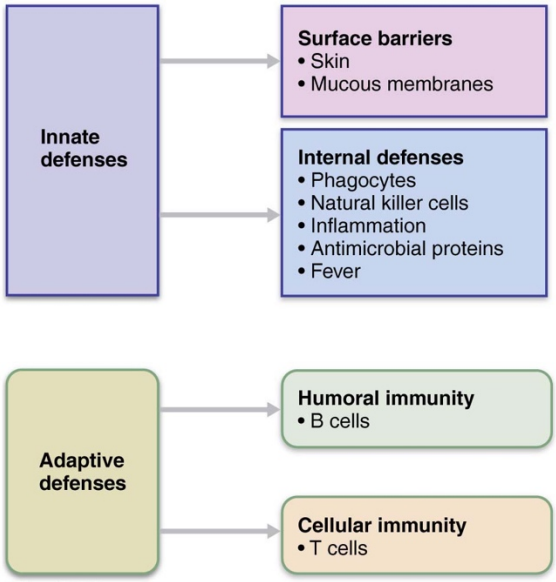
Immune System

Immune System: Intro

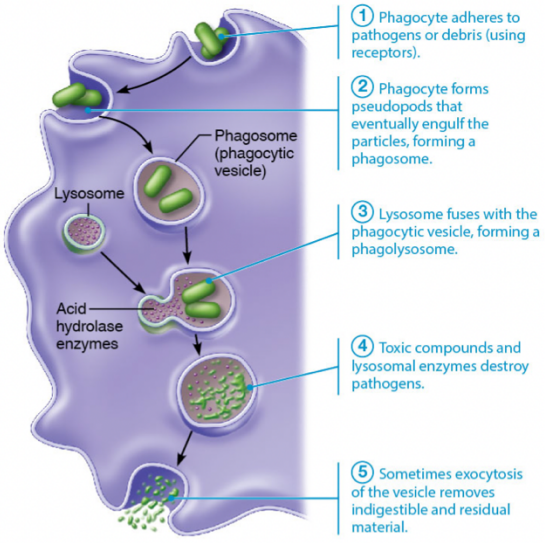
- Divided into 2 branches
  (1) Innate: makes sure nothing foreign comes in
  (2) Adaptive: specifically targets antigens to destroy them



- Nonspecific vs specific immunity
  - Nonspecific (innate)
    - Known as first line of defense
    - Provides physical barriers through skin and mucous membrane
      - If barrier is breached, there are internal defenses like phagocytes that stop foreign things that breached barrier
  - Specific (adaptive/acquired)
    - Known as third line of defense designed to target particular invading things
    - Humoral vs cellular
      - Humoral: B cells secrete antibodies to find target
      - Cellular: T cells attacks antigens

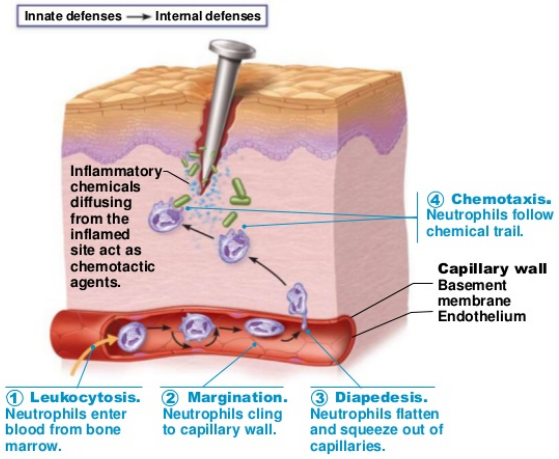
Phagocytosis and Natural T cells

- Phagocytosis: eating pathogens
  - Some pathogens are resistant to digestion and live inside phagocyte (ex: tuberculosis)
  - Performed by neutrophils and macrophages
  - Helper T cells: type of T cells that release lethal respiratory burst (superoxide or free radical killing) to kill pathogen



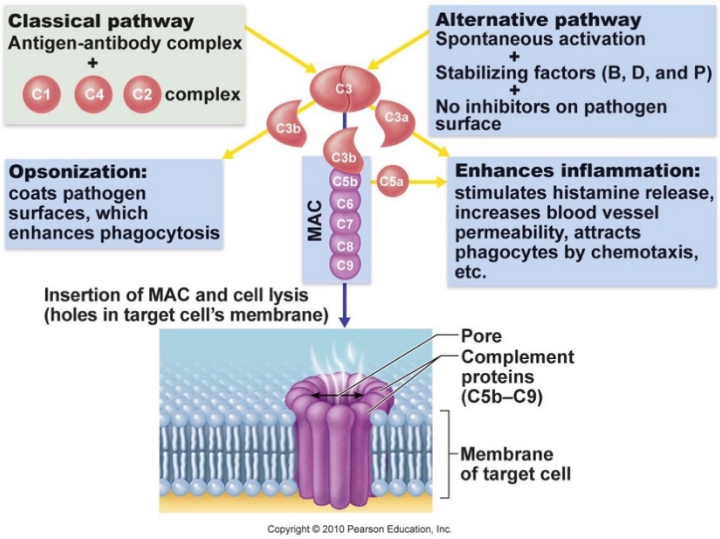
- Natural killer cells (NK cells)
  - Do not phagocytize targets but kill them via apoptosis (programmed cell death)
    - NK basically forces mutated/infected cells and foreign ells to commit suicide
  - Secrete chemicals to induce and enhance inflammatory response

Inflammation
- Beneficial effects:
  - Prevents spread of damaging agents
  - Disposes of debris and pathogens
  - Alerts adaptive immunity in case we need it (draws WBC)
  - Sets stage for repair when we have a breach to prevent infection
- Process:
  (1) Inflammatory chemical is released: histamine, kinins, prostaglandins, and complement
  (2) Leads to vasodilation and increased vascular permeability: hyperemia (increased blood influx to tissues) and exudate (cells and blood leaking out)
    - Vasodilation helps bringing essential material like WBC into area of damage
  (3) Phagocytes are mobilized via leukocytosis, margination, diapedesis, and chemotaxis



- Signs of inflammation
  - Heat
    - Due to local increase of blood flow
  - Redness
    - Due to local increase of blood flow
  - Pain
    - Due to release of inflammatory chemicals like histamine
    - Helps you to immobilize the damaged area to keep lymph stable until it fixes damage
  - Swelling
    - Due to increased capillary permeability which enables more fluid to accumulate in the area

Complement
- Definition: plasma protein activated during inflammation
- Functions: enhances effectiveness of innate and adaptive immunity
- Process:
  (1) Proteins circulate in blood as their inactive form
  (2) They get activated in 3 pathways: classical, lectin, or spontaneous
    - Classical pathway: antibodies tags pathogen or cell by coating target L
    - Lectin pathway: lectin binds to specific sugars on targets' surfaces
    - Alternative/spontaneous pathway: attacks cells that don't have molecules to identify themselves as part of the body's own cells
  (3) All 3 pathways converge at C3 (activator) to start final activation of complement

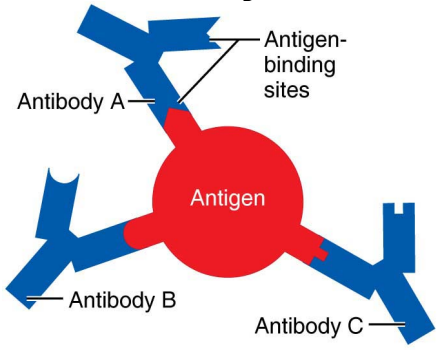


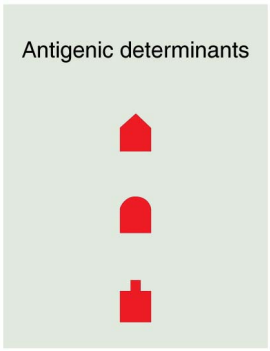
- C3 divides into 2 active killing and 1 indirect killing mechanism
  - C3a (opsonization): pathogen is coated with substances that attract macrophages to eat the pathogen
  - C3b: enhances inflammation by stimulating histamine release, increasing blood vessels permeability, and attracting phagocytes

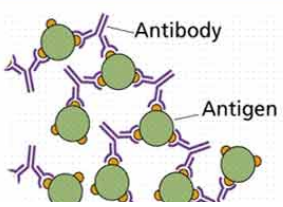
(4) Kills pathogen or cell 3 ways: release of inflammatory chemicals, lysing, or direct killing

Adaptive Immunity

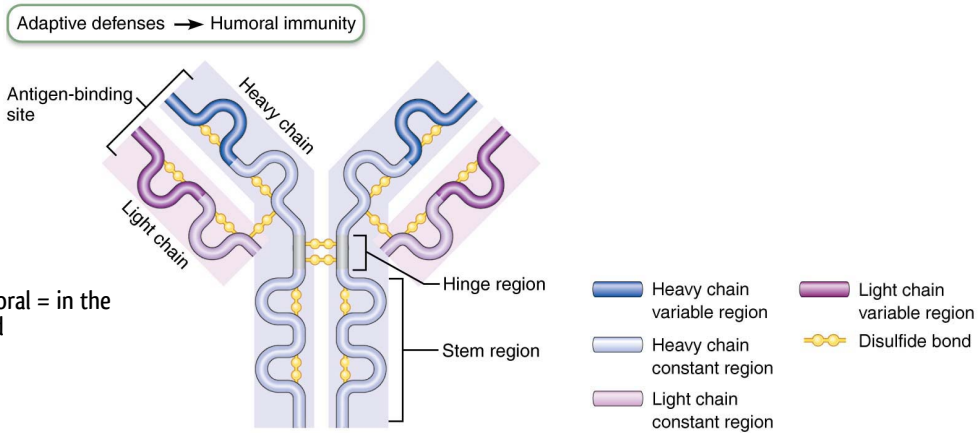
- Characteristics
  - Specific: recognizes and targets specific species of pathogens or foreign things
  - Systemic: not restricted to site of initial infection and goes all over body unlike innate immune which is local
  - Memory: recognizes and mounts stronger attack on previously encountered pathogens
    - Ex: you don't get chicken pox twice because your body remembers those pathogens and activate appropriate antigens that made during first infection
- Divided into cell-mediated and antibody-mediated immunity
  - Cell-mediated/cellular immunity: mediated by lymphocytes
    - Targets cellular pathogens (infected cells, cancer cells, and foreign grafts)
    - Either directly kill or release chemicals to increase inflammation or activate other lymphocytes or macrophages
  - Antibody-mediated/humoral immunity: mediated by antibodies
    - Antibodies circulate freely in blood until they find extracellular targets that they will tag for destruction or inactivate (no direct killing)
      - Phagocytes or complement will do the direct killing
- Antigens and antibodies
  - Antigens: substances that can mobilize adaptive defenses
    - Self-antigens: antigens on your own cells that do not trigger adaptive defense
      - Identified by MHC molecules so that our own cells are not attacked
    - Each antibody only attaches to one binding site –epitope-- of antigen
      - Thus, one antigen can be attacked by multiple antibodies if the antigen has many binding sites





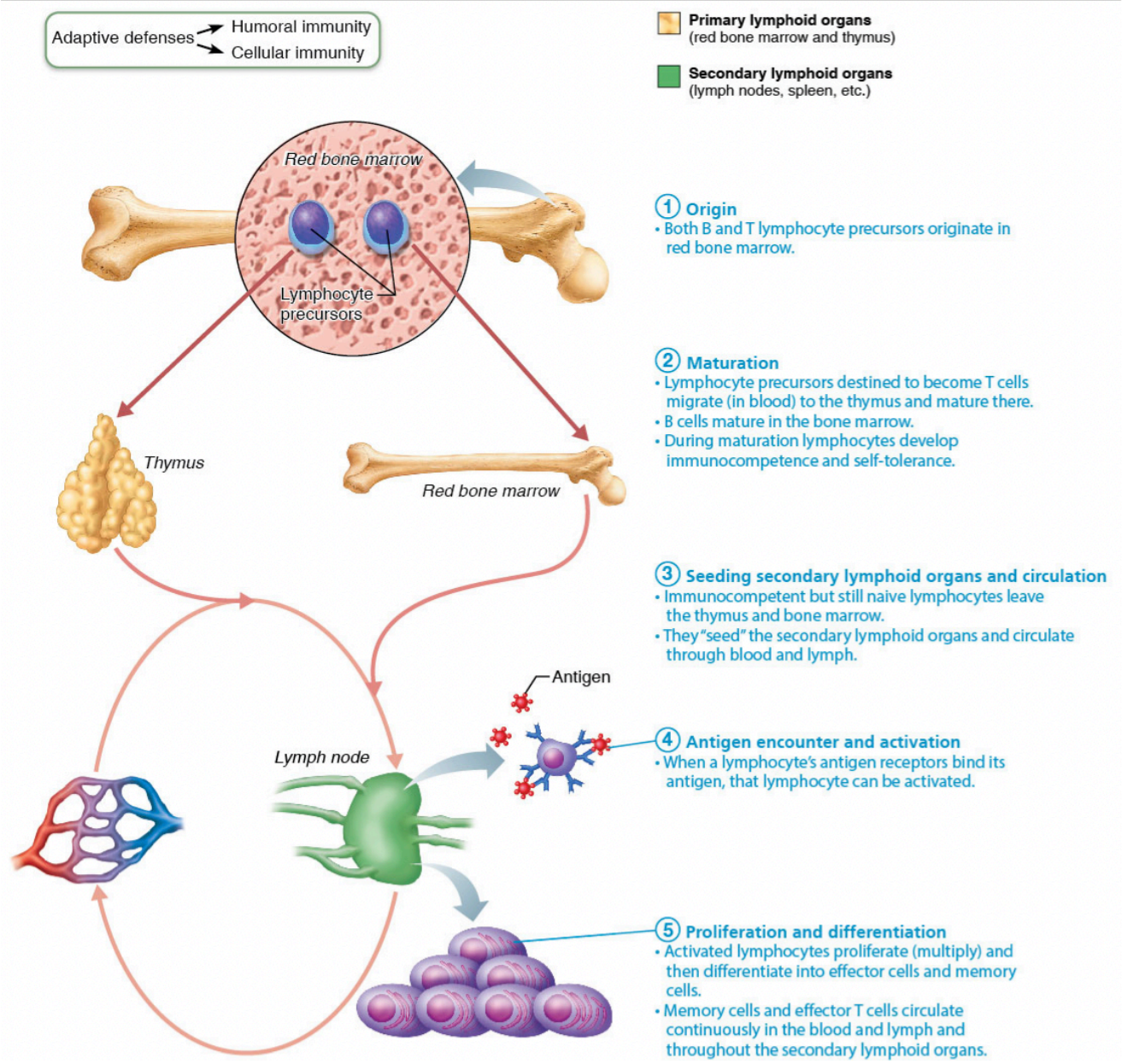


- Antibodies: protein secreted in response to an antigen by effector B cells (plasma cells)
  - Each B cells make one type of antibody that can only recognize a specific shape of an antigen
  - Made of 4 polypeptide chains
  - Also known as immunoglobins because they are made of gamma globulins of blood proteins
  - Function: specifically recognizes target antigen and binds on them



Humoral = in the blood

- Lymphocyte
  - Making process:
    (1) Origin: made in red bone marrow
    (2) Maturation: B cells are matured in bone marrow while T cells are matured in thymus
      - cells become immunocompetent and self-tolerant (being able to recognize your own cells and not attack them)
    (3) Seeding secondary lymphoid organs and circulation: at this point the cells are "naïve" (just matured) and goes to lymphoid organs and wait to be activated as well as circulate through blood
    (4) Antigen encounter activation: cells become activated once they see their specific antigens
      - You have a lot of lymphocytes that are not activated in your life time because they don't ever encounter their specific antigen
    (5) Proliferation and differentiation: activated cells differentiate into effector cells and memory cells

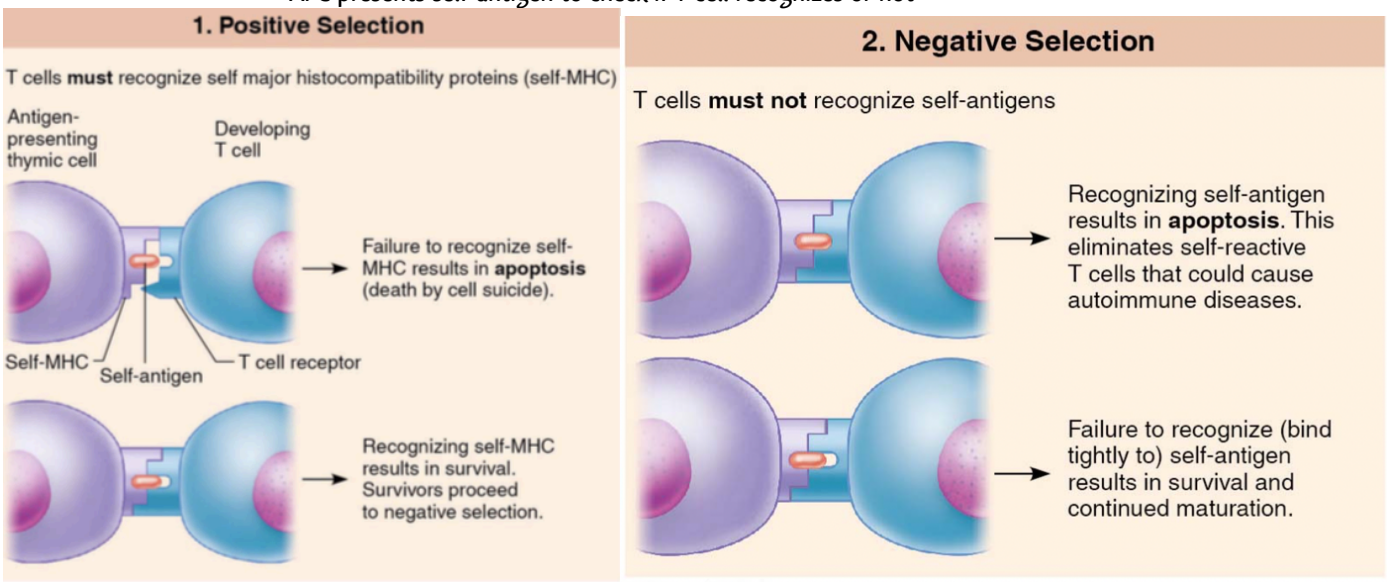


<u>T-cells maturation: 2 step process</u>

(1) Positive selection: T-cells must recognize self-major histocompatibility proteins (self-MHC)
  - T cells are presented an antigen via an APC
  - T cells have to have the ability to recognize what the MHC is holding out and if they can't, they are discarded
  - APC and MHC
    - APC: immune cells that circulate in blood until they encounter something foreign and bring it to naïve T cell in order to help the T cells to recognize it and mount an immune response

- MHC: antigen holders that present antigen to T cells

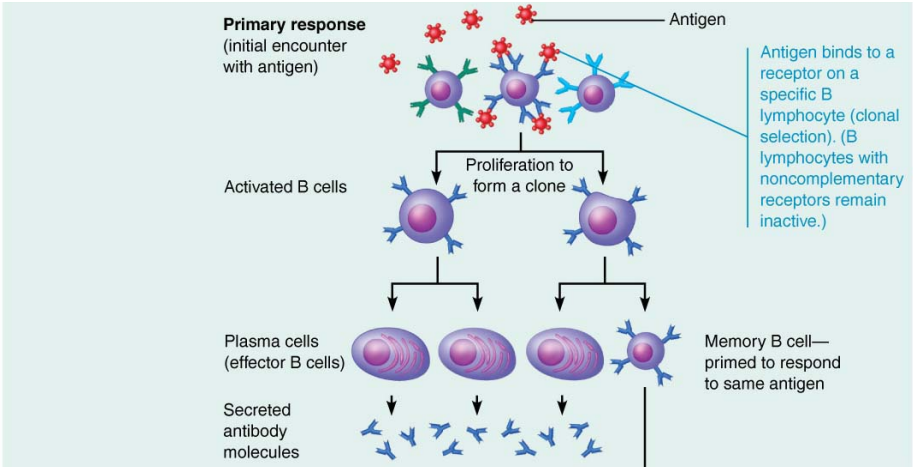
(2) Negative selection: T cells should not recognize self-antigens
- If a T cells recognize your own antigen, they are discarded because they can attack your own tissue
  - APC presents self-antigen to check if T cell recognizes or not

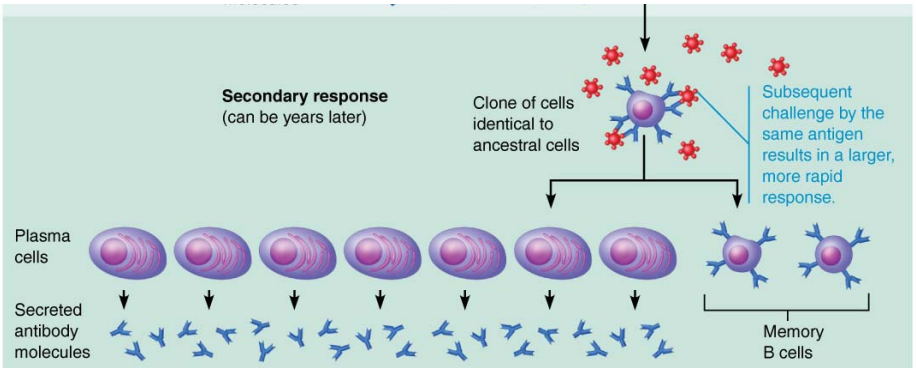


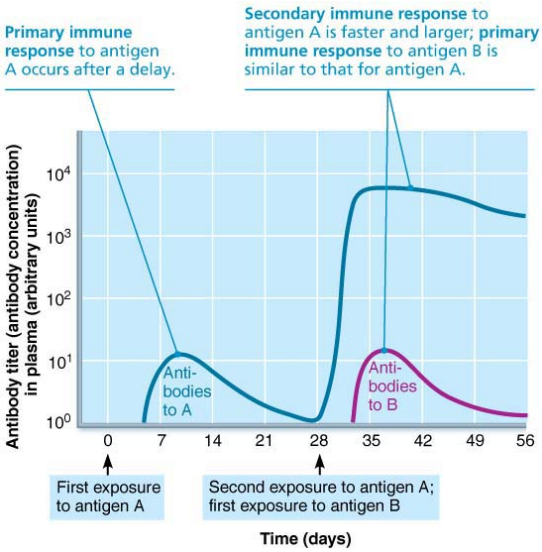
B vs T Cells

	B CELLS	T CELLS
TYPE OF IMMUNE RESPONSE	Humoral	Cellular
ANTIBODY SECRETION	Yes	No
PRIMARY TARGETS	Extracellular pathogens (bacteria, fungi, parasites, etc.) and pretty much anything (not necessarily cells but even just proteins)	Intracellular pathogens (virus) and abnormal cells (cancer cells)
SITE OF ORIGIN	Red bone marrow	Red bone marrow
SITE OF MATURATION	Red bone marrow	Thymus
EFFECTOR CELLS	Plasma cells	Cytotoxic T cells, helper T cells, and regulatory T cells
MEMORY CELL FORMATION	Yes	Yes
ACTIVATION	Via antibodies	Via MHC display display on other cells

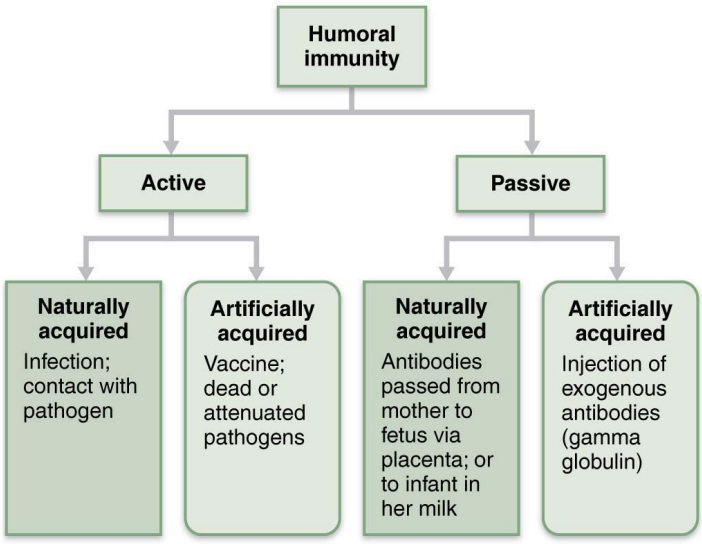
Immunological Memory
- Primary response: first time meeting the antigen
  (1) Antigen binds to receptor on specific B lymphocyte –clonal selection
    - Clonal selection/proliferation: making IDENTICAL B cells from the specific activated B cells
  (2) Creation of plasma cells and memory cells
    - Memory cells are primed to respond to same antigen much faster and stronger
- Secondary response: any encounters with antigen after first encounter
  - Larger response than primary response





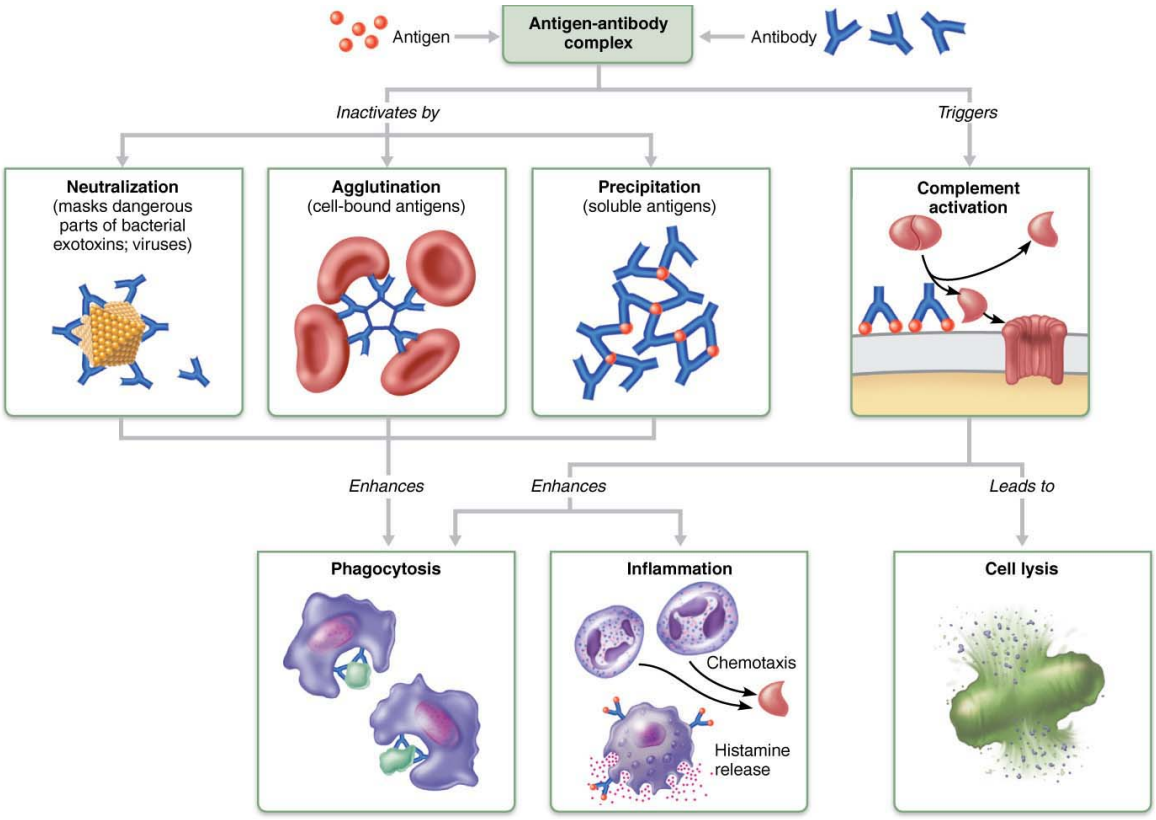


Humoral Immunity: Active vs Passive



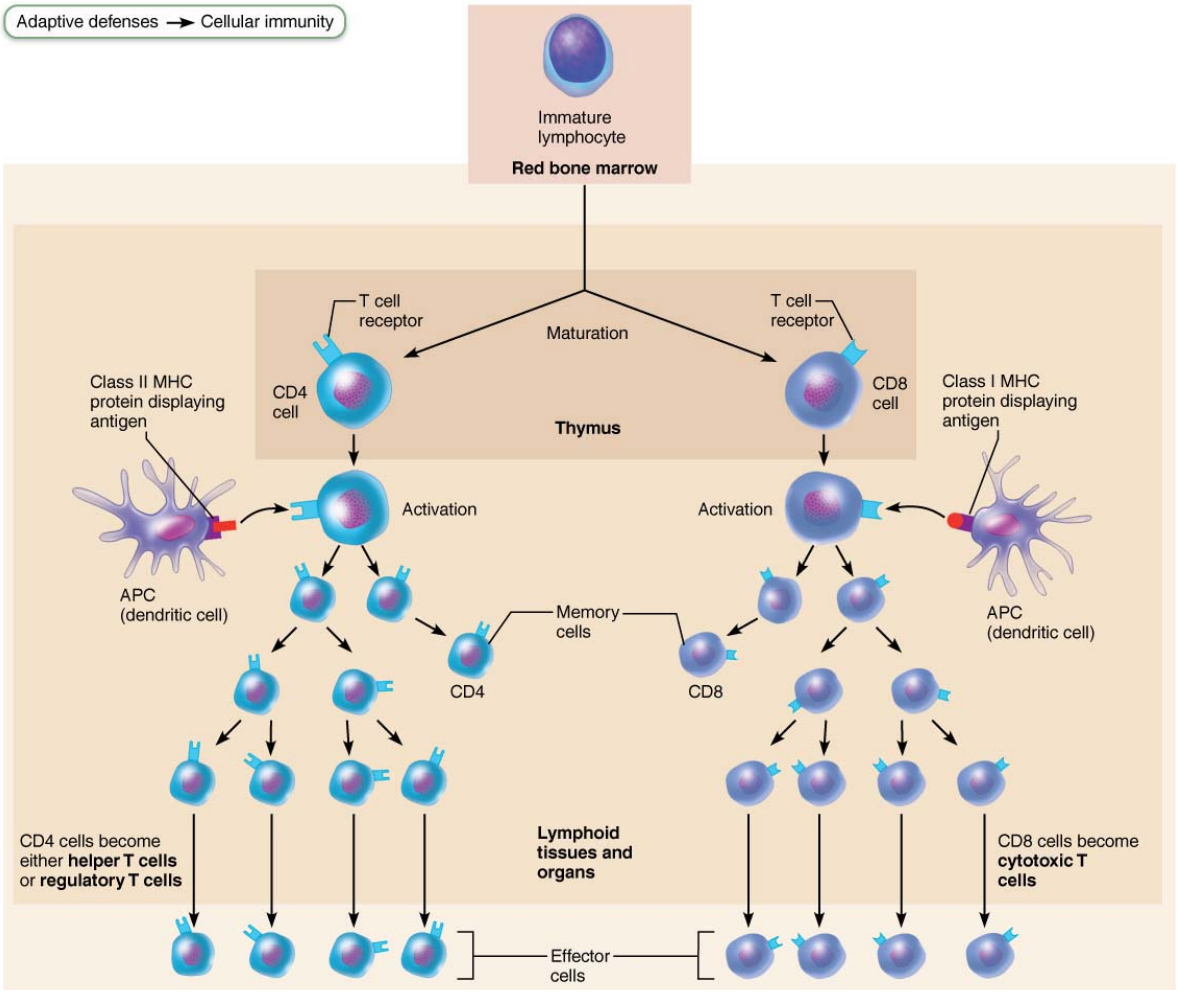
Functions of Antibodies

- Help immune system to do their job 4 ways
  (1) Neutralization: bunch of antibodies stick and coat virus so that they can't latch on our cells and infect them
  (2) Agglutination: clumping of cells to inhibit them to circulate and infect our cells
  (3) Precipitation: clumping of foreign soluble antigens (not cells)
  (4) Complement activation: trigger of complement so that it can enhance phagocytosis, inflammation, and cell lysis



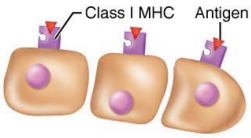
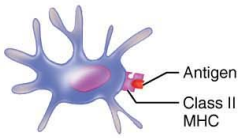
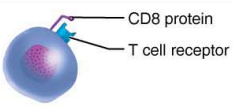
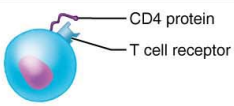
T Cell Differentiation and Activation

- T cells divide into 2 types:
  (1) CD4
    - Becomes helper T cells or regulatory T cells
  (2) CD8
    - Becomes cytotoxic T cells

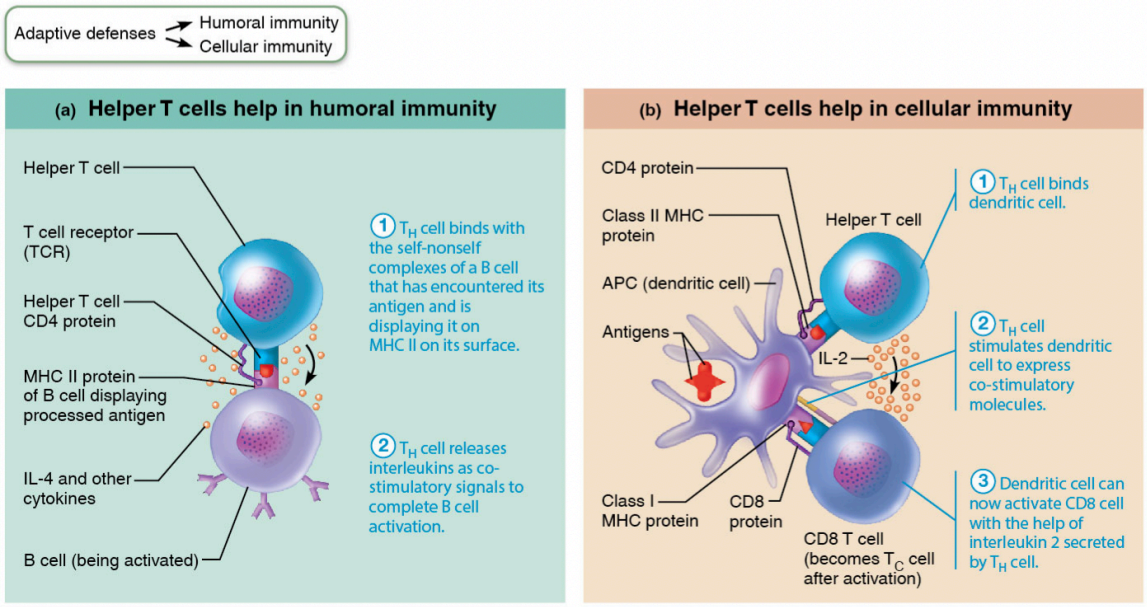


- BOTH CD4 and CD8 cells make memory cells
- T cells are activated with either Class I MHC or Class II MHC → this determines which type of T cell we have
  - Class I MHC makes CD8 cells and sends 2 messages
    - If the cell is an APC → I am your own cell but I captured a foreign that looks like this, so kill any cell that displays is
    - If the cell is not an APC → I am your own cell but I have been infected, so kill me
  - Class II MHC makes CD4 cells and sends 1 message
    - *I am your own cell, but I captured a foreign invader that looks like this, so help me mount a defense against it*

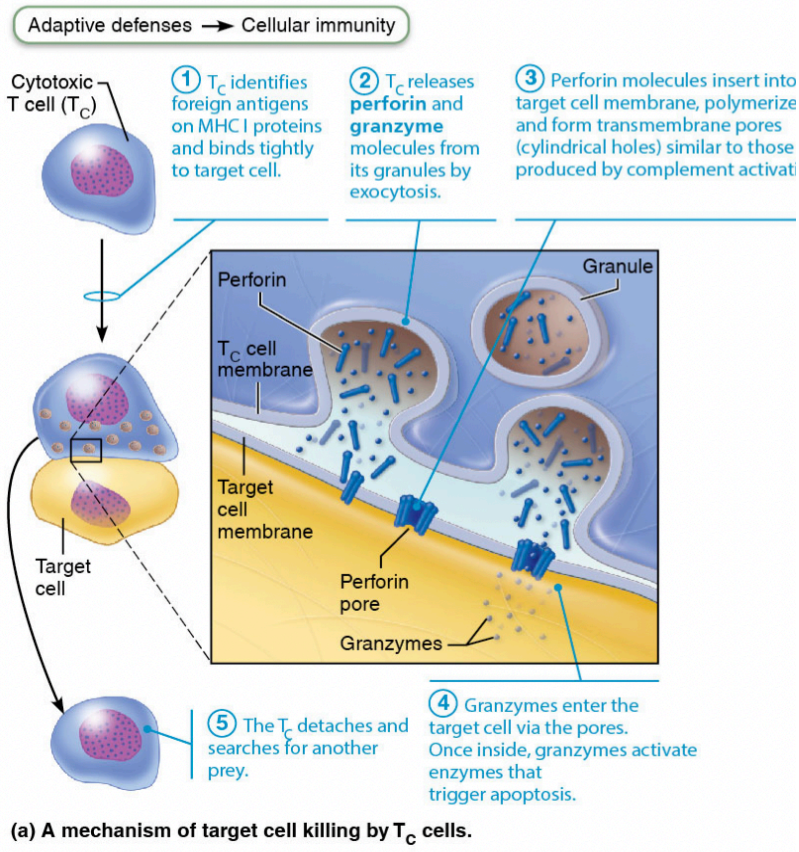
Table 21.6 Role of MHC Proteins in Cellular Immunity

	CLASS I MHC PROTEINS	CLASS II MHC PROTEINS
Displayed by	All nucleated cells 	APCs (dendritic cells, macrophages, B cells) 
Recognized by	Naive CD8 cells and cytotoxic T cells 	Naive CD4 cells and helper T cells 
Foreign antigens on MHC are	Endogenous (intracellular pathogens or proteins made by cancerous cells)* 	Exogenous (phagocytized extracellular pathogens) 
Cells displaying foreign antigens on MHC send this message	**If the cell is an APC:** "I belong to self, but have captured a foreign invader. This is what it looks like. Kill any cell that displays it." **If the cell is not an APC:** "I belong to self, but have been invaded or become cancerous. Kill me!"	"I belong to self, but have captured a foreign invader. This is what it looks like. Help me mount a defense against it."

- Helper T cells involved in humoral immunity vs cellular immunity
  - Humoral: complete B cell activation
  - Cellular: activates CD8



- Cytotoxic T cells kill messed up cells



(a) A mechanism of target cell killing by T_C cells.