Leucocyte physiology.

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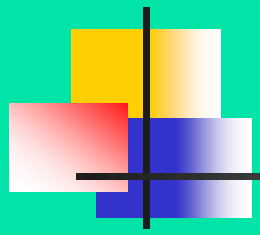
Physiology

Today's lecture



- Brainstorm
- Basic organization and function of the immune system
- Lymphocyte development
- Immune activation and response
- Immune suppression and tolerance

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- Natural killer cells

Brainstorm

- Why do organisms contract diseases?
- What happens when an organism contracts a disease?
- What factors can help (or hinder) the likelihood that we will contract a disease?
- What happens when an organism is injured?
- What factors can help (or hinder) the likelihood that we will recover from an injury?

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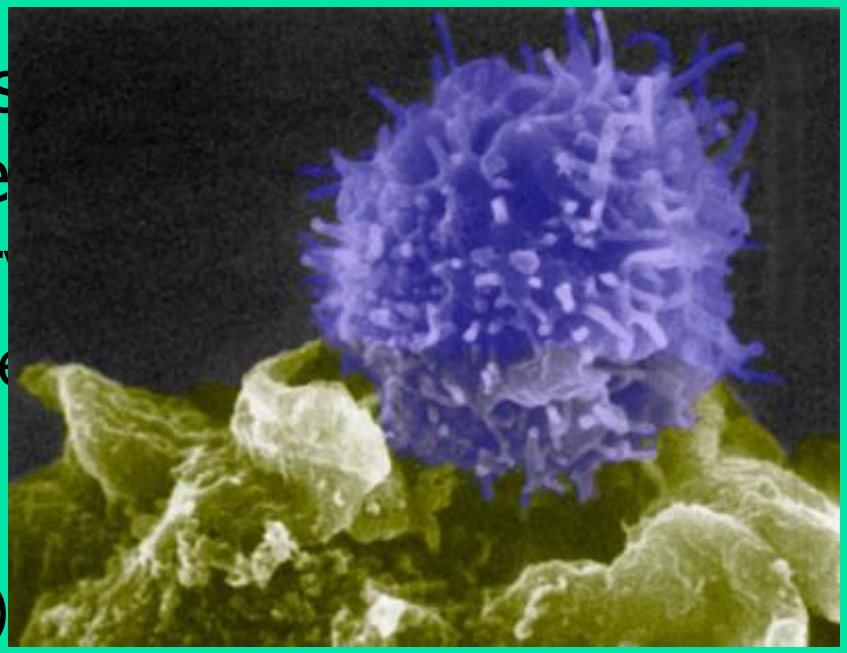
Basic Organization and Function of the Immune System

The immune system is
the body's response
to disease and injur

- Nonspecific response
(innate immunity)
- Specific response
(acquired immunity)

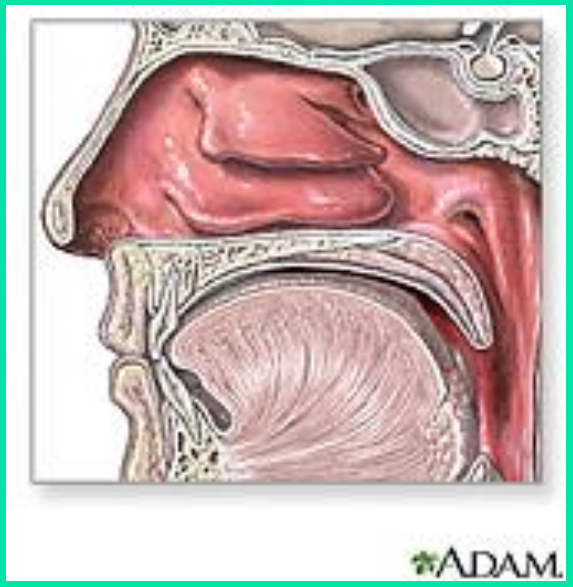


T-cell (part of the specific immune response)

Nonspecific response

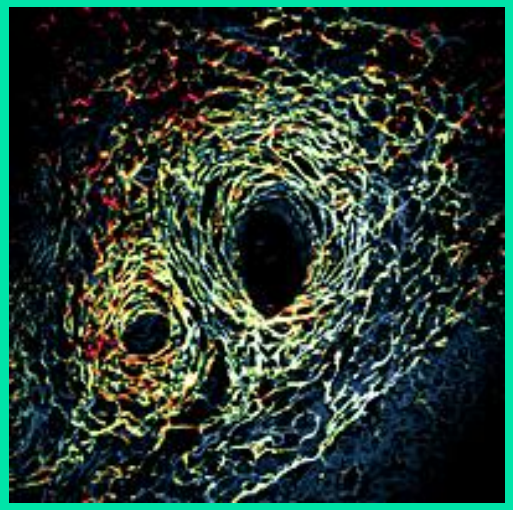
Exterior barriers

- Skin
- Mucous membranes
- Secretions

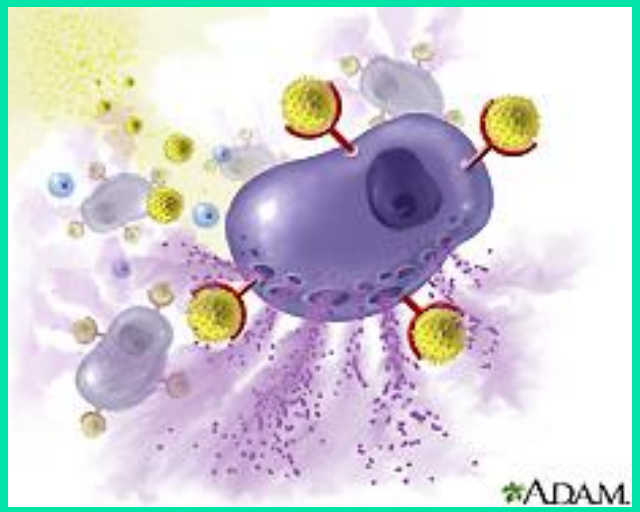


Nonspecific response

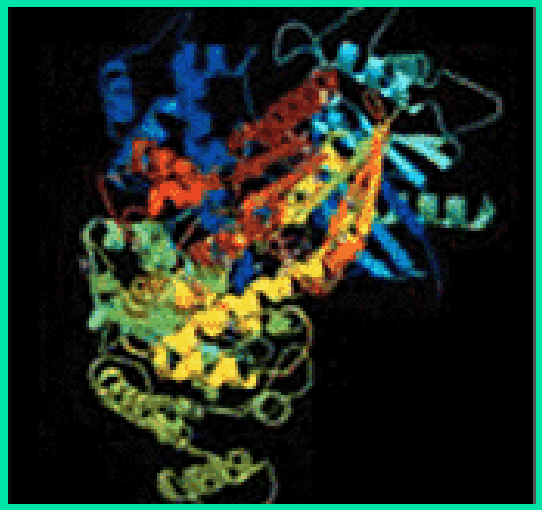
- Involves myeloid leukocytes (including all phagocytic cells) such as macrophages
- Participate in the inflammatory response to injury or disease
- Mast cells also involved
- Proteins (cytokines) signal between cells



inflammation



mast cell

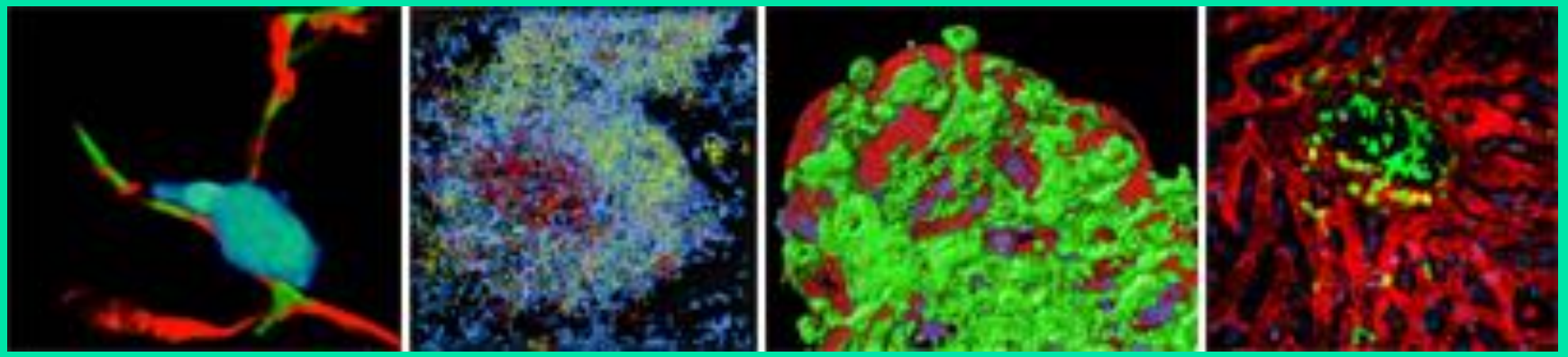


protein

cific Response

- Antigen-antibody relationship (acquired immunity)
- **Vaccinations depend on this**
- Involves lymphocytes (B, T and plasma cells)

Model of an antibody



T-cells, made visible by fluorescent dye

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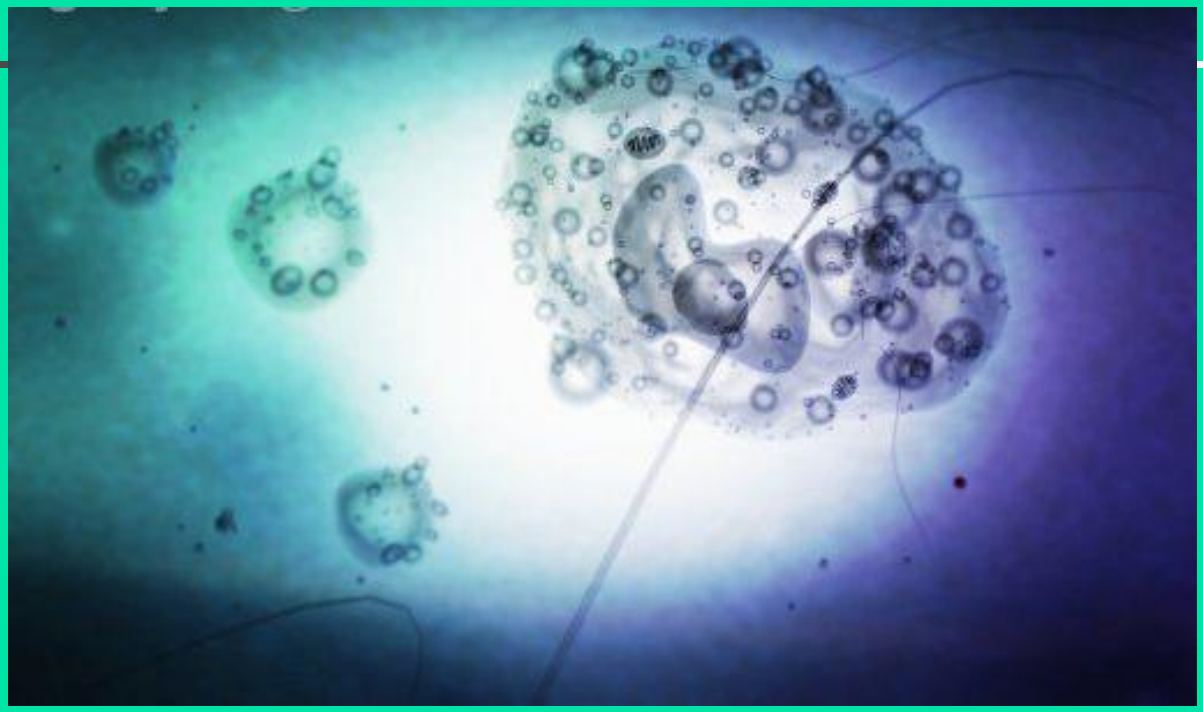
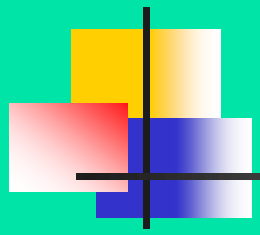
Lymphocyte development



Gettyimages
Conceptualization of a lymphoid progenitor cell

Origin, Lineage, Functions



Originates in bone marrow

- Rich supply of hematopoietic stem cells
- Asymmetric cell division (one daughter stays in bone marrow)
- *Lymphoid and Myeloid lineage cells begin and are released from here*

Differentiation into lymphoid stem cells in the bone marrow

- General B cells mature in the bone marrow

Differentiation into lymphoid stem cells in the thymus

- General T cells mature in the thymus

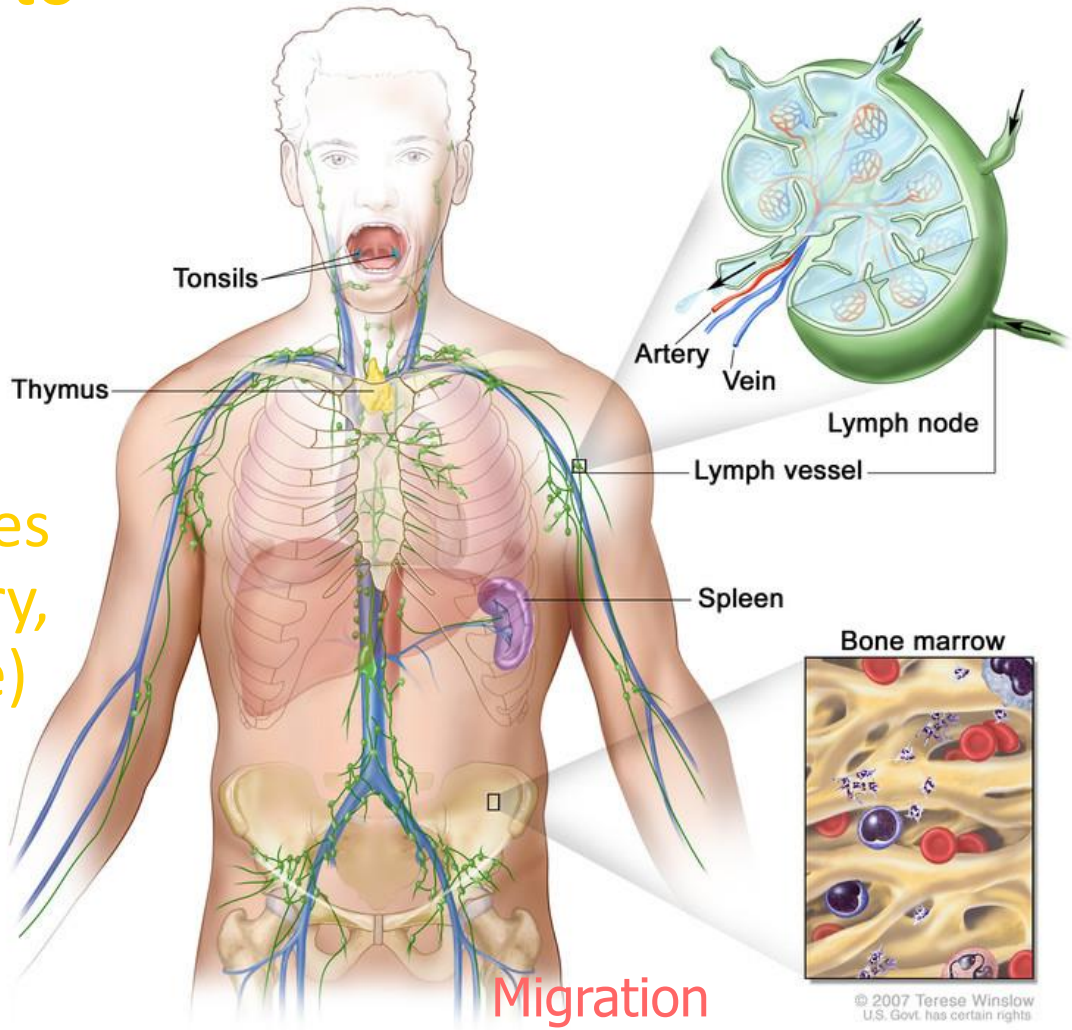
Play

"The Cell is Right"

to learn about the blood tree

Migration of mature general B and T cells to secondary lymphoid organs:

- Lymph nodes
- Spleen
- Tonsils
- External body surfaces (intestinal, respiratory, urinary, reproductive)



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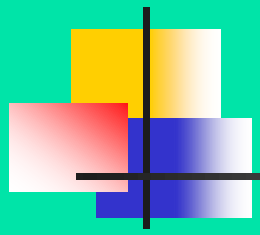

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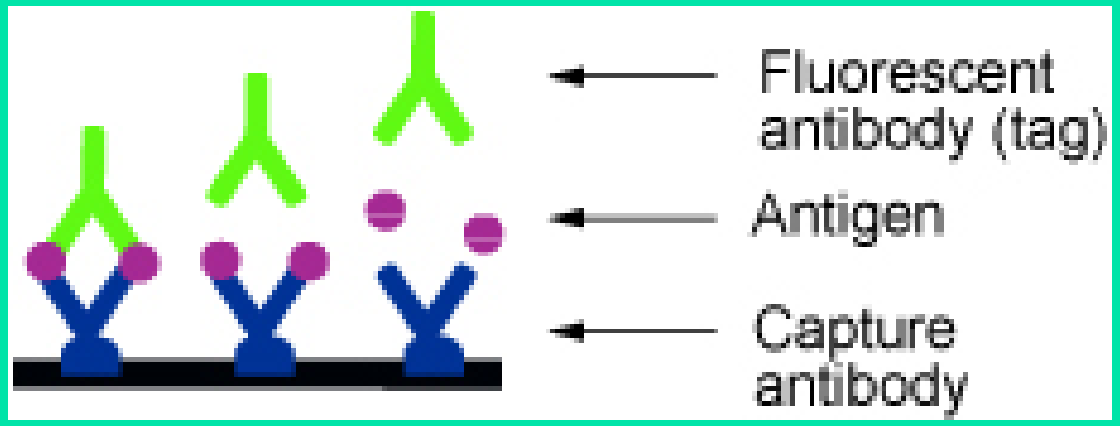
Immune activation and response

What triggers these cells to respond?



Antigen-antibody binding

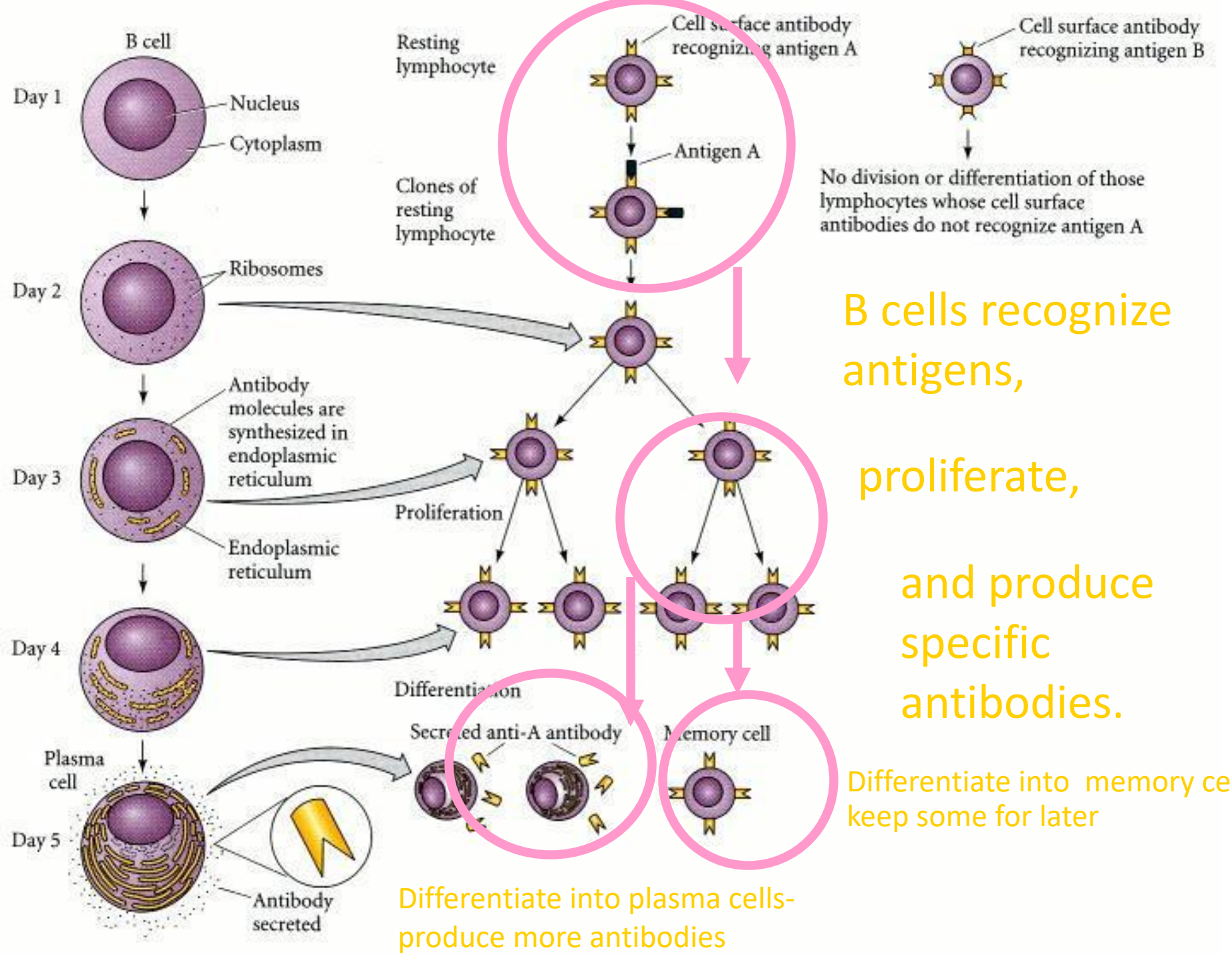
Structure, location and function of antibodies

1. Tag and disable antigen
2. Alert T cells, macrophages, leukocytes of presence

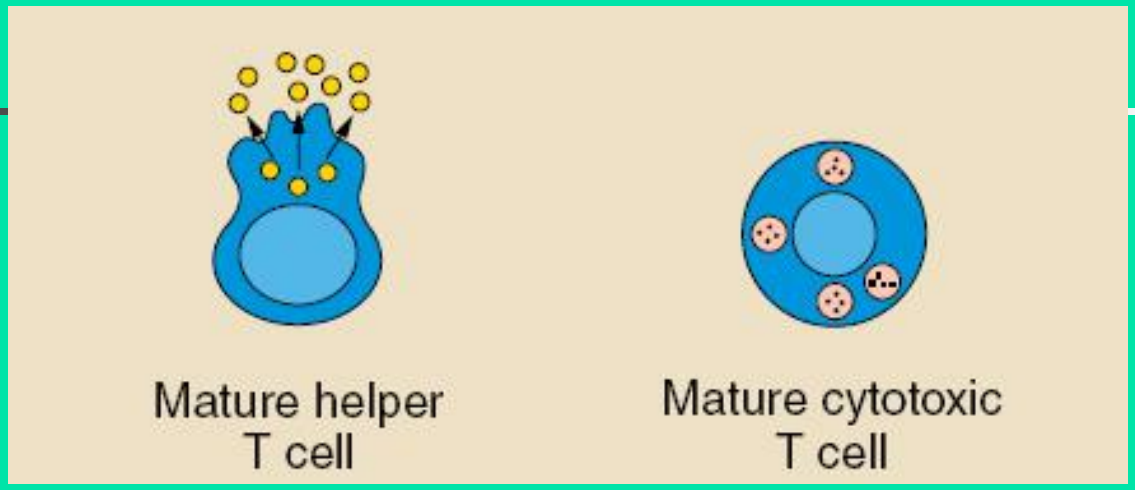
Cell response

B cells: recognize antigens, proliferate and produce specific antibodies.

- Differentiate into plasma cells- to produce more antibodies
- Differentiate into memory cells- keep antibodies in supply for activation from second encounter by same antigen

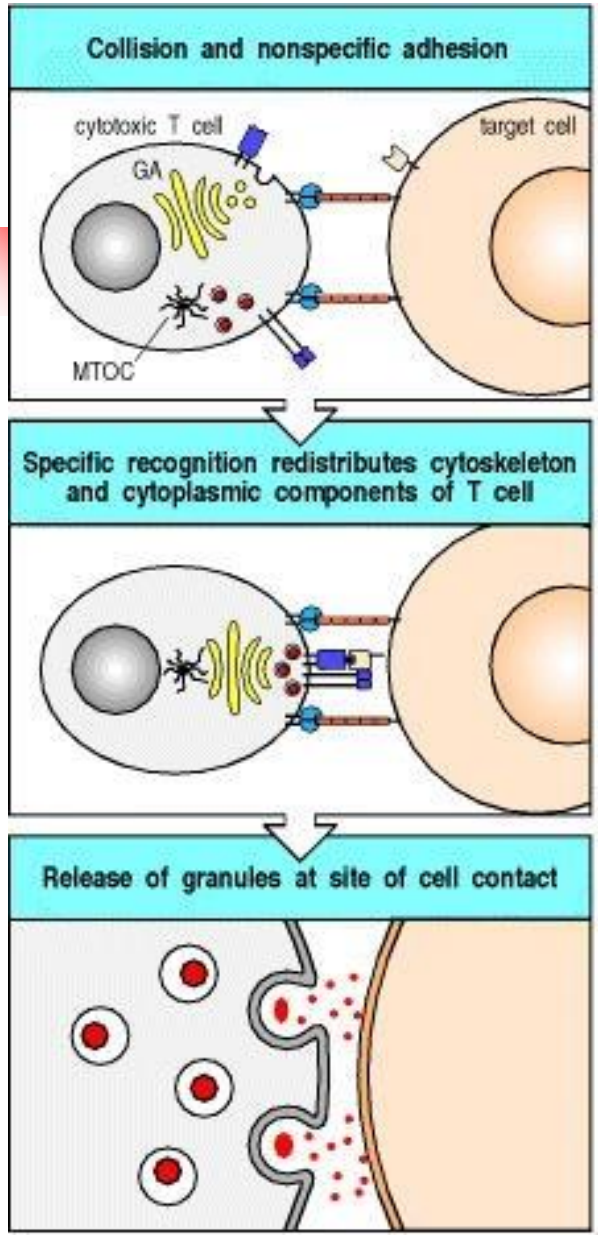

B cell
Day 1
Nucleus
Cytoplasm
Day 2
Ribosomes
Day 3
Antibody molecules are synthesized in endoplasmic reticulum
Endoplasmic reticulum
Day 4
Plasma cell
Day 5
Antibody secreted
Resting lymphocyte
Cell surface antibody recognizing antigen A
Antigen A
Clones of resting lymphocyte
Proliferation
Differentiation
Secreted anti-A antibody
Memory cell
Cell surface antibody recognizing antigen B
No division or differentiation of those lymphocytes whose cell surface antibodies do not recognize antigen A
B cells recognize antigens,
proliferate,
and produce specific antibodies.
Differentiate into memory cells- keep some for later
Differentiate into plasma cells- produce more antibodies

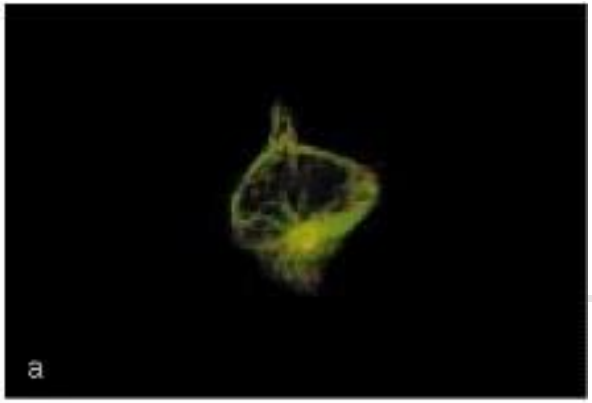
Cell response

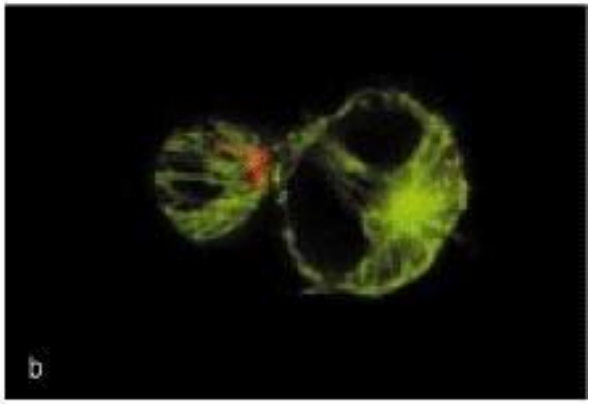


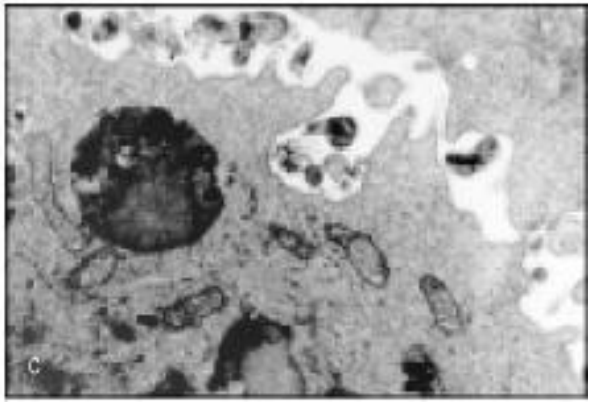
T cells: recognize and destroy tagged antigens and proliferate

- Cytotoxic T cells bind to antigen on plasma membrane of target cells and directly destroy the cells
- Helper T cells activate B cells, cytotoxic T cells, Natural Killer cells and macrophages
- *Remaining cells can respond to secondary exposure*

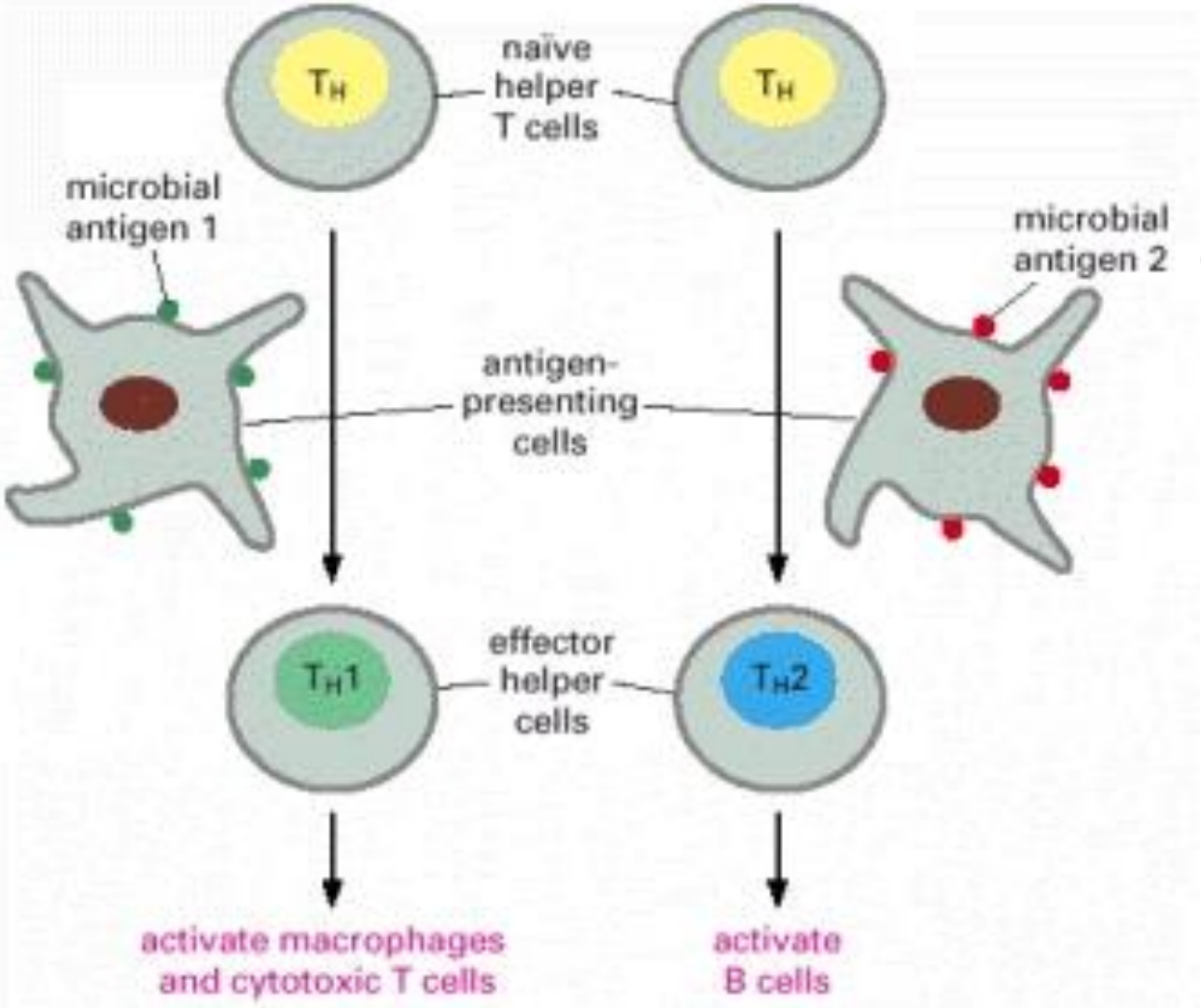








Cytotoxic T cell binds to antigen on plasma membrane of target cells and directly destroy the cells



Helper T cells activate B cells, cytotoxic T cells, natural killer cells and macrophages

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Why do stem cell transplants fail?

- Immune issues impact stem cell therapies
- Major Histocompatibility Complex is a person's combination of cell surface proteins that lymphocytes use to tell "self" from "non-self"
- **Allogeneic** transplants fail because there isn't a match, and lymphocytes destroy the non-self cells

Immune tolerance research

- Currently, transplant recipients need immune suppression - giving drugs for long periods of time to the patient
  - Dulls the immune response to non-self
  - Increases susceptibility to disease
- Immune tolerance: the future?
  - Antigen-specific immune tolerance would use drugs on the cell transplant to make them **tolerogenic**

Future of Immunotherapy

- Play video of Jeffrey Bluestone, UCSF