

The normal immune system



windows of my lab

**Prof. Allan Wiik, emeritus director
Department of Autoimmunology
Statens Serum Institute, Copenhagen**

The immune defence

The innate immune system

Cells:

- "Eater cells" (phagocytes)
- Killer cells

Soluble factors:

- Antibodies
- Enzyme cascades
- Signaling molecules

The adaptive immune system

Cells:

- T-lymphocytes
- B-lymphocytes
- macrophages (phagocytes)

Soluble factors:

- Specific antibodies
- Signaling molecules

The immune defence

The innate defence:

Cells:

- Phagocytes
- Killer cells

Soluble factors:

- Antibodies
- Enzyme cascades
- Signaling molecules

The adaptive immune defence:

Cells:

- T-lymphocytes
- B-lymphocytes
- macrofages (phagocytes)

Soluble factors:

- Specific antibodies
- Signaling molecules

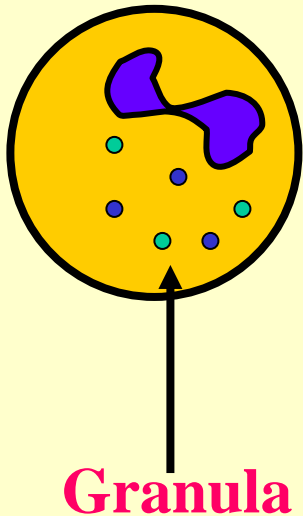


The two systems collaborate

The innate immune defence consists of:

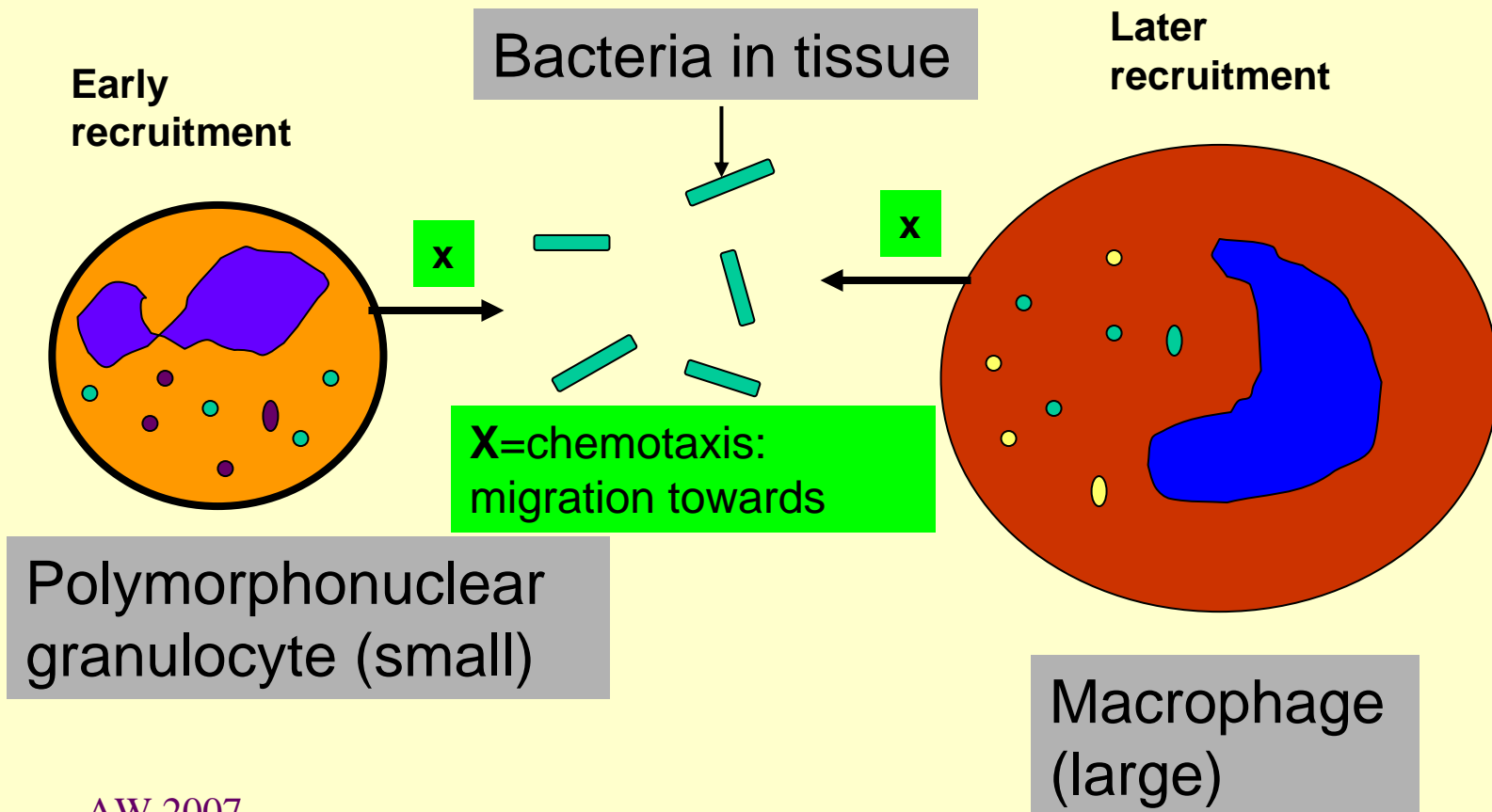
- natural killer cells (NK-cells)
- polymorphonuclear granulocytes (phagocytes)
- natural antibodies (IgM,IgG)
- complement (a series of proenzymes, that bind to cell surfaces after attaching to antibodies bound on the cell surface. They are activated into a series of proteins that help get rid of bacteria, virus, fungi, immune complexes.
- Signaling molecules, that activate cells to function adequately, so that both the innate and the specific immune defence act synergistically (potentiate each other) and in concert.

Polymorphonuclear granulocytes (PMNs)



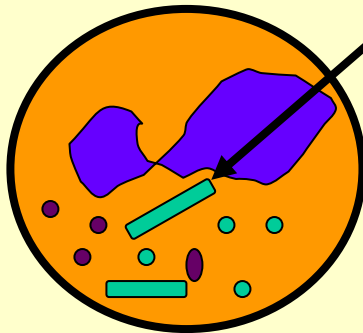
- Are produced from stem cells in the bone marrow and circulate in the blood stream
- Emigrate from the blood stream toward damaged tissue caused by foreign bodies, bacteria, combustion, chemicals etc. which are ingested (phagocytosed)
- Phagocytosed material is decomposed in the PMN into small inactive components
- PMNs constitute an immediate defence mechanism against invading foreign material (police force)
- They are attracted by chemotactically active molecules secreted by cells or created by the inflammatory process.

Phagocytosis by "eater cells".I

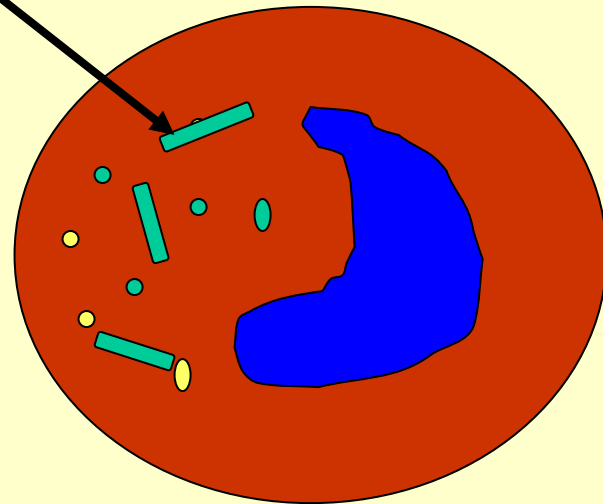


Phagocytosis (ctd.) II

Bacteria are killed and degraded

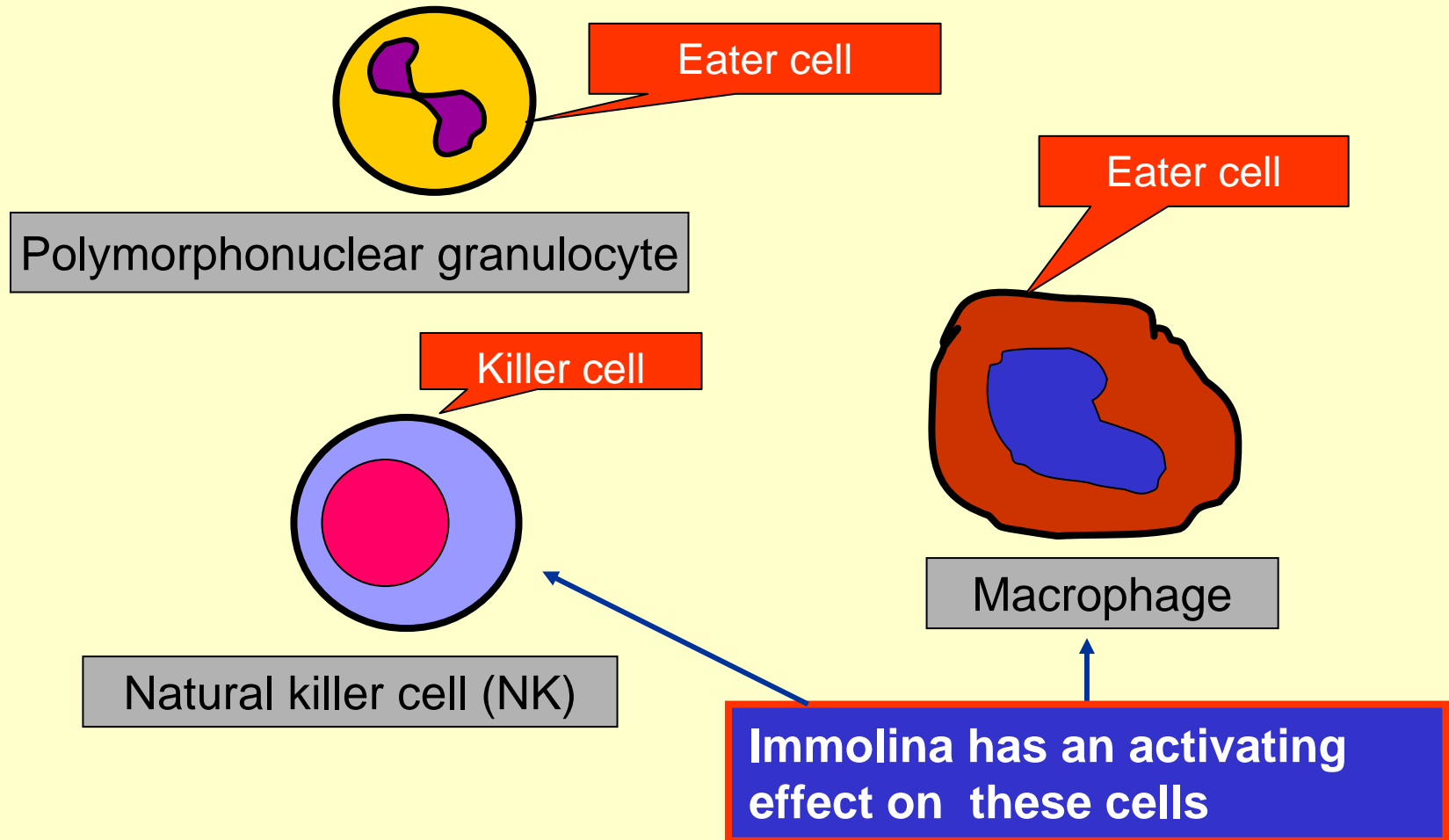


PMN with ingested
(phagocytosed) bacteria



Macrophage with
phagocytosed bact.

Interacting cells. I



Cells in the immune system

Plasma cell: produces and secretes antibodies

B-lymphocyte

Immobilina effect

Precursor of antibody-producing plasma cell

"Conductor"

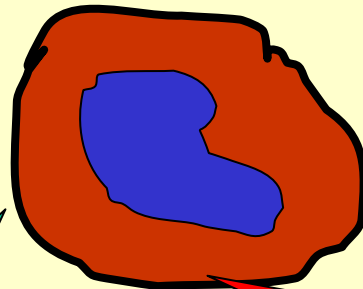
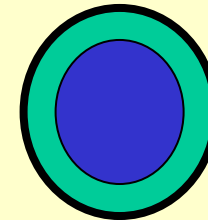
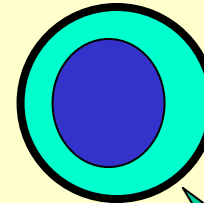
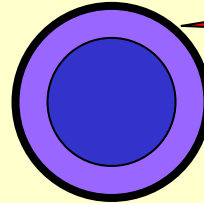
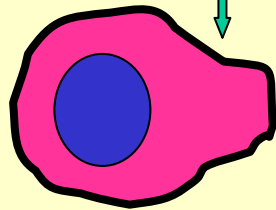
Th

Tc

T-lymphocytes

Macrophage

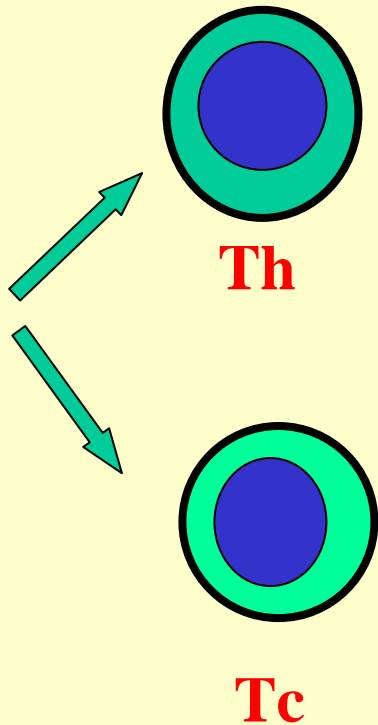
Antigen-presenting "eater cell"



Specific immune defence

- Constituted by **Th-lymphocytes**, that after contact with and presentation of antigen via macrophages stimulate specific B-lymphocytes to antibody production, resulting in antibodies fitting perfectly to the antigen shape.
- B-lymphocytes divide, multiply, and become plasma cells, that produce large amounts of specific antibodies.
- **Tc-lymphocytes**, that after contact with and presentation via macrophages are stimulated to divide and secrete lymphokines (small signaling molecules that give messages to other cells) and cytotoxic enzymes that kill target cells.

T-lymphocyte functions I



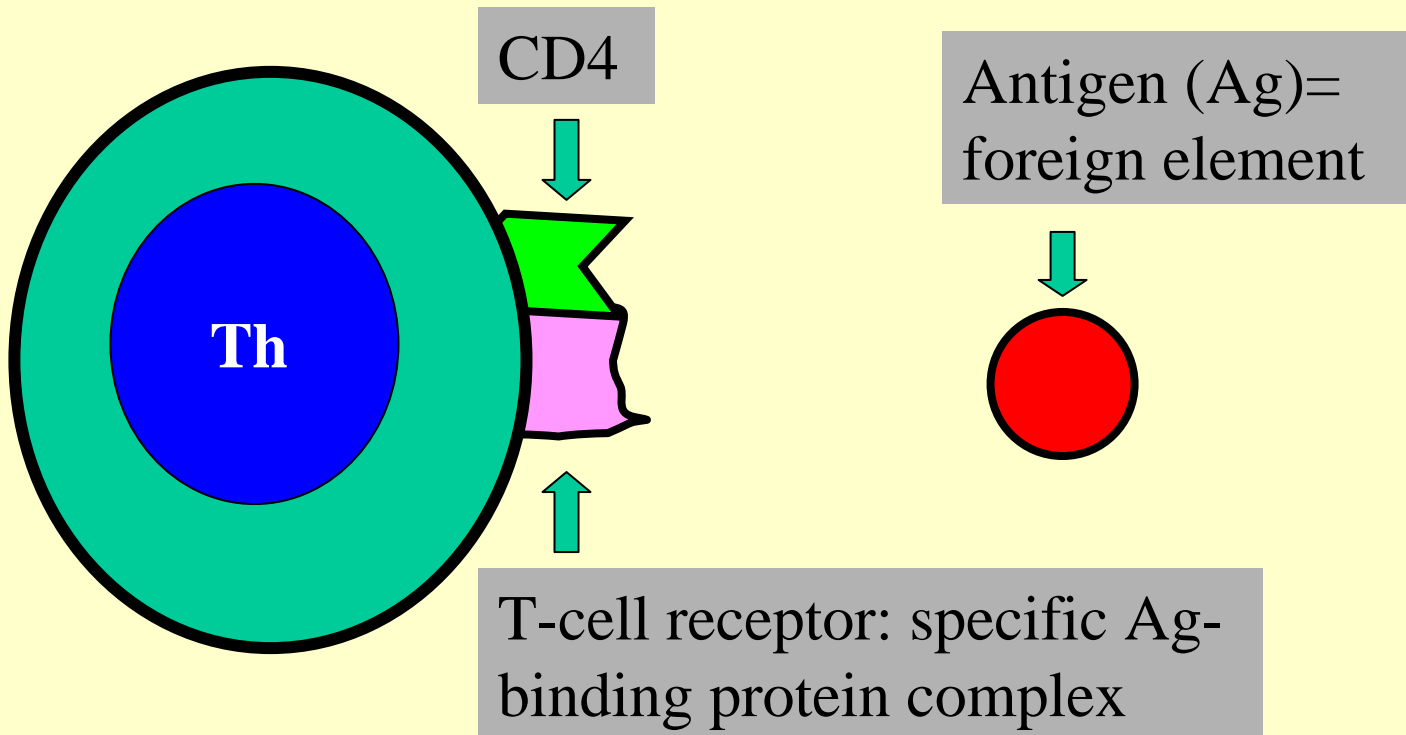
T-helper cells (*Th*)

- ”Conductors” in the immunological orchestra
- constitute around 1/2 of all lymphocytes
- made in the bone marrow, are matured in thymus
- after binding to antigen they are activated as Th cells and produce a number of signaling molecules (lymphokines)

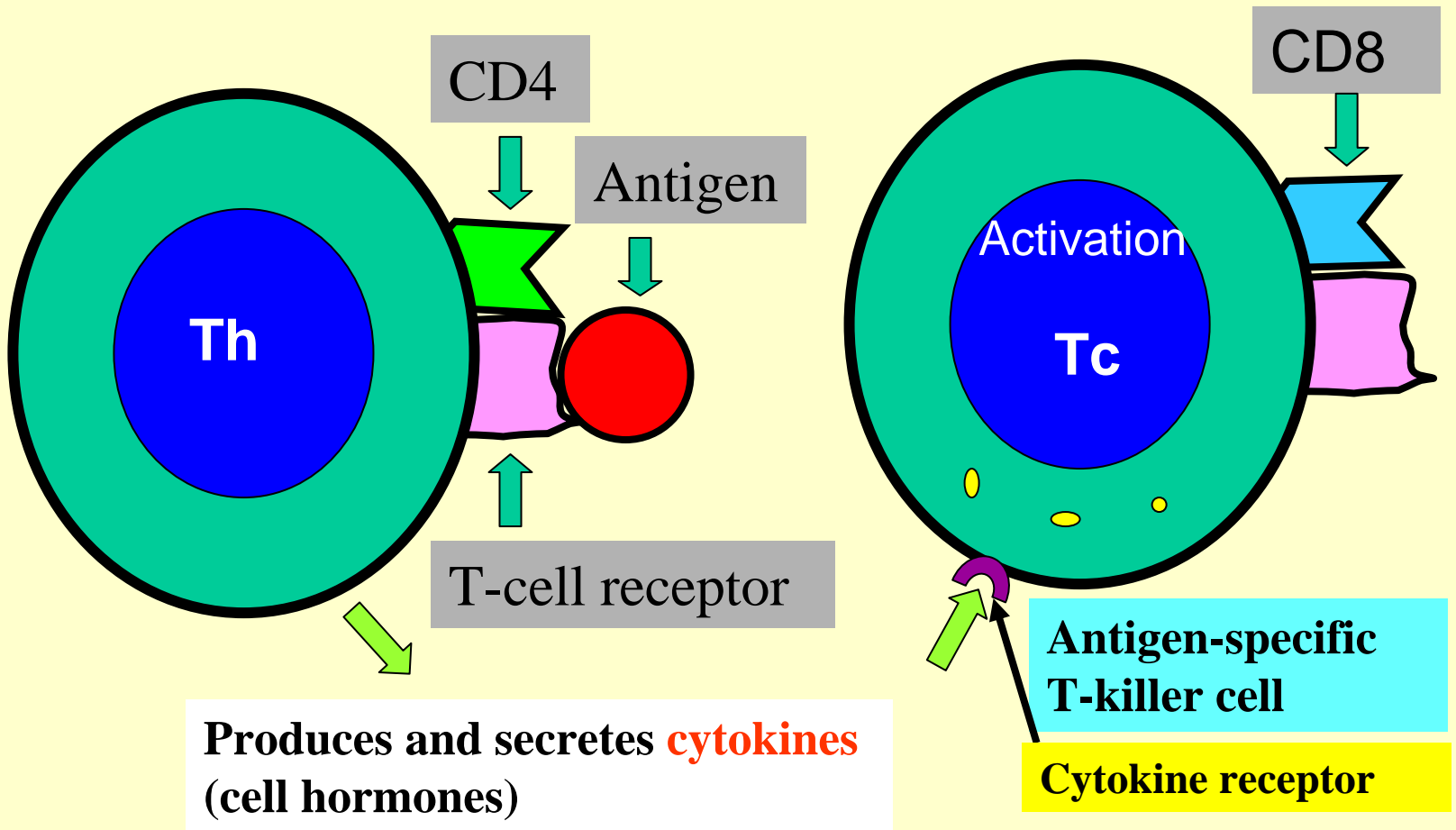
T-cytotoxic cells (*Tc*)

- have specific reactivity against a large number of foreign elements (antigens) on cell surfaces
- specifically kill altered cells (virus-infected cells, cancer)

T-lymphocyte functions II

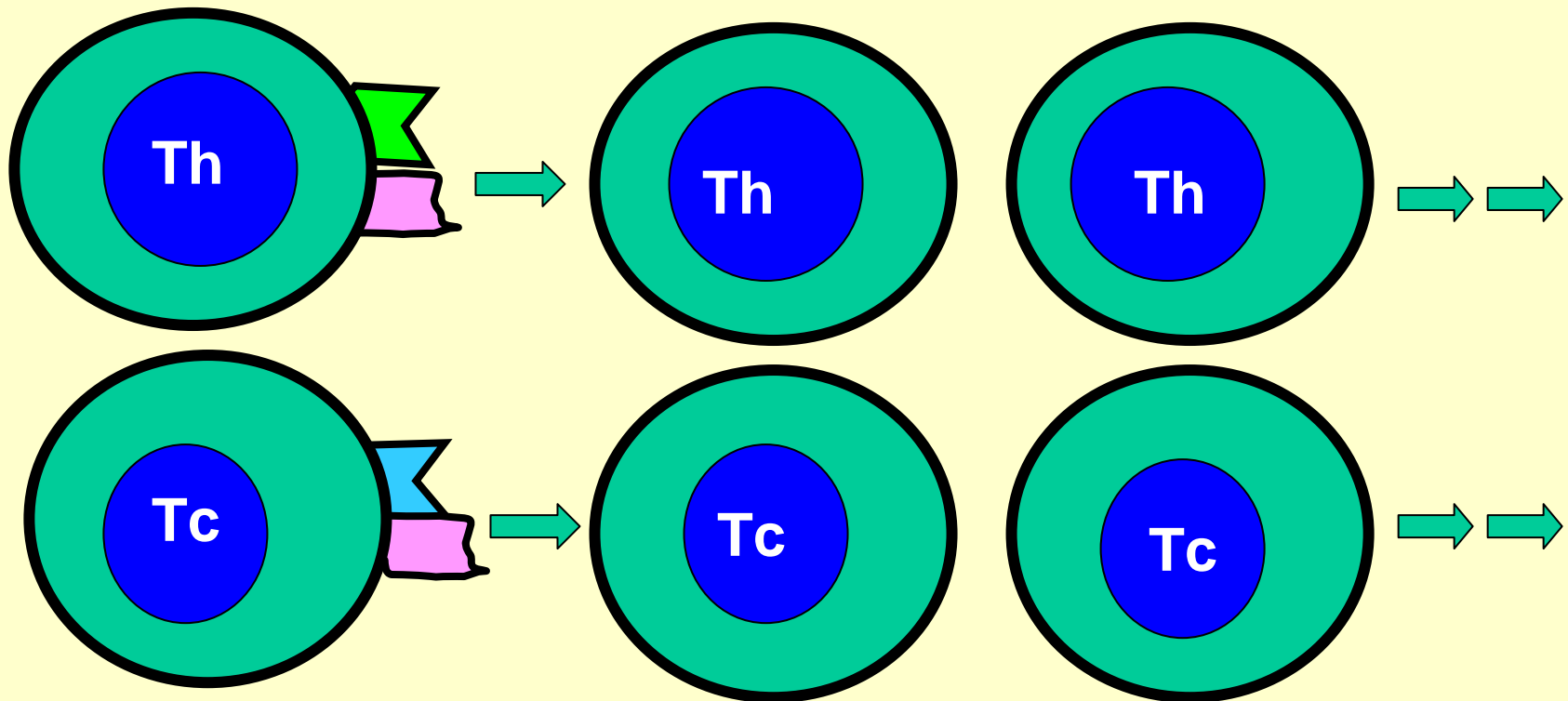


T-lymphocyte functions III



T-lymphocyte clone formation

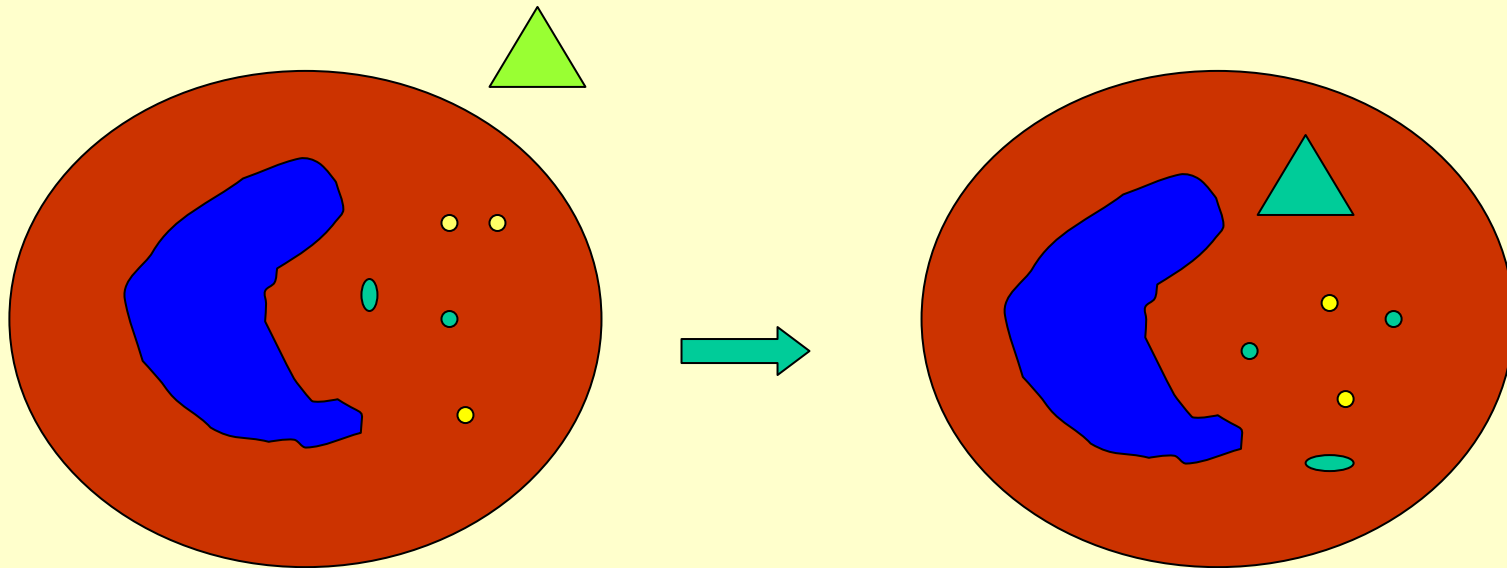
After stimulation Th og Tc proliferate into antigen-specific cell families (clones)with identical specificity, and reactivity, resulting in augmented helper and cytotoxic activity



Macrophage functions: Antigen presentation. I

Antigen (foreign material)

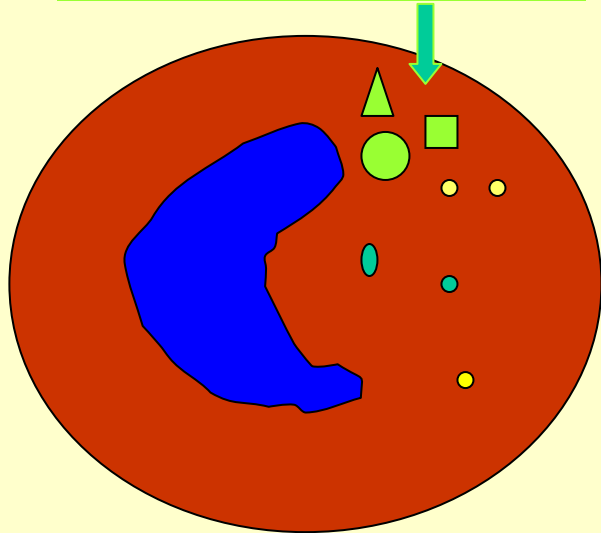
Phagocytosis (ingestion of
foreign antigen)



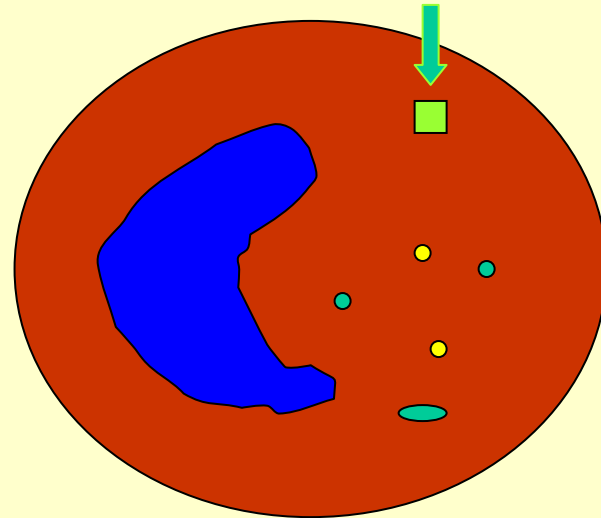
Macrophage

Macrophage functions: Antigen presentation. II

Antigen decomposition



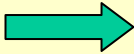
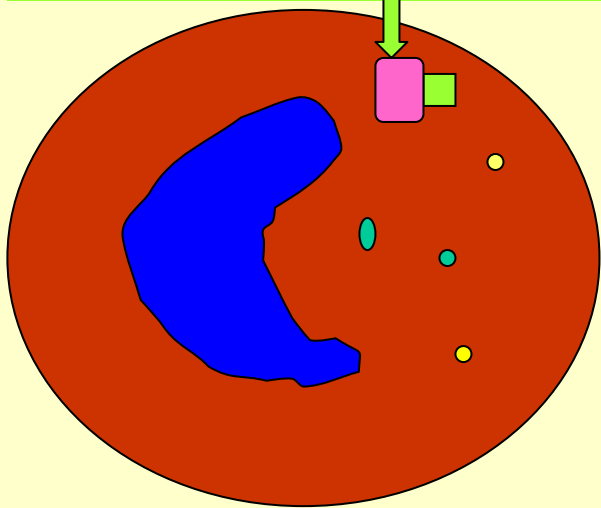
Immunogen fitting



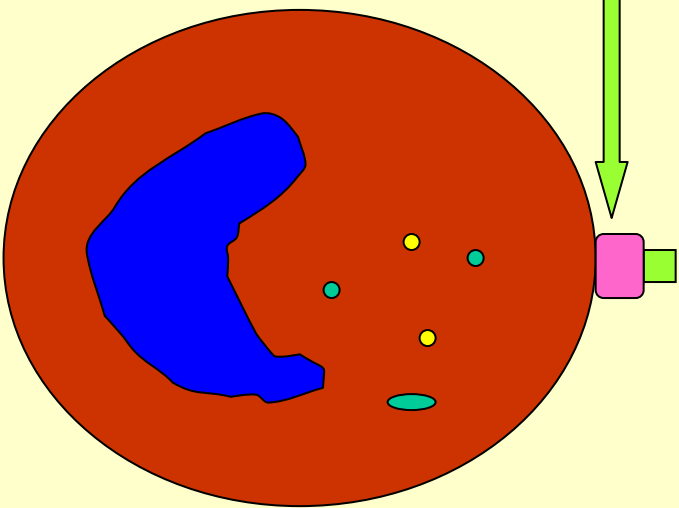
Macrophage

Macrophage functions: Antigen presentation. III

Immunogen binding to tissue type molecule in the cell

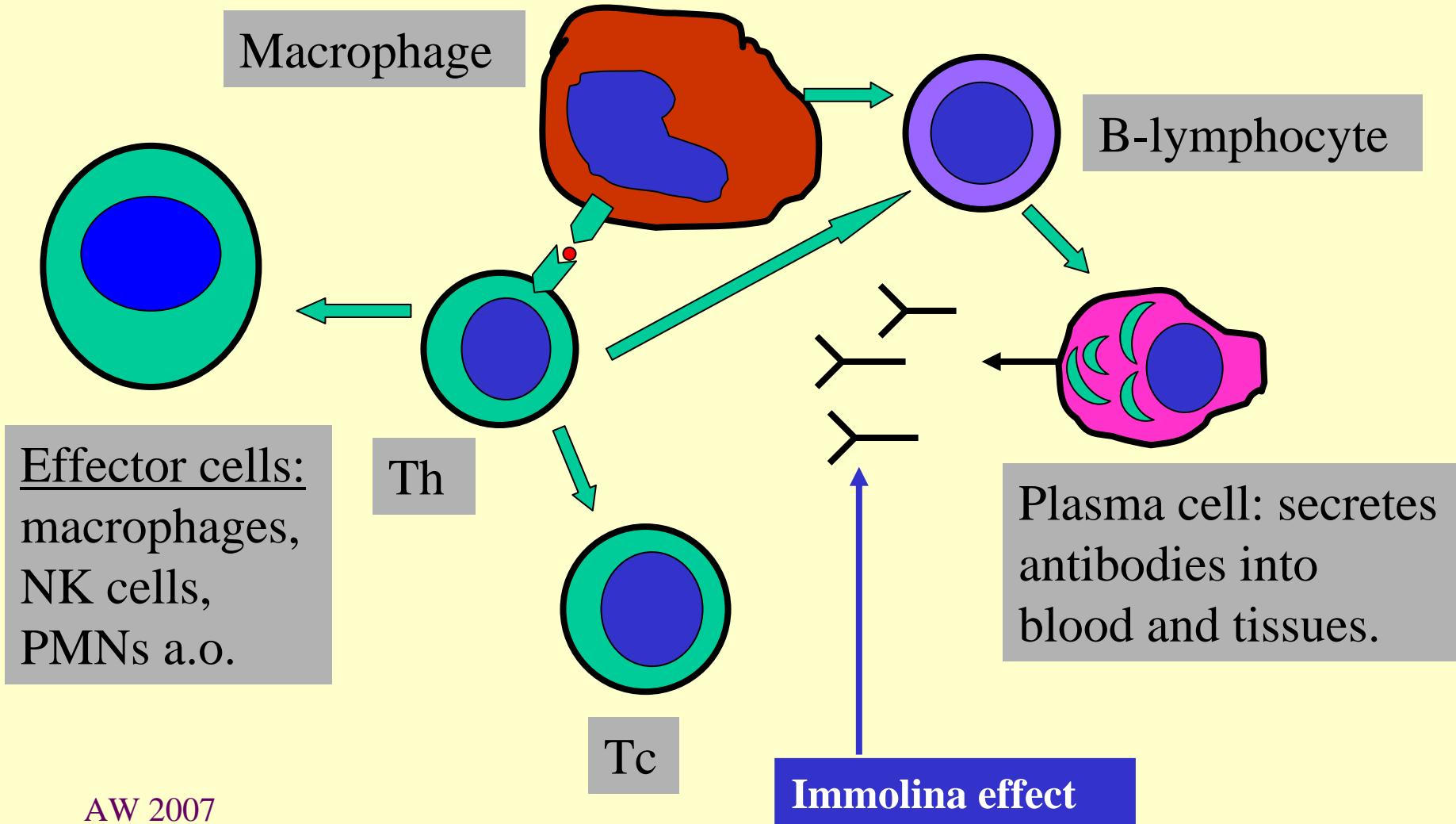


Immunogen presentation on tissue type molecule on the cell surface

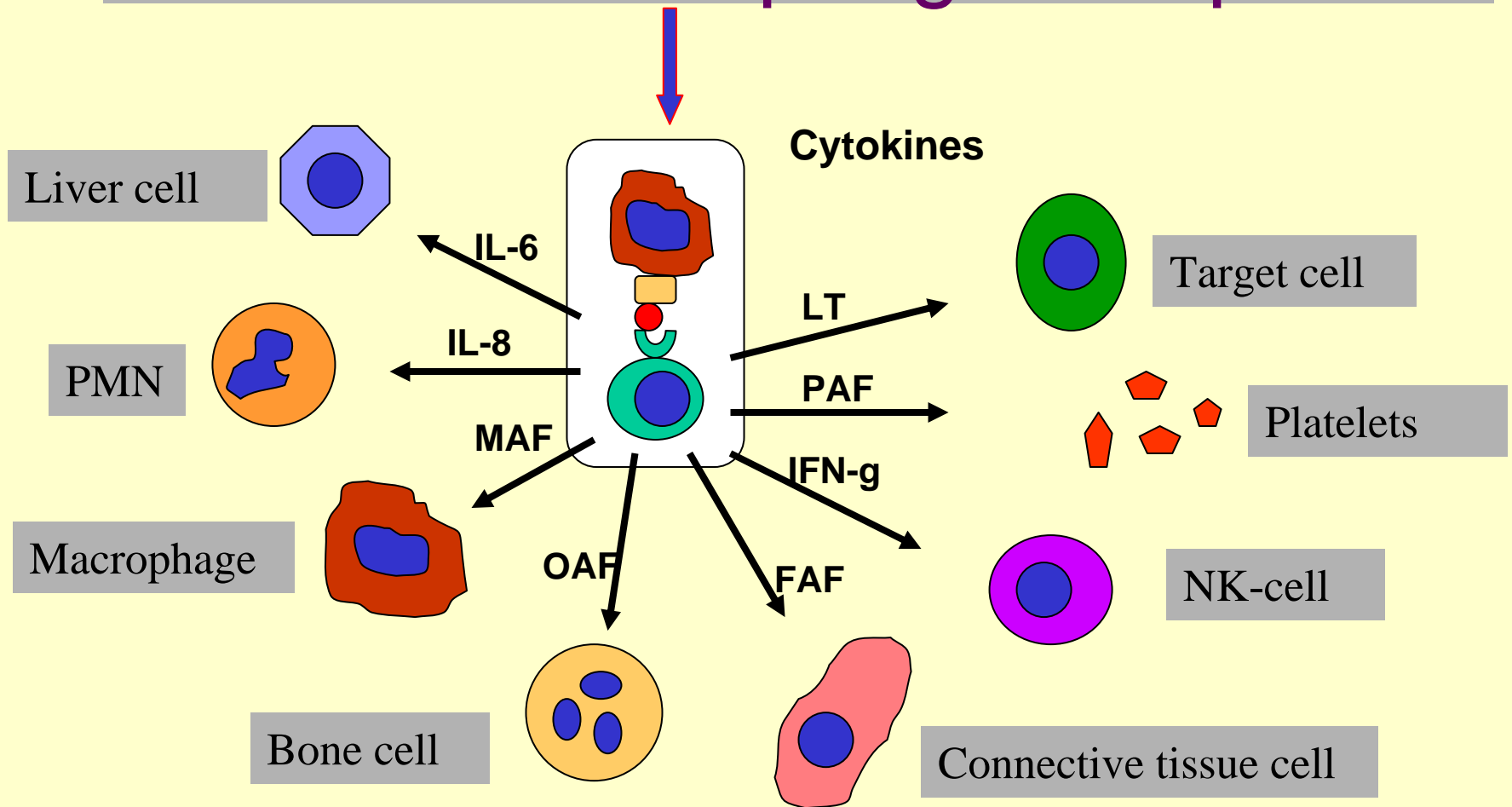


Macrophage

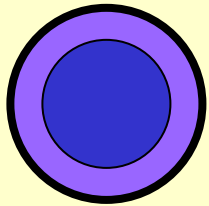
Cell communication and regulatory mechanisms



Effects of cytokines caused by the Th/macrophage complex



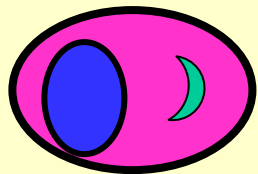
B-lymphocyte functions



B-ly



Pl.c



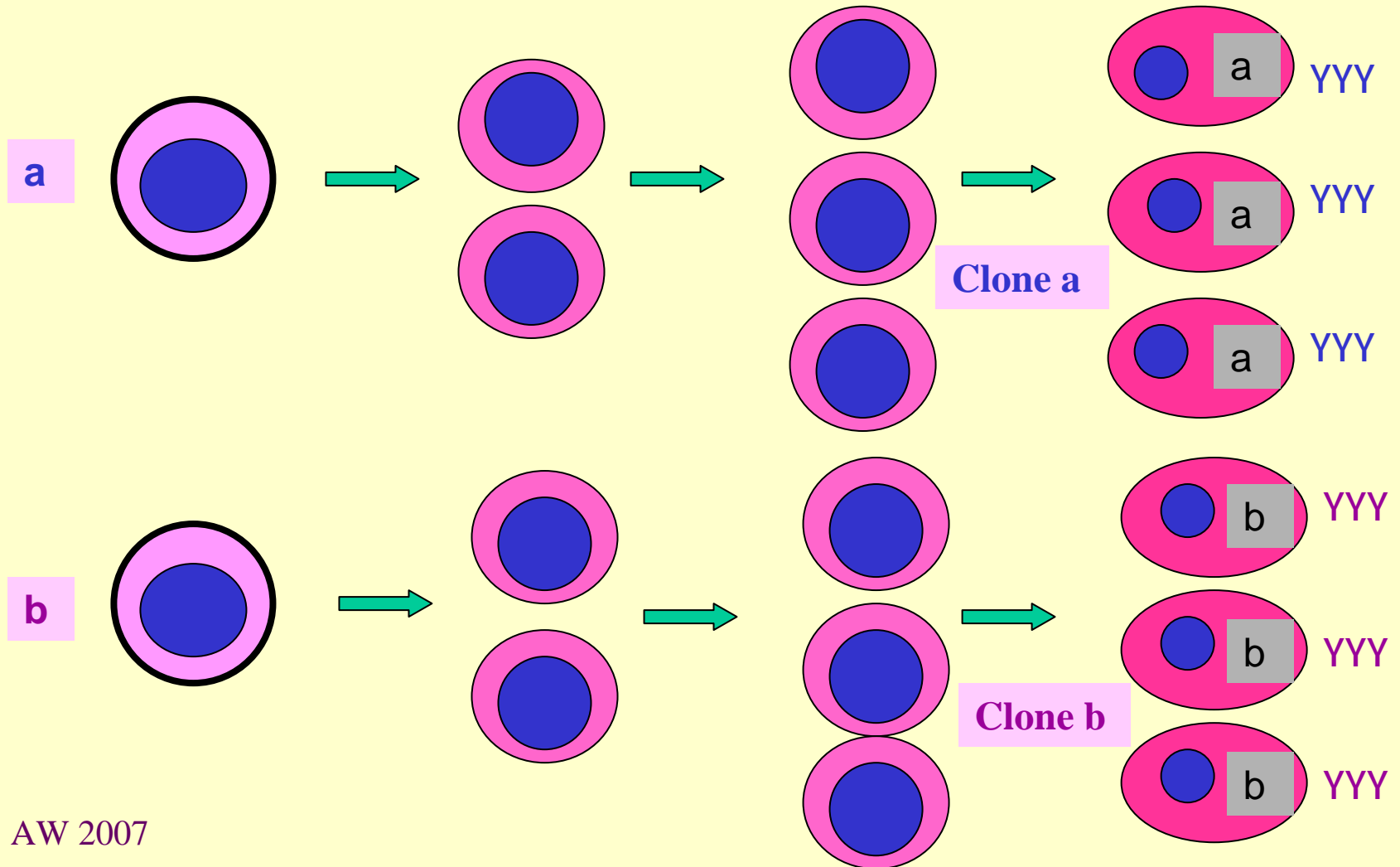
- Made and matured in bone marrow

- Produce small amounts of antibodies

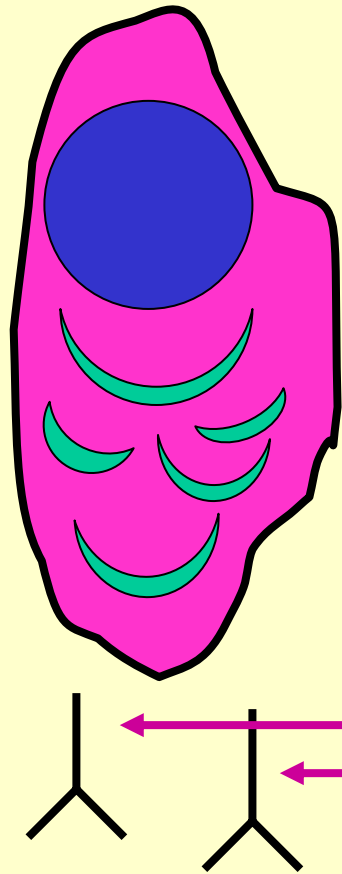
- These are presented in the cell membrane and function as antigen-specific receptors

- Are precursors of plasma cells, that are effective "factories" for mass production of antibodies for secretion into tissues and blood stream

B-cell clones and antibody production



Plasma cell function



- Developed from B-lymphocytes in lymphoid tissues (lymph nodes, spleen, intestinal wall and bronchial mucous membranes)
- Have pronounced capacity to produce antibody molecules for "export"(secretion)
- Strong production of antibodies directed against foreign elements (antigens), to which they specifically bind
- Antibodies belong to 5 classes of so-called immunoglobulins (IgG, **IgA**, IgM, IgD, IgE)

Immolina effect

The 5 immunoglobulin classes

IgG: Found in all body fluids and blood stream

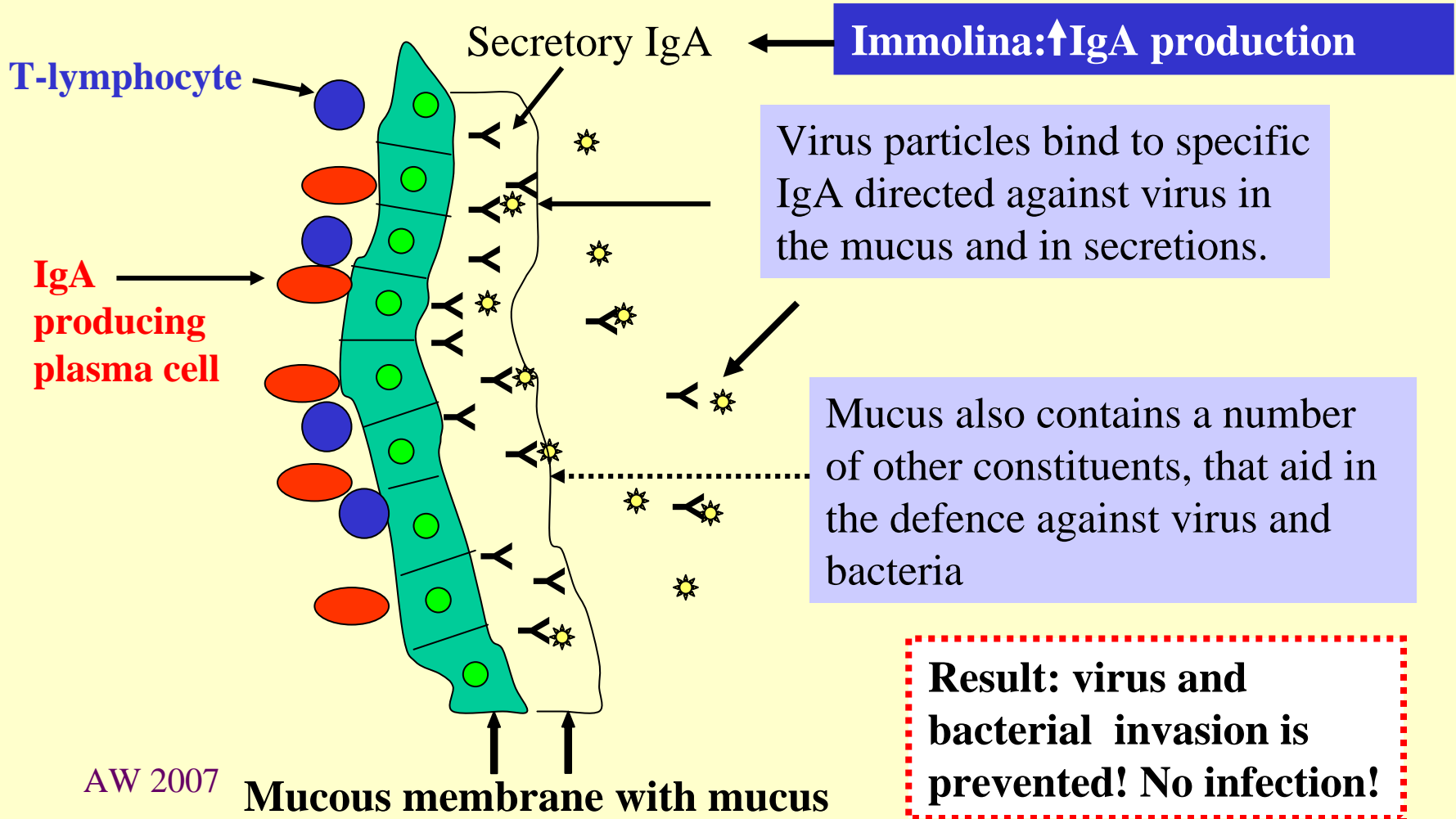
IgM: Only in the blood stream.

IgA: The most important immunoglobulin in and on mucous membranes (bronchi, intestinal tract, skin, bladder)

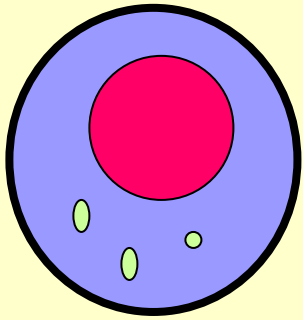
IgD: Not precisely known.

IgE: Concentrated on mast cell surfaces and basophil granulocyte surfaces.

Combat of virus on mucous membranes



Natural killer cells (NK-cells)

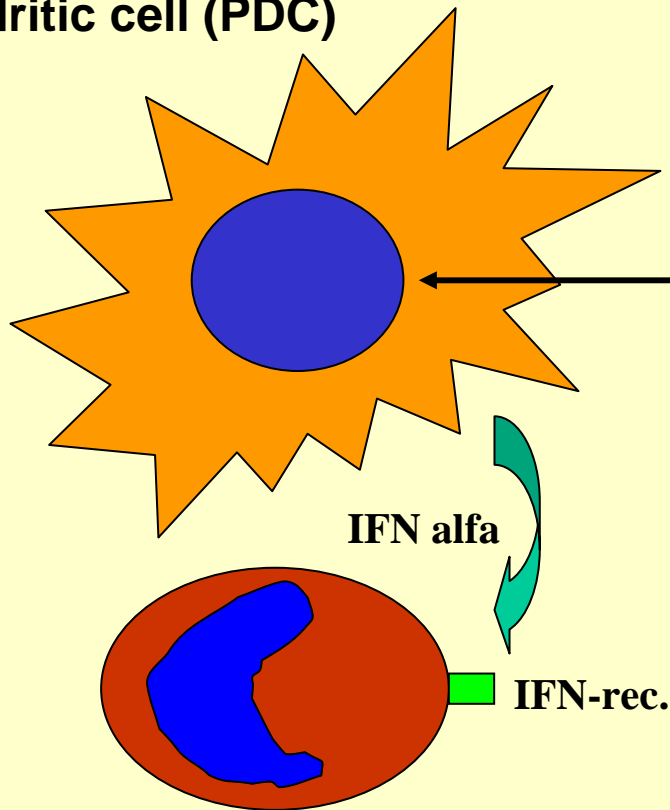


**NK-cell
with granula**

- Made in bone marrow
- Produces cell toxic products (cytotoxins), that can kill virus infected cells and cancer cells
- Toxins are pumped into the target cell after cell-to-cell contact has been established and target cells die
- Some of the enzymes degrade senescent and damaged cells, and peptides from these cells can be mistaken as being foreign antigens, causing immune responses (autoimmunity).

Co-operation between plasmacytoid dendritic cells and macrophages

Plasmacytoid dendritic cell (PDC)

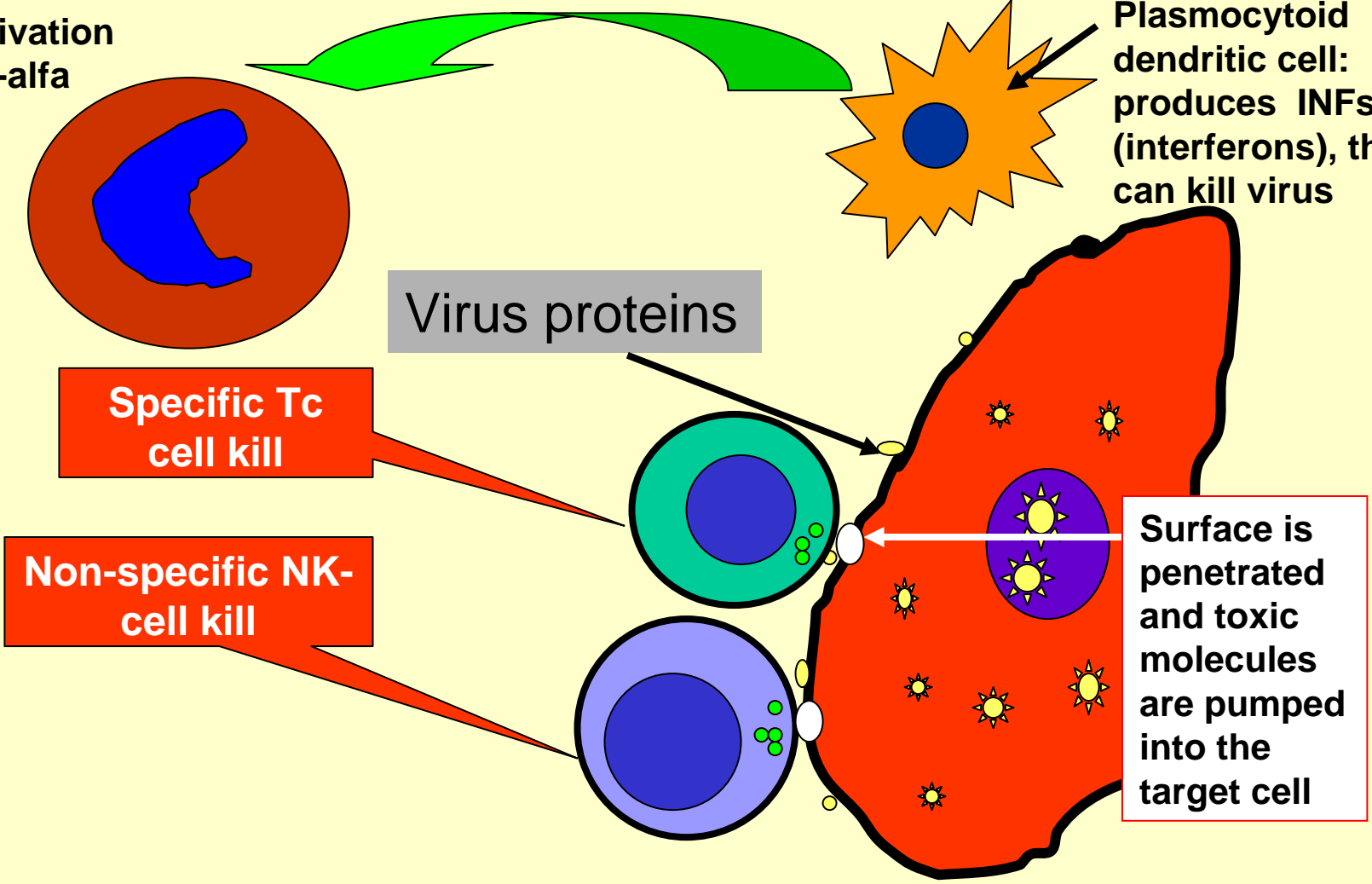


React to many different foreign agents, with which it gets into contact: functions as Ag-presenting cell for Th cells and as producer of many cytokines and other important signaling molecules, especially interferons, e.g. IFN-alfa, that stimulates macrophages, initiates strong cytokine production, and kill virus. Also react to immune complexes between IgG antibodies and virus-containing particles via specific Toll-like receptors (TLR). Can also react with autologous RNA-containing particles (RNP-RNA particles), so autoimmunity is started and connective tissue autoimmune disease is the result.

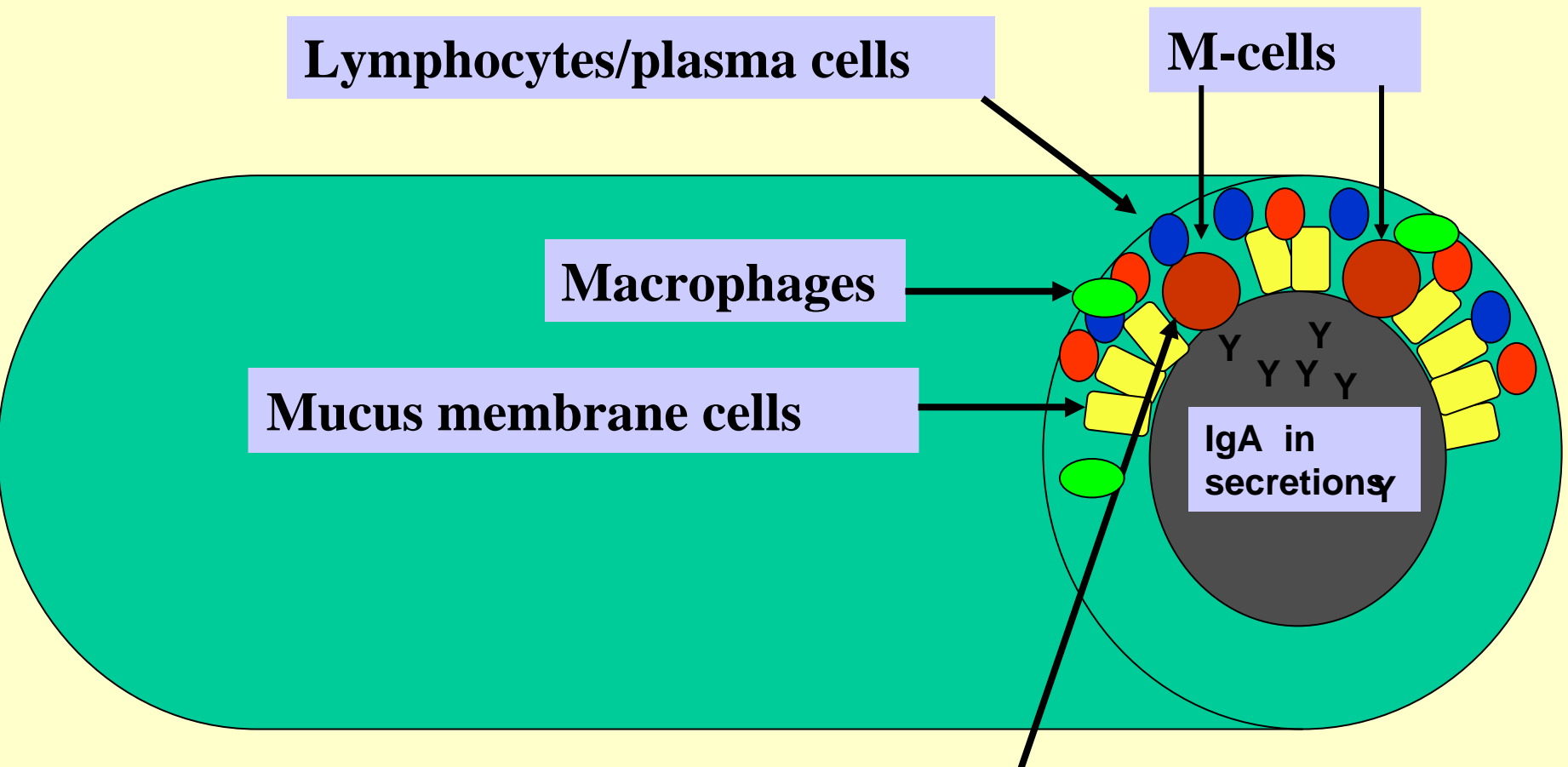
Killing of virus-infected cells

MØ activation
via INF-alfa

Plasmacytoid
dendritic cell:
produces INFs
(interferons), that
can kill virus

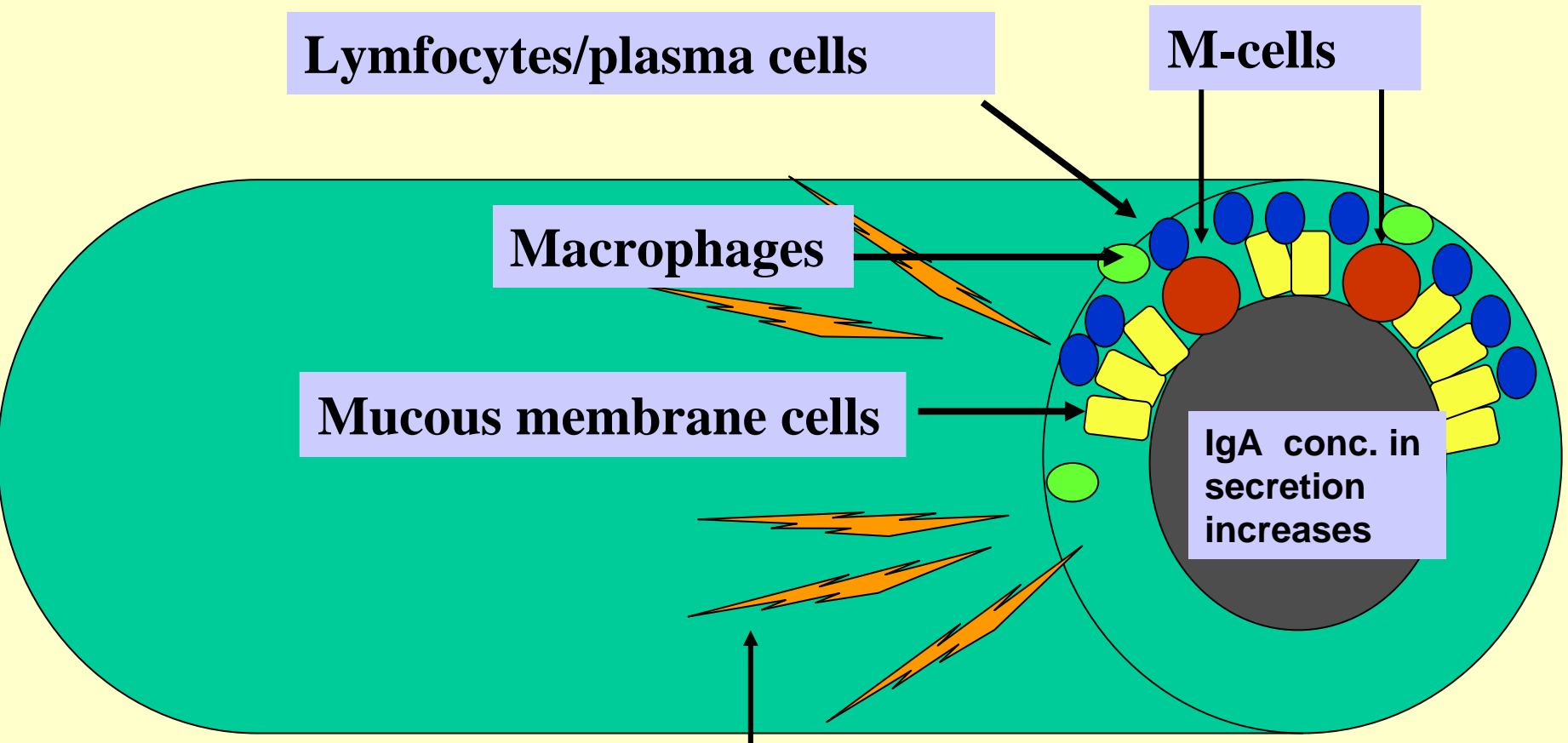


The intestinal immune system



Immolina has an effect on M-cells and thereby stimulates the surrounding immune cells (B, T, MØ, and NK cells).

The intestinal immune system



After stimulation by Immolina the effect is spread systemically to the rest of the innate and the specific immune system, whereby general defence is increased.

Conclusions

Immulina has an effect on the innate as well as the specific immune system via mucous membrane M-cells, Th-lymphocytes, Tc-effector lymphocytes, B-lymphocytes/plasma cells, antibody production (especially increased secretory IgA production), but also through a stimulating effect on NK cell activity towards virus-infected cells which they can kill.