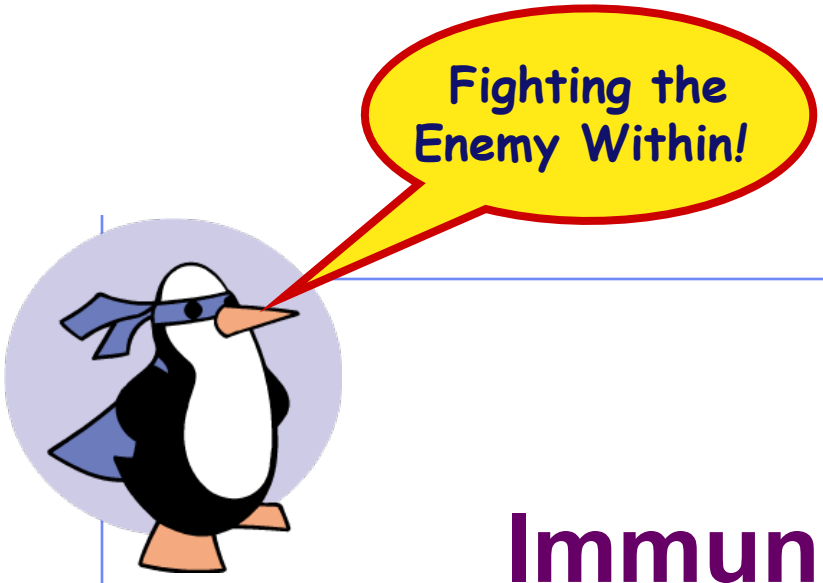
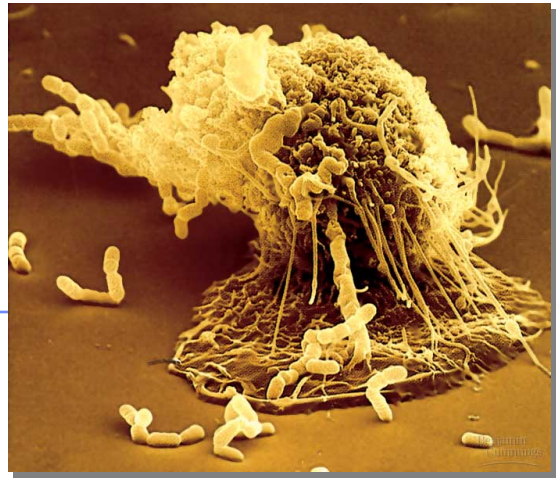
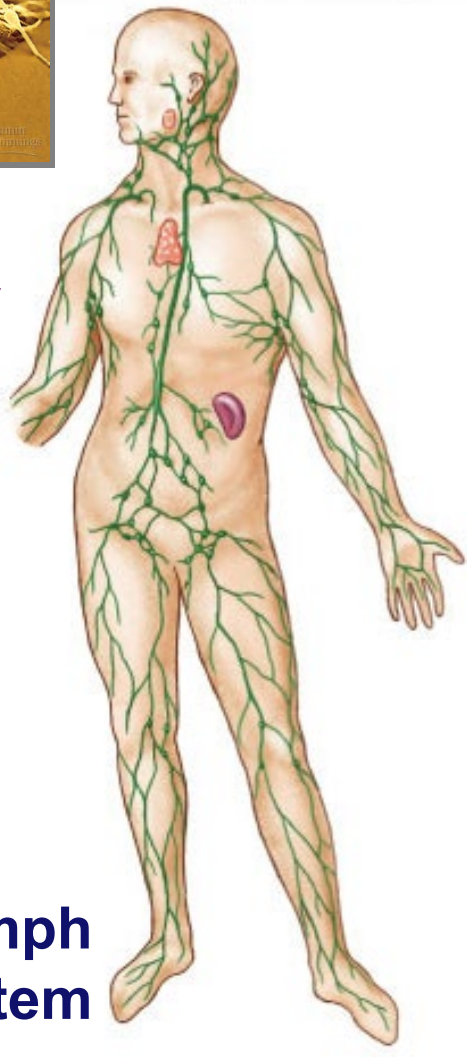




phagocytic leukocyte

Immune / Lymphatic System

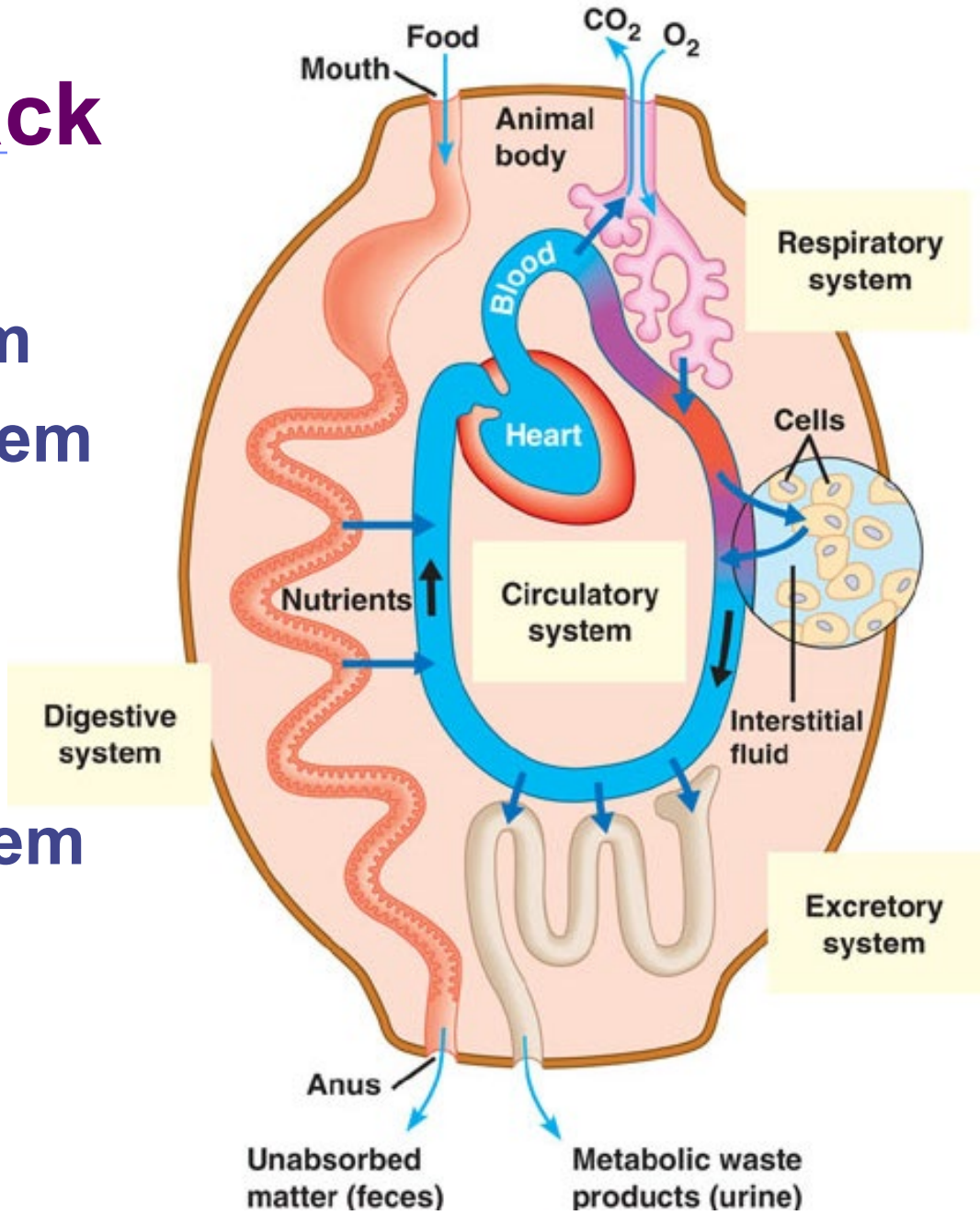
lymphocytes attacking cancer cell



lymph system

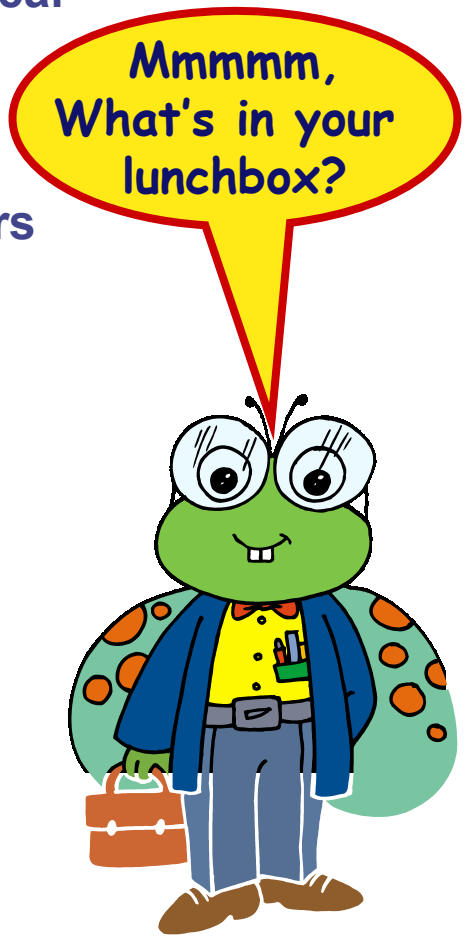
Avenues of attack

- Points of entry
  - digestive system
  - respiratory system
  - urogenital tract
  - break in skin
- Routes of attack
  - circulatory system
  - lymph system



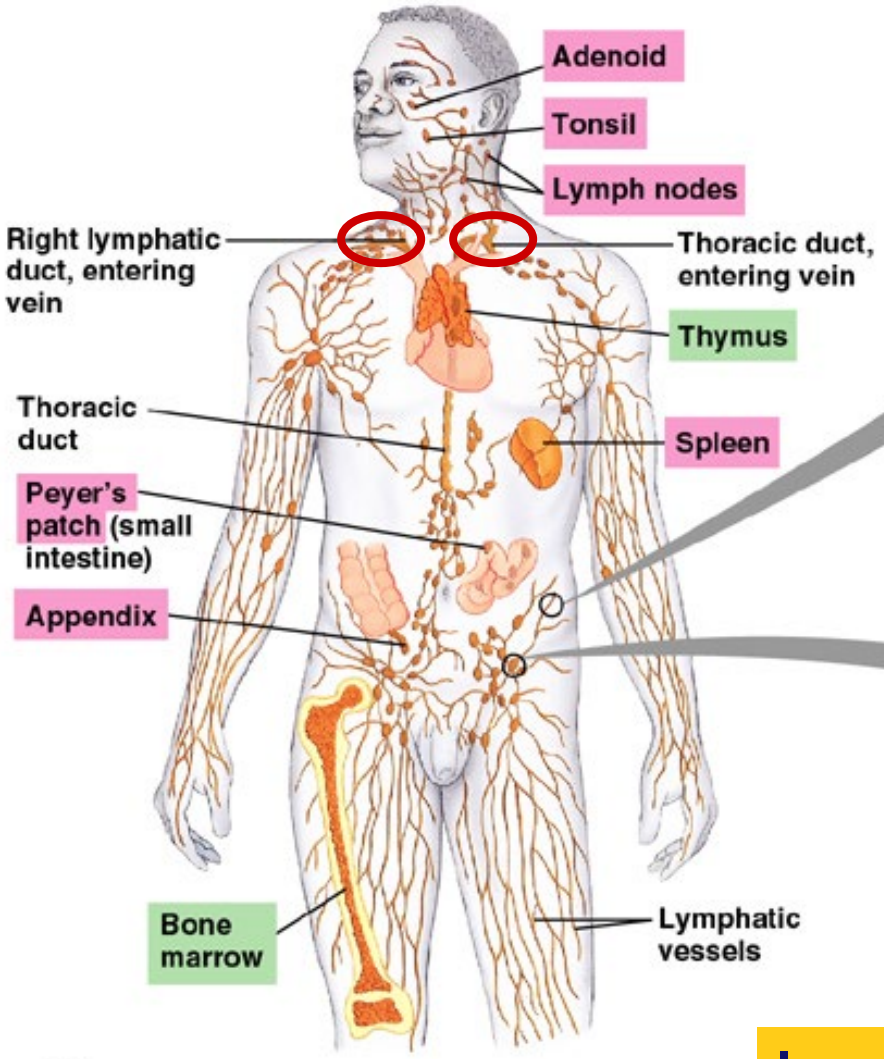
Why an immune system?

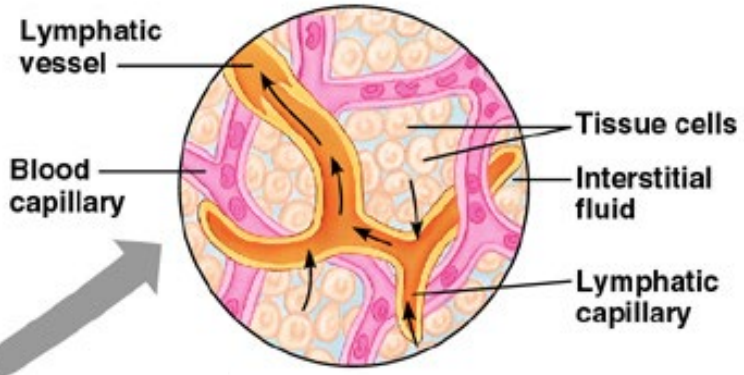
- **Attack from outside**
  - lots of organisms want you for lunch!
  - animals are a tasty nutrient- & vitamin-packed meal
    - cells are packages of macromolecules
    - no cell wall
      - traded mobility for susceptibility
  - animals must defend themselves against invaders
    - viruses
      - HIV, flu, cold, measles, chicken pox, SARS
    - bacteria
      - pneumonia, meningitis, tuberculosis
    - fungi
      - yeast
    - protists
      - amoeba, Lyme disease, malaria
- **Attack from inside**
  - defend against abnormal body cells = cancers



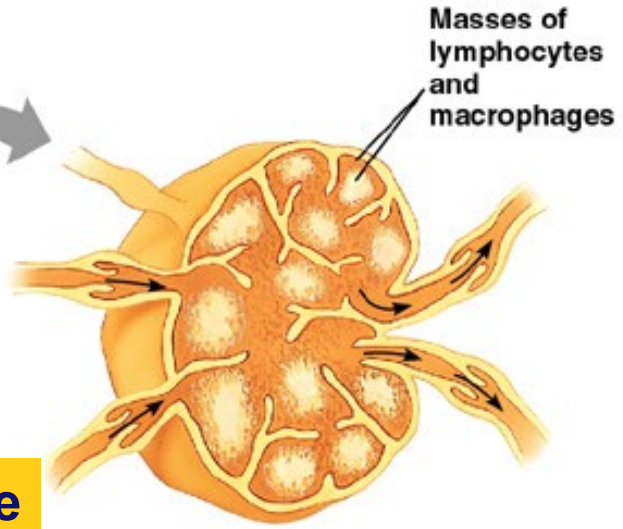
Lymph system

Production & transport of leukocytes
Traps foreign invaders





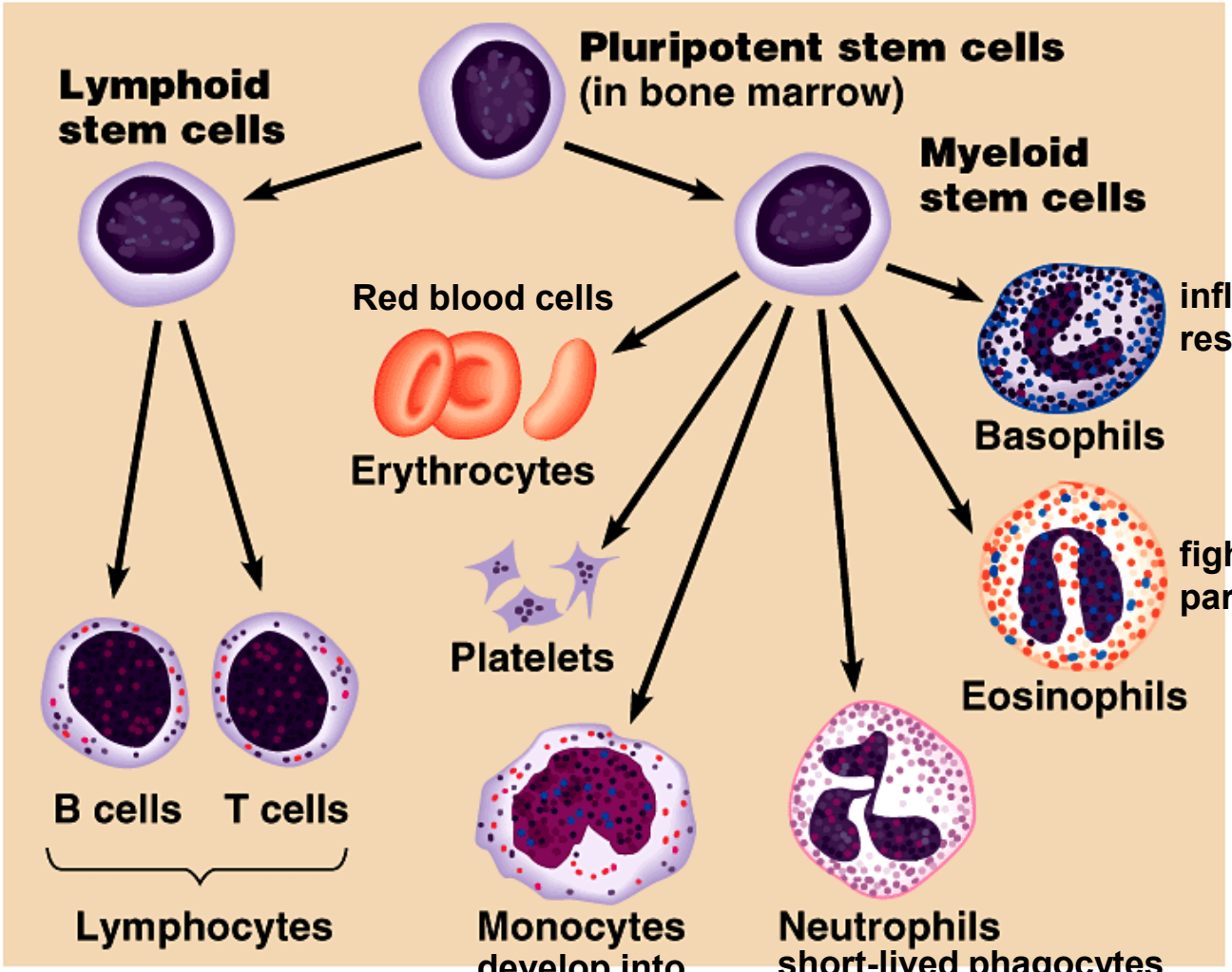
lymph vessels
(intertwined amongst blood vessels)



lymph node

A

Development of Red & White blood cells

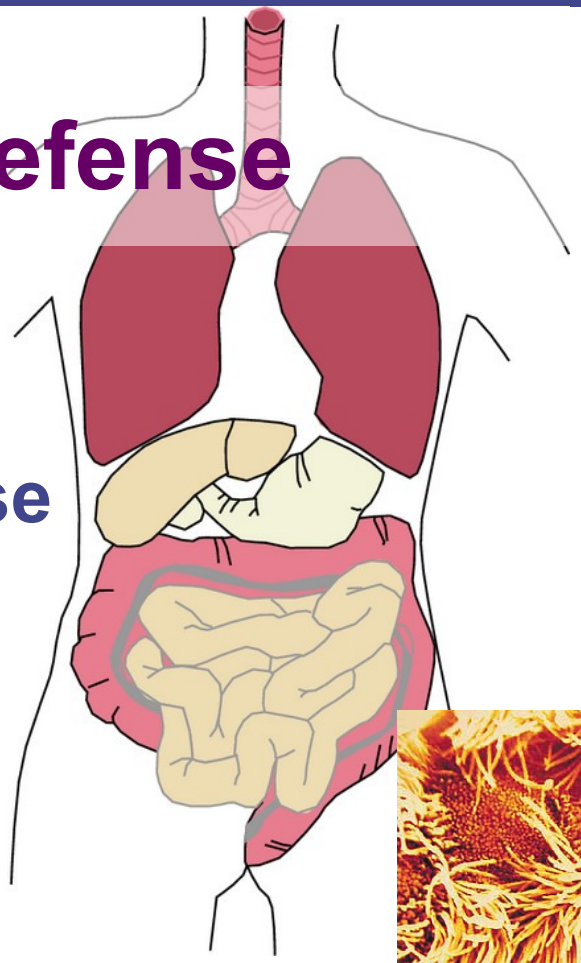


Lines of defense

- 1st line: Barriers
  - broad, external defense
    - "walls & moats"
  - skin & mucus membranes
- 2nd line: Non-specific patrol
  - broad, internal defense
    - "patrolling soldiers"
  - leukocytes = phagocytic WBC
    - macrophages
- 3rd line: Immune system
  - specific, acquired immunity
    - "elite trained units"
  - lymphocytes & antibodies
    - B cells & T cells

1st line: External defense

- Physical & chemical defenses
  - non-specific defense
- external barrier
  - epithelial cells & mucus membranes
    - skin
    - respiratory system
    - digestive system
    - uro-genital tract



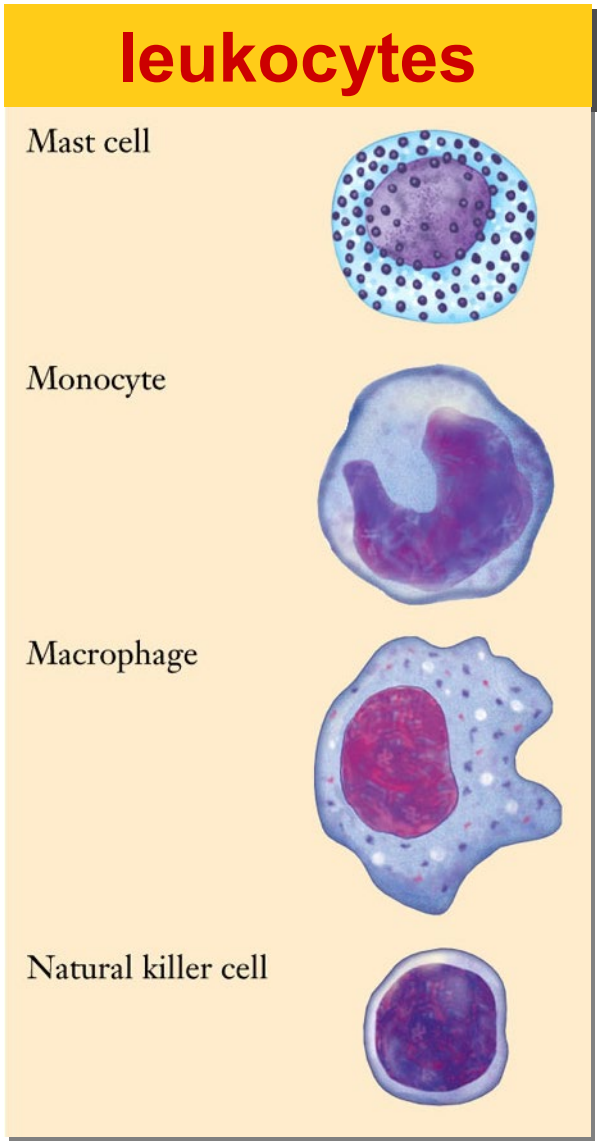
Lining of trachea:
ciliated cells & mucus secreting cells

1st line: Chemical barriers on epithelium

- Skin & mucous membrane secretions
  - sweat
    - pH 3-5
  - tears
    - washing action
  - mucus
    - traps microbes
  - saliva
    - anti-bacterial = “lick your wounds”
  - stomach acid
    - pH 2
  - anti-microbial proteins
    - lysozyme enzyme
      - digests bacterial cell walls

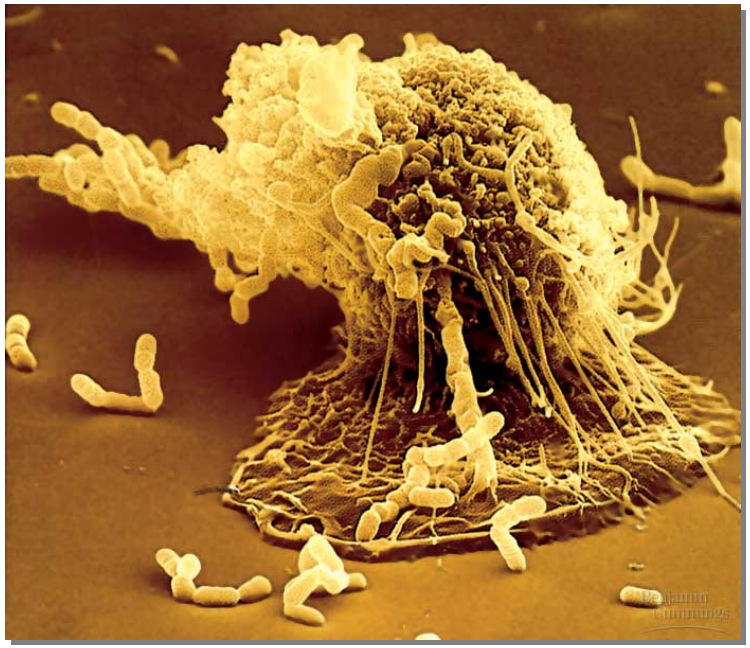
2nd line: Internal, broad range patrol

- Innate, general defense
  - rapid response
- Patrolling cells & proteins
  - attack invaders that penetrate body's outer barriers
    - leukocytes
      - phagocytic white blood cells
    - complement system
      - anti-microbial proteins
    - inflammatory response

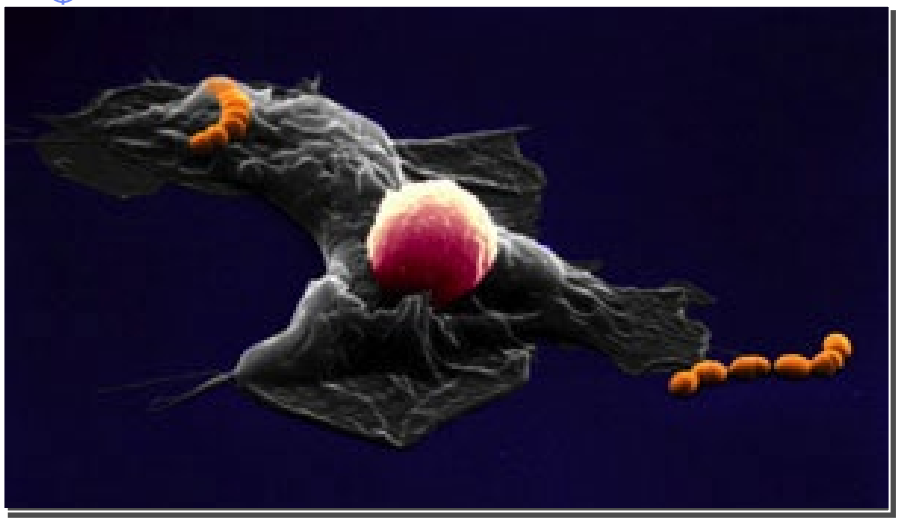


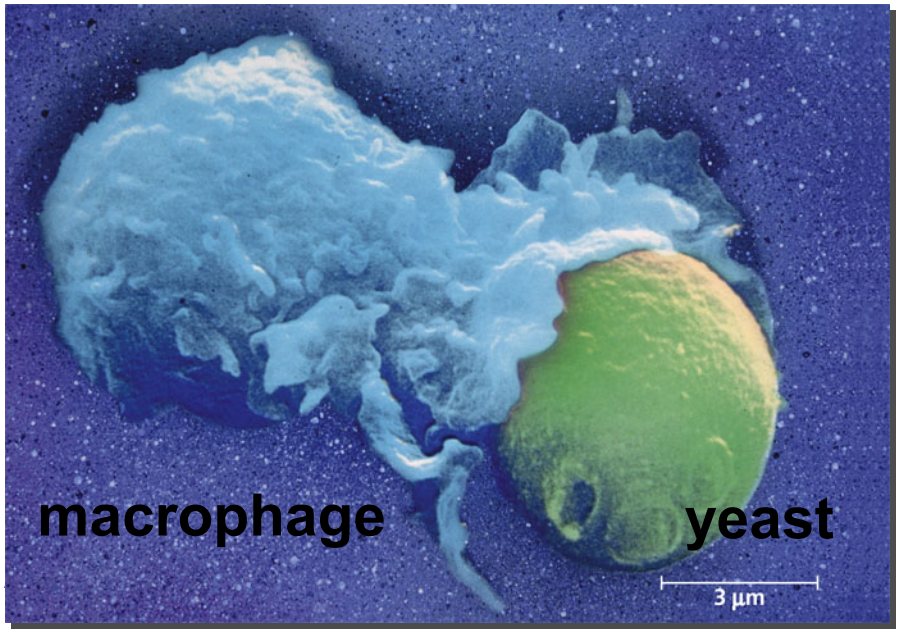
Leukocytes: Phagocytic WBCs

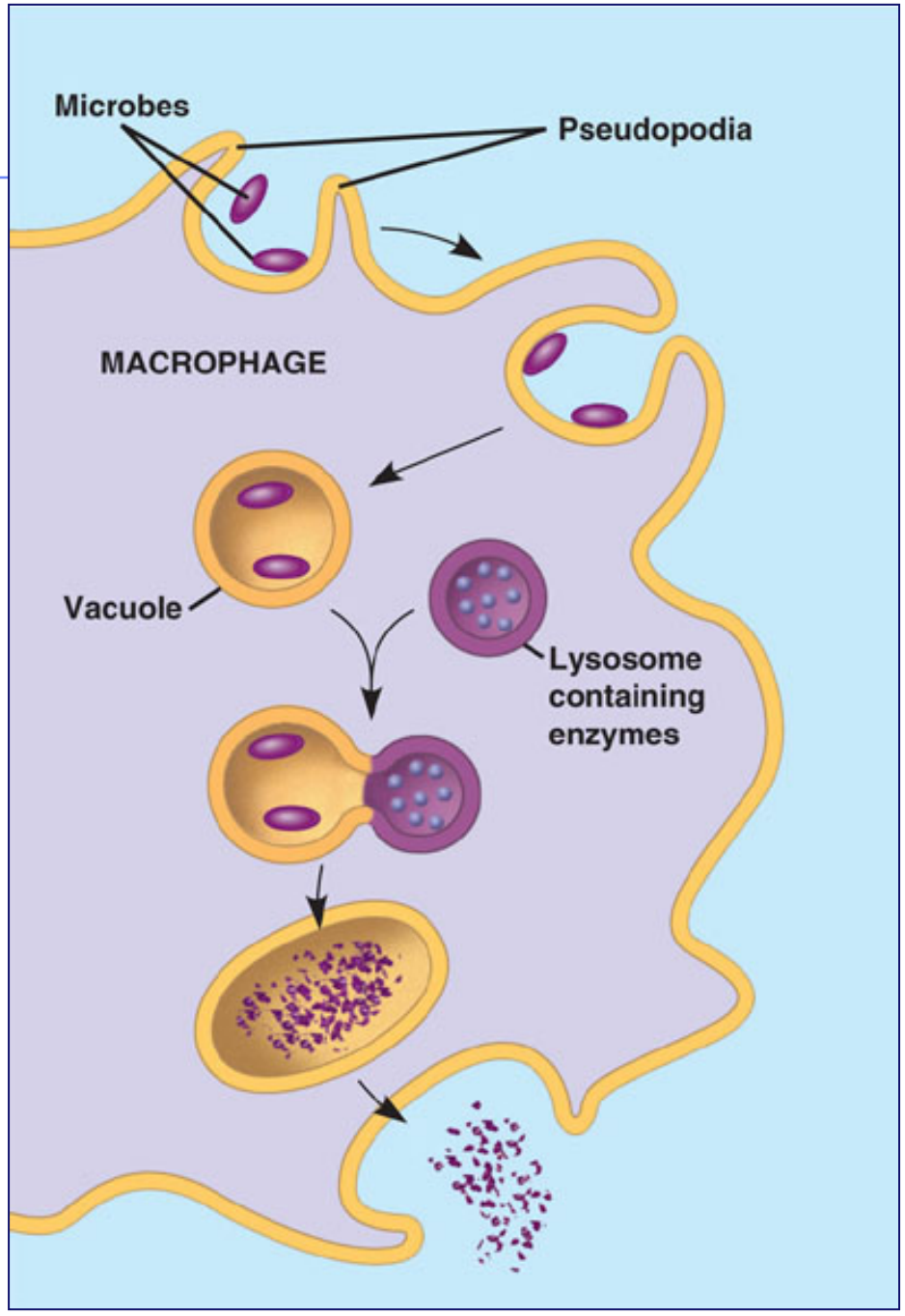
- **Attracted by chemical signals released by damaged cells**
  - enter infected tissue, engulf & ingest microbes
    - lysosomes
- **Neutrophils**
  - most abundant WBC (~70%)
  - ~ 3 day lifespan
- **Macrophages**
  - "big eater", long-lived
- **Natural Killer Cells**
  - destroy virus-infected cells & cancer cells



Phagocytes

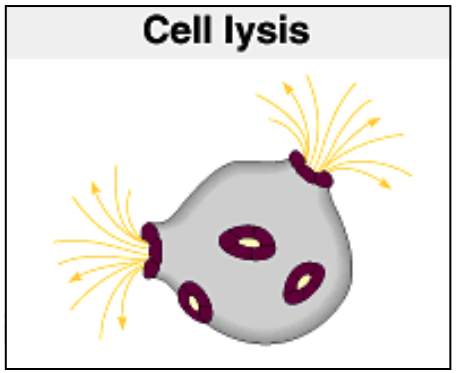



macrophage
yeast
3 µm


Microbes
Pseudopodia
MACROPHAGE
Vacuole
Lysosome containing enzymes

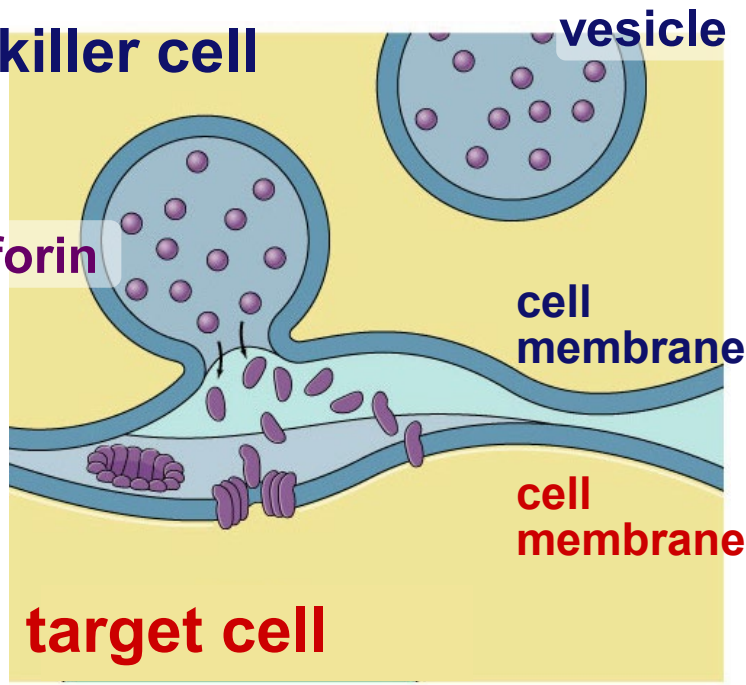
Destroying cells gone bad!

- Natural Killer Cells perforate cells
  - release perforin protein
  - insert into membrane of target cell
  - forms pore allowing fluid to flow into cell
  - cell ruptures (lysis)
    - apoptosis



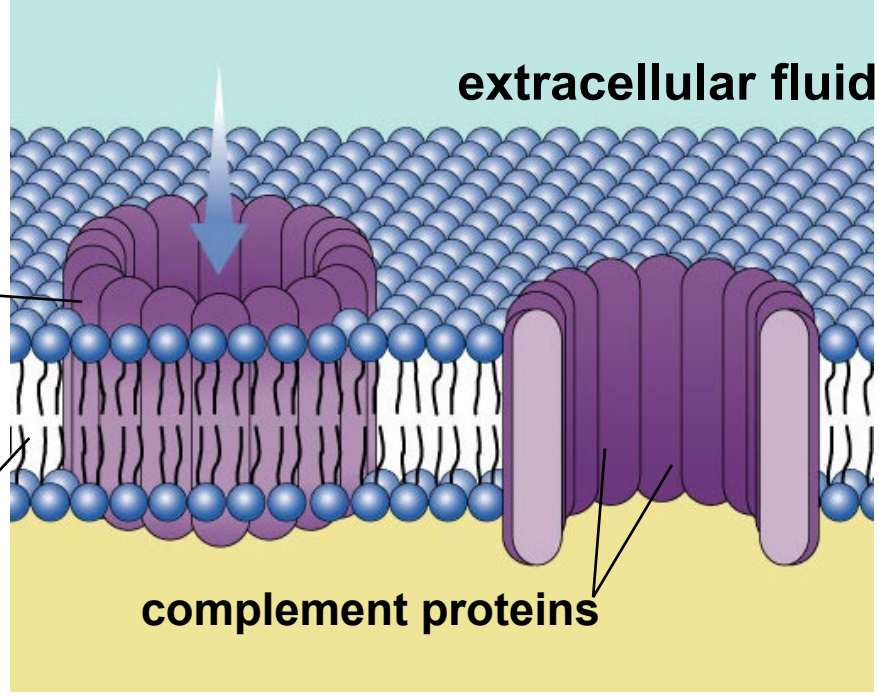
AP B

perforin punctures cell membrane



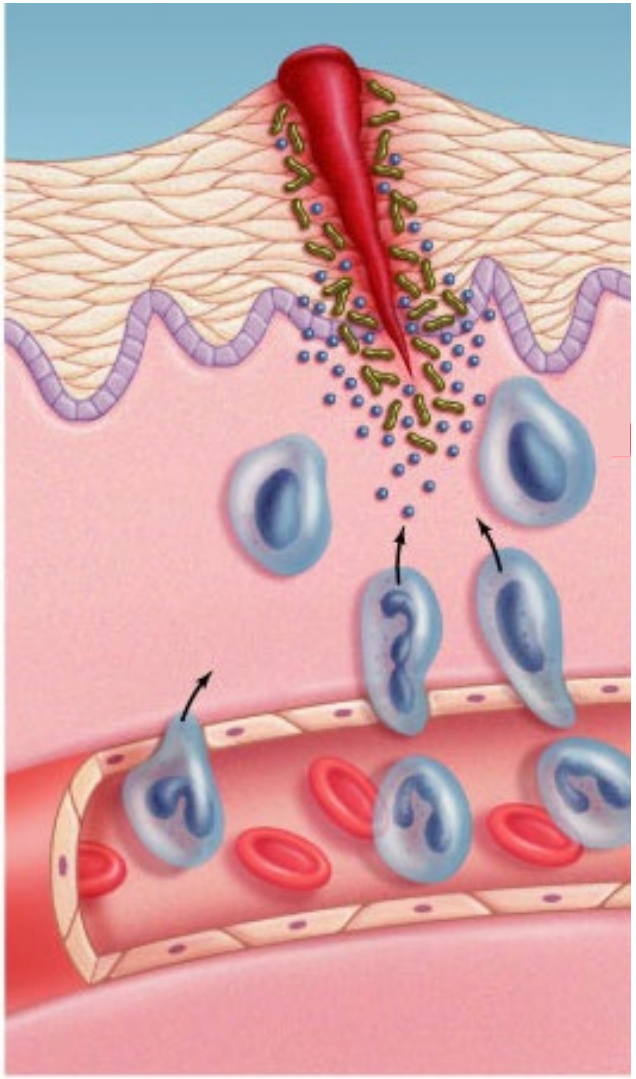
Anti-microbial proteins

- Complement system
  - ~20 proteins circulating in blood plasma
  - attack bacterial & fungal cells
    - form a membrane attack complex
    - perforate target cell
    - apoptosis
      - cell lysis



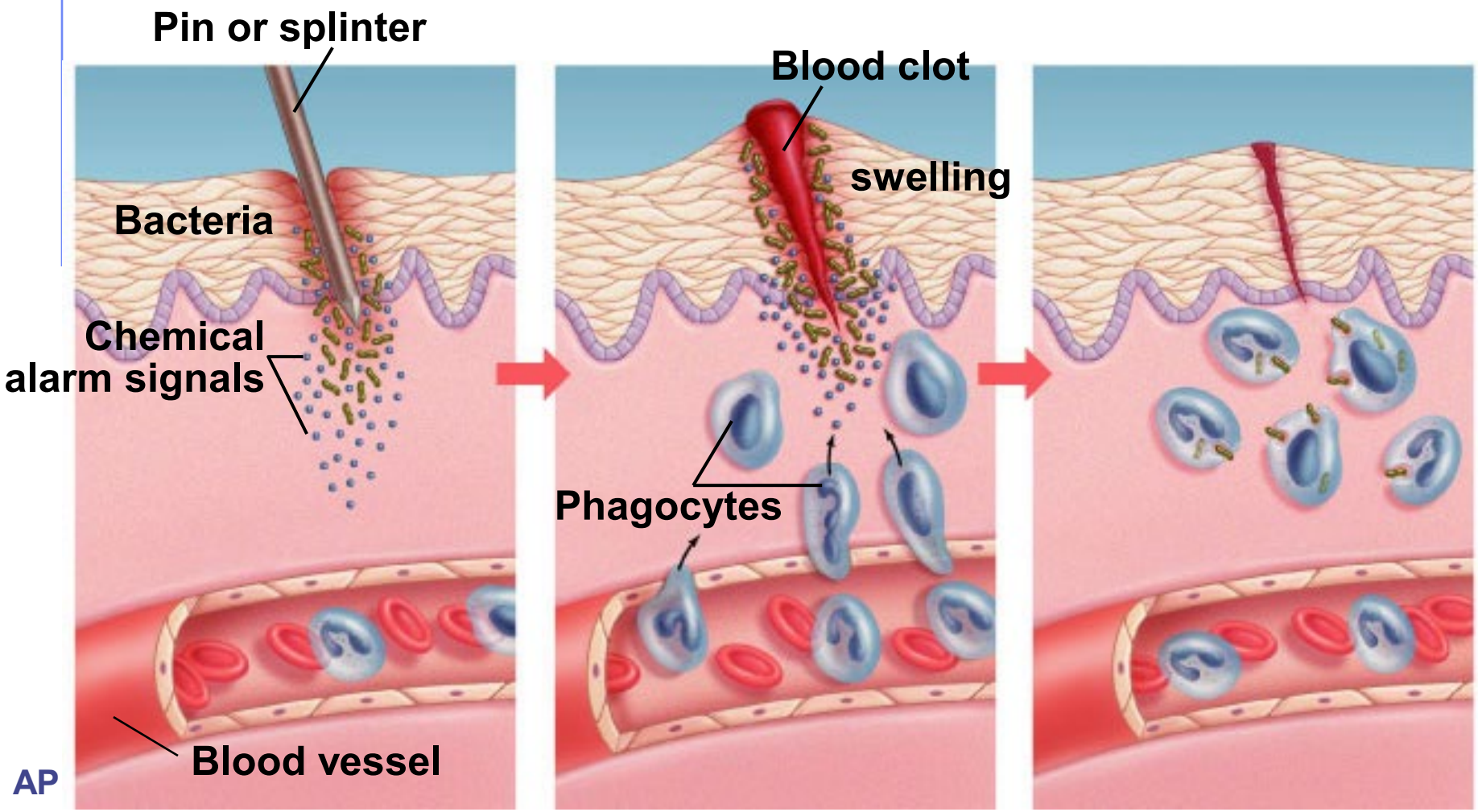
Inflammatory response

- Damage to tissue triggers local non-specific inflammatory response
  - release histamines & prostaglandins
  - capillaries dilate, more permeable (leaky)
    - increase blood supply
    - delivers WBC, RBC, platelets, clotting factors
    - fight pathogens
    - clot formation
    - accounts for swelling, redness & heat of inflammation & infection



Inflammatory response

- Reaction to tissue damage



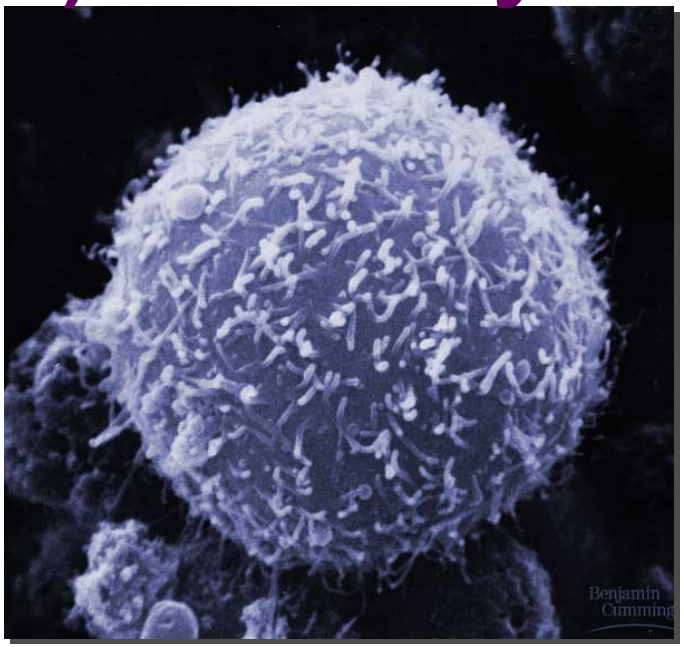
AP

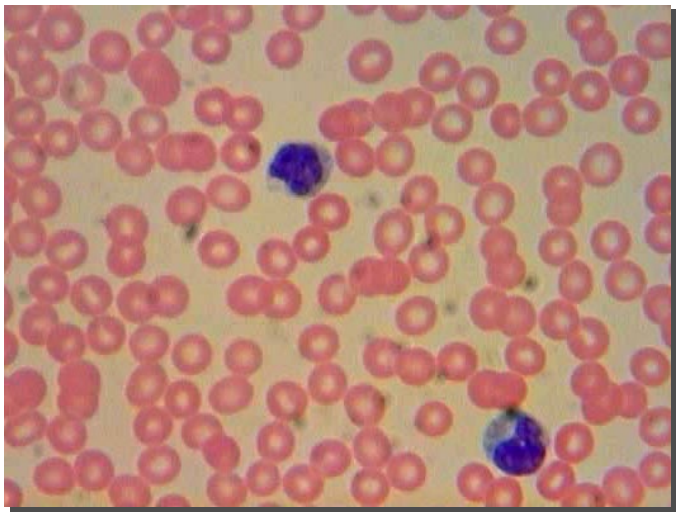
Fever

- When a local response is not enough
  - systemic response to infection
  - activated macrophages release interleukin-1
    - triggers hypothalamus in brain to readjust body thermostat to raise body temperature
  - higher temperature helps defense
    - inhibits bacterial growth
    - stimulates phagocytosis
    - speeds up repair of tissues
    - causes liver & spleen to store iron, reducing blood iron levels
      - bacteria need large amounts of iron to grow

3rd line: Acquired (active) Immunity

- Specific defense
  - lymphocytes
    - B lymphocytes (B cells)
    - T lymphocytes (T cells)
  - antibodies
    - immunoglobulins
- Responds to…
  - antigens
    - specific pathogens
    - specific toxins
    - abnormal body cells (cancer)

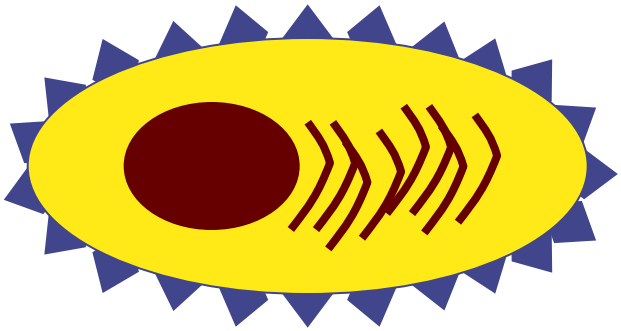




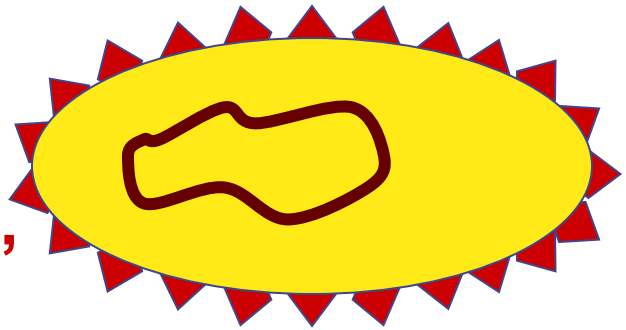
How are invaders recognized: antigens

- **Antigens**
  - proteins that serve as cellular name tags
    - **foreign antigens** cause response from WBCs
      - viruses, bacteria, protozoa, parasitic worms, fungi, toxins
      - non-pathogens: pollen & transplanted tissue
- **B cells & T cells respond to different antigens**
  - B cells recognize intact antigens
    - pathogens in blood & lymph
  - T cells recognize antigen fragments
    - pathogens which have already infected cells

"self"

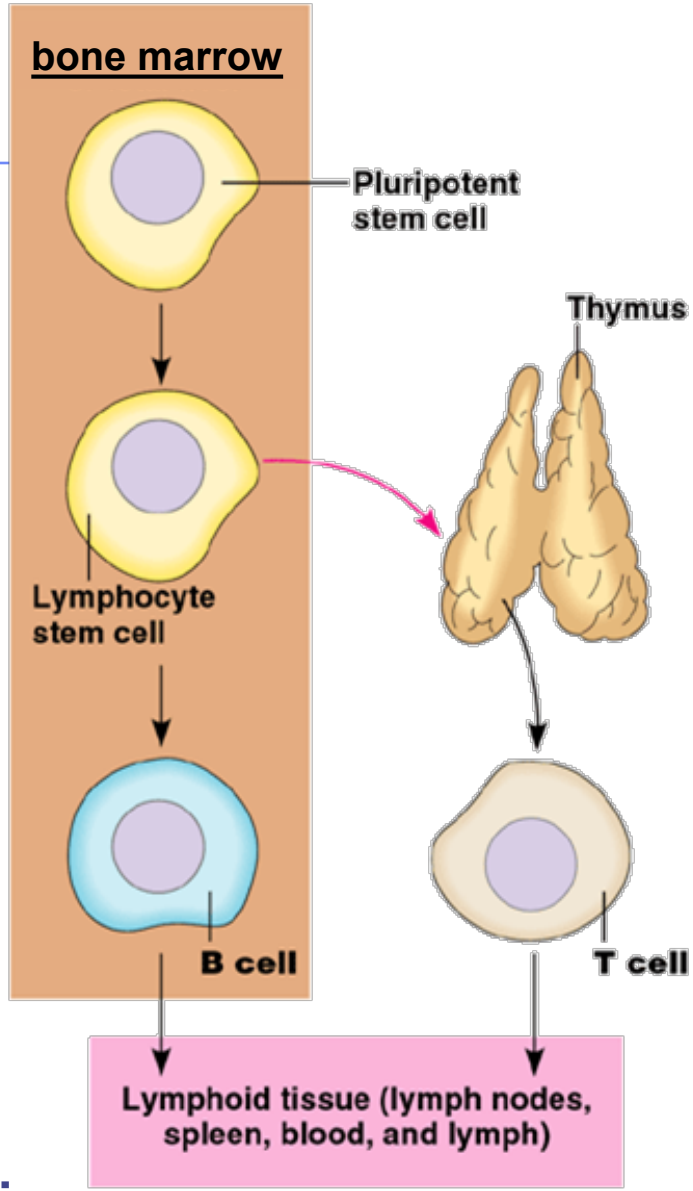


"foreign"



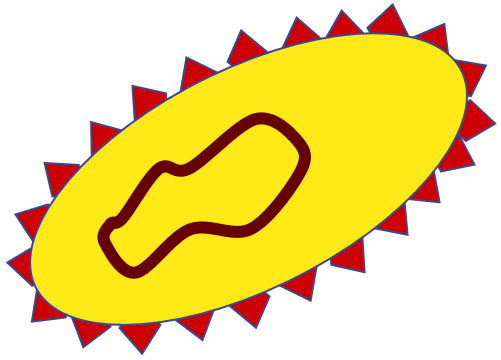
Lymphocytes

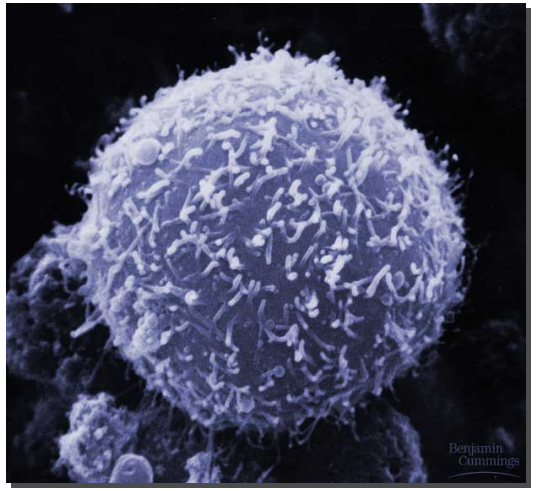
- **B cells**
  - mature in **bone marrow**
  - **humoral** response system
    - "humors" = body fluids
    - produce antibodies
- **T cells**
  - mature in **thymus**
  - **cellular** response system
- **Learn to distinguish "self" from "non-self" antigens during maturation**
  - if they react to "self" antigens, they are destroyed during maturation



B cells

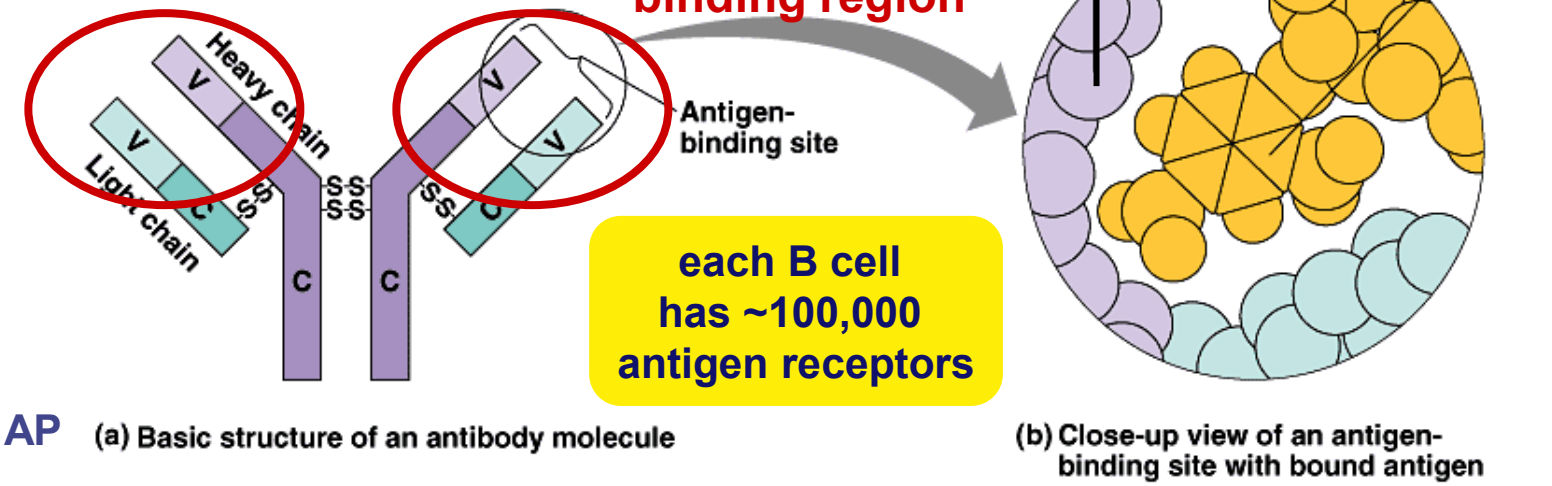
- Humoral response = "in fluid"
  - defense against attackers circulating freely in blood & lymph
- Specific response
  - produces antibodies against specific antigen
    - tagging protein = immunogloblin
      - millions of different B cells, each produces different antibodies, each recognizes a different antigen
  - types of B cells
    - plasma cells
      - immediate production of antibodies
      - rapid response, short term release
    - memory cells
      - long term immunity



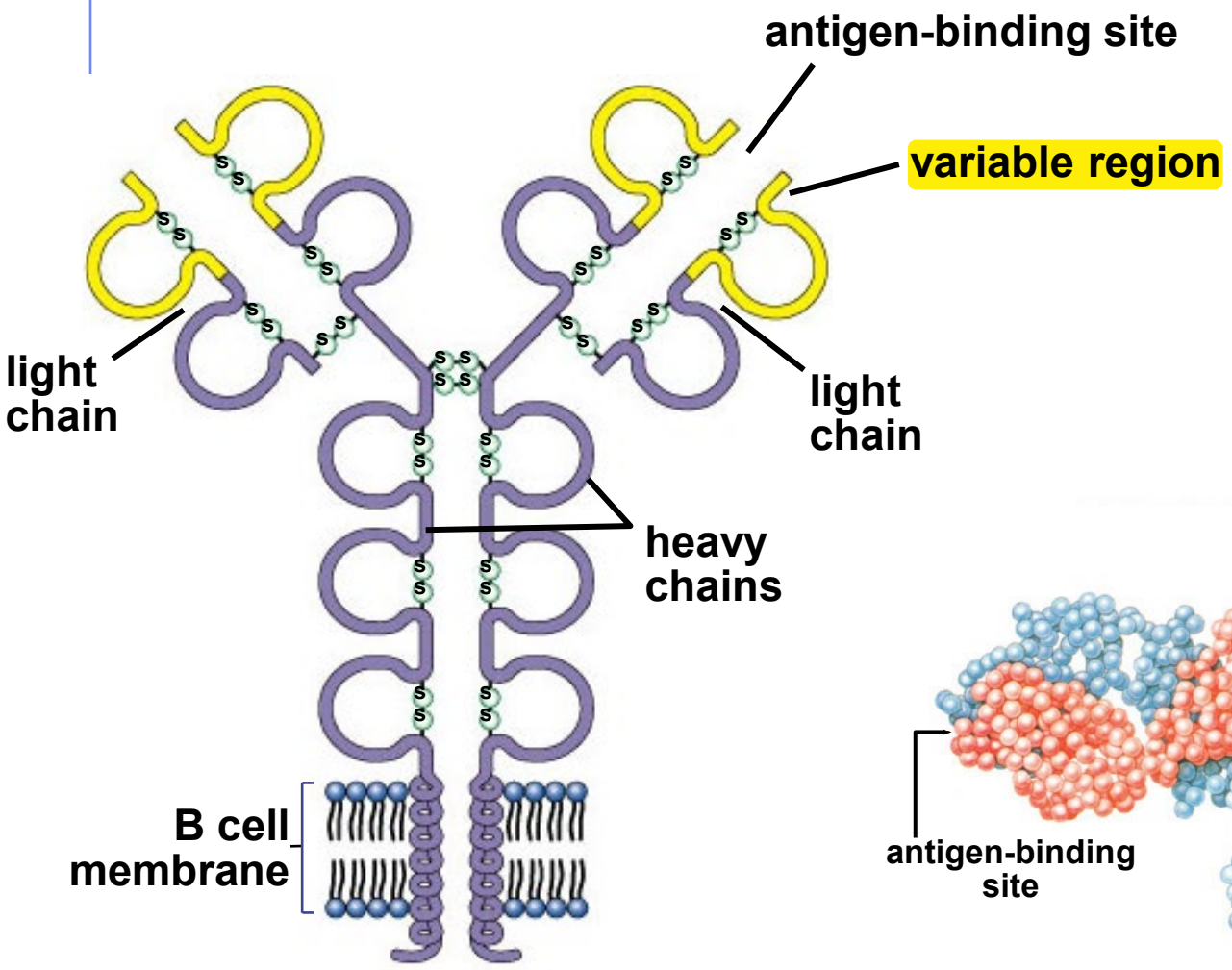


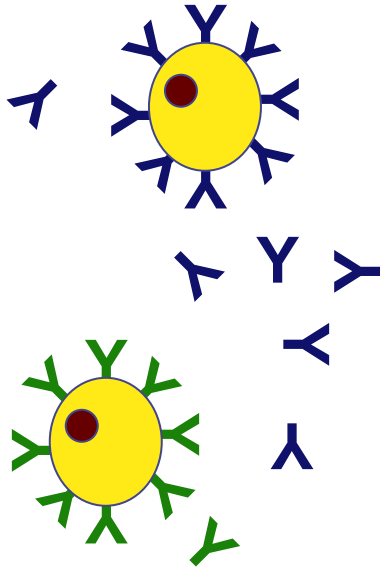
Antibodies

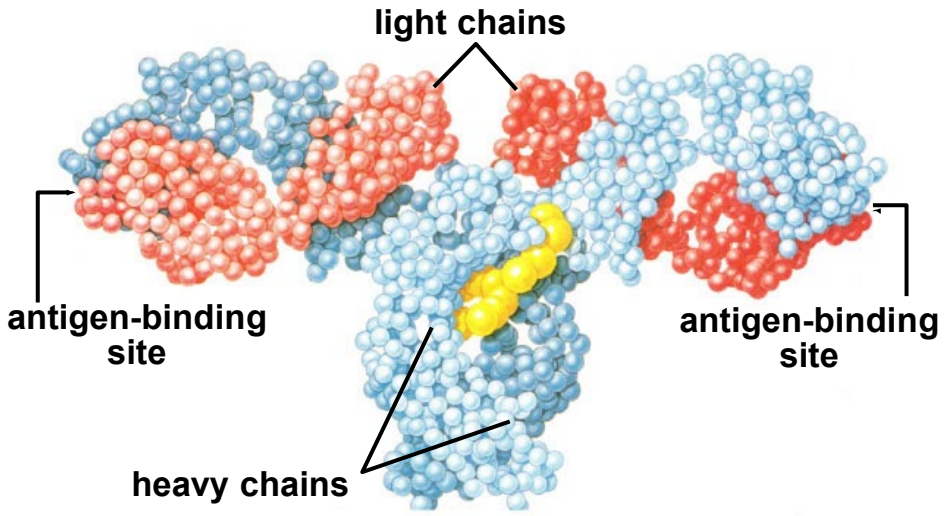
- **Proteins that bind to a specific antigen**
  - multi-chain proteins produced by B cells
  - antibodies match molecular shape of antigens
  - immune system has antibodies to respond to millions of foreign antigens
  - tagging system
    - "this is foreign!"



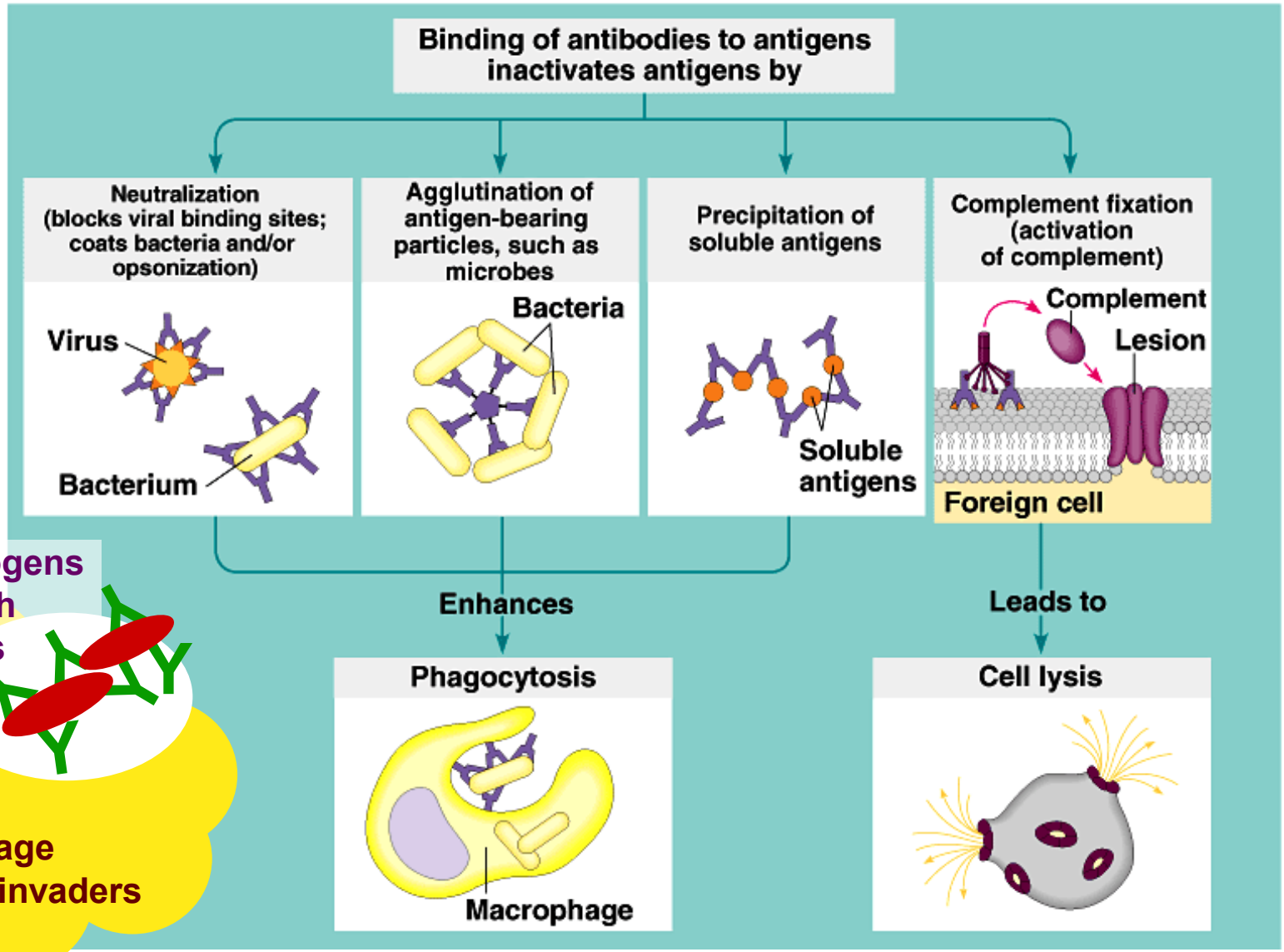
Structure of antibodies







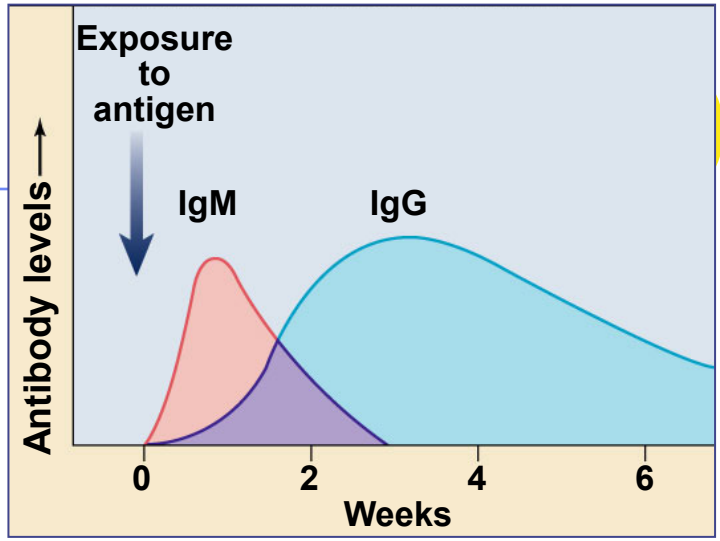
How antibodies work



invading pathogens tagged with antibodies

macrophage eating tagged invaders

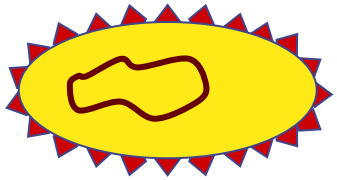
Classes of antibodies



- Immunoglobulins
  - IgM
    - 1st immune response
    - activate complement proteins
  - IgG
    - 2nd response, major antibody circulating in plasma
    - promote phagocytosis by macrophages
  - IgA
    - in external secretions, sweat & mother's milk
  - IgE
    - promote release of histamine & lots of bodily fluids
    - evolved as reaction to parasites
    - triggers allergic reaction
  - IgD
    - receptors of B cells???

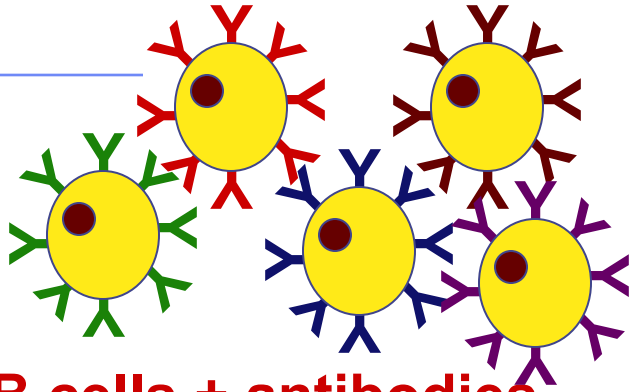
10 to 17 days for full response

B cell immune response



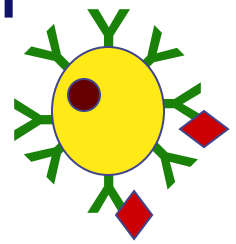
invader
(foreign antigen)

tested by
B cells
(in blood & lymph)

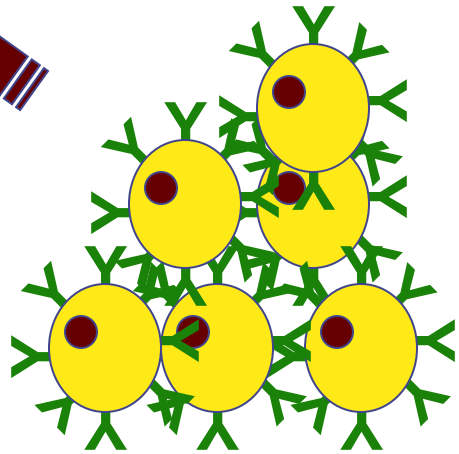


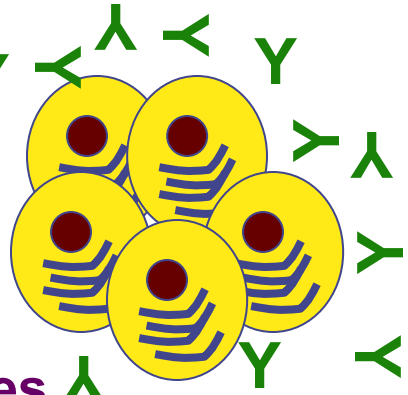
B cells + antibodies

recognition

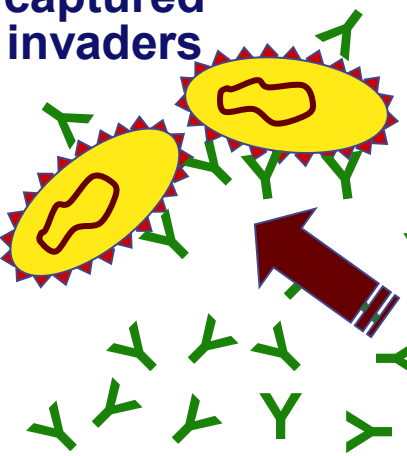


clone
1000s of clone cells

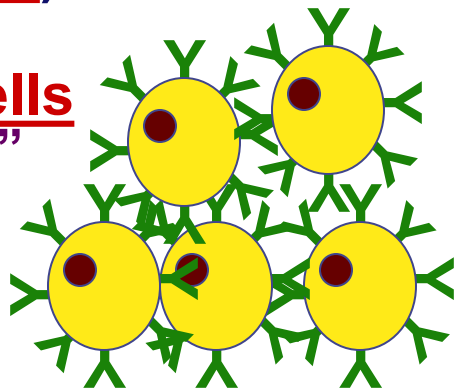




plasma cells
release antibodies



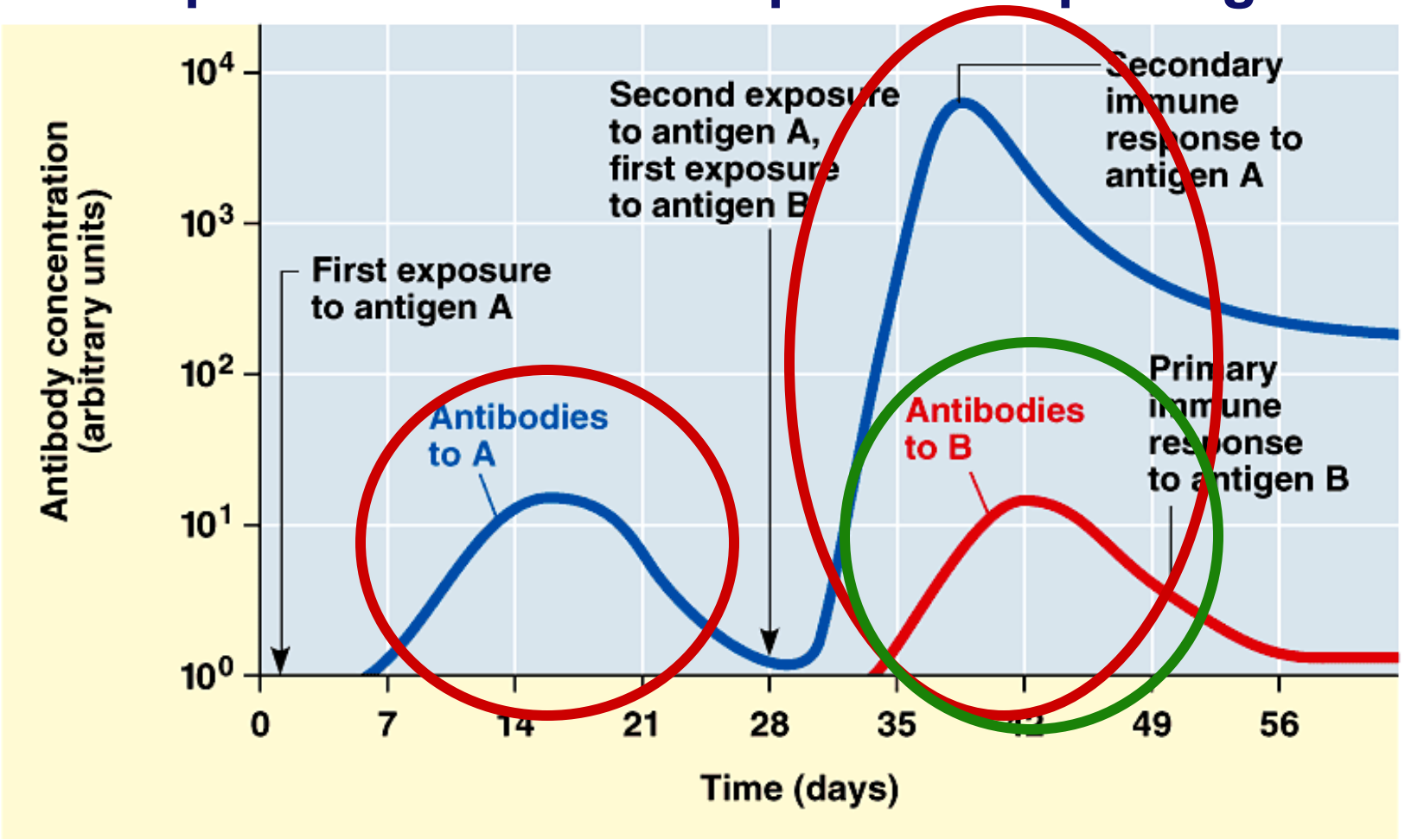
captured
invaders



memory cells
"reserves"

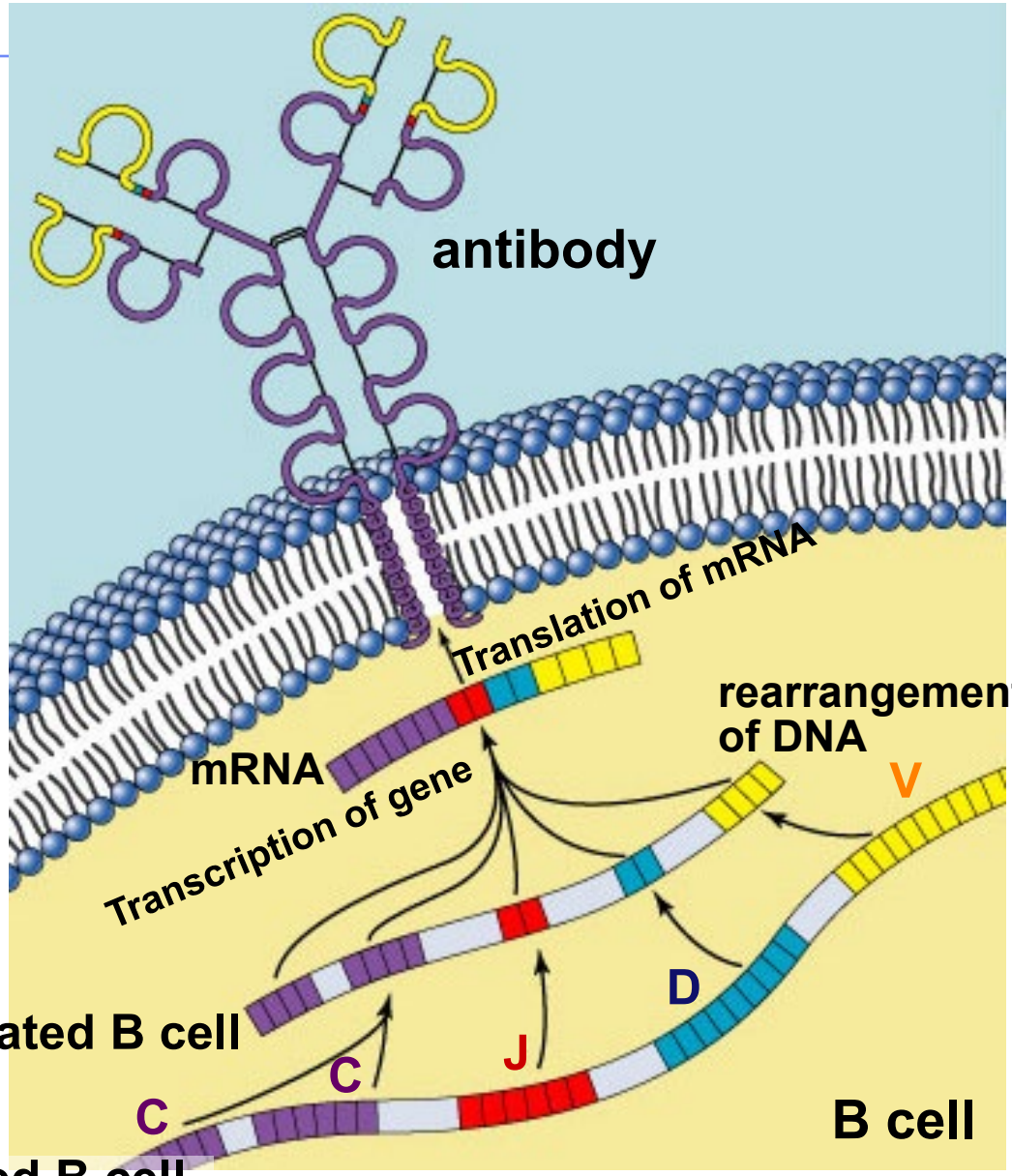
1° vs 2° response to disease

- Memory B cells allow a rapid, amplified response with future exposure to pathogen



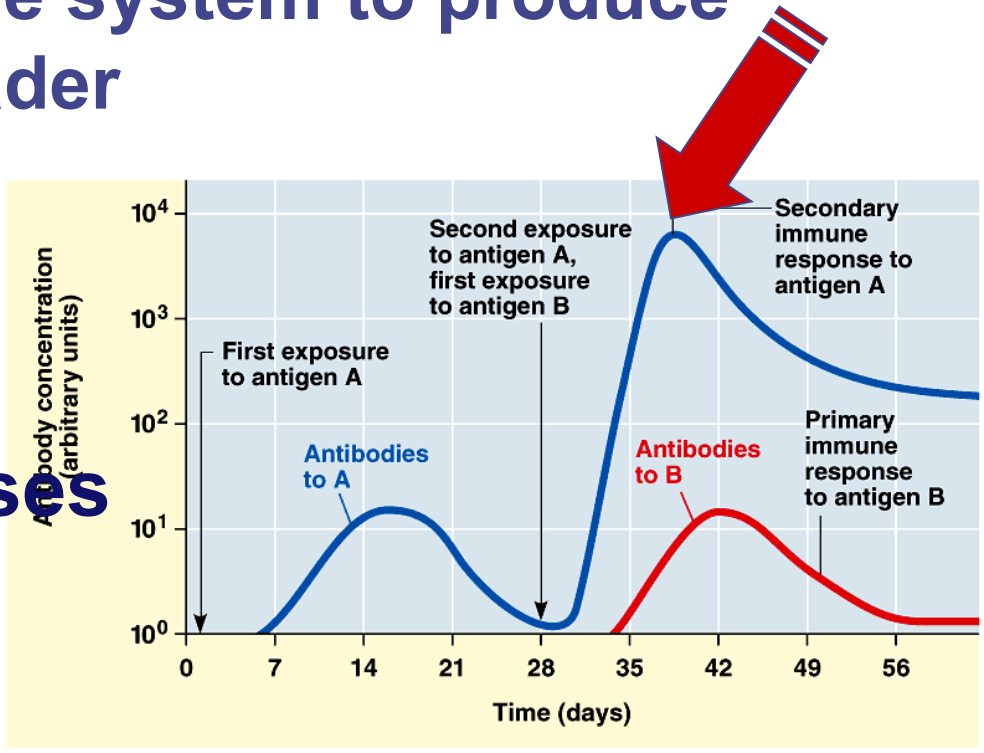
How do vertebrates produce millions of antibody proteins, if they only have a few hundred genes coding for those proteins?

By DNA rearrangement & somatic mutation vertebrates can produce millions of B & T cells



Vaccinations

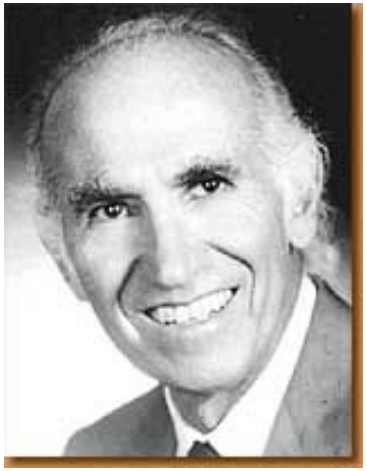
- Immune system exposed to harmless version of pathogen
  - triggers **active immunity**
  - stimulates immune system to produce antibodies to invader
  - rapid response if future exposure
- Most successful against viral diseases



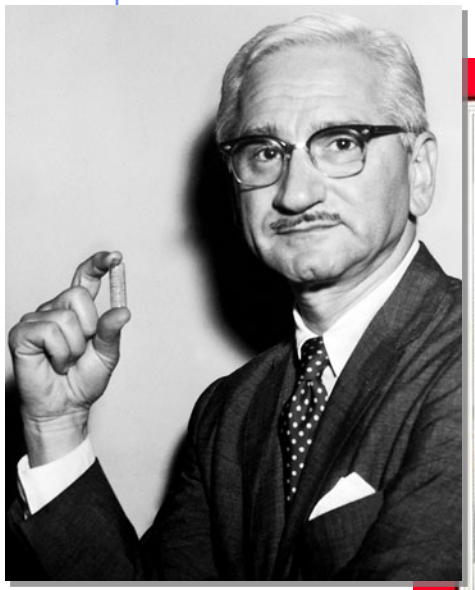
1914 – 1995

Jonas Salk

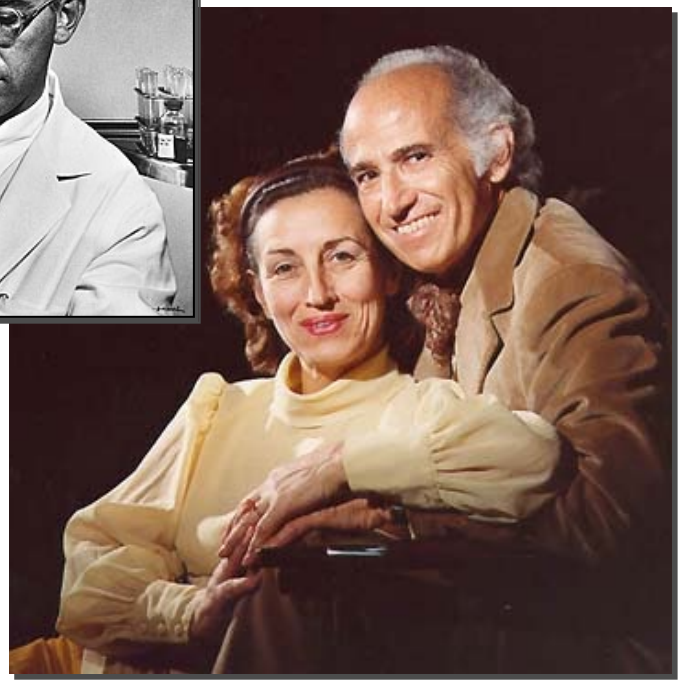
April 12, 1955



- Developed first vaccine
  - against polio
    - attacks motor neurons



Albert Sabin
1962
oral vaccine



Polio epidemics

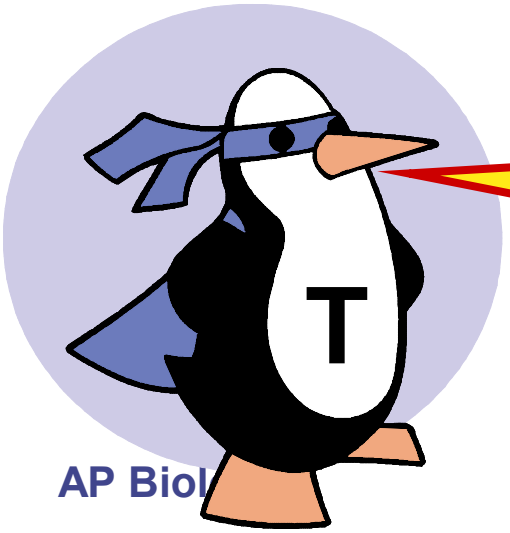
1994:
Americas polio free

Passive immunity

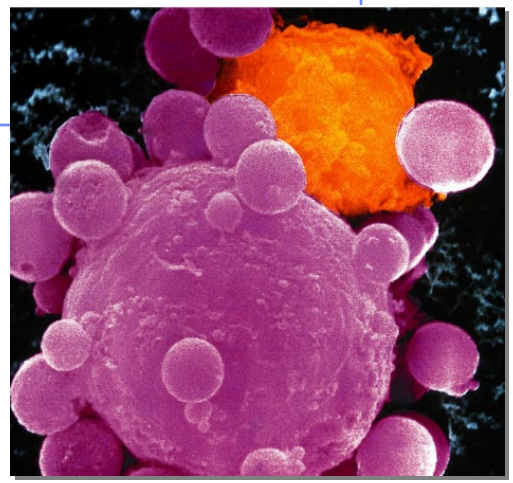
- Obtaining antibodies from another individual
- Maternal immunity
  - antibodies pass from mother to baby across placenta or in mother's milk
  - critical role of breastfeeding in infant health
    - mother is creating antibodies against pathogens baby is being exposed to
- Injection
  - injection of antibodies
  - short-term immunity

What if the attacker gets past the B cells in the blood & actually infects some of your cells?

You need trained assassins to kill off these infected cells!

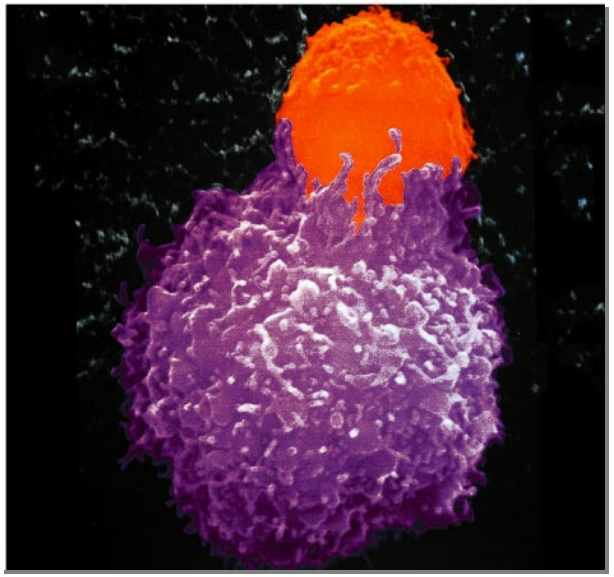


Attack of the Killer T cells!



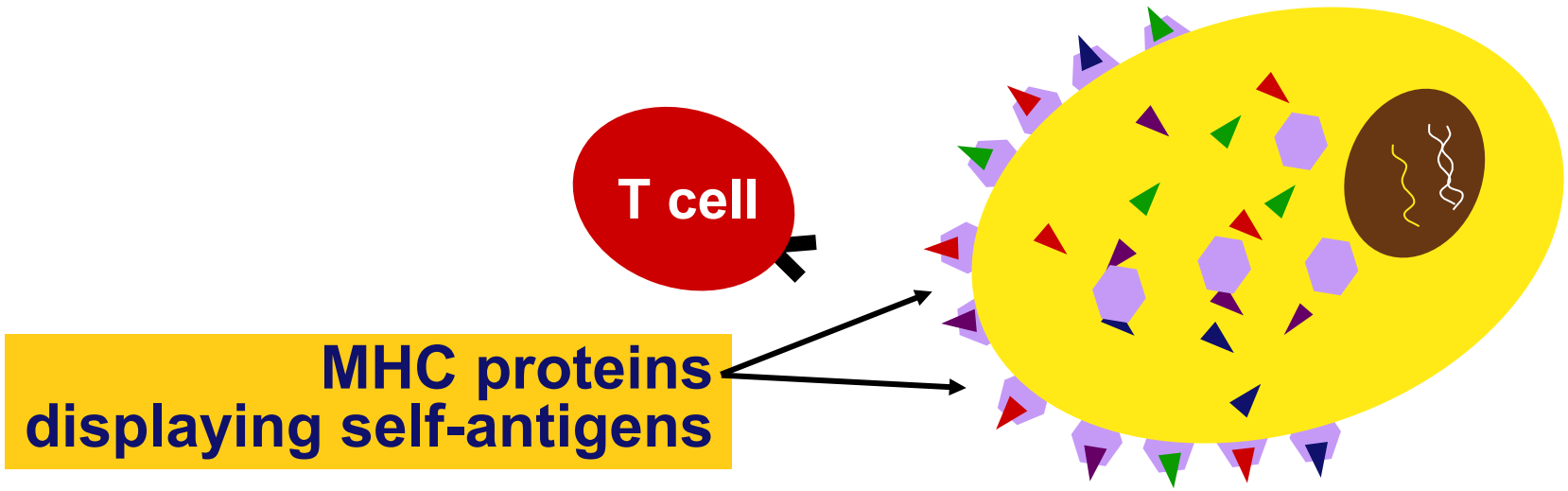
T cells

- **Cell-mediated response**
  - immune response to infected cells
    - pathogens inside cells
    - viruses, bacteria & parasites within cells
  - defense against "non-self" cells
    - cancer & transplant cells
- Types of T cells
  - helper T cells
    - alerts immune system
  - killer (cytotoxic) T cells
    - attack infected body cells



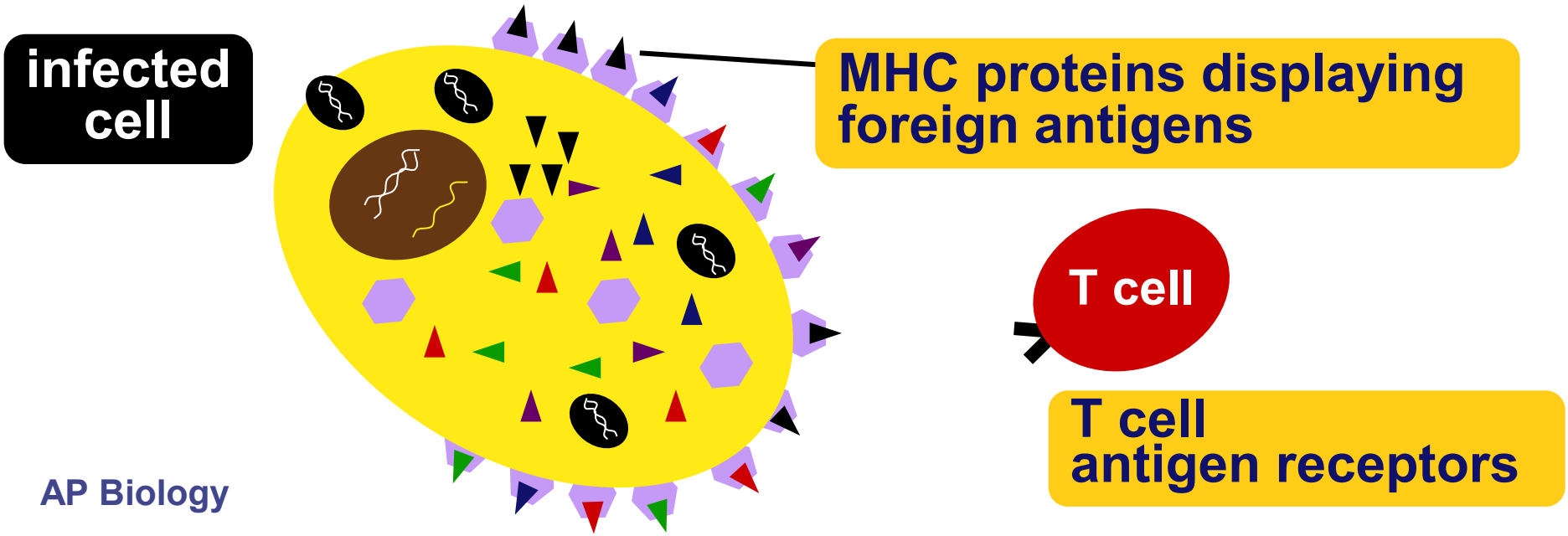
How are cells tagged with antigens

- **Glycoproteins** on surface of cells have unique "fingerprint"
  - major histocompatibility (MHC) proteins
- MHC proteins constantly carry bits of cellular material to the cell surface
  - "snapshot" of what is going on inside cell

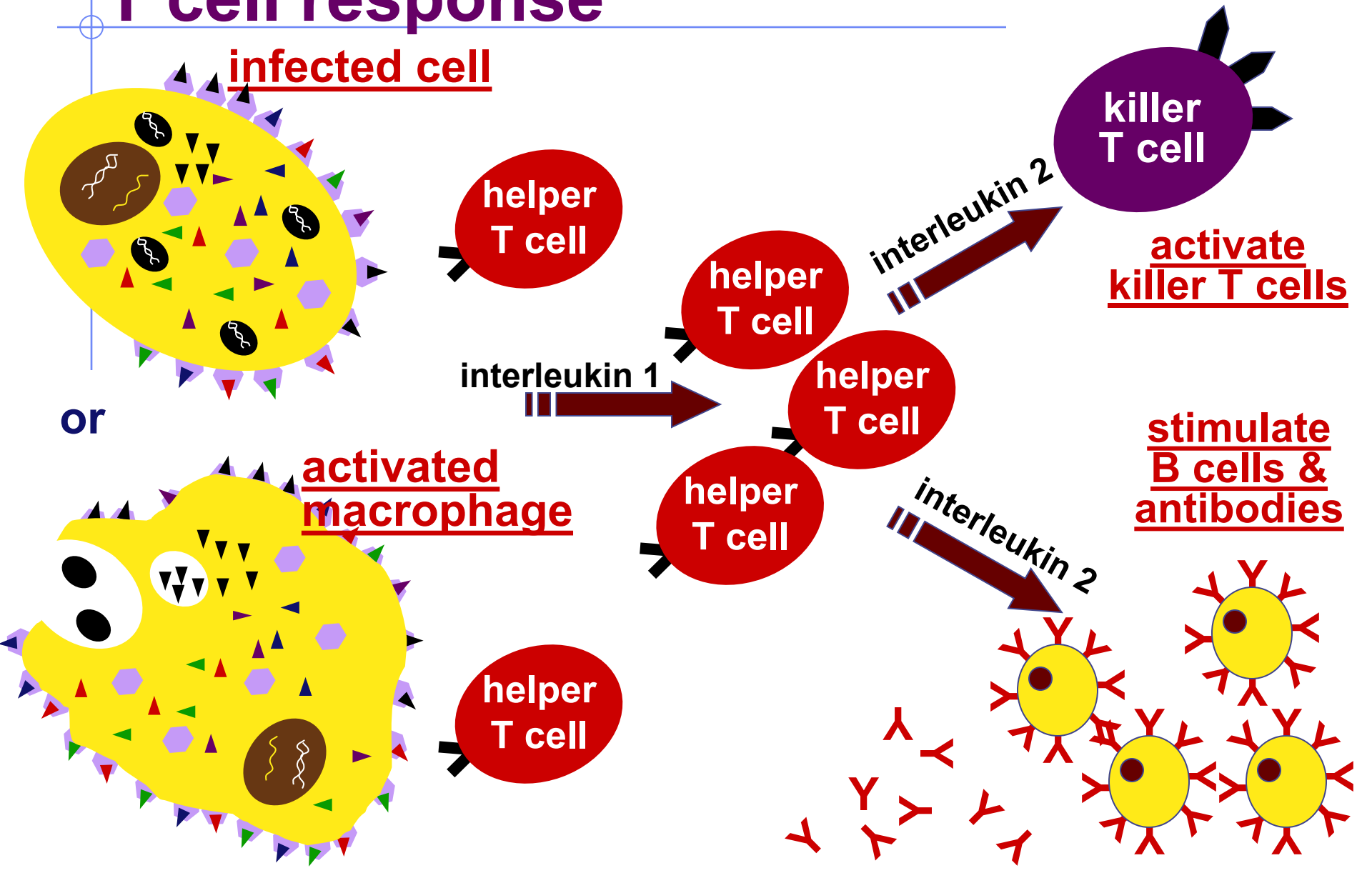


How do T cells know a cell is infected

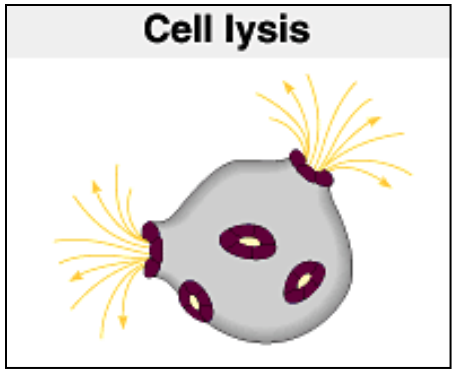
- Infected cells digest pathogens & MHC proteins bind & carry pieces to cell surface
  - "antigen presenting cells" (APC)
  - alerts helper T cells



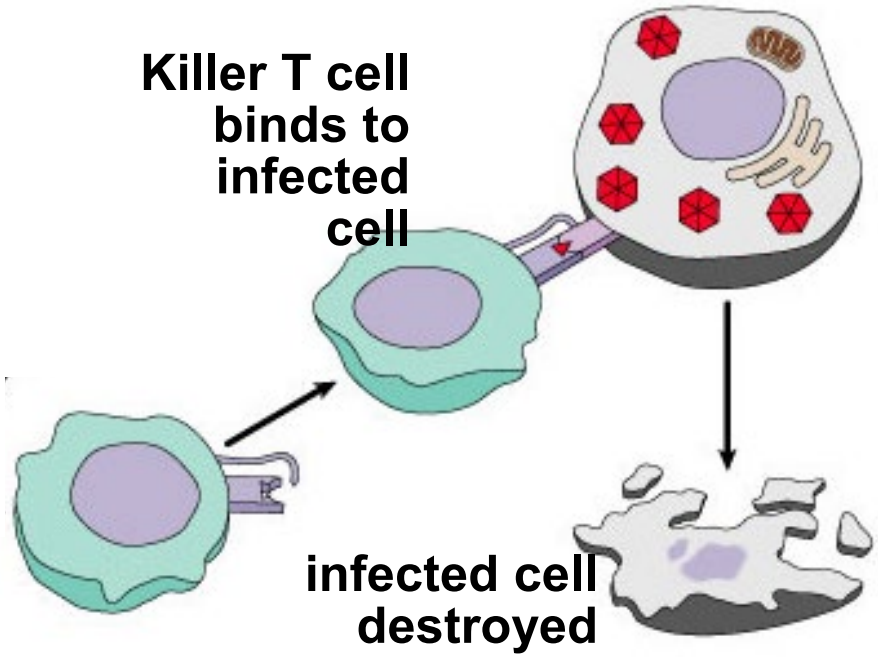
T cell response

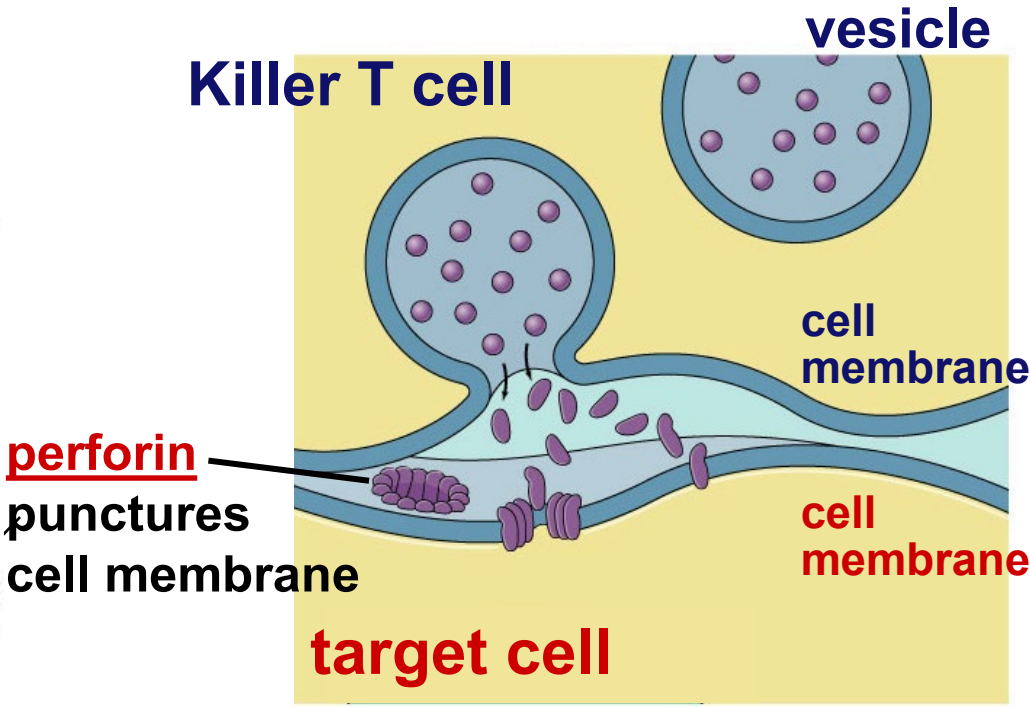


Attack of the Killer T cells

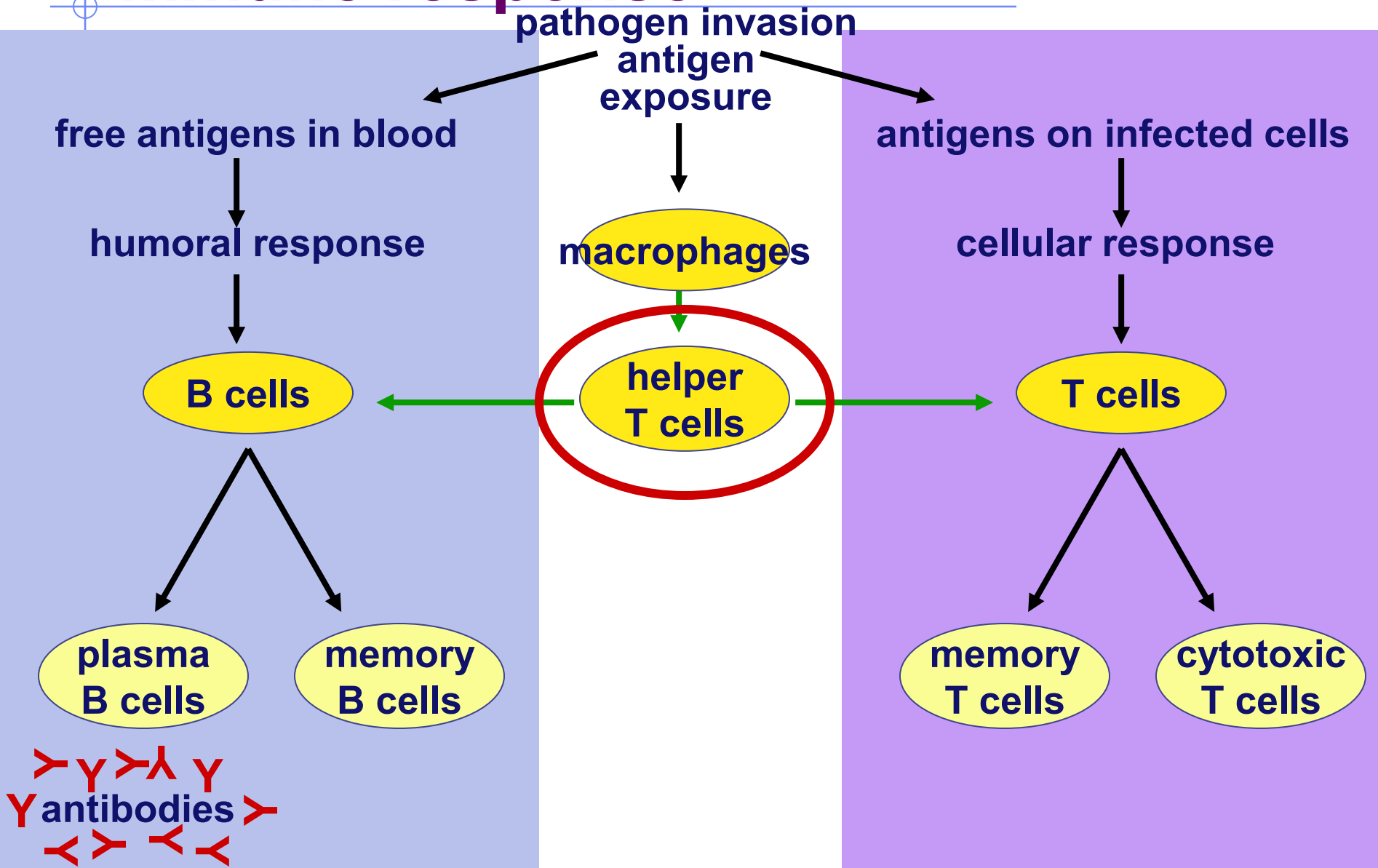


- Destroys infected body cells
  - binds to target cell
  - secretes perforin protein
    - punctures cell membrane of infected cell



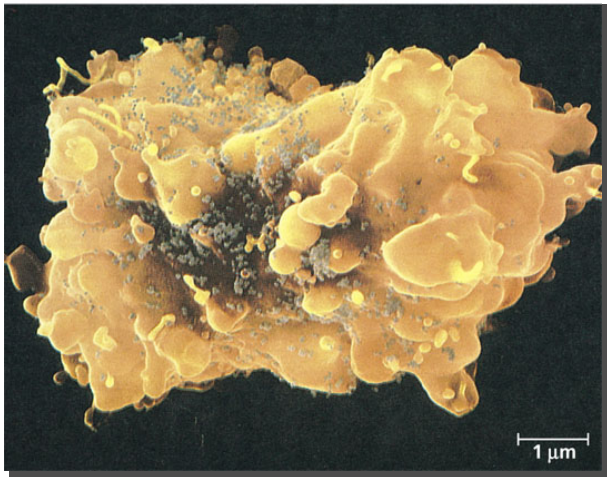


Immune response



HIV & AIDS

- Human Immunodeficiency Virus
  - virus infects helper T cells
  - helper T cells don't activate rest of immune system: T cells & B cells
    - also destroy T cells
- Acquired ImmunoDeficiency Syndrome
  - infections by opportunistic diseases
  - death usually from other infections
    - pneumonia, cancer



Immune system malfunctions

- **Auto-immune diseases**
  - immune system attacks own molecules & cells
    - lupus
      - antibodies against many molecules released by normal breakdown of cells
    - rheumatoid arthritis
      - antibodies causing damage to cartilage & bone
    - diabetes
      - beta-islet cells of pancreas attacked & destroyed
    - multiple sclerosis
      - T cells attack myelin sheath of brain & spinal cord nerves
- **Allergies**
  - over-reaction to environmental antigens
    - allergens = proteins on pollen, dust mites, in animal saliva
    - stimulates release of histamine

Key attributes of immune system

- 4 attributes that characterize the immune system as a whole
  - specificity
    - antigen-antibody specificity
  - diversity
    - react to millions of antigens
  - memory
    - rapid 2° response
  - ability to distinguish self vs. non-self
    - maturation & training process to reduce auto-immune disease