The normal immune system

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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
- macrofages (phagocytes)

Soluble factors:
- Specific antibodies
- Signaling molecules

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The innate defence:
Cells:
- Phagocytes
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The adaptive immune defence:
Cells:
- T-lymphocytes
- B-lymphocytes
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- 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".

Early recruitment

Polymorphonuclear granulocyte (small)

Later recruitment

Macrophage (large)

Bacteria in tissue

\[ X = \text{chemotaxis: migration towards} \]
Phagocytosis (ctd.) II

Bacteria are killed and degraded

PMN with ingested (phagocytosed) bacteria

Macrophage with phagocytosed bact.
Interacting cells. I

- Eater cell
- Killer cell
- Natural killer cell (NK)
- Polymorphonuclear granulocyte
- Macrophage

Immolina has an activating effect on these cells.
Cells in the immune system

Plasma cell: produces and secretes antibodies

B-lymphocyte

Immolina effect

Precursor of antibody-producing plasma cell

Antigen-presenting "eater cell"

Macrophage

"Conductor"

Tc

Th

T-lymphocytes

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Specific immune defence

• Constituted by **Th-lymphocytes**, that after contact with and presentation of antigen via macrophages stimulate specific B-lymfocytes 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-helper cells (Th)
- "Conductors" in the immunological orchestra
- constitute around $\frac{1}{2}$ 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

Antigen (Ag) = foreign element

T-cell receptor: specific Ag-binding protein complex

CD4
T-lymphocyte functions III

**Th**
- CD4
- T-cell receptor
- Produces and secretes **cytokines** (cell hormones)

**Tc**
- CD8
- Antigen-specific T-killer cell
- Cytokine receptor
- Antigen
- Activation
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
Macrophone functions: Antigen presentation. II

Macrophage functions:
- Antigen presentation
- Immunogen fitting
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

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Cell communication and regulatory mechanisms

**Effector cells:** macrophages, NK cells, PMNs a.o.

**Plasma cell:** secretes antibodies into blood and tissues.

**Macrophage**

**B-lymphocyte**

**Th**

**Tc**

**Immolina effect**

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Effects of cytokines caused by the Th/macrophage complex

Liver cell
PMN
Macrophage
Bone cell
Connective tissue cell
Target cell
Platelets
NK-cell

Cytokines

IL-6
IL-8
MAF
OAF
FAF
LT
PAF
IFN-g

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B-lymphocyte functions

- 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

Clone a

Clone b
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

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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

Virus particles bind to specific IgA directed against virus in the mucus and in secretions.

Mucus also contains a number of other constituents, that aid in the defence against virus and bacteria.

Result: virus and bacterial invasion is prevented! No infection!
Natural killer cells (NK-cells)

- 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 plasmocytoid dendritic cells and macrophages

Plasmocytoid 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 auto-immunity is started and connective tissue autoimmune disease is the result.
Killing of virus-infected cells

- **Virus proteins**

- **Specific Tc cell kill**

- **Non-specific NK-cell kill**

- **Surface is penetrated and toxic molecules are pumped into the target cell**

- **MØ activation via INF-alfa**

- **Plasmocytoid dendritic cell: produces INFs (interferons), that can kill virus**
Immolina has an effect on M-cells and thereby stimulates the surrounding immune cells (B, T, MØ, and NK cells).

The intestinal immune system

Mucus membrane cells

Macrophages

M-cells

Lymphocytes/plasma cells

IgA in secretions
The intestinal immune system

Lymphocytes/plasma cells

M-cells

Macrophages

Mucous membrane cells

IgA conc. in secretion increases

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

Immolina 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.