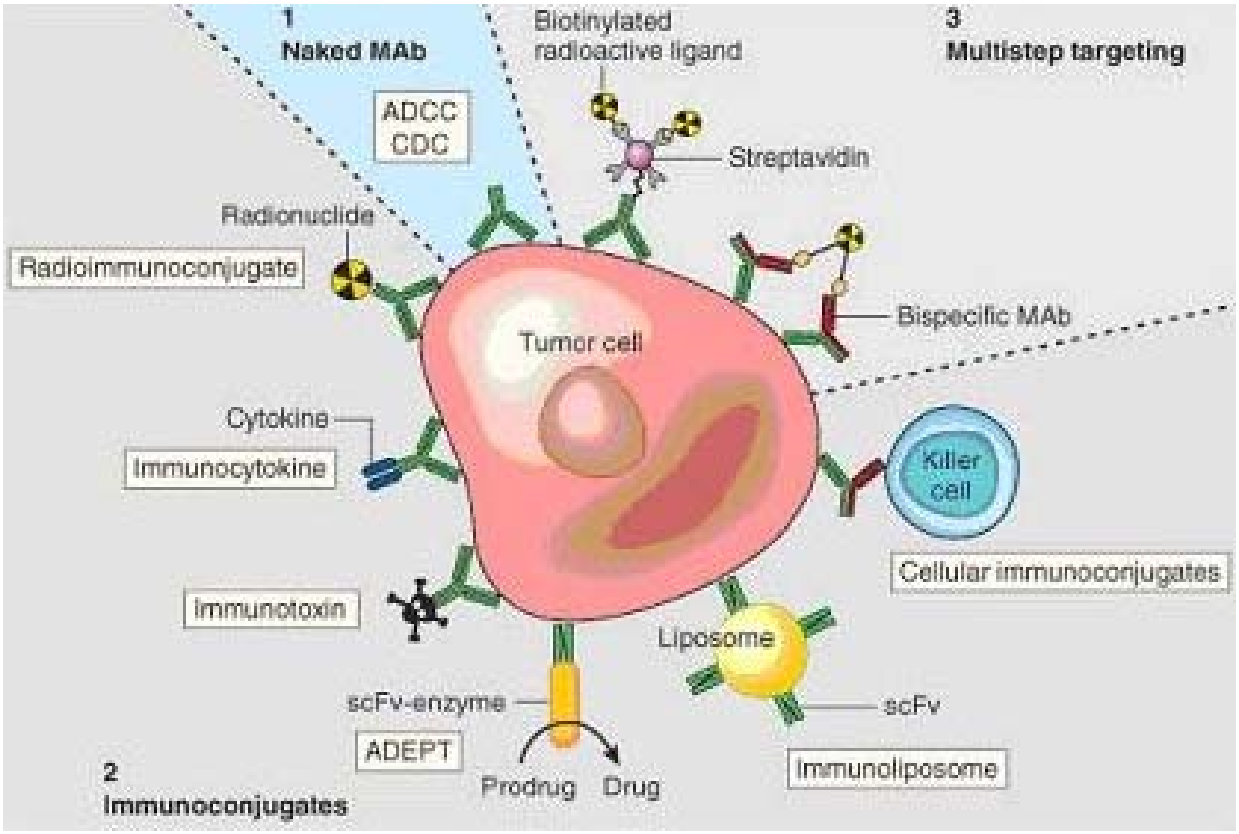
Biological Applications of Immunology Report

免疫學及其於生物醫學之應用期末報告



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Cancer Immunotherapy

What Is Immunotherapy

Immunotherapy is treatment that uses certain parts of the immune system to fight disease, including cancer. This can be done by stimulating your own immune system to work harder or by using an outside source, such as man-made immune system proteins. Immunotherapy is sometimes used by itself, but it is most often used as an adjuvant to add to the effects of the main therapy.

How the Immune System Works

Your immune system is a collection of organs, specialized cells, and substances that help protect you from disease. Immune system cells and the substances they make circulate throughout your body to protect it from germs that cause infections, and to some extent ,from cancer.

Reacting to Antigens

Anything that causes the immune response is called an *antigen*. Antigens cause an immune reaction that can lead to destruction of both the antigen and anything the antigen is attached to or part of, such as a bacterial cell or a cancer cell.

Germs such as viruses, bacteria, and parasites have substances on their outer surfaces, such as certain proteins, that are not normally present in the body. These foreign substances are recognized by the immune system as antigens. Cancer cells also have some unusual substances on their outer surfaces that can act as antigens, marking the cells as different or abnormal.

Generally, the immune system is much better at recognizing germs than cancer cells. Germs are truly "foreign" to the body, and their cells differ quite a bit from normal human cells. In contrast, the differences between normal cells and cancer cells may be less clear cut.

The Member Of The Immune System

The response to antigens is a highly coordinated process that uses the many types of cells of the immune system. Most cells of the immune system are *lymphocytes*. Several types of lymphocytes work together to attack cancer cells:

- **B cells (B lymphocytes)**
- **T cells (T lymphocytes)**

killer T cells

helper T cells

- **natural killer (NK) cells**

Antigen-presenting cells (APCs) are not lymphocytes but work closely with lymphocytes to fight cancer. The 2 main groups of antigen-presenting cells are:

- **monocytes and macrophages**
- **dendritic cells**

Other types of white blood cells, known as **granulocytes**, also make up an important part of the immune system.

Lymphocytes

B cells and plasma cells: are formed and develop in the bone marrow. B cells then move to and collect in lymph nodes, that are found throughout the body. lymphatic vessels connect the lymph nodes to each other. B cells also collect in some internal organs such as the spleen.

B cells can directly destroy germs or cancer cells by themselves, but they play an important role in immune defenses by producing antibodies. When a B cell comes into contact with a foreign antigen, it turns into another cell type called a **plasma cell**.

Plasma cells produce antibodies that specifically recognize and bind (attach) to the antigen. Antibodies are large proteins that circulate throughout the body They will not bind to other substances that are part of normal human cells and tissues. The antibodies may directly cause the cell to die, or they may mark it for destruction by other immune system cells, such as T cells.

T cells: Some lymphocytes that are formed in the bone marrow enter the bloodstream before they are fully mature. From the bloodstream, they enter the thymus. where they mature and gain new disease-fighting properties.

Once they leave the thymus gland, they are known as T lymphocytes or T cells. T cells gather in the lymph nodes and spleen, where they work together with other immune system cells. T cells have special proteins on their surfaces similar to antibodies. These proteins allow T cells to recognize and react to parasites, cancer cells, and cells infected by viruses.

There are 2 main kinds of T cells:

Killer T cells destroy unwanted cells in the body. When these cells come in contact with the specific cancer cells they recognize, they give off substances that kill the cells.

Helper T cells do not directly kill cancer cells or germs, but they release substances that help B cells and killer T cells to work more effectively.

Natural killer (NK) cells: Lymphocytes called natural killer (NK) cells are not as specific as killer T cells. They attach to cancer cells and release substances that split the cells open. After killing the cancer cells, the NK cells then find other cancer cells to attack.

Antigen-Presenting Cells (APCs)

Antigen-presenting cells (APCs) help lymphocytes recognize antigens on cancer cells. Antigen-presenting cells include monocytes and dendritic cells.

Monocytes and macrophages: Monocytes are produced by the bone marrow and released into the bloodstream. Some monocytes enter tissues and organs. Here they become macrophages, capable of surrounding and "eating" cells. They display antigens from the devoured cells on their outer surface, so that lymphocytes can recognize them.

Dendritic cells: Dendritic cells are the most powerful type of antigen-presenting cell. They are found in lymph nodes, the skin, and some internal organs. Dendritic cells are the focus of many cancer vaccines currently in development.

Types of Immunotherapy

We know the immune system can help fight cancer because people with weakened immune systems are more likely to get cancer. But many people with normal immune systems still develop cancer. This is because the immune system may not recognize cancer cells as foreign. Or the immune system may recognize cancer cells, but the response may not be strong enough to destroy the cancer. To overcome this, researchers have designed different types of immunotherapies to help the immune system recognize cancer cells and to strengthen the response so that it will destroy the cancer.

There are different types of immunotherapy. *Active immunotherapies* stimulate the body own immune system to fight the disease. *Passive immunotherapies* do not rely on the body to attack the disease; instead, they use immune system components created outside of the body.

Types of immunotherapies include:

- **cancer vaccines** (active specific immunotherapies)
- **monoclonal antibody therapy** (passive immunotherapies)
- **nonspecific immunotherapies and adjuvants**

Sometimes, will use 2 or more of these immunotherapy options together. Some tumors are more effectively attacked by one kind of immune system cell than another, so researchers use that knowledge when designing and applying immunotherapies.

Cancer Vaccines

A cancer vaccine contains cancer cells, parts of cells, or pure antigens. The vaccine increases the immune response against cancer cells that are already present in the body.

Active immunotherapies because substances injected into the body are meant to trigger your own immune system to respond.

Specific because they should only affect the cancer cells. Cancer vaccines cause the immune system to make antibodies to one or several specific antigens, and/or to make killer T cells to attack cancer cells that have those antigens.

Vaccines may be combined with other substances or cells called *adjuvants* that boost the immune response.

There are several types of cancer vaccines now under study.

Tumor Cell Vaccines

Tumor cell vaccines use cancer cells removed during surgery. The cells are killed, usually by radiation, so they cannot form more tumors. The cells are then injected into the patient to stimulate a specific immune system response. The immune system seeks out and attacks any similar cancer cells remaining in the body.

One reason for using whole tumor cells in vaccines, instead of individual antigens, is that not all cancer antigens have been identified yet. Using the whole tumor cell may expose the immune system to a large number of important cancer antigens, including some that researchers have not yet recognized.

The 2 basic kinds of tumor cell vaccines are autologous and allogeneic.

> **Autologous vaccines:** Autologous means "coming from the self." An autologous tumor cell vaccine is made from killed tumor cells taken from the same person in whom they will later be used. Autologous cancer cells may be reinjected shortly after surgery, or they may be grown in the lab or preserved by freezing and reinjected later.
>
> Although autologous tumor cell vaccines remain promising, there are some potential drawbacks. It can be expensive to create a new, unique autologous tumor cell vaccine for each patient. Cancer cells also tend to mutate (change) over time, so an autologous tumor vaccine might become less effective later if the cancer cells in your body change. Finally, depending on the surgery and the size of your tumor(s), you may not have enough usable cells in the removed tumor to make a vaccine.

Allogeneic vaccines: Allogeneic means "coming from another patient." These vaccines use cells of a particular cancer type that originally come from someone other than you. The cells are grown in the lab from a stock of cancer cells kept for that purpose. Some allogeneic tumor vaccines use a mixture of cells, originally removed from several patients.

While the **US Food and Drug Administration (FDA)** has not yet approved any tumor cell vaccines for general use, they are being studied in clinical trials against several types of cancer, including:

- melanoma
- kidney cancer
- ovarian cancer
- breast cancer
- colorectal cancer
- lung cancer
- leukemia

Dendritic Cell Vaccines

Dendritic cells are specialized antigen-presenting cells that help the immune system to recognize cancer cells. They break down the antigens from the cancer cells into smaller pieces, then hold out those antigen pieces to T cells, making it easier for the immune system cells to react with and attack them.

Dendritic cell vaccines are patient-specific and must be made individually for each patient. The process used to create them is involved and expensive:

- Scientists remove some dendritic cells and treat them in the lab to make them reproduce rapidly, creating many more than were withdrawn.
- These dendritic cells are then "taught," in the lab, to recognize cancer antigens. This is done by exposing them to the antigens in a dish, or by genetically modifying them so that they make their own antigens. *Some newer studies are even looking at fusing dendritic cells with tumor cells, creating dendritic cells with tumor antigens on their surface.*
- The dendritic cells are then injected back into the body.
- The "trained" dendritic cells are better able to help the immune system recognize and destroy cancer cells that have those antigens on them.

The dendritic cell vaccine approach has shown a great deal of promise in tests done in lab animals and in early studies in humans. They are being studied for use in people with these and other cancers:

- prostate cancer
- melanoma
- kidney cancer
- colorectal cancer

- lung cancer
- breast cancer
- leukemia
- non-Hodgkin lymphoma

Antigen Vaccines

Antigen vaccines stimulate the immune system by using individual antigens, rather than whole tumor cells that contain many thousands of antigens. These antigens are usually proteins or pieces of proteins called peptides. While antigen vaccines may be specific for a certain type of cancer, they are not made for a specific patient. This new technology means that large amounts of these very specific antigens can now be given to many patients.

In fact, some antigens can now be produced entirely from man-made chemicals. Scientists can change these antigens to make them more easily recognized by the immune system.

Antigen vaccines are being studied for use against these cancers, among others:

- breast cancer
- prostate cancer
- colorectal cancer
- ovarian cancer
- melanoma
- kidney cancer
- pancreatic cancer

Anti-Idiotype Vaccines

Every B lymphocyte or plasma cell that produces antibodies produces only one kind of antibody. The unique part of each type of antibody is called an *idiotype*.

Sometimes the immune system also makes some antibodies that treat other antibodies like antigens. Immunologists believe these antibodies against other antibodies are important in regulating the immune system.

Because the anti-idiotype antibodies look like the antigen, the immune system attacks the anti-idiotypes, along with the antigens themselves, when they are injected into a patient. Scientists have learned how to mass-produce these anti-idiotype antibodies. They can be used as part of a cancer-specific vaccine because they look like the antigens originally on the cancer cells in the patient body. Therefore they can trigger an immune response against that specific cancer. Anti-idiotype vaccines are not made for a specific patient.

Researchers consider lymphomas to be the most promising targets for anti-idiotype vaccines. This is because all lymphoma cells have unique antigen receptors not present on normal lymphocytes or other normal cells of the body. These unique antigens can be used for preparing lymphoma vaccines.

DNA Vaccines

When antigens or anti-idiotypes are injected into the body as a vaccine, they may produce the desired immune response at first but often become less effective over time. This is because antibodies recognize them as foreign and rapidly attach to them, after which immune system cells destroy them. Without any further stimulation, the immune system often returns to its normal state of activity. **To get around this, scientists have looked for a way to provide a steady supply of antigens to keep the immune response going.**

DNA vaccines are injecting bits of DNA that would be taken up by cells and would instruct them to continuously make specific antigens. Scientists may be able to do this by removing cells from the body, treating them with DNA containing instructions for making a particular antigen, and then returning them. The altered cells would then make the antigen on an ongoing basis to keep the immune response strong.

DNA vaccines are now being studied in clinical trials for use against the following cancers, among others:

- melanoma
- leukemia
- prostate cancer
- head and neck cancer

Other Active Specific Immunotherapies

Lymphokine-Activated Killer (LAK) Cell Therapy

Scientists can produce large numbers of active, cancer-fighting T cells in the lab by treating a small number of T cells in a test tube with a interleukin-2 (IL-2).After being returned to a patient bloodstream, these special cells, called lymphokine-activated killer (LAK) cells, are more effective against cancer cells.

LAK cell therapy has shown promising results in animal studies, where it caused shrinkage of tumors in animals with lung, liver, and other cancers. While clinical trials in human patients have not yet produced results as successful as those in animals, researchers are constantly improving LAK cell techniques. They are testing these newly improved methods against melanoma and other cancers.

Tumor-Infiltrating Lymphocyte (TIL) Vaccine with Interleukin-2 (IL-2)

Researchers examining tumors have discovered immune system cells deep inside the tumor tissue and have named these cells **tumor-infiltrating lymphocytes (TILs)**. These cells can be removed from tumor

samples taken from a patient and made to reproduce in test tubes by treating them with IL-2. When injected back into the patient, these cells may be active cancer fighters.

Success with TILs in lab animals has led researchers to try several different methods to increase the anti-tumor activity of TILs. Immunotherapies using TILs are being tested in clinical trials for people with melanoma, kidney cancer, and other cancers.

In one study, researchers from the National Cancer Institute (NCI) used a newer technique involving TILs in patients with advanced melanoma. After removing TILs from the body, the researchers treated the patients with chemotherapy to reduce the numbers of other white blood cells in the body. When the TILs were reintroduced, tumors shrank significantly in about half of the patients, and almost all of the patients have lived longer than expected.

Monoclonal Antibody Therapy

Monoclonal antibody therapy is a form of passive immunotherapy because the antibodies are made in large quantities outside the body rather than by a person immune system. These treatments do not require the person immune system to take an "active" role in fighting the cancer.

Antibodies are mass-produced in the lab by fusing a myeloma cell from a mouse with a mouse B cell that makes a specific antibody. The cell that results from this fusion is called a **hybridoma**. The combination of a B cell that can recognize a particular antigen and a myeloma cell that lives indefinitely makes the hybridoma cell a kind of perpetual antibody-producing factory. Because the antibodies are all identical clones produced from a single (mono) hybridoma cell, they are called **monoclonal antibodies**

We can make monoclonal antibodies that react with specific antigens on certain types of cancer cells. As researchers discover more cancer-associated antigens, they will be able to direct monoclonal antibodies against more and more cancers.

Clinical trials of monoclonal antibody therapy are in progress for people with almost every type of cancer, and **the FDA has already approved several for the treatment of certain cancers:**

MAb Name	Trade Name	Used to Treat:	Approved in:
Rituximab	Rituxan	Non-Hodgkin lymphoma	1997
Trastuzumab	Herceptin	Breast cancer	1998
Gemtuzumab ozogamicin*	Mylotarg	Acute myelogenous leukemia (AML)	2000

Alemtuzumab	Campath	Chronic lymphocytic leukemia (CLL)	2001
Ibritumomab tiuxetan*	Zevalin	Non-Hodgkin lymphoma	2002
Tositumomab*	Bexxar	Non-Hodgkin lymphoma	2003
Cetuximab	Erbitux	Colorectal cancer	2004
Bevacizumab	Avastin	Colorectal cancer	2004

*conjugated monoclonal antibodies

Two types of monoclonal antibodies are used in cancer treatments:

- **Naked monoclonal antibodies** are those without any drug or radioactive material attached to them.
- **Conjugated monoclonal antibodies** are those joined to a chemotherapy drug, radioactive particle, or a toxin.

Naked Monoclonal Antibodies

Naked antibodies attach themselves to specific antigens on cancer cells. They can be used in different ways:

- Some mark the cancer cell for the immune system to destroy it.
- Others attach to certain antigen sites, called receptors, where other molecules that stimulate the cancer cells growth might otherwise attach. By blocking the other molecules from attaching there, the monoclonal antibodies prevent the cancer cells from growing rapidly.

The FDA has approved several naked MAbs for use in the United States:

- **Rituximab (Rituxan):** Rituximab is used to treat B cell non-Hodgkin lymphoma. It is a monoclonal antibody against the CD20 antigen, found on B cells.
- **Trastuzumab (Herceptin):** Trastuzumab is an antibody against the HER2 protein, which is present in large numbers on cells in some cases of breast cancer. It is used to treat advanced cases of the disease.
- **Alemtuzumab (Campath):** Alemtuzumab is an antibody against the CD52 antigen, which is present on both B cells and T cells. It is used to treat B cell chronic lymphocytic leukemia (B-CLL) in patients who have already had chemotherapy.
- **Cetuximab (Erbitux):** Cetuximab is an antibody against the EGFR protein, which is present in high amounts on some tumor cells. It is used along with the chemotherapy drug irinotecan to treat advanced colorectal cancer.

- **Bevacizumab (Avastin):** Bevacizumab works against the VEGF protein, which normally helps tumors develop new blood vessels in order to get nutrients. This antiangiogenesis therapy is used along with chemotherapy to treat metastatic colorectal cancer.

Recent progress with these antibodies, and others currently being tested in clinical trials, is very encouraging. These antibodies can help some people after standard treatments have stopped working. And if clinical trials continue to demonstrate their effectiveness, they may be used as standard (initial) treatment instead of, or in addition to, chemotherapy.

Conjugated Monoclonal Antibodies

Conjugated monoclonal antibodies are joined to drugs, toxins, or radioactive atoms. They are used as delivery vehicles to take those substances directly to the cancer cells. The MAb acts as a homing device, circulating in the body until it finds a cancer cell with a matching antigen. It delivers the toxic substance to where it is needed most, minimizing damage to normal cells in other parts of the body. But conjugated antibodies still generally cause more side effects than do naked antibodies. The actual effects depend on which type of substance they attached to.

Conjugated MAbs are also sometimes referred to as "tagged," "labeled," or "loaded" antibodies.

- MAbs with chemotherapy drugs attached are generally referred to as **chemolabeled**.
- MAbs with radioactive particles attached are referred to as radiolabeled, and this type of therapy is known as **radioimmunotherapy (RIT)**.
- MAbs attached to toxins are called **immunotoxins.**

Conjugated MAbs are now being tested in clinical trials for use in treating many types of cancer.

Chemolabeled antibodies:

These are presently available in the United States only through clinical trials.

Radiolabeled antibodies:

In 2002, the FDA approved the first radiolabeled MAb to treat cancer outside of clinical trials. **Ibritumomab tiuxetan (Zevalin)** delivers radioactivity directly to cancerous B lymphocytes.

A second radiolabeled MAb, **tositumomab (Bexxar)**, was approved by the FDA in 2003. It is used to treat certain types of non-Hodgkin lymphoma that no longer respond to rituximab (Rituxan) or chemotherapy.

Aside from being used to treat cancer, radiolabeled antibodies can also be used along with special cameras to detect areas of cancer spread in the body. Radiolabeled antibodies that have been approved by the FDA to detect cancer include **OncoScint** (for colorectal and ovarian cancer) and **ProstaScint** (for prostate cancer).

Immunotoxins:

Immunotoxins are made by attaching toxins to monoclonal antibodies. Various immunotoxins have been made by attaching monoclonal antibodies to bacterial toxins such as **diphtherial toxin (DT)** or **pseudomonal exotoxin (PE40)**, or to plant toxins such as **ricin A** or **saporin**.

The only immunotoxin which FDA approval for treating cancer is **gemtuzumab ozogamicin (Mylotarg)**. It is attached to an antibody directed against the CD33 antigen, which is present on most leukemia cells. Gemtuzumab is used to treat **acute myelogenous leukemia (AML)** in people who have already had chemotherapy or are not eligible to receive it.

Another immunotoxin, **BL22**, has shown promising results in early studies against hairy cell leukemia, even in patients who no longer respond to chemotherapy.

Clinical trials of immunotoxins are also in progress for people with certain leukemias, lymphomas, brain tumors, and other cancers.

Other Targeted Therapies Containing Toxins

Scientists are also experimenting with toxins linked to hormone-like substances called growth factors. Many cancer cells have large numbers of receptors for growth factors on their surfaces, which stimulate them to reproduce and allow them to grow faster. Growth factors are therefore more likely to attach to these cells.

When the growth factor/toxin reaches the cancer cell's growth factor receptors, it delivers its payload of toxin that kills the cell. The concept behind these growth factor/toxin drugs is similar to that of immunotoxins. But because the growth factor/toxin drugs do not contain antibodies, they are not classified as immunotoxins.

The only growth factor/toxin approved by the FDA thus far is **denileukin diftitox (Ontak)**. It consists of a cytokine known as interleukin-2 (IL-2), attached to a toxin from the germ that causes diphtheria.

Improving Monoclonal Antibody Therapy

Chimeric and Humanized Monoclonal Antibody

In some cases, the patient immune system recognizes the mouse antibodies as "foreign" after a while, and starts destroying them as soon as they enter the body. For this reason, we can combine the part of the mouse antibody gene responsible for recognizing a specific tumor antigen with other parts from a human antibody gene. The mouse-human antibody gene product two types of monoclonal antibody call **chimeric and humanized monoclonal antibody**. It looks more like a normal human antibody, so there a better chance it won't be destroyed by the patient own immune system. This means the antibody therapy may still be effective if used more than once.

Nonspecific Immunotherapies and Adjuvants

Nonspecific immunotherapies stimulate the immune system in a very general way. The overall boost in immune system activity can result in more activity against any cancer cells present. Some nonspecific immunotherapies can be given as main therapies by themselves. Others are used as **adjuvants** to boost immune system function to improve how well another therapy works. And some immunotherapies are used by themselves against some cancers and as adjuvants against others.

Cytokines

Cytokines are hormones made by immune system cells. They have a crucial role in regulating the growth and activity of other immune system cells and blood cells. At the present time, the main use of cytokines in cancer treatment is to lessen the side effects of other treatments such as chemotherapy. Manmade versions of cytokines can help the bone marrow make more white blood cells, red blood cells, or platelets when the levels in the body have become too low.

Granulocyte-macrophage colony-stimulating factor (GM-CSF):

GM-CSF is a cytokine/growth factor that causes the bone marrow to make more of certain types of immune system cells and blood cells. A manmade version is commonly used to boost white blood cell counts after chemotherapy.

GM-CSF is also being tested against cancer as a nonspecific immunotherapy and as an adjuvant given with other types of immunotherapies.

Clinical trials of GM-CSF, alone or with other immunotherapies, are in progress for people with these cancers and others:

- melanoma
- leukemia
- lymphoma
- neuroblastoma
- Kaposi sarcoma
- mesothelioma
- lung cancer
- breast cancer
- prostate cancer
- colorectal cancer
- brain tumors
- kidney cancer
- cervical cancer

Interleukins:

Interleukins are cytokines that act as chemical signals between white blood cells. When interleukin-2 (IL-2) was approved by the FDA in 1992 for the treatment of advanced kidney cancer, it became the first true immunotherapy approved for use alone in treating cancer. Since that time, it has also been approved to treat people with metastatic melanoma.

IL-2 can be used as a single drug treatment for these cancers, or it may be combined with other forms of immunotherapy, such as vaccines. The use of IL-2 together with chemotherapy or with other cytokines (such as INF-α) may increase their effectiveness against some cancers, but the side effects of the combined treatment are also increased.

Other interleukins, such as IL-4, IL-6, and IL-12, are now being studied for use against cancer as well, both as adjuvants and as stand-alone agents.

INFs: This family of cytokines is important in the body resistance to virus infections and cancers. The types of interferon (IFN) are named: **IFN-α**, **IFN-β**, and **IFN-γ**. While all 3 types of interferon are FDA approved for various conditions, only **IFN-α** is used to treat cancer. Not all of its properties are well understood, but it may work by:

- directly slowing the growth of cancer cells
- slowing down angiogenesis, the growth of new blood vessels that tumors must have to continue to grow
- causing cancer cells to produce more antigens, making them easier for the immune system to recognize and destroy
- boosting the cancer cell-killing ability of natural killer (NK) cells and of other immune system cells that attack cancer with help from antibodies

The FDA has approved IFN-α for use against these cancers:

- hairy cell leukemia (HCL)
- chronic myelogenous leukemia (CML)
- follicular non-Hodgkin lymphoma
- cutaneous (affecting the skin) T cell lymphoma
- renal cell (kidney) cancer
- melanoma
- Kaposi sarcoma

Adjuvants Other than Cytokines

Aluminum hydroxide (alum): Alum is one of the most common adjuvants used in clinical trials for cancer vaccines.

BCG: BCG is a bacterium that is related to the germ that causes tuberculosis. Unlike its bacterial "cousin," BCG does not cause serious disease in humans, but it does:

- infect human tissues
- attract immune system cells to areas of infection
- activate the immune system

This makes this bacterium useful as a form of anticancer immunotherapy. BCG was one of the earliest immunotherapies used against cancer. It is FDA approved as a routine treatment for superficial bladder cancer. Its usefulness in other cancers as an adjuvant is also being tested. Researchers are looking at injecting BCG to give an added boost to the immune system when using chemotherapy, radiation therapy, or other types of immunotherapy.

Keyhole limpet hemocyanin (KLH): KLH is another adjuvant used to boost the effectiveness of cancer vaccine therapies. It is extracted from a type of sea creature related to the snail.

Incomplete Freund's adjuvant (IFA): IFA is given together with some experimental therapies to help stimulate the immune system and to increase the immune response to cancer vaccines.

QS-21: QS-21 is a relatively new immune stimulant made from a plant extract that increases the immune response to vaccines used against melanoma.

DETOX: DETOX is another relatively new adjuvant. It is made from parts of the cell walls of bacteria and a kind of fat. It is used with various immunotherapies to stimulate the immune system.

Levamisole: Levamisole, a drug first used to treat parasites, has been found to improve survival rates among people with colorectal cancer when used together with some chemotherapy drugs. It is often used as an immunotherapy adjuvant because it can activate T lymphocytes. Levamisole is being tested in clinical trials as a treatment for other types of cancer.

Dinitrophenyl (DNP): DNP is a small molecule that can attach to tumor antigens and cause an enhanced immune response. It is used to modify tumor cells in certain cancer vaccines.

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