



# VIROLOGY LIVE

WITH VINCENT RACANIELLO

## Adaptive Immunity

Session 14

Virology Live

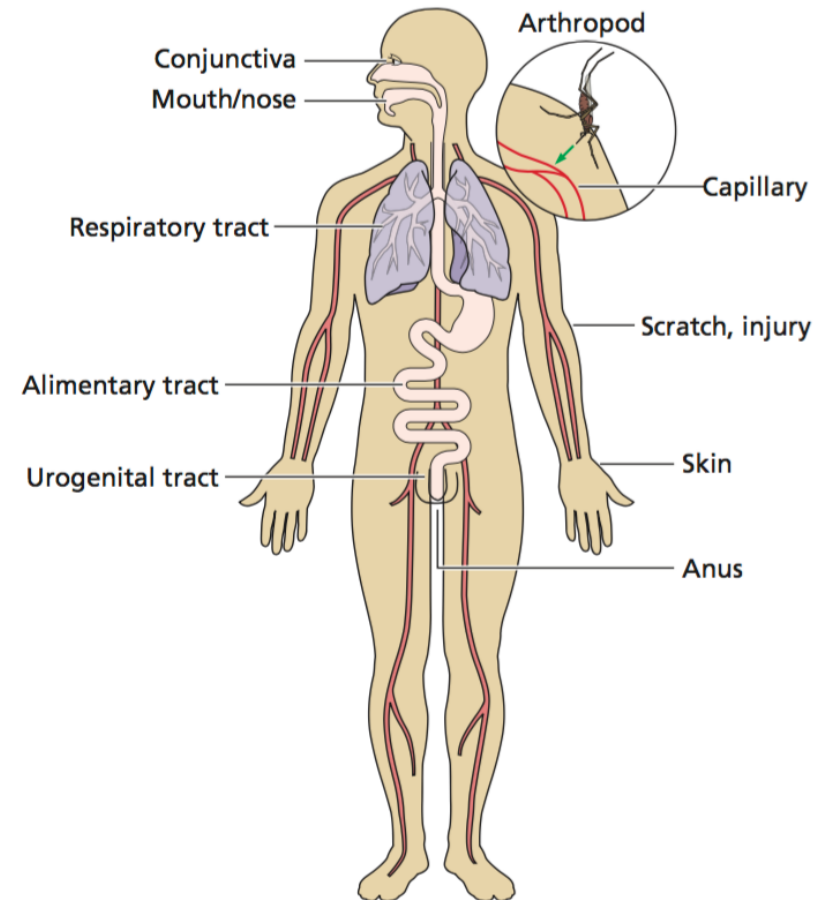
Fall 2021

*Life is simple, but we insist on making it complicated*

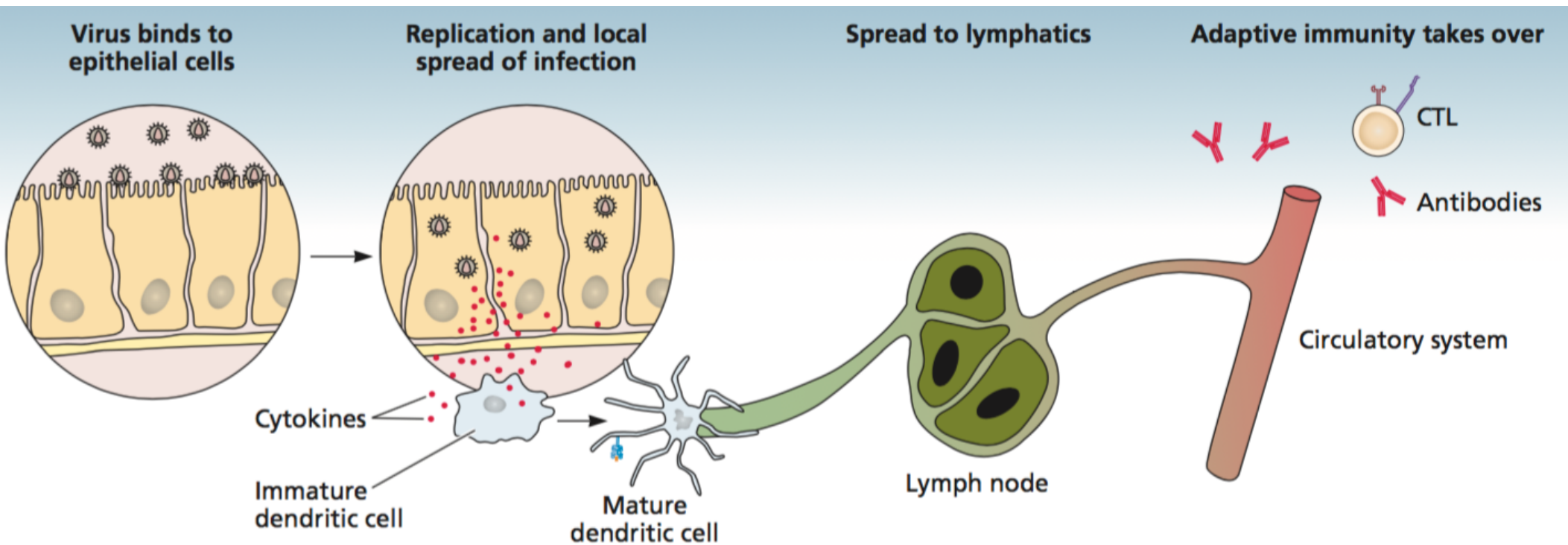
–CONFUCIUS

# 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*

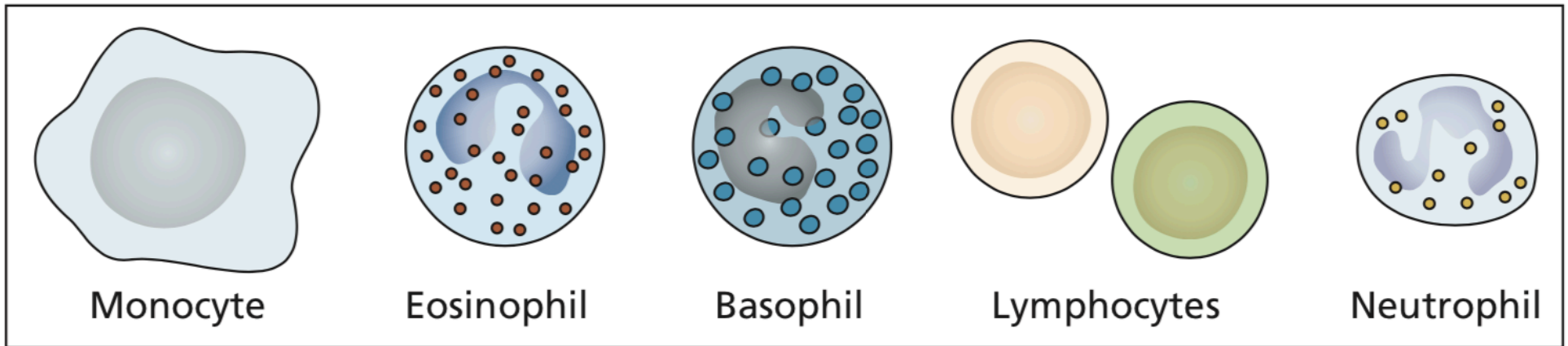




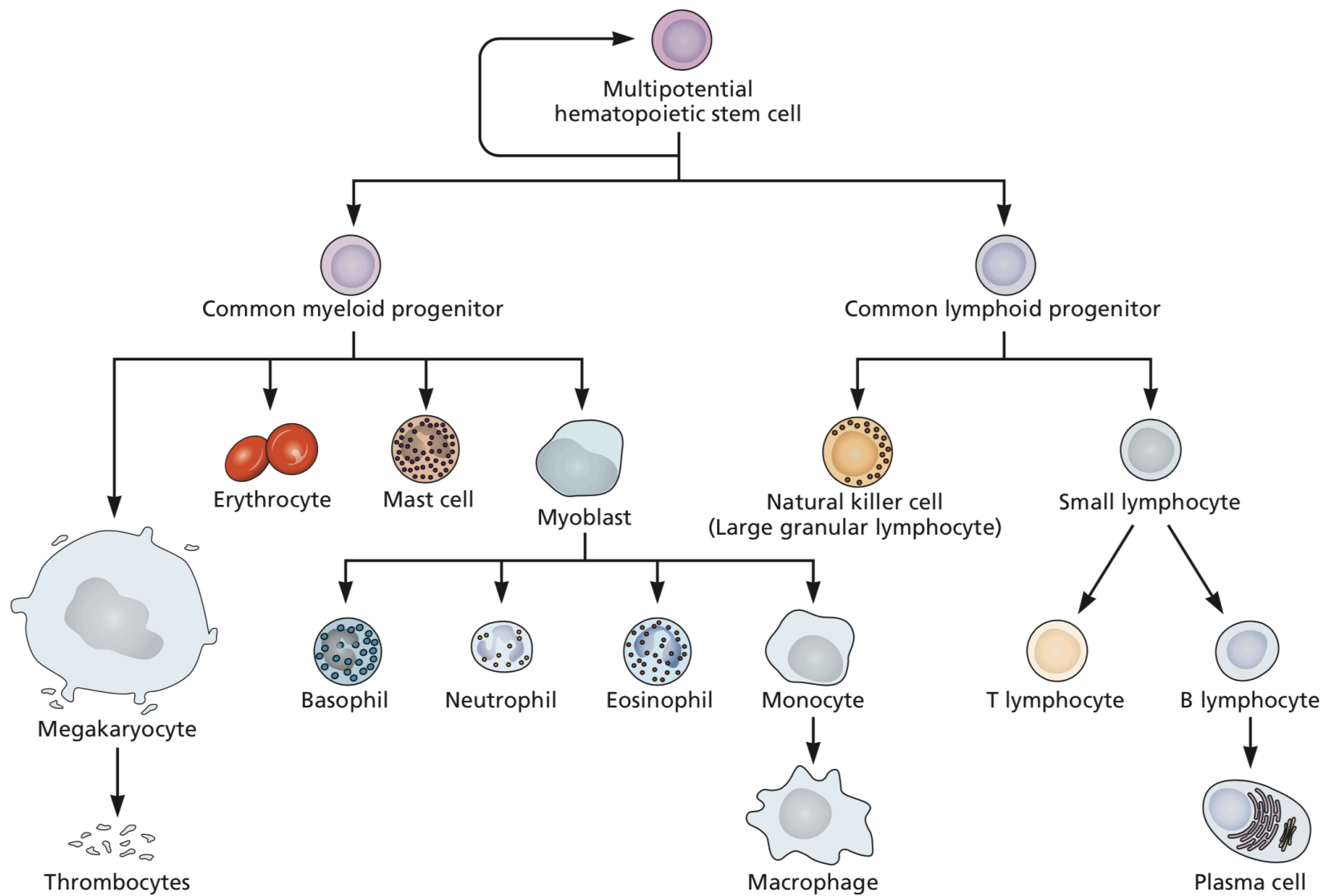


# Leukocytes and Lymphocytes

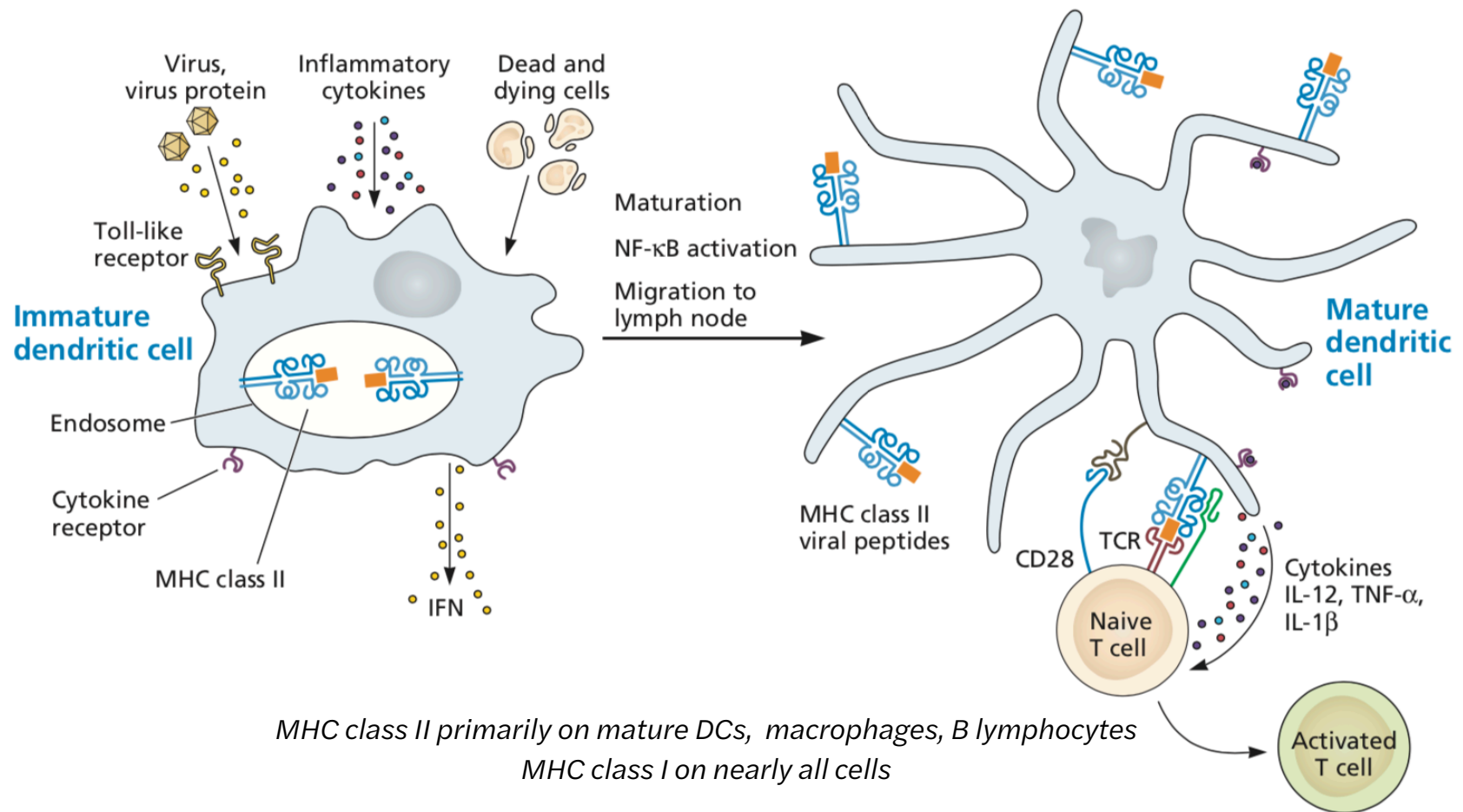
## Leukocytes



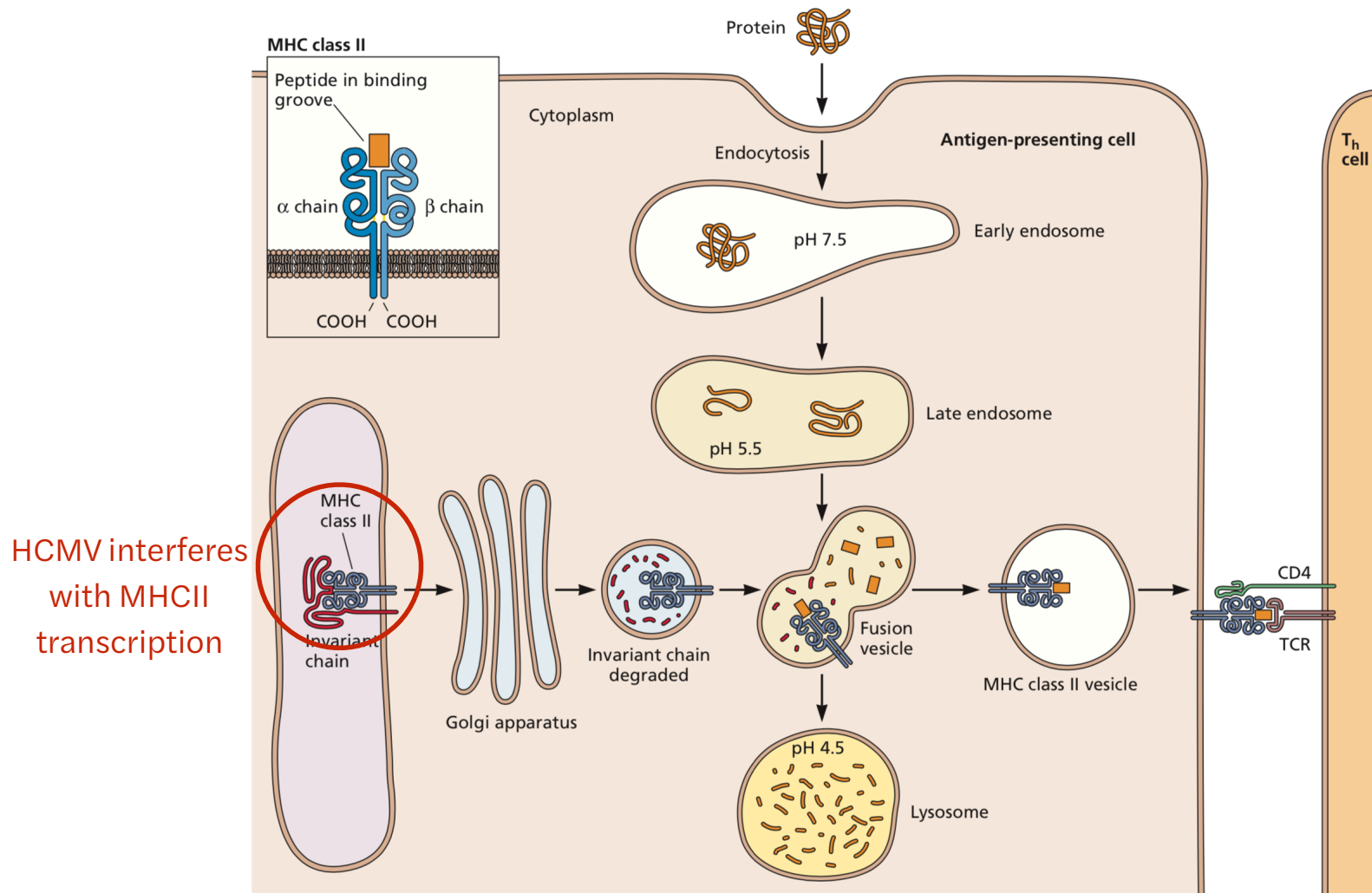
- Leukocyte: general term for white blood cell (lymphocytes, neutrophils, eosinophils, macrophages)
- Lymphocyte: Subset of leukocytes (T, B, NK cells; have variable antigen-detecting cell surface receptors)



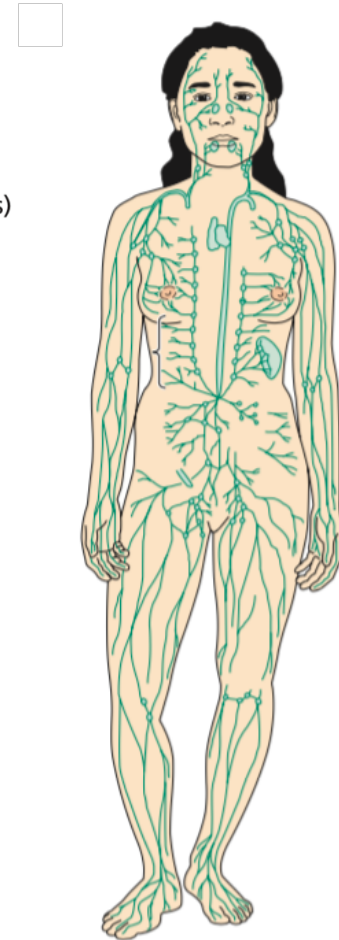
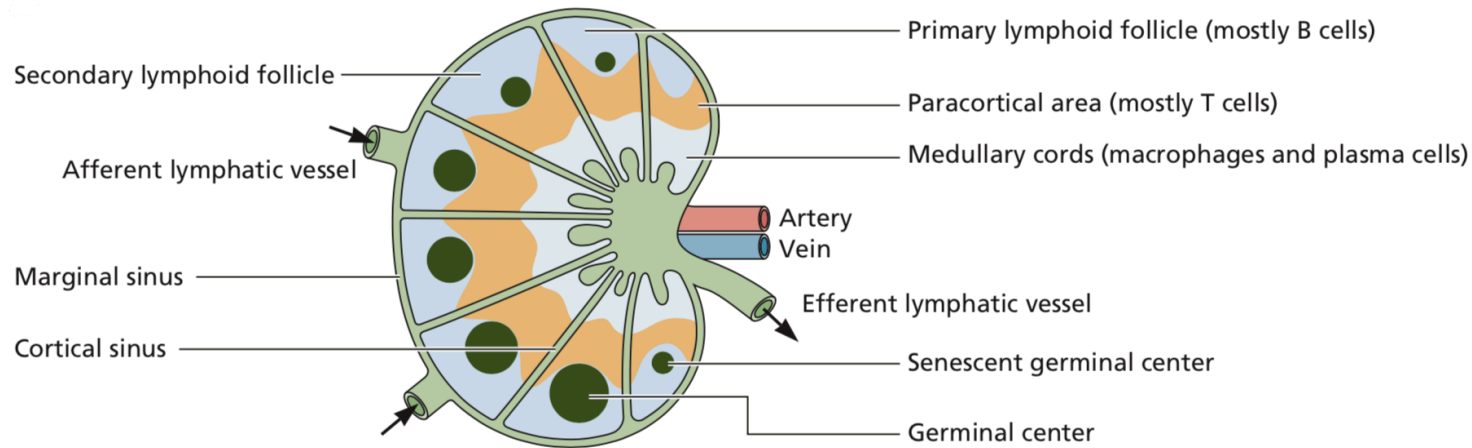
# Innate instruction of adaptive immunity



# Exogenous antigen presentation

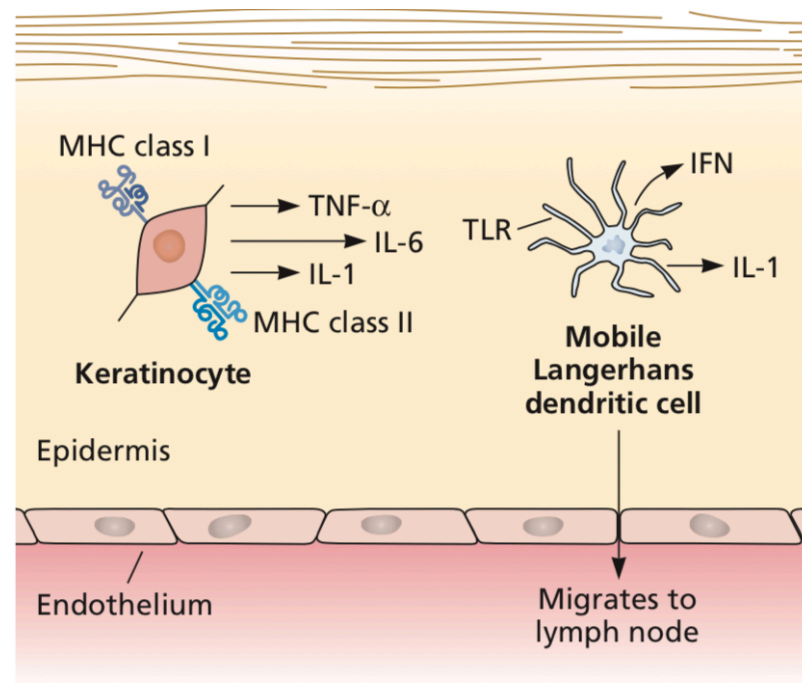
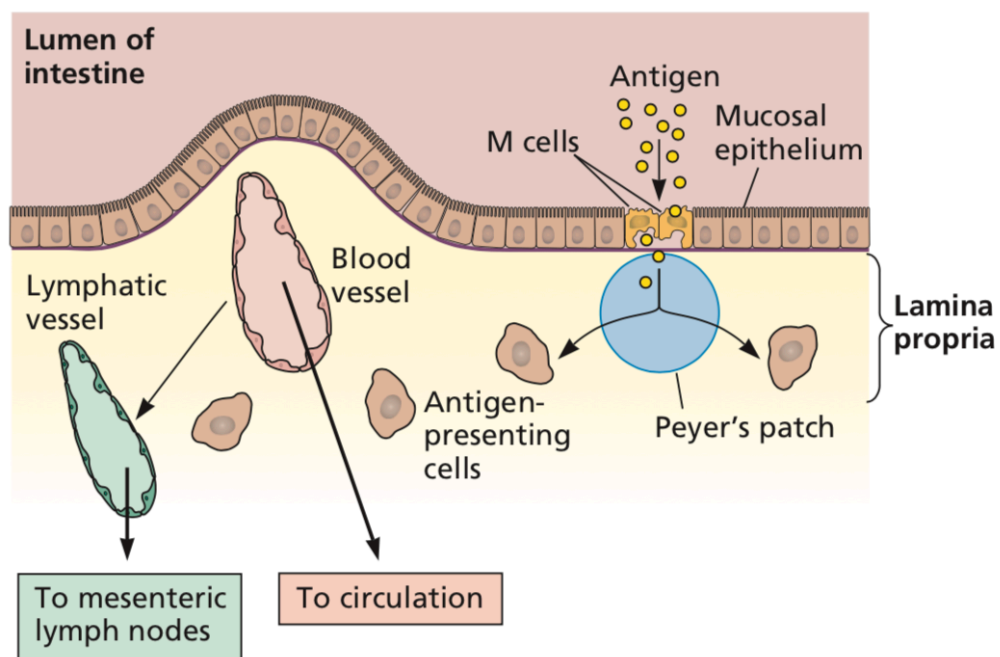


# Lymphocyte activation triggers massive cell proliferation



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

# Mucosal and cutaneous immune system



**GALT = gut-associated lymphoid tissue**

**MALT = mucosa-associated lymphoid tissue**

**Go to:**

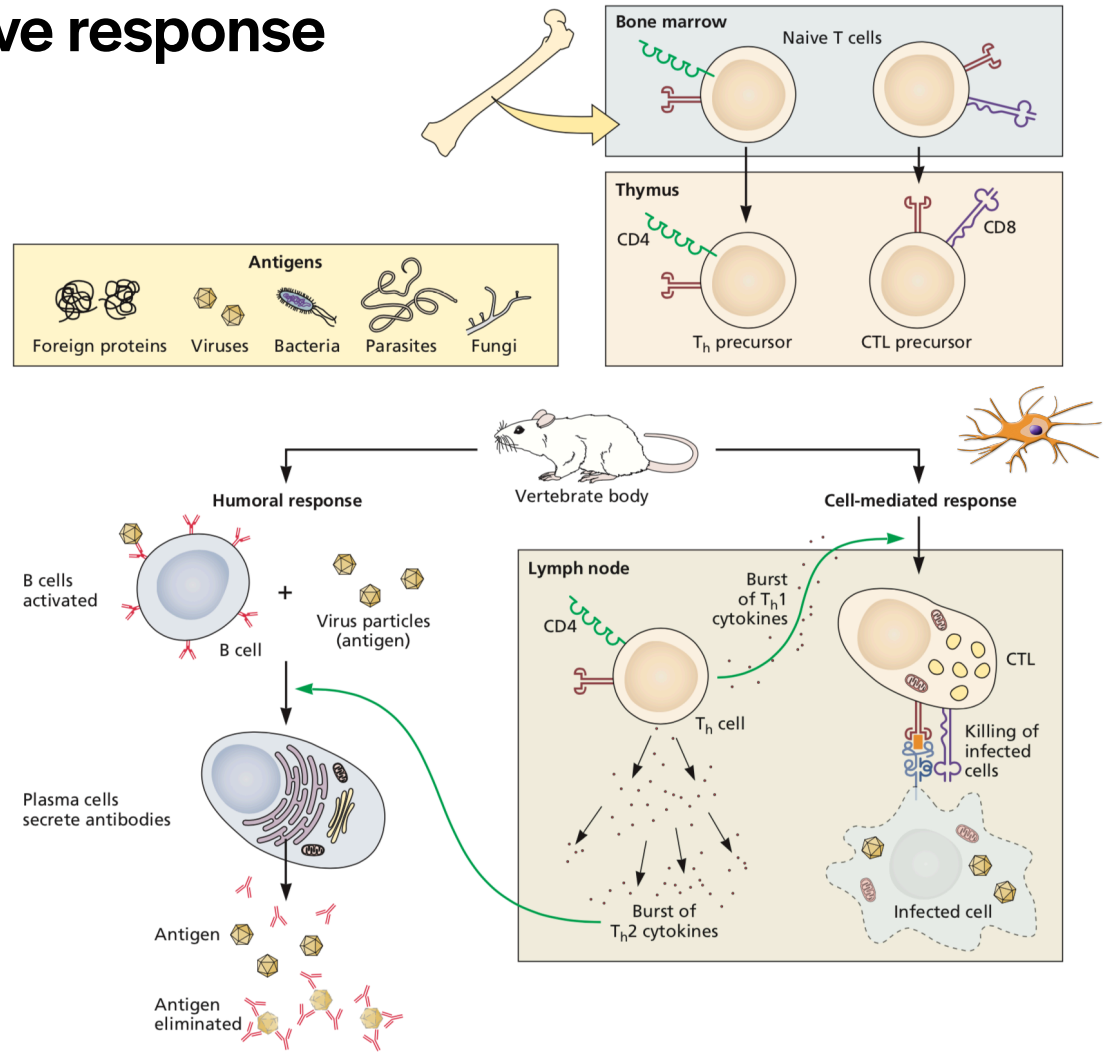
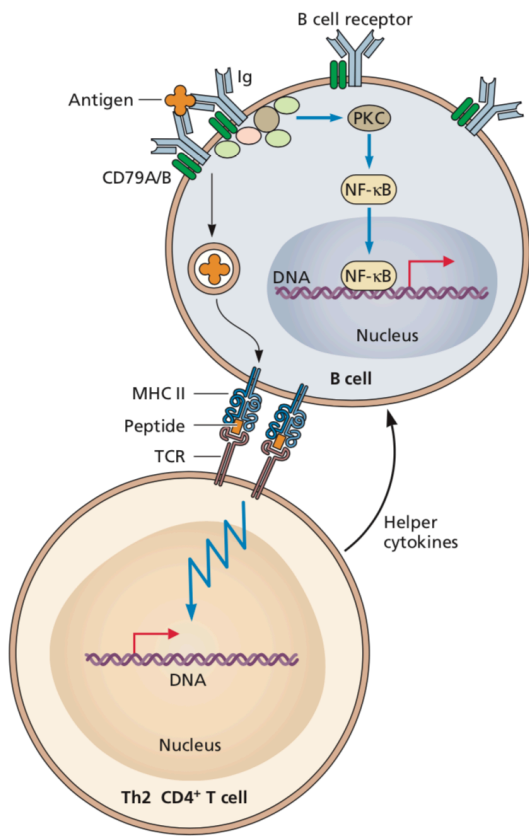
**[b.socrative.com/login/student](https://b.socrative.com/login/student)  
room number: virus**

**What is a property of innate instruction of adaptive immunity?**

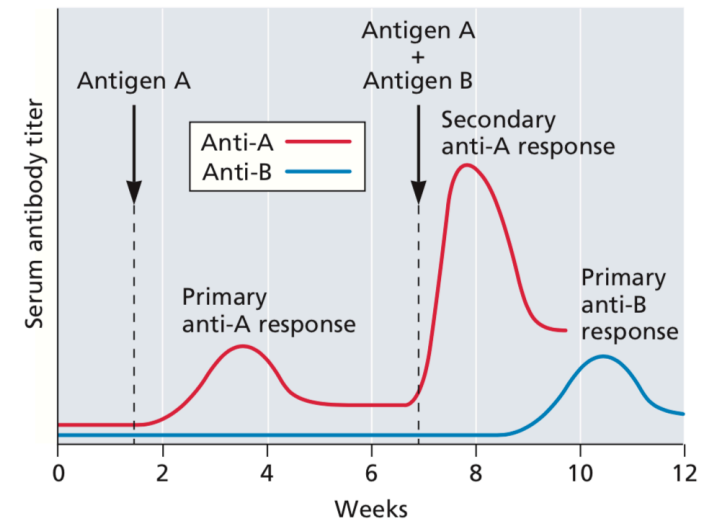
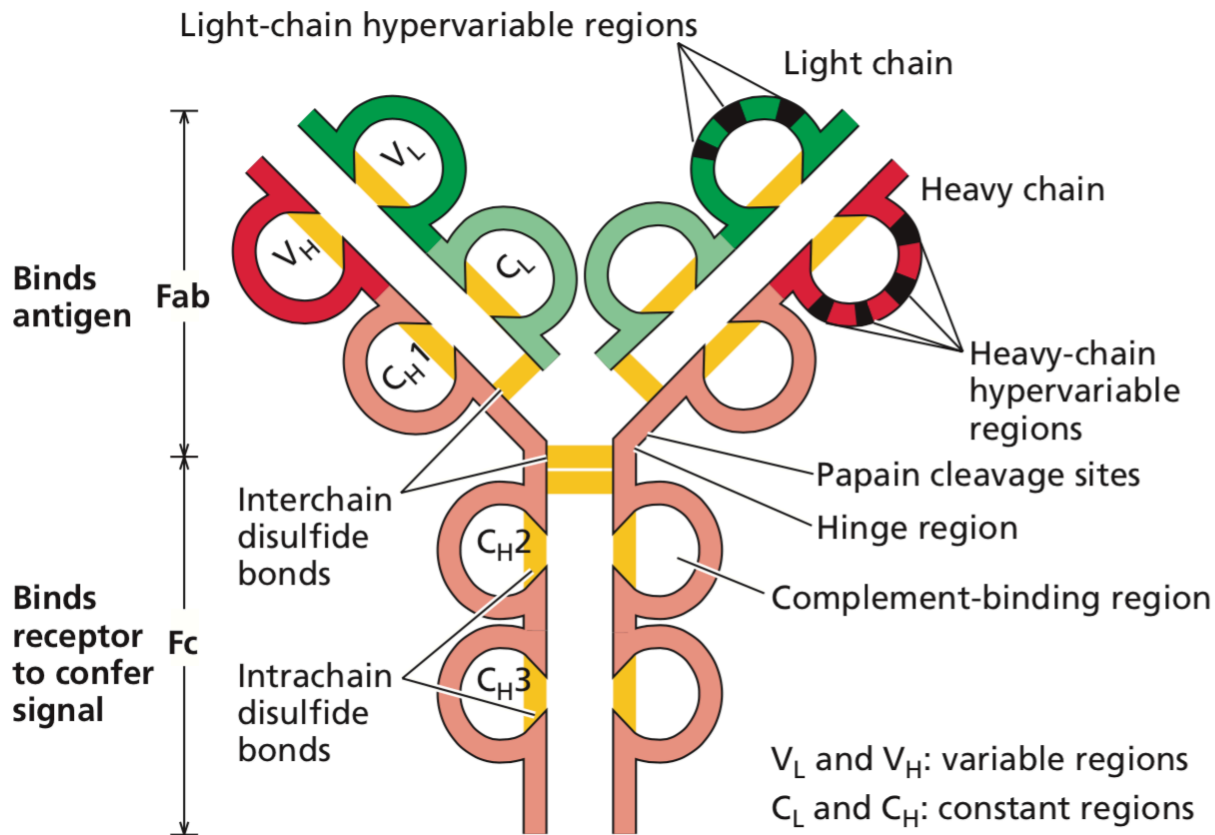
- A. Presentation of viral peptides on MHC II to CD4 T cells
- B. Endocytosis of viral proteins
- C. Activation of DCs by cytokines
- D. Sensing by TLRs
- E. All of the above



## Effectors of the adaptive response



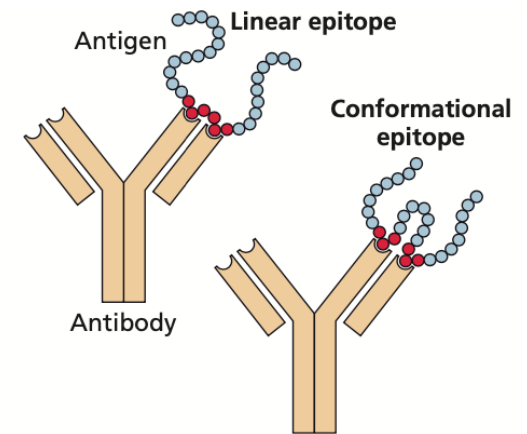
# Antibodies



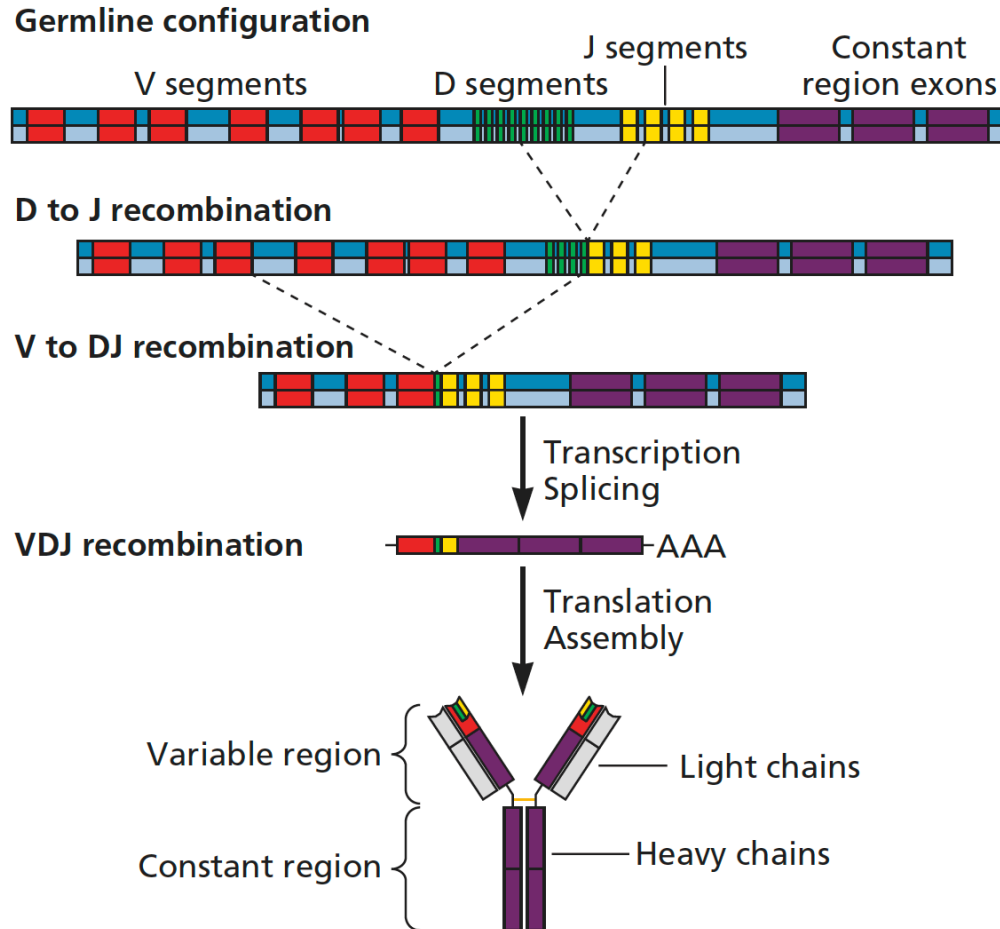
*Contraction not waning!*

# Antibodies, antigens, and epitopes

- *Antigen*: molecule that induces an immune response (protein, DNA, RNA, lipid, polysaccharide)
- *Epitope*: part of antigen bound by antibody or T-cell receptor
- *Monoclonal antibody*: against a single epitope
- Serum contains a mixture of monoclonal antibodies: *polyclonal*

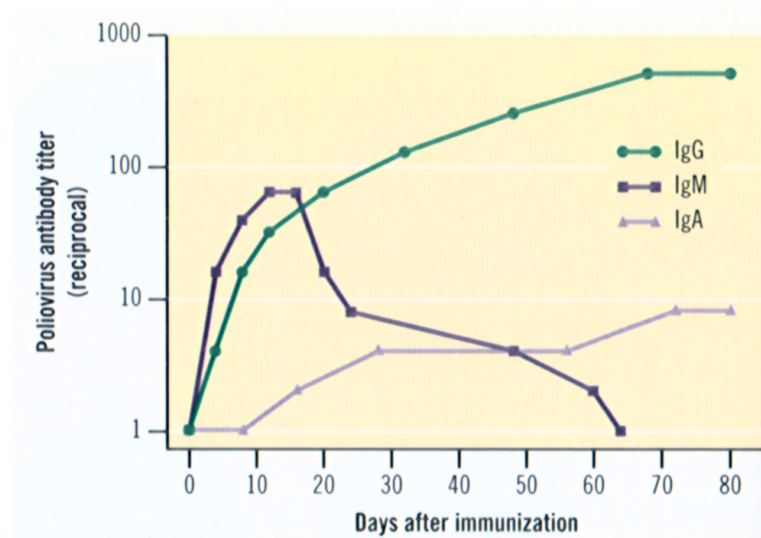
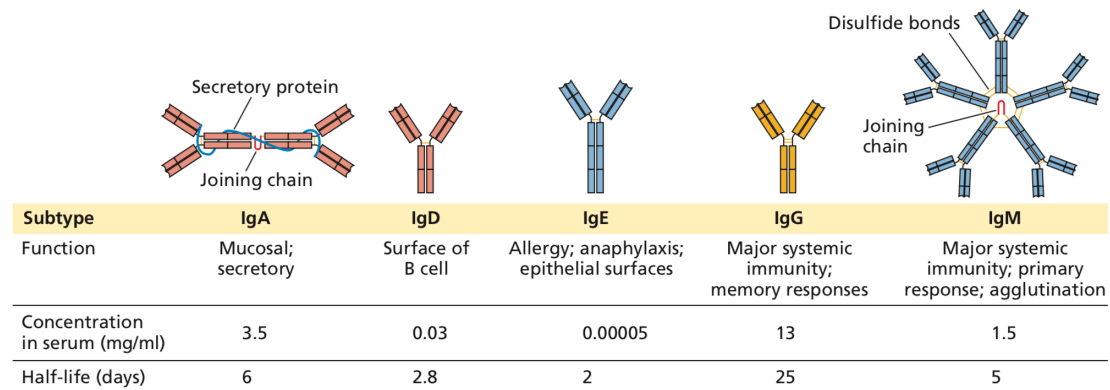


# Generation of B cell receptor diversity

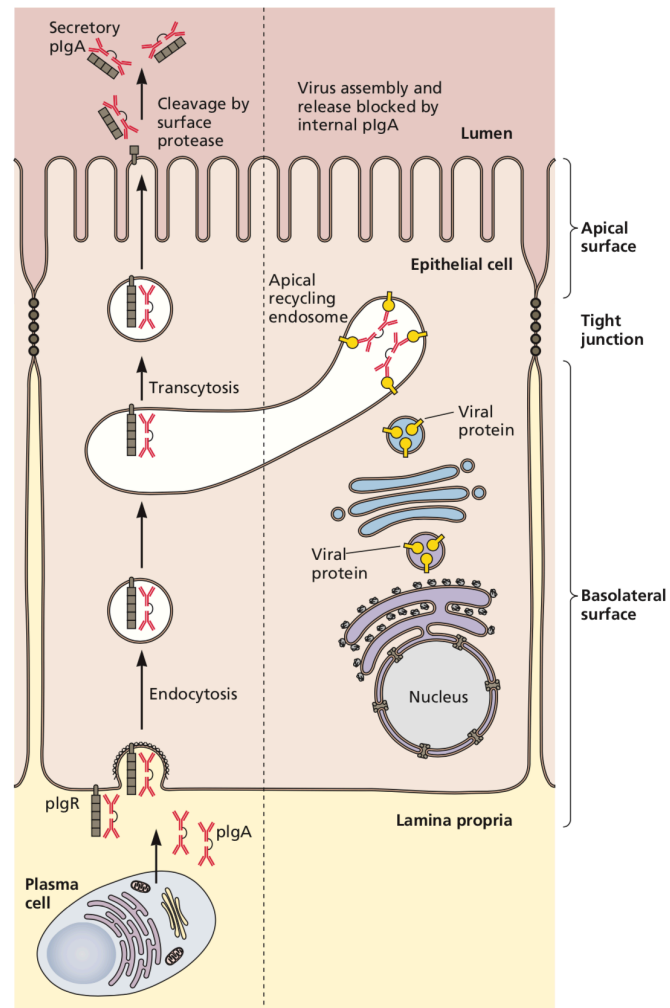


*VDJ recombination occurs in B cells in the bone marrow*

# Antibody response



# Secretory IgA



# A rapid assay for serum antibodies to SARS-CoV-2



Collect blood sample



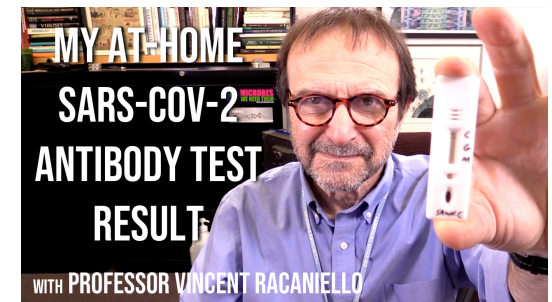
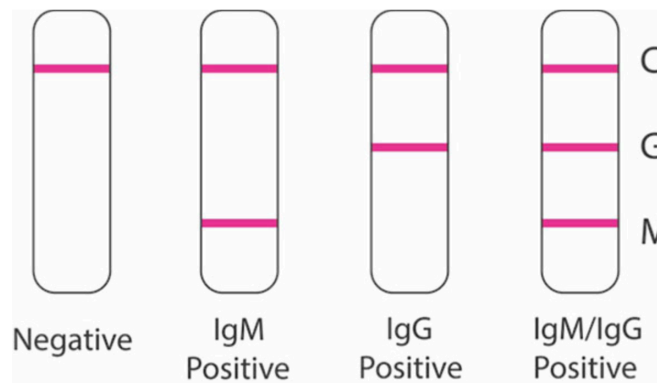
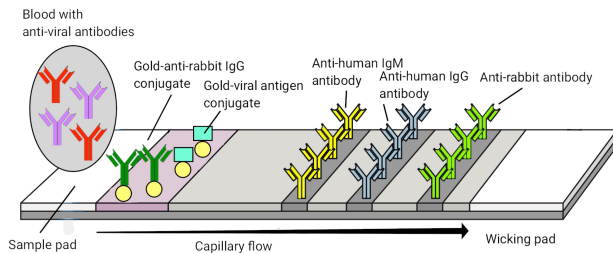
Add blood sample to sample well



Place 2-3 drops of buffer in sample well



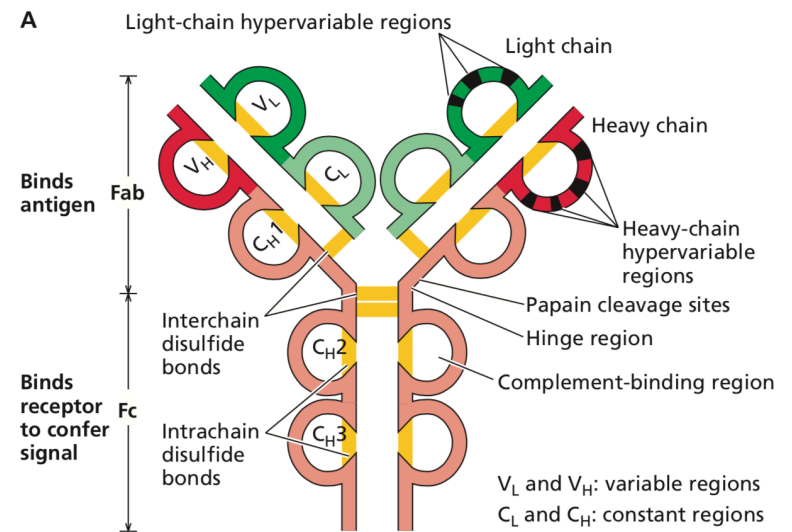
Read results after 15 minutes



<https://youtu.be/HvXCISbrK9Q>

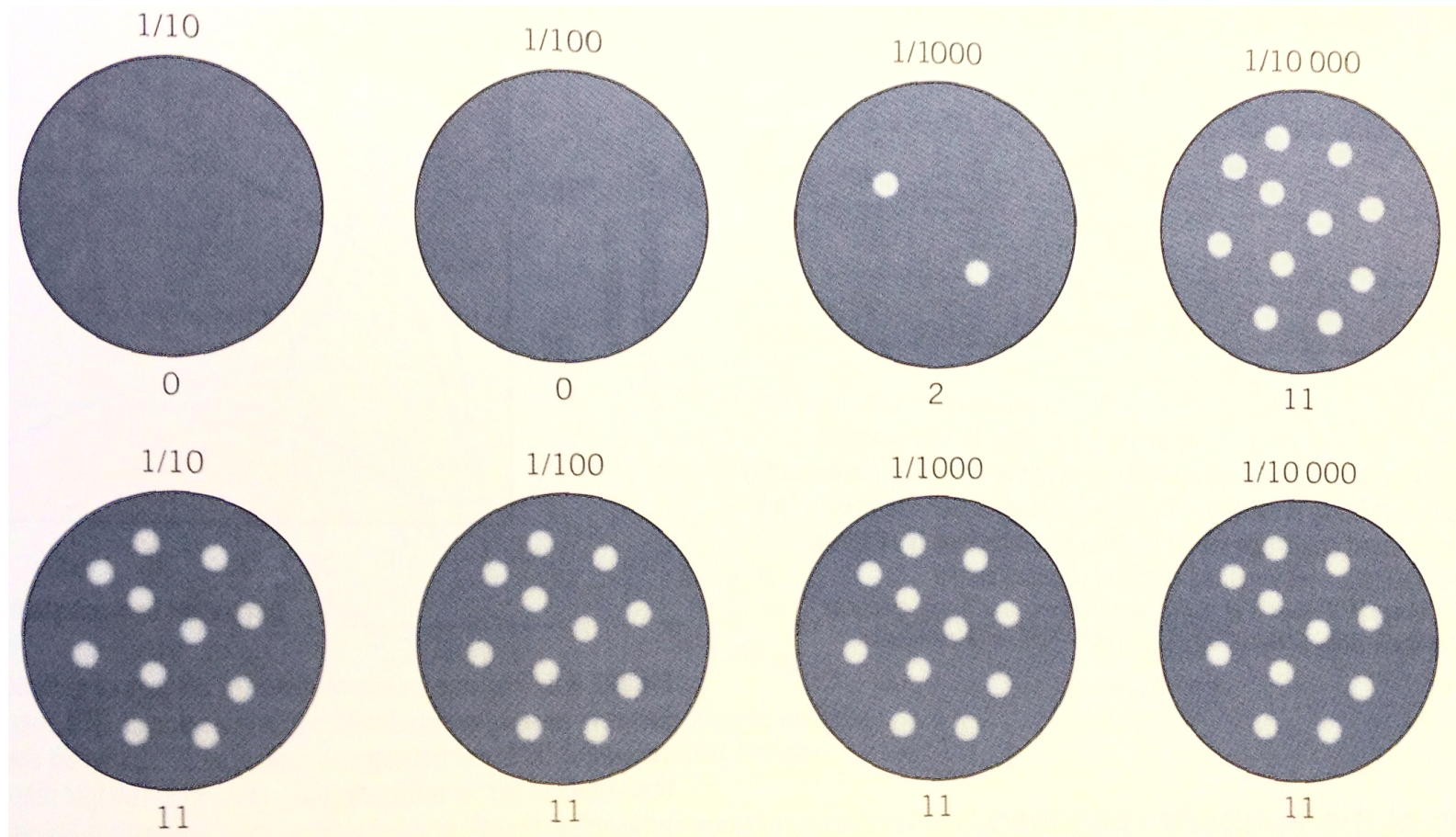
# Neutralizing antibodies

- 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
- Not all anti-viral antibodies neutralize infection!

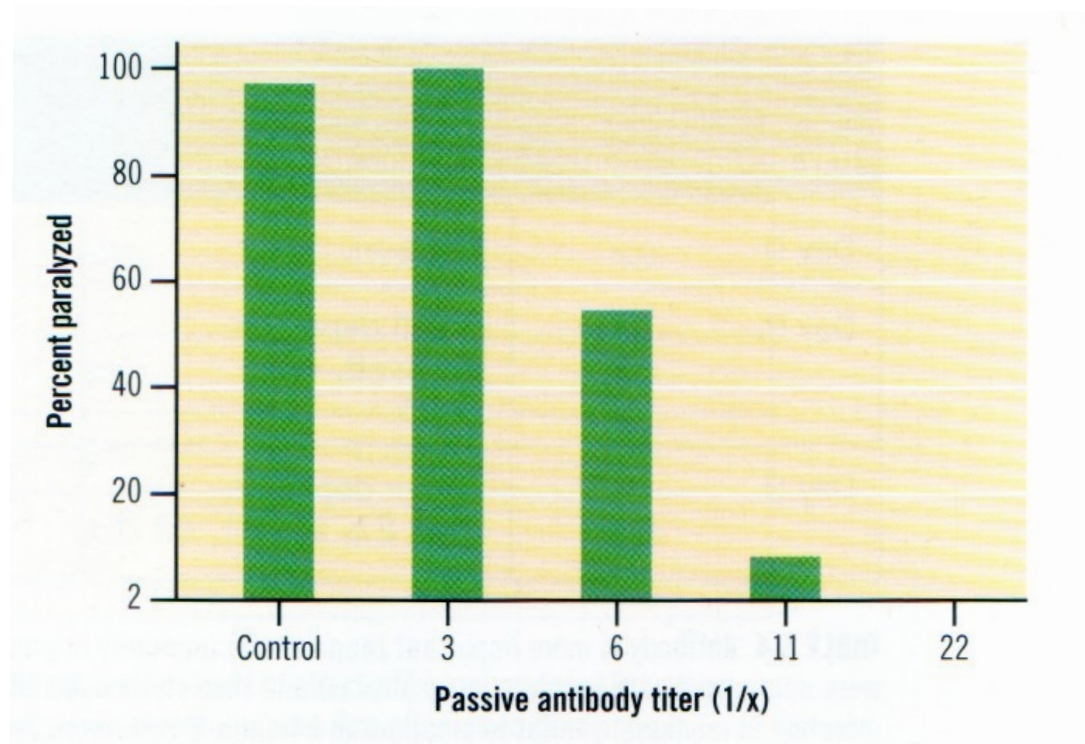




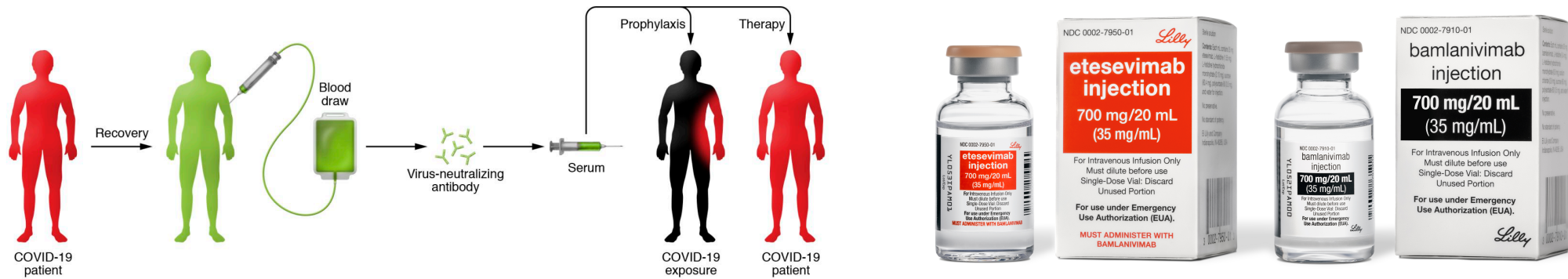
# Neutralizing antibodies



# Passive antibody protects against poliomyelitis



# Convalescent sera and monoclonal antibodies for COVID-19 treatment or prevention



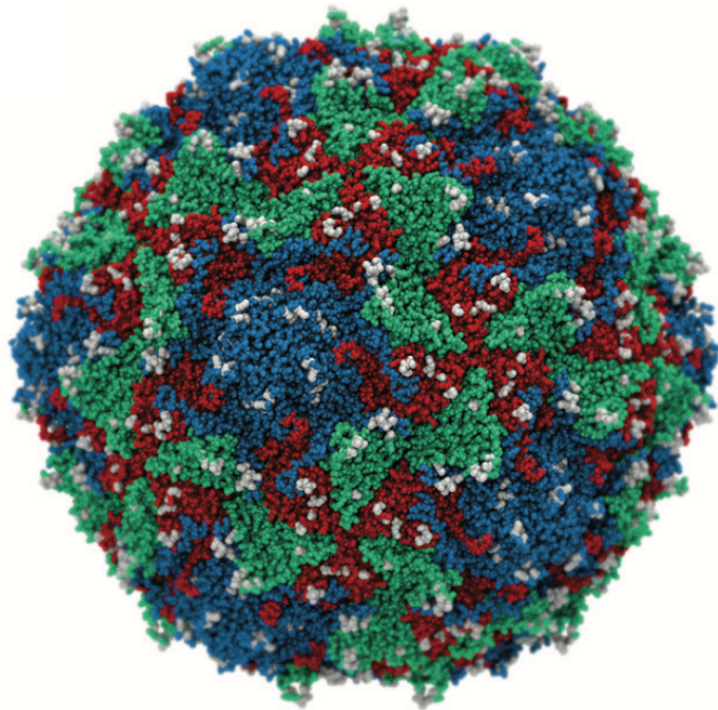
*Serum* is the liquid that remains after the blood has clotted

*Plasma* is the liquid that remains when clotting is prevented with the addition of an anticoagulant.

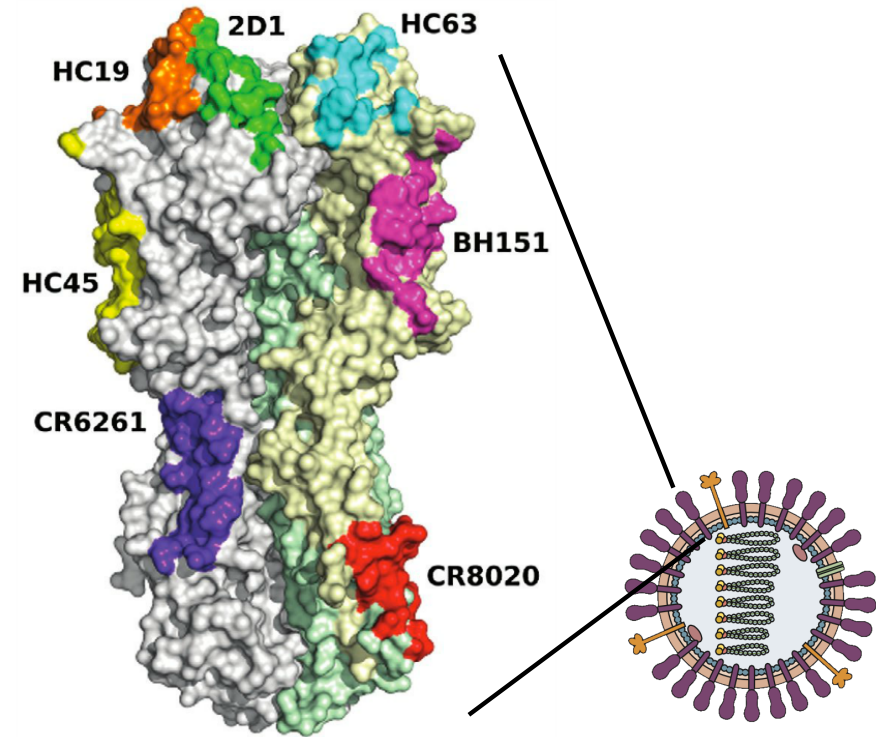


# Neutralization antigenic sites

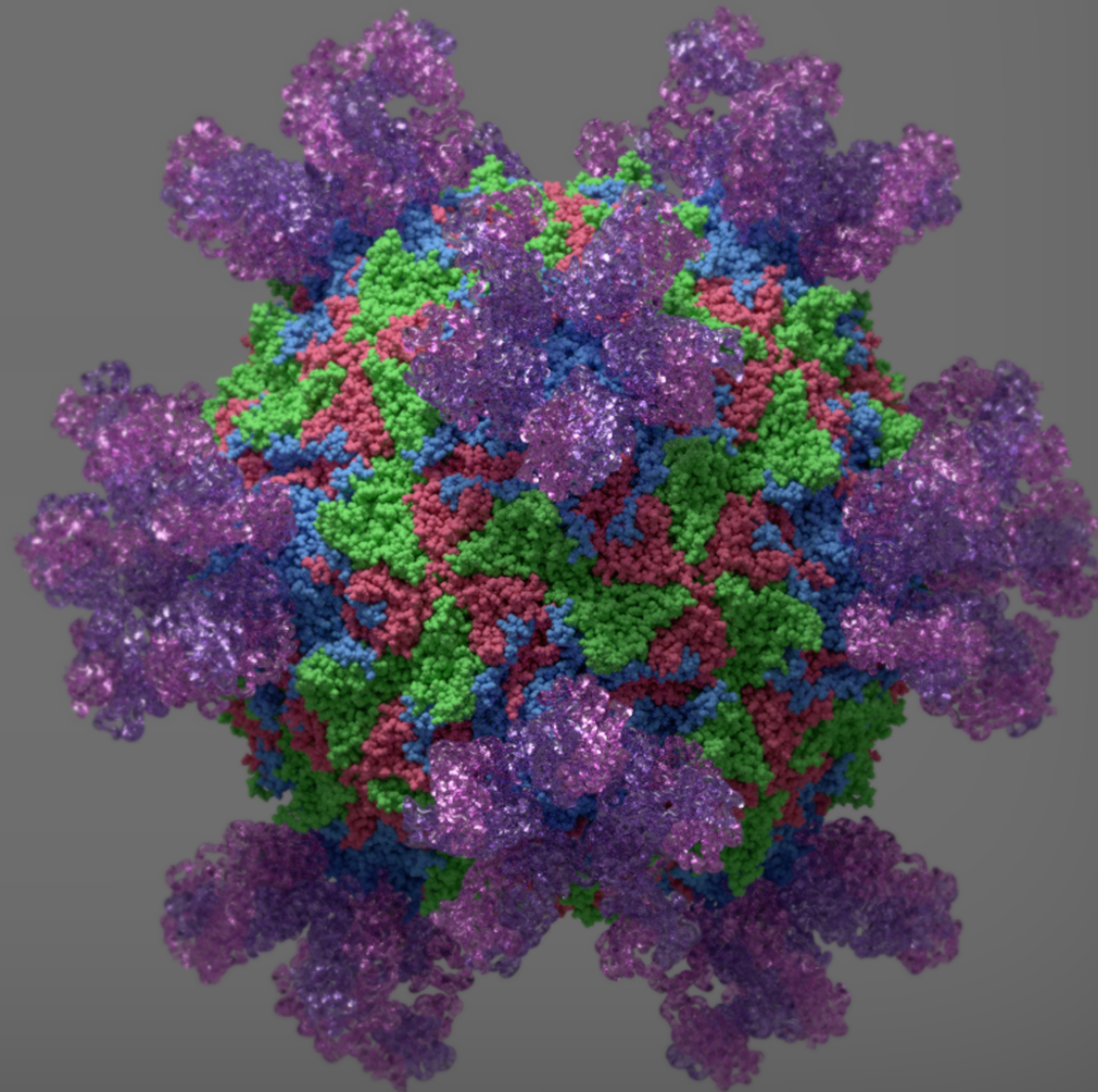
*Some antibodies bind but do not neutralize!*

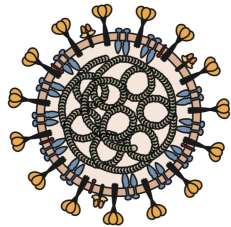


**Poliovirus**

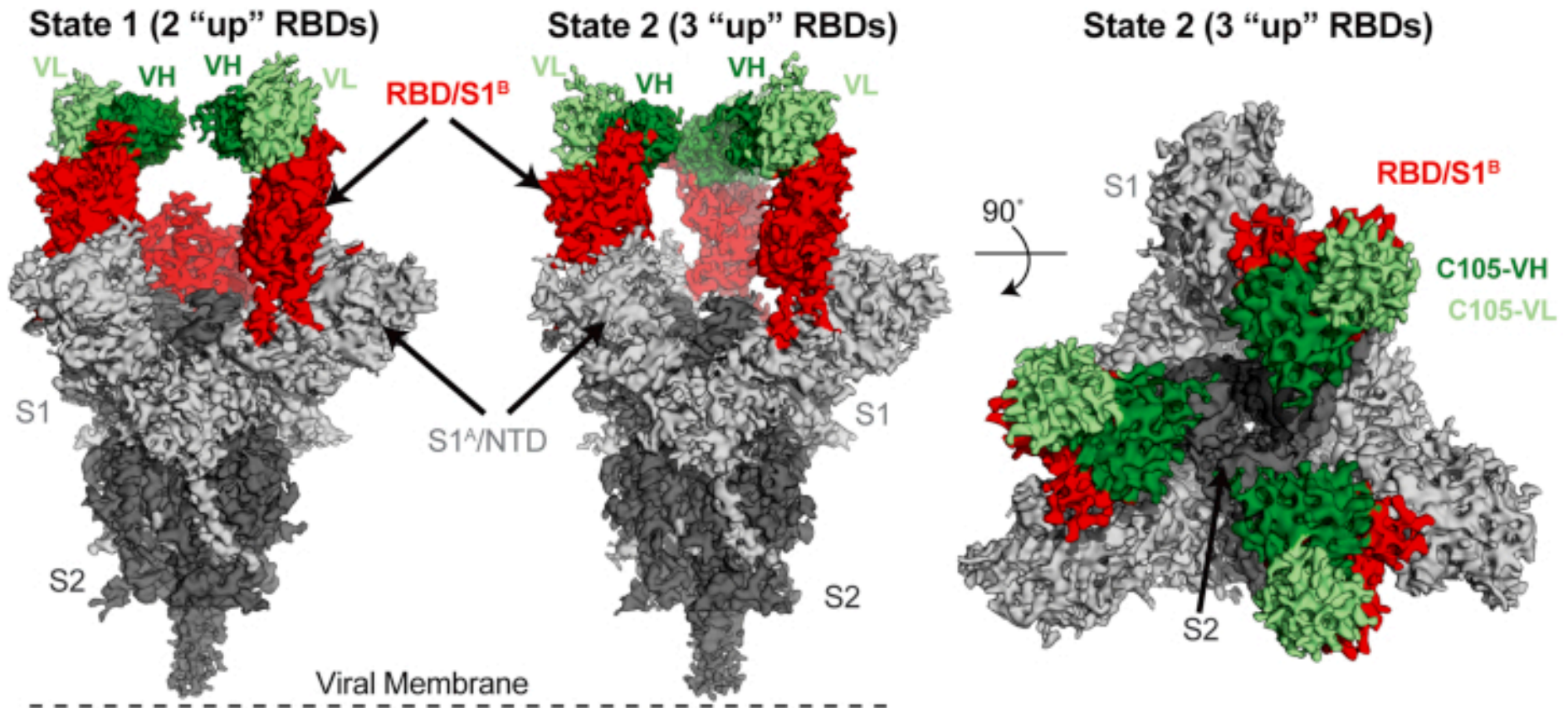


**Influenza virus HA**



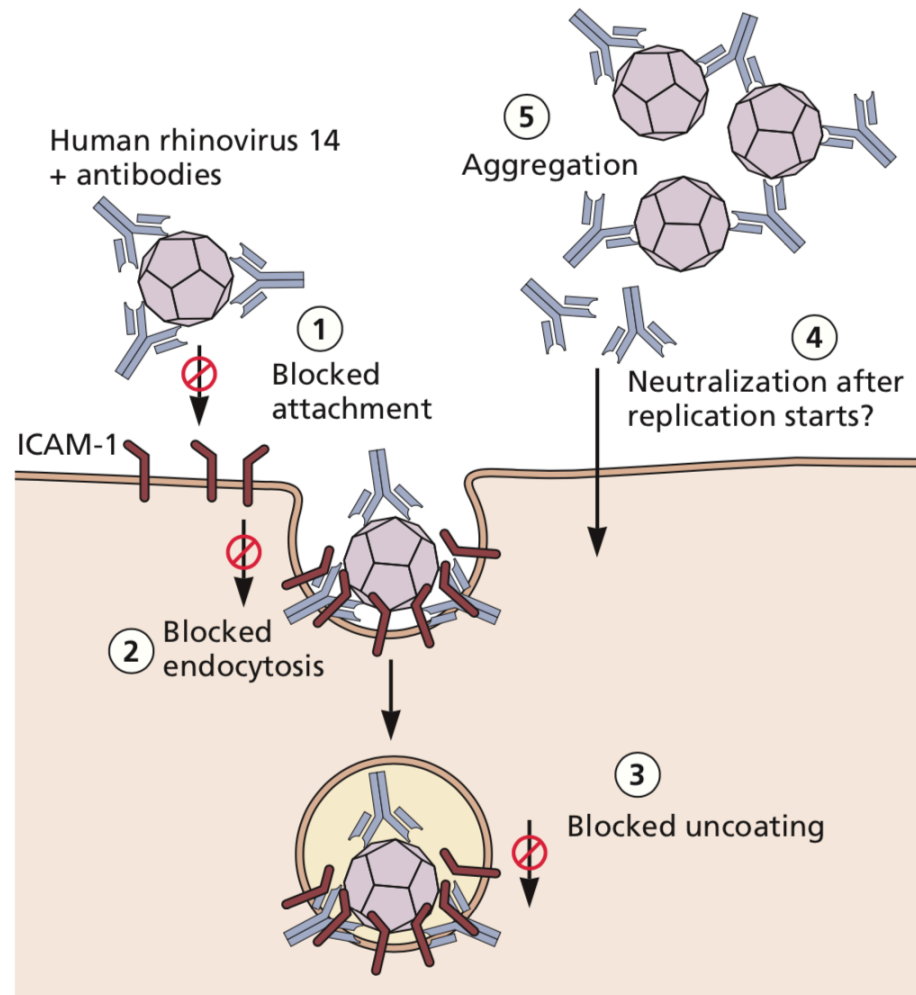


# mAb Fab fragment bound to SARS-CoV-2 spike

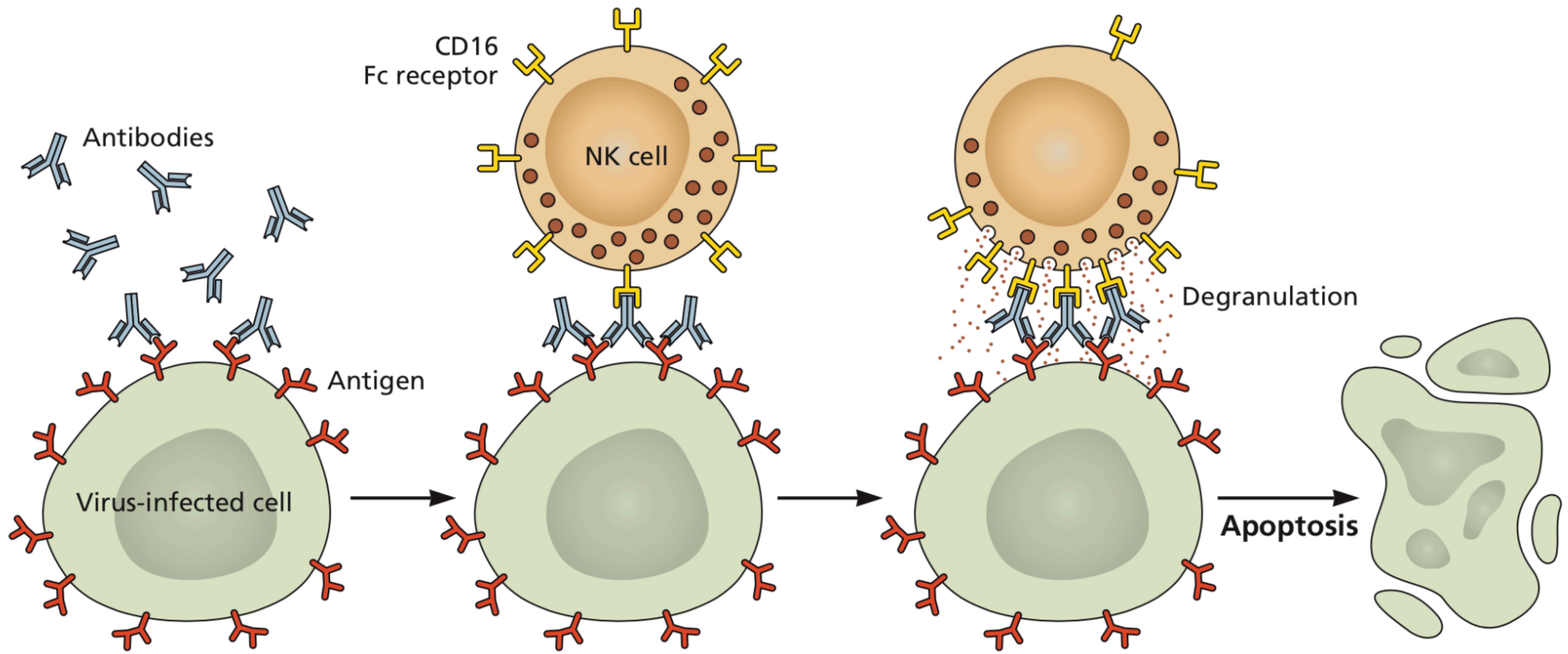




# Neutralizing antibodies

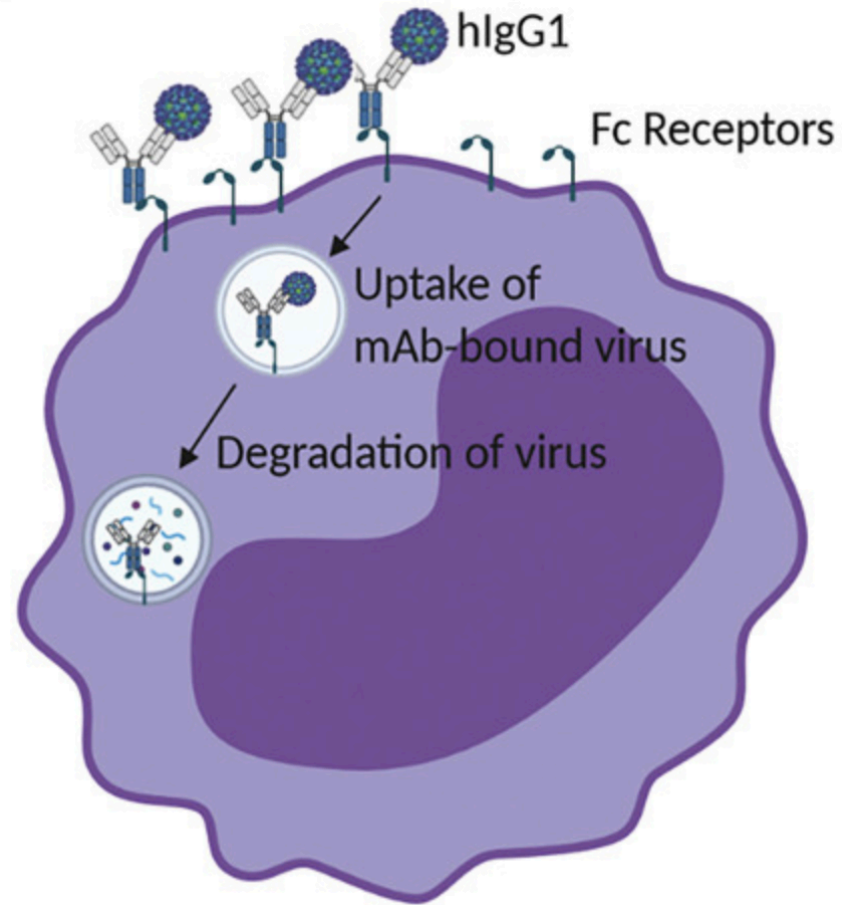


# Antibody-dependent cellular cytotoxicity

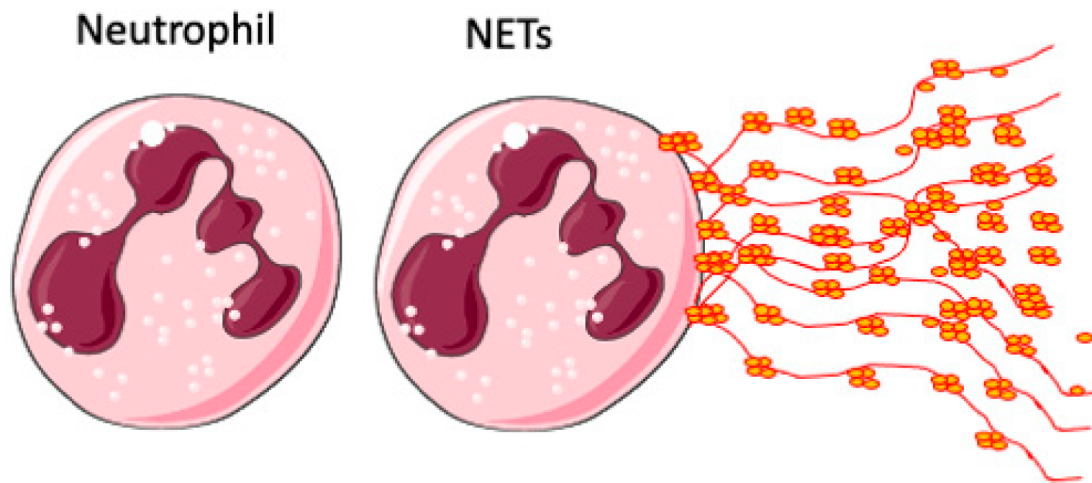




# Disease protection by non-neutralizing antibodies

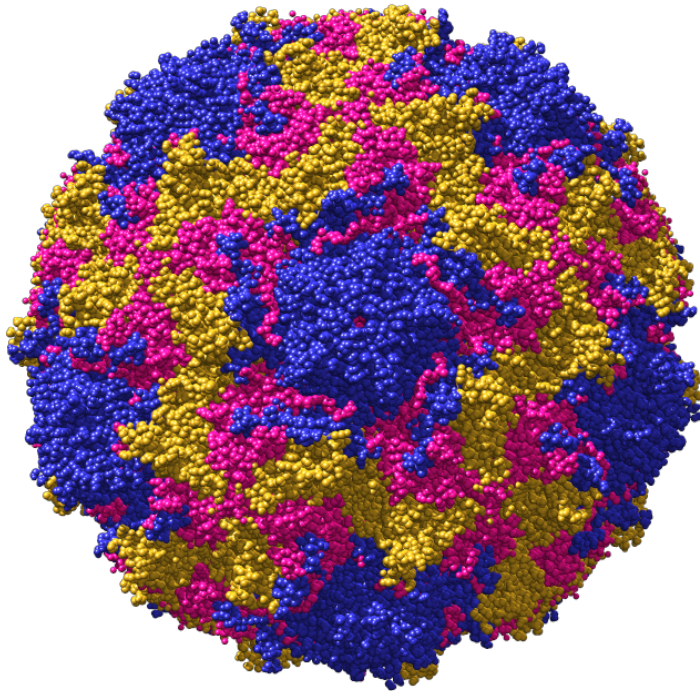


# IgA-stimulated NETosis



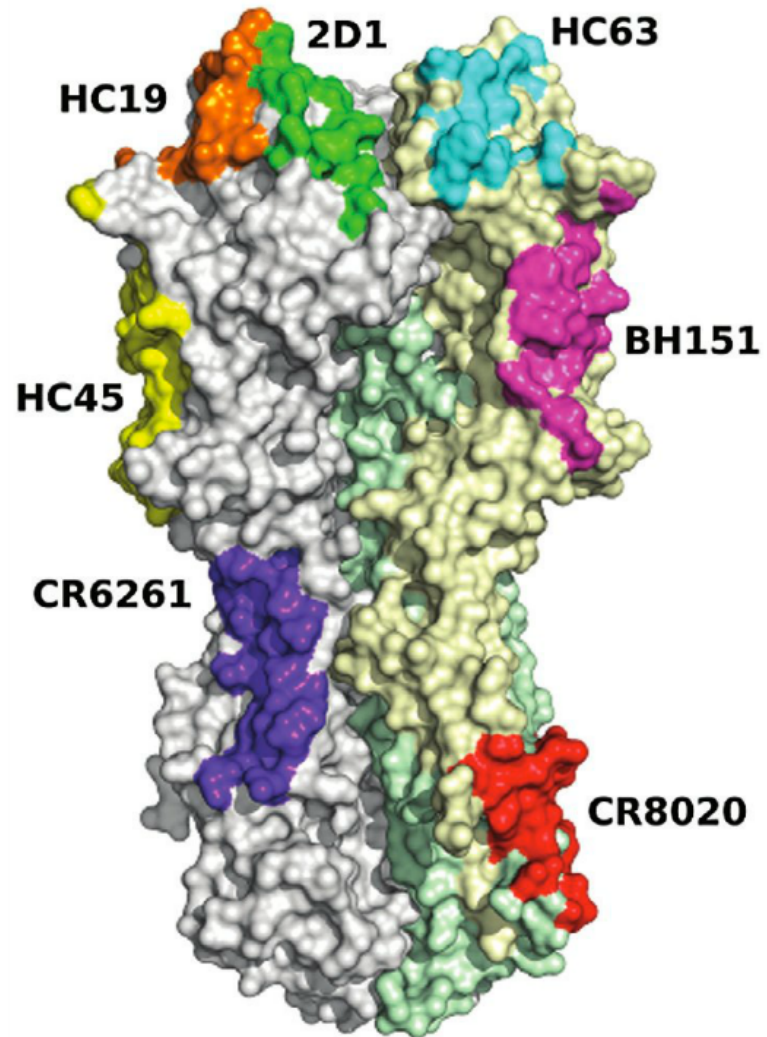
- Stimulated by IgA-virus complexes
- Non-neutralizing Ab
- Involves Fc receptors on neutrophils

## Evasion of antibody



**Rhinovirus**

>100 serotypes



**Influenza HA**

Antigenic variation

Fields Virology, Wolters Kluwer

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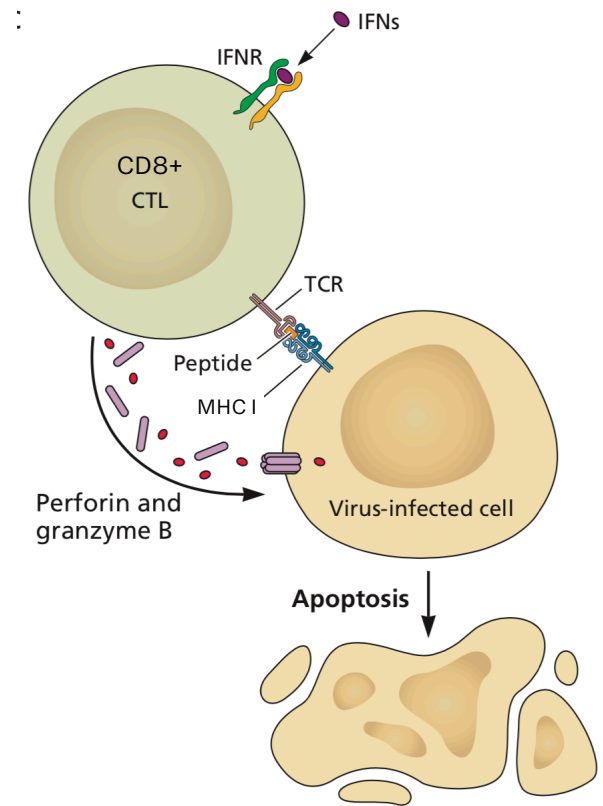
**b.socrative.com/login/student  
room number: virus**

**Which statement about anti-viral antibodies is incorrect:**

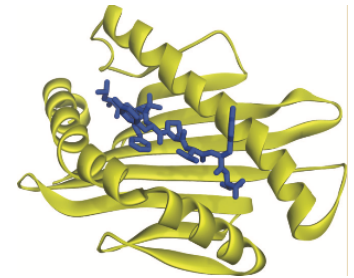
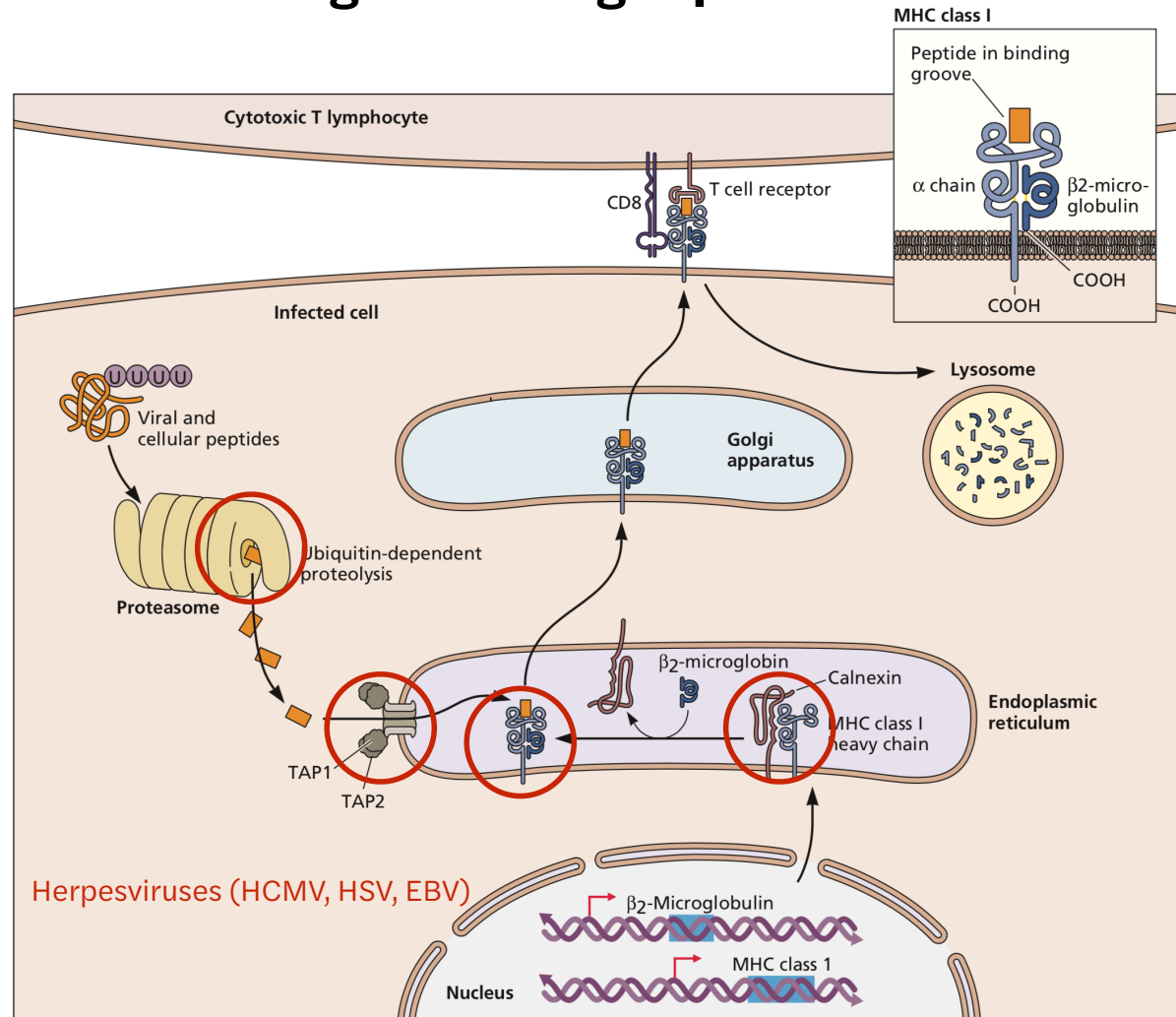
- A. They are important for protection against viral infections
- B. They only neutralize virus infectivity
- C. They may block virus attachment to cells
- D. They can be found at mucosal surfaces
- E. IgM is the first to appear, then IgG

# Cell mediated immunity

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



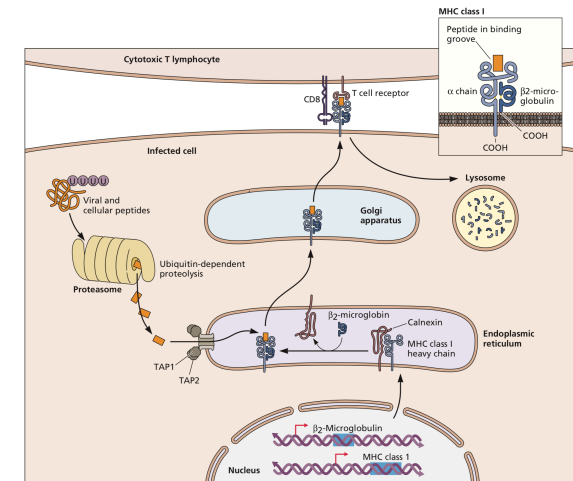
# Endogenous antigen presentation



TAP = transporter associated with antigen processing

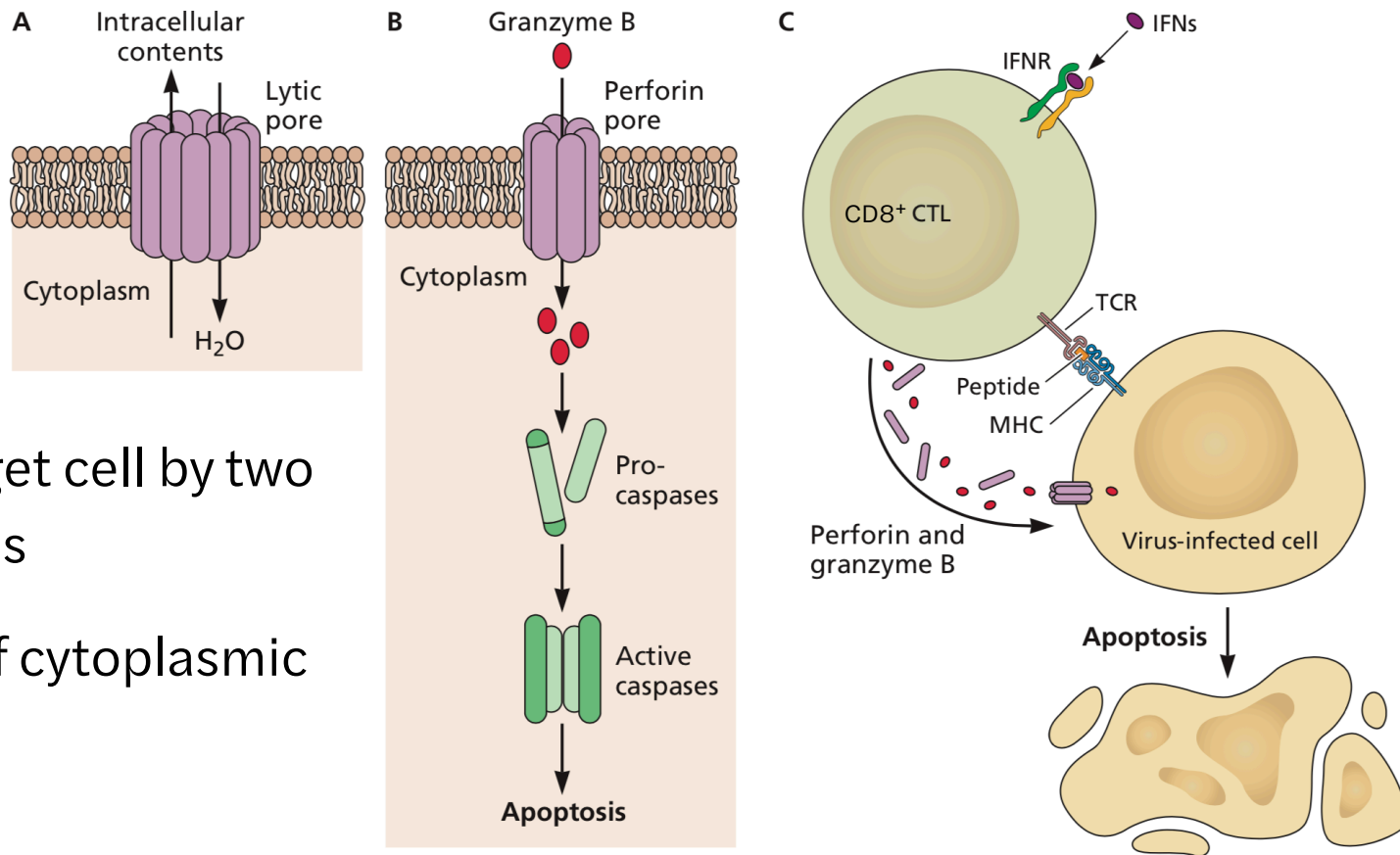
# Countering MHC I

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





# Cytotoxic T lymphocyte (CTL) lysis



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



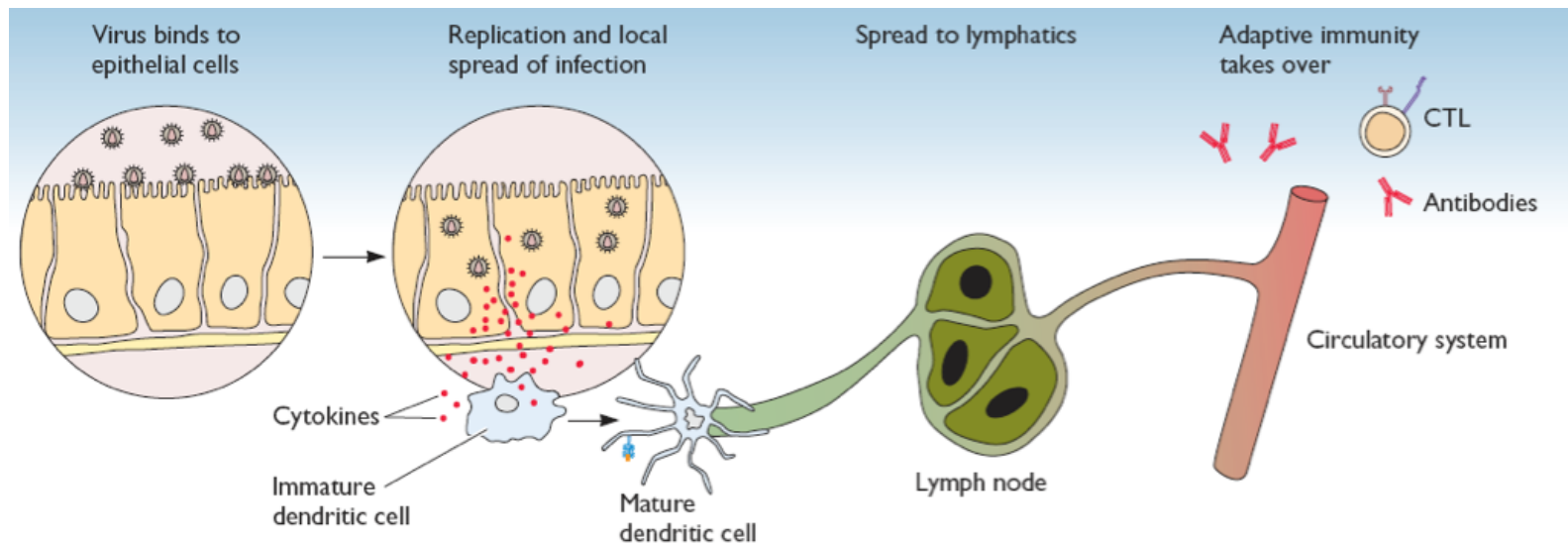
## Antibody vs cellular immunity in protecting against monkeypox virus disease

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

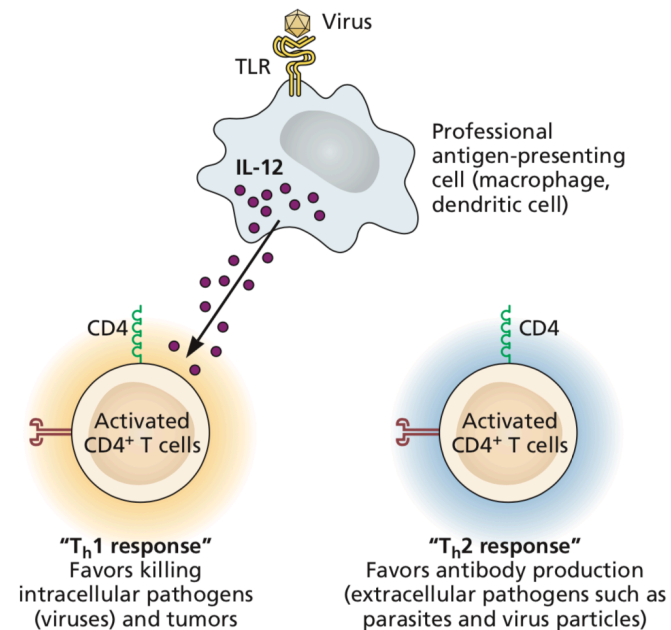
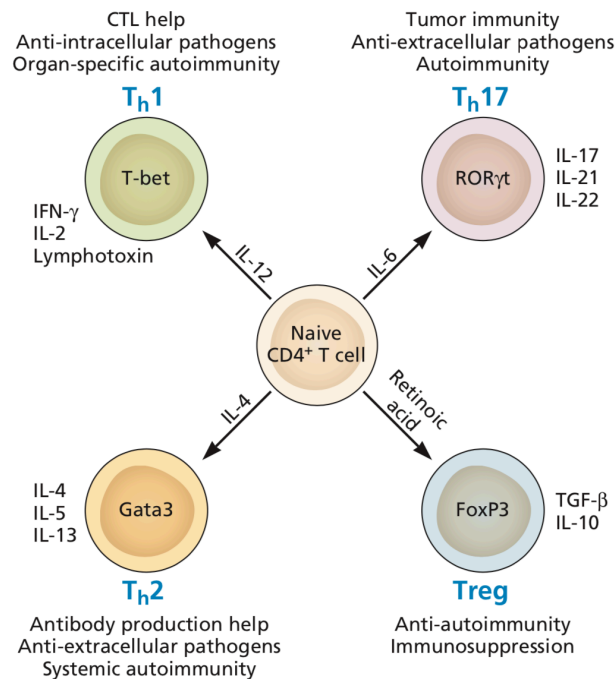
## How is the correct response made?

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



# 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



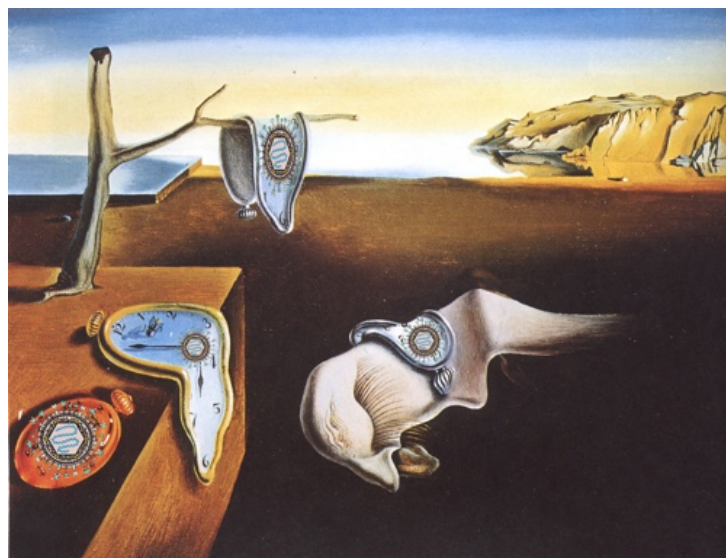
**Go to:**

**[b.socrative.com/login/student](https://b.socrative.com/login/student)  
room number: virus**

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

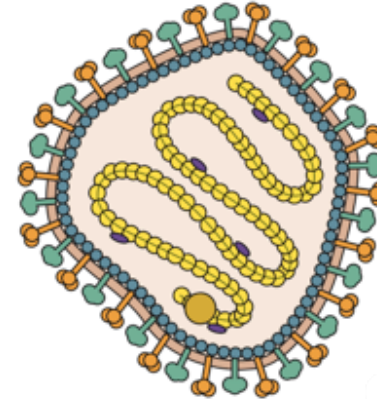
- A. By B lymphocytes
- B. By intrinsic defenses
- C. By autophagy of infected cells
- D. By the mix of peptides and cytokines presented by DCs
- E. It depends on whether the capsid is icosahedral or helical

## Adaptive responses also provide *memory*



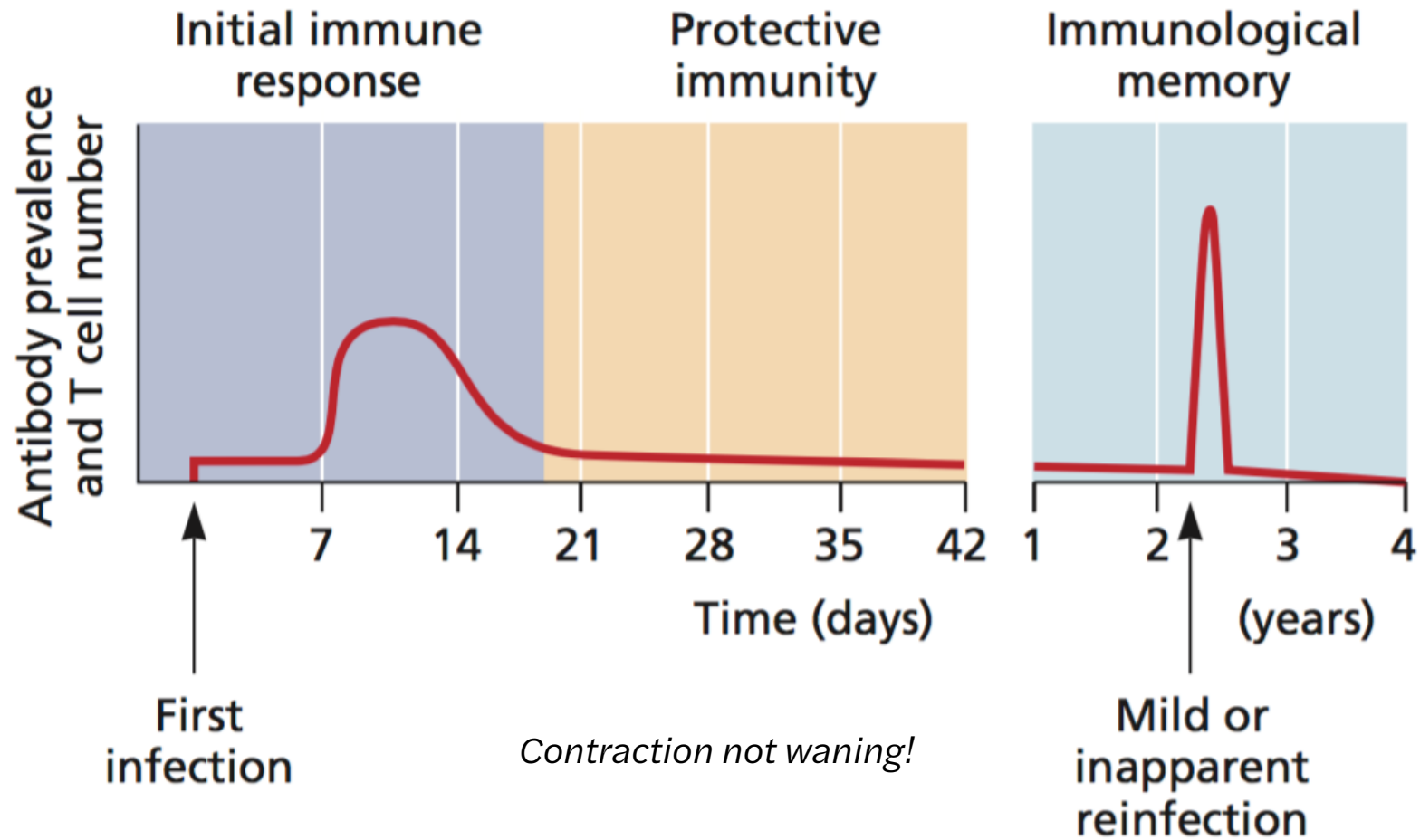
- If the host is subsequently infected by the same virus, the response will be **rapid and specific**
  - *Innate responses don't have memory*
- Memory: the basis for **vaccination**

# Infection provides immune memory



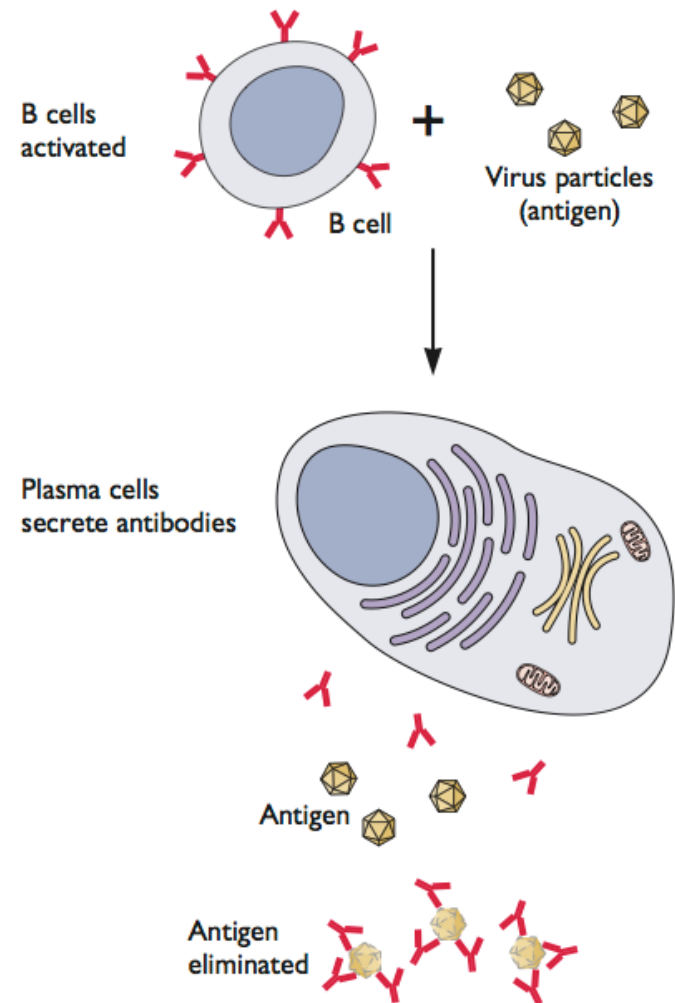
- 1781: outbreak of measles on Faroe Islands
- Next 65 years, islands free of measles
- 1846: another outbreak of measles; none of those who survived the 1781 epidemic were infected
- Immune memory may last a long time, maintained without re-exposure to virus

# Immunological memory



# 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

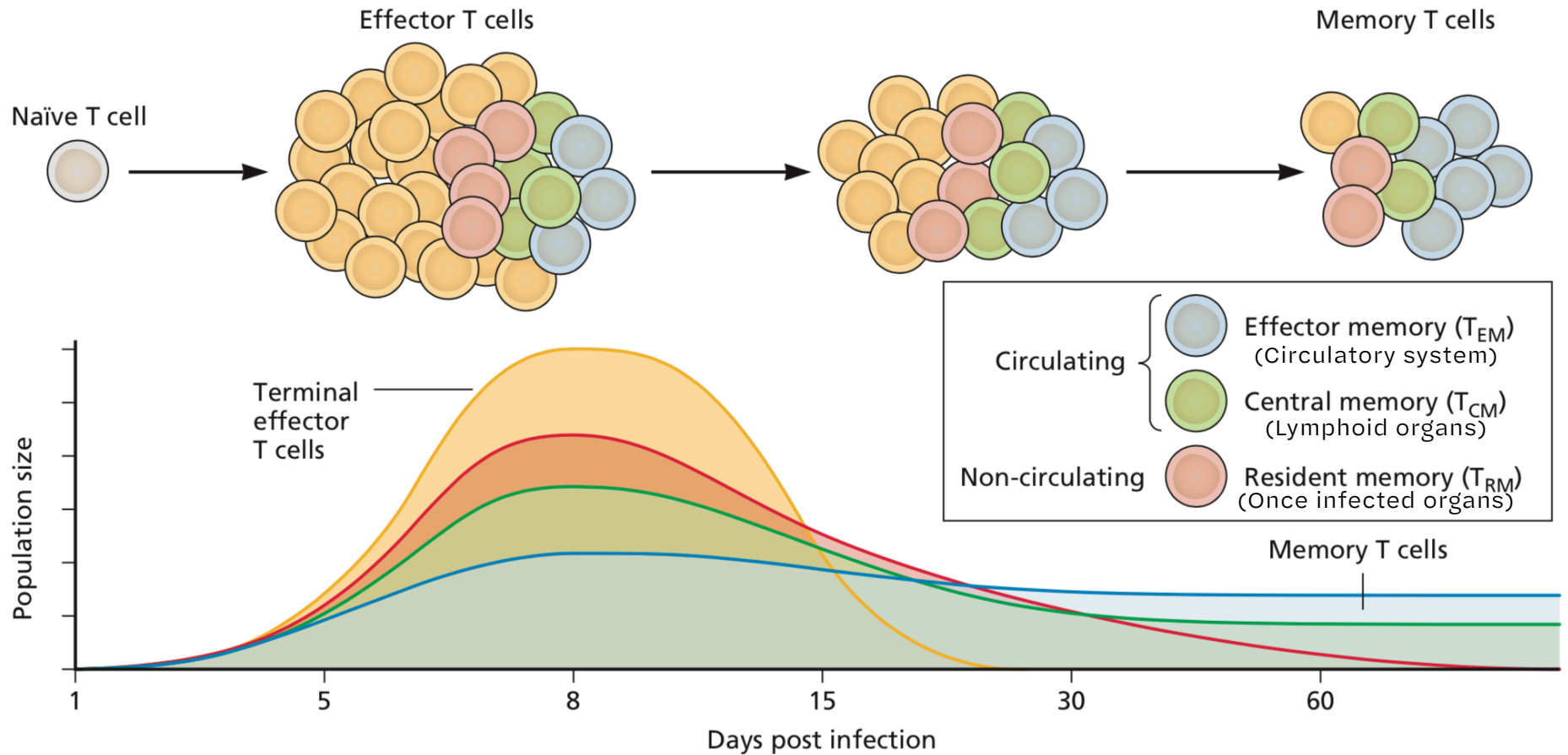


Principles of Virology, ASM Press



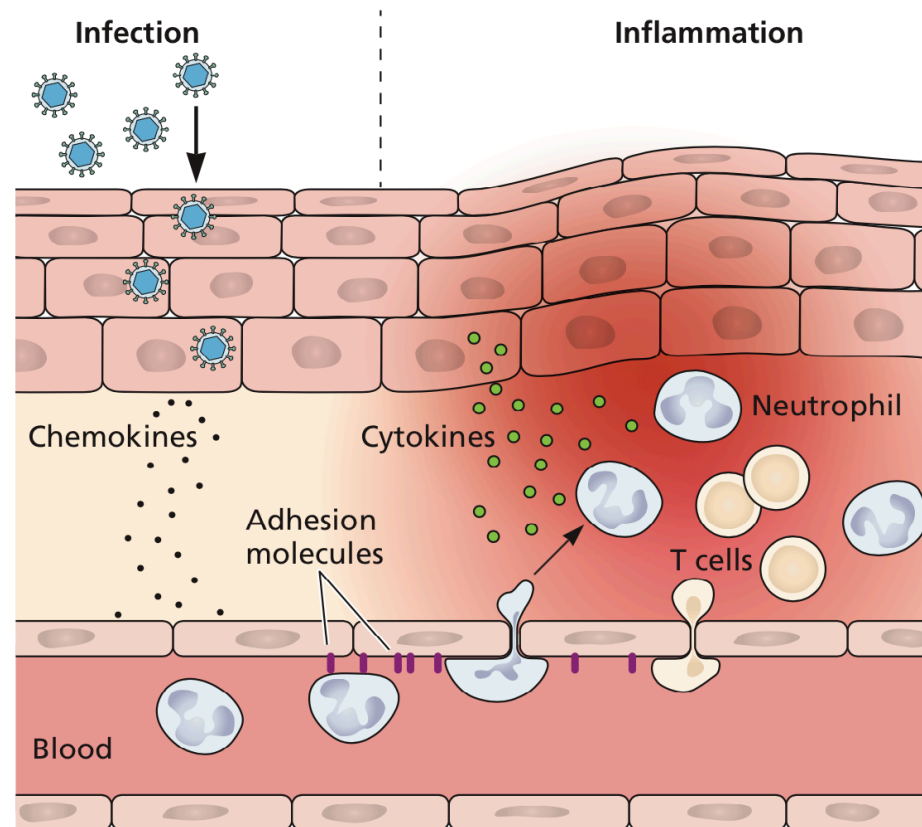
Disease	Persistence of antibody
<b>Systemic infections</b>	
Chikungunya	30 yr
Rift Valley fever	12 yr
Dengue	32 yr
Yellow fever	75 yr
Measles	65 yr
Mumps	12 yr
Poliomyelitis	40 yr
Hepatitis A	25 yr
Smallpox	40 yr
Vaccinia	75 yr
Rubella	14 yr
<b>Mucosal Infections</b>	
Coronavirus disease	12 mo
Influenza	30 mo
RSV disease	3 mo
Rotavirus gastroenteritis	12 mo

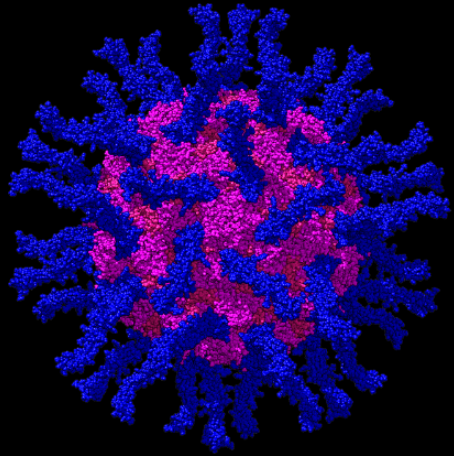
# Generation of memory T cell diversity



*Contraction not waning!*

# Inflammation provides integration and synergy within the immune system





# **VIROLOGY LIVE**

**WITH VINCENT RACANIELLO**

**Next time: Mechanisms of pathogenesis**