



PERSONALIZED ACTIVE IMMUNOTHERAPY

A Resource for People With B-Cell Non-Hodgkin's Lymphoma, Including Chronic Lymphocytic Leukemia



TM


Genitope Corporation

Delivering on the promise of personalized medicine™



Personalized Active Immunotherapy

Personalized active immunotherapy is an investigational treatment currently being studied in **clinical trials** for people with **B-cell** malignancies, including **non-Hodgkin's lymphoma (NHL)** and **chronic lymphocytic leukemia (CLL)**. The word “**immunotherapy**” means that a treatment uses a person's own **immune system** to fight the cancer growing in his or her body. The immune system is the body's natural defense mechanism. It is designed to prevent and combat disease. It works by distinguishing between the body's own cells and those of foreign invaders, such as viruses or bacteria. Personalized active immunotherapy is designed to work by helping the patient's immune system to recognize his or her cancer as foreign (ie, something that should be attacked). Personalized active immunotherapy is custom-made for each individual person to target that person's cancer. Therefore, only cancer cells, and not normal healthy cells, should be affected.

The Immune System and Cancer

The immune system is a natural defense mechanism that the body uses to prevent and fight disease. The immune system is always on alert against foreign substances, such as bacteria and viruses (Figure 1). This is called “immune surveillance.” When the immune system encounters a foreign substance, the response can be a **humoral response** (involving **antibodies** made by B cells) or a **cellular response** (involving **T cells**) (Figure 2). However, the immune system is generally unable to defend the body against a cancer once it has developed. Since cancer cells arise from the body’s own cells, they generally avoid detection by the immune system. In addition, cancer cells themselves have developed ways to reduce or even eliminate the immune system’s ability to attack them (Figure 3).

Figure 1

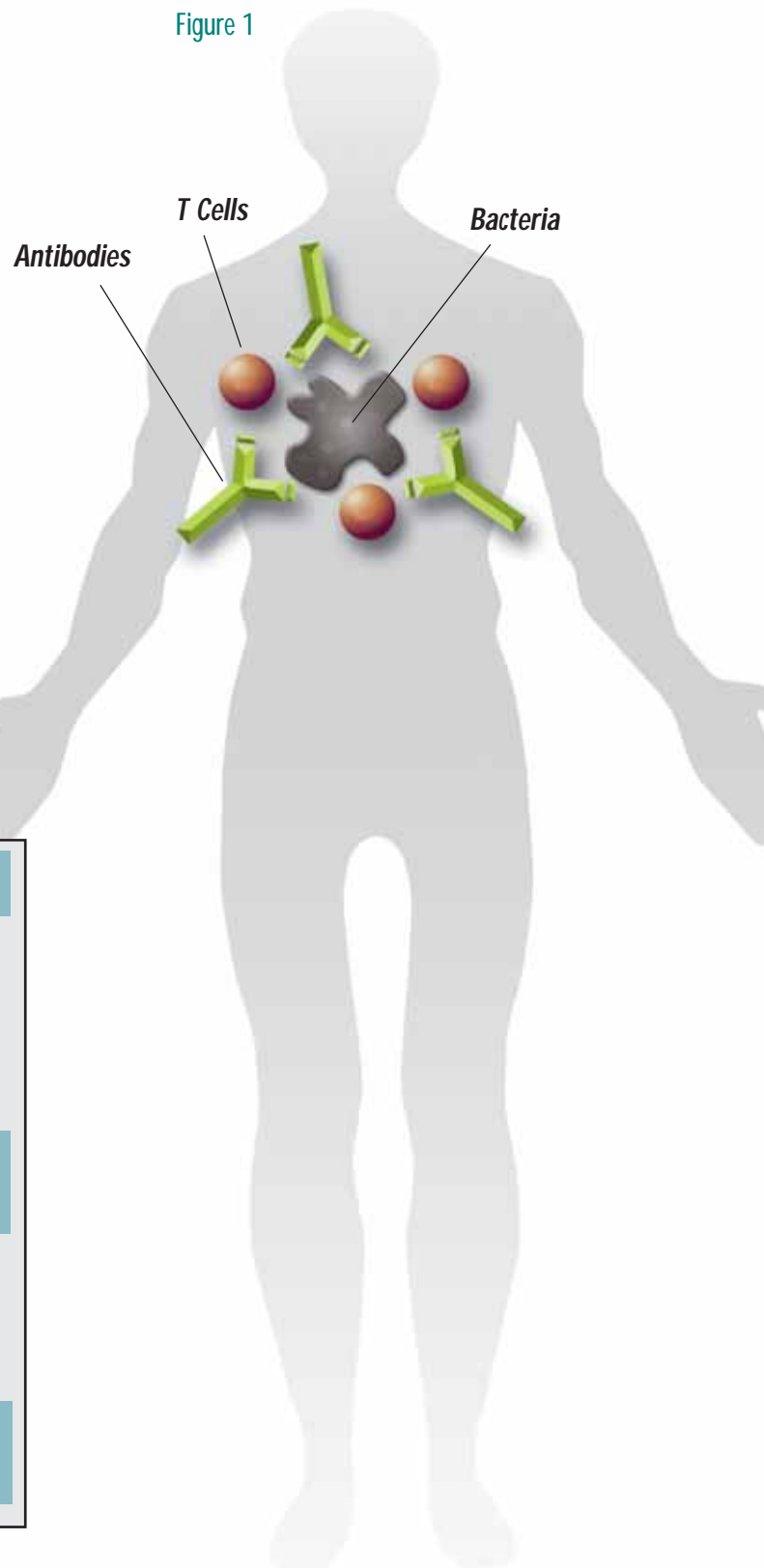


Figure 2




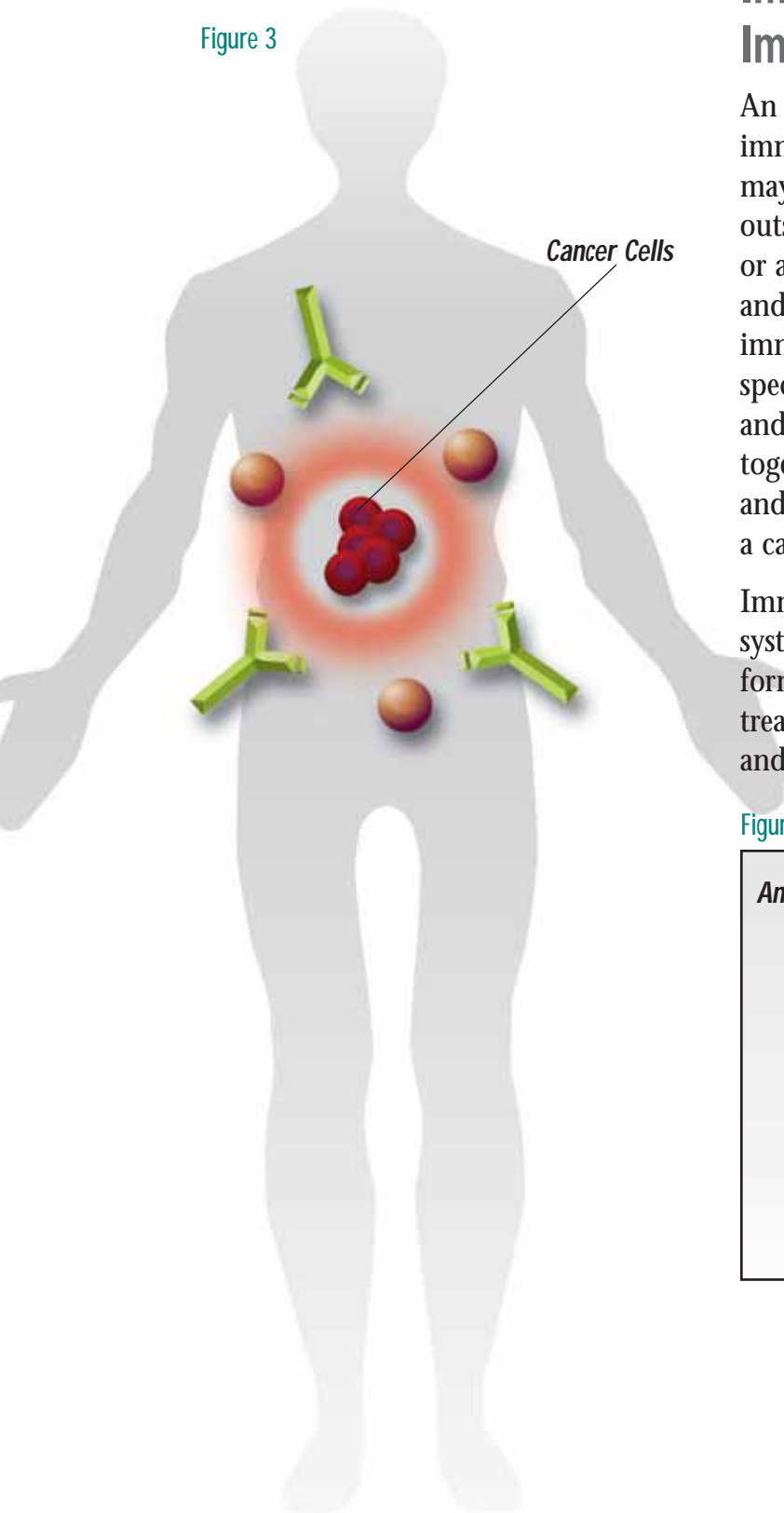
	B cells: White blood cells that produce antibodies
	Antibody: Specialized protein produced by B cells and used by the immune system to identify and destroy foreign substances
	T cells: Lymphocytes , a type of white blood cell, that can recognize and destroy foreign substances
	Humoral response: Immune response involving antibodies made by B cells
	Cellular response: Immune response provided by T cells

Figure 3

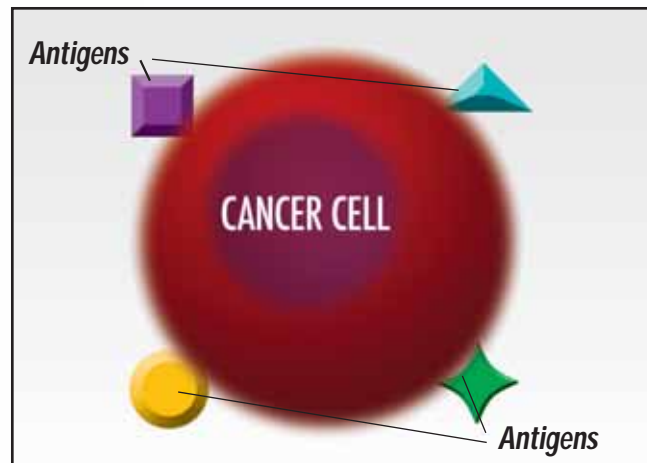


Immunotherapy: Using the Immune System to Fight Cancer

An **antigen** is a substance that causes the immune system to react and fight. An antigen may be a foreign substance that comes from outside the body (such as a bacteria or virus), or an antigen may be formed within the body and found on cells. Once cells from the immune system are activated, they produce a specific response to the antigen. The humoral and cellular arms of the immune system work together to identify and destroy the antigen and anything the antigen is attached to, such as a cancer cell (*Figure 4*).

Immunotherapy uses a person's own immune system to fight diseases, including cancer. Two forms of immunotherapy have been used to treat various diseases: passive immunotherapy and **active immunotherapy**.

Figure 4



Passive Immunotherapy

In passive immunotherapy, antibodies specific to a particular antigen are manufactured in large quantities. In this type of immunotherapy, antibodies are directed at antigens that are commonly found on cancer cells and on normal cells as well. When these antibodies are infused into a person with cancer, they attach to any cell that has that particular antigen. Rituxan® and Campath® are both **monoclonal antibodies** that are examples of passive immunotherapy. Rituxan targets the CD20 antigen and Campath targets the CD52 antigen, both found on normal and cancer cells. When these antibodies are infused into a person with cancer, the antibodies attach to the cells that display the antigen and cause direct cell destruction (*Figure 5*). The effects of passive immunotherapy are immediate and have proven successful against certain types of cancer. However, the effects of passive immunotherapy are temporary and repeated administration is required. Also, unless the particular antigen is found only on cancer cells and never on normal cells, the infused antibodies will cause destruction of healthy cells as well as the cancer cells (*Table 1*).¹

Figure 5

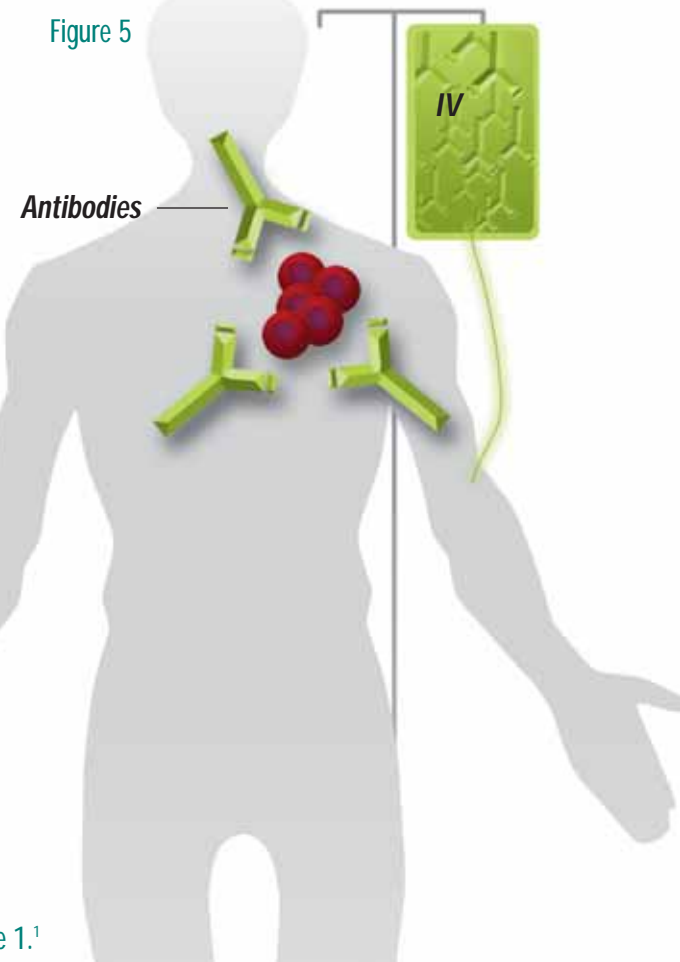
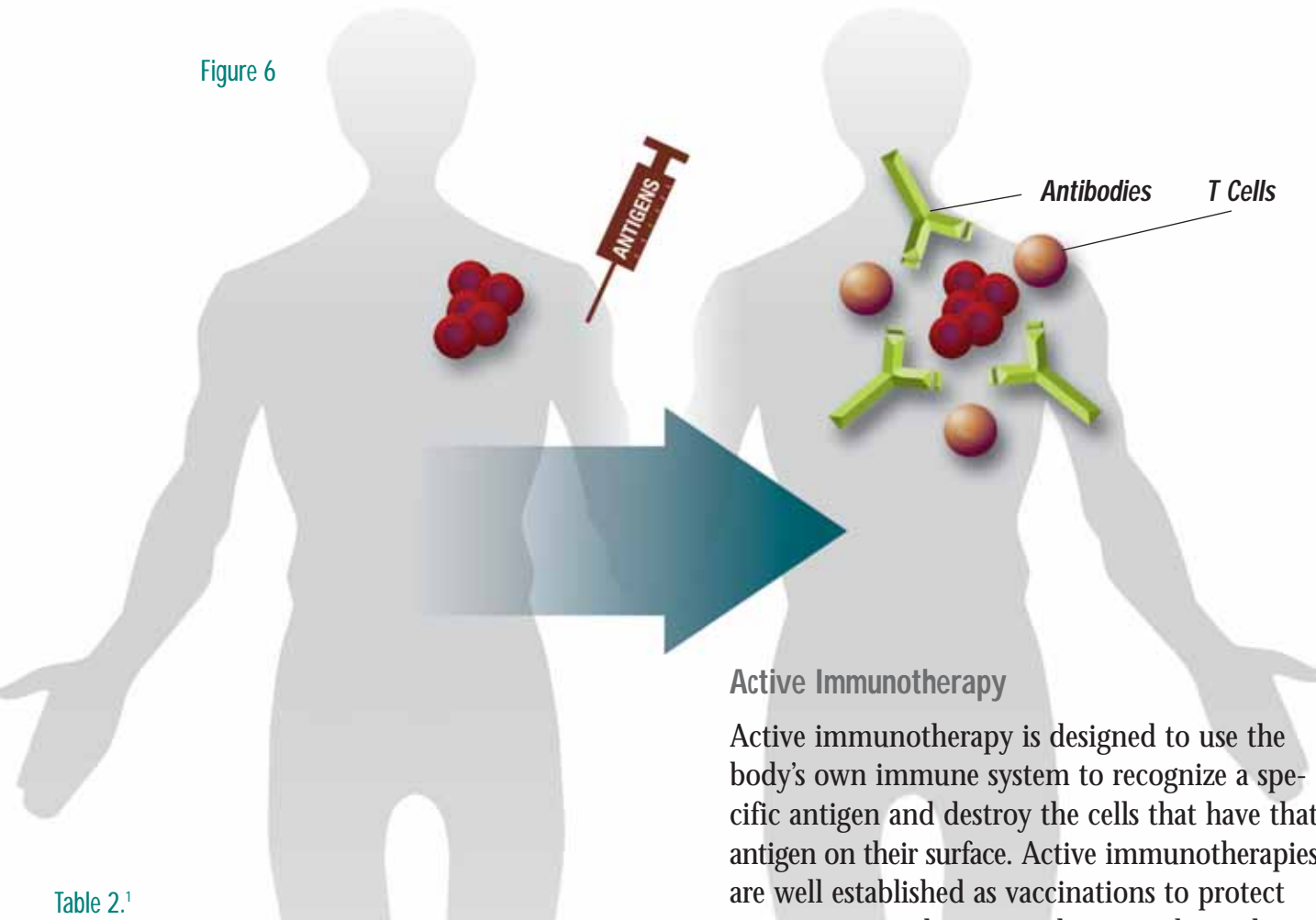


Table 1.¹

Passive Immunotherapy
Not tumor specific (mass produced)
Does not stimulate patient's immune system
Temporary anticancer effect
Requires retreatment
Uses only humoral arm of the immune system (B cells)
Does not require sample of patient's cancer cells

Adapted from Vose J. *Clin Adv Hematol Oncol*. 2005;3:923-932.

Figure 6



Active Immunotherapy

Active immunotherapy is designed to use the body's own immune system to recognize a specific antigen and destroy the cells that have that antigen on their surface. Active immunotherapies are well established as vaccinations to protect against certain diseases such as measles and mumps, and they are currently under investigation to treat cancer. An active and potentially long-lasting immune response in a person may be achieved by injecting the antigen into the person's body, often in combination with other substances that can enhance the immune response to the antigen. Importantly, both humoral (antigen-specific antibodies from B cells) and cellular (antigen-specific T cells) responses can be produced (*Figure 6, Table 2*). The immune system has the ability to remember the immune response it used before to attack a foreign invader such as a virus or bacteria. This is referred to as immunologic memory.

Table 2.¹

Personalized Active Immunotherapy
Tumor specific (custom-made for each patient)
Stimulates patient's immune system
Potential long-lasting anticancer effects
May induce immunologic memory
Uses both the humoral and cellular arms of the immune system (B cells and T cells)
Requires sample of patient's cancer cells for production

Adapted from Vose J. *Clin Adv Hematol Oncol*. 2005;3:923-932.

B-Cell Malignancies

Cancers can occur in many kinds of cells, including B cells. Some **genetic mutations** or errors that occur in cells can cause them to overproduce or underproduce proteins that abnormally affect the cell's behavior. Examples of this abnormality can be to cause a cell to divide too fast or fail to die when it should. The descendants of this abnormal cell can then go on to form a cancer.

B-Cell Malignancies Are Excellent Targets for Immunotherapy

There are a number of antigens that appear only on B cells. Although these antigens are specific to B cells, most appear on both normal B cells *and* cancerous B cells. This means that therapies directed against these antigens would destroy normal B cells along with the cancerous B cells. Fortunately, however, every B cell has a unique antigen on its surface called an **idiotype protein (Id)**, which is like a fingerprint (*Figure 7*).

Most cancers develop from a single malignant cell. When it is a B cell that undergoes malignant transformation and subsequently divides and expands into a cancer, the Id found on the original cancer cell is found on the other malignant cells. Because the particular Id is only on the cancer cells and not on normal B cells, it represents an excellent target for immunotherapy (*Figure 8*).

Figure 7

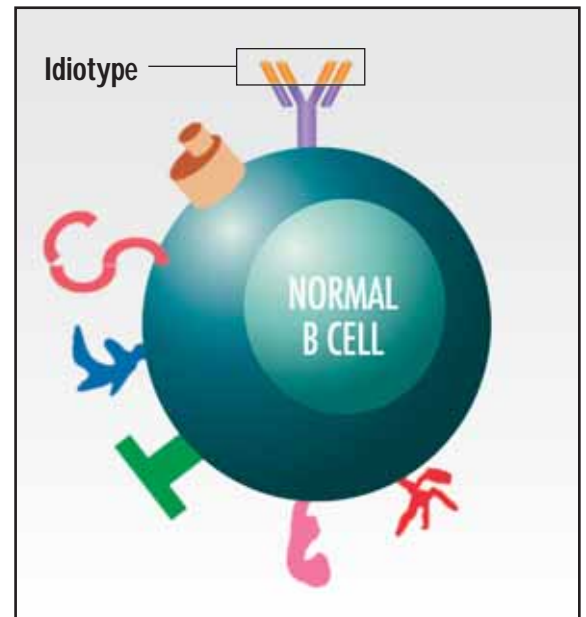
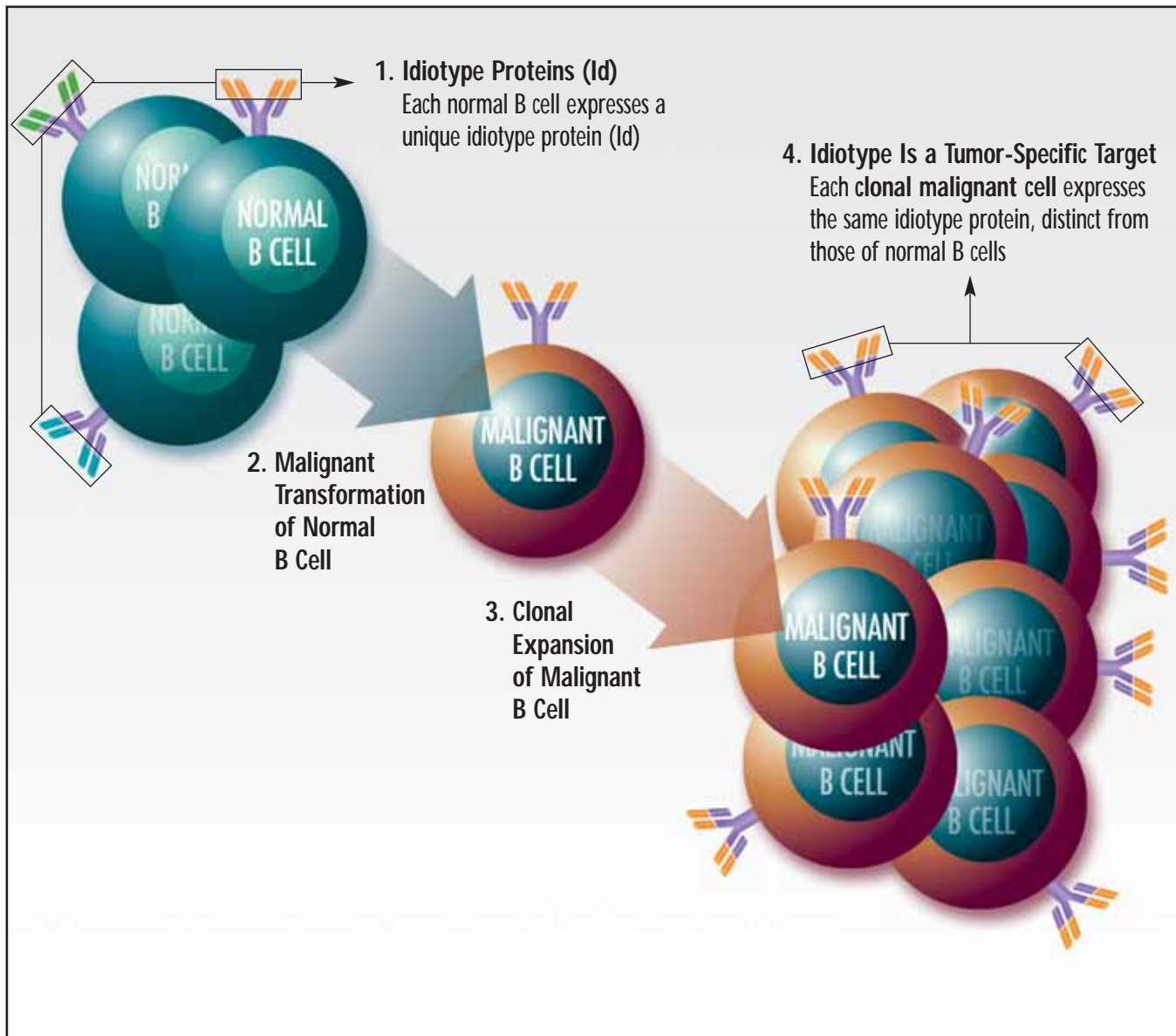


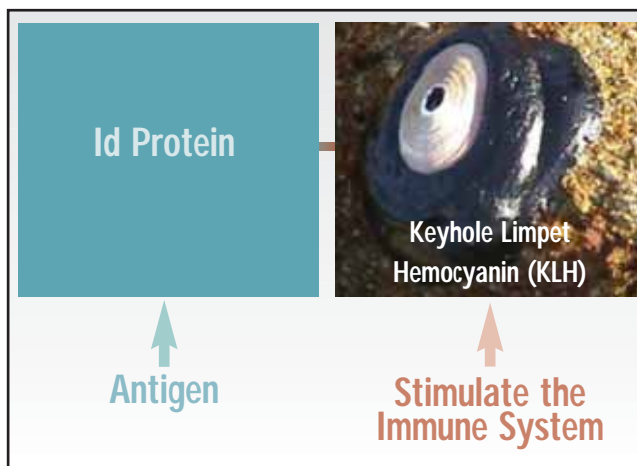
Figure 8



The Development of Personalized Active Immunotherapy

Personalized active immunotherapy was first investigated by researchers at the Stanford University Medical Center in the late 1980s for the treatment of patients with NHL (*Figure 9*).

Figure 9



Use of Personalized Active Immunotherapy in Clinical Trials

- **Patient and Tumor Specific:** Personalized active immunotherapy is unique to each patient because it is made from a sample of the patient's cancer cells.

The personalized active immunotherapy is made by re-creating and modifying the Id found on the cancer. This Id is attached to a foreign protein or a protein not normally found in the human body. This foreign protein is called **keyhole limpet hemocyanin (KLH)**. The Id, together with the KLH protein, makes up the personalized active immunotherapy.

The personalized active immunotherapy is given as an injection. The immunization is

followed by an injection of an **adjuvant**, which is an immunological agent added to a therapy to increase or aid its effect. An adjuvant commonly used with personalized active immunotherapy is a product called **granulocyte macrophage colony-stimulating factor (GM-CSF)**. GM-CSF is used because it is thought to boost the immune system. The personalized active immunotherapy, together with the adjuvant, is thought to help the immune system recognize the cancer as something to destroy and clear from the body.

- **Immunologic Memory:** The immune system has the ability to remember the immune response it used before to attack the Id. If a person's cancer returns and still **expresses** that particular Id (that is, a return of the original cancer and not the development of a completely new cancer), the person's immune system may recognize it and destroy it. This may result in longer cancer remissions.
- **Generally Well Tolerated:** Normal cells are not affected, so personalized active immunotherapy is generally well tolerated. The most commonly reported reactions involve redness, swelling, and some pain at the site of injections (these are also called injection-site reactions). Typically, these reactions are easily treated (eg, with ice and acetaminophen to relieve the discomfort) and disappear within a few days after each series of injections is completed. These reactions are generally mild compared to the significant reactions and toxicities associated with the chemotherapy drugs presently used to treat NHL and CLL. Some patients also experience flu-like symptoms, including fever, chills, nausea, and muscle soreness. These reactions may be

related to the Id-KLH immunotherapy and generally last for a few days after the injection, although they can last longer.

Administration of Personalized Active Immunotherapy

Figure 10 shows a person receiving an Id-KLH injection. A circle is drawn on the skin to aid in identifying the location for subsequent injections of the GM-CSF, which enhances the immune response.

Figure 11 shows the same person with an injection-site reaction. Redness indicates immune cells going to the site of injection. This occurred within 30 minutes following Id-KLH and GM-CSF administration.

Figure 10



Figure 11



Photographs courtesy of Maribeth Hohenstein, RN, BSN, OCN; Clinical Research Nurse Coordinator; University of Nebraska Medical Center; Omaha, Nebraska

Initial Results of Personalized Active Immunotherapy in Patients with NHL

- Personalized active immunotherapy has been studied in patients since the mid 1980s and appears to be safe and well tolerated.
- In early small studies, personalized active immunotherapy has shown anti-tumor activity, with long-term durable remissions (median of 42+ months from the completion of **chemotherapy**) observed in some patients.^{2,3} Personalized active immunotherapy is now under evaluation in larger **phase 3 studies**.
- In a more recent phase 2 study, nine of 21 patients remained in remission for between 57 and 78 months measured from the end of chemotherapy.⁴ To date, these patients have not required any additional **lymphoma** treatments.
- Personalized active immunotherapy can be made for more than 99% of people with cancers that express an Id antigen. To date, Genitope Corporation has manufactured hundreds of personalized active immunotherapies for use in clinical trials.

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4. Timmerman J, Vose J, Levy R, et al. Long-term follow-up of patients treated in a phase 2 trial with MyVax® personalized immunotherapy (recombinant Id-KLH plus GM-CSF) after chemotherapy as initial treatment for follicular non-Hodgkin's lymphoma (NHL). Presented at: 47th Annual Meeting and Exposition of the American Society of Hematology; December 10-13, 2005; Atlanta, Ga. Poster 2348.

Frequently Asked Questions

About MyVax[®] Personalized Active Immunotherapy

What is MyVax[®] personalized active immunotherapy?

MyVax[®] personalized active immunotherapy (“MyVax[®]”) is the proposed brand name for an exciting potential treatment currently being studied in clinical trials for patients with B-cell malignancies, including non-Hodgkin’s lymphoma (NHL) and chronic lymphocytic leukemia (CLL). It is a type of treatment that uses a person’s immune system (thus, the term immunotherapy) in an attempt to combat disease. MyVax[®] is called personalized active immunotherapy because it is developed from a protein called an idiotype, or Id, which is identified from the patient’s cancer cells and is unique to that patient’s tumor. In fact, the Id can be thought of as a tumor “fingerprint.” MyVax[®] is different from currently available therapies in that it is made individually and specifically for each patient. Because it has been custom-designed to work with each patient’s specific immune system and to target each patient’s particular tumor, healthy cells within the patient’s body should not be affected.

Are there other names for personalized active immunotherapy?

Yes, you may also hear personalized active immunotherapy referred to as **active idiotype immunotherapy**, **idiotype (Id) vaccines**, or **therapeutic idiotype vaccines**. These are simply different names for the same therapeutic approach.

What is MyVax[®] personalized active immunotherapy made of?

MyVax[®] personalized active immunotherapy is composed of (1) the patient’s tumor-specific idiotype (Id) protein, and (2) a second protein called keyhole limpet hemocyanin (KLH). KLH comes from a giant sea mollusk that lives off the coast of California. It is highly **immunogenic**, meaning that when it is injected into the body, the immune system responds strongly to it—and to anything attached to it.

Although technically not part of the personalized active immunotherapy, an adjuvant, or substance that enhances the immune response, is administered with MyVax[®]. This adjuvant is called granulocyte-macrophage colony-stimulating factor (GM-CSF).

How does MyVax[®] personalized active immunotherapy work?

The immune system is the body’s natural defense mechanism. It is designed to prevent and combat disease. It works by distinguishing between the body’s own cells and those of foreign invaders, such as viruses or bacteria. While the immune system is good at defending the body against infectious disease, it is generally ineffective in defending the body against cancer because cancer develops from the body’s own cells. Because of this, the immune system thinks the cancerous cells are part of the body, and thus, they are not attacked.

MyVax[®] personalized active immunotherapy works by helping the patient’s immune system to recognize his or her tumor as foreign (ie, something that should be attacked). When the

patient's tumor-specific idiotype (Id) is joined to KLH and the Id-KLH immunotherapy is then injected into the body, a strong immune response is typically generated against KLH and—because the Id protein is attached—theoretically against the Id protein. This immune response not only targets the Id proteins attached to KLH, but also the Id proteins on the cancer cells from which the sample used to make MyVax® was originally taken. The treatment is tumor-specific so the patient's immune system should target only the cancer cells for destruction while leaving normal cells unharmed.

What is the difference between MyVax® personalized active immunotherapy and vaccines given to prevent diseases such as measles, mumps, or polio?

Therapeutic idiotype (Id) vaccines such as MyVax® personalized active immunotherapy are used to treat diseases (ie, cancer) that are already present in the body, in an effort to prevent them from coming back or to keep them from getting worse. Vaccines for measles, mumps, polio, and other diseases, on the other hand, are **prophylactic, or preventative, vaccines** used to prevent disease from occurring in the first place. Another difference between the two vaccines is that MyVax® personalized active immunotherapy is made individually for each patient, while preventative vaccines are mass-produced.

Since it is made from the patient's tumor, can MyVax® personalized active immunotherapy cause the patient's cancer to come back?

MyVax® personalized active immunotherapy

contains a **recombinant, or genetically engineered, form of the idiotype (Id) protein**, not live cancer cells. Therefore, it cannot cause a recurrence of cancer. Disease recurrence is thought to be due to residual circulating cancer cells (ie, cells not destroyed by previous therapies) and/or genetic mutations related to the disease.

For what diseases is Genitope Corporation testing MyVax® personalized active immunotherapy?

MyVax® personalized active immunotherapy is currently being tested in patients with **B-cell NHL** and chronic lymphocytic leukemia (CLL). Specifically, a phase 3 study in patients with **follicular lymphoma (fNHL)** in first remission following chemotherapy is ongoing. A study in CLL is also ongoing. Other studies may be conducted in patients with other B-cell or T-cell malignancies.

Making MyVax® Personalized Active Immunotherapy

What is needed from the patient to make MyVax® personalized active immunotherapy?

Since MyVax® personalized active immunotherapy is made specifically for each individual patient, a sample containing cancer cells is needed. In lymphoma, this often involves a lymph node **biopsy**. **Excisional lymph node biopsies** are best, but it is possible to work with cancer cells obtained from a **core needle biopsy, fine needle aspiration, or bone marrow sample** or peripheral blood sample. In CLL, peripheral blood samples are often used because

the blood contains a high number of circulating cancer cells. Only a small amount of tissue or blood containing cancer cells is required to manufacture the therapy, but additional samples may be needed for lab work or other studies. The cells do not need to be alive, so tissue samples can be frozen. Cells that are preserved, or “**fixed**,” cannot be used.

In lymphoma, tissue obtained during the diagnostic biopsy can often be frozen and used to make a personalized active immunotherapy. In some instances, a second biopsy may be needed to obtain enough cancer cells.

How is MyVax[®] personalized active immunotherapy made?

Once Genitope Corporation has a patient’s sample containing cancer cells, the next step is to identify and isolate the genetic material associated with the specific idiotype (Id) the patient’s specific tumor is expressing, or producing. This genetic material is then used to produce a recombinant, or genetically engineered, version of the Id protein, which is then purified and combined with KLH. (See “*What is MyVax[®] personalized active immunotherapy made of?*” on page 10.)

How does Genitope Corporation make sure patients get their own specific personalized active immunotherapy?

At multiple points during the production process, the idiotype (Id) contained in the patient’s immunotherapy is compared to the Id from the original specimen. This ensures that they match and that the patient is getting a personalized active immunotherapy that specifically targets his/her cancer.

Can MyVax[®] personalized active immunotherapy be made for every patient?

Currently, MyVax[®] personalized active immunotherapy is an **investigational therapy** and, as such, MyVax[®] can be made only for patients involved in clinical trials. In a small number of cases, it may not be possible to produce a personalized active immunotherapy for a specific patient due to the biology of his/her disease (ie, the cancer cells may not express an idiotype [Id] protein or may not produce enough of the Id protein).

What to Expect When Receiving MyVax[®] Personalized Active Immunotherapy

Why do some patients have chemotherapy before receiving MyVax[®] personalized active immunotherapy?

Experts believe that lowering the amount of cancer in the body with chemotherapy before giving MyVax[®] personalized active immunotherapy may optimize the effects of the personalized active immunotherapy, giving it the best possible chance to work. However, in clinical trials, patients treated with MyVax[®] alone have been able to mount an immune response to the immunotherapy.

How is MyVax[®] personalized active immunotherapy given?

Each MyVax[®] personalized active immunotherapy injection is given just under the skin, or **subcutaneously**, via a small needle. Each MyVax[®] injection is followed by a GM-CSF injection. In some series, an additional three days of GM-CSF injections may be given.

What reactions do patients experience with MyVax[®] personalized active immunotherapy?

Reactions that patients should expect to experience with MyVax[®] personalized active immunotherapy include injection-site reactions, such as redness, swelling, bruising, itching, soreness, and/or pain at the site of the injection. Some patients also experience flu-like symptoms, including fever, chills, nausea, and muscle soreness. These reactions may be related to the Id-KLH immunotherapy and generally last for a few days after the injection, although they can last longer.

Side effects seen with the adjuvant, GM-CSF, include fever, bone or joint pain, flu-like symptoms (nausea, headache, tiredness), and mild skin reactions at the injection site. More information about GM-CSF side effects can be found at www.leukine.com.

As with any medication, there is a possibility of allergic reactions with MyVax[®]. Allergic reactions have been seen only in a small number of patients, and patients are monitored closely after each injection for signs of such a reaction. There are very effective medications available should they be required to counteract allergic reactions. MyVax[®] should not be used in patients with known allergy to the product.

What can be done to manage these reactions?

Patients should discuss any injection-site reactions or side effects they are experiencing with their doctor, who will be able to recommend treatment options. Ice or heat may be applied to the injection site to minimize discomfort. Over-the-counter medications such as acetaminophen, aspirin, antihistamines, and ibuprofen can be useful in helping to combat flu-like symptoms and injection-site reactions. Use of these medications is permitted in most clinical trials. Use of oral, inhaled, and/or topical corticosteroids or other medications that suppress the immune system are not permitted in MyVax[®] personalized active immunotherapy clinical trials, as they may interfere with the immune response. If you are a patient in one of Genitope Corporation's clinical trials and you are unsure about a medication, consult with your healthcare team.

For suggestions on how to manage side effects associated with GM-CSF, visit www.leukine.com.

Talking to Your Healthcare Team About MyVax[®] Personalized Active Immunotherapy

I want to talk to my doctor about the possibility of receiving MyVax[®] personalized active immunotherapy. What should I say?

Currently, the only way for patients to receive MyVax[®] personalized active immunotherapy is to be enrolled in a clinical trial. Ask your doctor if any of the trials now enrolling patients are right for you. To learn more about MyVax[®] clinical trials, call 1-866-436-4687, send an email to clinicalinfo@genitope.com, or visit www.genitope.com.



What Patients Say About MyVax[®] Personalized Active Immunotherapy

In this section, people who have received personalized active immunotherapy in clinical trials relate their experiences:

Receiving Immunizations

“You are almost always going to feel some pain when getting a shot, but it’s relatively minor.”

“The vaccine shots went quicker than expected...”

Self-Injecting GM-CSF

“At first I never thought I would be able to give myself a shot, but after getting encouraging feedback from someone who had already done the shots, my attitude slowly began to change to where I now thought, ‘I bet I can do this.’ ”

“I was able to do the first injection [of GM-CSF] at the doctor’s office, under guidance, which made me more confident.”

“There is a little more discomfort giving yourself the GM-CSF shots on days 3 and 4 when the injection site is swollen and red.”

Injection-Site Reactions

“I had no significant reactions...muscle pain and cramps in [the] back and neck post injection...”

“I did have some lower back pain... It went away after I finished with the vaccine.”

Advice to Other Patients

“Get educated. Learn the protocol for giving the [GM-CSF] shots... Knowledge is power!”

“Just relax. It’s a piece of cake compared to chemo!”

Concerns About Working After Receiving Immunizations

“[I had] no problems whatsoever or [with] any other activity during vaccines. [I] felt fine and was very active throughout.”

Glossary

Active Idiotype Immunotherapy - A type of treatment that uses the immune system in an effort to fight cancer. Uses a substance called an idiotype protein (Id), which is unique to each person's cancer. Given via a series of subcutaneous injections. May also be referred to as *personalized active immunotherapy*, *idiotype (Id) vaccines*, or *therapeutic idiotype vaccines*.

Active Immunotherapy - A type of treatment that uses the immune system in an effort to fight disease.

Adjuvant - A substance that aids another; for example, a medication given together with another therapy to make that therapy more effective.

Antibody - A specialized protein produced by B cells used by the immune system to fight foreign invaders or disease.

Antigen - A marker on the surface of a cell that can stimulate production of an antibody. With immunotherapies for cancer, the antibody targets the antigen on the cancer cell to kill that cell.

B Cells (B Lymphocytes) - White blood cells that produce antibodies.

B-Cell Non-Hodgkin's Lymphoma (NHL) - Any malignant lymphoma not classified as Hodgkin's lymphoma, where the malignant cells develop from immune system B cells.

Biopsy - The removal of tissue, cells, or fluid from the body (also refers to the sample removed), often performed in order to make a diagnosis. Types of biopsies include excisional lymph node biopsy, core needle biopsy, and fine-needle aspiration (FNA). Bone marrow

and peripheral blood samples may also be referred to as biopsies in the context of making a personalized active immunotherapy.

Bone Marrow Sample - A type of biopsy in which a very small amount of the soft tissue found in some of the body's larger bones is removed. Is usually performed in a doctor's office. The sample is usually taken from the hipbone using a hollow needle.

Cancer Vaccine - Cancer vaccines are designed to stimulate the immune system to recognize cancer cells as foreign and destroy them. The goal of cancer vaccines is preventing disease recurrence.

Cellular Response - Immune response provided by T cells (T lymphocytes).

Chemotherapy - In the treatment of cancer, a general term for chemical agents (ie, drugs) used to kill cancer cells by targeting a specific part of the cancer cell growth cycle. Because the growth cycle of healthy cells is often similar to that of cancer cells, side effects related to the destruction of healthy cells are also seen. Chemotherapy often involves more than one drug (combination chemotherapy).

Chronic Lymphocytic Leukemia (CLL) - A type of lymphoma characterized by an uncontrolled accumulation of large numbers of lymphocytes (white blood cells) in the blood, bone marrow, lymph nodes, and other organs. CLL is usually referred to as leukemia because its initial effects are on the blood and bone marrow.

Clinical Trials - Research studies conducted in humans to answer specific health-related questions. A common type of clinical trial is the interventional clinical trial, in which the safety and effectiveness of a new type of investigational therapy is compared to that of other commonly used therapies or, in some cases, no treatment.

Clonal Malignant Cells - Cancer cells that result from the original malignant B cell dividing and replicating.

Core Needle Biopsy - A biopsy that involves using a hollow (“core”) needle to remove a small tissue sample. The needle used for this type of biopsy has a cutting edge and is larger than that used for fine needle aspiration (FNA). The procedure typically takes only a few minutes and is usually performed in a doctor’s office.

Deoxyribonucleic Acid (DNA) - An individual’s cellular genetic information or coding.

Excisional Lymph Node Biopsy - The removal of an entire lymph node via a small cut in the skin. This type of biopsy is done with a local anesthetic in a doctor’s office or outpatient surgical center. The procedure often leaves a small scar.

Expressing (Gene Expression) - The process by which information contained within a gene is converted into cell structures/functions. For example, if a cell has a gene that codes for a particular protein, and the cell is currently manufacturing that protein, the cell is said to be “expressing” that gene.

Fine Needle Aspiration (FNA) - A biopsy obtained using a small needle to aspirate, or

suck out, fluid or small clusters of tissue cells. The procedure typically takes only a few minutes and is usually performed in a doctor’s office.

Fixed - A term used to describe the way in which a biopsy specimen is preserved for microscopic study through the use of chemicals to kill, harden, and preserve the tissue.

Follicular Lymphoma (fNHL) - A slow-growing or low-grade lymphoma.

Genetically Engineered Protein - A protein that is produced by recombining the genetic material of two different organisms. A number of medications and vaccines contain genetically engineered proteins.

Genetic Mutation - A permanent change in a cell’s genetic material (DNA). Can be the result of natural errors that occur during the cell division process or caused by external factors such as radiation, chemicals, or viruses.

Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF) - A growth factor naturally produced in the body, or its synthetic equivalent (ie, drug), that tells the bone marrow to manufacture new white blood cells and thus enhances the functioning of the immune system.

Humoral Response - An immune response brought about by antibodies that recognize antigens on cancer cells.

Id - Abbreviation for idiotypic protein.

Idiotypic (Id) - The patient-specific “fingerprint,” or unique protein on the patient’s tumor, that is identified and used to manufacture a patient-specific vaccine.

Idiotype Protein (Id) - A protein produced, or expressed, by B cells. When the protein is expressed by cancerous B cells, the idiotype is unique to that cancer.

Idiotype (Id) Vaccines - A type of treatment that uses the immune system in an effort to fight cancer. Uses a substance called an idiotype protein (Id), which is unique to each person's cancer, given by a series of subcutaneous injections. May also be referred to as *active idiotype immunotherapy*, *personalized active immunotherapy*, or *therapeutic idiotype vaccines*.

Immune System - The body's natural defense system. Designed to protect the body against harmful substances by recognizing antigens (large molecules) on the surface of these substances and subsequently destroying them. Viruses, fungi, and bacteria are examples of harmful substances that contain antigens. The immune system has a difficult time defending the body against cancer because cancer cells develop from the body's own cells.

Immunogenic - Related to or producing an immune response (ie, a substance that stimulates the immune system to react specifically to it).

Immunotherapy - Therapies that stimulate the immune system to fight disease.

Investigational Therapy - Any experimental treatment currently being studied to determine whether it is safe and effective. Investigational therapies may be compared to other commonly used treatments or no treatment.

Keyhole Limpet Hemocyanin (KLH) - A protein or substance derived from a giant sea mollusk found off the coast of California. The

body's immune system reacts strongly to its presence, so it is considered highly immunogenic. It is combined with the idiotype protein (Id) derived from a patient's cancerous B cells to form an idiotype immunotherapy and given to stimulate the patient's immune system to respond to the cancer.

Lymphocyte - A type of white blood cell that is part of the immune system.

Lymphoma - A type of cancer that originates in the lymphatic system from B or T lymphocytes.

Monoclonal Antibody (MAb) - An antibody that is developed in the laboratory from a single cell. MAb therapies to treat cancer target the antigen on the tumor. They kill the abnormal cell but also kill normal cells that express the same antigen.

Non-Hodgkin's Lymphoma (NHL) - A type of cancer that occurs when there is an uncontrolled or malignant growth of abnormal lymphocytes. Arising from the lymphatic system, NHL may be characterized by enlarged lymph nodes due to the collection of cancer cells in these areas.

Patient-Specific Vaccine - Another term for *personalized active immunotherapy* (see below).

Personalized Active Immunotherapy - A type of treatment that uses the immune system in an effort to fight cancer. Uses a substance called an idiotype protein (Id), which is unique to each person's cancer. Given via a series of subcutaneous injections. May also be referred to as *active idiotype immunotherapy*, *idiotype vaccine*, or *therapeutic idiotype vaccines*.

Phase 3 Study - A clinical trial in which an investigational drug or treatment is given to a large number of people. It is conducted to confirm effectiveness in a specific disease, monitor for reactions, compare the investigational therapy to other commonly used treatments, and gather information about the safe use of the investigational treatment.

Prophylactic (Preventative) Vaccines - Immunizations used to prevent, rather than treat or cure, disease. These vaccines are used before illness develops, are mass produced, and are administered to large numbers of people. Examples include measles, mumps, and polio vaccines.

Recombinant - A term used to describe the manufacture of a new molecule by recombining the original molecule's DNA.

Recombinant Protein - A protein that is produced by recombining the genetic material of two different organisms (hence the term *recombinant*). A number of medications and vaccines contain recombinant proteins.

Subcutaneous - Under the skin (ie, a subcutaneous injection is one that is administered just beneath the skin).

T Cells - Lymphocytes involved in cellular immunity. By recognizing antigens on cancer cells, killer T cells cause tumor destruction.

Therapeutic Idiotypic Vaccines - Immunizations used to treat diseases (such as cancer) already present in the body. They differ from prophylactic vaccines, which are used to prevent diseases such as measles, mumps, and polio from occurring.

Patient Resources

Lymphoma

Lymphoma Research Foundation (LRF)

Provides information on lymphoma, current treatments, research, clinical trials, and patient support issues.

www.lymphoma.org

Patients Against Lymphoma (PAL)

Provides information on lymphoma, current treatments, and clinical trials.

www.lymphomation.org

The Leukemia & Lymphoma Society (LLS)

Provides information and support to patients with blood-related cancers.

www.leukemia-lymphoma.org

Chronic Lymphocytic Leukemia

CLL Topics

Provides information on CLL, current treatments, research, and clinical trials, plus tools to help organize medical information.

www.clltopics.org

HealthTalk: CLL Education Network

Offers audio programs and transcripts on the latest advancements in CLL diagnosis and treatment, and practical advice for people living with CLL.

www.healthtalk.com/chroniclymphocyticleukemia/index.cfm

Lymphoma Research Foundation (LRF)

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The Leukemia & Lymphoma Society (LLS)

Provides information and support for patients with blood-related cancers.

www.leukemia-lymphoma.org

Government Agencies

National Cancer Institute (NCI)

Provides a wide variety of up-to-date cancer information.

www.cancer.gov

NCI's Cancer Vaccine Fact Sheet

Provides answers to commonly asked questions regarding cancer vaccines.

www.cancer.gov/newscenter/pressreleases/cancer_vaccines

NCI's Animation of the Immune System and Cancer Vaccines

Provides an animated illustration of the immune system and cancer vaccines.

www.cancer.gov/newscenter/benchmarks-vol3-issue1/Video

NCI's Biological Therapies for Cancer: Questions and Answers

Provides an overview of how the immune system functions and describes the actions of available biological therapies.

www.cancer.gov/cancertopics/factsheet/Therapy/biological

National Institutes of Health (NIH)

Provides a searchable database of clinical trials and information about clinical trials.

www.clinicaltrials.gov

Patient Support

Cancer Care, Inc.

Provides counseling, information, referrals, and financial assistance.

www.cancercares.org

Gilda's Club

Provides free support and networking groups, lectures, and social events for cancer patients and caregivers.

www.gildasclub.org

National Coalition For Cancer Survivorship (NCCS)

Information, programs, and resources on cancer survivorship—the experience of living with, through, and beyond a diagnosis of cancer.

www.canceradvocacy.org

Patient Advocate Foundation (PAF)

A national network for access to care, job retention, and reimbursement appeals.

www.patientadvocate.org

Patient Advocate Foundation's Co-Pay Relief (CPR) Program

Co-payment assistance funding for patients with lymphoma.

www.copays.org

The Wellness Community

Provides free support services and educational workshops to patients and their loved ones.

www.wellnesscommunity.org

