Introductory Immunology Presentation

by

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Introduction

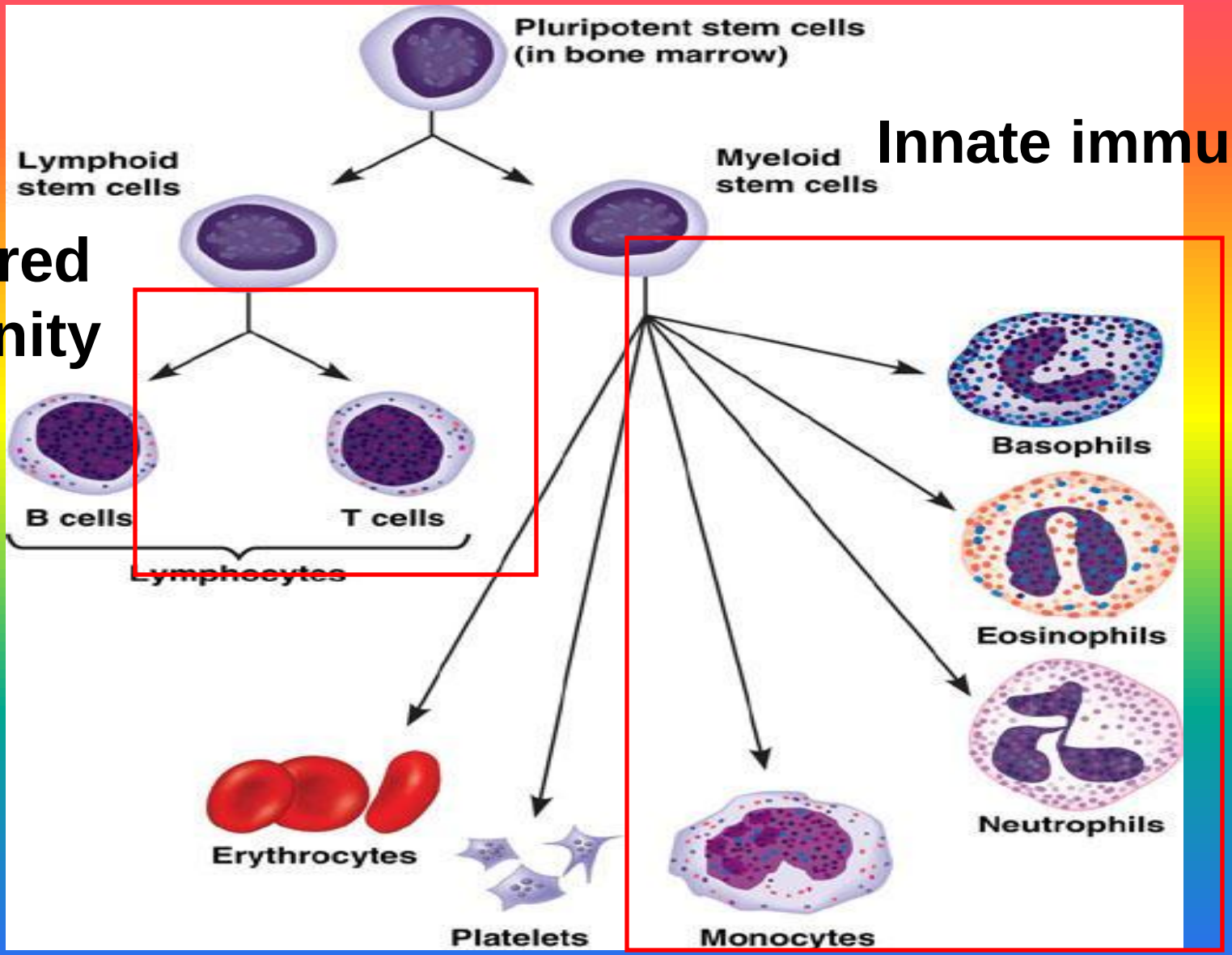
- ***Immunology*** is the study of host defence mechanisms.
- ***Immunity*** is the ability of the host to protect itself against pathogenic foreign organisms.
- The immune system comprises the tissues, cells & molecules which mount ***the immune response***.

Types of Immune System

- ***Natural (innate) immune system***
  - Skin, tears, saliva, mucus, acids, etc.
  - Property of all living creatures

- ***Adaptive (acquired) immune system***
  - Specialist cells, cytokines, antibodies
  - Specific and has 'memory'
  - Specialised mucosal lymphoid tissue

Two Major Kinds of Defense



Innate immunity

Acquired immunity

Immunogenicity and Antigenicity

- ***Immunogenicity*** is the capacity to induce an immune response by foreign, complex and high molecular weight compounds, mostly proteins.
- ***Antigenicity*** is the ability to bind to Ig(s) or immune cells; an immune response may not arise. All immunogens are antigens but all ag's need not necessarily be immunogens.
- ***Haptens ; Hapten carrier conjugate***

The Innate Immune System

- A reliable mean of protecting the host in the first instance against many extracellular organisms.
- It is a property of every living organism.
- Unable to deal with all intracellular organisms (e.g., protozoa, viruses & certain bacteria are not killed). Non- specific, has no memory involved.

The Innate Immune System

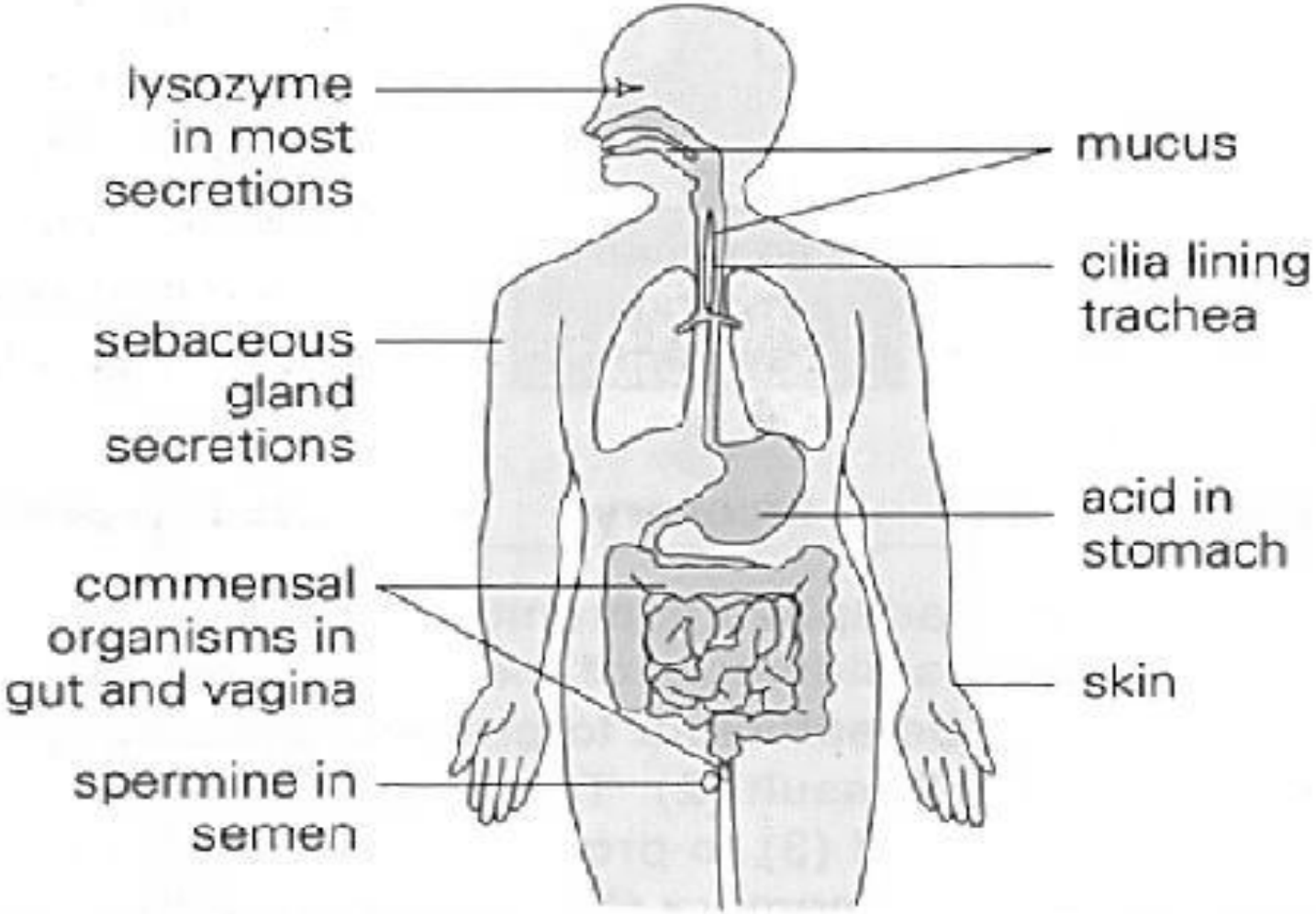
- Synonyms are the ***natural*** or ***native*** immune system.
- Rapidly mobilised first line of defence.
- Not dependent on prior exposure to a foreign invader.
- Non-specific.
- May not be sufficient to prevent foreign material persisting in the host.

Components of the Innate Immune System

- Innate immunity comprises:
  - Physio-chemical barriers.
  - Molecules normally present in body fluids e.g. lysozyme, complement, anti-proteases.
  - Phagocytic & cytotoxic cells such as neutrophils, macrophages, natural killer cells.

EXTERIOR DEFENCES

biochemical	chemical and physical



Mode of Threat Neutralization by the Innate Immune System

- The ***Respiratory Burst :***
  - Also known as the ***oxidative burst*.**
  - membrane-bound NADPH oxidase in combination with other enzyme produces
    - Superoxide Anion
    - Hypochlorous Acid
    - Hydrogen Peroxide
    - Chloramines

The Acquired Immune System

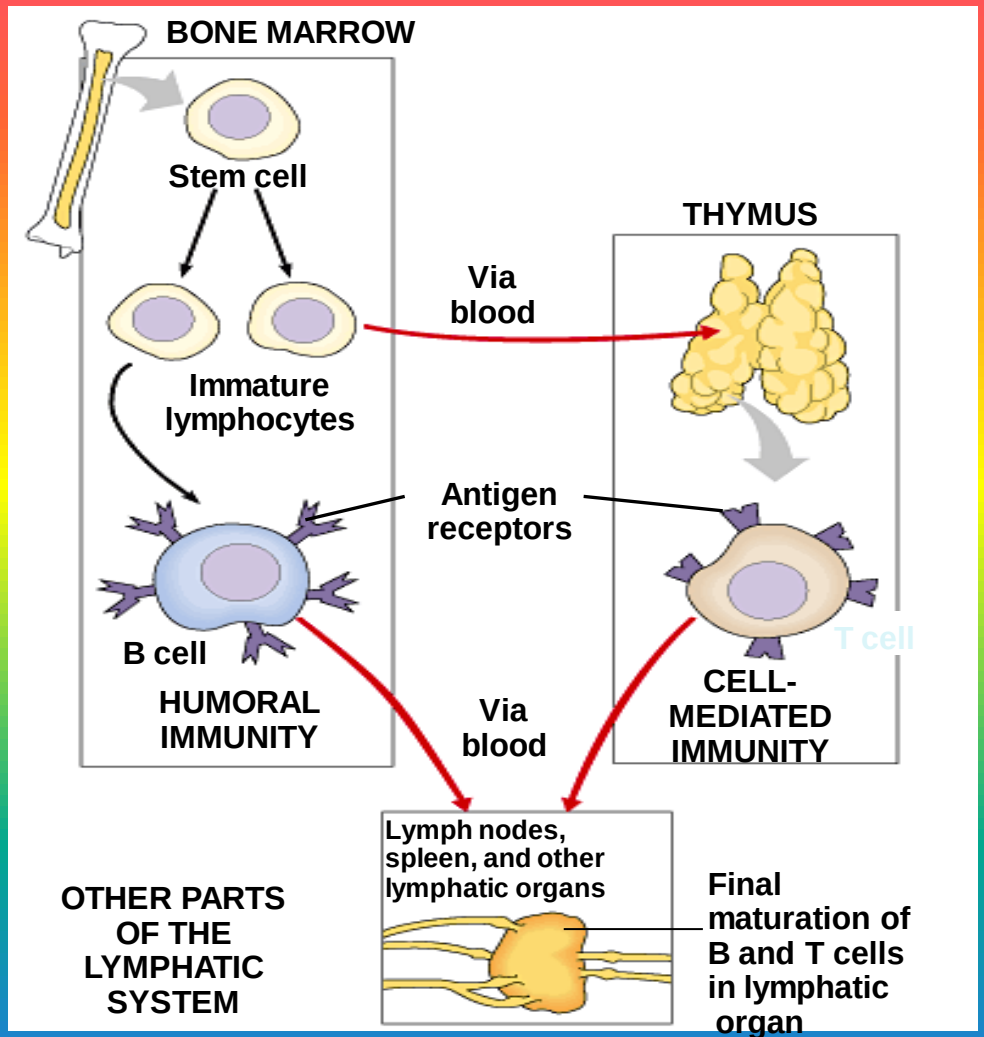
- Specific and has ***immunologic memory***
- Dedicated immune cells - ***the lymphoid cells (lymphocytes)***
- Molecules that ***specifically counteract*** antigens (**antibodies or immunoglobulins**)
- Specific immune systems associated with barrier surfaces e.g. **M**ucosa and **G**ut-**a**ssociated **L**ymphoid **T**issue (MALT and GALT) respectively.
- Lymphocyte also secrete cytokines eg. interleukins.

The Acquired Immune System

- ***Antigen specificity*** is the single most important aspect of the acquired immune system (mediated by lymphocytes).
- Each clone of a lymphoid cell ***responds only to a single antigen.***
- T-cells deal with ***surface bound processed antigen*** (usually cell associated); Self-MHC restriction.
- B-cells deal with ***soluble (extracellular) native antigen.***

Humoral and Cell-mediated Immunity

- Specific immunity is termed **humoral** when ***antibodies*** are involved in removing the antigen.
- It is termed **cell-mediated** when ***T-cells & macrophages*** are involved in pathogen clearance .



Active and Passive Immunity

- ***Immunity after infection*** is termed active immunity (because the host has responded actively to the stimulus).
- Immunity may be ***transferred passively*** by antibodies or cells (breast milk, vaccination, maternal IgG ab's, through placenta antivenom to snake venom).
- Vaccination may be passive (using Ig) or active (using antigen or attenuated organism, toxoid).

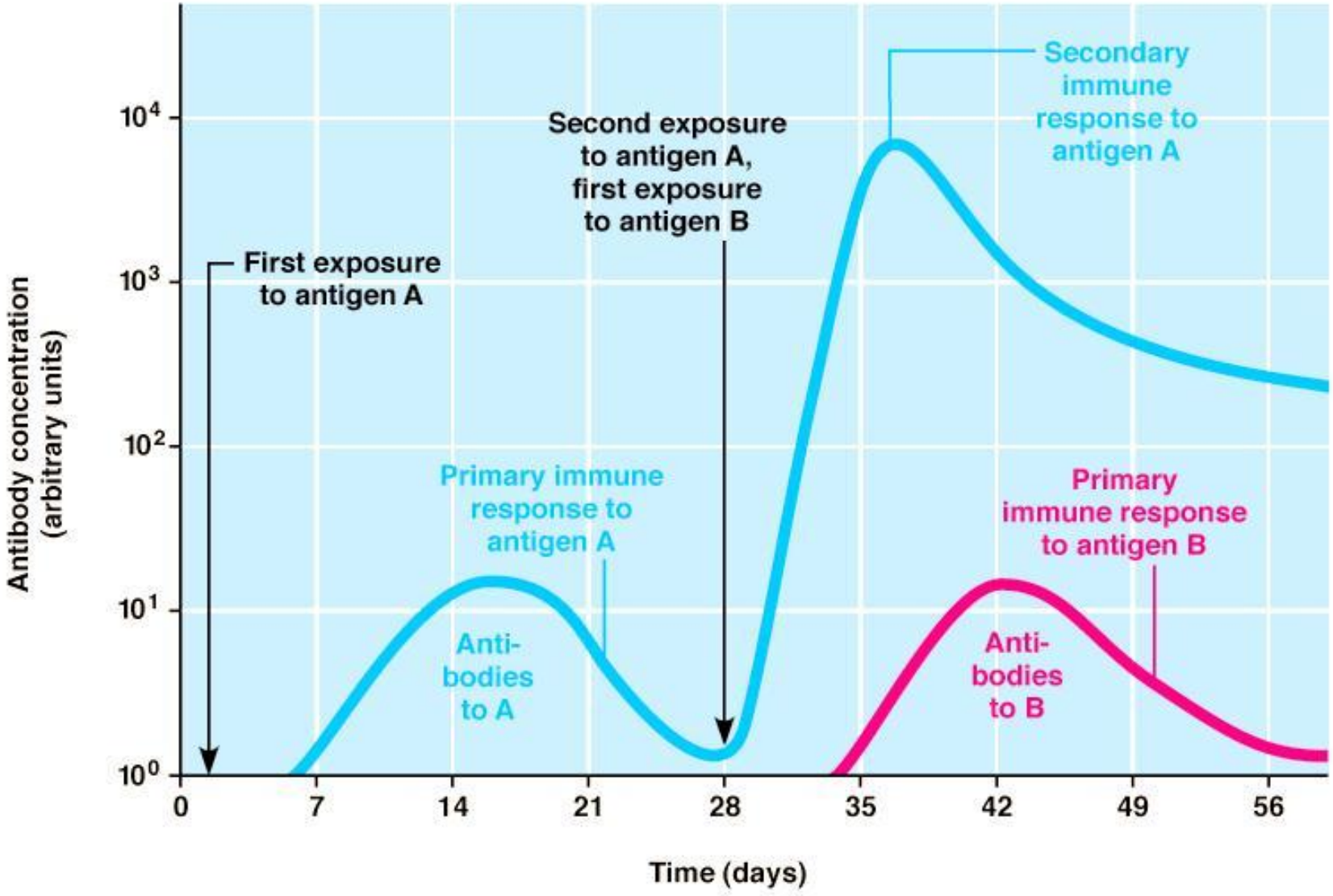
Primary Immune Response

- The development of acquired immunity begins with a ***primary immune response***:
  - an afferent phase involving APCs. Trapping and capture of ag's by DC's.
  - T-cell *transformation* from a resting (naive) to an active state.
  - an effector phase - induction of other cells (B-cells & macrophages) by active T-cells secreting cytokines such as IL-2,IL-4,IL-5.

Secondary Immune Response

- The primary immune response is accompanied by the appearance of antigen-specific T-cells(Th cells and CTL's) & Ig-secreting B-cells.
- The ***secondary immune response***:
  - on second (and subsequent) exposure to the same antigen, antigen-specific memory T- & B-cells are recruited much sooner & more efficiently.
  - Ig levels are consequently much higher.

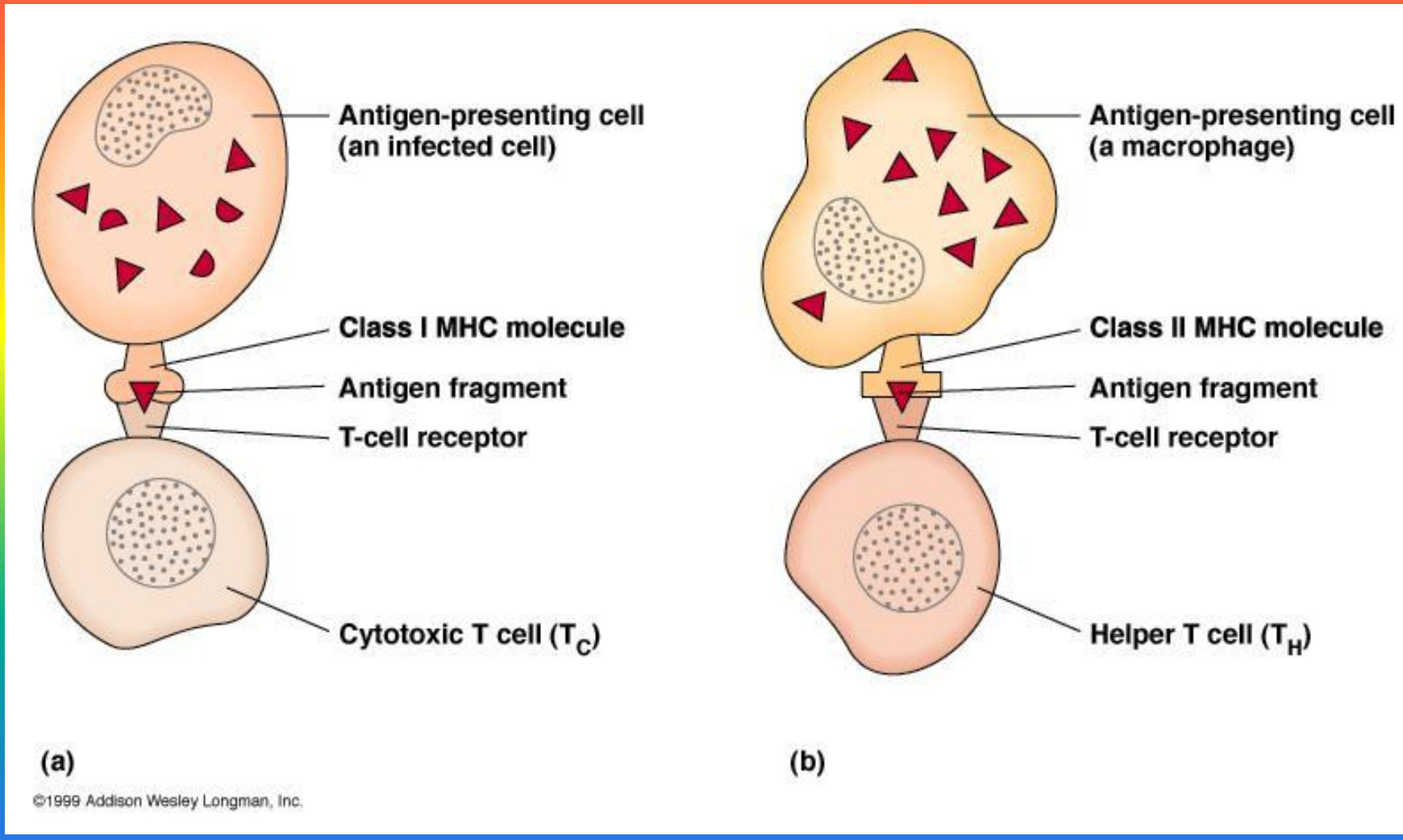
Antibody Response After Exposure to Antigen



T Cells and Cell-mediated Immunity

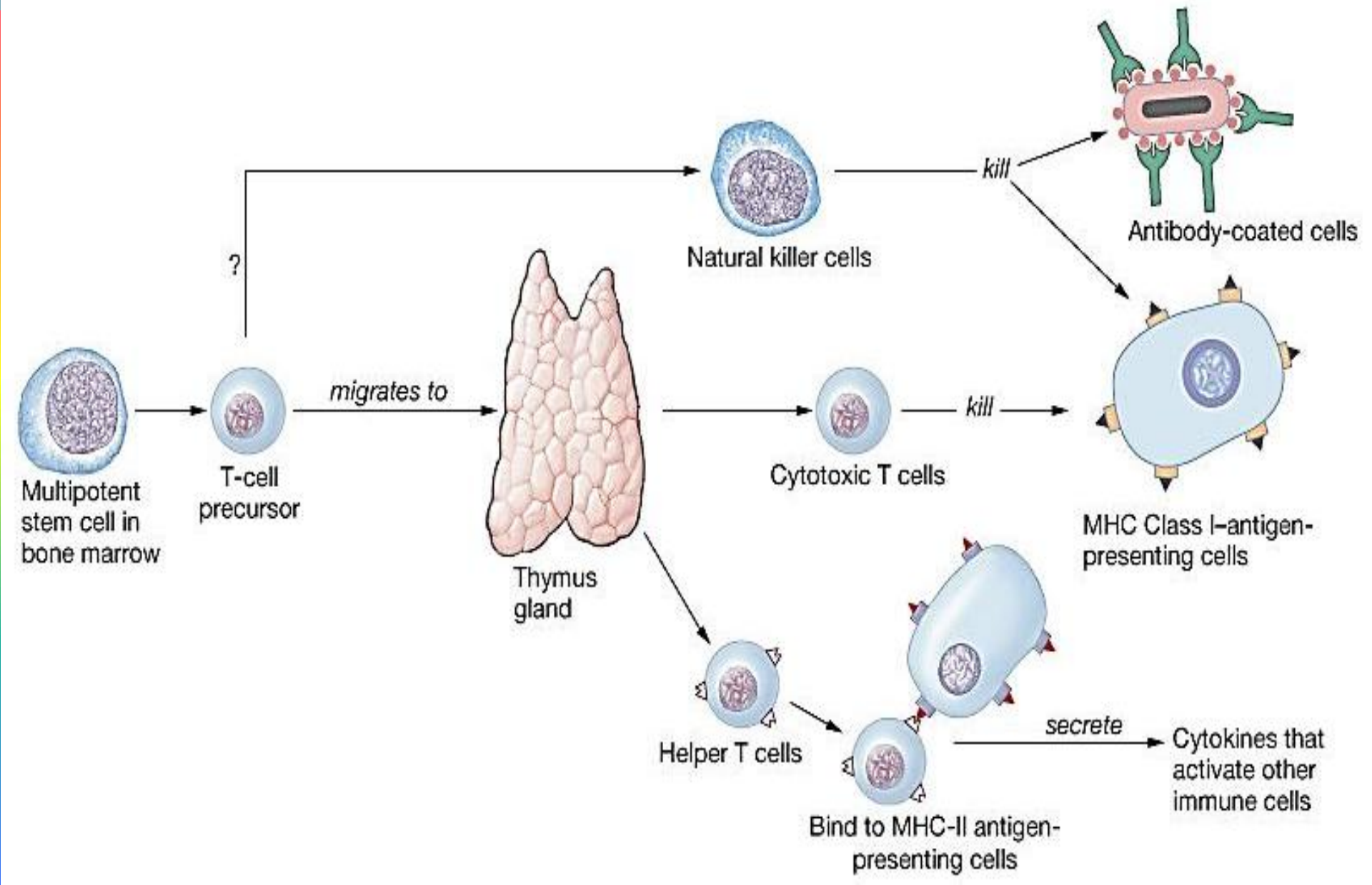
- T cells develop from stem cells in bone marrow and mature in the thymus gland.
- After maturation they migrate to lymphoid organs.
- T cells are key cellular component of immunity.
- T cells have an antigen receptor that recognizes and reacts to a specific *intracellular* antigen via T cell receptor.
- T cell receptor only recognize antigens combined with Major Histocompatibility Complex (MHC) proteins on the surface of cells.
  - ***MHC Class I***: Found on all nucleated cells
  - ***MHC Class II***: Found on phagocytes, B cells and DC's.

T Cells Only Recognize Antigen Associated with MHC Molecules on Cell Surfaces



- **Clonal selection** increases number of effector T cells and destroy the invader.
- T cells regulate proliferation and activity of other cells of the immune system: B cells, macrophages, neutrophils, etc.
- Defense against:
  - Bacteria ,Viruses, Fungi, protozoa, and helminths.
  - Cancer cells & Transplanted tissue.
- Unlike humoral immunity, cell mediated immunity is not transferred to the fetus (no passive immunity).

T-cell Specific Responses



Types of T cells

1. **Helper T ($CD4+$ T_H) Cells**: have central role in immune response, these activate macrophages and help form cytotoxic T cells.
2. **Cytotoxic T (CD8+ CTLs)**: destroy target cells on contact by producing perforin and granzymes that lyse an infected cells.
3. **Delayed hypersensitivity T (T_D) Cells:** Mostly T helper and a few cytotoxic T cells that are involved in some allergic reactions and rejection of transplanted tissue.
4. **Suppressor T (Ts) Cells**: inhibit the production of CTL cells to shut down immune response once they are unneeded, least they cause more damage than necessary. (Now called regulatory T cells).

Type of Recognition by $CD4^+$ and $CD8^+$ Cells

- $CD4^+$ cells recognize antigens that have been taken up by **A**ntigen **P**resenting **C**ells (APCs) which present antigen fragments on the cell surface.

- $CD8^+$ cells recognise cells infected with virus, altered self cells such as tumor cells which they then kill after recognition.

$CD4^+$ T_h Lymphocytes

- $CD4^+$ (T_h) cells interact directly with other cells by releasing cytokines to control development of the immune response.
- Two types of T_h cells:
  - T_{h1} cells activate macrophages to destroy pathogens by phagocytosis and subsequent respiratory burst.
  - T_{h2} cells help B-cells to make antibody.

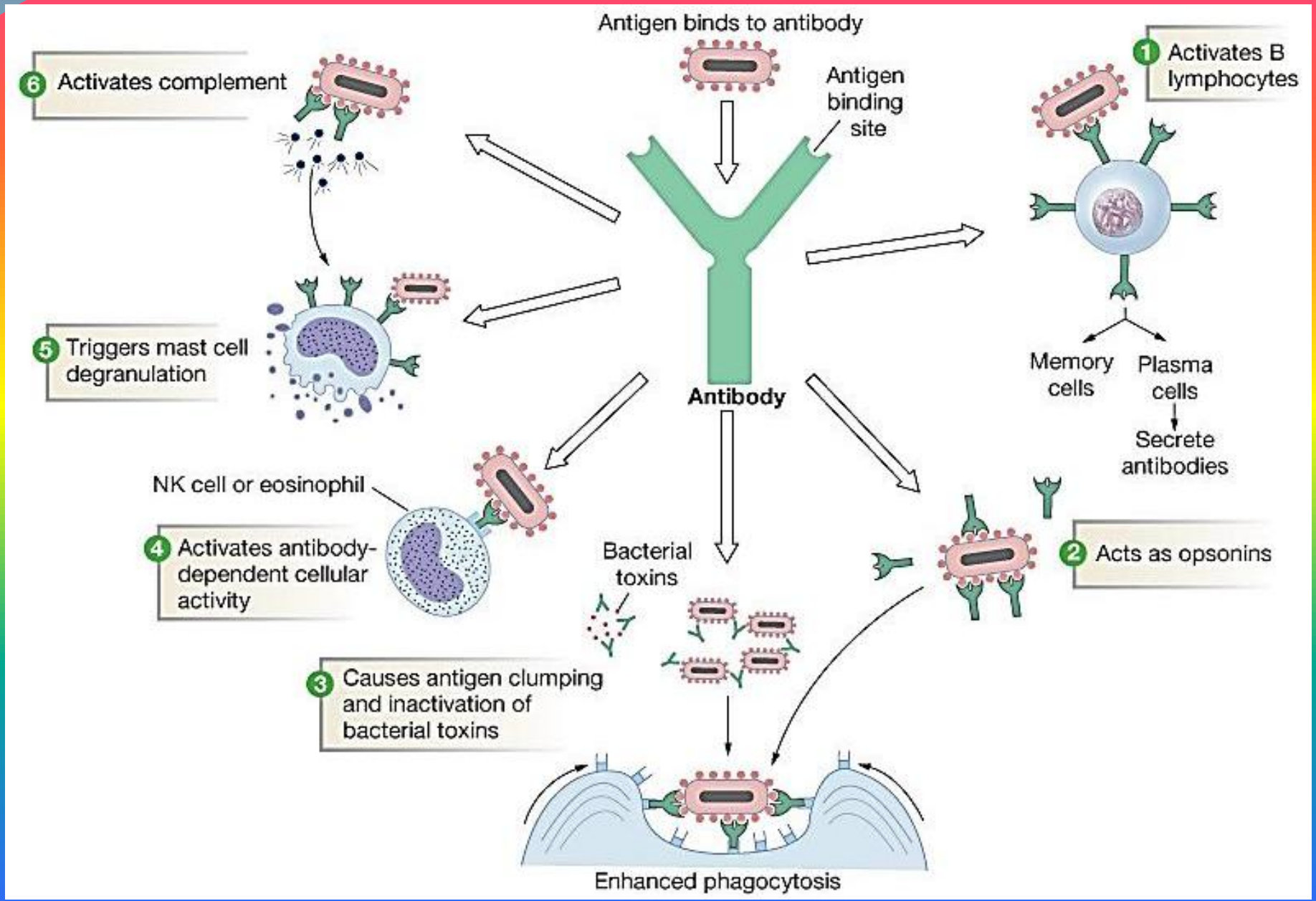
B-Lymphocytes

- Specialised for the production of immunoglobulins after differentiation into plasma cells.
- Controls pyogenic bacteria (bacteria that causes pus formation).
- Prevents blood-borne infections.
- Neutralise toxins produced by pathogens.
- 12% of total lymphocytes.

B-Lymphocytes

- Can respond to peptide, carbohydrate & glycolipids.
- Usually require T-cell help to respond to antigen (interleukins) but can also recognise antigen directly through surface Ig.
- TD and TI antigens.
- B cells mature & proliferate in lymph nodes.

Ag-Specific Responses

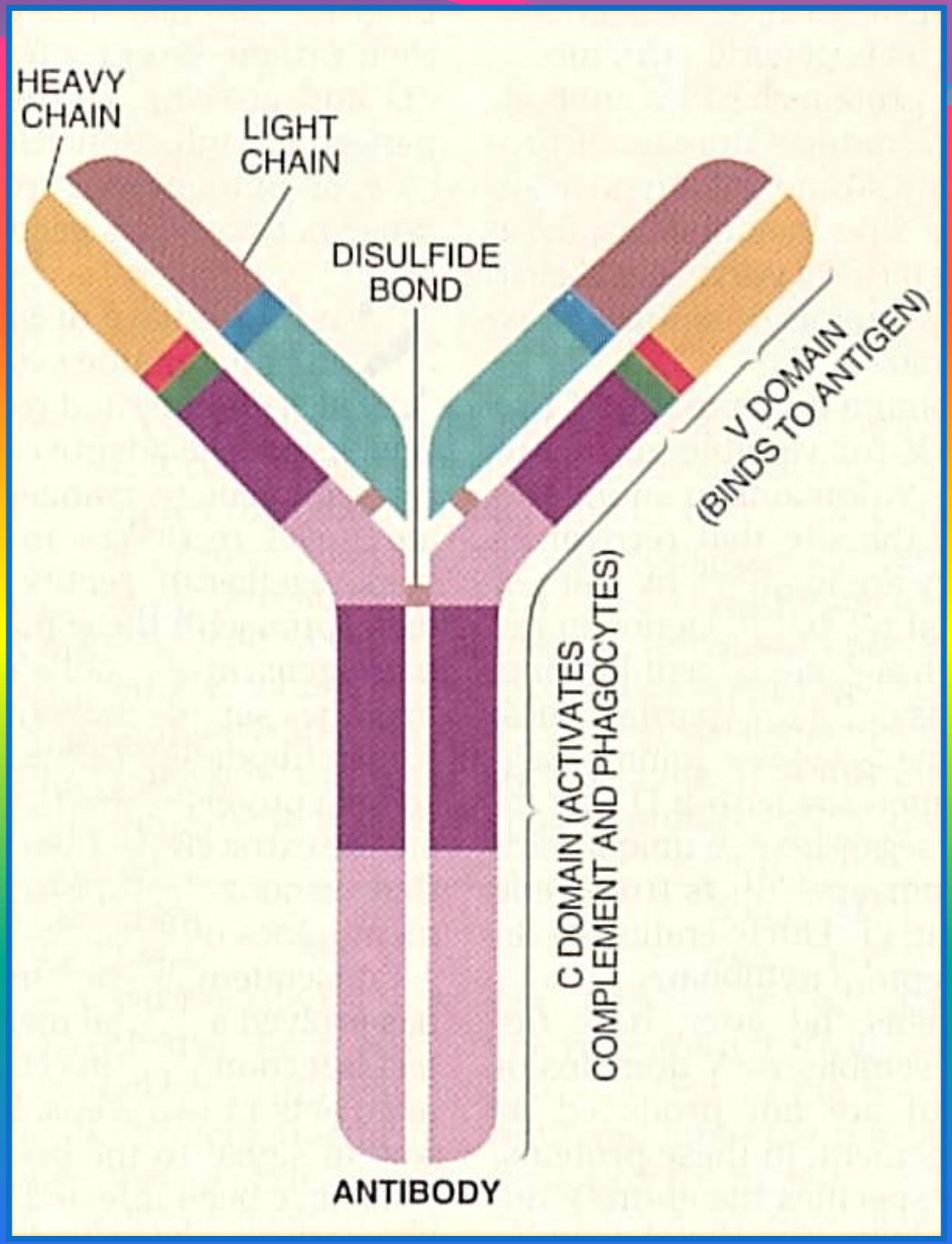


Classes of Immunoglobulins

- The 5 classes of Ig are:
  - IgM
  - IgA
  - IgD
  - IgG
  - IgE

Structural Biology of Immunoglobulins

- 4-chain structure
  - 2 light chains
  - 2 heavy chains
- Chains linked by disulphide bonds.
- Chains are coiled into “domains”.
  - 110 amino acids.
  - stabilised by intrachain disulphide bond.


HEAVY CHAIN
LIGHT CHAIN
DISULFIDE BOND
V DOMAIN (BINDS TO ANTIGEN)
C DOMAIN (ACTIVATES COMPLEMENT AND PHAGOCYTES)
ANTIBODY

- Terminal regions of H & L chains are the variable regions.
- The variable region is the site where Ig combines with antigen.
- This region's variability is responsible for wide range of antigen specificity. **Antibody diversity**.
- The other domains are the constant regions which are similar within isotypes of Ig.
- Using enzymes, a number of Ig fragments have been identified. Important ones are ***Fab*** and ***Fc***.

- F_c regions is formed from H chains & determine isotype & so biological function.
- Hinge region also has effect on function.
- These functions are distinct from antigen binding.
- Opsonization,complement activation, ADCC etc.

IgG (Immunoglobulin γ)

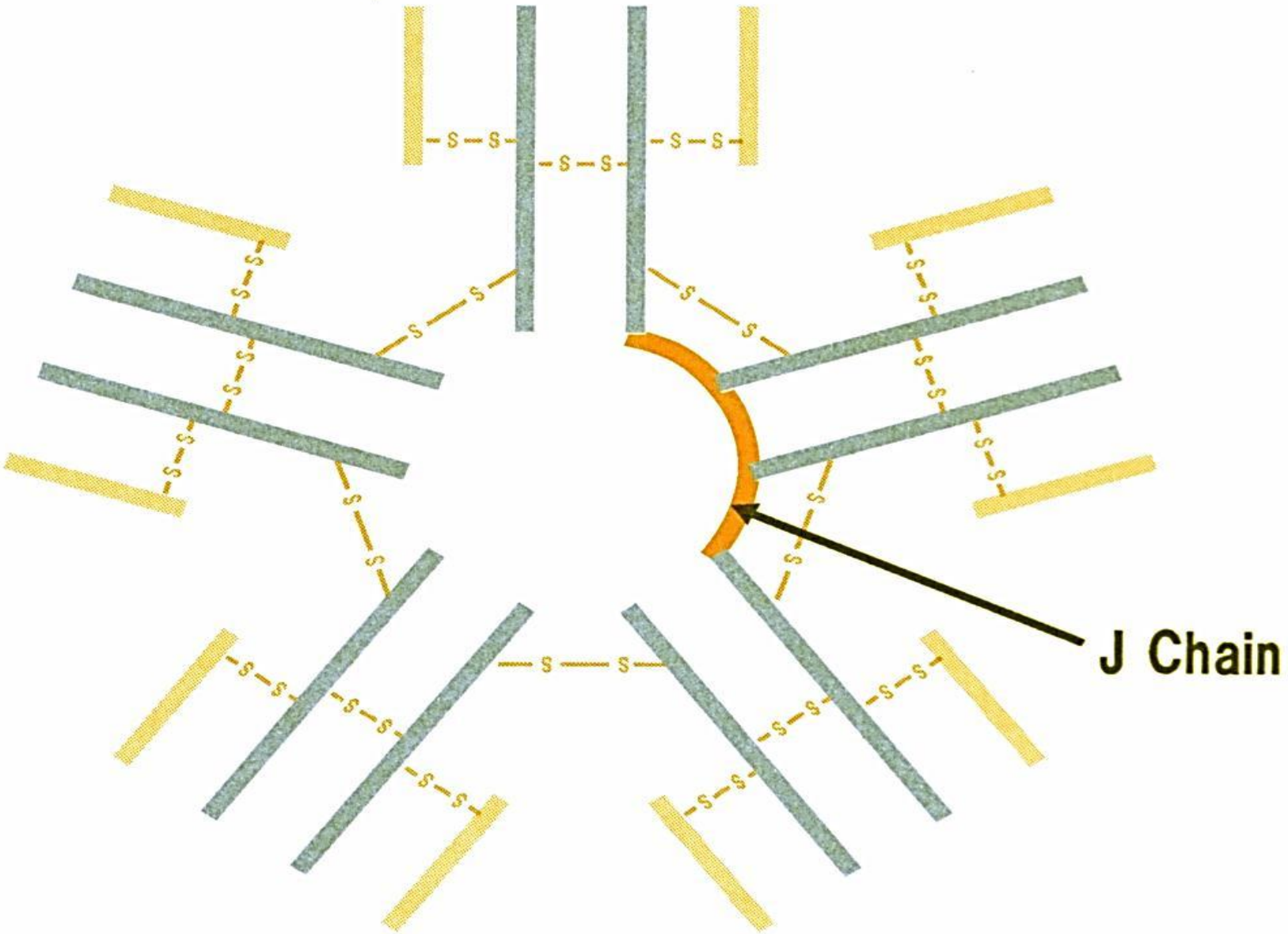
- IgG
  - neutralises toxins.
  - activates complement.
  - Opsonisation.
  - able to cross placental barrier (only Ig that can).
  - Four subclasses : IgG1,IgG2,IgG3,IgG4.
  - Present in the highest concentration in blood.

IgA (Immunoglobulin α)

- IgA
  - monomeric & dimeric forms.
  - dimeric form is ***secretory IgA*** and is found in secretions such as tears, saliva, breast milk.
  - important antiviral Ig.
  - Is the signature molecule of mucosal immunity.

IgM (Immunoglobulin μ)

- IgM
  - pentameric
  - good agglutinator
  - good at activating complement
  - First class of ab to be synthesized by B cells after exposure to an ag.
  - mIg.
  - 10 ag binding sites


J Chain

IgE (Immunoglobulin ε)

- IgE :
  - Active against parasitic infections especially of helminths.
  - F_c portion binds to receptors on mast cells, basophils.
  - Triggers mast cell degranulation.
  - Expressed in high concentrations in atopic individuals in response to allergens such as pollen, animal dander, RSPM etc.
  - **Mediate Type I hypersentivity reactions such as asthma.**

Major Histocompatibility Complex (MHC)

- Class I molecules expressed on all nucleated cells.
- Class II molecules expressed on a small group of antigen presenting cells.
- Class II molecules may also be induced to be expressed on other cells during immune reactions by interferon-γ.

Cytokines

- Cytokines are short-range, multifunctional, short-acting mediators of cellular activities, especially within the immune system.
- Released primarily by activated T-cells & other immune and non-immune cells.
- Act in a autocrine or paracrine manner.

Classes of Cytokines

- There are 4 major classes of cytokines :
  - Interleukins (IL-1 to IL-12)
  - Interferons (IF-α, IF-β & IF-γ)
  - **C**olony **S**timulating **F**actors (CSFs)
  - **T**umour **N**ecrosis **F**actor(s) (TNF-α & TNF-β)

Natural Killer Cells

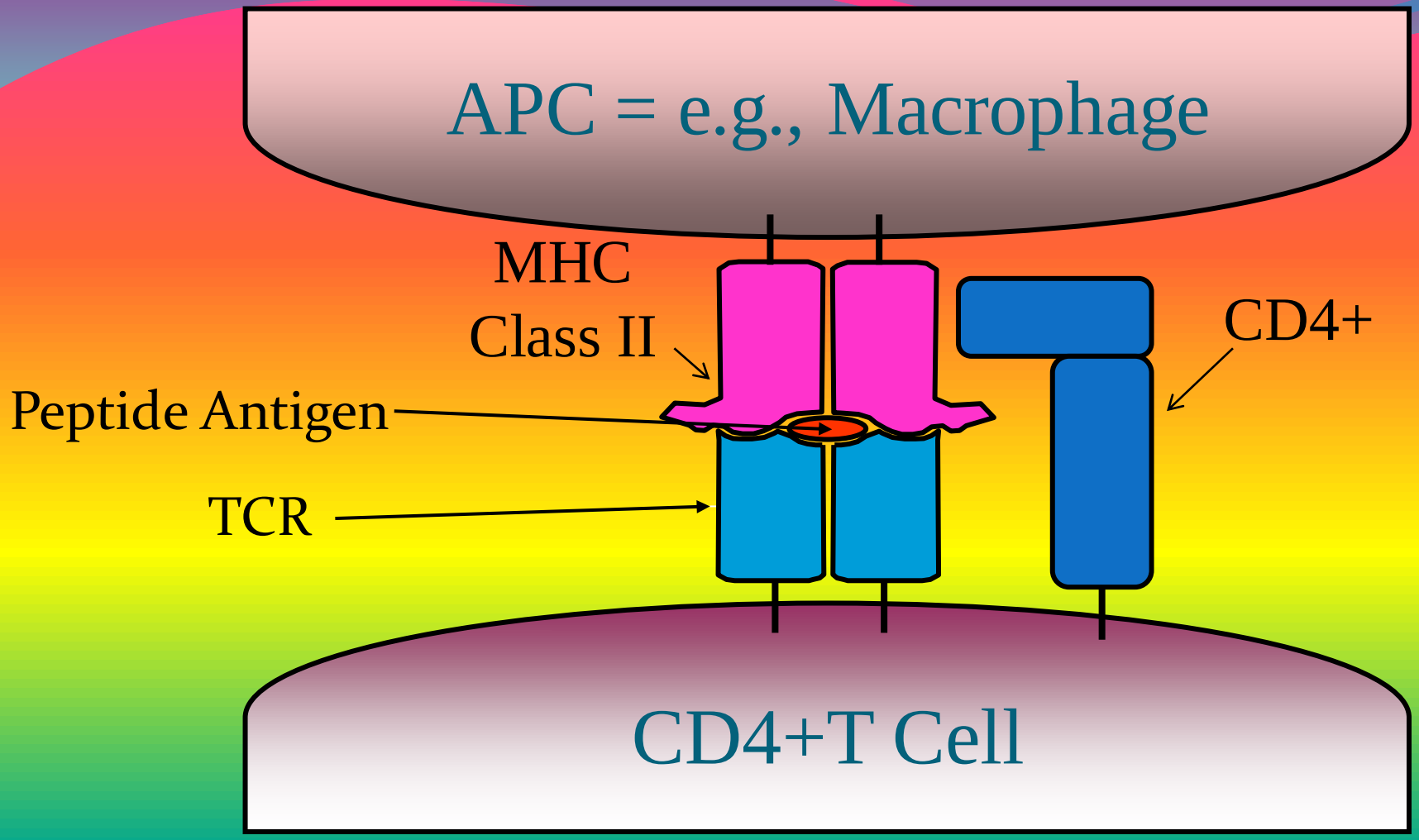
- Natural Killer (NK) cells:
  - Classed as part of the lymphoid system but have no differentiating surface markers.
  - They are particularly effective against virus-infected & tumour cells.
  - Also called large granular lymphocytes.
  - Kill via granzymes and perforins.

Antigen Presenting Cells

- Antigen Presenting Cells (APCs):
  - normally, initiation of the acquired immune response does not take place at the site of injury or penetration of foreign organisms.
  - antigen is taken up (trapped and captured) by APCs at the site of inflammation and transported to regional lymph nodes and/or spleen where it is presented to T- & B-cells.

Antigen Presenting Cells

- Examples of APCs are:
  - macrophages
  - B-cells
  - dendritic cells
- Macrophages & B-cells recognise antigen through the Ig molecule.
- Dendritic cells process & present antigen to naive T-cells via MHC Class II. Most potent APC's.



Antigen Recognition by CD4+ T-cell Presented by APC

Complement System

- **The complement system :**
  - comprises at least ***9 plasma proteins*** & some ***regulatory factors***, that mediate several functions of the ***inflammatory process.***
  - synthesised by ***macrophages*** or ***hepatocytes.***
  - usually circulate as inactive pro-enzymes.
  - heat labile

Complement Pathways

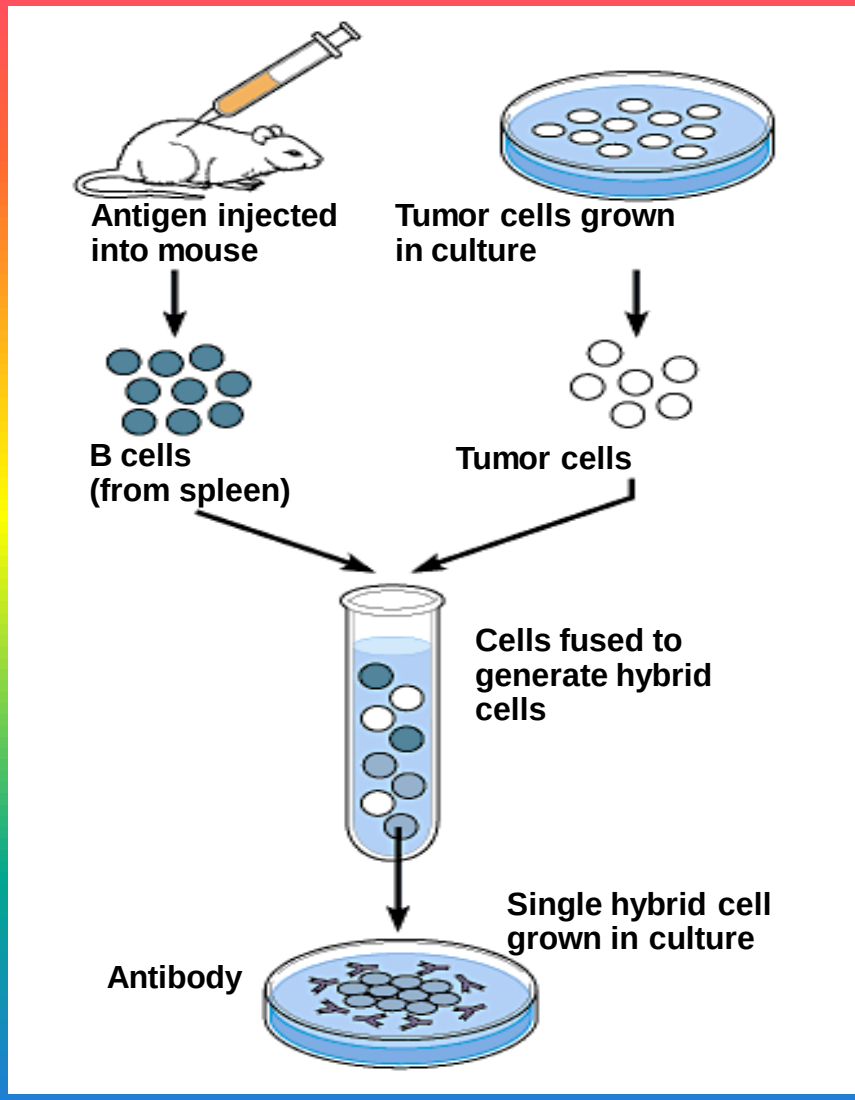
- Complement pathways :
  - Cascade of sequential activation converts each proenzyme into its active state & amplifies the response.
  - Three main pathways:
    - ***Classical*** pathway - bound IgG, IgM
    - ***Alternative*** pathway - certain antigens (LPS, endotoxin, etc.)
    - ***Lectin*** pathway

Functions of Complement System

- opsonisation, chemotaxis, immune adherence (MAC)
- acceleration of acute inflammation
- immune cytolysis
- virus neutralisation
- MAC causes the killing of the microbe through osmotic lysis.

Monoclonal Antibodies

- Monoclonal antibodies are pure antibody preparations
- Specific for a single antigenic determinant
- Produced from descendants of a single cell
- ***Hybridomas*** – cell hybrids made from a fusion of a *tumor cell* (easy-to-grow) and a *B cell* (specific for a single antigenic determinant)



Hybrid cell culture, producing monoclonal antibodies

Uses of Monoclonal Antibodies

- **Monoclonal Abs are powerful tools in the lab. Commercially prepared antibodies are used:**
- **In research & clinical testing.**
- **To provide passive immunity .**
- **These cells are useful in medical diagnosis.**
- **They are also useful in the treatment of certain cancers. Magic bullets.**
- Have desirable properties of both parent cells – indefinite proliferation as well as the ability to produce a single type of antibody.

THANK YOU