M.Sc. Pharmaceutical Chemistry

Semester IV

COURSE : 16P4CPHT15EL – PHARMACEUTICAL CHEMISTRY III

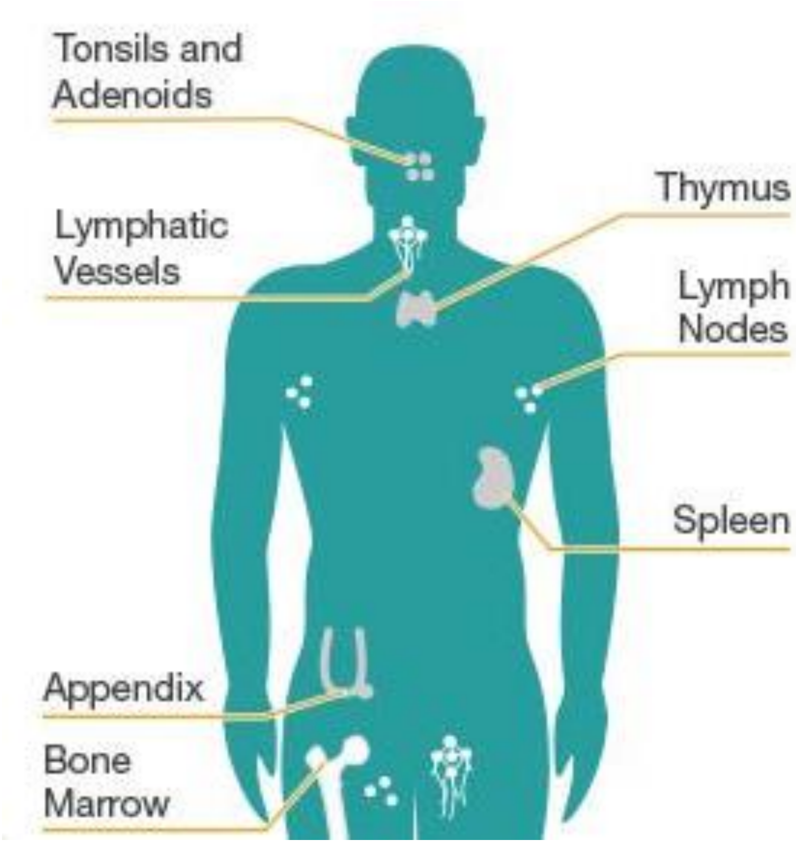
MODULE : ANTINEOPLASTIC DRUGS

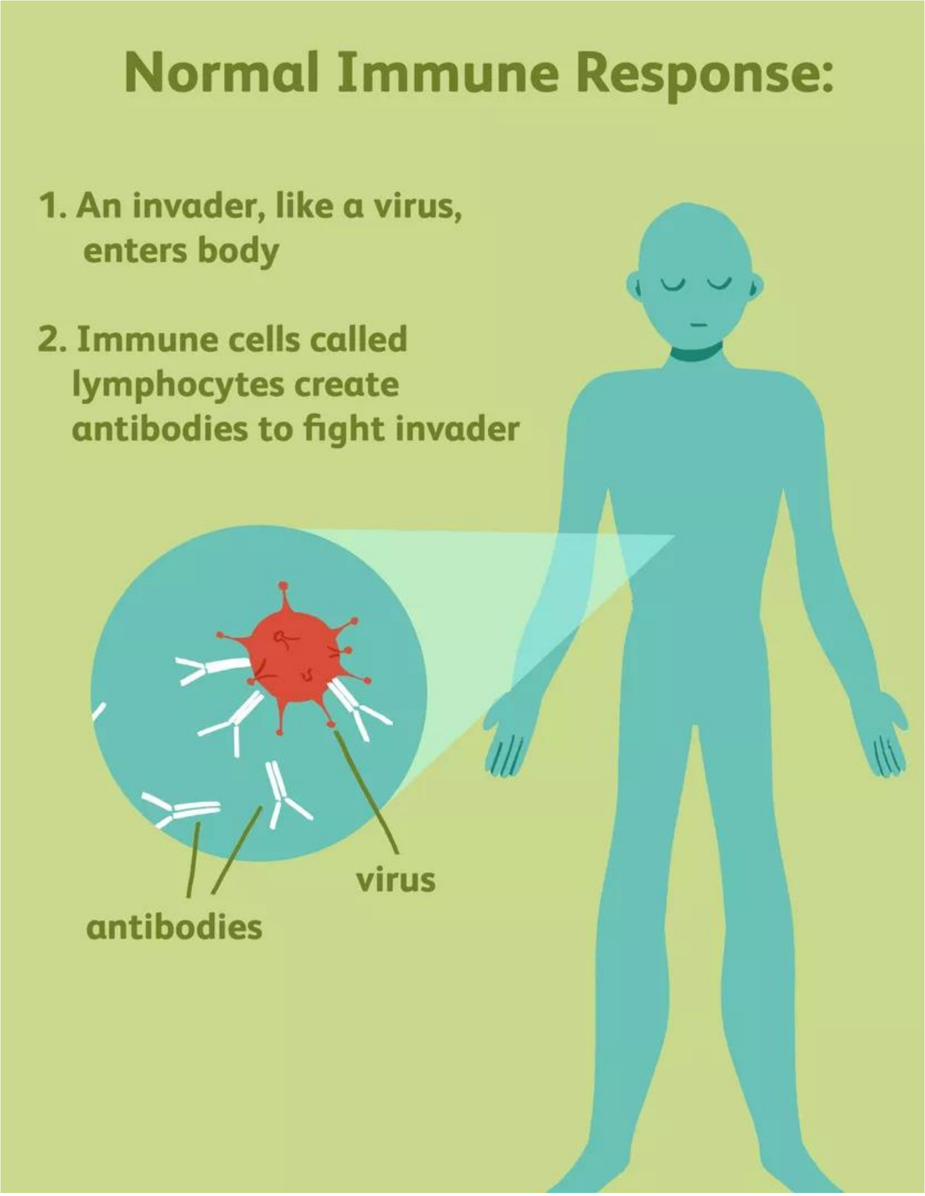
TOPIC : *CANCER IMMUNOTHERAPY*

IMMUNOLOGICAL INTERVENSIONS IN ANTI-CANCER TREATMENT

CANCER IMMUNOTHERAPY:

- Uses the immune system and its components to mount an anti-tumor response.
- Boosts the body's natural defenses to fight the cancer.
- Uses substances made by the body or in a laboratory to improve or restore immune system function.
- Involves the exploitation of the immune system’s machinery to recognize, target and destroy cancer cells.


Tonsils and Adenoids
Lymphatic Vessels
Thymus
Lymph Nodes
Spleen
Appendix
Bone Marrow


Normal Immune Response:
1. An invader, like a virus, enters body
2. Immune cells called lymphocytes create antibodies to fight invader
virus
antibodies

Working of Immunotherapy:

- Stopping or slowing the growth of cancer cells.
- Stopping cancer from spreading to other parts of the body.
- Helping the immune system work better at destroying cancer cells.

Properties of Immune cells utilized for immunotherapy:

- Provide constant surveillance, as they continuously travel throughout the body
- They are specifically stimulated against tumors, which are by definition *antigenic and often immunogenic*
- protect against tumor relapse, due to induction of specific and long-lasting memory.

Landmarks in the Immunotherapy Treatment:

- ***The 1973 discovery of dendritic cells (DCs)***

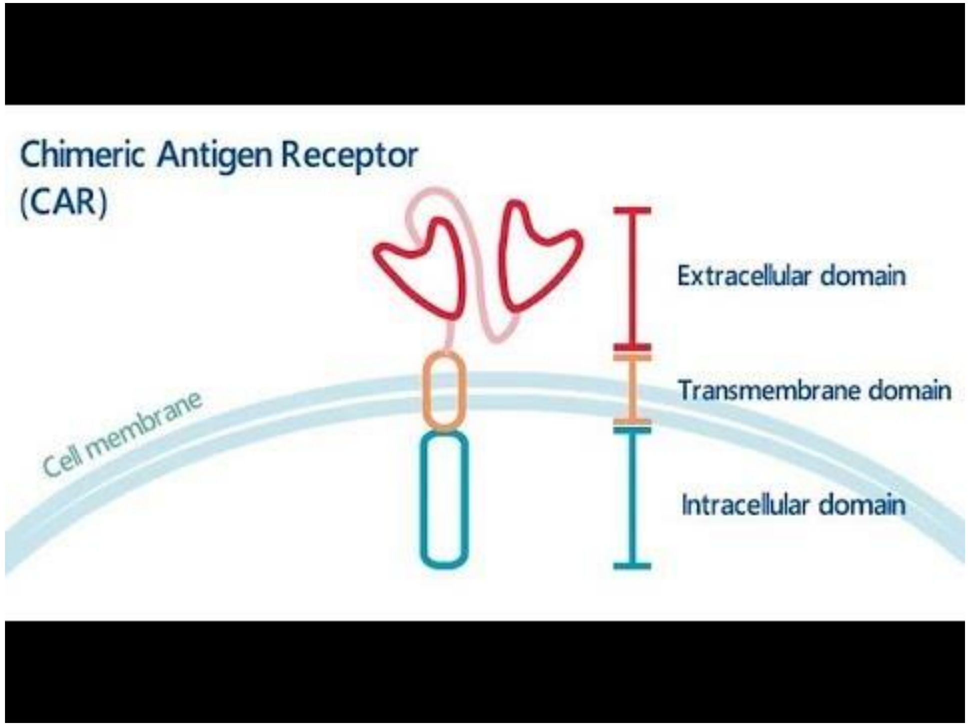
o Dendritic cells are central to the initiation of primary immune responses.

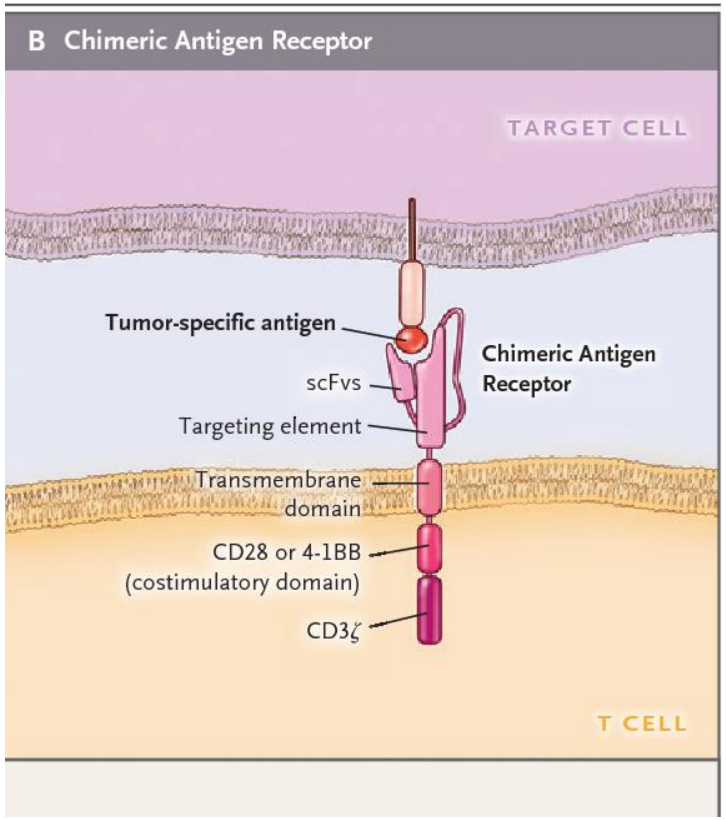
o antigen-presenting cell capable of stimulating naive T cells,

o Dendritic cells also interact with and influence the response of cells of the innate immune system.

1989 development of the first chimeric antigen receptors (CARs)

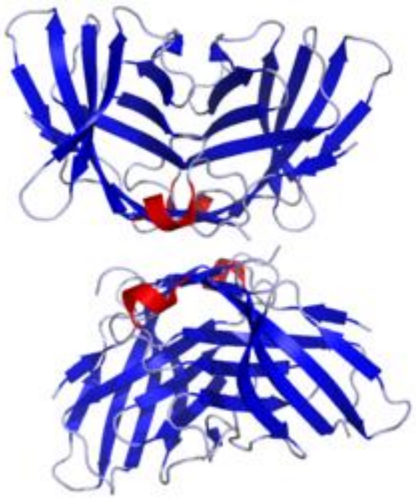
CARs are receptor proteins that have been engineered to give T cells the new ability to target a specific protein.





- the 1991 cloning of the first tumor antigen

- the 1995 identification of the first checkpoint molecule, namely the cytotoxic T lymphocyte-associated protein 4 (CTLA-4)



protein receptor that, functioning as an immune checkpoint, (or checkpoint inhibitor), downregulates immune responses.

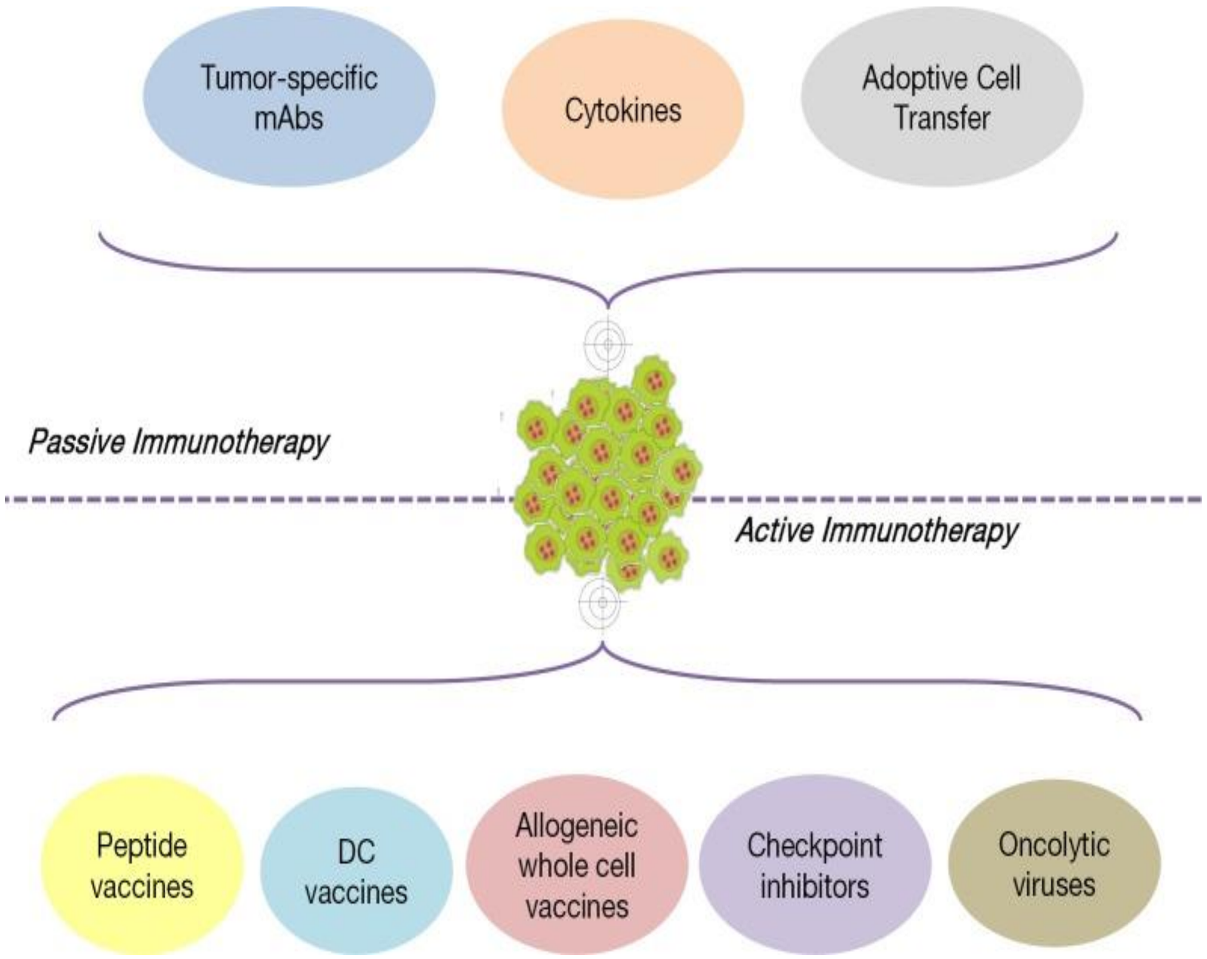
PASSIVE IMUNOTHERAPY

- passive immunotherapeutics are used in cancer patients with weak, unresponsive, or of low responsiveness immune systems.
- Passive protocols consist of *ex vivo*-activated cells or molecules that once found inside the body, compensate for missing or deficient immune functions.
- Among others, this category includes the infusion of tumor-specific antibodies, the systemic administration of recombinant cytokines and the adoptive transfer of immune cells pre-activated to lyse tumors *in vivo*.

ACTIVE IMMUNOTHERAPY

- strategies aim to stimulate effector functions *in vivo*.
- To apply active immunotherapeutics, the patient’s immune system should be able to respond upon challenge, get competently stimulated and mediate effector functions.
- The most important active protocols comprise vaccination strategies with tumor peptides or allogeneic whole cells, the use of autologous DCs as vehicles for tumor antigen delivery, and the infusion of antibodies targeting crucial checkpoints of T cell activation.

ACTIVE AND PASSIVE IMMUNOTHERAPY



MONOCLONAL ANTIBODIES

Monoclonal antibodies are a specific type of antibodies made in a laboratory.

monoclonal antibodies (mAb) can be used as a **targeted therapy** to block an abnormal protein in a cancer cell. Monoclonal antibodies can also be used as flags an immunotherapy.

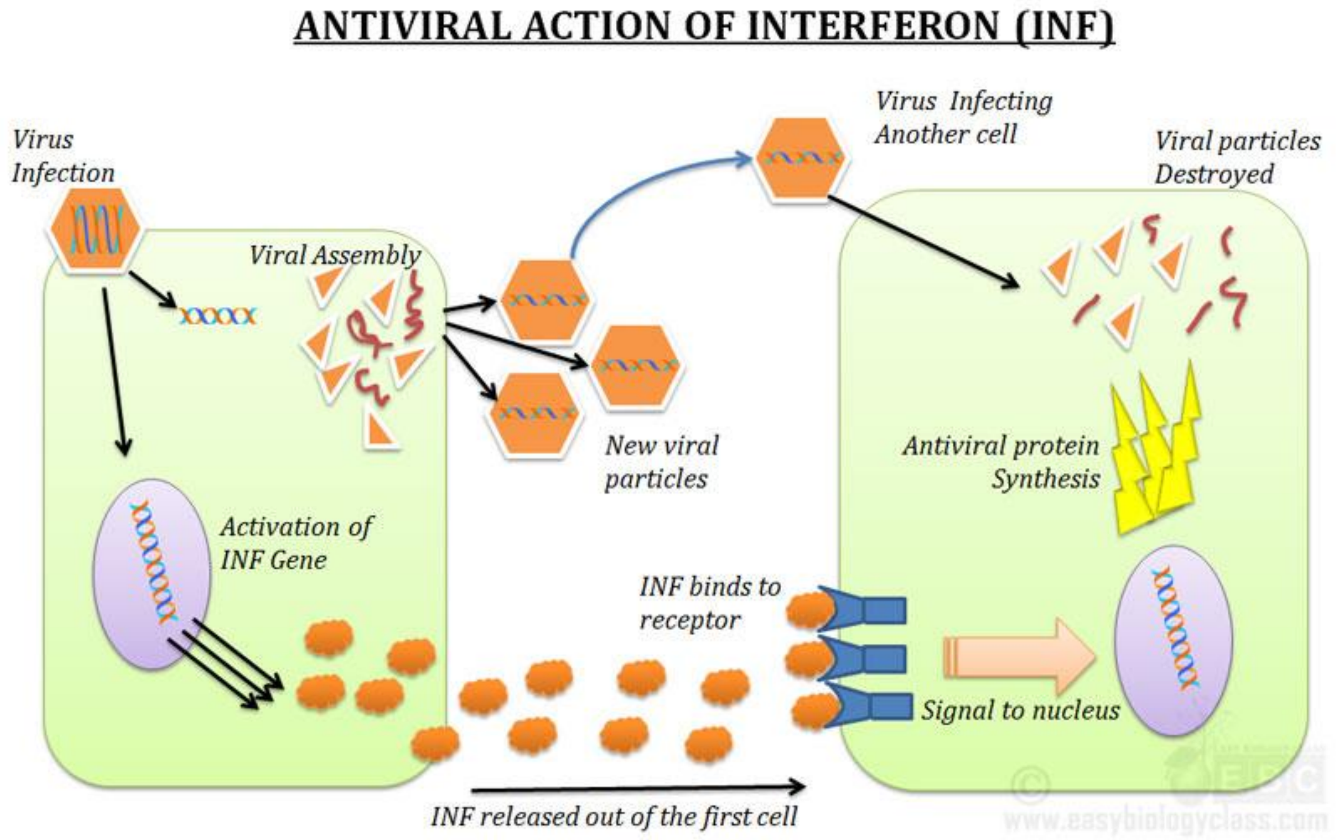
CTLA-4 pathways - immune checkpoints

The immune system responds to the cancer by blocking these pathways with specific antibodies called immune ***checkpoint inhibitors***.

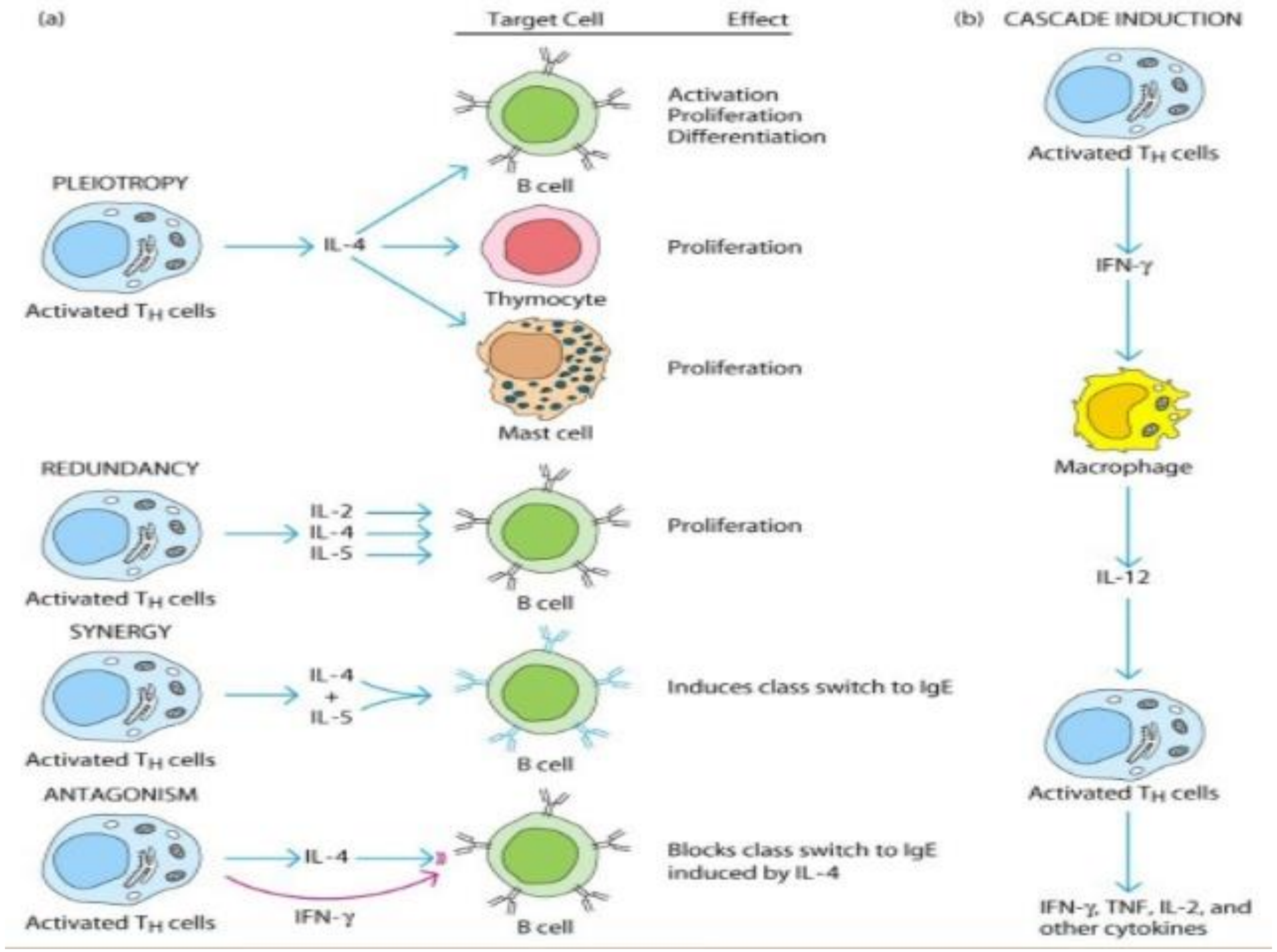
Once the immune system is able to find and respond to the cancer, it can stop or slow cancer growth.

Non-specific immunotherapies

Interferons. Interferons help the immune system fight cancer and may slow the growth of cancer cells. An interferon made in a laboratory is called an interferon alpha (Roferon-A [2a], Intron A [2b], Alferon [2a]).
Related proteins that are produced by the body's cells as a defensive response to <u>viruses</u>. They are important modulators of the <u>immune response</u>.



Interleukins. Interleukins help the immune system produce cells that destroy cancer. An interleukin made in a laboratory is called interleukin-2, IL-2, or aldesleukin (Proleukin).



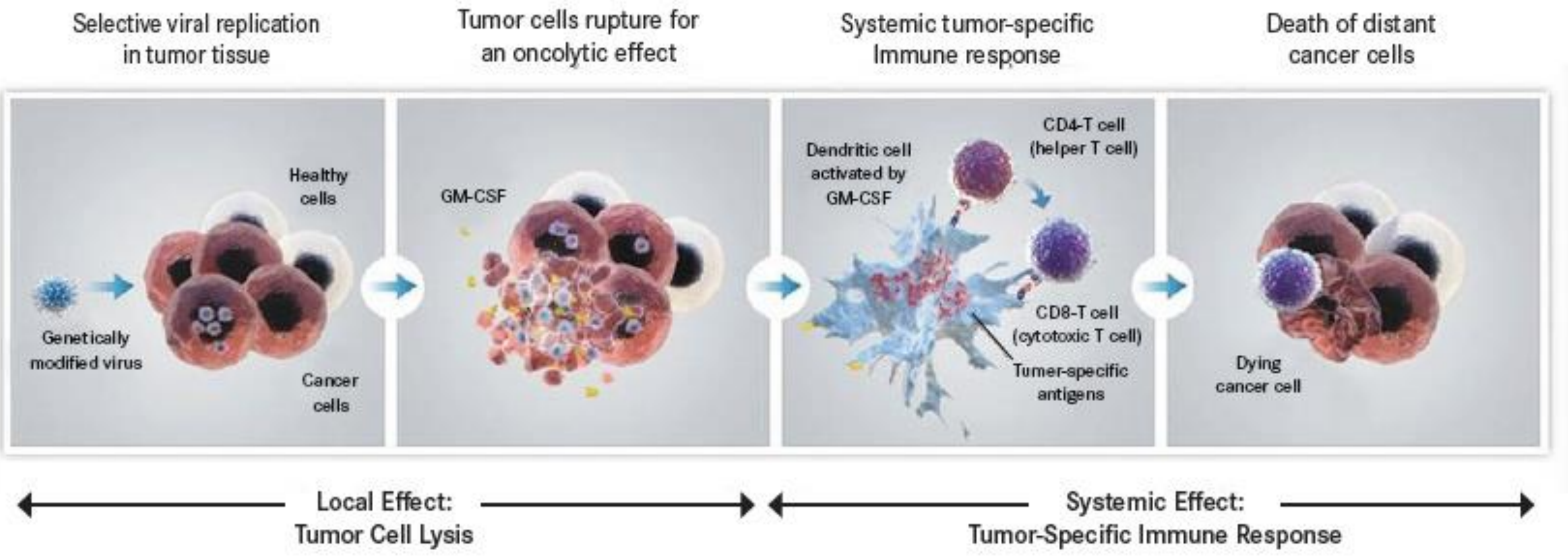
ONCOLYTIC VIRUS THERAPY

Oncolytic virus therapy uses genetically modified viruses to kill cancer cells.

First, the doctor injects a virus into the tumor. The virus enters the cancer cells and makes copies of itself. As a result, the cells burst and die. As the cells die, they release specific substances called antigens.

This triggers the patient’s immune system to target all the cancer cells in the body that have those same antigens. The virus does not enter healthy cells.

FIGURE 1. Talimogene laherparepvec (T-VEC) is a viral oncolytic immunotherapy designed to produce both local and systemic effect resulting in tumor lysis and death.



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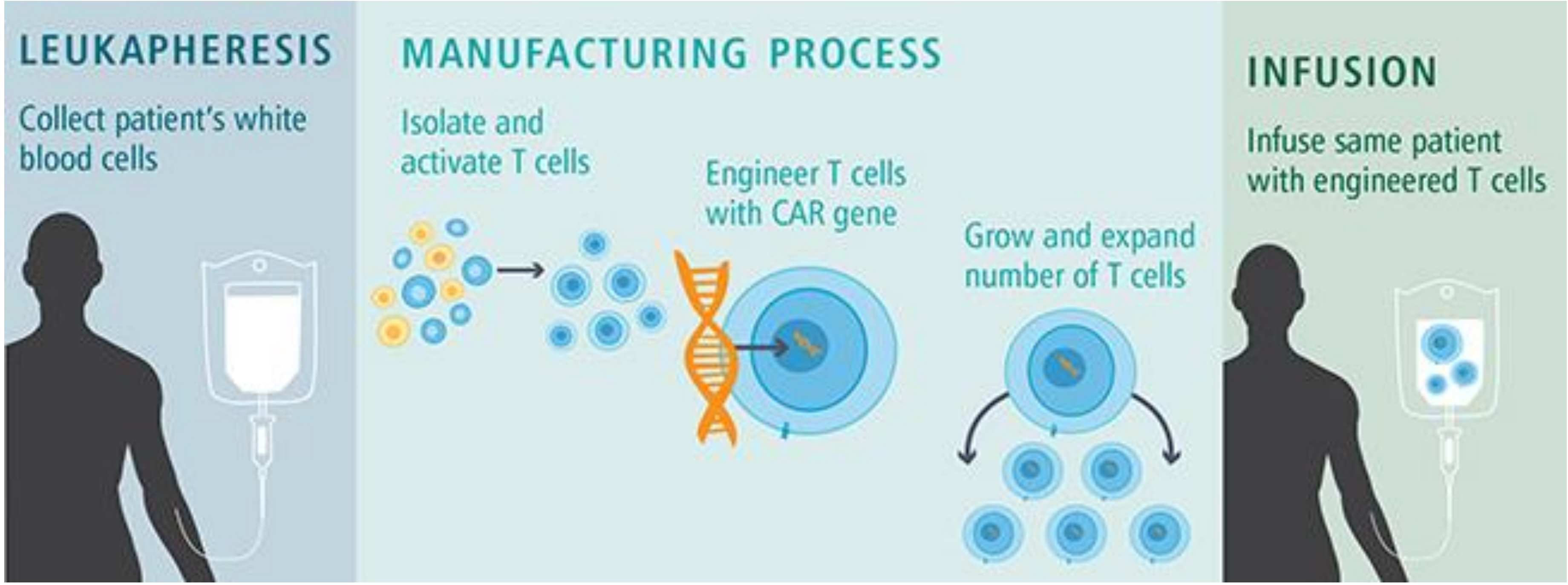
GM-CSF indicates granulocyte-macrophage colony-stimulating factor.

T-cell therapy:

In T-cell therapy, some T cells are removed from a patient's blood. Then, the cells are changed in a laboratory so they have specific proteins called receptors. The receptors allow those T cells to recognize the cancer cells. The changed T cells are grown in large numbers in the laboratory and returned to the patient's body. Once there, they seek out and destroy cancer cells. This type of therapy is called ***chimeric antigen receptor (CAR) T-cell therapy***.



Cancer vaccines

A vaccine is another method used to help the body fight disease. A vaccine exposes the immune system to an antigen. This triggers the immune system to recognize and destroy that antigen or related materials.

There are 2 types of cancer vaccines: prevention vaccines and treatment vaccines.