Immunotherapy for Cancer

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Cancer Immunotherapy

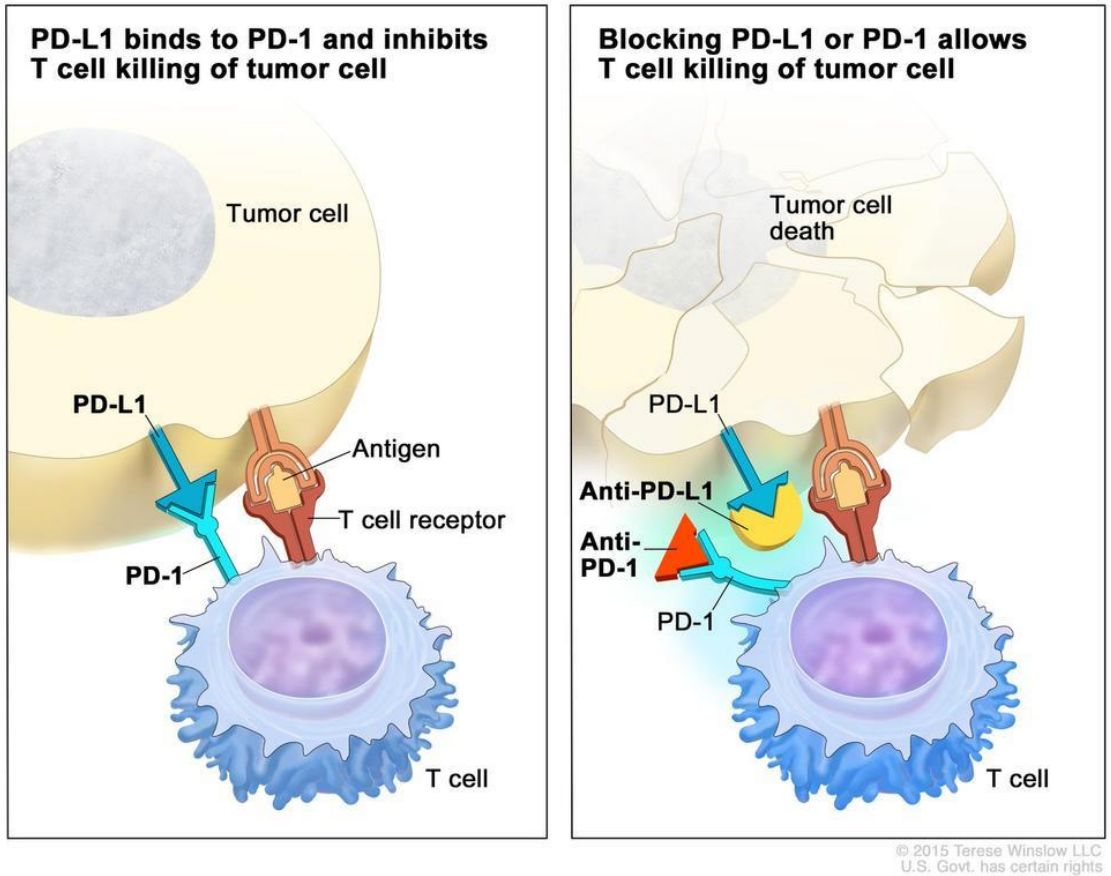
- Immunotherapy is a type of cancer treatment.
- It uses substances made by the body or in a laboratory to boost the immune system and help the body find and destroy cancer cells. Immunotherapy can treat many different types of cancer.
- It can be used alone or in combination with chemotherapy and/or other cancer treatments.

Types of Cancer Immunotherapy

- Immune check point inhibitors- drugs that block immune checkpoints
- T cell transfer therapy-
- Monoclonal antibodies/ therapeutic Ab
- Treatment Vaccines
- Immune system modulators

Immune check point inhibitors

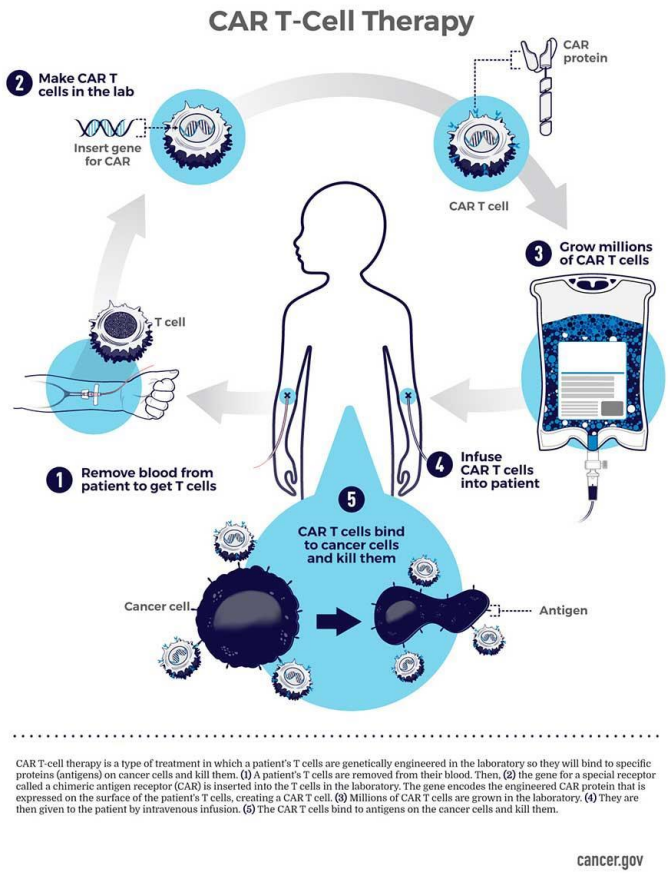
- Their role is to prevent an immune response from being so strong that it destroys healthy cells in the body.
- Immunotherapy drugs called immune checkpoint inhibitors work by blocking checkpoint proteins from binding with their partner proteins. This prevents the “off” signal from being sent, allowing the T cells to kill cancer cells.
- One such drug acts against a checkpoint protein called CTLA-4. Other immune checkpoint inhibitors act against a checkpoint protein called PD-1 or its partner protein PD-L1.
- Some tumors turn down the T cell response by producing lots of PD-L1.
- many types of cancer, including melanoma, lung, kidney, bladder, and lymphoma.

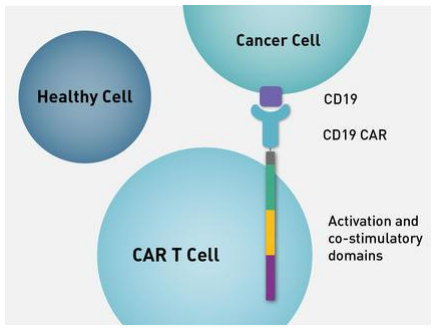


https://www.cancer.gov/about-cancer/treatment/types/immunotherapy

T cell transfer therapy-5th pillar

- There are two main types of T-cell transfer therapy:
  - tumor-infiltrating lymphocytes (or TIL) therapy : T cells called tumor-infiltrating lymphocytes that are found in your tumor . dentifying TILs that recognize cancer cells with mutations specific to that cancerExit Disclaimer and identifying people whose cancers are more likely to respond to TIL therapy.
  - CAR T-cell therapy: CAR stands for chimeric antigen receptor. CARs are designed to allow the T cells to attach to specific proteins on the surface of the cancer cells, improving their ability to attack the cancer cells.
- Both involve collecting your own immune cells, growing large numbers of these cells in the lab, and then giving the cells back to you through a needle in your vein.
- T-cell transfer therapy is also called adoptive cell therapy, adoptive immunotherapy, and immune cell therapy.
- 2017, six CAR T-cell therapies have been approved by the Food and Drug Administration (FDA). All are approved for the treatment of blood cancers, including lymphomas, some forms of leukemia, and, most recently, multiple myeloma.





2017, with FDA's approval of tisagenlecleucel (Kymriah), the first CAR T-cell therapy to be approved by the agency, based on clinical trials demonstrating it could eradicate cancer in children with relapsed ALL.

BCMA and CD19-targeted CAR T cells are also offering hope to adults and children with advanced aggressive lymphomas

One of the most frequent and serious side effects is cytokine release syndrome (CRS). neurologic effects, including severe confusion, seizure-like activity, and impaired speech.

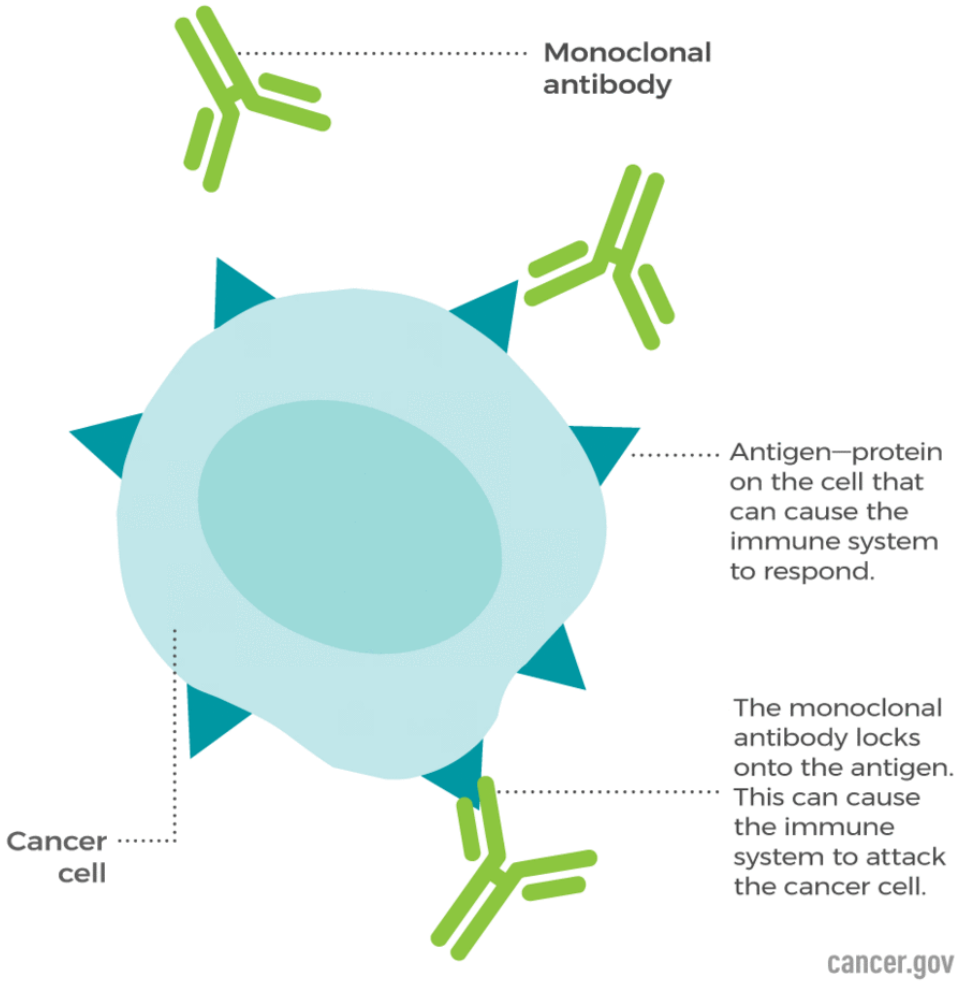
Unsuccessful for solid tumors

Gene-editing technologies like TALON and CRISPR are being used to induce the donated T cells to produce CARs.

NKT cells

using nanotechnology and mRNA-based approaches that allow CAR T cells to be created inside the body.

Therapeutic antibodies/ Monoclonal antibodies.



- Mab mark cancer cells so that the immune system will better recognize and destroy them. Eg rituximab, which binds to a protein called CD20 on B cells and some types of cancer cells, causing the immune system to kill them.
- Pembrolizumab, trastuzumab-HER 2R
- Blinatumomab (Blincyto®), which binds to both CD19, a protein found on the surface of leukemia cells, and CD3, a protein on the surface of T cells. This process helps the T cells get close enough to the leukemia cells to respond to and kill them.

https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/monoclonal-antibodies

Cancer Treatment Vaccines/ Oncolytic Virus therapy

- Cancer treatment vaccines are a type of immunotherapy that treats cancer by strengthening the body's natural defenses against the cancer.
- Unlike cancer prevention vaccines, cancer treatment vaccines are designed to be used in people who already have cancer—they work agai
- Treatment vaccines against tumor associated antigens (not present in healthy) can help the immune system learn to recognize and react to these antigens and destroy cancer cells that contain them.

Cancer treatment vaccines may be made in three main ways

- Own tumor cells: custom-made so that they cause an immune response against features that are unique to your cancer.
- Made from tumor-associated antigens that are found on cancer cells of many people with a specific type of cancer. Such a vaccine can cause an immune response in any patient whose cancer produces that antigen. This type of vaccine is still experimental.
- Dendritic cell vaccines stimulate your immune system to respond to an antigen on tumor cells. One dendritic cell vaccine has been approved, sipuleucel-T, which is used to treat some men with advanced prostate cancer. Sipuleucel-T is used to treat people with prostate cancer:
  - that has spread to other parts of the body
  - who have few or no symptoms
  - whose cancer does not respond to hormone treatment

Oncolytic virus therapy

- The first FDA-approved oncolytic virus therapy is talimogene laherparepvec (T-VEC, or Imlygic®). It is based on herpes simplex virus type 1. Although this virus can infect both cancer and normal cells, normal cells are able to kill the virus while cancer cells cannot. Melanoma treatment

- T-VEC is injected directly into a tumor. As the virus makes more and more copies of itself, it causes cancer cells to burst and die. The dying cells release new viruses and other substances that can cause an immune response against cancer cells throughout the body.

Immune System Modulators

- Types of immune system modulators include cytokines, BCG, and immunomodulatory drugs.
- Cytokines that are sometimes used to treat cancer:
  - **Interferons (INFs).** Researchers have found that one type of interferon, called INF-alfa, can enhance your immune response to cancer cells by causing certain white blood cells, such as natural killer cells and dendritic cells, to become active. INF-alfa may also slow the growth of cancer cells or promote their death.
  - **Interleukins (ILs).** There are more than a dozen interleukins, including IL-2, which is also called T-cell growth factor. IL-2 boosts the number of white blood cells in the body, including killer T cells and natural killer cells. Increasing these cells can cause an immune response against cancer. IL-2 also helps B cells (another type of white blood cell) produce certain substances that can target cancer cells.
  - Cytokines that are sometimes used to reduce side effects from cancer treatment are called hematopoietic growth factors. They promote the growth of blood cells that are damaged by chemotherapy:
  - **Erythropoietin**, which increases the production of red blood cells.
  - **IL-11**, which increases the production of platelets.
  - **Granulocyte-macrophage colony-stimulating factor (GM-CSF) and granulocyte colony-stimulating factor (G-CSF)**, which both increase the number of white blood cells. Boosting white blood cells reduces the risk of infections. G-CSF and GM-CSF can also enhance the immune system response against cancer by increasing the number of cancer-fighting T cells.

- BCG (live attenuated vaccine form of *Mycobacterium bovis*) is used to treat bladder cancer. When inserted directly into the bladder with a catheter, BCG causes an immune response against cancer cells. It is also being studied in other types of cancer. BCG stands for Bacillus Calmette-Guérin.
- Immunomodulatory drugs (also called biological response modifiers) stimulate the immune system. They include
  - thalidomide (Thalomid®)
  - lenalidomide (Revlimid®)
  - pomalidomide (Pomalyst®)
  - imiquimod (Aldara®, Zyclara®)
- Thalidomide, lenaliodomide, and pomalidomide cause cells to release IL-2. They also stop tumors from forming new blood vessels. Tumors need to form new blood vessels to grow beyond a certain size. These three drugs may also be called angiogenesis inhibitors.
  - Imiquimod is a cream that you rub on the skin. It causes cells to release cytokines.

Reference

- https://www.cancer.gov/about-cancer/treatment/types/immunotherapy
- "Targeted Therapy to Treat Cancer was originally published by the National Cancer Institute.“
- https://en.wikipedia.org/wiki/Cancer_immunotherapy
- Hamden F, Cerullo V. Cancer immunotherapies: A hope for the incurables. Front. Mol. Med. Vol 3. 2023 https://doi.org/10.3389/fmmed.2023.1140977