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Cancer Action Network℠ American Cancer Society®

ACS CAN, the nonprofit, nonpartisan advocacy affiliate of the American Cancer Society, supports evidence-based policy and legislative solutions designed to eliminate cancer as a major health problem. ACS CAN works to encourage elected officials and candidates to make cancer a top national priority. ACS CAN gives ordinary people extraordinary power to fight cancer with the training and tools they need to make their voices heard. For more information, visit acscan.org.

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IMMUNOTHERAPY

HOW IT CAN HELP THE FIGHT AGAINST CANCER

GENERAL IMMUNOLOGY

YOUR IMMUNE SYSTEM IS A COLLECTION OF SPECIAL CELLS THAT HELP PROTECT YOU FROM INFECTIONS AND SOME OTHER DISEASES. IT CAN ALSO HELP PROTECT YOU FROM SOME CANCERS.

Special immune cells travel through your body looking for foreign substances that don't belong, such as germs. In their travels, they also encounter your body's own cells. Your immune system can tell the difference between your own cells and cells that don't belong. This is very important because it keeps your immune system from attacking your own healthy cells.

Any new substance in your body that the immune system doesn't recognize can raise an alarm and cause your immune system to attack and attempt to kill or remove it. Substances that cause an immune response are called antigens. For example, germs have substances, such as certain proteins, on their outer surfaces that aren't normally found in the human body. Your immune system sees these foreign substances (antigens) as an enemy and attacks the cells that have them on their surface.

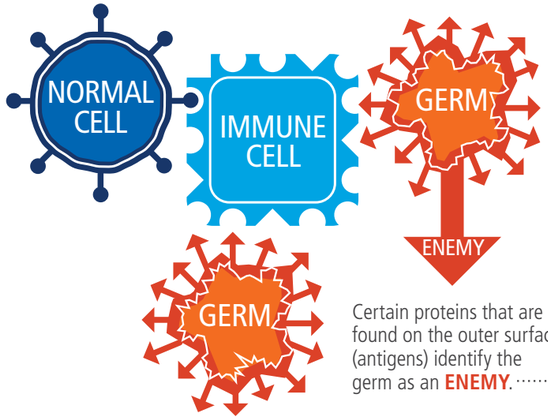
Cancer cells are actually your own cells, but due to some change in the cells' genes, they have begun to grow out of control. While they are your own cells, cancer cells can sometimes look different from normal cells, such as having unusual substances on their outer surfaces that can act as antigens. These differences are sometimes enough of a red flag to cause the cancer cells to be attacked and destroyed by your immune system. However, sometimes cancer cells don't look different enough to be noticed. It's also possible your immune system recognizes the cancer cells, but its response may not be strong enough to destroy them. Lastly, cancer cells have the ability to use natural defense mechanisms that identify them as a friend and keep the immune system from attacking them.

To make sure your immune system has the best chance of recognizing and killing cancer cells, researchers have found ways to help strengthen the immune system response. Some of these new therapies have been approved by the Food and Drug Administration (FDA), but many are still only available in clinical trials. While strengthening the immune response can help the body eliminate cancer cells, side effects of an overly strong immune response can include damage to healthy cells and organs. When your immune system attacks your own body it's known as autoimmunity. This can be very dangerous, but fortunately it's relatively rare.

TAKEAWAYS

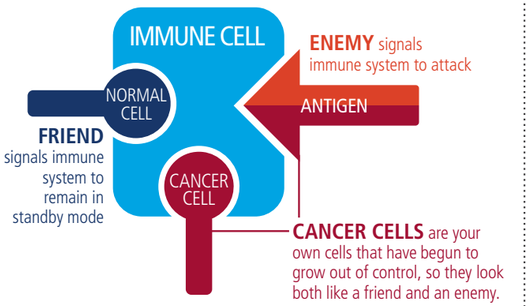
1. **Your immune system has the potential to help fight cancer.**
2. **The ability for your immune system to successfully kill cancer cells can be limited by natural processes.**
3. **New treatment approaches, recently developed and still being researched, can help overcome some of these natural limitations.**
4. **Many of these new treatments are only available in clinical trials.**
5. **Efforts to increase your immune system's power to kill cancer cells can also lead to your immune system attacking healthy cells and organs (autoimmunity).**

IMMUNE CELLS LOOK FOR FOREIGN ANTIGENS, LIKE **GERMS,** THAT DON'T BELONG.

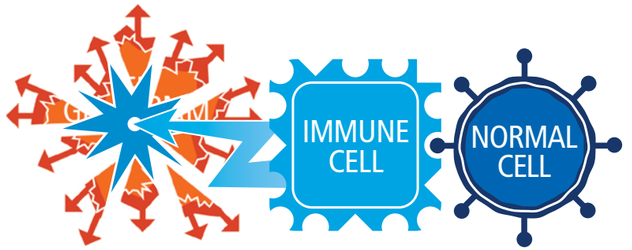


Certain proteins that are found on the outer surface (antigens) identify the germ as an **ENEMY.**

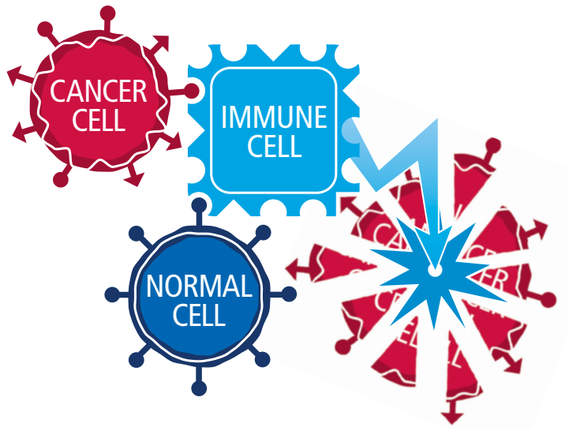
The identification of these proteins works like a **LOCK AND KEY SYSTEM** between the immune cell, normal cell, cancer cell and any foreign substance.



IMMUNE CELLS REMOVE CELLS THAT ARE IDENTIFIED AS AN ENEMY.



CANCER CELLS CAN HAVE PROTEINS THAT IDENTIFY THEM AS BOTH A **FRIEND** & **ENEMY,** SO SOMETIMES THE IMMUNE SYSTEM HAS A HARD TIME RECOGNIZING CANCER CELLS AS AN ENEMY.



CHECKPOINT INHIBITORS

YOUR IMMUNE SYSTEM HAS IMPORTANT CHECKS AND BALANCES. THESE CHECKS AND BALANCES CONTROL WHEN YOUR IMMUNE SYSTEM GOES INTO ATTACK MODE TO REMOVE UNWANTED CELLS AND WHEN IT STAYS IN STANDBY MODE.

This is very important because if your immune system is overly active, it can attack normal cells in your body and cause damage.

T cells are natural immune cells that travel through your body to look for cells that don't belong, like germs. T cells look for unwanted cells using receptors on their own surface that match up with proteins on the surface of unwanted cells. The system works like a lock and key – T cells have a series of locks (receptors) that fit with keys (surface proteins) usually found on germs – when a match is made the T cell turns to attack mode and destroys the germ.

To keep T cells from attacking normal cells in your body, you have immune checkpoints. Checkpoints are like circuit breakers. They can turn off the T cell's attack mode if it might attack your body's own cells. Much like the protein interactions that turn on the attack, checkpoints rely on protein interactions to turn off the attack, but it's through the interactions of a different set of proteins.

In the case of cancer, your immune system is sometimes able to identify cancer cells and destroy them, but some cancer cells seem to be well adapted at using checkpoints to shut down natural immune system attacks. Researchers have developed a number of different drugs that block this checkpoint process, which are known as checkpoint inhibitors. When checkpoint inhibitors are used, the ability of cancer cells to switch T cells back into standby mode is taken away, and your immune system is better able to attack and kill cancer cells.

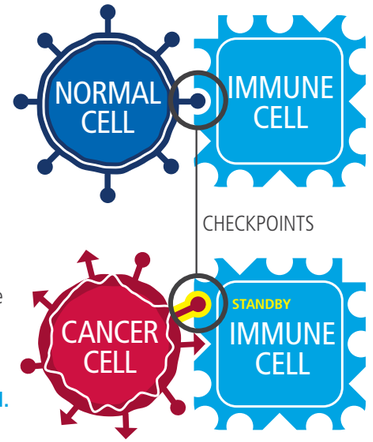
The immune checkpoint process exists so your own healthy cells are not mistakenly killed by your immune system, a process known as autoimmunity. Autoimmunity is a rare but potentially dangerous side effect of using drugs to shut down the checkpoint process and can lead to serious organ damage.

Currently, three checkpoint inhibitors have been approved to treat cancer, two of them for use in treating melanoma, and one for both melanoma and lung cancer.

Checkpoint inhibitors are an area of intense research, with many of the approved drugs, as well as other experimental drugs, being tested in clinical trials for a variety of cancers.

IMMUNE CELLS AND YOUR OWN **NORMAL CELLS** INTERACT THROUGH CHECKPOINTS.

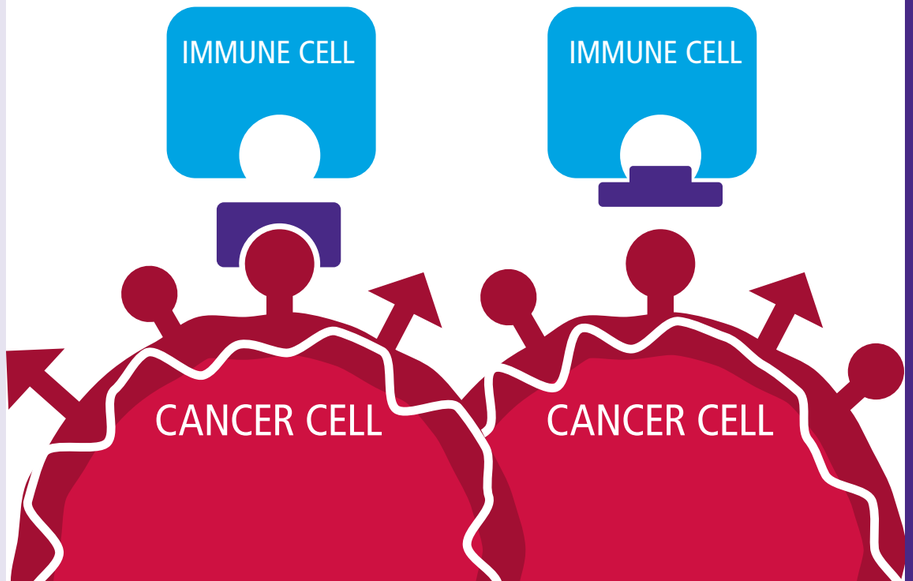
The checkpoint process identifies your own cells as **FRIENDS** and prevents your **IMMUNE SYSTEM** from attacking them.



Since **CANCER CELLS** are your own cells, they can use the checkpoint process by appearing as a friend to protect against an attack by your **IMMUNE SYSTEM.**

CHECKPOINT INHIBITORS ARE DRUGS THAT BLOCK CHECKPOINTS, REMOVING THE ABILITY FOR CANCER CELLS TO APPEAR AS A **FRIEND** TO THE **IMMUNE SYSTEM.**

CHECKPOINT INHIBITORS CAN BE DESIGNED TO BLOCK THE PROTEINS ON **CANCER CELLS,** OR BLOCK THE RECEPTORS ON **IMMUNE CELLS.**



TAKEAWAYS

1. **Checkpoint inhibitors are a rapidly developing type of immunotherapy and an active area of current cancer research.**
2. **Current, FDA-approved checkpoint inhibitors are:**
   - **Yervoy (ipilimumab)**
   - **Keytruda (pembrolizumab)**
   - **Opdivo (nivolumab)**
3. **Checkpoint inhibitors are biologic therapies (antibodies), but they work by enhancing the body's own immune response.**
4. **Checkpoint inhibitors are administered intravenously (IV or into vein) in a physician's office and are typically covered by the medical portion of a health insurance benefit.**
5. **Checkpoint inhibitors will likely expand from their original approved use to additional approvals and potential off-label use in other cancer types.**

CHIMERIC ANTIGEN RECEPTOR (CAR) T CELL THERAPY

IN GREEK MYTHOLOGY THE CHIMERA IS A FIERCE CREATURE MADE FROM PARTS OF SEVERAL DIFFERENT ANIMALS – A LION, A GOAT, AND EVEN A SNAKE. CHIMERIC ANTIGEN RECEPTOR T CELLS, OR "CAR T CELLS" FOR SHORT, GET THEIR NAME BECAUSE THEY COMBINE SEVERAL FEATURES FROM DIFFERENT CELLS IN YOUR BODY THAT MAKE THEM ESPECIALLY GOOD AT FINDING AND KILLING CANCER CELLS.

T cells are immune system cells that find and kill unwanted cells in your body, like germs, by looking for unusual proteins (antigens) on the surface of cells. T cells travel through the body and look for proteins on the surfaces of other cells that indicate the cell should be killed. The system works like a lock and key – T cells have a series of locks (receptors) that fit with keys (surface proteins) usually found on germs. When a match is made, the T cell turns to attack mode and eliminates the germ. While germs look very different from normal human cells and are easily seen as foreign, that is not always the case with cancer cells. Cancer cells are your own cells that have begun to grow out of control, and the special proteins found on their surface sometimes are not as easily recognized by T cells as foreign.

CAR T cells are a type of special T cell; they are created in the lab to be better able to identify cancer cells. To do this, T cells are removed from the cancer patient's own blood and are genetically altered in the lab to have specific antigen receptors (chimeric antigen receptors, or CARs) on their surface that are designed to recognize common proteins found on cancer cells and trigger the CAR T cells to attack. The CAR T cells are multiplied in the lab and then put back into the patient's blood, where they can seek out cancer cells and launch a precise immune attack against them.

This type of treatment is different from many traditional treatments because it doesn't use a drug to treat cancer, but instead uses the patient's own living cells that have been modified in the laboratory. The cells continue to live once returned to the patient's body, and can reproduce without the need for repeated infusions of additional CAR T cells. This treatment is not without side effects, including high fevers and low blood pressure, which in some cases can be severe. As more people get this treatment, doctors are learning how to better manage CAR T cell therapy side effects.

Just as it's important to match blood types for blood transfusions or organ donations, it's also important to match CAR T cells. Currently, each patient must have their own T cells removed from their blood, modified and returned, which means this treatment cannot be mass-produced in the same way traditional chemotherapy drugs can. However, efforts are underway to find ways to use the same transformed CAR T cells for multiple people.

This technique has shown very encouraging results in early clinical trials against some advanced, hard-to-treat types of leukemia and lymphoma. However, at this time there are no CAR T cell therapies approved by the FDA, so this treatment is only available in clinical trials.

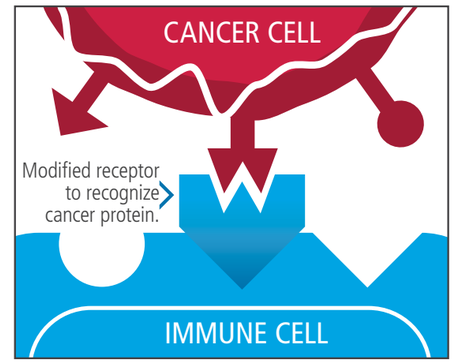
T CELLS ARE TAKEN FROM A PATIENT.

THE **CELLS** ARE THEN TRANSFORMED SO THEY WILL HAVE **CHIMERIC ANTIGEN RECEPTORS (CARs). CAR T CELLS** BETTER RECOGNIZE PROTEINS OFTEN FOUND ON A PATIENT'S **CANCER CELLS.**

CANCER CELL

CANCER CELLS may have unique proteins on their surface that are not normally identified by **IMMUNE CELLS** as an **ENEMY.**

CARs WORK LIKE ADAPTORS THAT TURN ON THE **IMMUNE CELL'S** ENEMY RESPONSE WHENEVER IT IDENTIFIES PROTEINS COMMONLY FOUND ON **CANCER CELLS.**



Normal antigen receptors trigger an **ENEMY** response.

CARs are designed to trigger an **ENEMY** response specifically for **CANCER CELLS.**

THE **TRANSFORMED IMMUNE CELLS** ARE THEN REINTRODUCED INTO THE PATIENT SEVERAL DAYS OR WEEKS AFTER THEIR INITIAL REMOVAL.

THESE CELLS ATTACK THE PATIENT'S **CANCER CELLS**, AND CAN CONTINUE TO REPRODUCE IN THE PATIENT'S BODY.

THE PATIENT'S **TRANSFORMED IMMUNE CELLS** ARE GROWN IN A LAB, TURNING THOUSANDS OF CELLS INTO BILLIONS OF CELLS.

TAKEAWAYS

1. **CAR T cell therapies are regulated by the FDA as biologic therapies.**
2. **CAR T cell therapies are unique to each patient, so their safety and efficacy are strongly reliant on process controls.**
3. **Federal funding is key to the development of CAR T cell therapies. The development of most drugs typically shifts from academic laboratories to private industry early in the drug development cycle. Commercial funding of CAR T cell therapy development, however, tends to come much later in the development cycle. This means the development of treatments like this are strongly dependent on academic research support.**
4. **Provenge, a similar cell-based therapy, took a long time to be covered by insurance after FDA approval.**