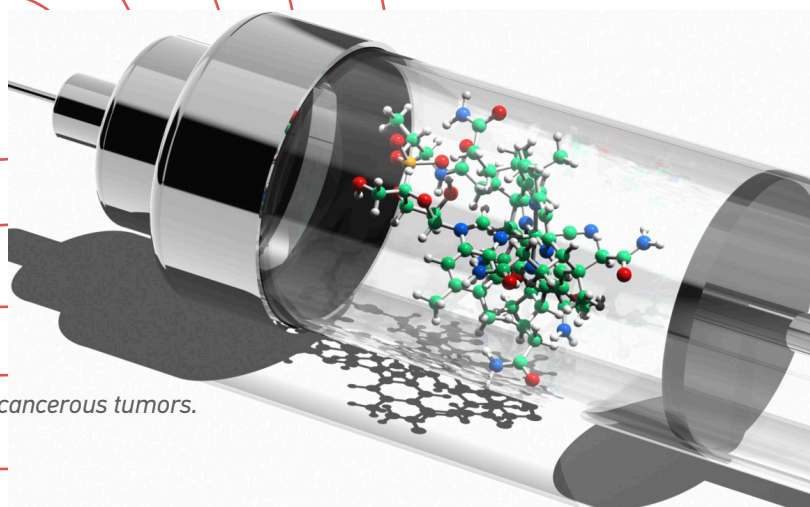


Targeted Cancer Killers

Physicians are arming the immune system to seek and destroy cancerous tumors.

By Jeff Samoray



Traditionally, most cancer treatments involve some combination of chemotherapy, radiation therapy, and surgery. But what if physicians could supplement these therapies by helping the immune system—our body’s natural defense mechanism—detect these tumors and destroy them? What if you could receive a vaccination that helped your body fight cancer indefinitely?

That’s the exciting direction researchers are taking toward potentially groundbreaking treatments with immunotherapy.

Recently, encouraging developments in the field of immunotherapy are offering exciting evidence that this form of cancer treatment may offer hope for patients facing aggressive cancers. Within the past two years, the US Food and Drug Administration (FDA) approved two new immunotherapy drugs—one for prostate cancer and one for melanoma.

Additionally, the 2011 Nobel Prize in physiology was awarded to three scientists who are credited with discoveries that have helped create new vaccines that enable the immune system to attack tumors. All of these developments speak to the expanding role that immunotherapy may play in the cancer treatment landscape of the future—and to the possibilities they offer today’s patients.

Boosting the Immune System

“Immunotherapy is any kind of treatment that works by stimulating the patient’s immune system,” says David Berd, MD, national director of immunotherapy and a medical oncologist at Cancer Treatment Centers of America® in Philadelphia, Pennsylvania. “With cancer patients, immunotherapy usually works best against small tumors. The best candidates are patients who have a small number of

cancer cells remaining after surgery.”

Immunotherapy treatments can stimulate the patient’s immune system to work harder, slow the growth or spread of tumors, and enhance normal immune system functions. Researchers have explored the impact of immunotherapy against most cancer types, though the majority of studies have involved melanoma and kidney cancer.

There are three main types of immunotherapy treatments:

- **Active immunotherapy** involves vaccine injections (similar to the polio vaccine) that stimulate the patient to generate a permanent immune response to disease.
- **Passive immunotherapy** works by administering lab-created antibodies (or immune system components) to fight off disease. The rabies antiserum is one example: it kills the virus but does not provide permanent immunity.

- *Adoptive immunotherapy* is the most complex form. Scientists harvest T-cells from the patient by drawing blood. In the laboratory the T-cells are activated with a specific antibody, which programs them to find and attack tumors. After the “boosted” T-cells are transferred back to the body, they not only seek and destroy tumors but also transfer their function to existing cells, thereby enhancing the patient’s natural immune system.

“Adoptive immunotherapy can potentially generate a permanent immune system response to the disease,” says Dr. Berd. “The T-cells are trained to respond to a particular type of cancer cell. Once transferred back to the body, the T-cells can remain active indefinitely.”

Applying immunotherapy to cancer is not a new idea. Researchers have studied and tested the treatment with cancer patients since the 1920s. Interest in continuing the research has wavered since then, based on the variable success of clinical studies.

“Every time there’s been an advance in basic immunology, researchers have tried to apply immunotherapy to cancer,” Dr. Berd says. “Some immunotherapy studies are spectacularly effective; others aren’t. Clinical outcomes depend on a number of factors. Currently, there is great interest in immunotherapy because of the two drugs that have received FDA approval: Provenge® (sipuleucel-T) for prostate cancer and Yervoy® (ipilimumab)

for late-stage melanoma patients. These are the first effective cancer-fighting immunotherapy drugs on the market.”

Long-Term Therapy

At the Karmanos Cancer Institute in Detroit, Michigan, researchers are conducting a clinical study applying adoptive immunotherapy to several patient groups, including women with one of the deadliest forms of the disease: triple-negative breast cancer.

This type of breast cancer is generally more aggressive than other forms of the disease. It’s also more difficult to treat because the cancer cells have few or no receptors that respond to traditional chemotherapy. About 26 percent of African-American women with breast cancer are triple-negative compared with 15 percent of White women. The recurrence rate can be as high as 80 percent after chemotherapy and surgery due to the persistent nature of the disease.

The Karmanos study will help determine if activated T-cells in combination with neoadjuvant chemotherapy (administered before surgery) increase complete pathologic remission or elimination of the disease.

“The usual incidence of complete pathologic remission [no disease found at the time of surgery] after neoadjuvant chemotherapy for patients without immunotherapy is 20 percent; our goal is to double that,” says Lawrence Lum, MD, DSc, professor of oncology, medicine, immunology, and microbiology at Karmanos and Wayne State University School of Medicine. Dr. Lum is the principal investigator on the study and a pio-

neer in developing new antibodies that target specific tumors.

“Our immune system’s T-cells mount the body’s strongest anti-tumor response,” Dr. Lum says. “The exciting part about adoptive immunotherapy is the potential long-term result. If we can vaccinate the patient’s immune system using activated T-cells, the tumor-killing effect can last from months to years.”

It’s too early to tell if targeted T-cell infusion can improve outcomes for patients with triple-negative breast cancer, but a separate clinical study conducted by Dr. Lum has shown some promise.¹ Patients with stage IV breast cancer who received infusions of activated T-cells had an overall survival rate nearly two to three times longer than that of patients who received conventional treatment.

“Vaccinating patients against their own tumors and achieving a long-term anti-tumor effect is our goal,” Dr. Lum says. “I think immunotherapy has great potential for the future, and investigators are making some progress. We don’t expect to hit a home run with immunotherapy itself, but if we can discover the optimal method of using immunotherapy in combination with standard therapies, we’ll take the next step toward finding a cure.” **CFThrive**

Reference

1. Lum LG, Rathore R, Al-Kadhimi Z, et al. T-cells targeted with anti-CD3 x anti-HER2 bispecific antibody for treatment of women with stage IV breast cancer (phase I): Clinical and immune function results. Paper presented at: 47th Annual Meeting of the American Society of Clinical Oncology; June 3-7, 2011; Chicago, IL. Abstract 2518.