

LEC 7: THE IMMUNE SYSTEM AND CANCER

Lucentis Update

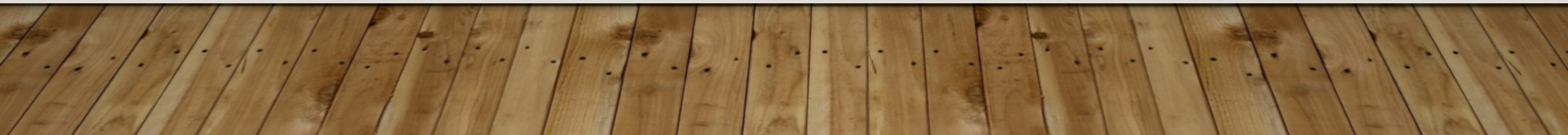
Last week, Novartis and Bayer were defeated in a UK lawsuit – brought by a group of NHS organisations – allowing them to continue using Roche's cheaper drug Avastin (bevacizumab) in place of Lucentis and Eylea for AMD, even though Avastin isn't approved for the indication. Meanwhile, Eylea has been gaining ground in wet AMD thanks to less frequent dosing, accord to GlobalData.

Strep, HIV, pregnancy test

Immunologic memory

Organ transplant

Spontaneous regression



DEFENDING THE HOST

Lymph nodes

In the lymph nodes are the cells (lymphocytes) of the immune system. These recognise and eliminate invading pathogens



White blood cells

How white blood cells attack pathogens both in the blood itself and in other tissues of the body



Spleen

The spleen assists the body in protecting itself against bacterial infections



Stomach and intestines

Stomach acid kills most harmful bacteria. Antibodies secreted by the intestinal cells attack viruses and other pathogens that have landed in the intestinal tract



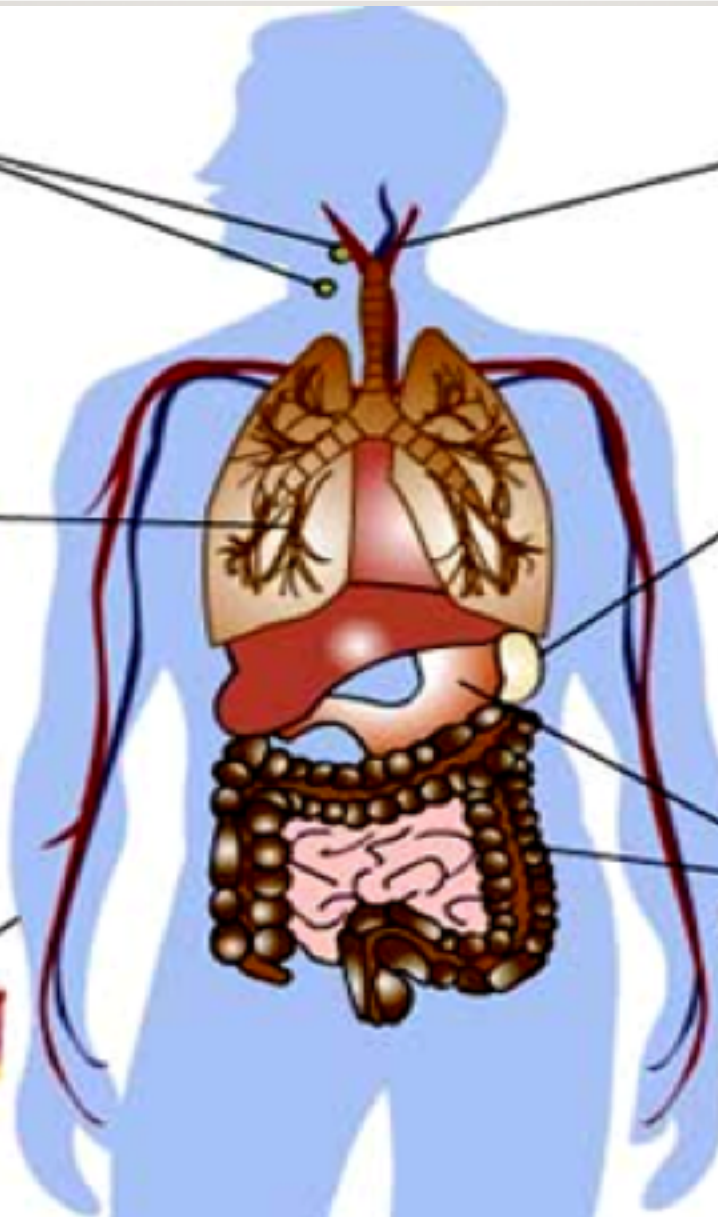
Respiratory system

The cilia (fine hair-like projections) line the airway and move mucus and contaminants upward and out of the respiratory tract



Skin

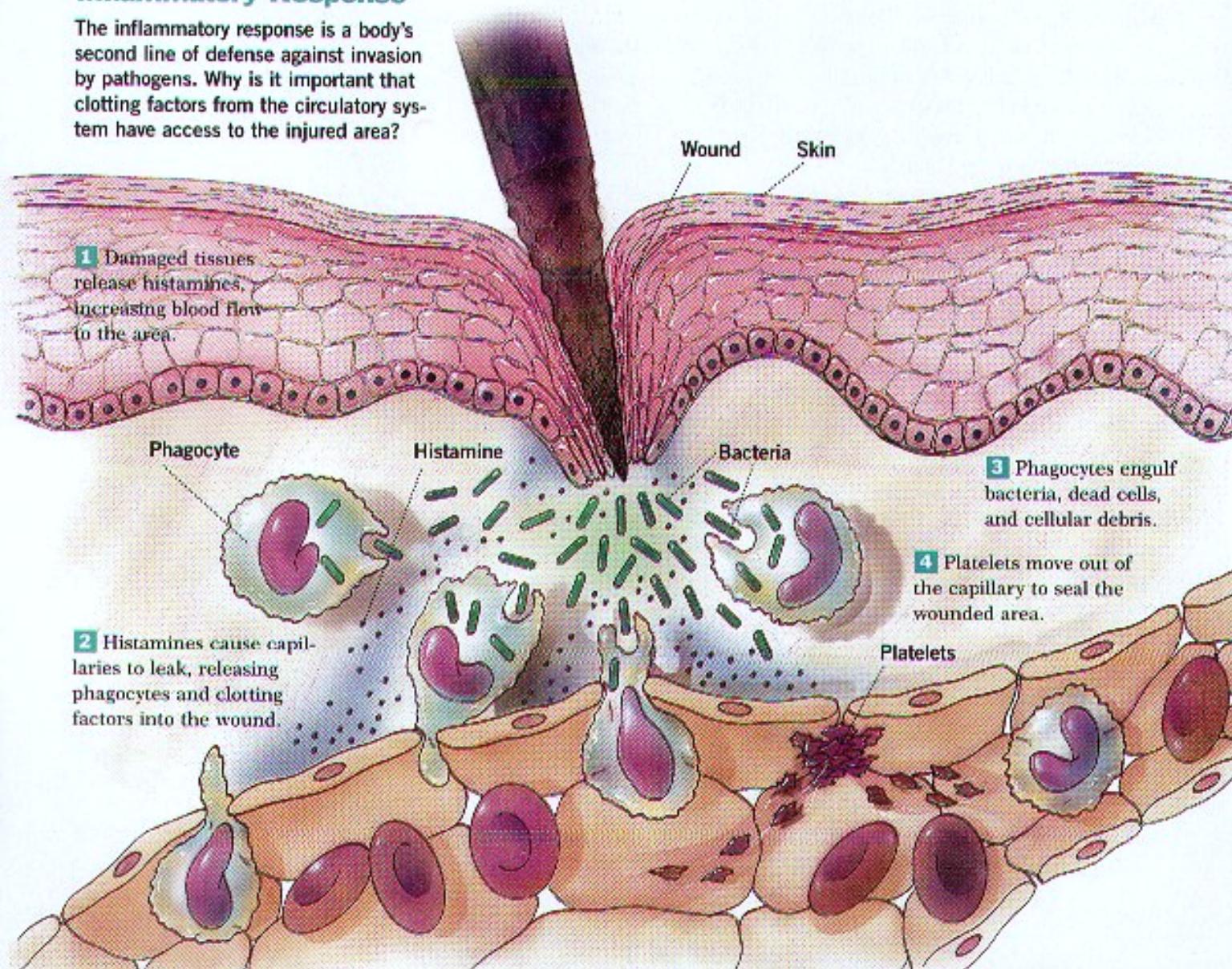
The skin forms a very effective barrier against invading pathogens



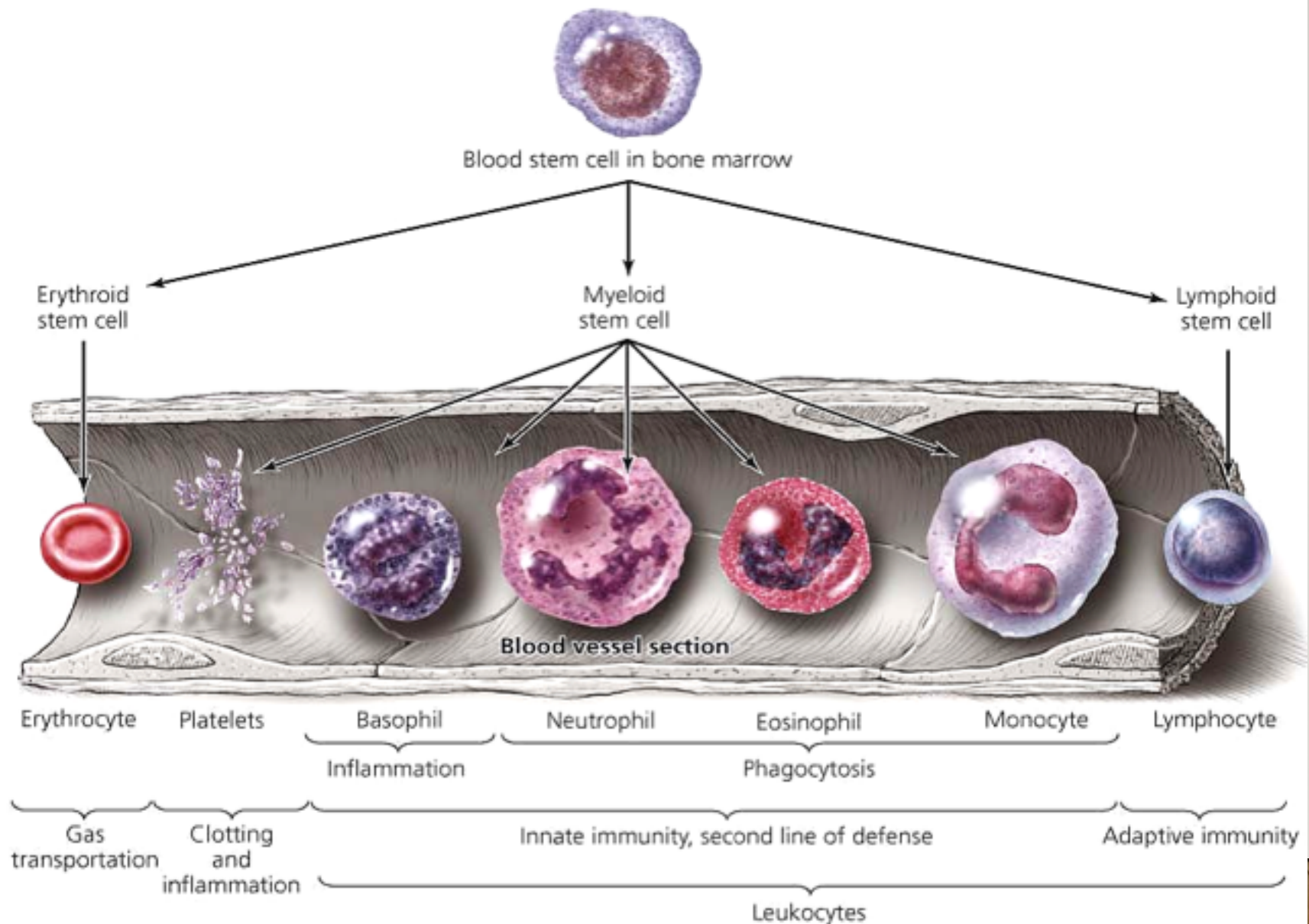
Swelling, redness, warmth

Steps of the Inflammatory Response

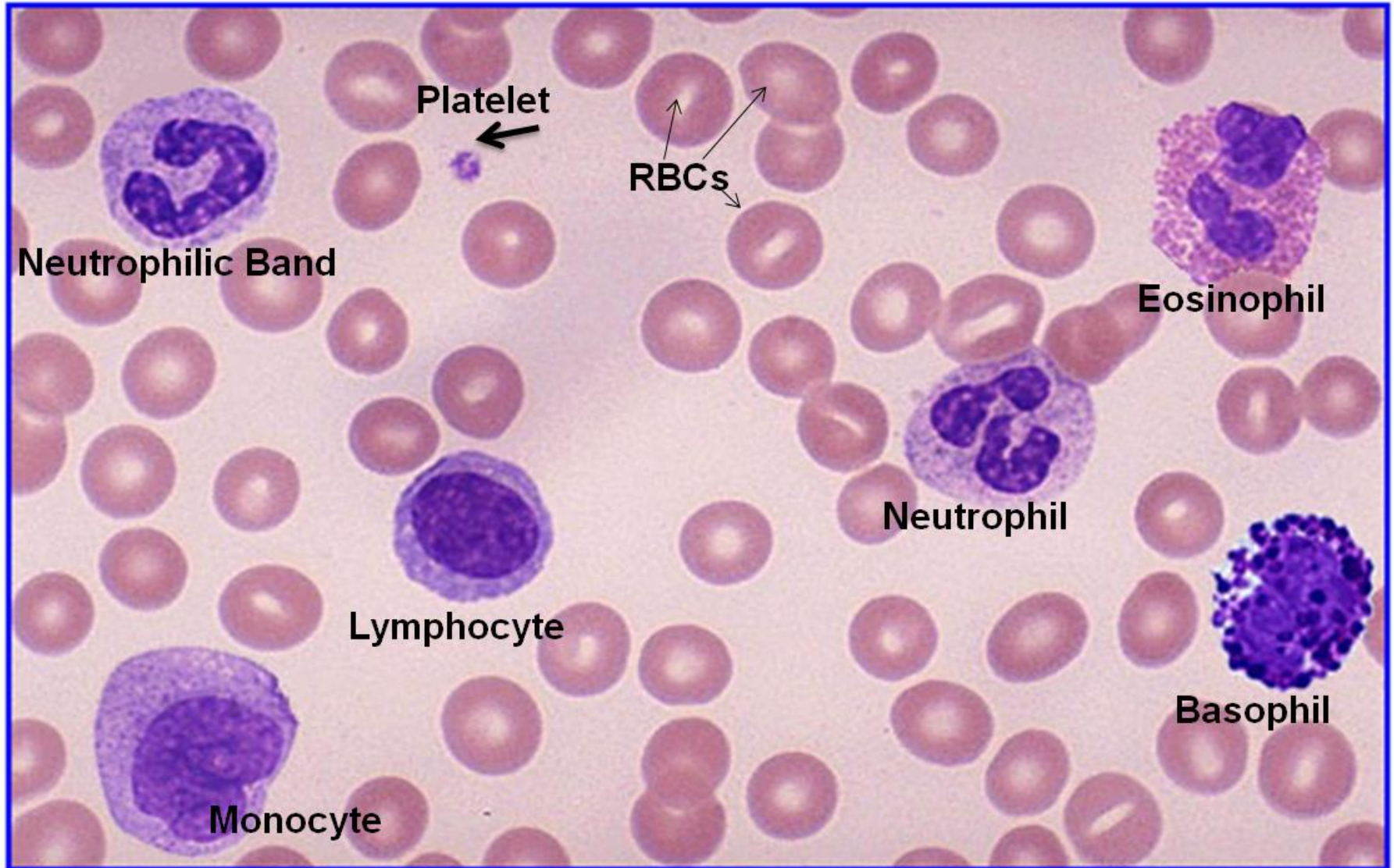
The inflammatory response is a body's second line of defense against invasion by pathogens. Why is it important that clotting factors from the circulatory system have access to the injured area?



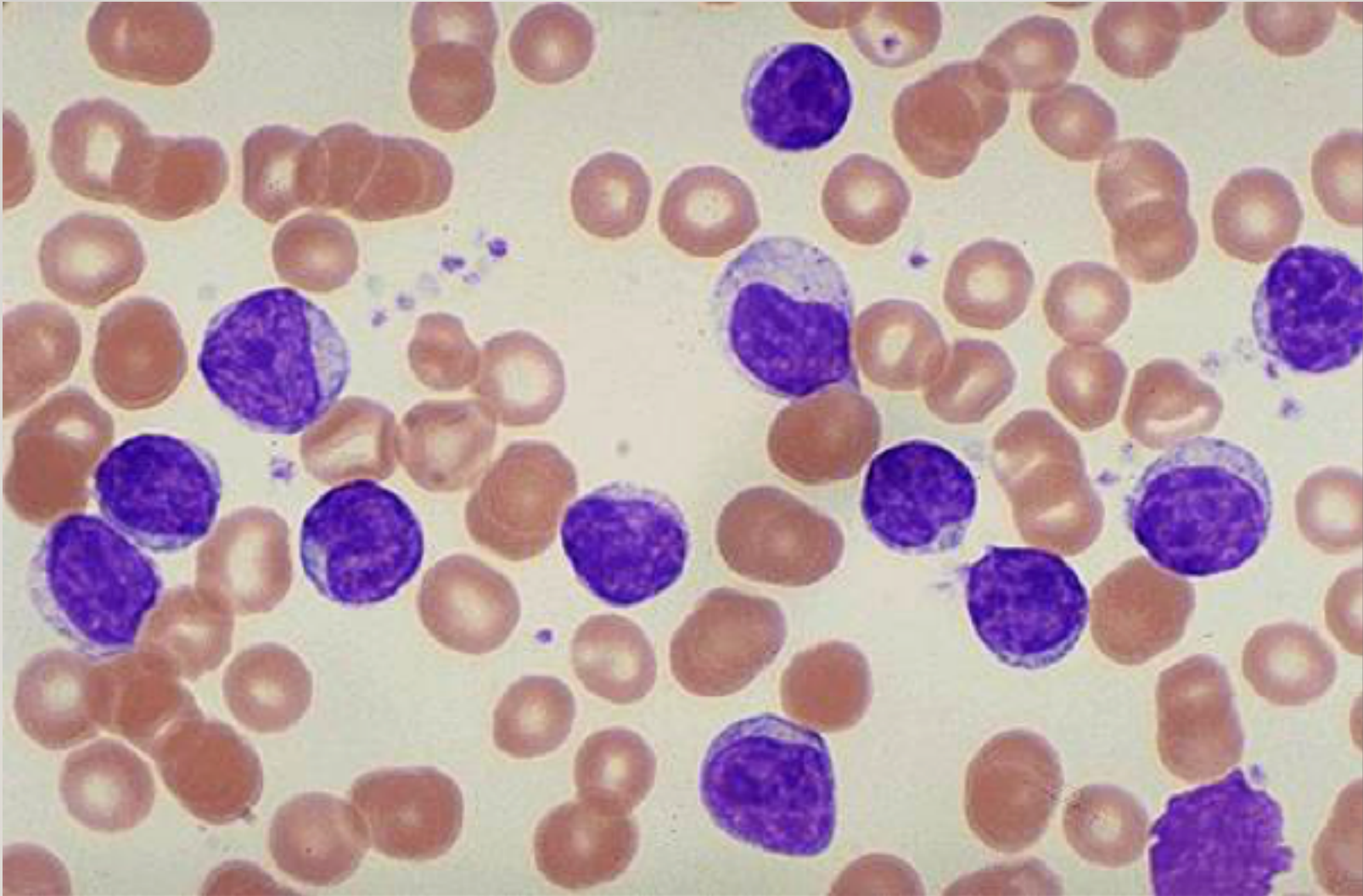
CELLS OF THE INNATE IMMUNE SYSTEM



PERIPHERAL BLOOD CELLS

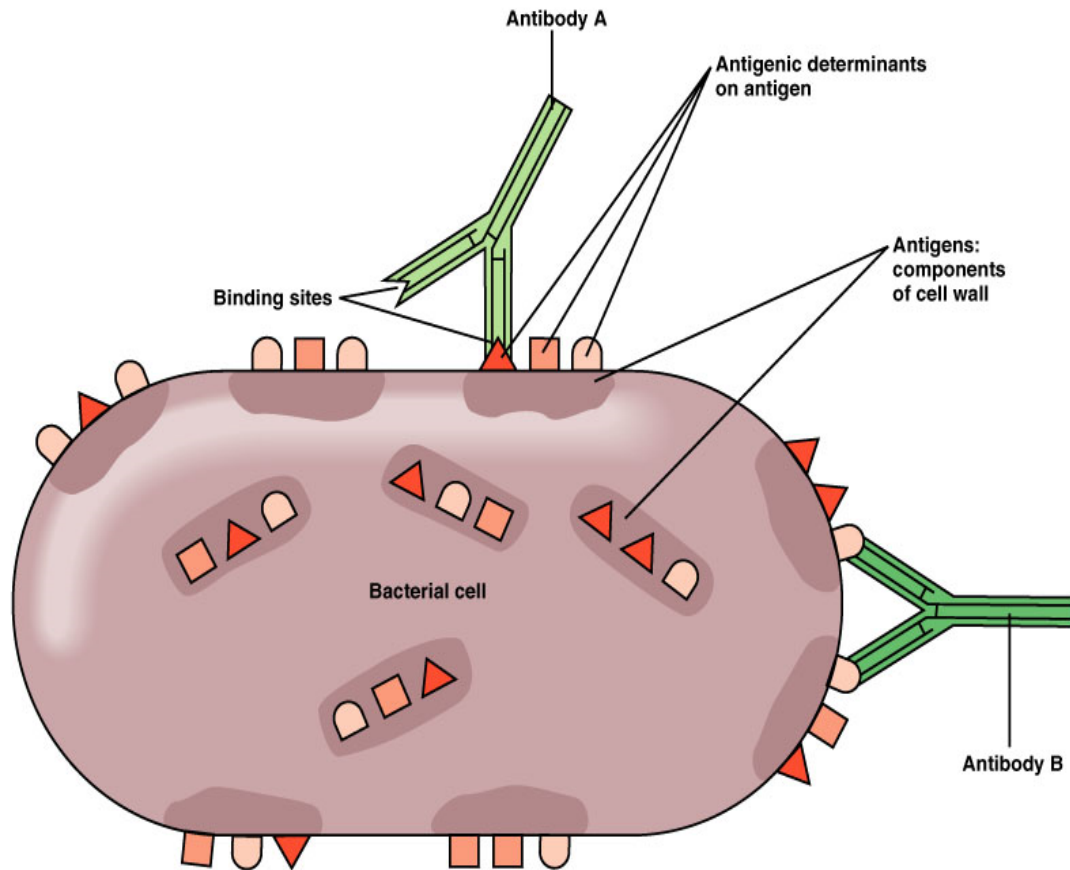


CHRONIC LYMPHOCYTIC LEUKEMIA



A common type of indolent (slowly progressing) cancer in which too many lymphocytes (white blood cells) are found in the peripheral blood and bone marrow. Most patients with CLL are older than 50 years and have no symptoms at the time of their diagnosis.

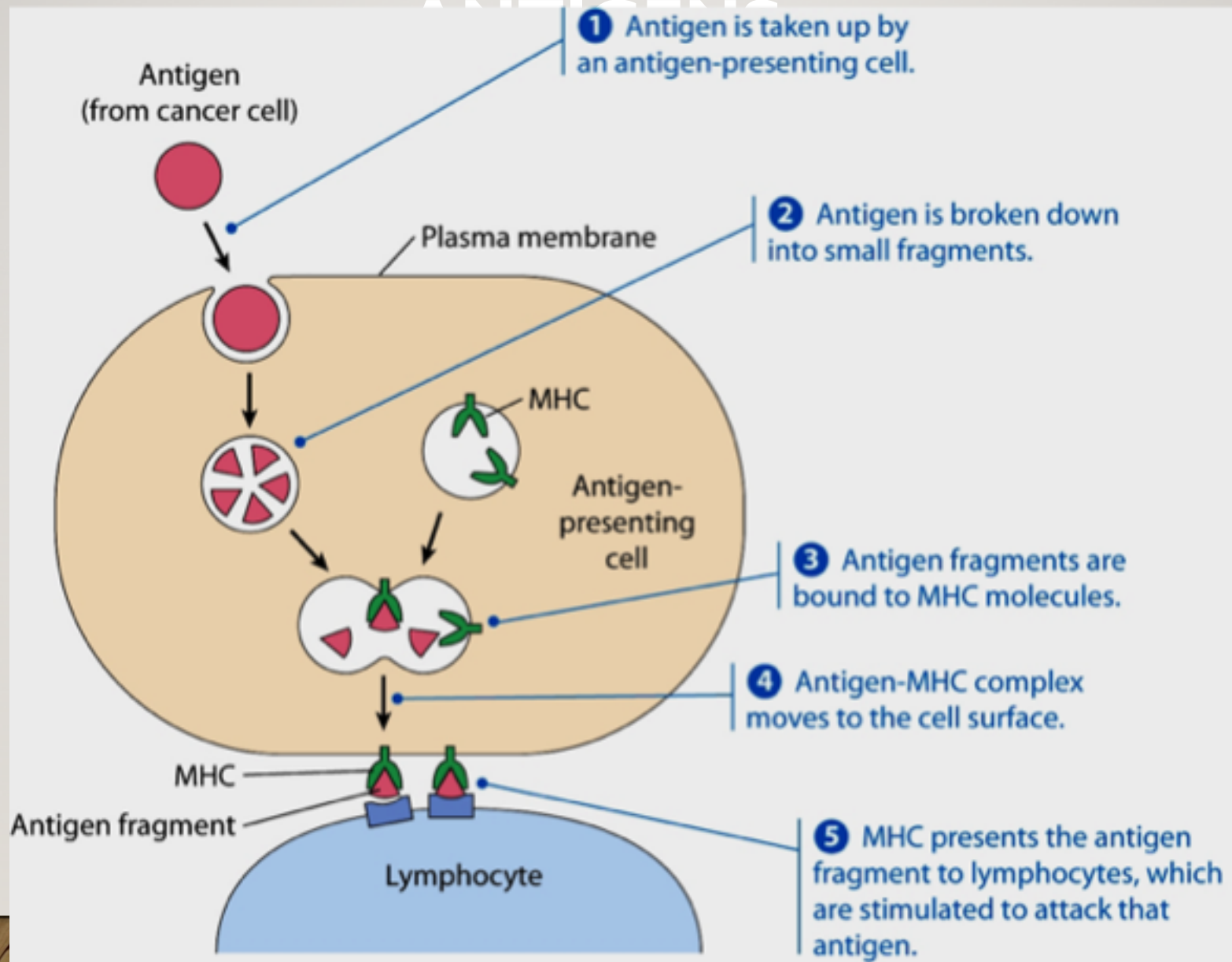
Antigen & Antibody



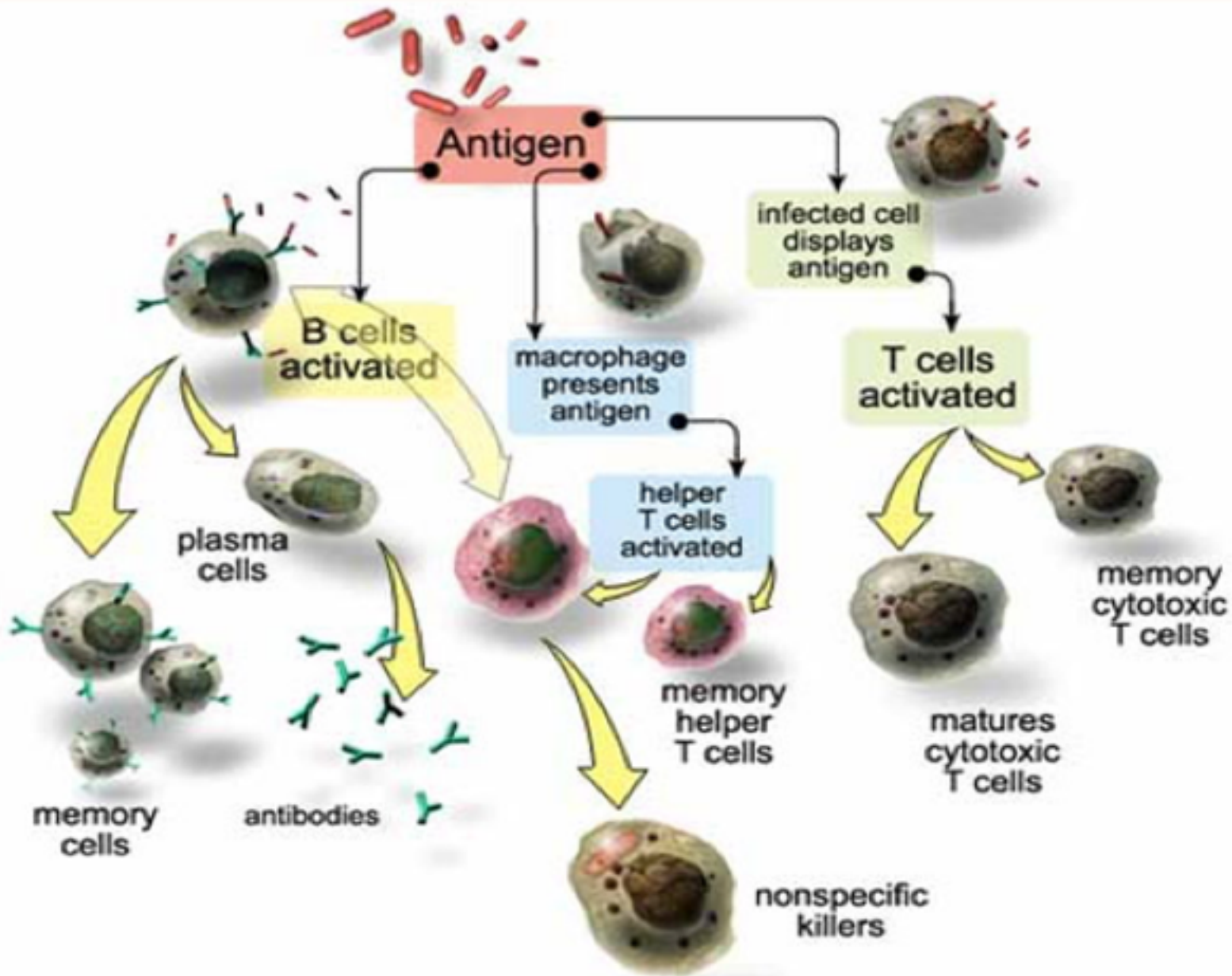
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- ❑ **Antigen** is a “foreign” substance that induces the production of antibodies because it is recognized by the immune system as a threat
- ❑ **Antibody** is a protein produced in response to antigen invasion

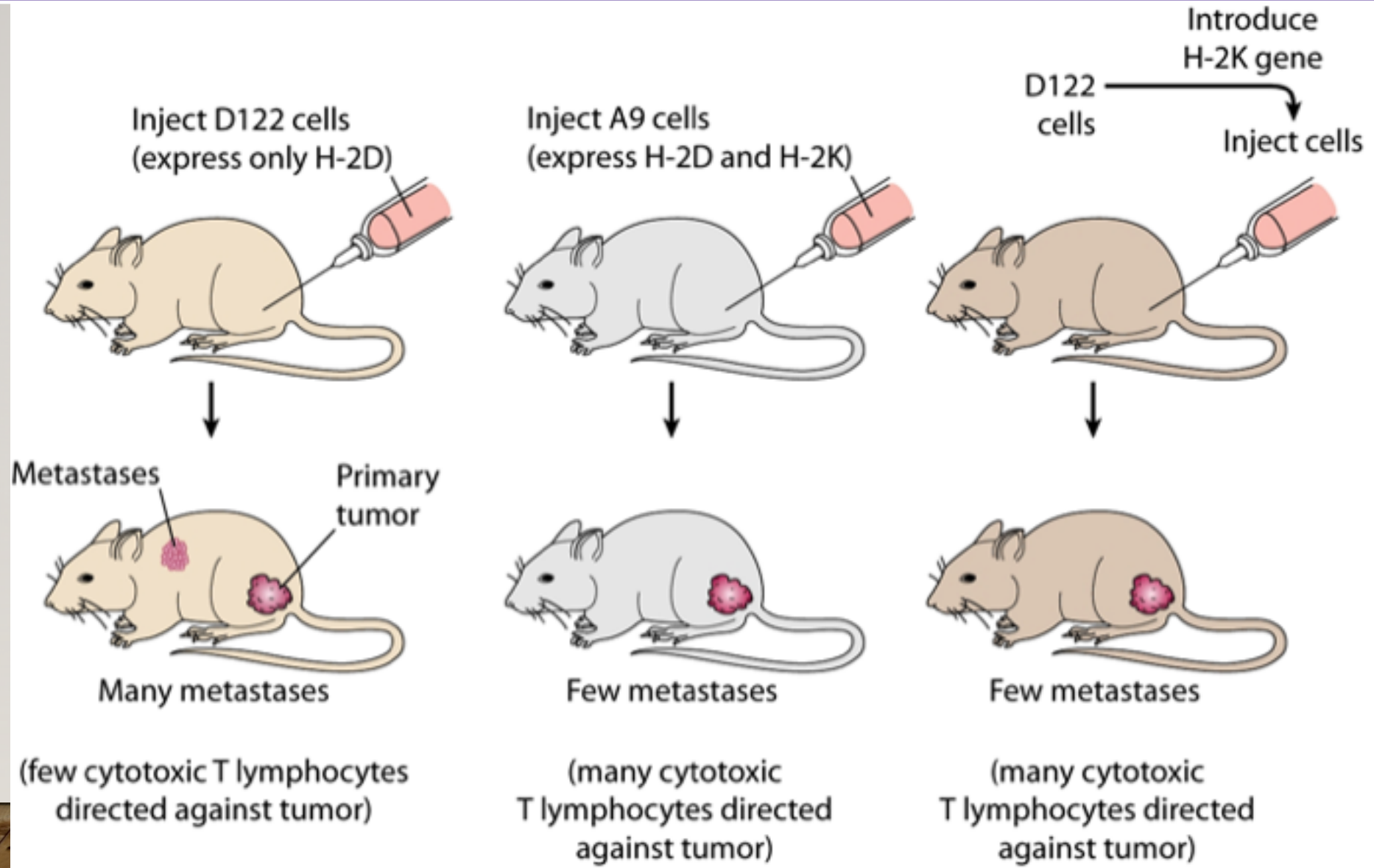
PRESENTATION OF CANCER



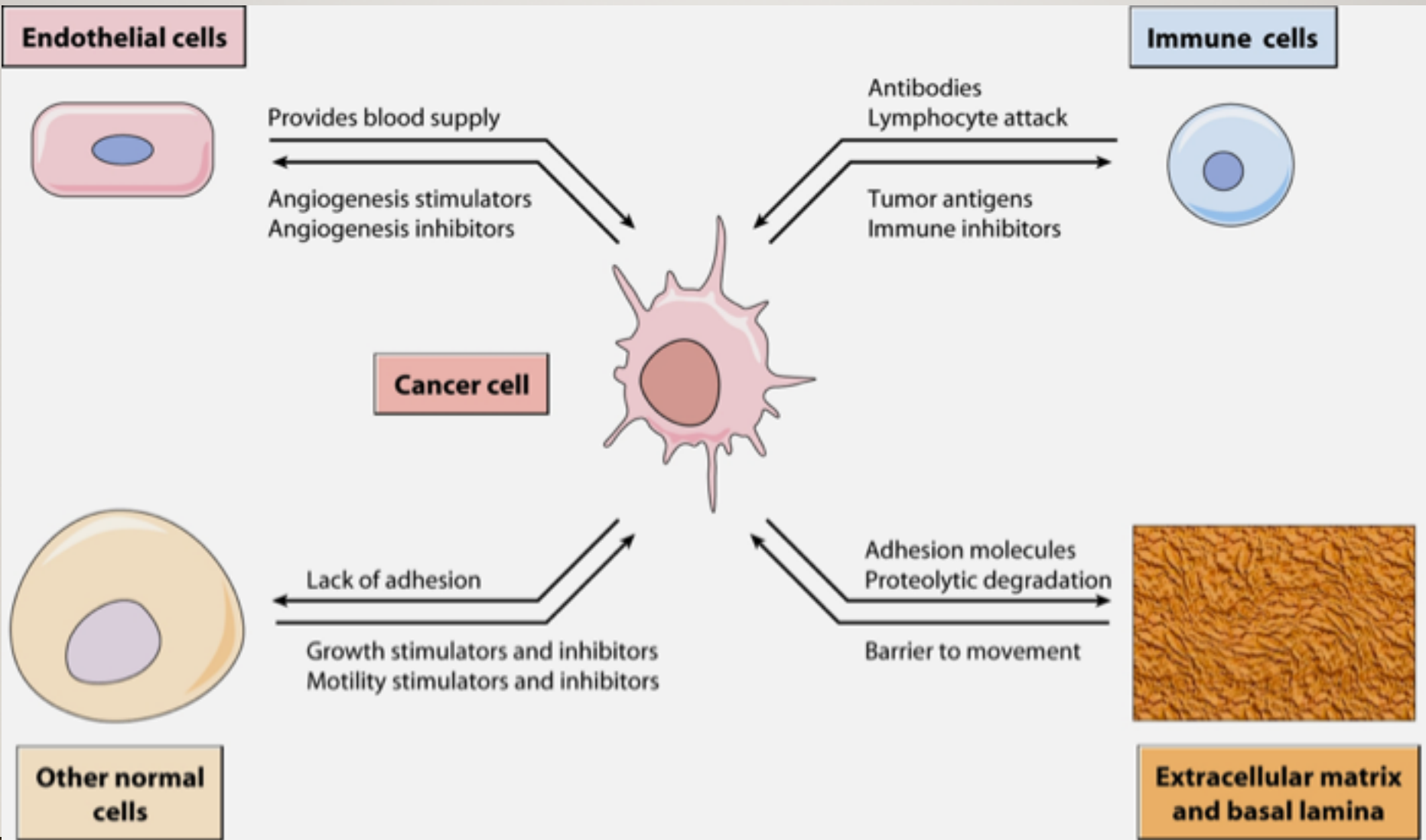
HOW THE IMMUNE SYSTEM WORKS



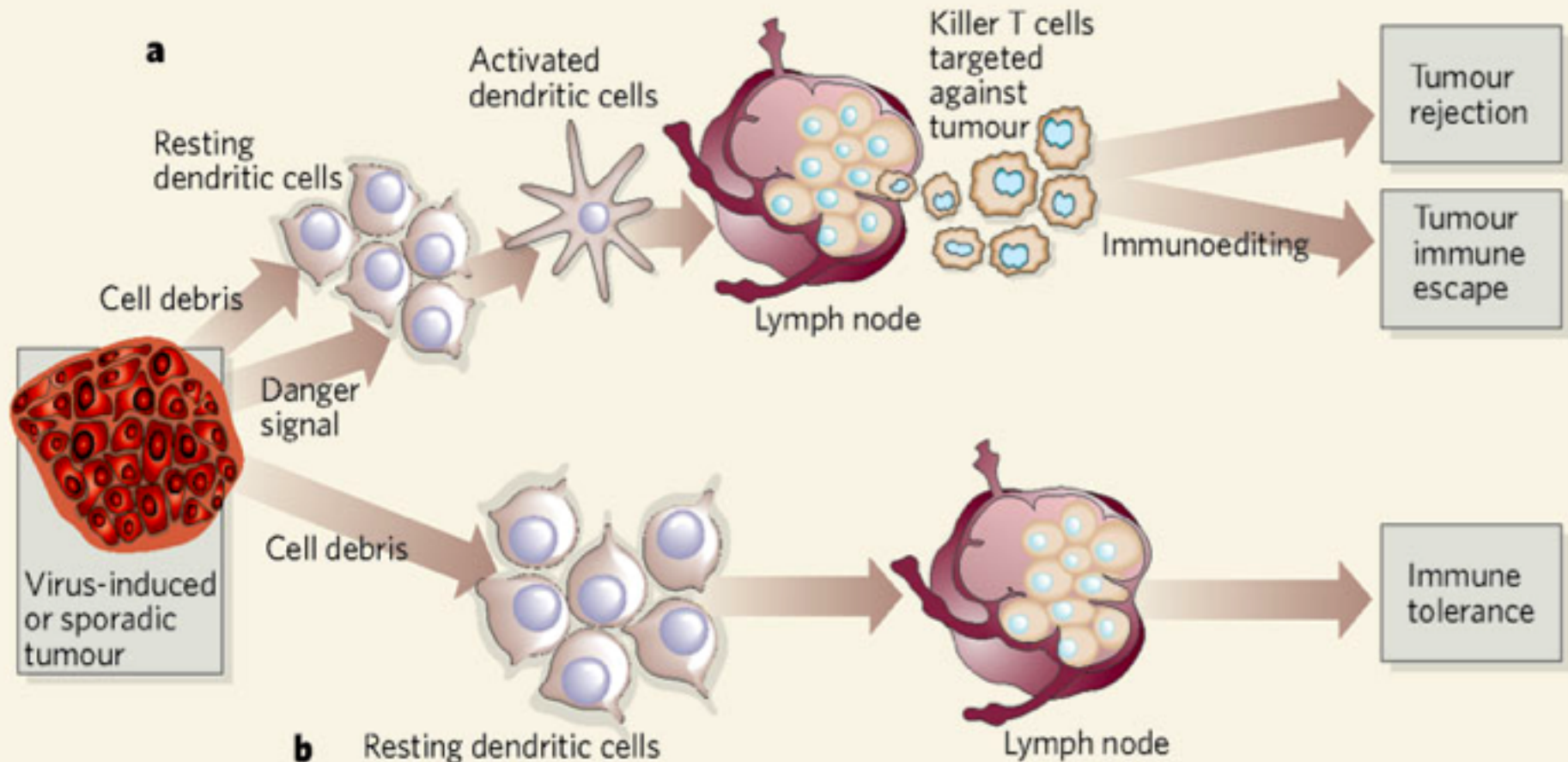
EFFECTS OF IMMUNE RECOGNITION ON METASTATIC COMPETENCE OF CANCER CELLS



TUMOR HOST INTERACTIONS



CANCER IMMUNOLOGY: CAT AND MOUSE GAMES



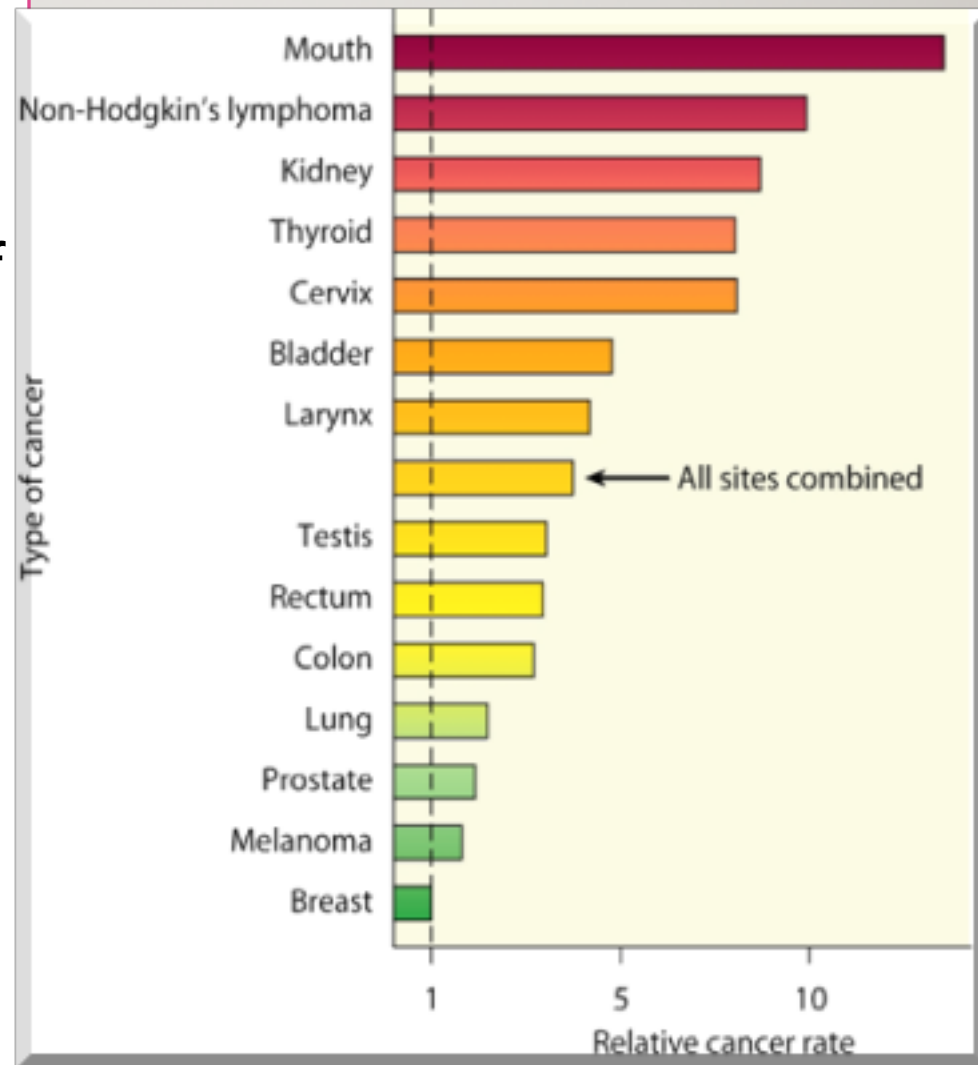
Immunoediting: immune system shapes the tumor

IMMUNE EVASION BY CANCER

- ❑ Tumor cells look like normal host cells
- ❑ *Tumor progression*- natural selection favors cancer cells that do not induce strong immune response; strongly immunogenic cells are killed off
- ❑ Cancer cells surround themselves with dense connective tissue that shields from immune attack
- ❑ Some cancers divide so quickly that they overwhelm the immune system
- ❑ Some cancer cells produce molecules that destroy T cells

EVIDENCE FOR IMMUNE REACTIVITY TO TUMORS

- ❑ Certain tumors regress spontaneously (e.g., *melanomas*, *neuroblastomas*).
- ❑ There is an increased incidence of malignancies (particularly *lymphoreticular tumors*) in immunodeficient patients.
- ❑ Antibodies and immune T-lymphocytes have been detected in patients with tumors.
- ❑ The young and the very old have an increased occurrence of tumors
- ❑ We can be immunized against tumors.



From L. J. Kleinsmith, *Principles of Cancer Biology*. Copyright (c) 2006 Pearson Benjamin Cummings.

IMMUNOTHERAPIES

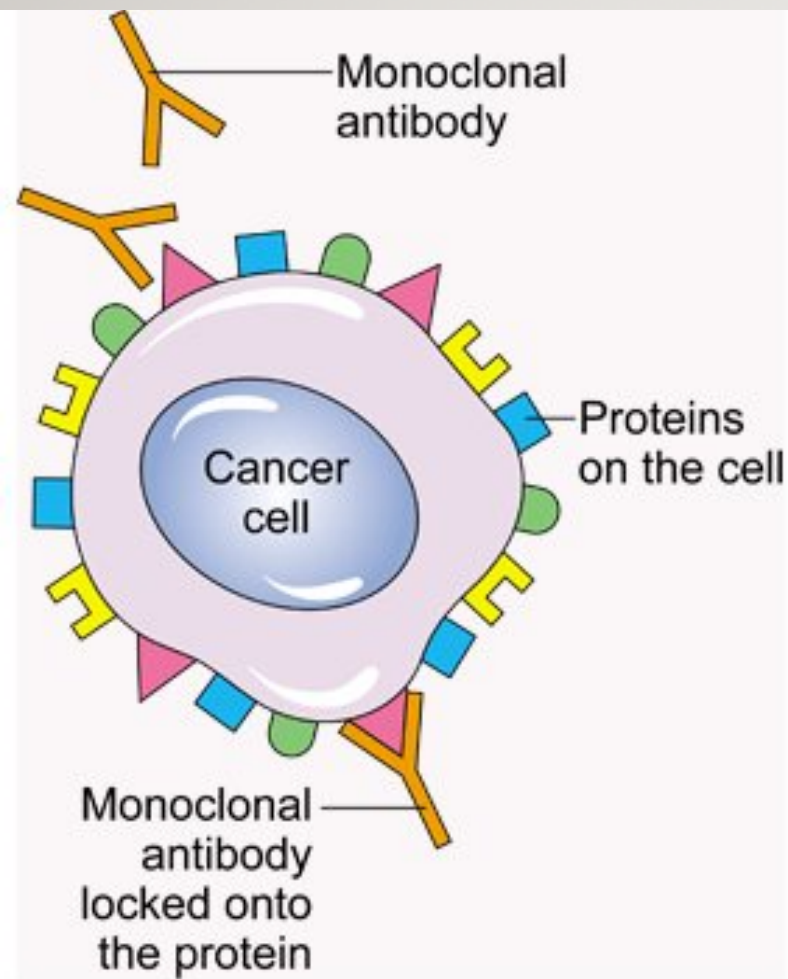


Diagram showing a monoclonal antibody attached to a cancer cell
© CancerHelp UK

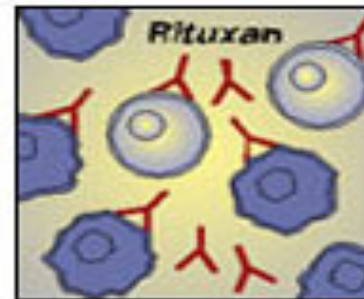
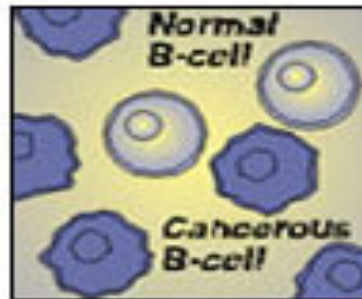
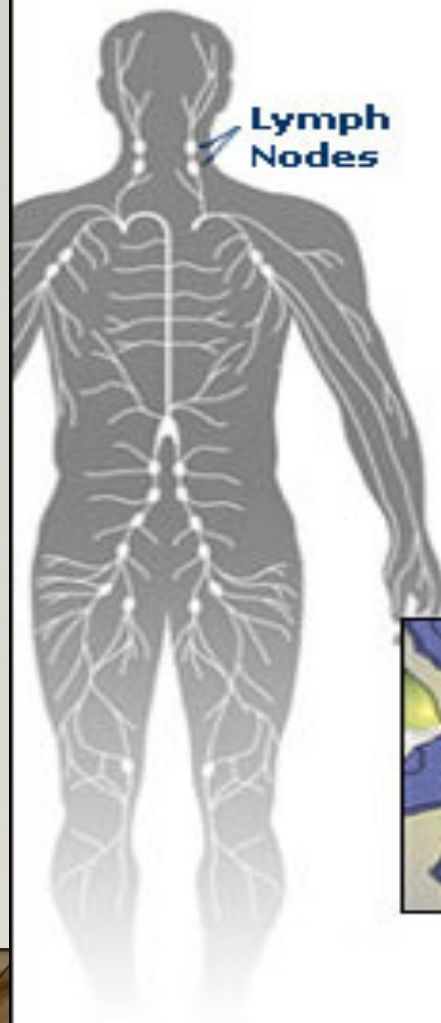
- ❑ Rituximab (Mabthera) recognizes CD20 protein on the outside of non-Hodgkin's lymphoma cells
- ❑ Bevacizumab (Avastin) targets growth factors and is used to treat bowel cancer and breast cancer
- ❑ Trastuzumab (Herceptin) recognizes breast cancer cells that produce too much of the protein HER 2 (are 'HER 2 positive')

RITUXAN AND LYMPHOMA TREATMENT

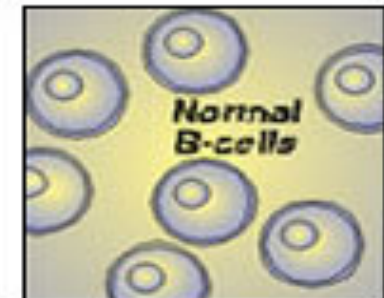
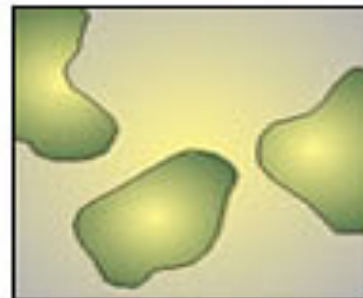
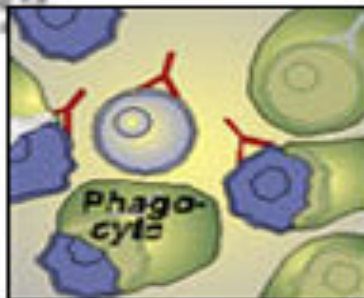
PERSONALIZED IMMUNOTHERAPY

Non-Hodgkin's lymphoma most commonly occurs in the lymph nodes and is a cancer of B-cells.

Rituxan, a therapeutic antibody, binds to the CD20 protein found on normal and cancerous B-cells in vitro.



Rituxan recruits components of the body's immune system (phagocytes, etc.) to destroy B-cells.

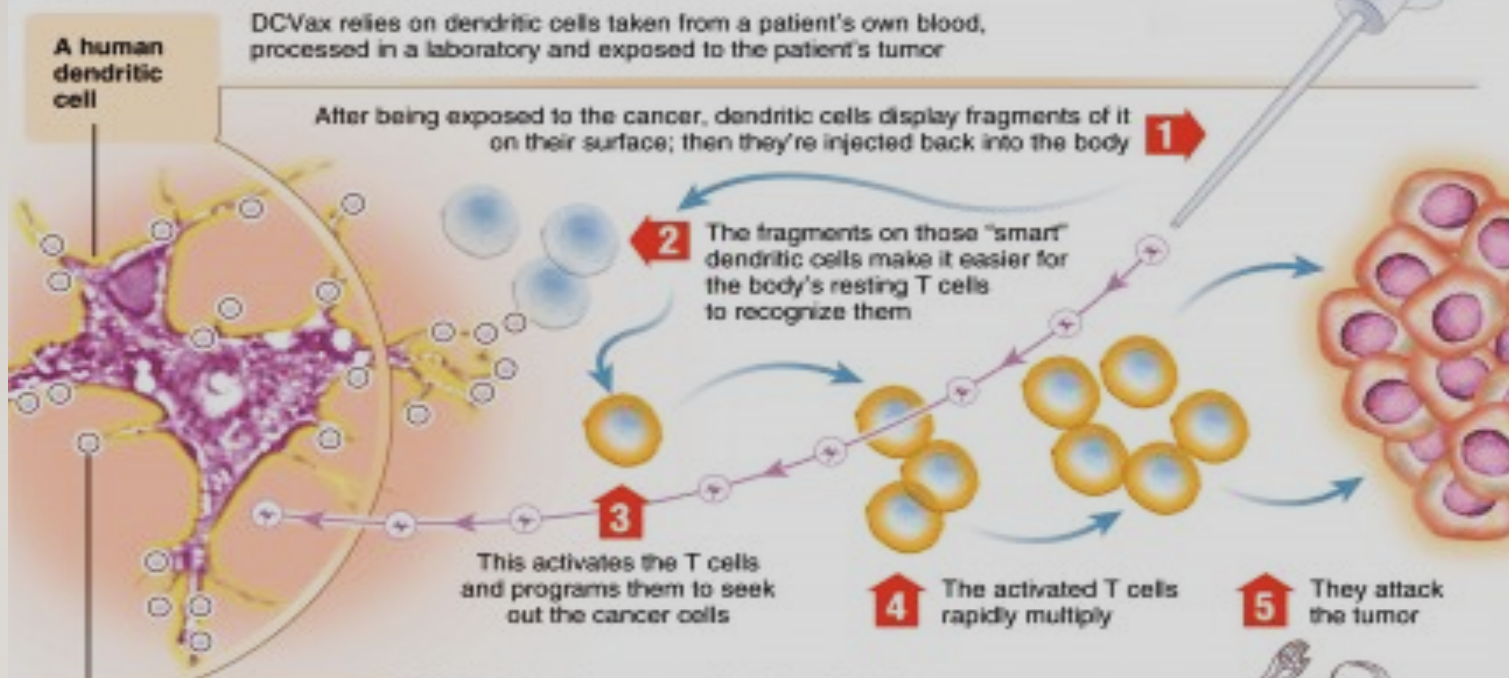


Once Rituxan has cleared the body, normal B-cells can begin to grow again.

Teaching the body's immune system to fight cancer

DCVax is an experimental cancer vaccine designed to trigger an immune response and direct it to attack the cells of cancerous tumors. A look at how it's supposed to work:

How the vaccine is designed to operate



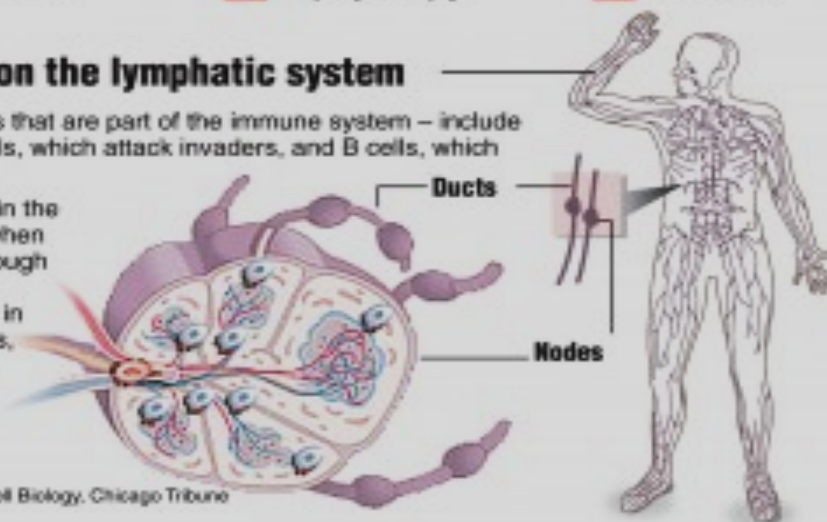
Specialized white blood cells whose job is to find an attacking foreign cell in the body, break it down and carry fragments of it (antigens) into the immune system via the lymphatic system

There, dendritic cells present the antigens to T and B cells, telling these defenders of the body where to find the invader and to attack it

Why it relies on the lymphatic system

Lymphocytes – cells that are part of the immune system – include killer cells and T cells, which attack invaders, and B cells, which make antibodies

They are produced in the lymph nodes and, when activated, travel through the lymph ducts; lymphocytes collect in the adenoids, tonsils, spleen, appendix, small intestine



Why cancer is so hard for our immune system to fight

- The body's immune system fights infection by attacking any foreign substance it detects

- But cancer cells are mutated versions of the body's own cells, and they usually don't trigger the immune system

- The goal of new vaccines is to help the immune system identify, "target" and kill cancer cells, to teach them to see cancer as an invader

Cancer Vaccine

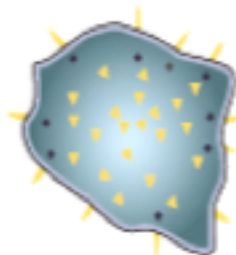
On Thursday, an FDA advisory panel endorsed the safety and effectiveness of Provenge, which could become the first approved treatment to specifically direct the immune system to attack tumors. Here is how it works:



1. White blood cells are drawn from the patient. Certain immune system cells are isolated.



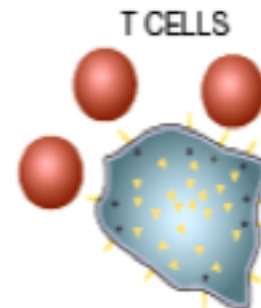
2. The immune system cells are exposed to a protein often found in prostate cancer cells.



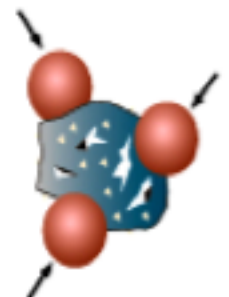
3. These immune system cells display part of the protein on their surface, alerting the immune system.



4. Days after the white cells are drawn, these immune system cells are put back in the patient.



5. The body's T cells are stimulated...



6. ...multiplying in the body and attacking cancer cells bearing the protein.