

Natural killer & cytokines

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Natural killer cells

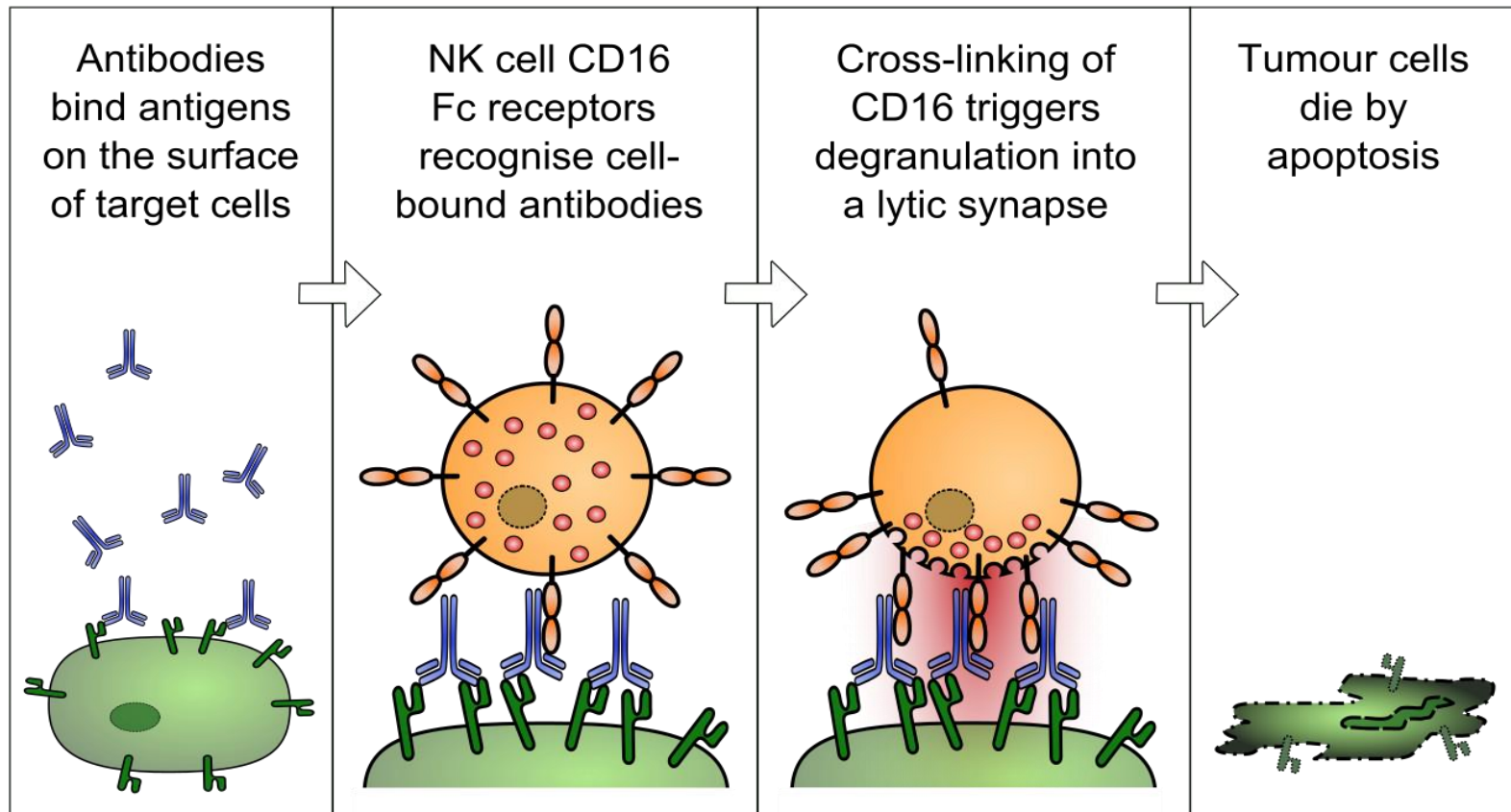
- Natural Killer” cells are large granular lymphocytes which are an important part of innate immunity and typically constitute about 10% of total blood lymphocytes.
- NK cells (belonging to the group of innate lymphoid cells) are defined as large granular lymphocytes (LGL) and constitute the third kind of cells differentiated from the common lymphoid progenitor - generating B and T lymphocytes in the bone marrow , it complete development without the influence of the thymus.

Key surface markers (Receptors on the NK surface) :

- 1- CD16 (Fc γ RIII), binds IgG and promotes the antibody-dependent cytotoxicity (ADCC) of NK cells
- 2- CD56 (adhesion molecule) Activation receptors, bind to signals from infected cells, enhance killing
- 3- Killer cell Immunoglobulin-like Receptor (KIR): recognize MHC class I molecules (HLA-A, B, C) delivers a *negative* signal to the NK cell (inhibit killing activity).

If a viral infection causes the target cell to express *reduced levels of HLA-A , B or C* molecules (several viruses can do this), then the negative signal to the NK cell is reduced and the target cell may be killed.

Alternatively, if the target cell expresses modified glycoproteins in its membrane (which can also result from viral infection, or from malignant transformation), then an increased *positive* signal may also result in target cell killing.



Key cytokines:

- Interleukin-15: required for NK cell development
- IL-12, IL-18 & IFN- γ : cause activation & cytotoxicity.

NK function

1- Surveillance function: NK cells are found in:

- Peripheral blood
- Secondary lymphoid organs: spleen and activated lymph nodes
- Peripheral tissue: liver, lung and the decidual lining of the uterus

2- Specific NK cell functions :-

- 1- Control of viral infections
- 2- Control of malignant cells
- 3- Role in hematopoietic stem cell transplantation
- 4- NK cells has a role in maintain or lost of pregnancy

Cytokines: are immunomodulatory proteins representing a group of proteins and peptides that are used in organisms as signaling compounds allowing communication between the cells. **They are particularly important in both innate and adaptive immune responses.**

Due to their central role in the immune system, cytokines are involved in a variety of immunological, inflammatory and infectious diseases, also they are involved in several developmental processes during embryogenesis.

Cytokine -mediated effects

- **Cell growth**
- **Cell differentiation**
- **Cell death**
- **Induce non-responsiveness to other cytokines/cells**
- **Induce responsiveness to other cytokines/cells**
- **Induce secretion of other cytokines**

- They are produced by a variety of cells (both haemopoietic and non-haemopoietic) and same cytokine is even produced by different types of cells at the same time in response to any foreign particle
- Although various classifications for cytokines have been suggested on the basis of their mode of action, structure, receptors, etc. but depending on their inflammatory reactions, they are broadly categorized into :-

1- Pro-inflammatory cytokines :- are produced by Th-1 , they are TNF- α , TNF- β , IFN- γ , IL-1, IL-2, etc. and they activated Tc and macrophages to stimulate cellular immunity and inflammation,

2- Anti-inflammatory cytokines :- are produced by Th-2 cells , they are IL-4, IL-5, IL-10, IL-12, etc. which stimulate antibody production by B cells.

- **Interleukins:** Communication between WBCs.
- **Interferons:** Protect against viral infections.
- **Chemokines:** Attract WBCs to infected areas.

What are the differences between Ig and cytokines?

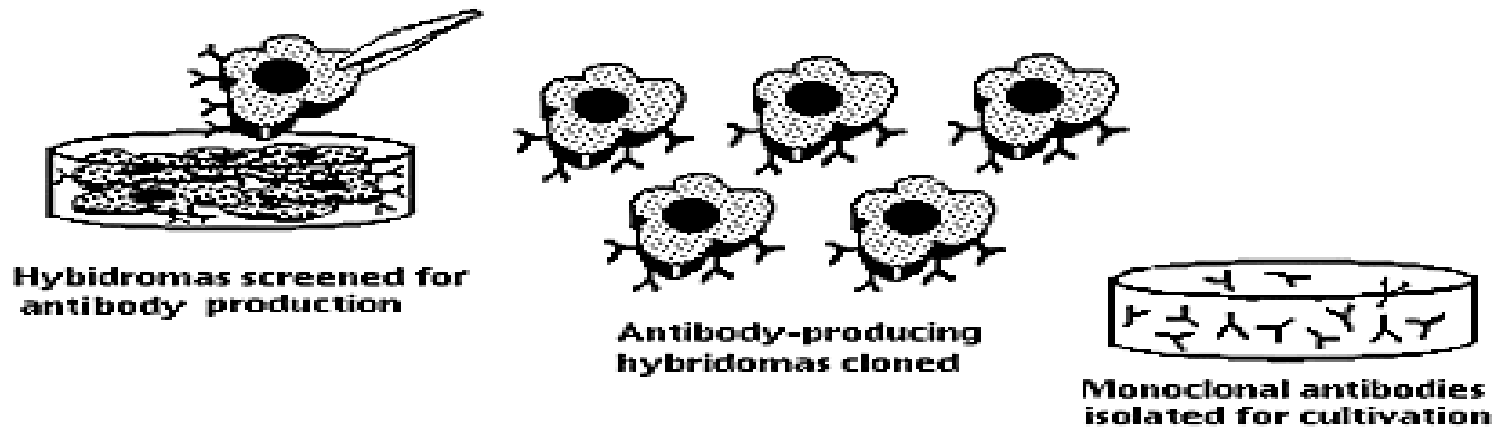
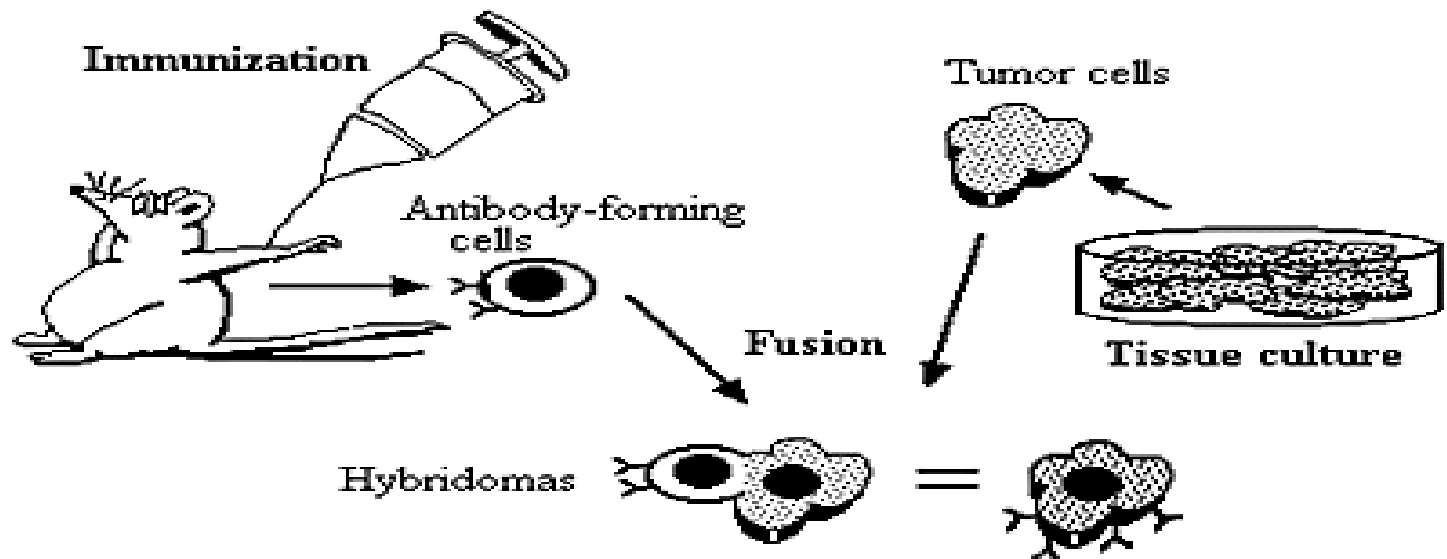
Cluster of differentiation (often abbreviated as **CD**) is a protocol used for the identification and investigation of cell surface molecules present on WBC, providing targets for immunophenotyping of cells.

Physiologically, CD molecules can act in numerous ways, often acting as receptors or ligands (the molecule that activates a receptor) important to the cell.

All T and B cells have about $10^5 = 100,000$ molecules on their surface. **B** cells are coated with CD19, CD21, CD35, CD40, and CD45, while **T** cells express CD2, CD3, CD4, CD8, CD28, CD45R.

Monoclonal Antibody

MoAb :-Process by which large quantities of specific antibodies (targeted against a particular antigen) can be produced.



Monoclonal Antibody Production

Monoclonal Antibody Production

- 1- A mouse is immunized by injection of an antigen X to stimulate the production of antibodies targeted against X.
- 2- The antibody forming cells are isolated from the mouse's spleen.
- 3- Antibody-forming cells are fusing with tumor cells grown in culture. The resulting cell is called a **hybridoma**.
- 4- Each hybridoma produces relatively large quantities of identical antibody molecules.
- 5- hybridoma cells allowed to multiply in culture to produce a population of cells, each of which produces identical antibody molecules and these antibodies are called "**monoclonal antibodies**" because they are produced by the identical offspring of a single, cloned antibody producing cell.

Application

- Diagnostic tests like:- **Immunofluorescence** is a technique depend on using specific fluorescent dye to identify specific biomolecule within a cell allow visualization of the target molecule through the sample. Ex:- CD (MoAb), immunohistochemistry.
- Therapeutic treatment :- Ex:- Cancer treatment ;one possible treatment for cancer involves monoclonal antibodies that bind only to cancer cell and induce an immunological response against the target cancer cell