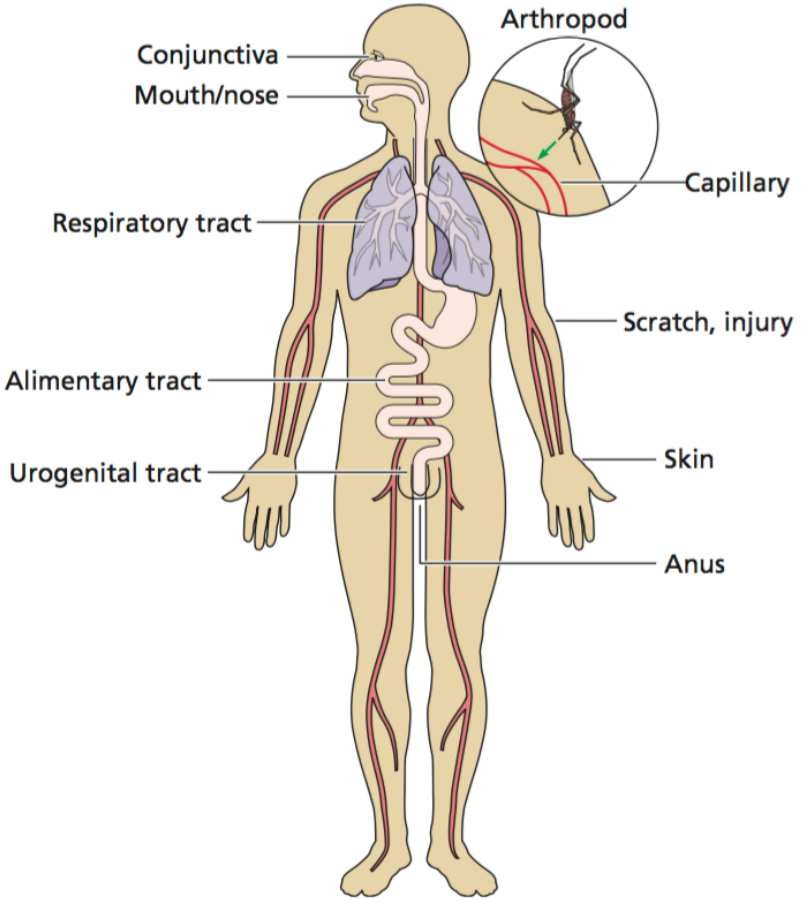
Adaptive Immunity

Lecture 14
Biology 3310/4310
Virology
Spring 2017

Life is simple, but we insist on making it complicated
–CONFUCIUS

Host defenses

- Intrinsic
  - *Always present* in the uninfected cell
  - Apoptosis, autophagy, RNA silencing, antiviral proteins
- Innate immune system: *Induced* by infection
- Adaptive immune system: *Tailored* to pathogen; *memory*



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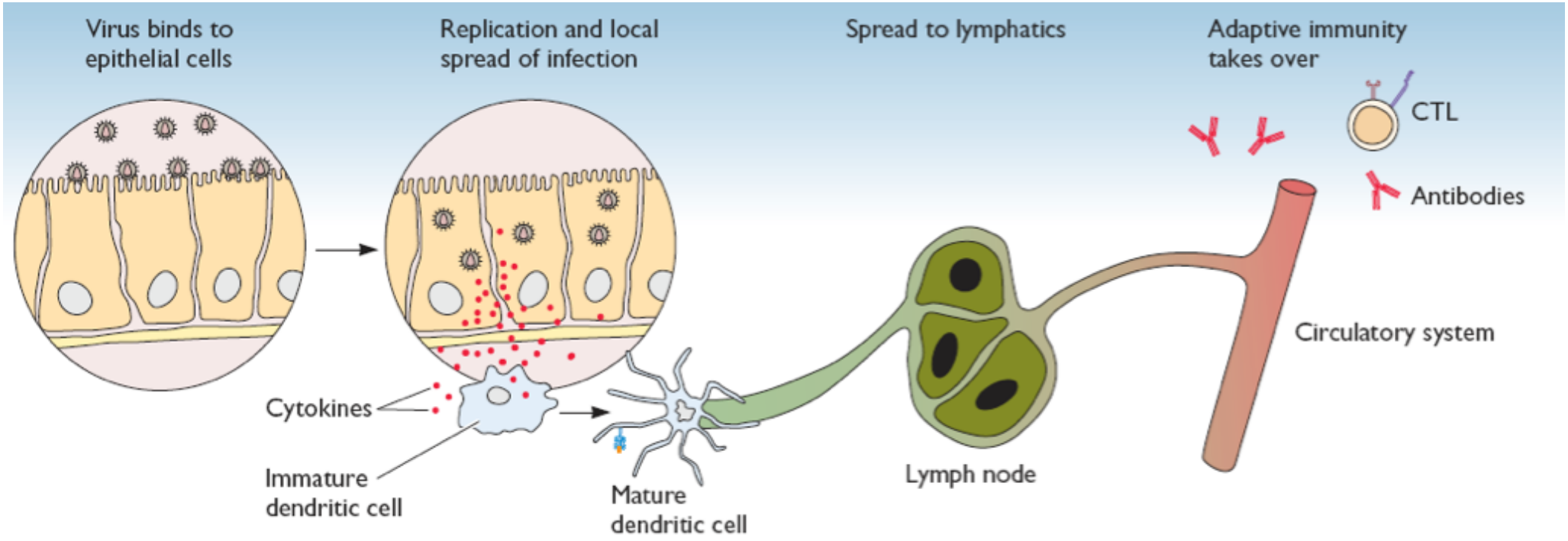

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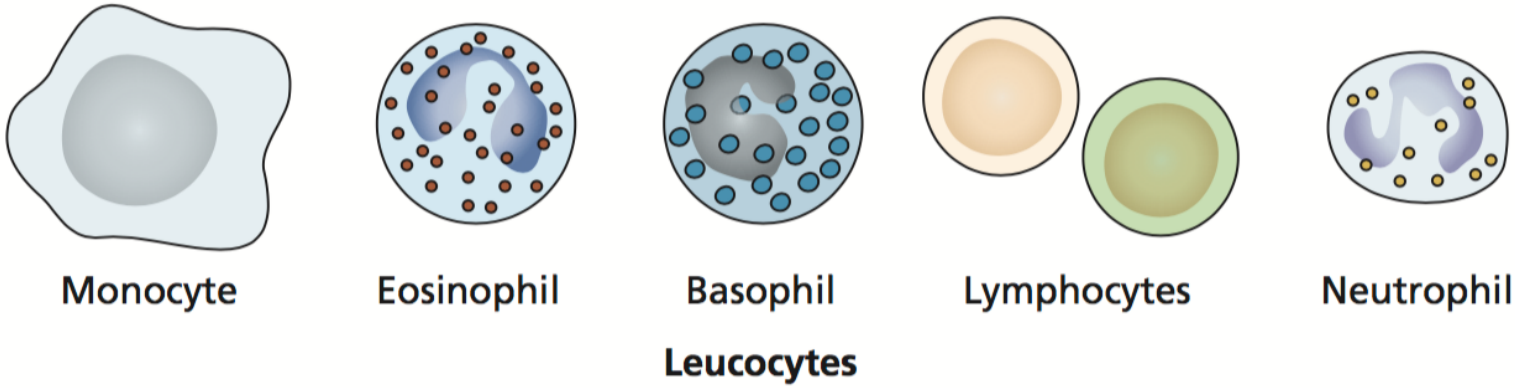
Leukocytes and Lymphocytes



- Leukocyte: general term for white blood cell (lymphocytes, neutrophils, eosinophils, macrophages)
- Lymphocyte: Subset of leukocytes (T, B, NK cells; have variable antigen-detecting cell surface receptors

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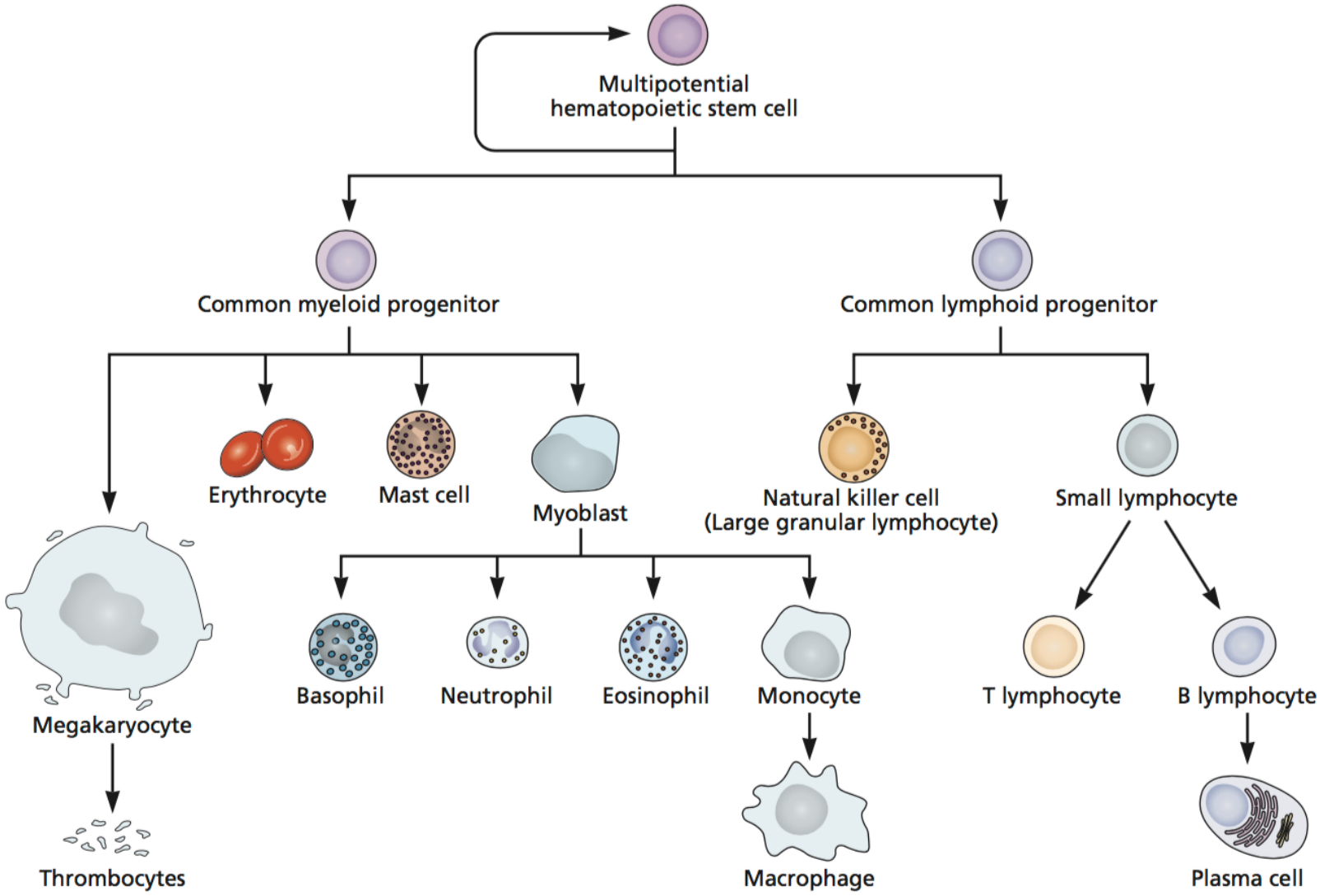
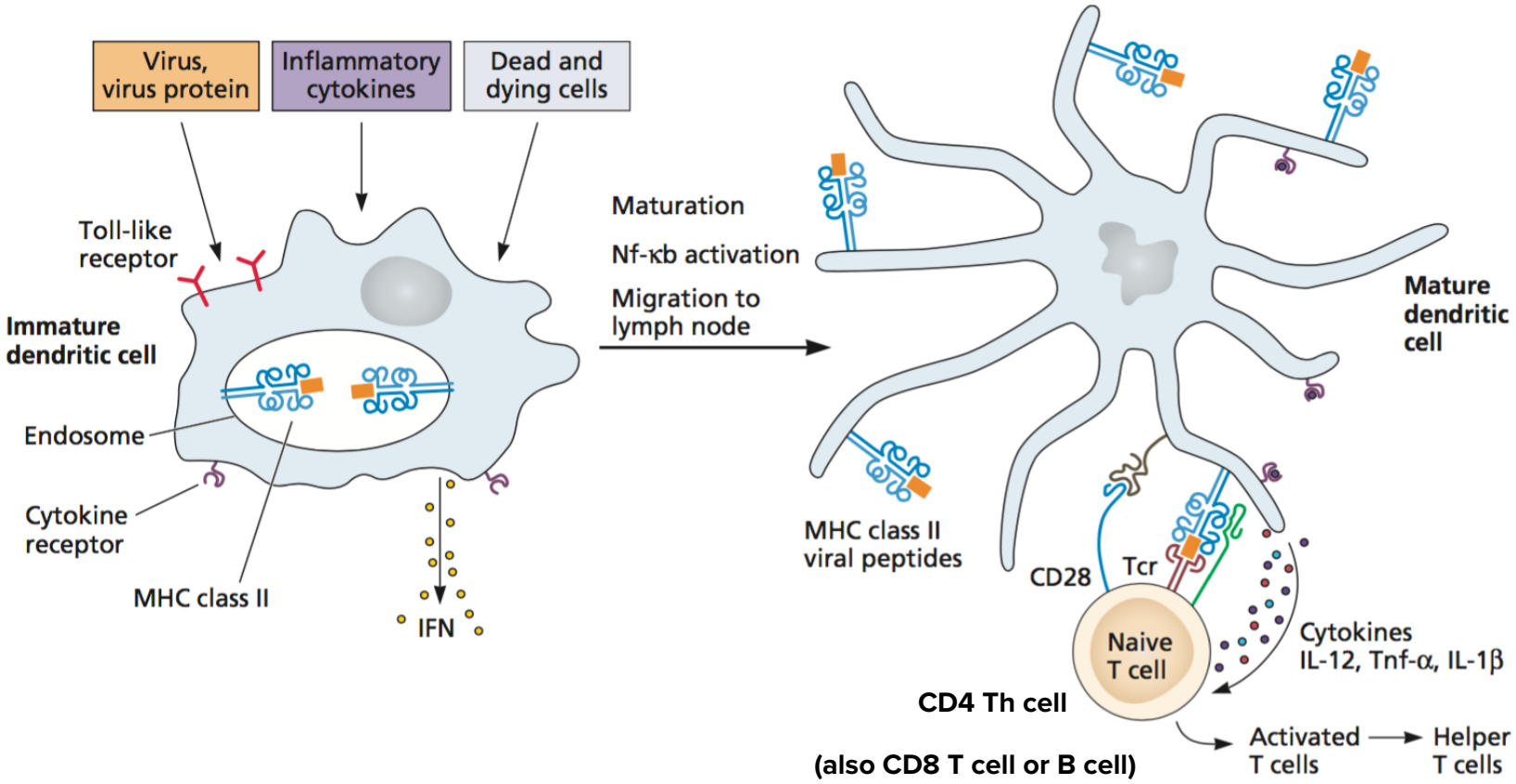

Multipotential
hematopoietic stem cell
Common myeloid progenitor
Common lymphoid progenitor
Erythrocyte
Mast cell
Myoblast
Natural killer cell
(Large granular lymphocyte)
Small lymphocyte
Megakaryocyte
Basophil
Neutrophil
Eosinophil
Monocyte
T lymphocyte
B lymphocyte
Thrombocytes
Macrophage
Plasma cell

Innate instruction of adaptive immunity



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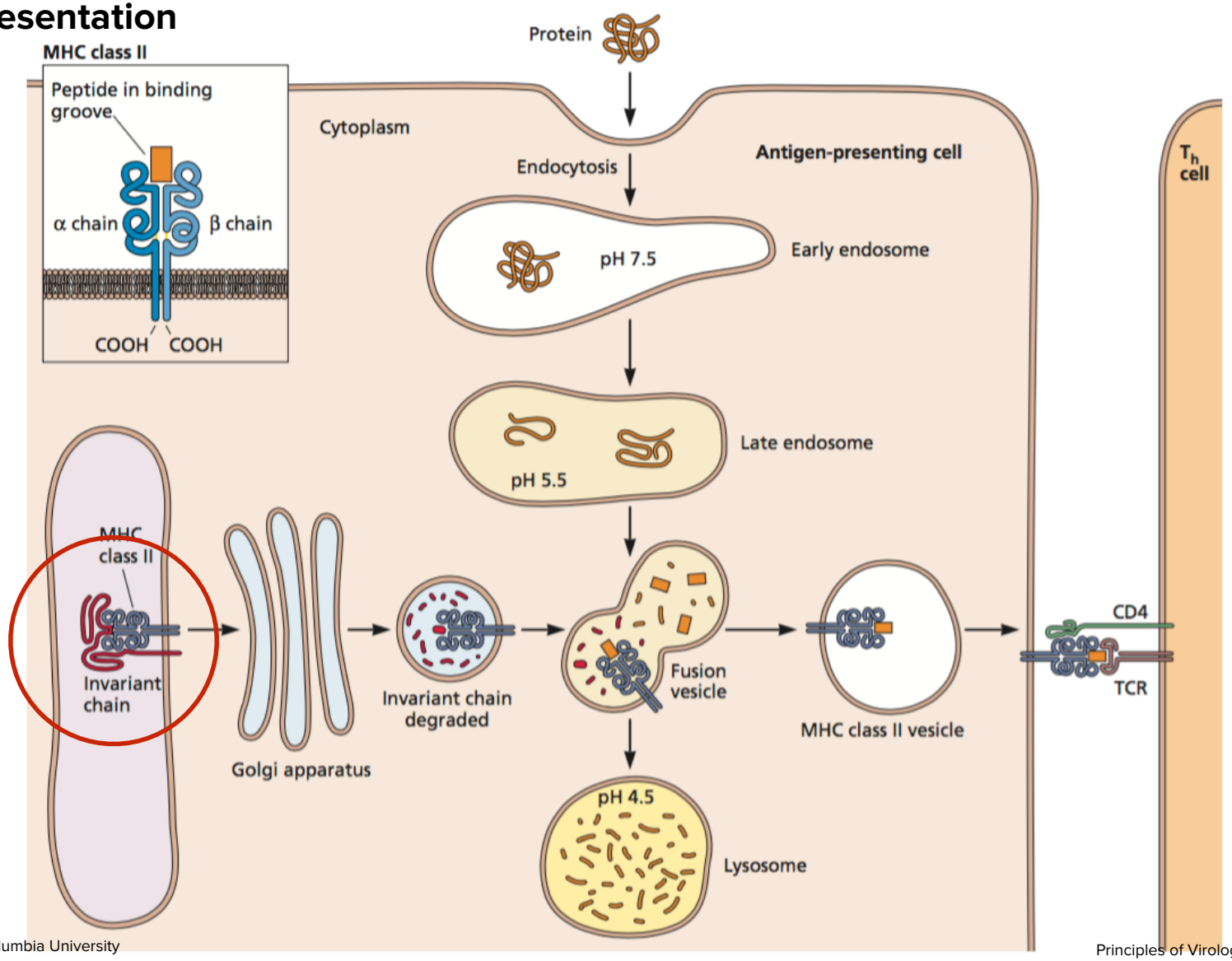
Exogenous antigen presentation

HCMV interferes with MHCII transcription



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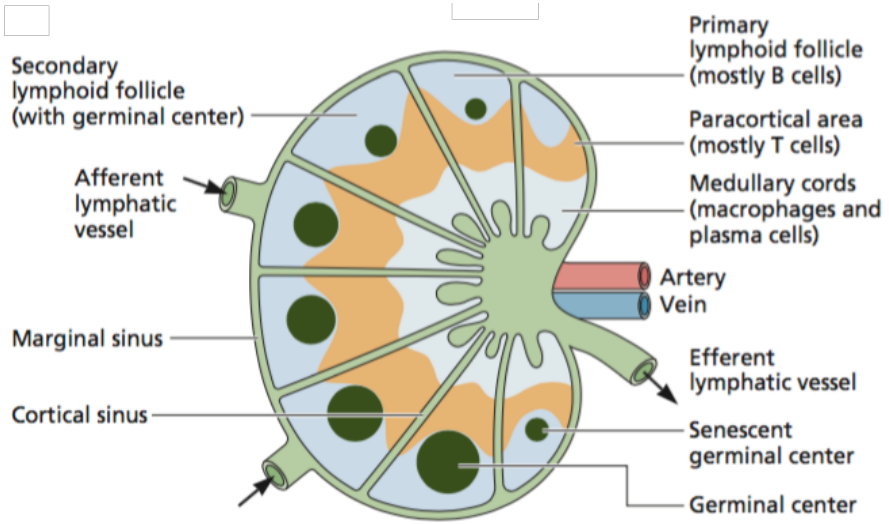
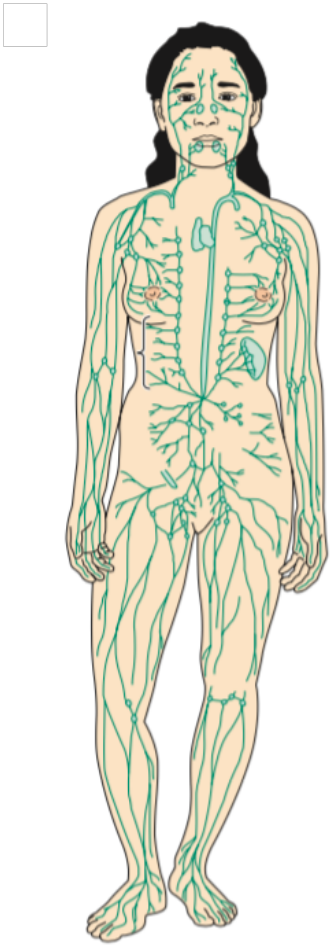
Lymphocyte activation triggers massive cell proliferation





- 1/10,000 - 1/100,000 B or T cells recognize antigen
- 1-2 weeks: 1,000 - 50,000 fold amplification
- Lymphadenopathy

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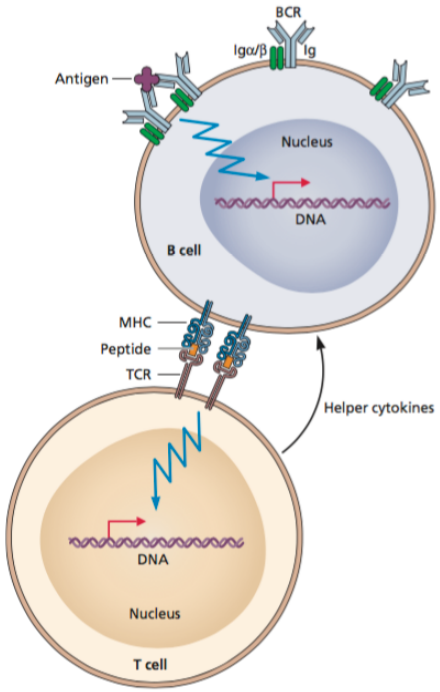
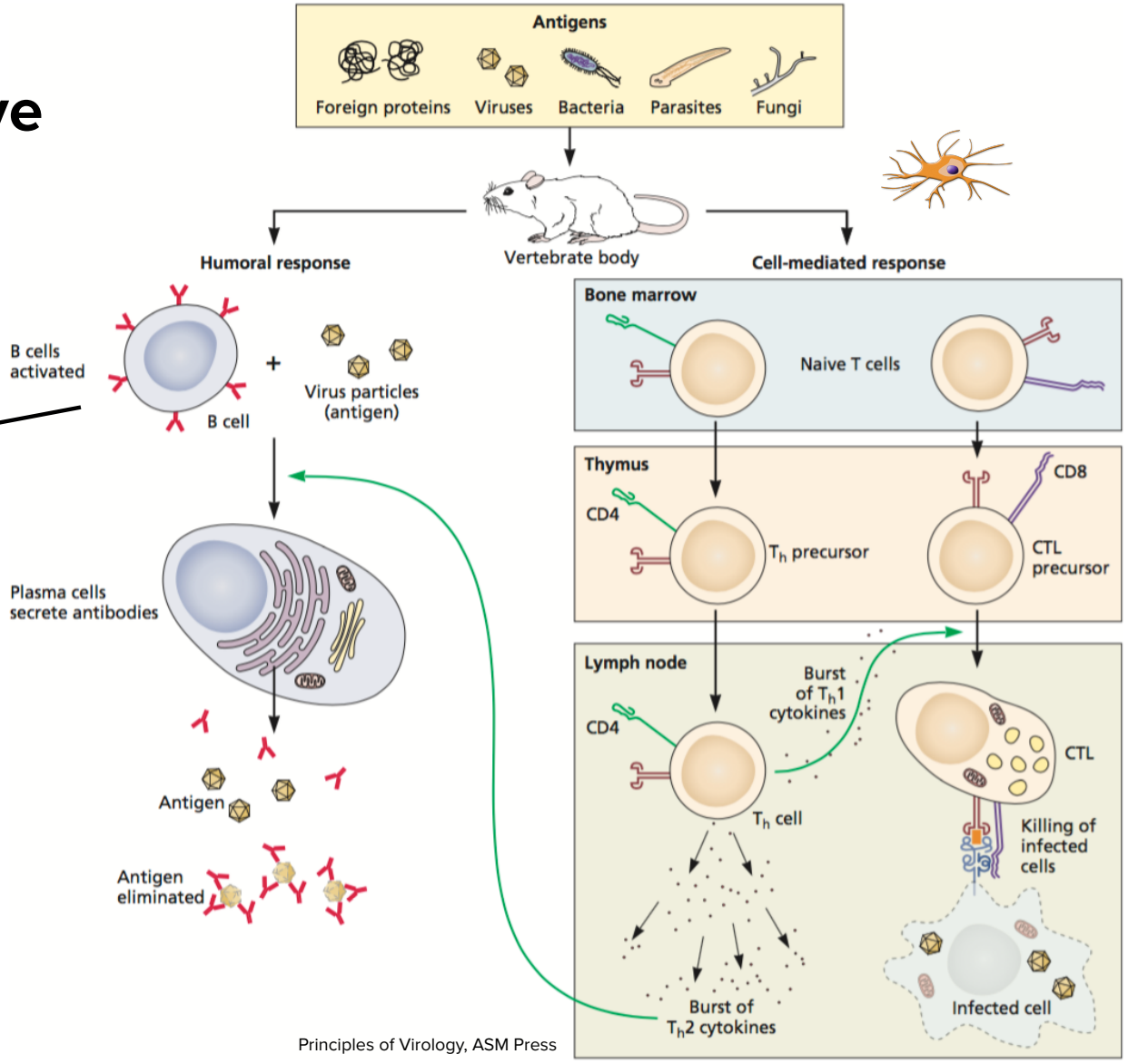
What is a property of innate instruction of adaptive immunity?

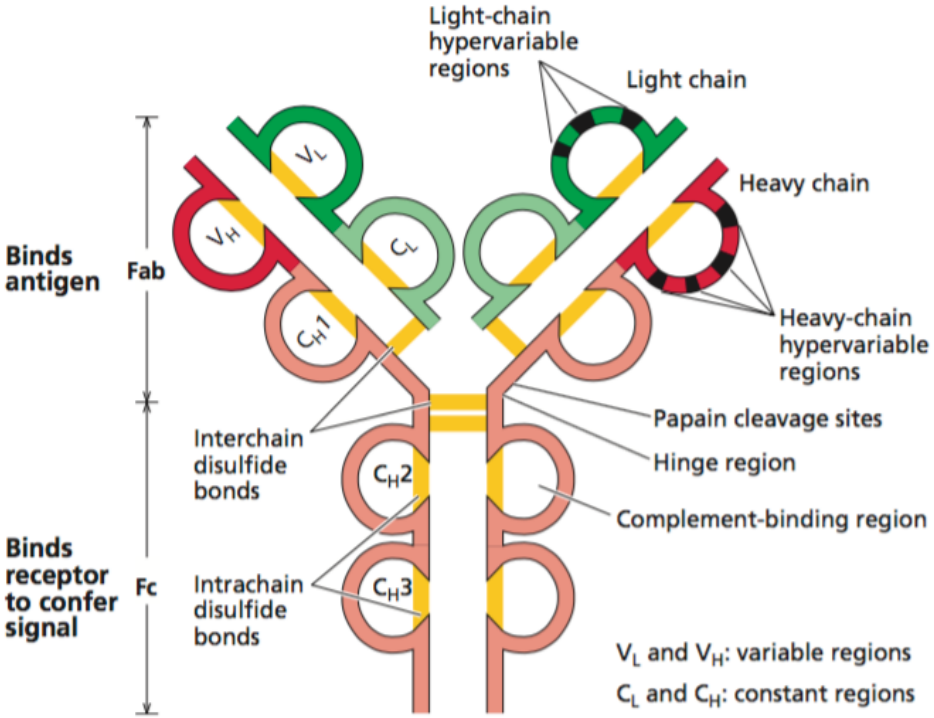
A. Presentation of viral peptides on MHC II to CD4 T cells
B. Endocytosis of viral proteins
C. Activation of DCs by cytokines
D. Sensing by TLRs
E. All of the above

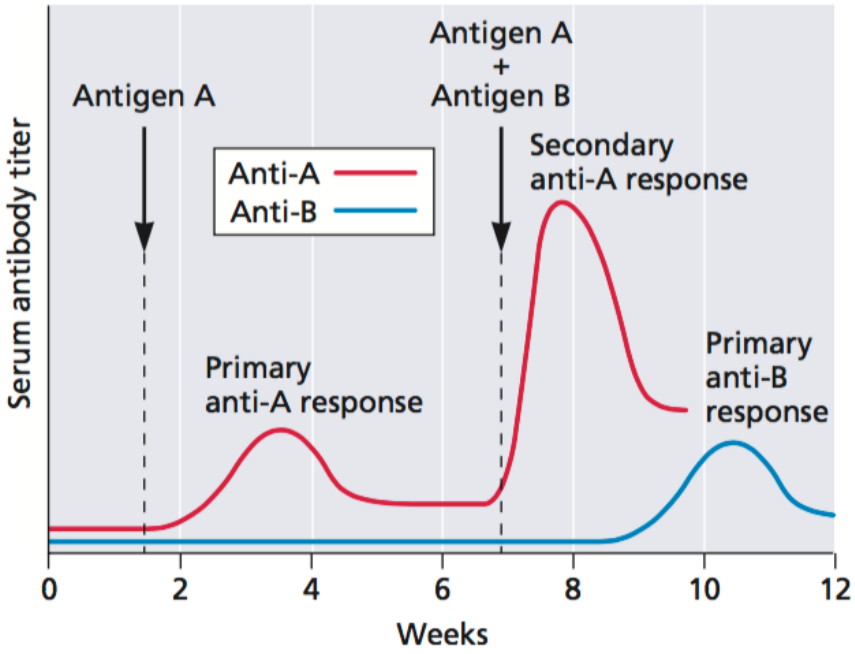
Effectors of the adaptive response





Antibodies





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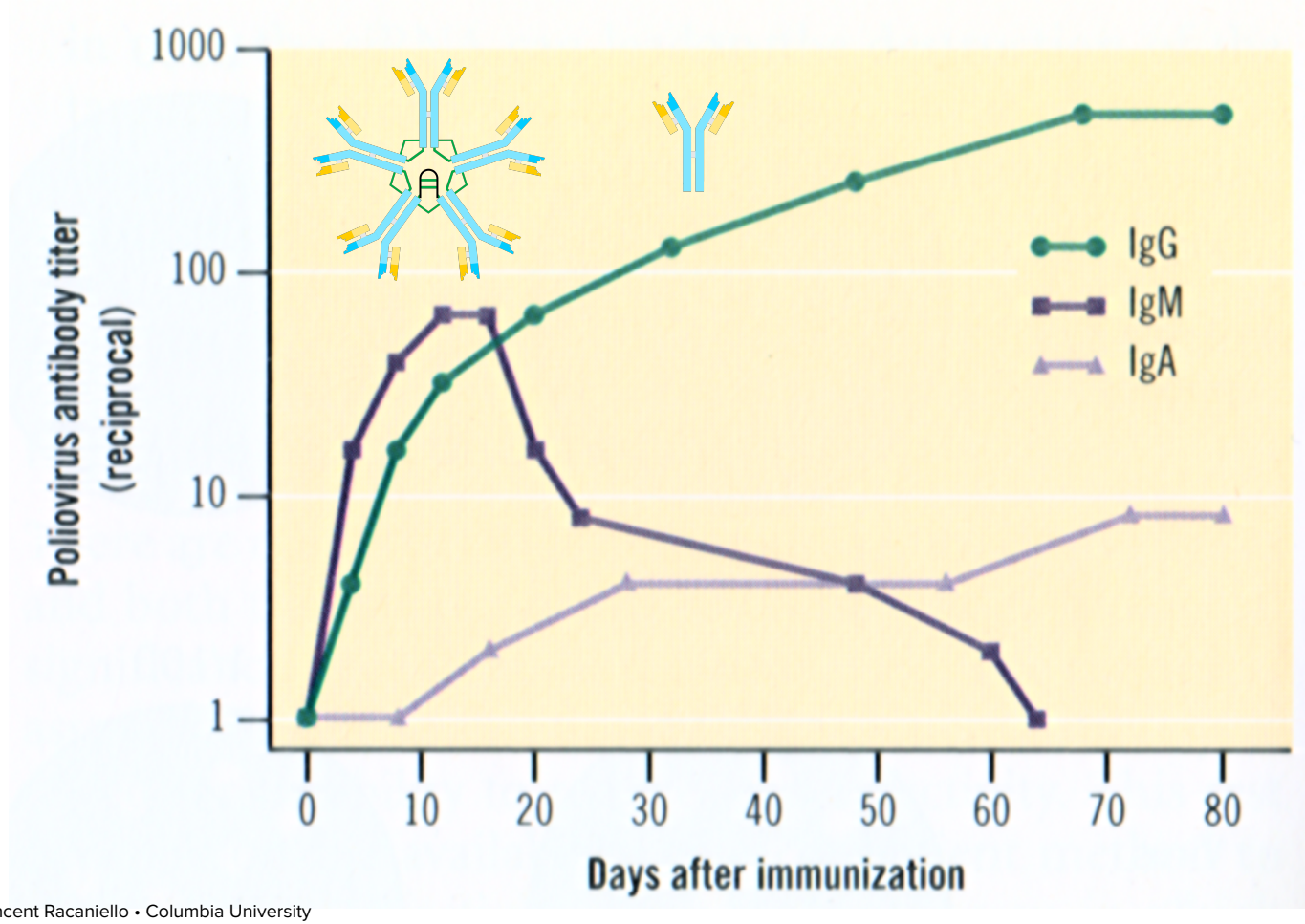
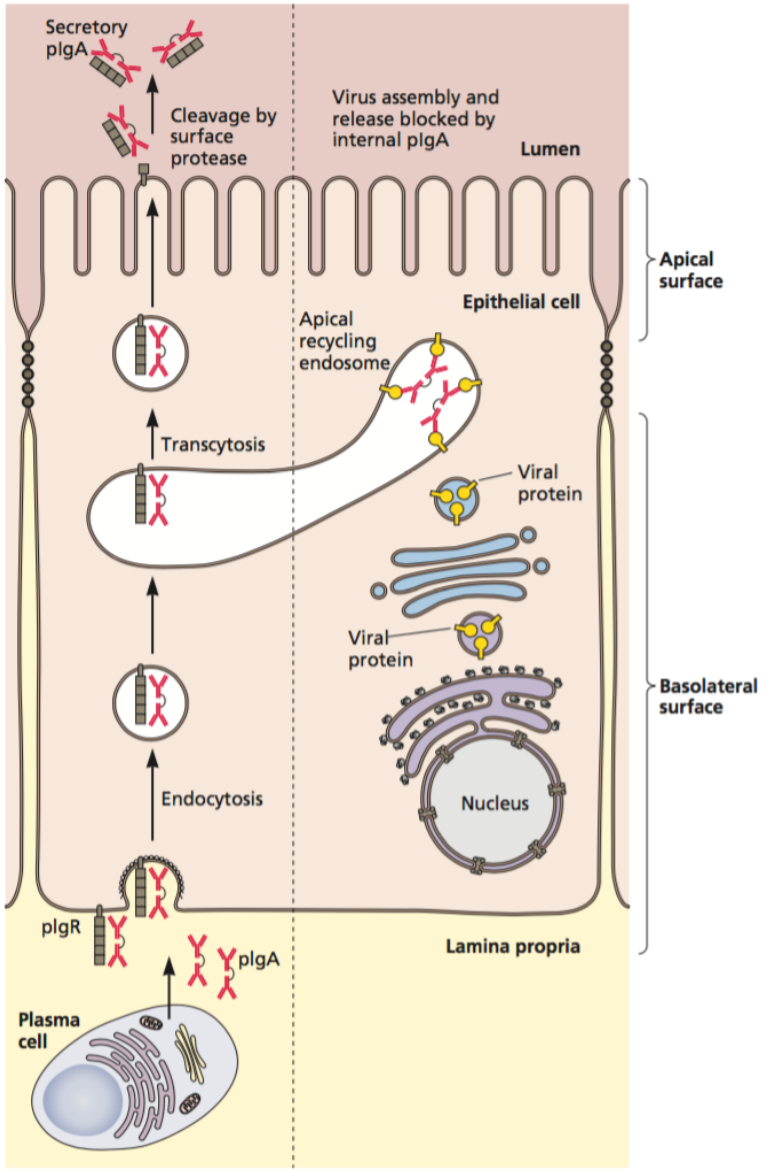
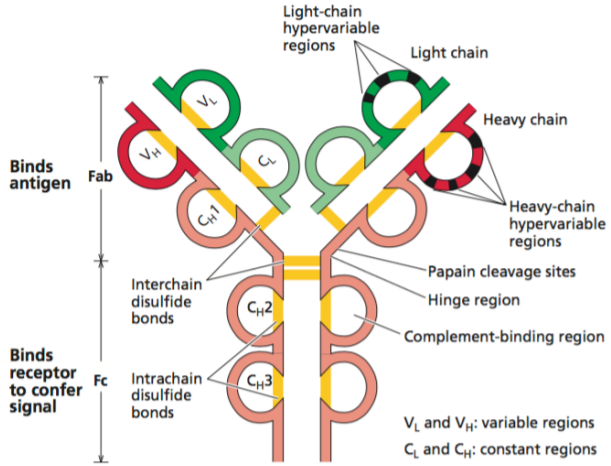
Antibody response



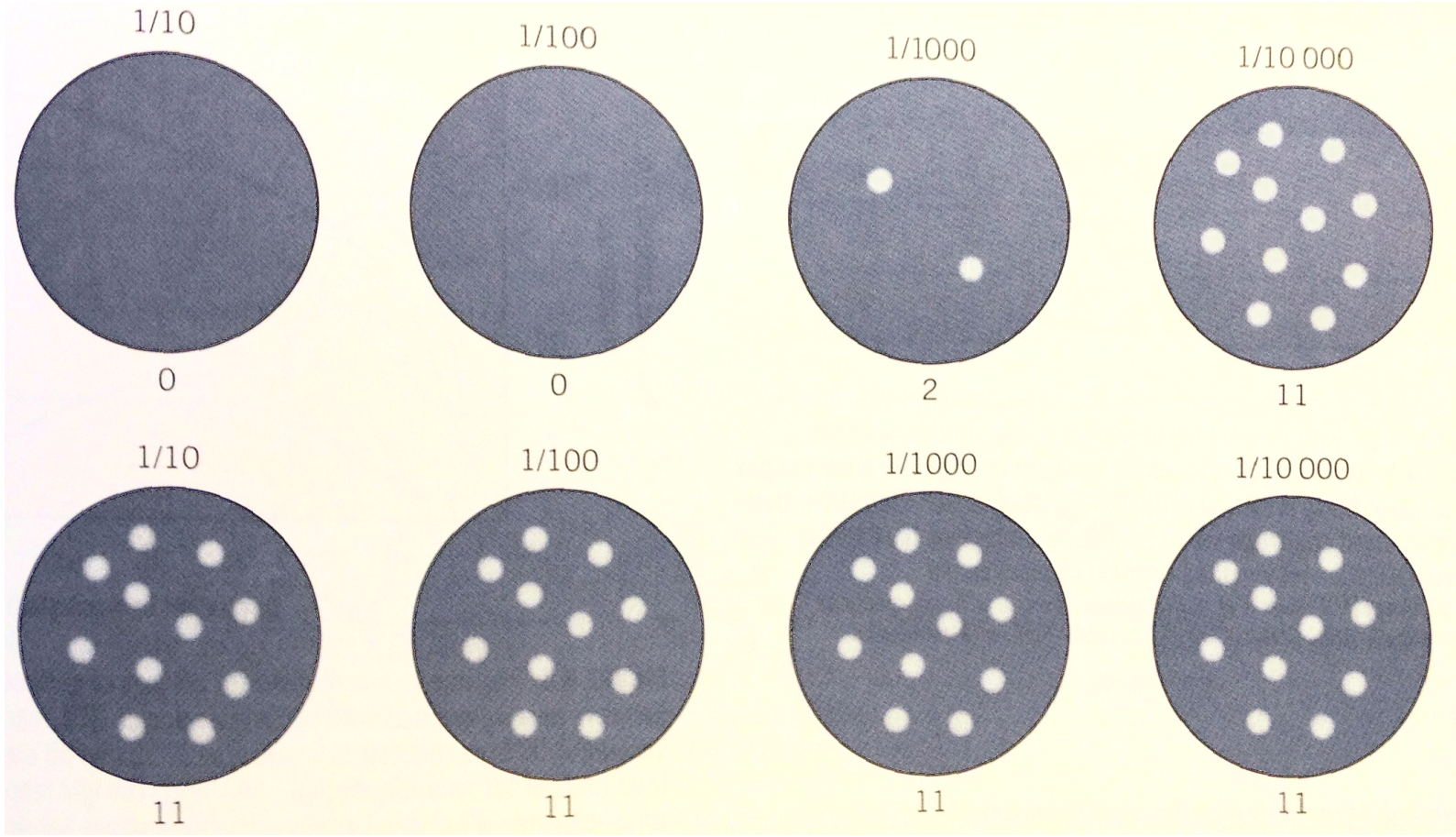

Secretory pIgA
Cleavage by surface protease
Virus assembly and release blocked by internal pIgA
Lumen
Apical surface
Epithelial cell
Apical recycling endosome
Transcytosis
Viral protein
Viral protein
Basolateral surface
Endocytosis
Nucleus
pIgR
pIgA
Lamina propria
Plasma cell

Neutralizing antibodies

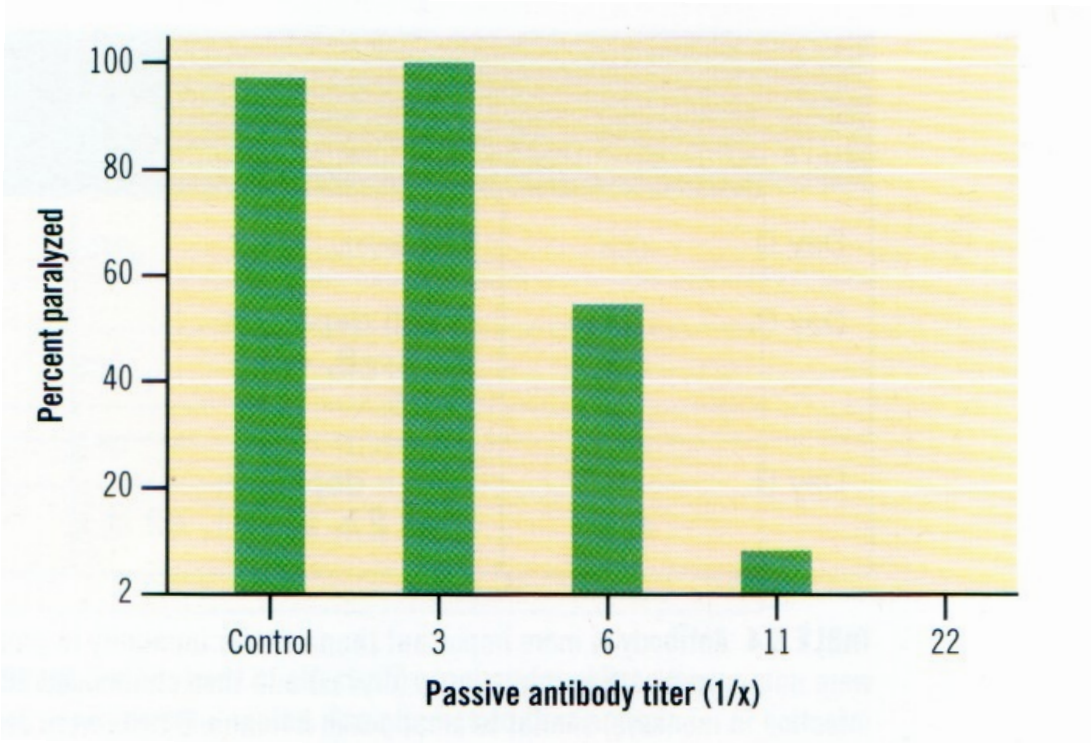


- Essential *defense* against many virus infections
- Neutralize virus particles in the blood, prevent virus spread
- IgA at mucosal surfaces (secretory antibody) blocks entry
- Some neutralizing antibodies are important for *recovery* from infection

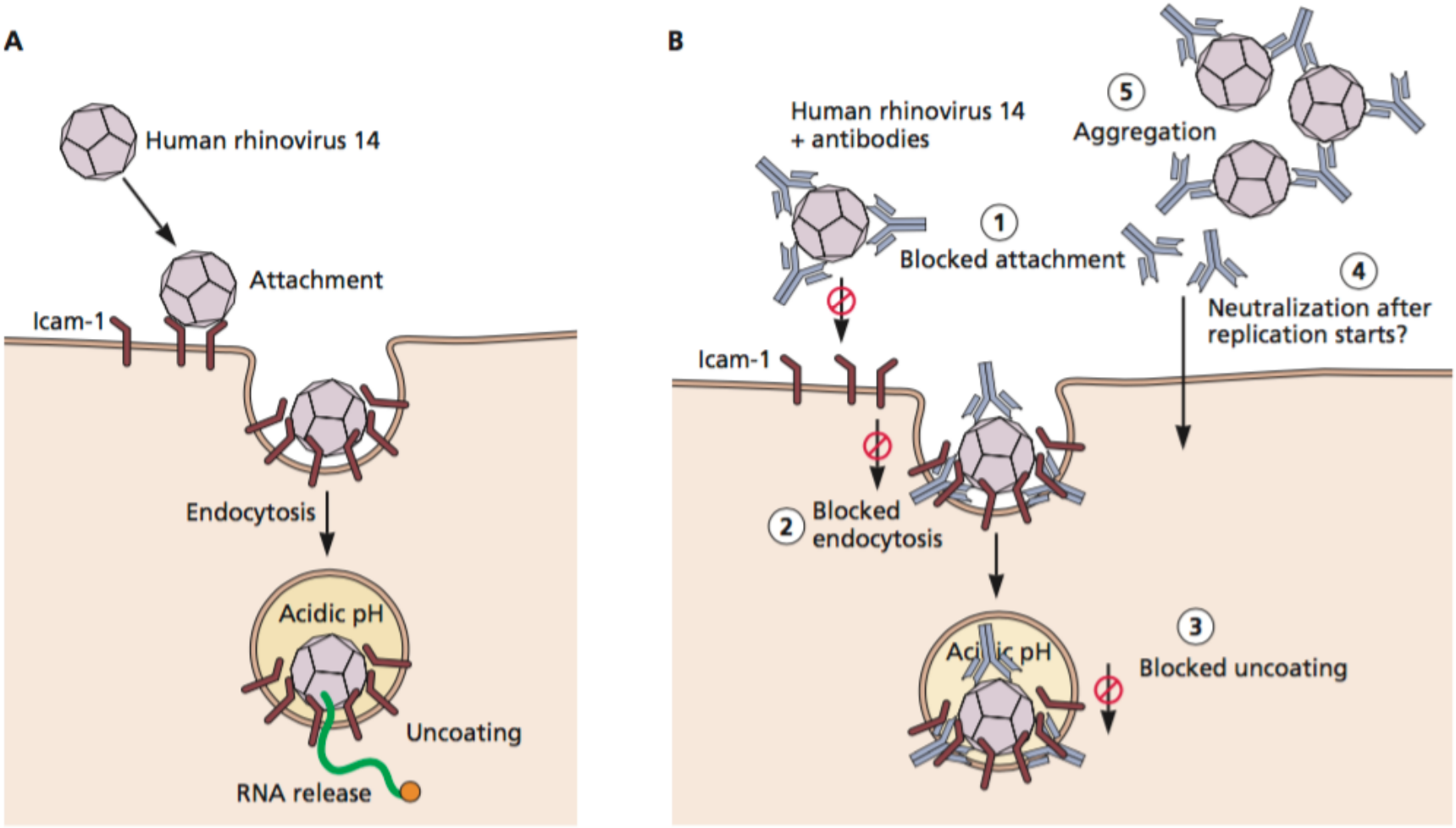
Neutralizing antibodies



Passive antibody protects against poliovirus infection



Neutralizing antibodies



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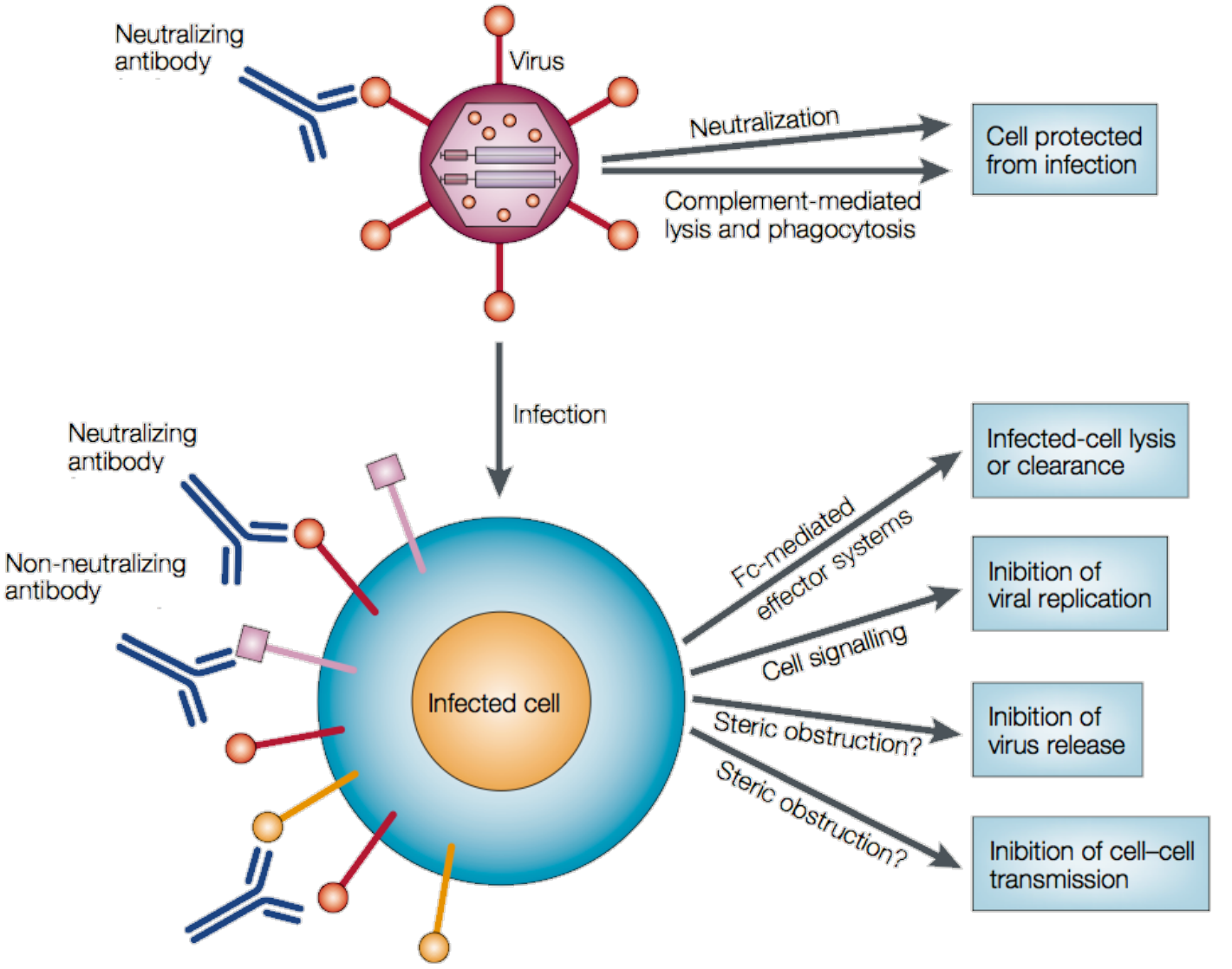
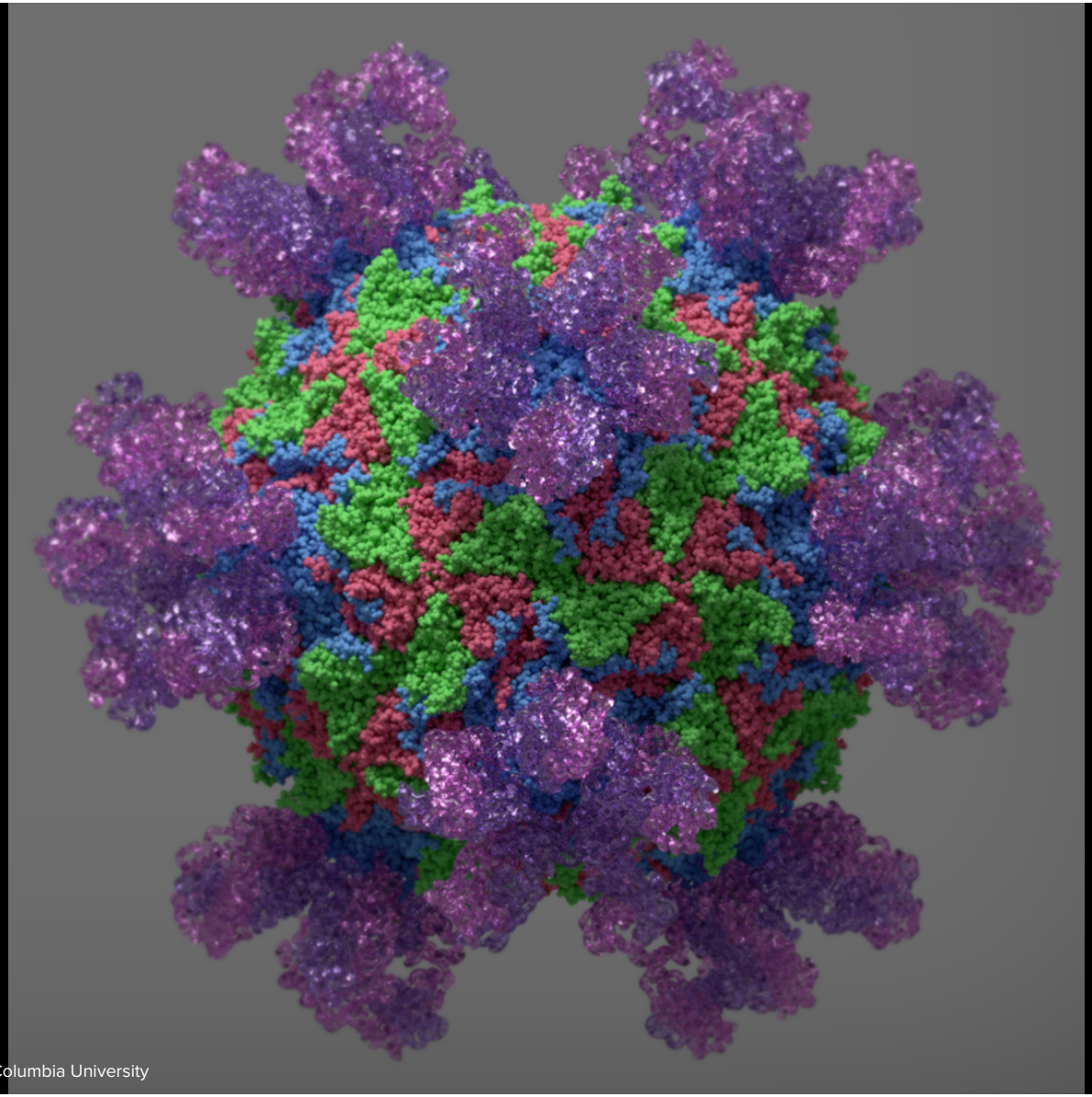
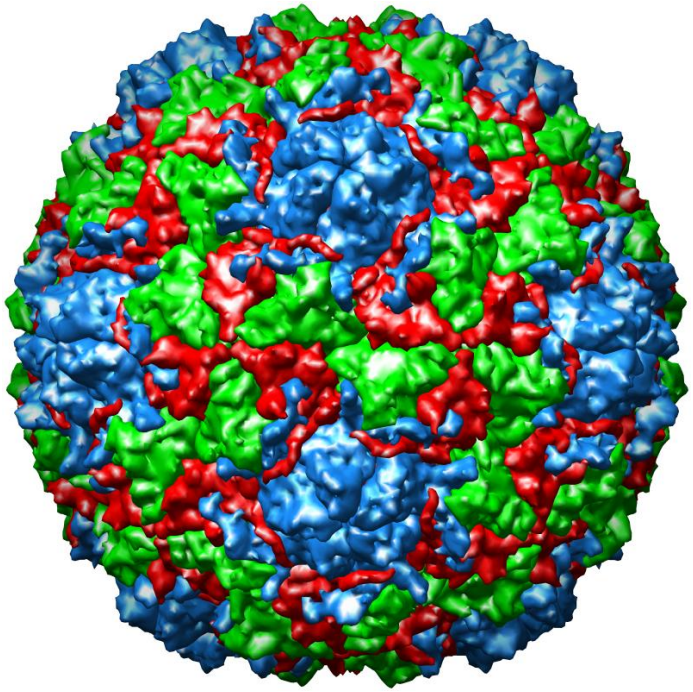


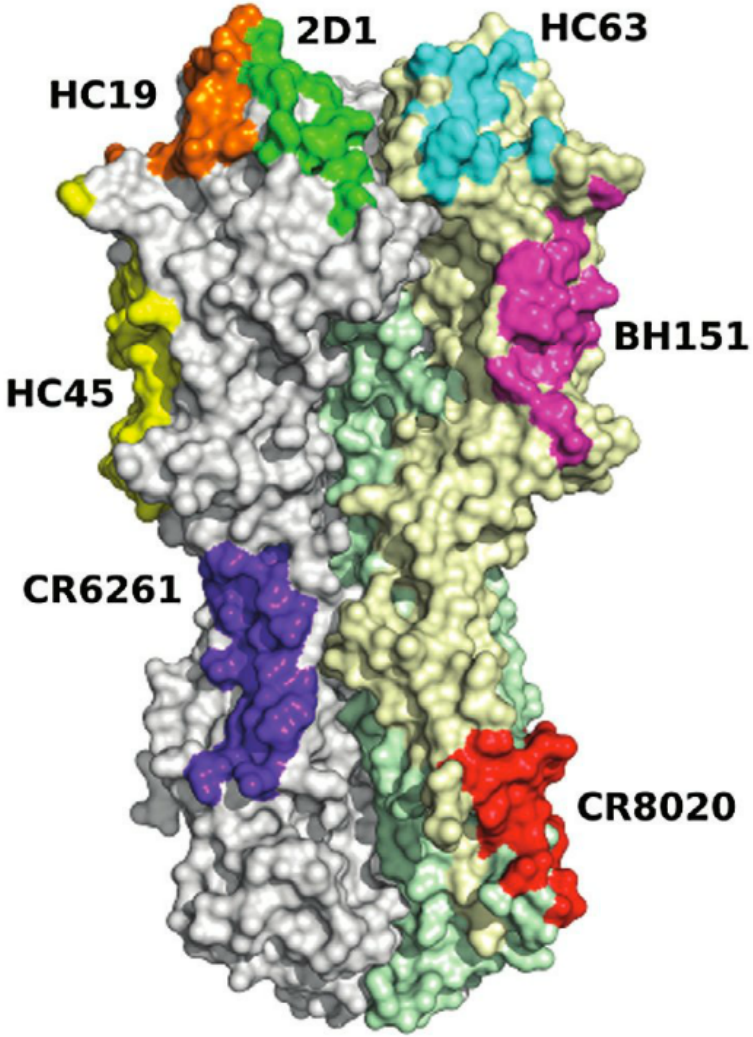
Nature Immunology 2:707, 2002



Evasion of Ab



Rhinovirus



Influenza HA

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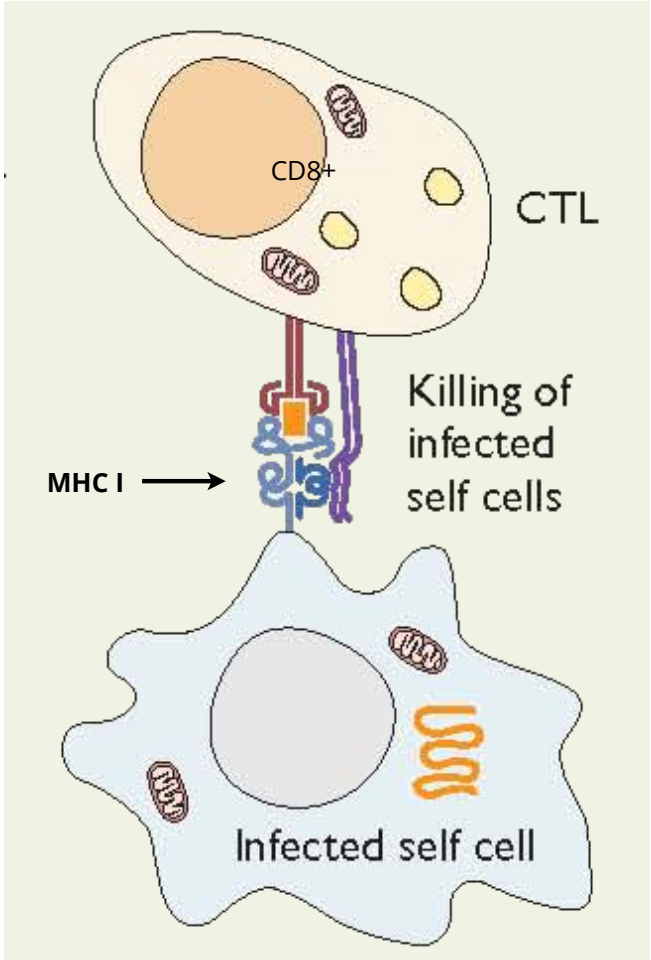
Which statement about anti-viral antibodies is incorrect:

A. They are important for protection against viral infections
B. They only neutralize virus infectivity
C. They may block virus attachment to cells
D. They can be found at mucosal surfaces
E. IgM is the first to appear, then IgG

Cell mediated immunity

- Essential for clearing most viral infections
- CTL and target cells form an immunological synapse
- Lysis of target cell
- Countermeasures



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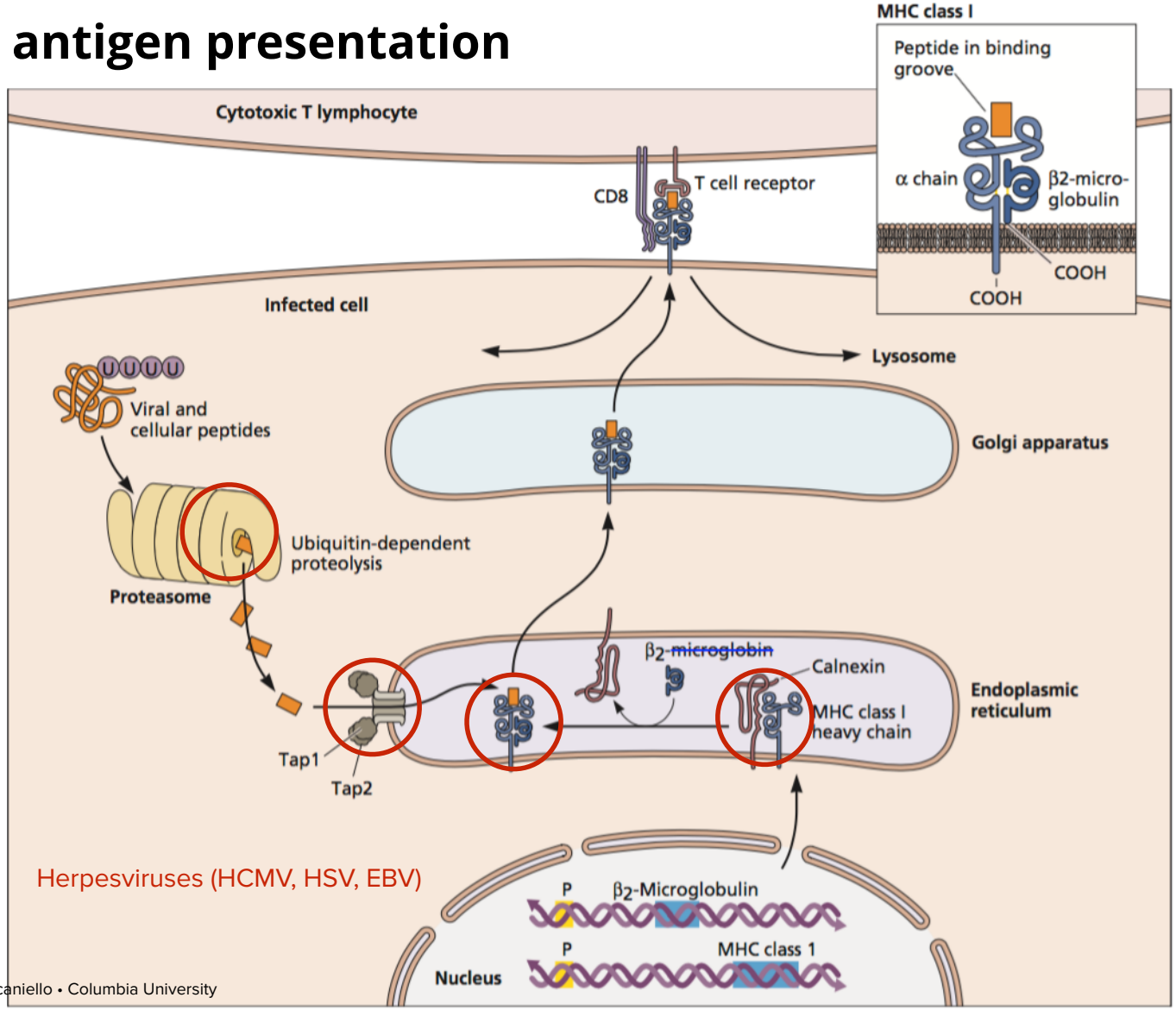
Endogenous antigen presentation

TAP = transporter associated with antigen processing



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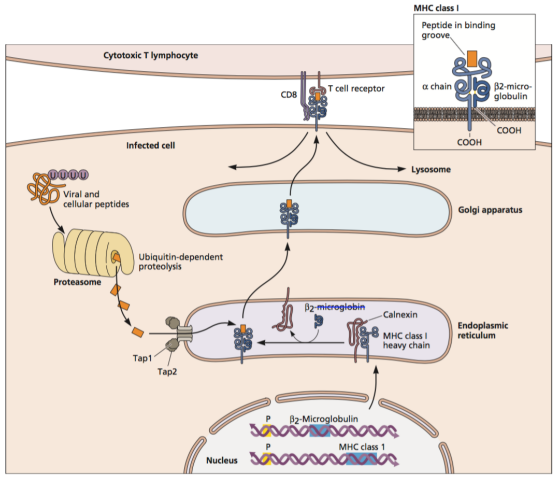
Countering MHC I

MHC I pathway	Viral protein
MHC I synthesis	Lentivirus Vpu
TAP synthesis TAP function	EBV vIL-10, HCMV UL111A HCMV US6, HSV ICP47
MHC I transport Retain in ER Dislocate to cytoplasm Increase MHC I endocytosis	HCMV US3, Ad E3-19K HCMV US11, US2 HIV nef, HHV-7 K3, K4



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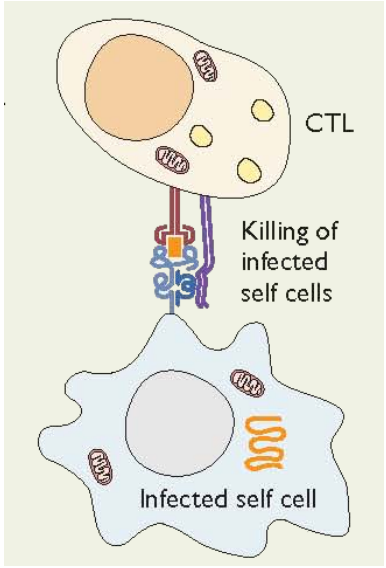
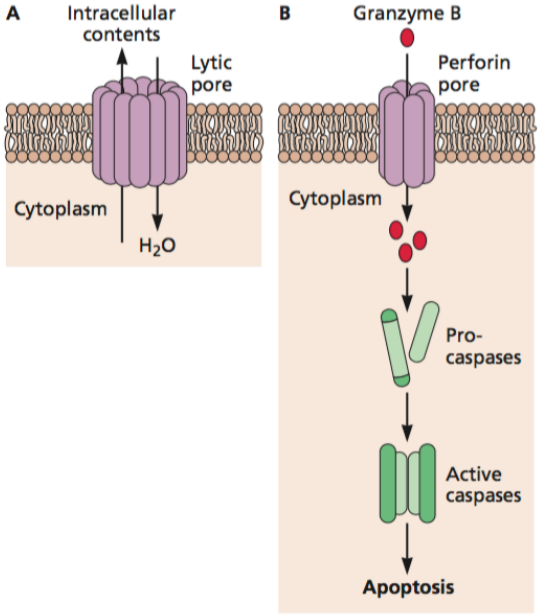
CTL lysis

- Lysis of target cell by two mechanisms
  - Release of cytoplasmic content
  - Apoptosis





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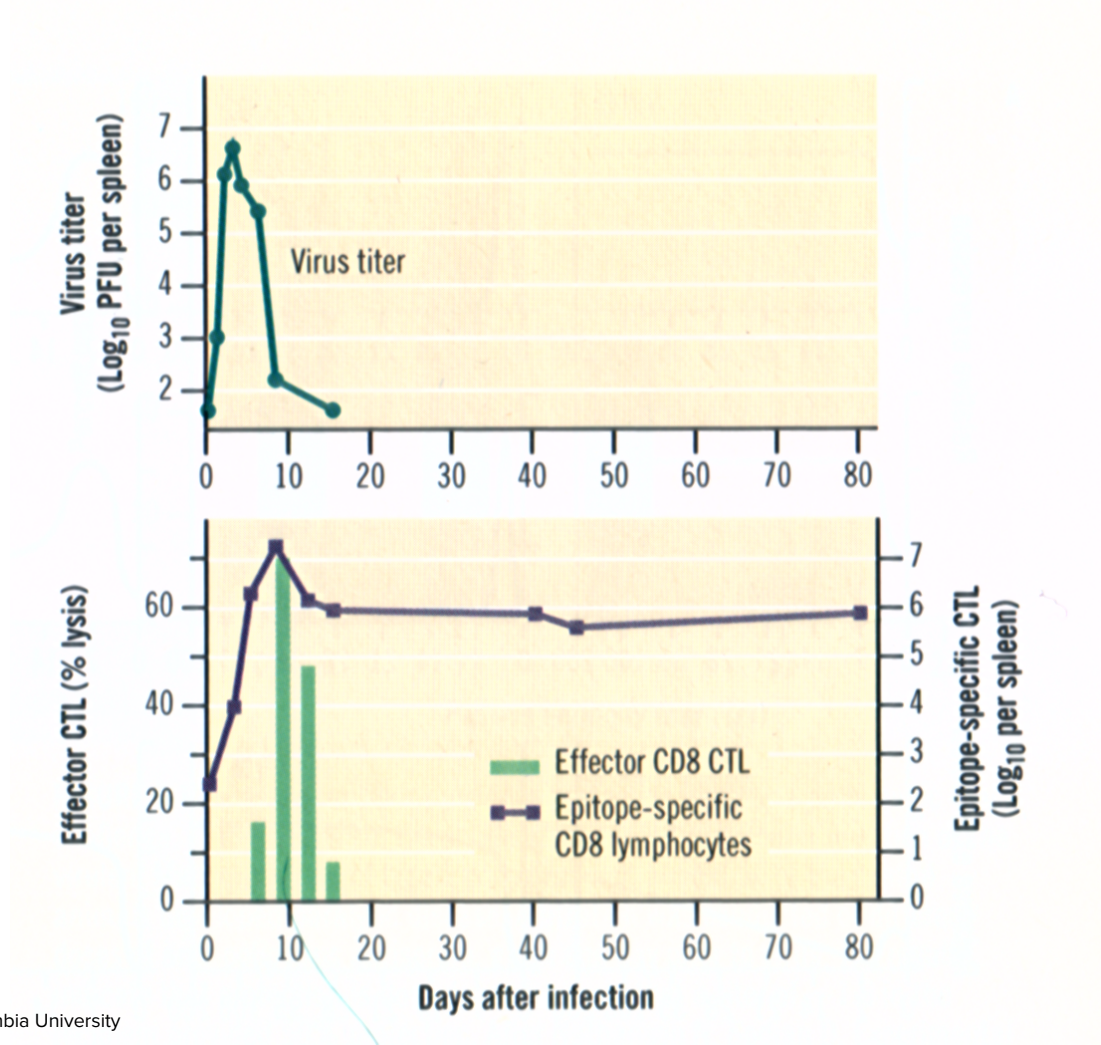
Kinetics of CD8 T cell (CTL) production



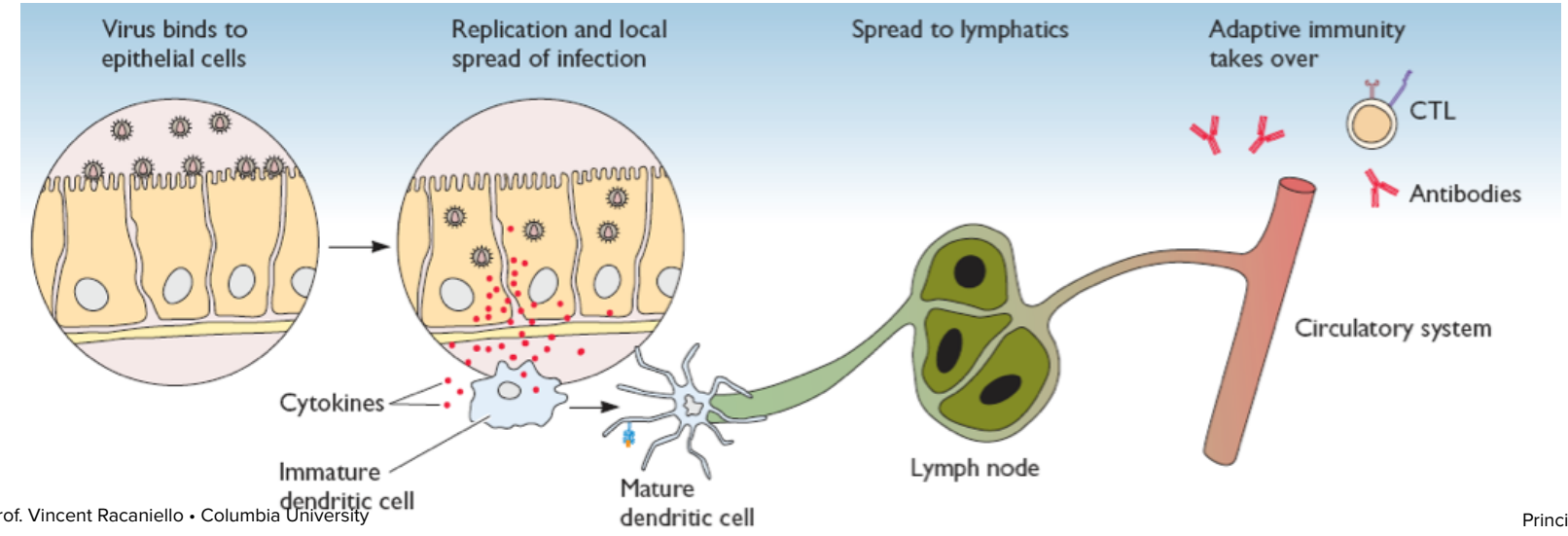
Antibody vs cellular immunity in protecting against monkeypox virus infection

Day of vaccination	Immune manipulation	Neutralizing Ab day 22	Monkeypox infection	Fatality
0	None	800-6400	Day 28	0/4
0	B cell depletion	42-59	Day 28	3/4
0	CD8 cell depletion	268-2963	Day 28	0/4

For some infections, CTL response is more important than the antibody response

How is the correct response made?

Begins in lymph tissues where sentinels tell naive B and T cells nature of invader



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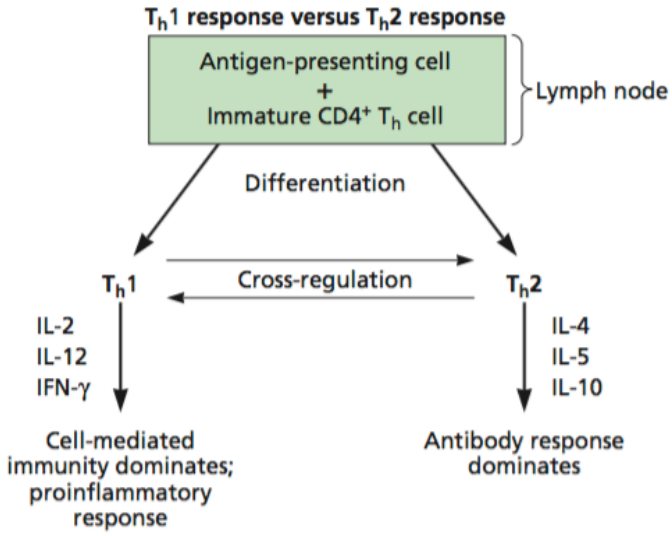
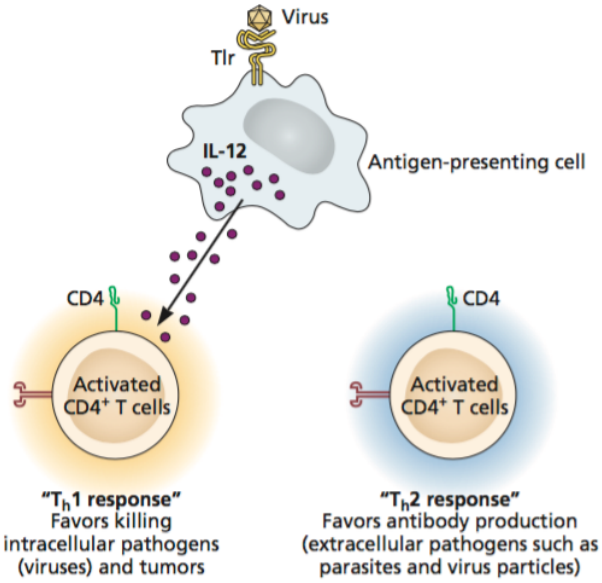
This decision is made in part by special T helper cells (Th cells)

- Th cells make contact in the lymph nodes with sentinel DCs and macrophages
- Information exchanged (peptides, cytokines) causes differentiation to Th1 or Th2





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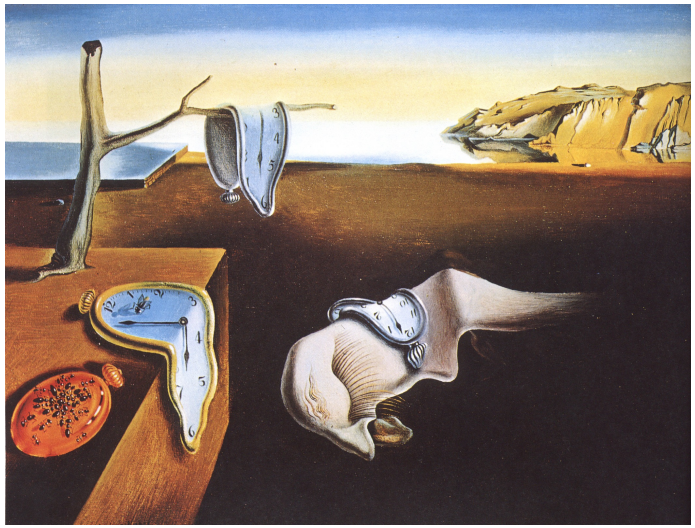
For some infections, CTLs are more important for protection than antibody. How is the CTL-antibody balance determined?

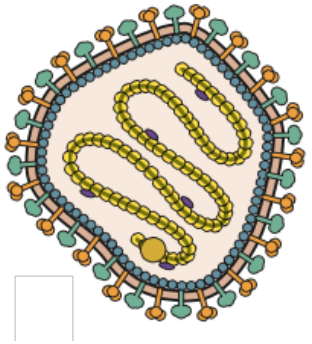
A. By toll-like receptors
B. By intrinsic defenses
C. By autophagy of infected cells
D. By the mix of peptides and cytokines presented by DCs
E. It depends on whether the capsid is icosahedral or helical

Adaptive responses also provide *memory*



- If the host is subsequently infected by the same virus, the response will be **rapid and specific**
  - *Innate responses don't have memory*
- Memory: the basis for **vaccination**

Infection provides immune memory



- 1781: outbreak of measles on Faroe Islands
- Next 65 years, islands free of measles
- 1846: another outbreak of measles; none of those who survived the 1781 epidemic were infected
- Immune memory lasts a long time, maintained without re-exposure to virus

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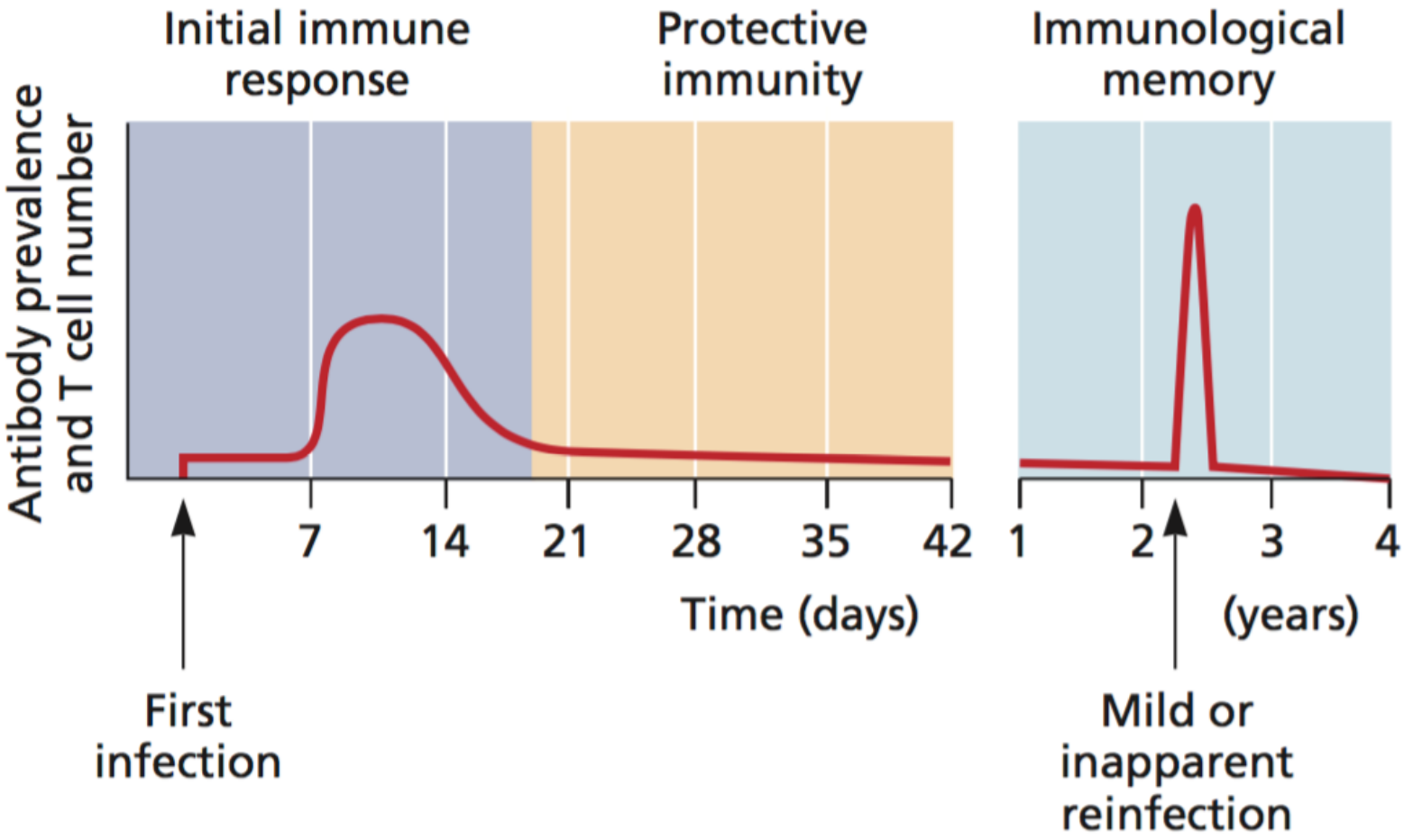
Immunological memory



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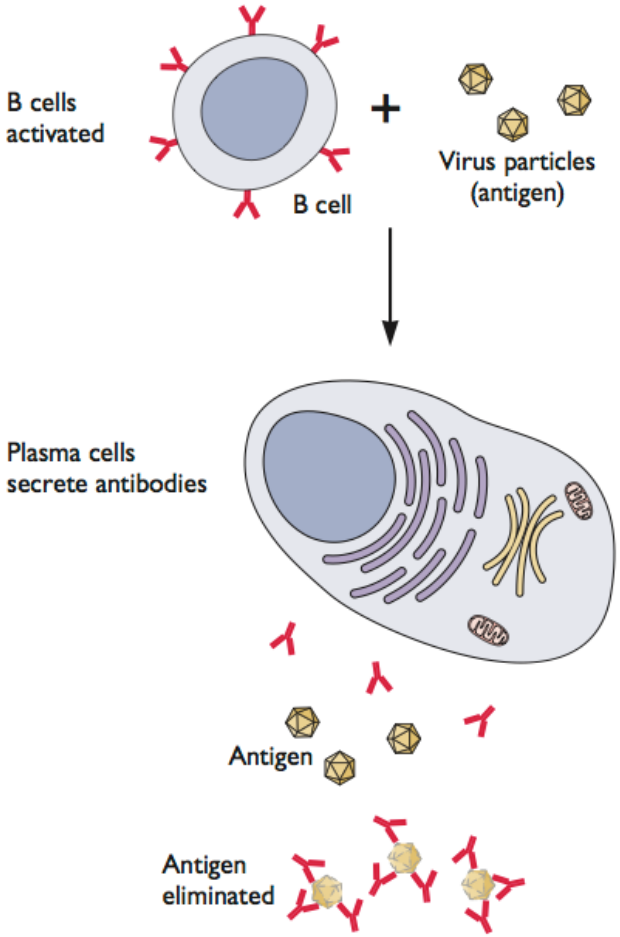
Immunological memory

- Memory B cells
  - In spleen, lymph nodes
  - Do not produce antibodies unless stimulated by Ag
- Long lived plasma cells
  - Bone marrow
- Memory T cells



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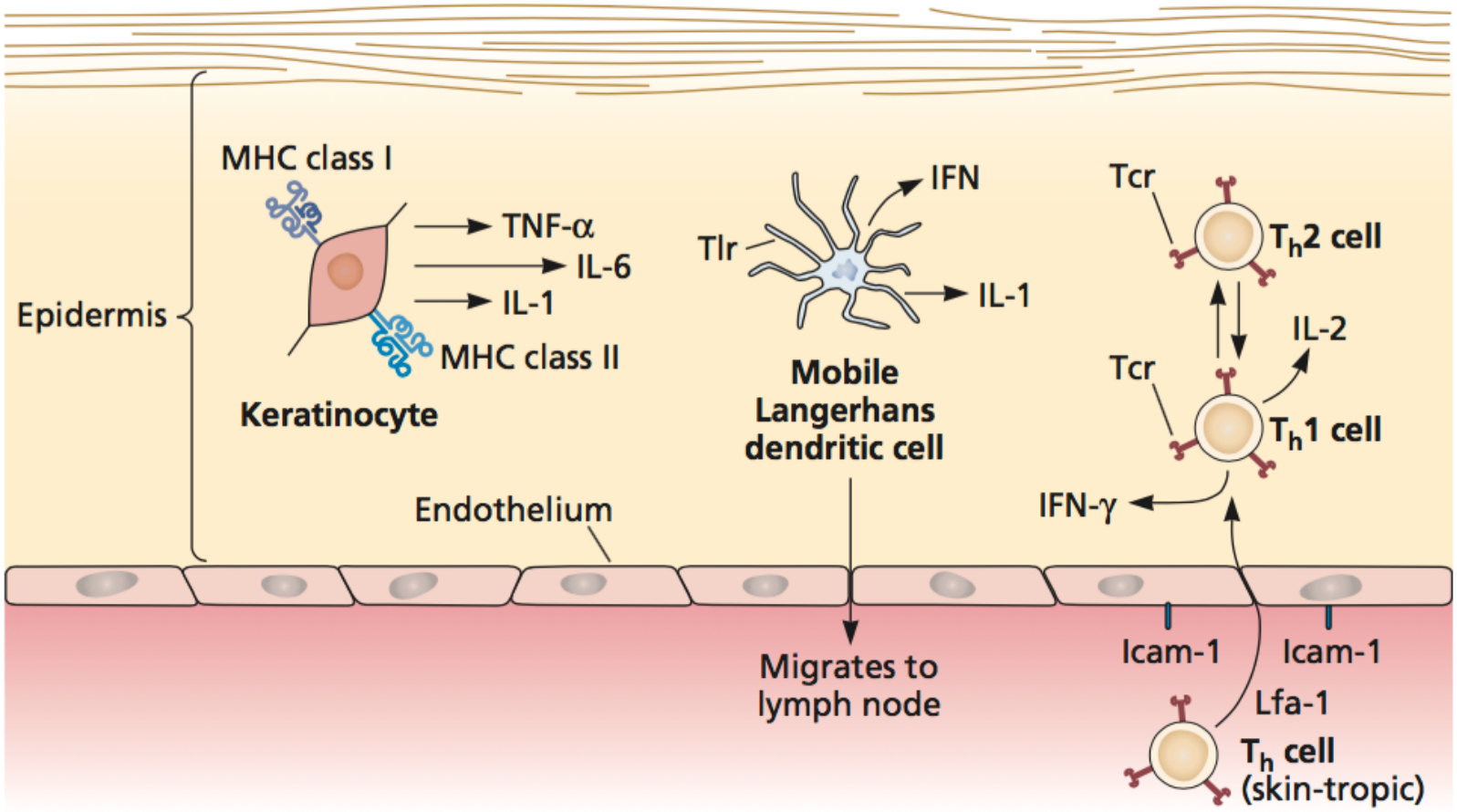
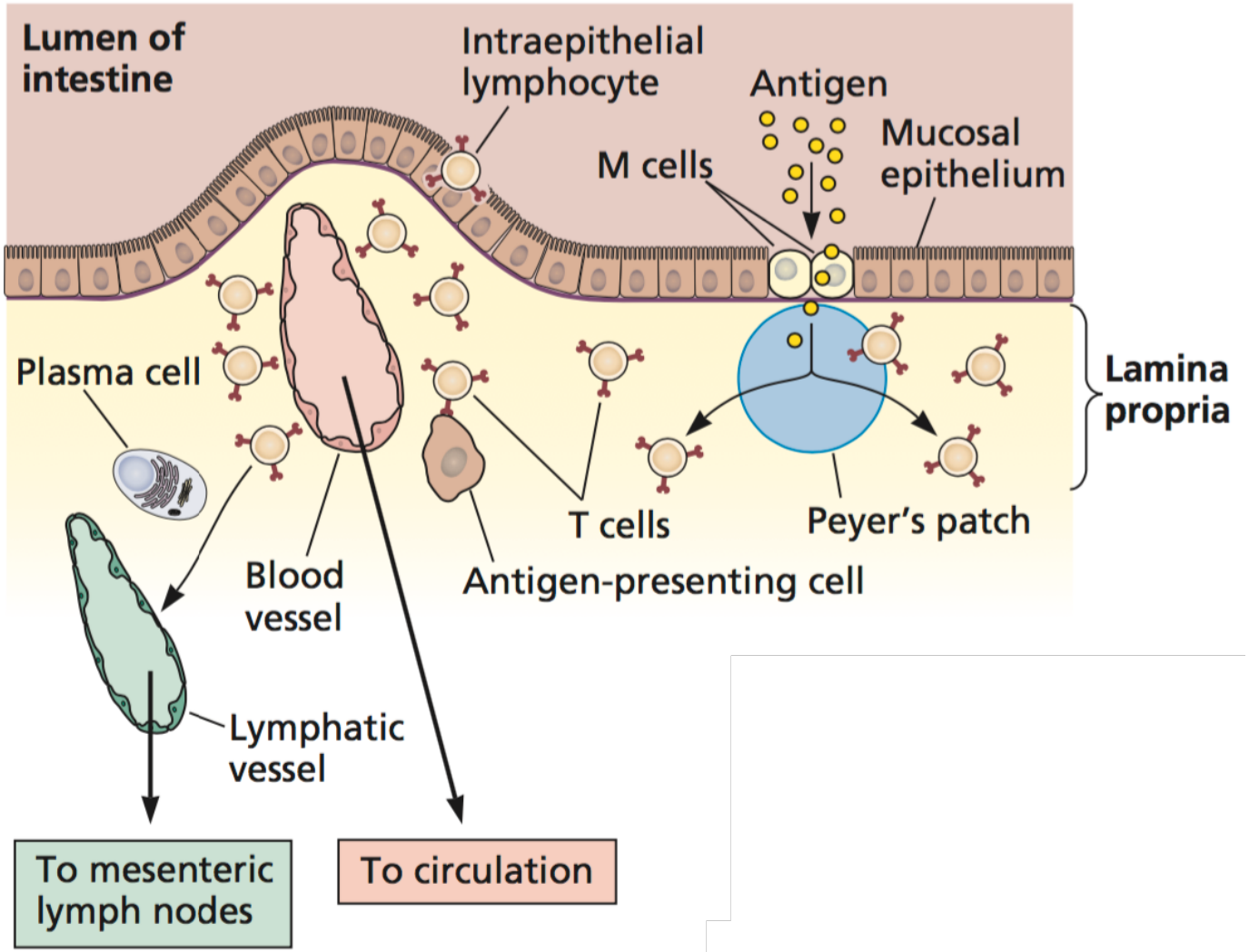
Cutaneous immune system



Mucosal immune system in gut



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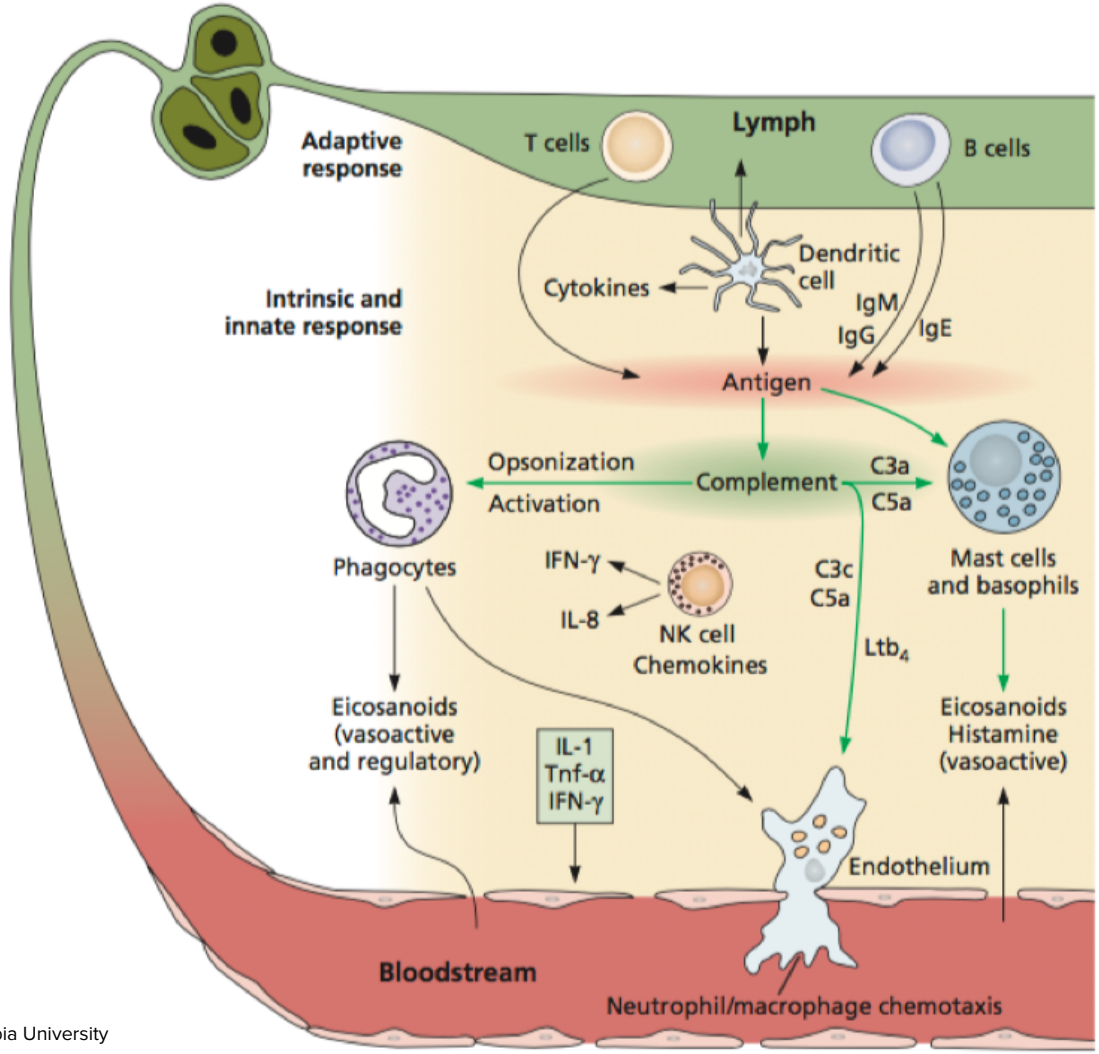
Inflammation provides integration and synergy



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