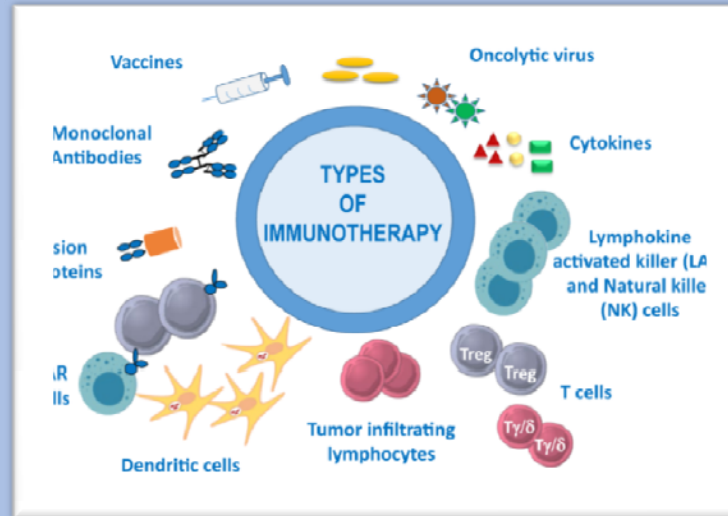
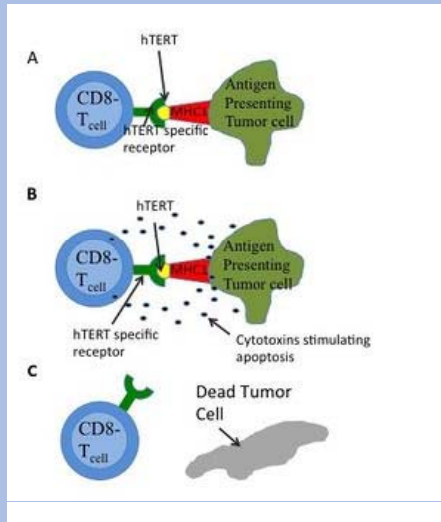


Immunotherapy



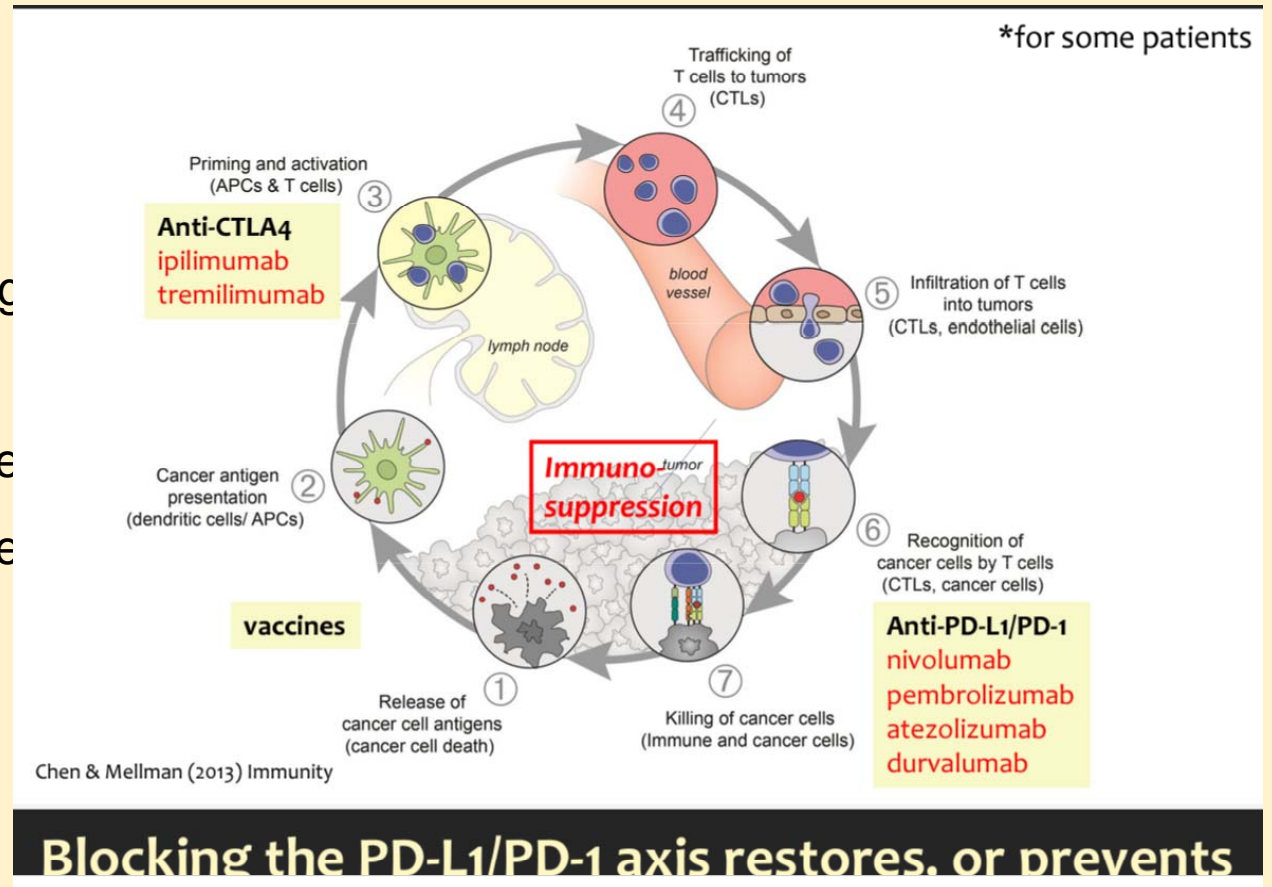
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What is immunotherapy?

- ❖ Immunotherapy is defined as one of the methods of treatment by inducing, enhancing, or suppressing an immune response.
- ❖ Immunotherapy is a relatively new form of treatment whereby the immune system is modulated to control diseases, for example autoimmune disease, allergies, or cancer.
- ❖ Therapies include immunosuppressants, biologicals (e.g. cytokines, monoclonal antibodies), vitamins and minerals (e.g., zinc, vitamin C, and vitamin B6), transplantation (e.g., bone marrow) and oncolytic viruses and cancer vaccines.
- ❖ It is one of the types of biological therapy in which the substances obtained from living organisms are used to treat cancer.

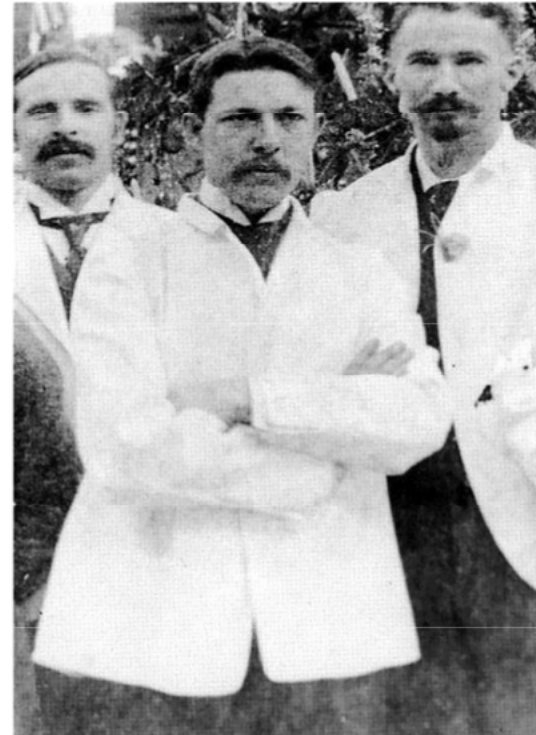
Immunotherapies are classified into two groups:

- **Activation immunotherapies:** includes immunotherapies employed for amplifying an immune response.
- **Suppression immunotherapies:** include immunotherapies that suppress or reduce an immune response.



- Mostly, immunotherapies have been found to be promising to cure varieties of cancer.
- Also, it often has fewer side effects in comparison to the existing drugs.
- Immunotherapy helps to enhance immune cells by providing with additional components.
- Immunotherapy instructs the immune system to identify and defend specific cancer cells.
- Immunotherapy helps to eradicate cancer by boosting immune cells.

William Coley and the birth of cancer immunotherapy



New York Times - July 29, 1908

ERYSIPELAS GERMS AS CURE FOR CANCER

Dr. Coley's Remedy of Mixed
Toxins Makes One Disease
Cast Out the Other.

MANY CASES CURED HERE

Physician Has Used the Cure for 15
Years and Treated 430 Cases—
Probably 150 Sure Cures.

Following news from St. Louis that
two men have been cured of cancer in
the City Hospital there by the use of
a fluid discovered by Dr. William B.
Coley of New York. It came out yester-

Types of Immunotherapy for cancer:

There are various types of immunotherapy.
They are listed as follows:

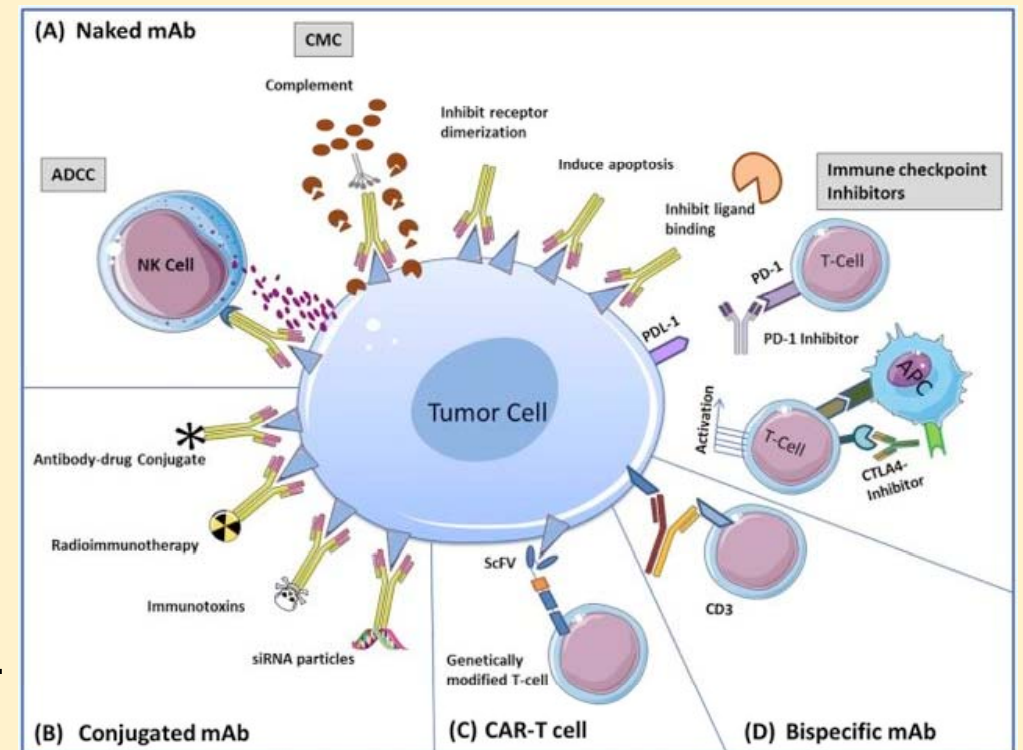
1. Monoclonal antibodies and tumor-
diagnostic treatments, such as checkpoint
inhibitors
2. Oncolytic virus therapy
3. CAR T-cell therapy
4. Cancer vaccines
5. Immune checkpoint inhibitors

Monoclonal antibodies (mAbs or MoAbs) and tumor-agnostic treatments:

- When a threat is sensed by the immune system, it produces antibodies.
- Antibodies are proteins that interact with antigens and initiate an immune response in the body.
- Monoclonal antibodies are defined as antibodies that are prepared in laboratory in order to boost the natural antibodies or to defend the foreign threats itself.
- Monoclonal antibodies help to fight cancer in several ways, for instance, monoclonal antibodies can be designed to fight with a specific cancer cell.
- Thus, it is also termed as targeted therapy.
- Basically, three types of mAbs are introduced, they are:

1. Naked monoclonal antibodies:

- Most commonly used for treatment of cancer.
- They are not attached to any other substance.
- These antibodies instruct the immune system to defend cancer cells or block proteins within tumor.

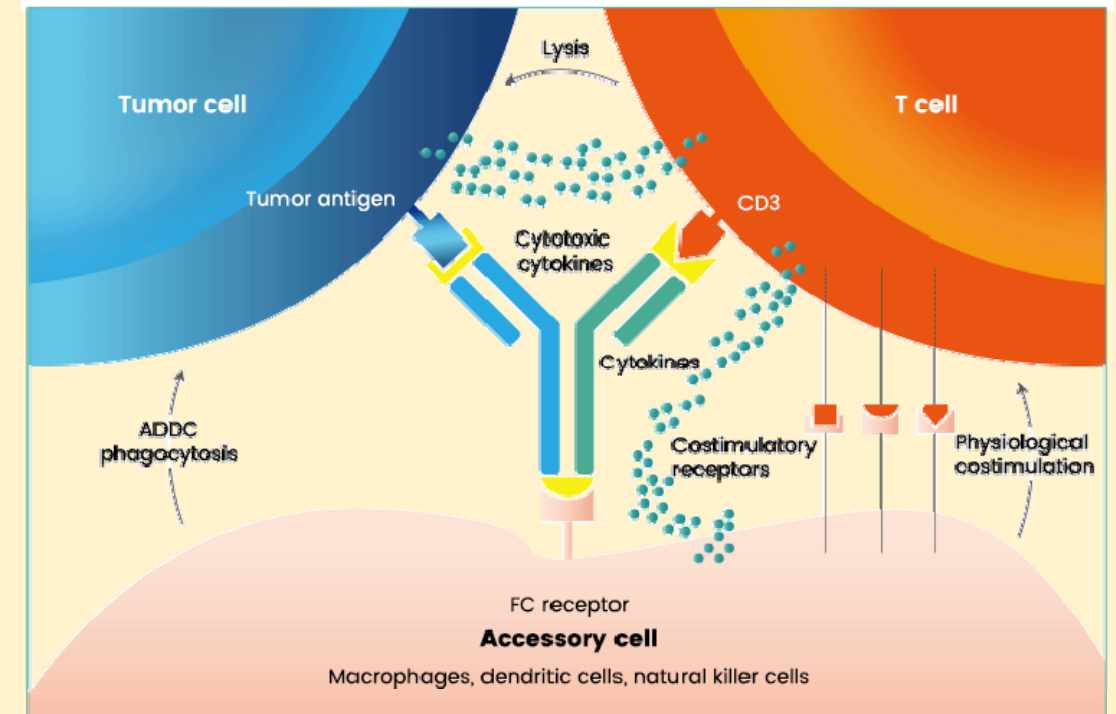
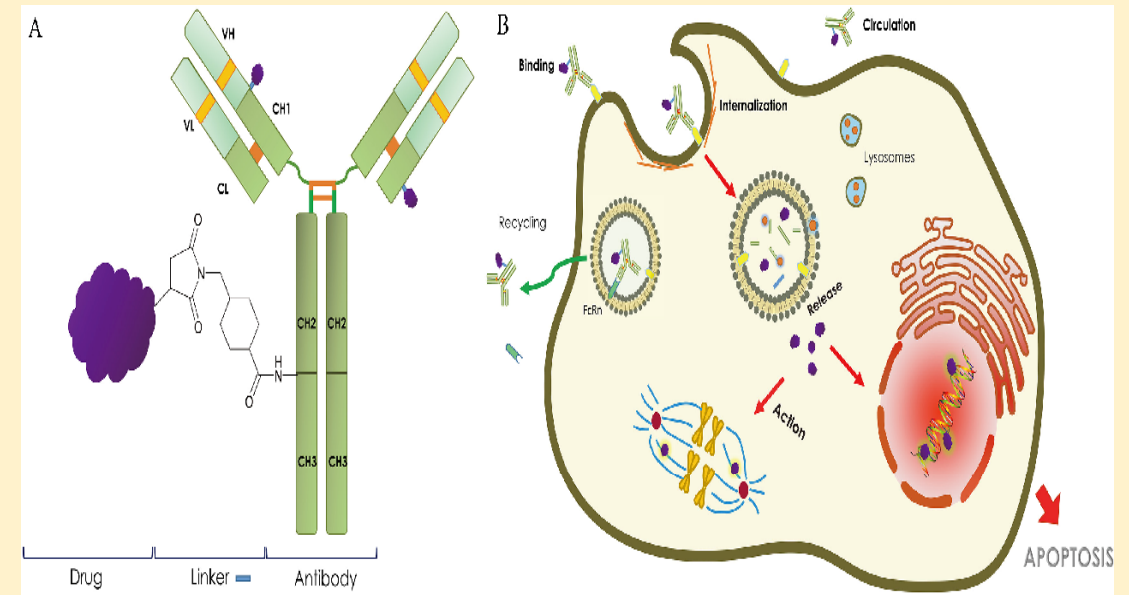


2. Conjugated monoclonal antibodies:

- These are attached with either a radioactive particle or chemotherapy drug.
- They are capable of attaching directly to the cancer cells.
- It works by delivering the drug to the location of utmost requirement.
- There are reduced or less chance of side effects and enhances the chemotherapy as well as radiation.

3. Bispecific monoclonal antibodies (BsMAb):

- These are antibodies designed in order to bind with two proteins at once.
- Few can bind to both cancer cells and an immune system cell facilitating the immune response on cancer.



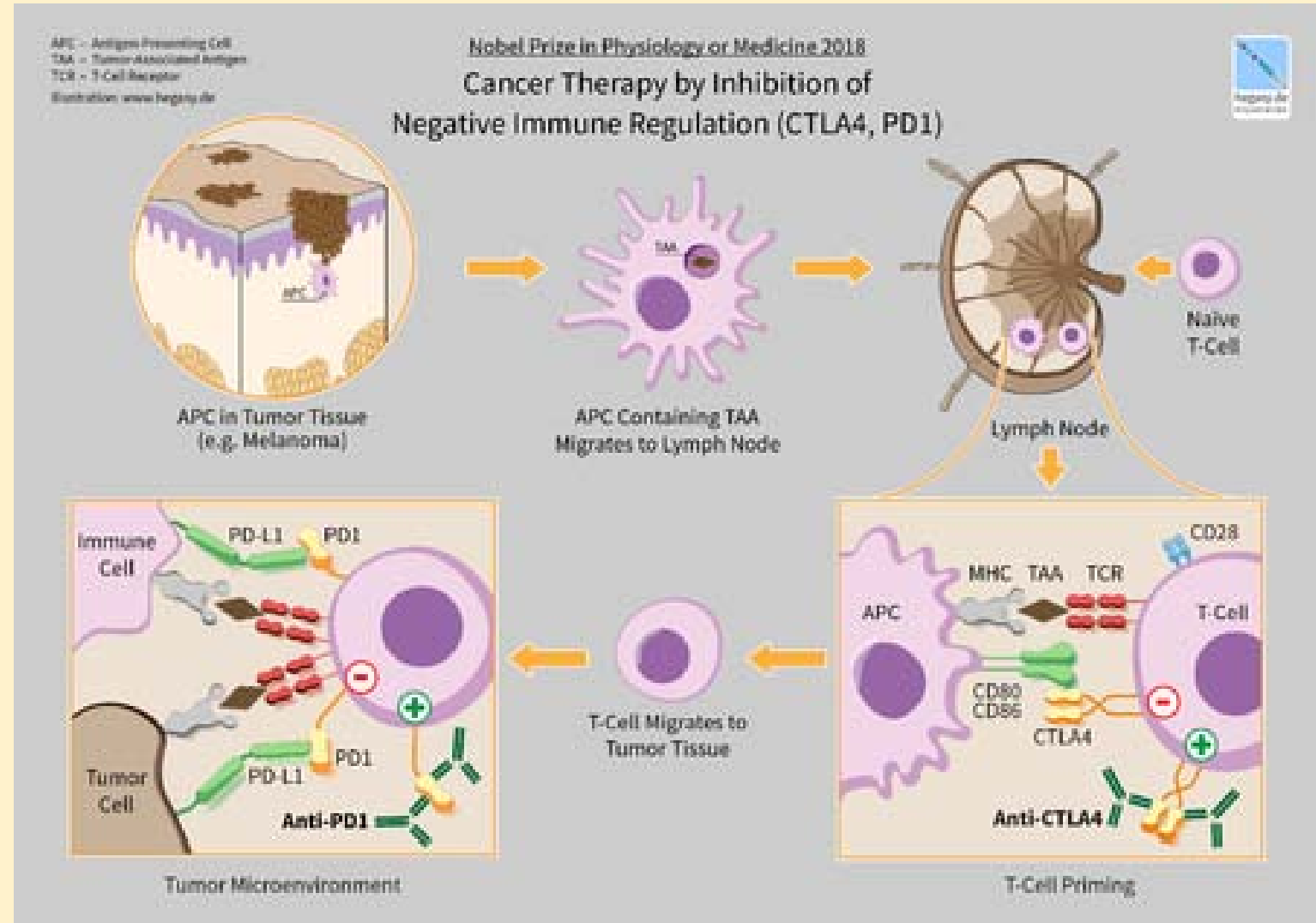
Checkpoint inhibitors

- Cancer cells can find ways to hide from the immune system by activating these checkpoints.

- These drugs basically take the 'brakes' off the immune system, which helps it recognize and attack cancer cells. Common checkpoints that these inhibitors affect are the PD-1/PD-L1 and CTLA-4 pathways. Examples of immune checkpoint inhibitors are: Ipilimumab (Yervoy); Nivolumab (Opdivo).

- Checkpoint inhibitors are used to treat cancers such as [melanoma skin cancer](#) and [lung cancer](#).

- Researchers are also looking at them in clinical trials for other types of cancer.



Oncolytic virus therapy:

- In this type of treatment, viruses used are modified in the lab with a motive to infect and kill specific tumor cells.

• Procedure of Oncolytic virus therapy:

- First, the genetically modified virus is injected into the tumor.
- Then the virus reaches the cancer cells and make copy of itself.
- This leads to the disruption of cancer cells and ultimately their death.
- As soon as the cells die, it stimulates the immune system to attack any cancer cells on the body having alike proteins as that of dead cells.

- This modified oncolytic virus doesn't affect healthy cells.

- This therapy is considered superior to all other immunotherapies as it does not depend on any specific antigen expression patterns.

- The features that makes it an ideal candidate for the treatment of diverse malignancies are as follows:

- Oncolytic viruses enhance the recruitment of tumor-infiltrating lymphocytes (TILs)
- Reprogramming of immunosuppressive tumor micro-environment (TME)
- Boosts systemic anti-tumor immunity

CAR T-cell therapy:

- It stands for **chimeric antigen receptor T-cell therapy (CAR T-cell therapy)**.
- T cell, a type of leukocytes is one of the main constituents of the adaptive immune system.
- In CAR T-cell therapy, the doctor reprograms T cells after taking out T cells from blood in order to find cancer cells more easily in contrast to it, T-cell therapy instruct the T-cells to search for tiny bits of specific antigens inside the cancer cells.
- **Procedure of CAR T-cell therapy:**
 - At first T cells are isolated from patient's blood.
 - Then, the receptors, which are specific proteins are added to it in the laboratory.
 - The receptors permit the T cells to identify cancer cells.
 - Then, the programmed T cells are then re-entered into the body.
 - Now, these cells find and destroy cancer cells.
- Side effects such as low blood pressure, fever, confusion, and in rare cases, seizures are observed.

Cancer vaccines:

- These are also termed as therapeutic vaccines.
- The vaccines are employed to people already diagnosed with cancer with a motive to increase body's natural defense in order to fight cancer.
- The vaccines may either prevent the cancer from recurrence, destroy any cancer cells remnant even after the accomplishment of other treatments or stop a tumor from spreading.

Procedure of cancer vaccine therapy:

- As we know, when the antibodies are produced in response to the antigens, the immune system develops memory cells, which will respond to these antigens in future.
- Cancer vaccines enhance the immune system's capacity to identify and destroy antigens.
- Certain molecules termed as cancer specific antigens are present on the surface of the cancer cells, which are lacked by healthy cells.
- These molecules act as antigens when given to a person, and trigger the immune system to identify and kill cancer cells having these molecules on the surface.
- Few cancer vaccines also consist of adjuvants that may enhance the immune response.

Immune-checkpoint inhibitors:

- It is the significant function of immune cells to be able to differentiate between the own normal cells and foreign cells.
- Checkpoints are thus required, in order to monitor the foreign cells.
- In general term, immune checkpoints are molecules on specific immune cells that needs to be either activated or inactivated for starting an immune response.
- Drugs targeting these checkpoints are found to be promising for cancer treatment.
- These drugs are hence termed as checkpoint inhibitors.
- Two types of checkpoint inhibitors are described on the basis of proteins they target, they are:

•i. Checkpoint inhibitors that target PD-1 or PD-L1:

- T cells are immune cells and PD-1 is a checkpoint protein on it.
- PD-1 protein prevents the T-cells from attacking other cells in the body, acting as a type of off switch.
- It occurs when it is bound to PD-L1, which is a protein on some normal and cancer cells.
- After the binding, it stops T-cells from attacking any cells favoring the cancer cells with high PD-L1 protecting it from immune attack.
- Monoclonal antibodies targeting either PD-1 cells or PD-L1 cells can prevent the binding and enhance immune response against cancer cells.

•**Drugs targeting PD-1 (PD-1 inhibitors):**

- Pembrolizumab (Keytruda)
- Nivolumab (Opdivo)
- Cemiplimab (Libtayo)

•**Drugs targeting PD-L1 (PD-L1 inhibitors):**

- Atezolizumab (Tecentriq)
- Avelumab (Bavencio)
- Durvalumab (Imfinzi)

ii. Checkpoint inhibitors that target CTLA-4

- Some T cells contain CTLA-4 protein that also acts as a off switch in order to regulate immune system.
- The CTLA-4 is inhibited by Ipilimumab (Yervoy) which is a monoclonal antibody that attaches to CTLA-4.
- The body's immune response is hence improved.
- This drug is proved to treat melanoma of skin.

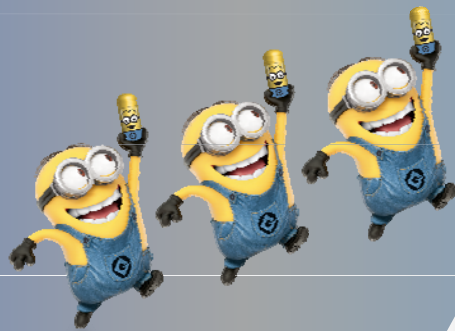
•**Side effects of checkpoint inhibitors include:**

- – Inflammation in the lungs
- – Rashes along with itchiness
- – Kidney infections
- – Diarrhea

Benefits

- ✓ Only a tiny minority of patients expected to die from cancer will benefit from immunotherapy.
- ✓ Immunotherapies have been used for a hundred years eg the deliberate injection of bacteria into the body to stimulate the immune system,
- ✓ 2011 marked the approval of the first immunotherapy for cancer, a checkpoint inhibitor named ipilimumab (Yervoy). This class of drugs unleashes the body's immune system against cancer, and is the subject of much enthusiasm.
- ✓ When immunotherapy works the results are terrific.
- ✓ Patients with otherwise life-threatening cancers live far longer than expected and some may even be cured by immunotherapy however today few patients can expect to be among the lucky ones.
- ✓ Several common cancers, like colon and breast cancer, these drugs work poorly for.
- ✓ The ability to manipulate components of the immune system with drugs and to manipulate and activate an individual patient's cells in the laboratory are the areas with great interest and activity now," said Clifford A. Hudis, MD, the chief of breast cancer medicine service at Memorial Sloan Kettering Cancer Center in New York City, although he warned that clinicians should avoid creating unreasonable expectations among patients.
- ✓ The key point physicians have to convey to lay audiences is the power of the immune system and the fact

THANK YOU



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