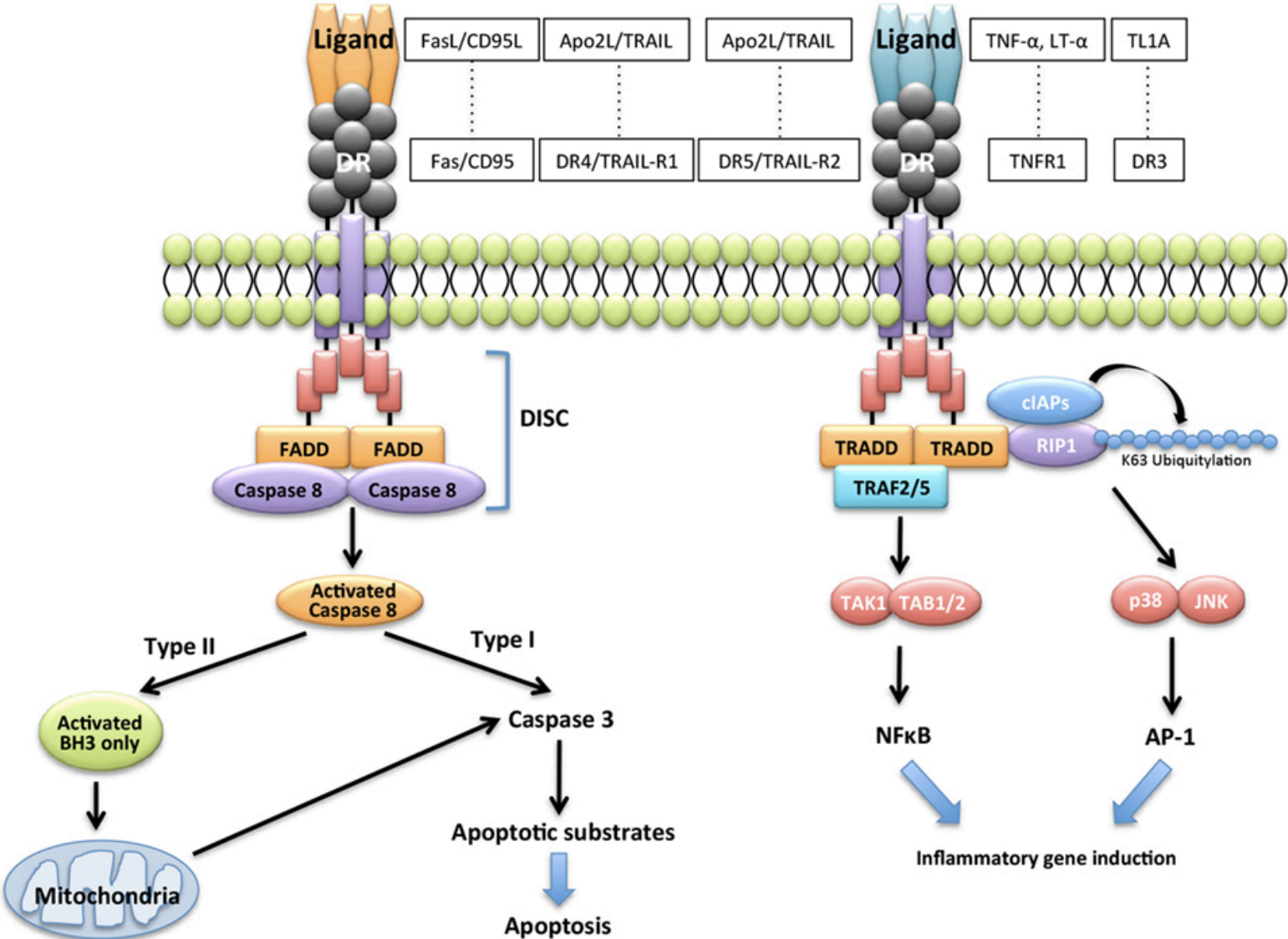
CD8 – cytotoxic mechanisms



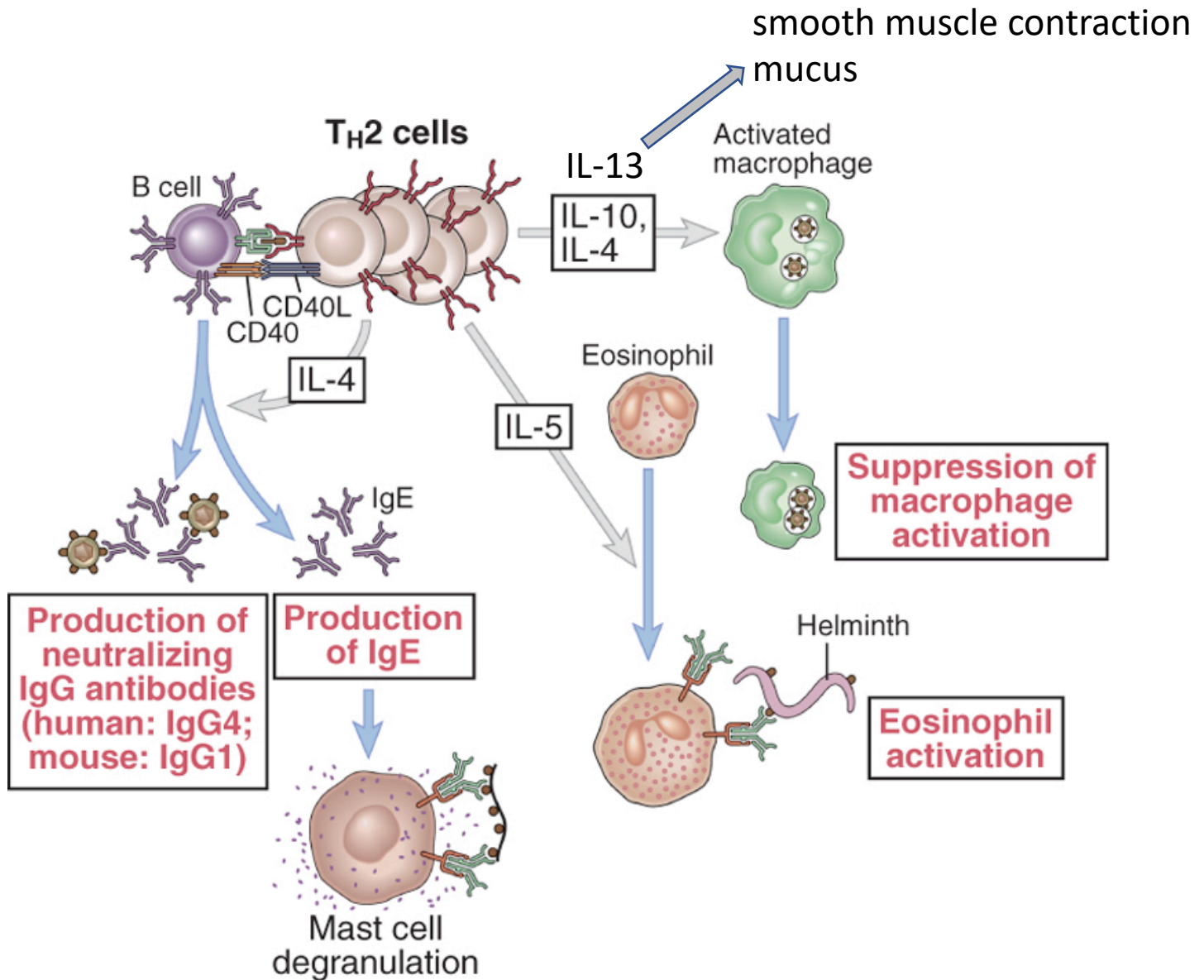
Perforin/granzyme cell death induction



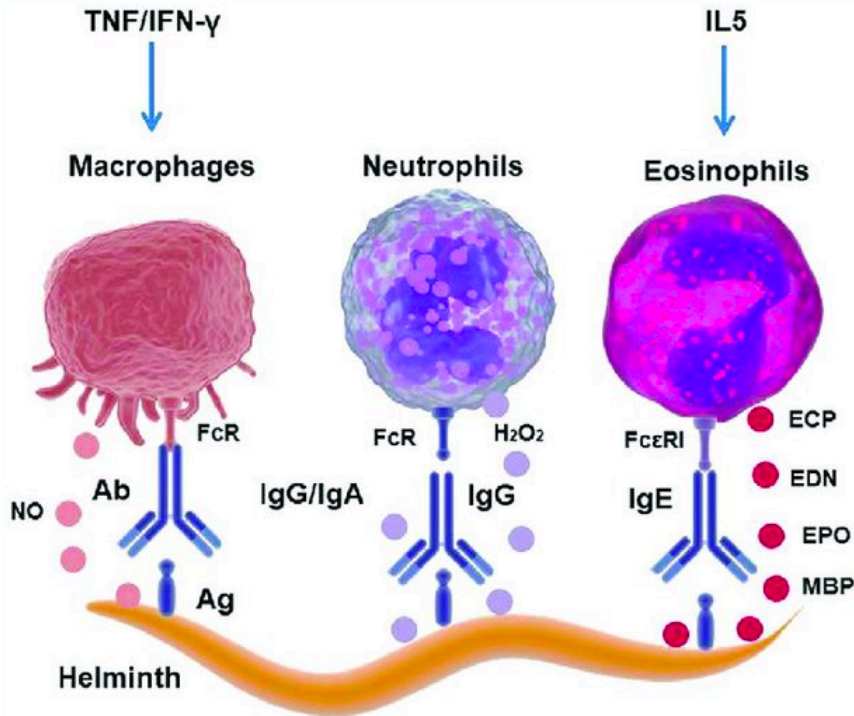
TNFR family – cell death induction



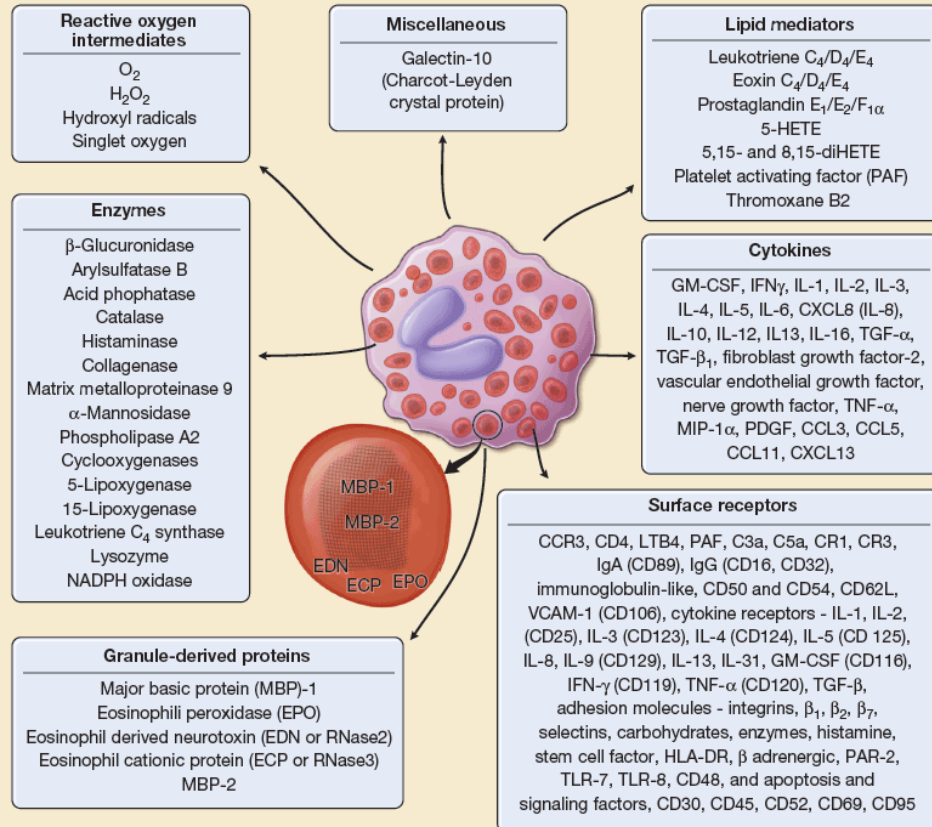
Th2 – extracellular/multicellular pathogens



Th2 effector mechanisms



Products of eosinophils and localization of distinctive granule proteins



Source: Goldsmith LA, Katz SI, Gilchrist BA, Paller AS, Leffell DJ, Wolff K: *Fitzpatrick's Dermatology in General Medicine, 8th Edition*: www.accessmedicine.com

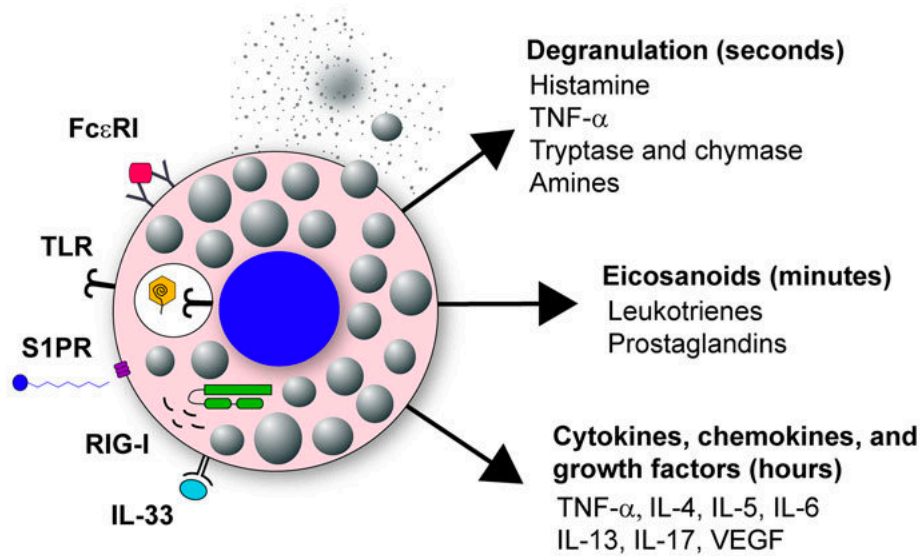
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eosinophils

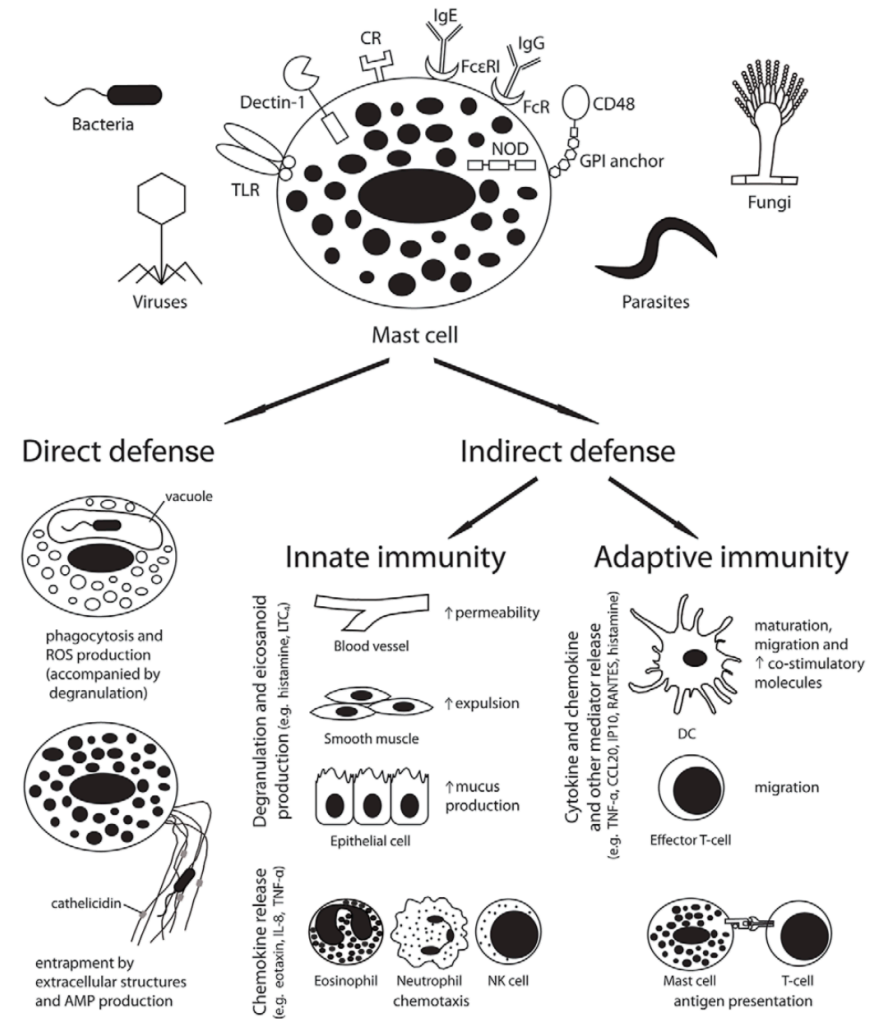
<https://www.instagram.com/p/BeQg8fglkpf/>

<https://www.youtube.com/watch?v=dDn9hFdn7n8>

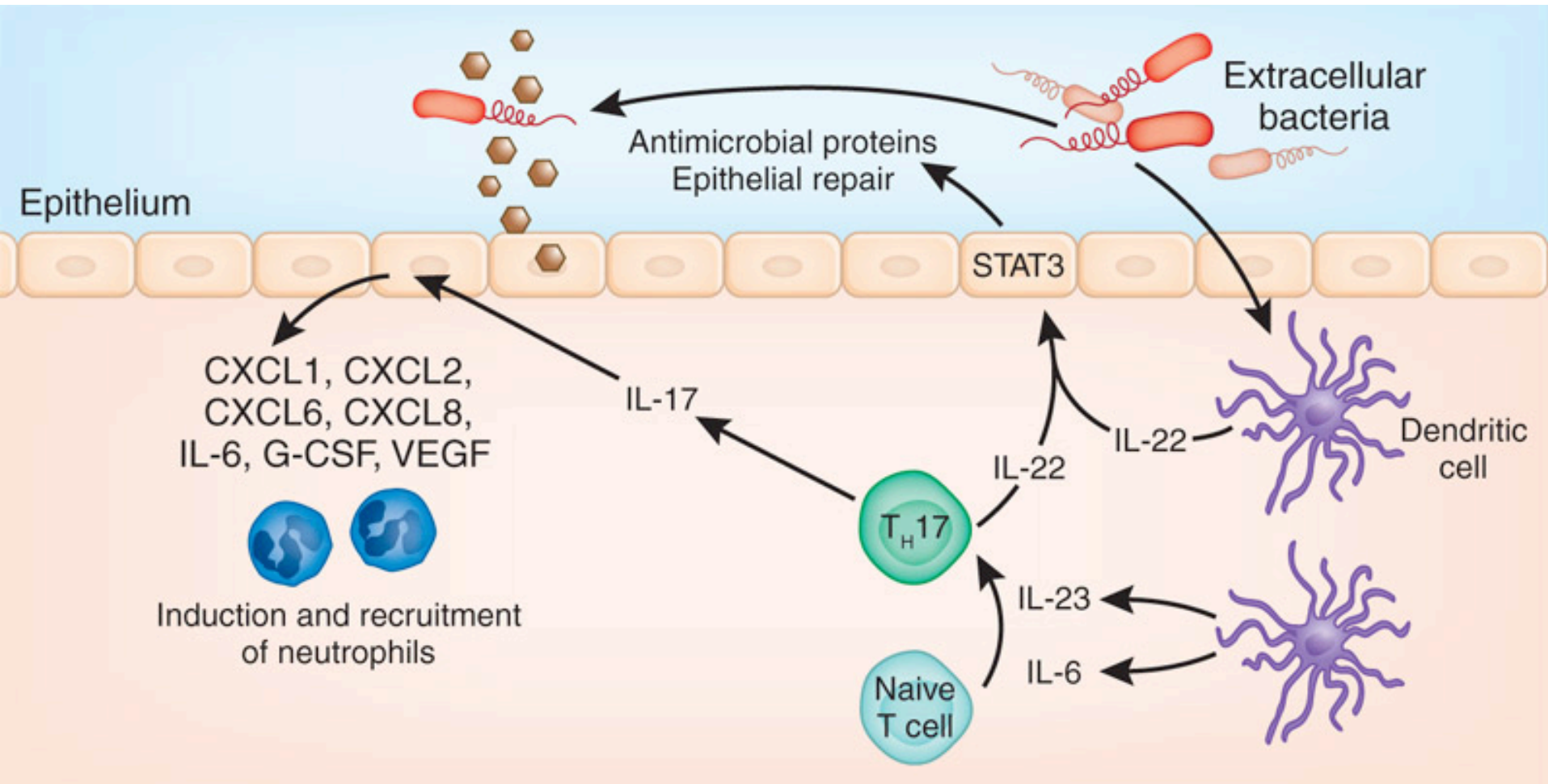
Mast cells



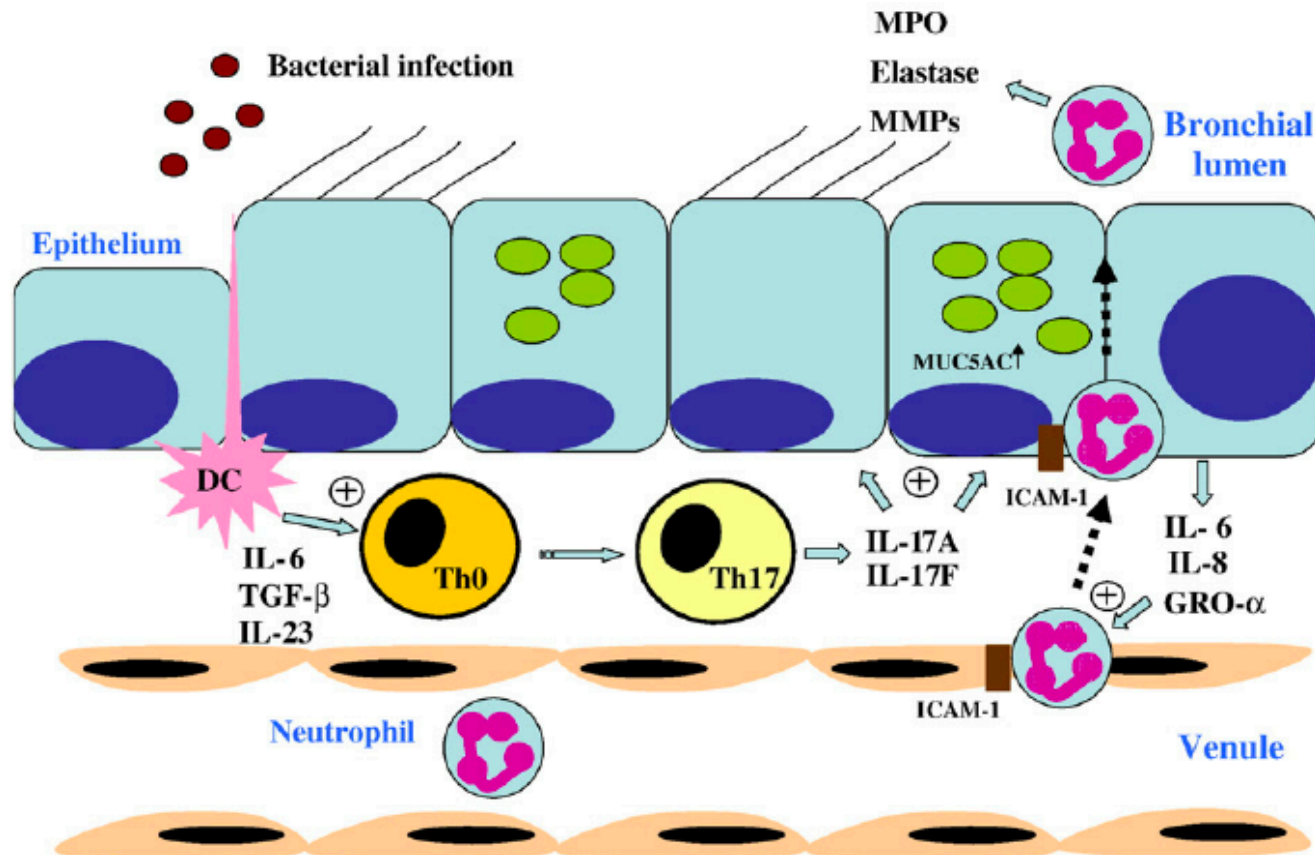
Mast cell protease 2 → Worm elimination



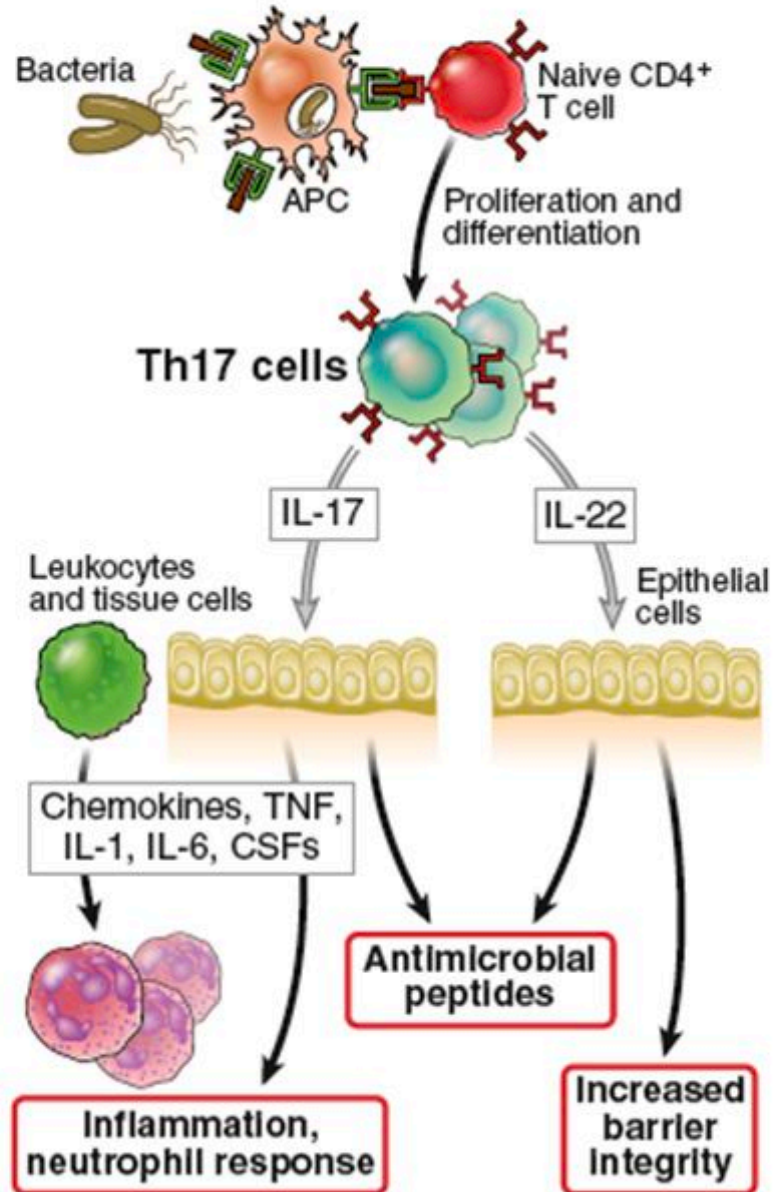
Th17 – extracellular pathogens



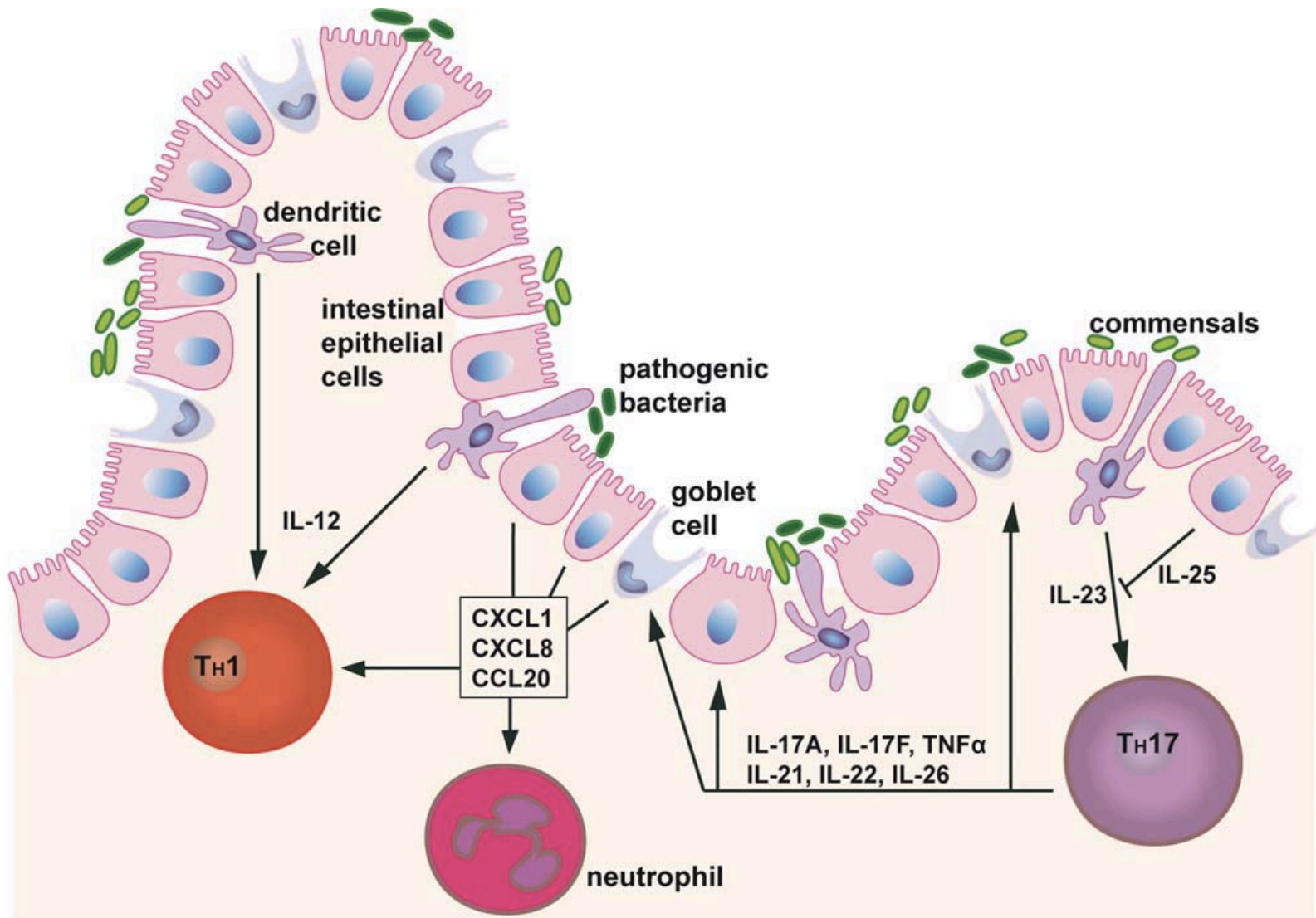
Neutrophils are an important part of the Th17 effector mechanism



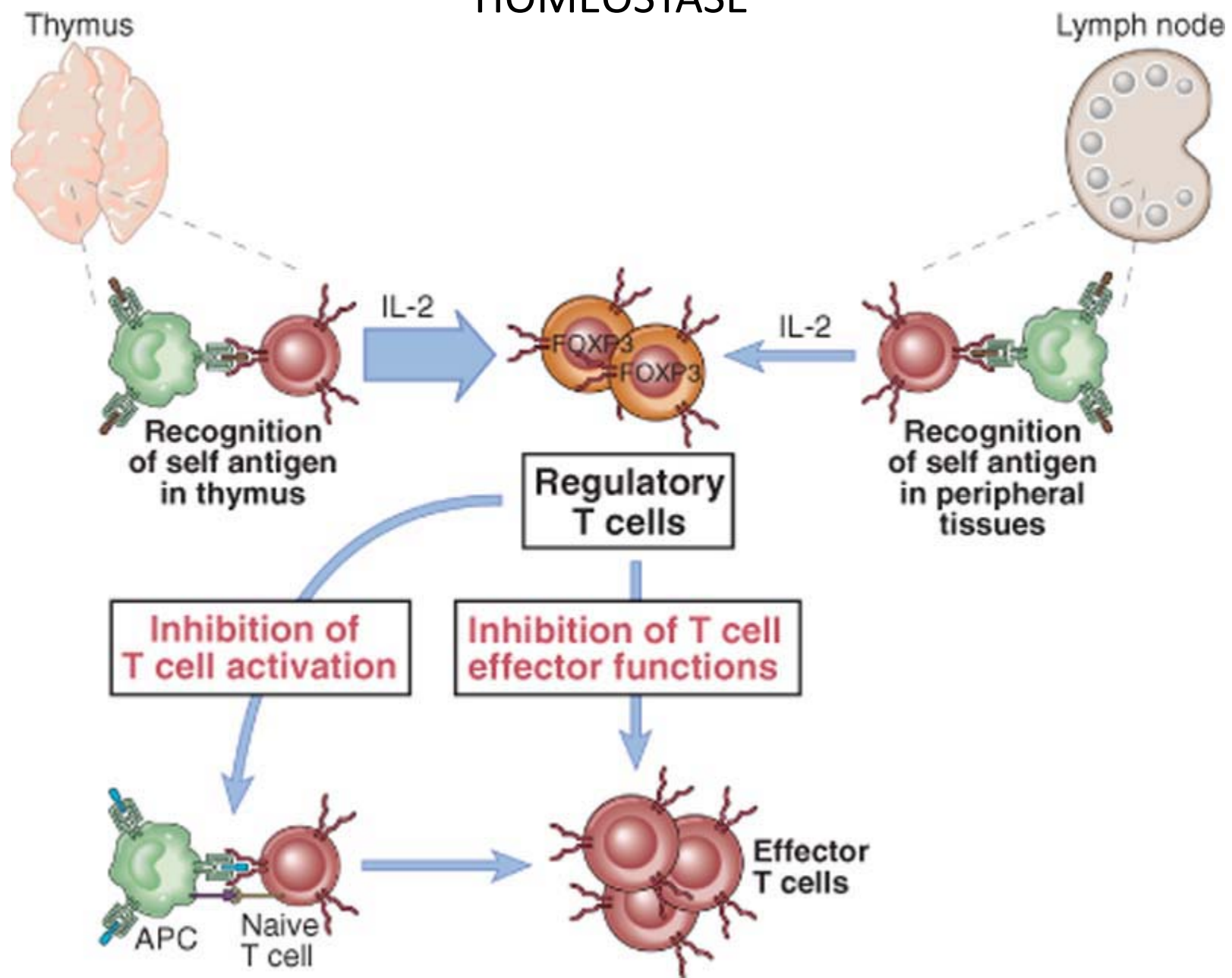
Effector mechanisms Th17



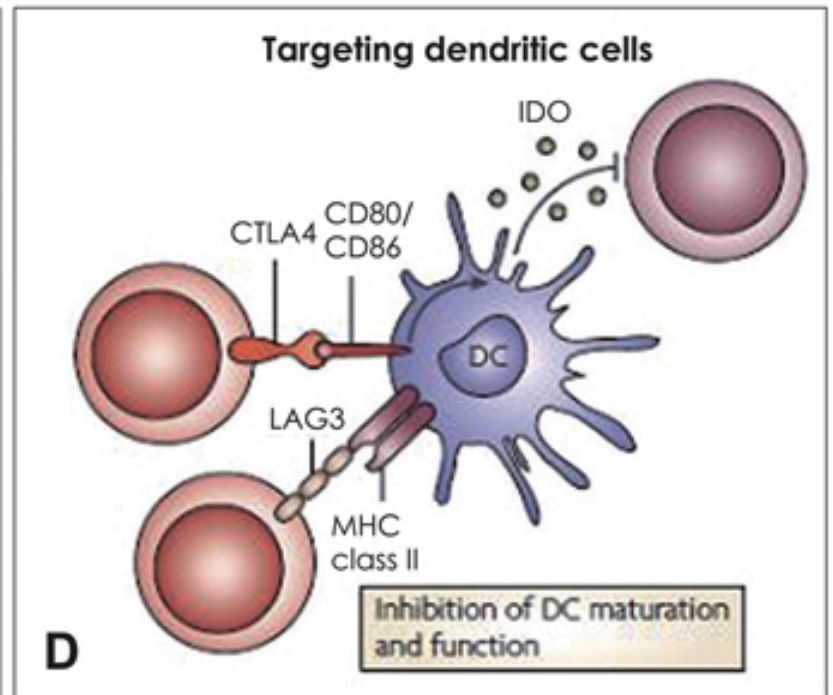
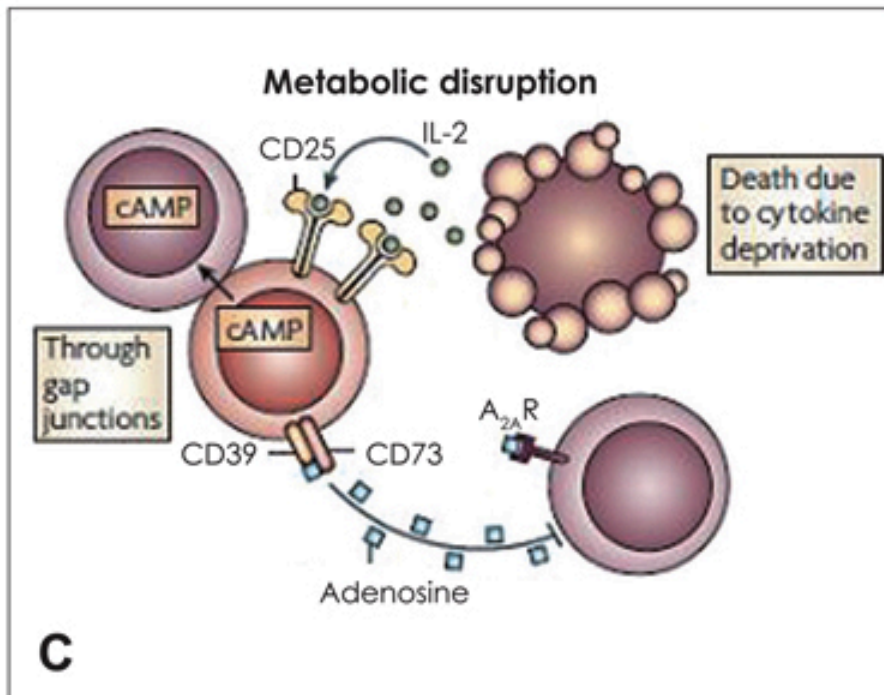
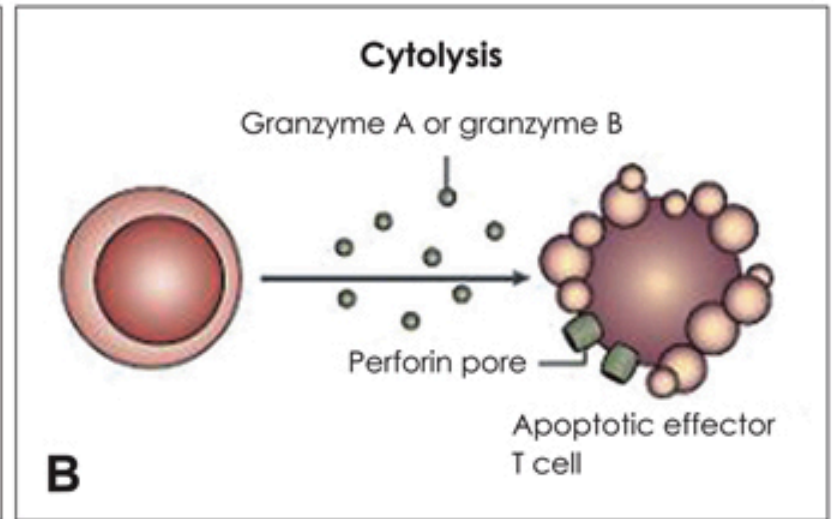
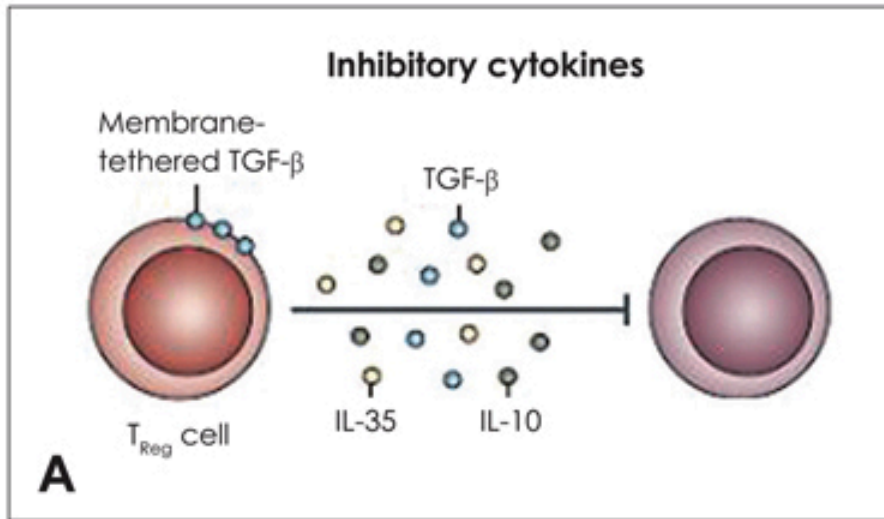
IL-17 – recruitment of Th1 cells



CÉLULAS T REGULADORAS CONTROLAM RESPOSTA EFETORA E MANTÊM HOMEOSTASE

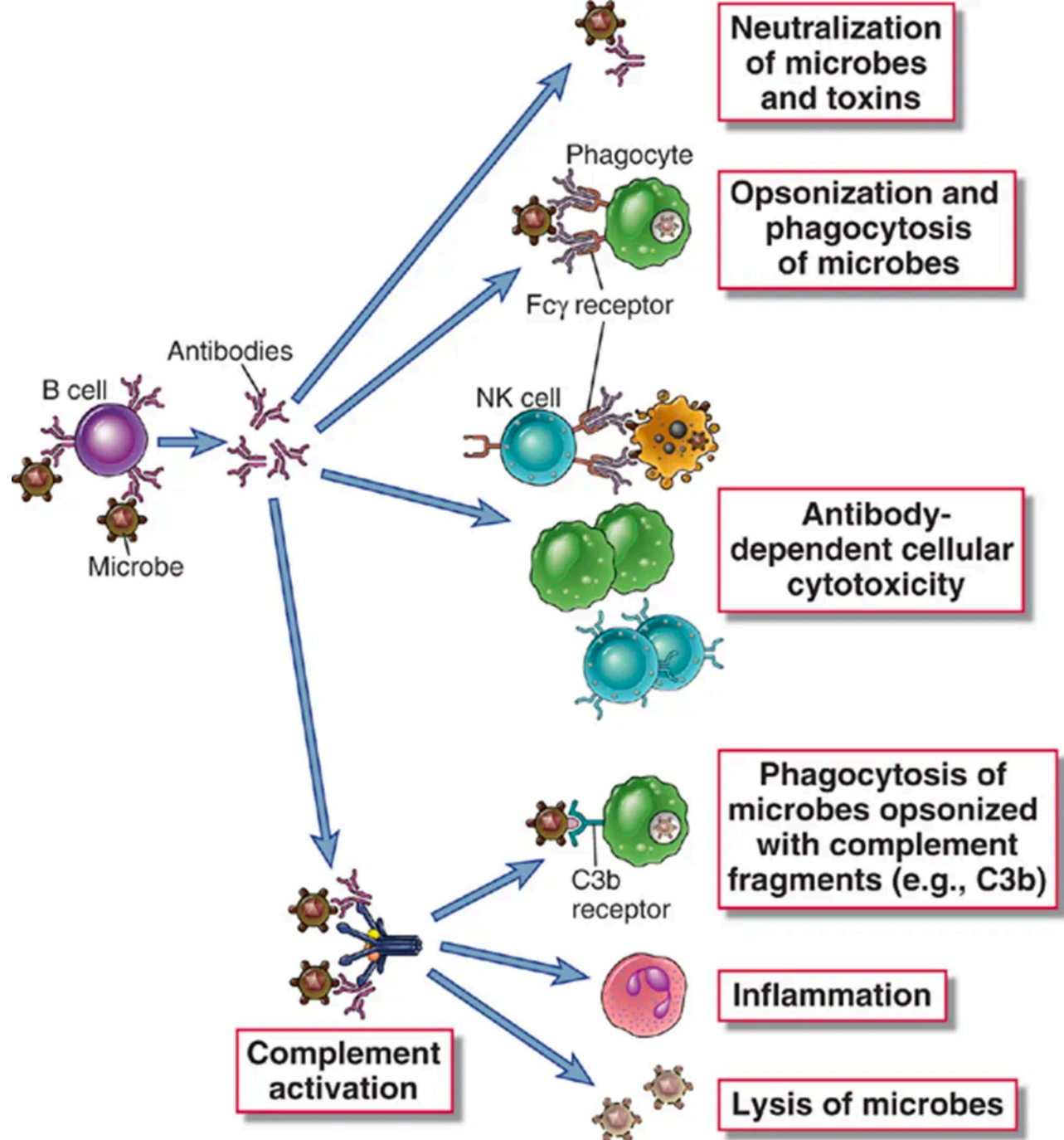


REGULATORY T CELLS



ANTIBODIES

Effector functions



antibodies localization and function

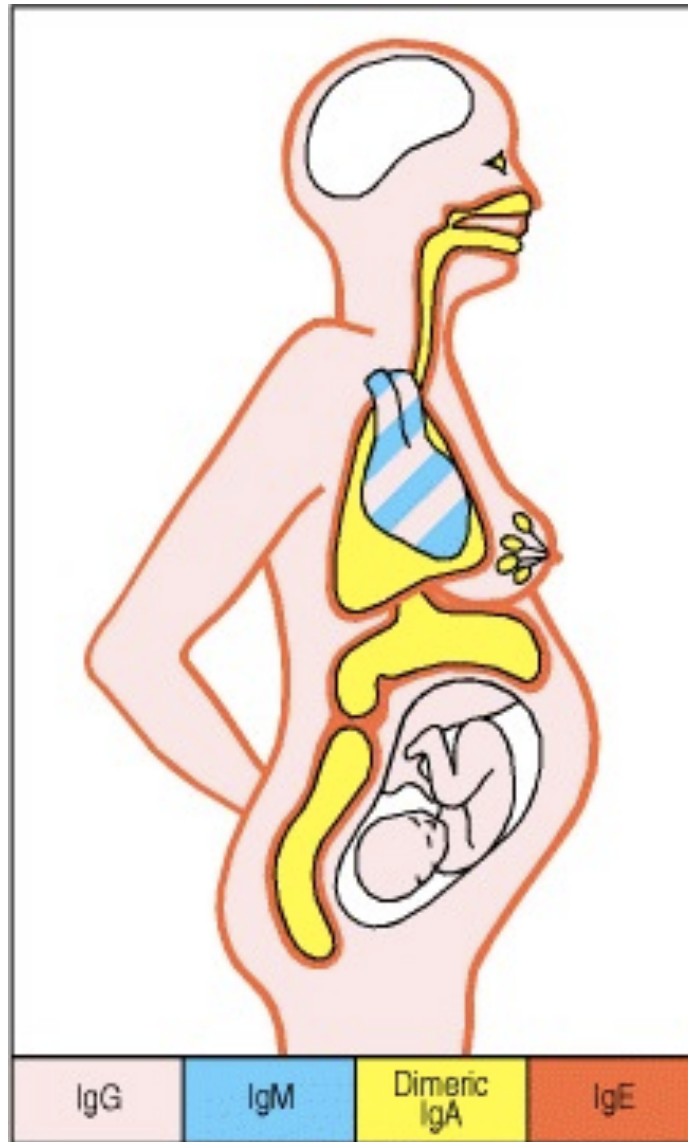
Function	IgM	IgG1	IgA	IgE
neutralização	+	+++	+++	-
opsonização	-	+++	+	-
Ativação de NK	-	++	-	-
Ativação de mastócitos	-	+	-	+++
Ativação de SC	+++	++	+	-

Property	IgM	IgG1	IgA	IgE
Transporte pelo epitélio	+	-	+++ (dimer)	-
Transporte pela placenta	-	+++	-	-
Difusão extracelular	+/-	+++	++ (monomer)	+
mg/ml no soro	1.5	9	2.5	5×10^{-5}

Figure 4.32 The Immune System, 3ed. (© Garland Science)

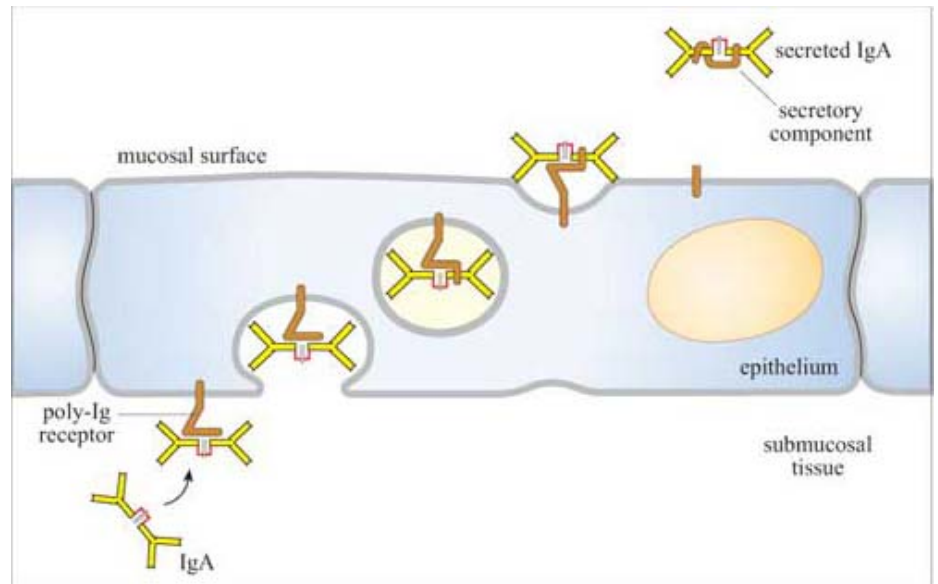
Localization

IgM pentamers stay in the blood

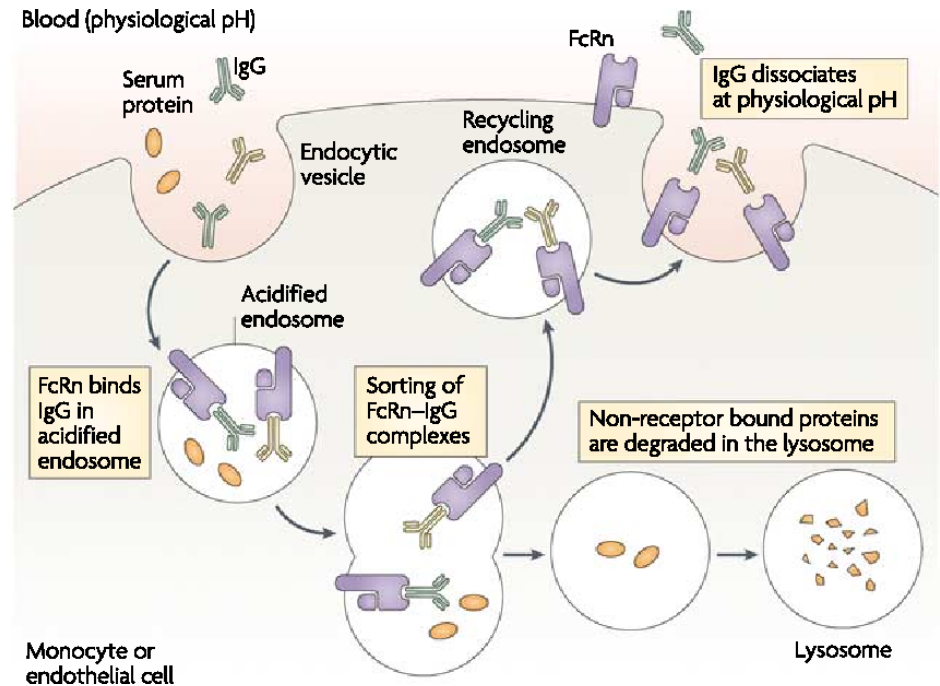


Localization

IgA dimers transcytosis

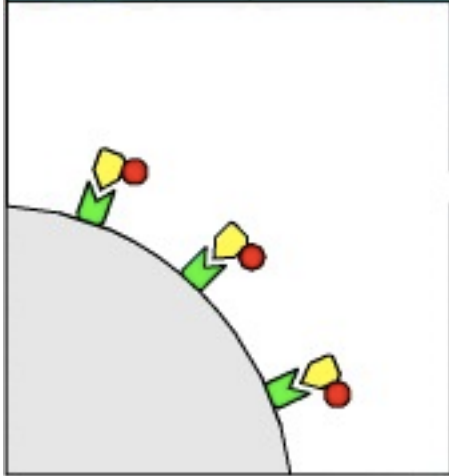


IgG transport through the placenta

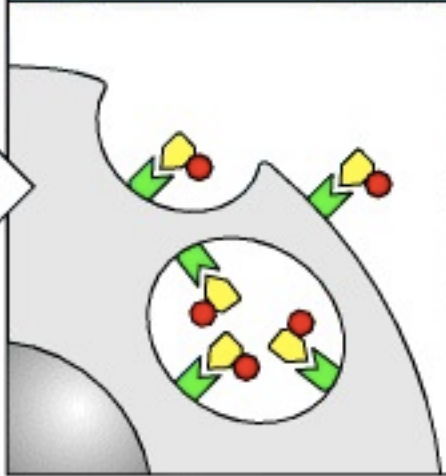


Neutralization

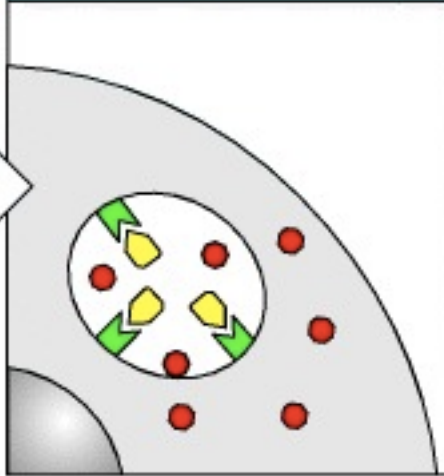
Toxin binds to cellular receptors



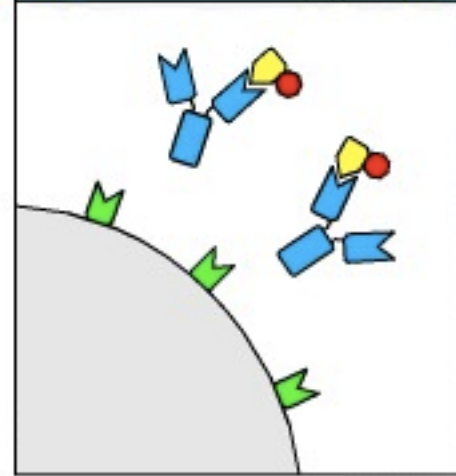
Endocytosis of toxin:receptor complexes



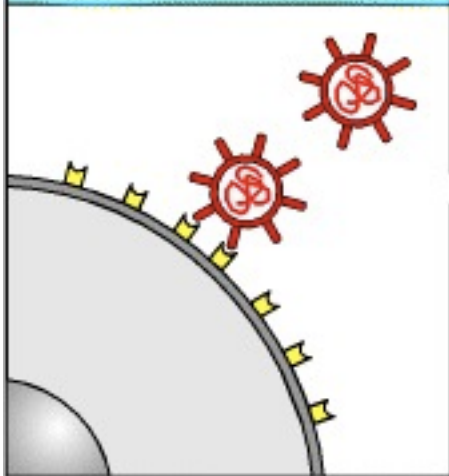
Dissociation of toxin to release active chain, which poisons cell



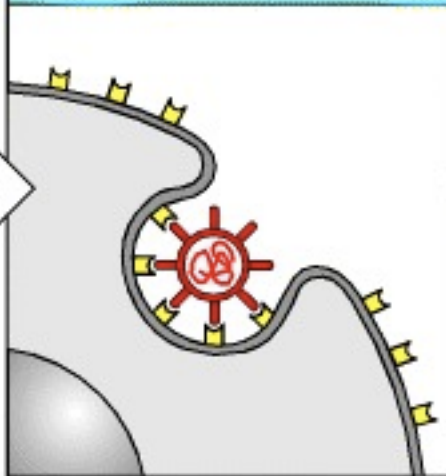
Antibody protects cell by blocking binding of toxin



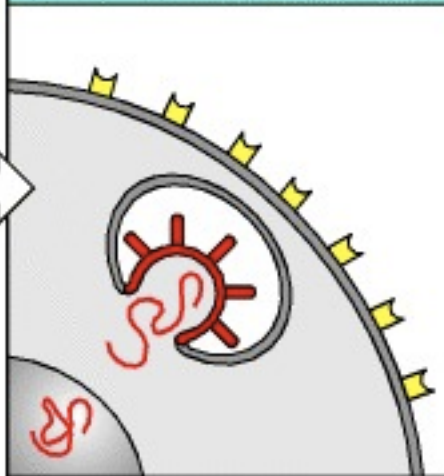
Virus binds to receptors on cell surface



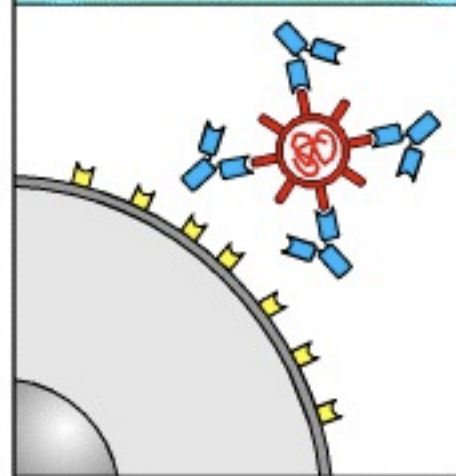
Receptor-mediated endocytosis of virus



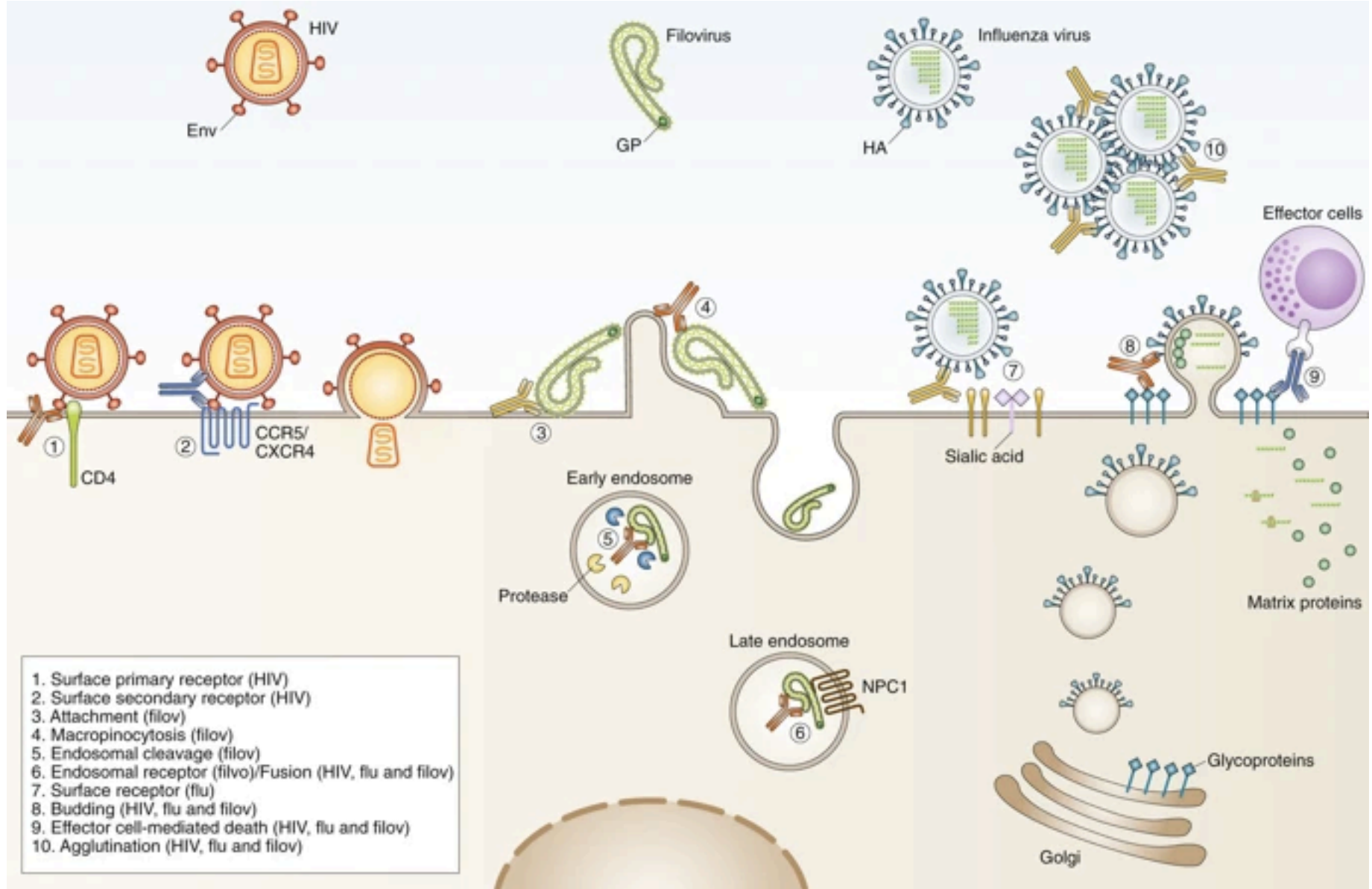
Acidification of endosome after endocytosis triggers fusion of virus with cell and entry of viral DNA



Antibody blocks binding to virus receptor and can also block fusion event

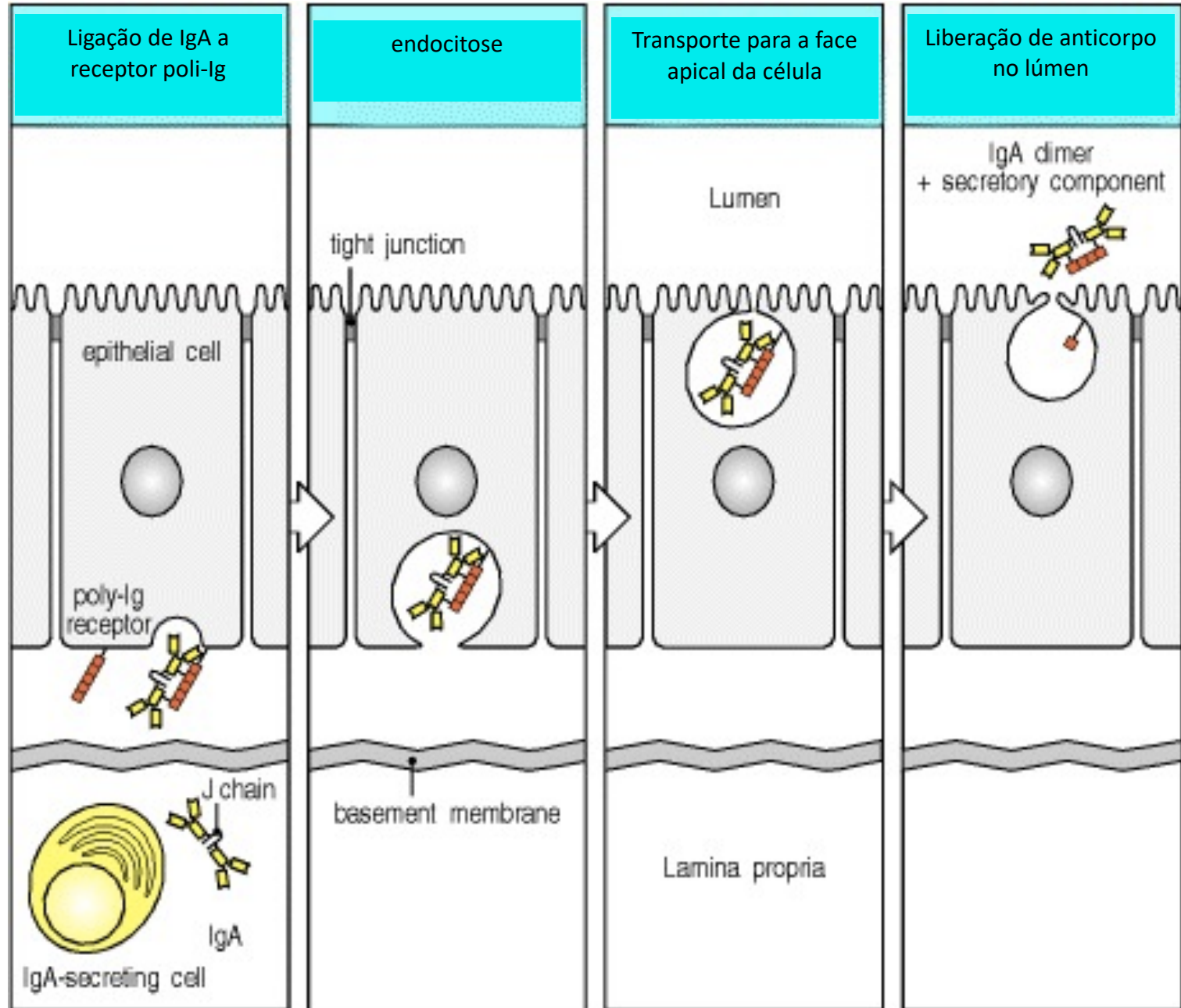


Neutralization



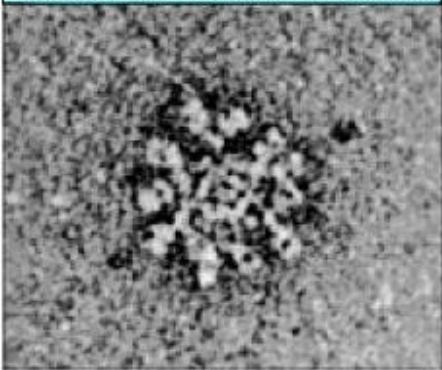
1. Surface primary receptor (HIV)
2. Surface secondary receptor (HIV)
3. Attachment (filov)
4. Macropinocytosis (filov)
5. Endosomal cleavage (filov)
6. Endosomal receptor (filvo)/Fusion (HIV, flu and filov)
7. Surface receptor (flu)
8. Budding (HIV, flu and filov)
9. Effector cell-mediated death (HIV, flu and filov)
10. Agglutination (HIV, flu and filov)

IgA E TRANSCITOSE



Complement activation

IgM 'planar' conformation

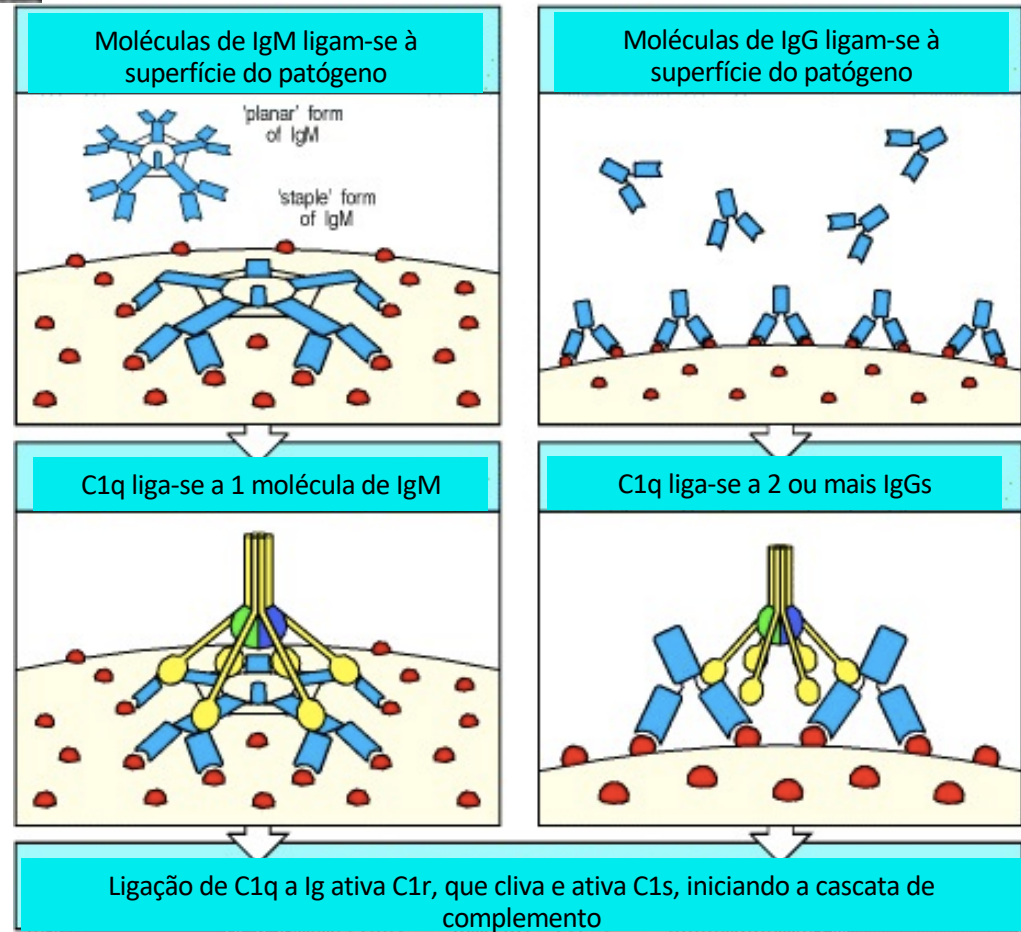


IgM 'staple' conformation



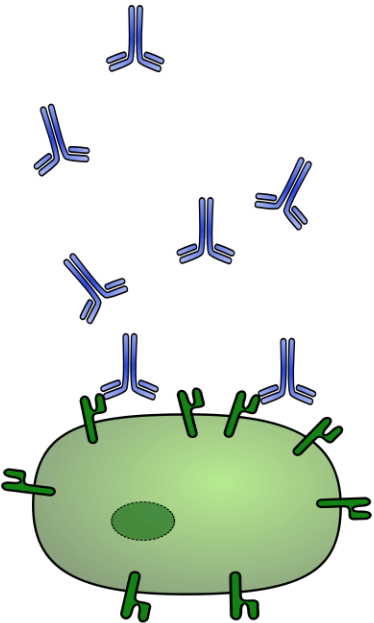
IgM e IgG

IgM, em geral, tem baixa afinidade ao antígeno, mas por ter 10 sítios de ligação forma uma plataforma ideal para ativação do sistema complemento

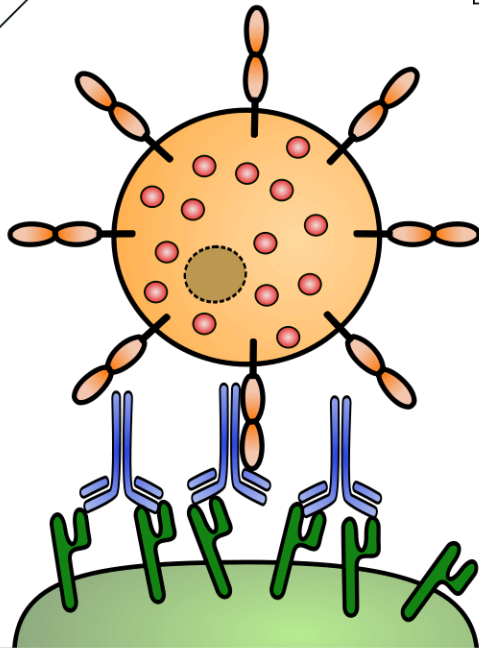


Antibody mediated cytotoxicity

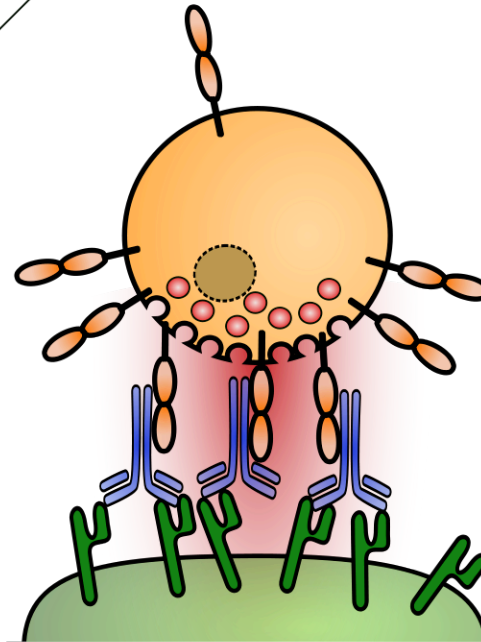
Antibodies bind antigens on the surface of target cells



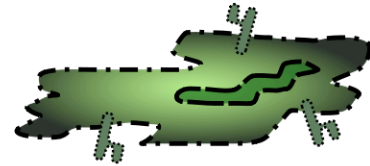
NK cell CD16 Fc receptors recognise cell-bound antibodies



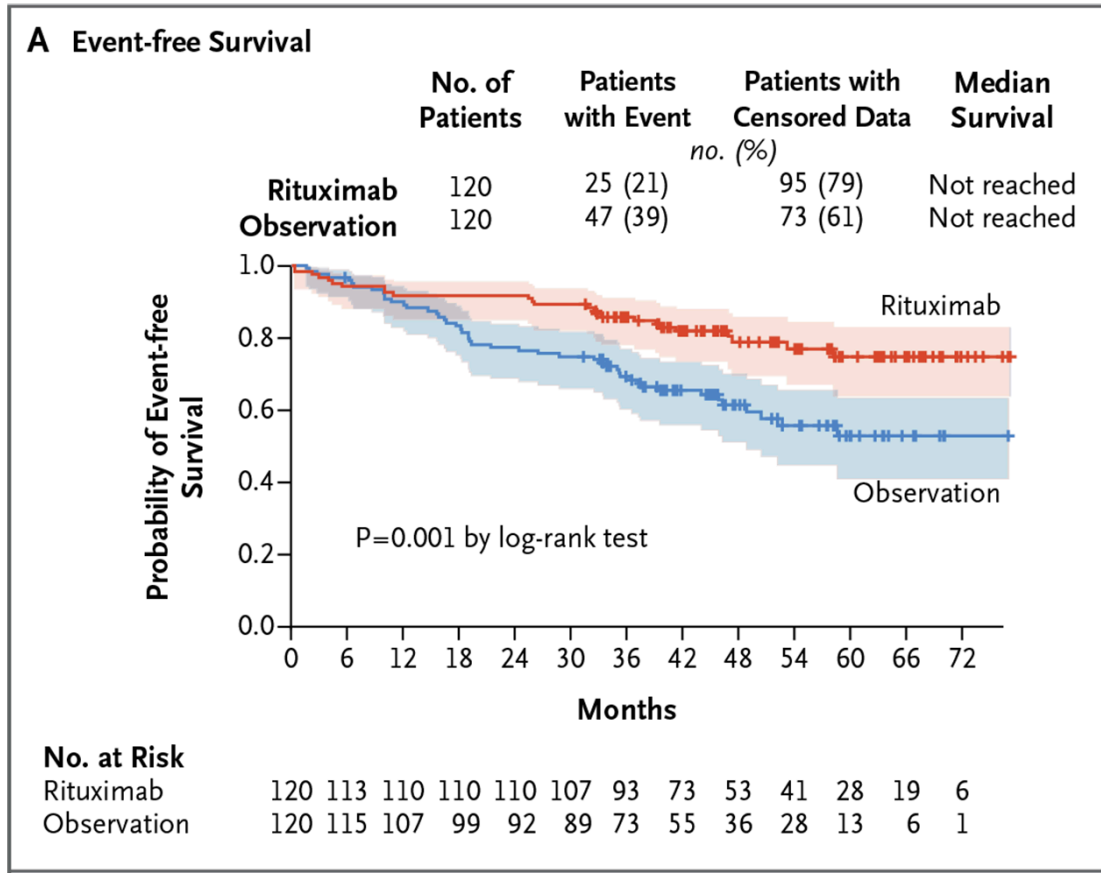
Cross-linking of CD16 triggers degranulation into a lytic synapse



Tumour cells die by apoptosis



translation – lymphoma – treatment with Rituximab



Karen Sokal-Gutierrez, NEJM, 2017

Rituximab after transplantation in mantle-cell lymphoma

Opsonization – phagocytosis, neutralization, CS activation

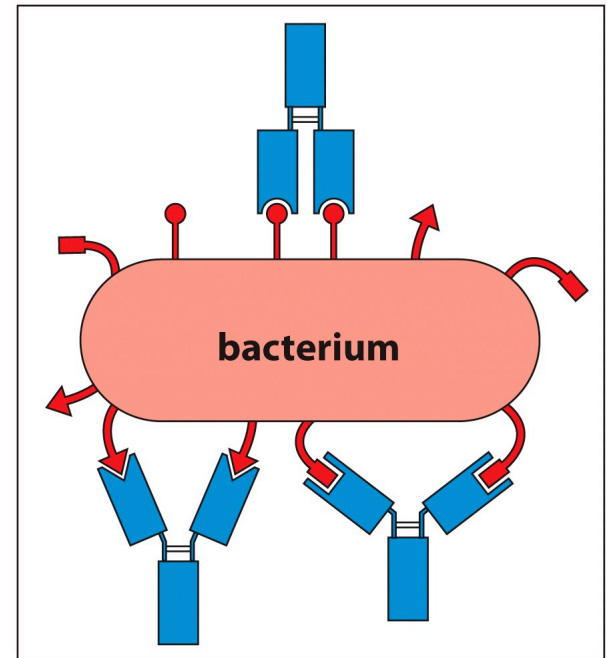
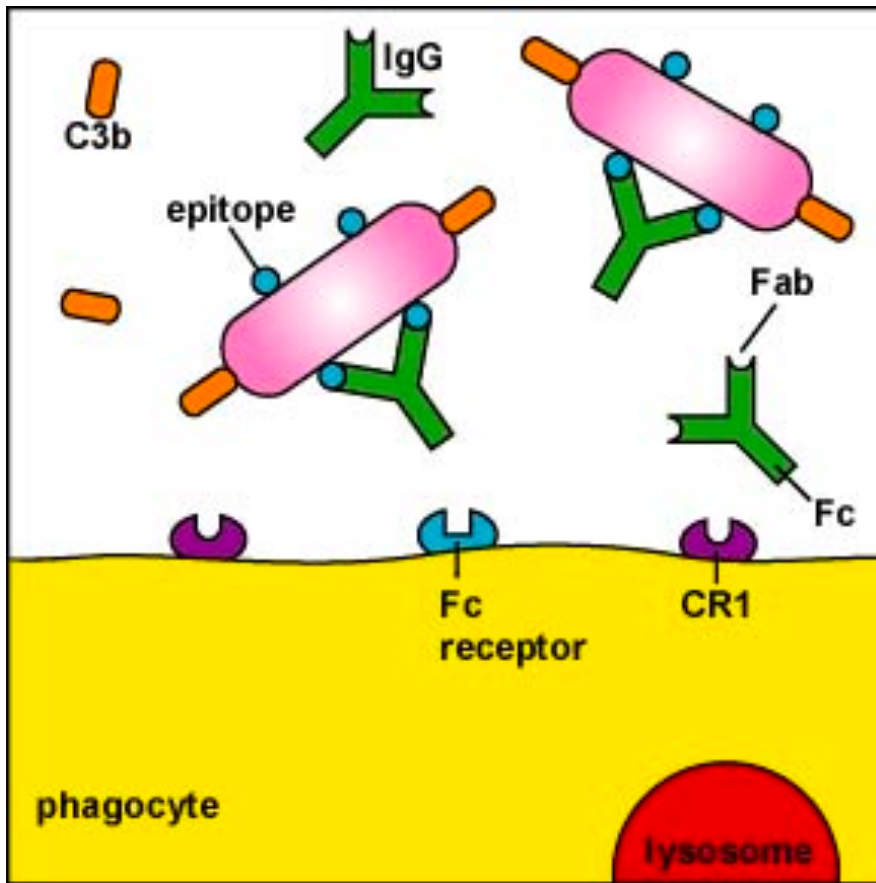
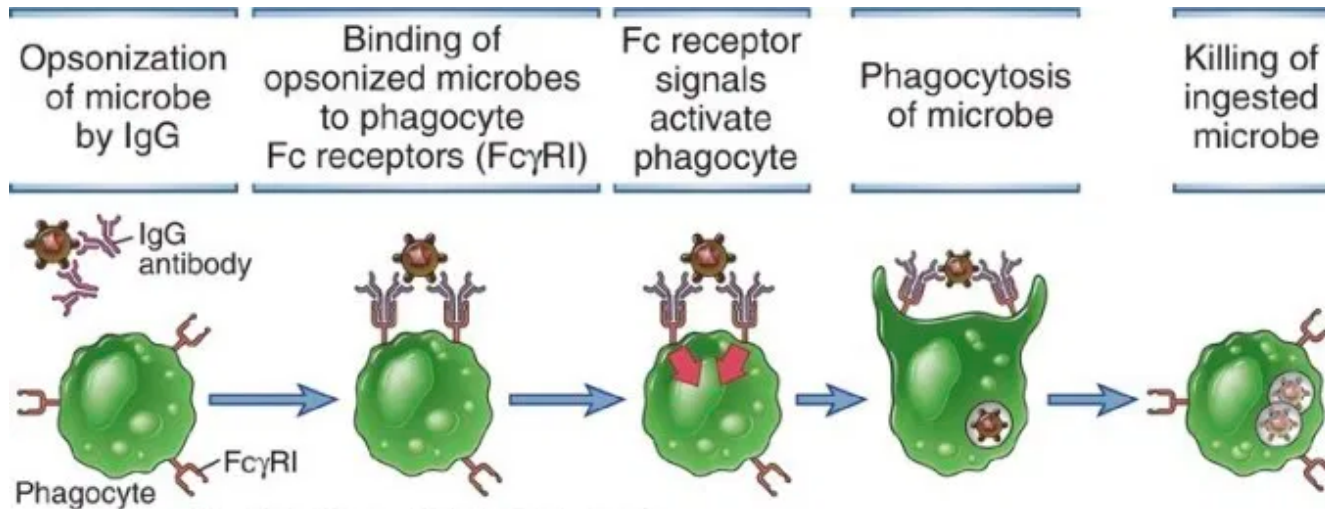


Figure 4.4 The Immune System, 3ed. (© Garland Science 2009)

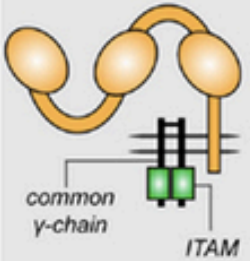
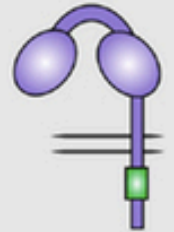
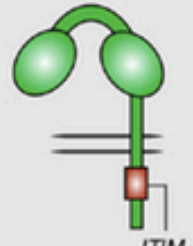

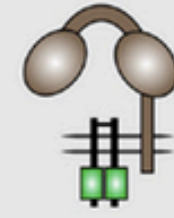
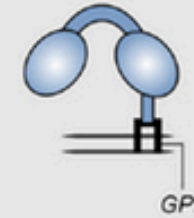
Opsonization and phagocytosis



Abbas et al: Cellular and Molecular Immunology, 7e.

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Fcγ receptors

Name	FcγRI CD64	FcγRIIa CD32a	FcγRIIb C32b	FcγRIIc CD32c	FcγRIIIa CD16a	FcγRIIIb CD16b
Structure	 <p>Diagram of FcγRI structure showing two orange extracellular domains, a common γ-chain, and an ITAM signaling domain.</p>	 <p>Diagram of FcγRIIa structure showing two purple extracellular domains and a green ITAM signaling domain.</p>	 <p>Diagram of FcγRIIb structure showing two green extracellular domains and a red ITIM signaling domain.</p>	 <p>Diagram of FcγRIIc structure showing two green extracellular domains and a purple ITAM signaling domain.</p>	 <p>Diagram of FcγRIIIa structure showing two brown extracellular domains and a green ITAM signaling domain.</p>	 <p>Diagram of FcγRIIIb structure showing two blue extracellular domains and a GPI anchor.</p>
Function	Activating	Activating	Inhibitory	Activating	Activating	Activating
Affinity	High	Low	Low	Low	Low	Low
SNP		131H/R R: reduced affinity to IgG2	232I/T T: decreased inhibitory activity	57Q/X X: stop codon (non-functional protein)	158F/V V: increased affinity to IgG1/3/4	NA1/2 NA2: reduced affinity to IgG1/3