

Immunotherapy: Update on a Promising Cure for Cancer

by Dr. David N. Krag

Editor's note: Dr. David N. Krag is a surgical oncologist and cancer researcher at the University of Vermont College of Medicine. Krag led the world's largest surgical trial in breast cancer, which nearly eliminated the need to remove all the lymph nodes. Krag, along with other researchers across the United States, has been working to develop new treatments for breast cancer, brain cancer, and other types of cancers, using patients' own immune systems.

Immunotherapy is a promising and exciting new treatment for cancer—and the excitement is well justified. However, we are at the beginning stages of developing this new therapy: if all the discoveries we need were hidden away in a big house, we would just be coming through the front door.

We hear about our immune system all the time, but what is it? First of all, it is phenomenally complex. Many types of cells make up the immune system, with names like B cells, T cells, dendritic cells, and macrophages. Scientists try to understand the function of each of these cells. It is difficult to understand how the immune system works because these immune cells do not act alone. The immune system is like an orchestra. If we take dendritic cells alone and work with them in the lab, it is like trying to understand an entire symphony by learning what the oboe is playing.

Why all the excitement now about immunotherapy for cancer? The reason is that some new drugs have made the disease disappear in some patients with advanced cancer. As a cancer surgeon and researcher, I have never seen anything like this in the 30 years I have been practicing. It is truly a breakthrough time for cancer treatments.

Targeting Mutated Cell Parts

Let's dive in a bit to understand what these new drugs are doing. Till now, almost every anticancer drug that has been developed has worked by attacking cancer cells. Great science goes into understanding the weak points or vulnerabilities of cancer cells. Chemicals are created to take advantage of those vulnerabilities by blocking highly specific things in cancer cells.

The problem is that cancer cells are not all alike. One chemical may cause some cancer cells to die but then other cancer cells may regrow, which are not harmed by the anticancer chemical. This has been the chemotherapy story for more than 50 years, and there does not appear to be an end to this situation anytime soon.

The new immunotherapy drugs are totally different from all previous cancer drugs. These drugs do not directly attack cancer cells at all. Instead, they act on immune cells. The drugs broadly stimulate immune cells to move forward and attack the cancer cells. When our body reacts to an infection, like the flu or a cut that gets infected, the immune cells ramp up to fight the infection. The body knows just how far to ramp up and then, like magic, ramp down: the redness and swelling around the cut goes away. The immune cells have cues that tell them to slow down. Researchers have discovered some of the ways these messages or cues work that tell the immune cells to back off.

Cancer cells tap into the messages that tell immune cells to slow down, which is not good. It appears that just as the immune cells are beginning to go after cancer cells, those cells send a message that turns off the immune cells. The new immunotherapy drugs

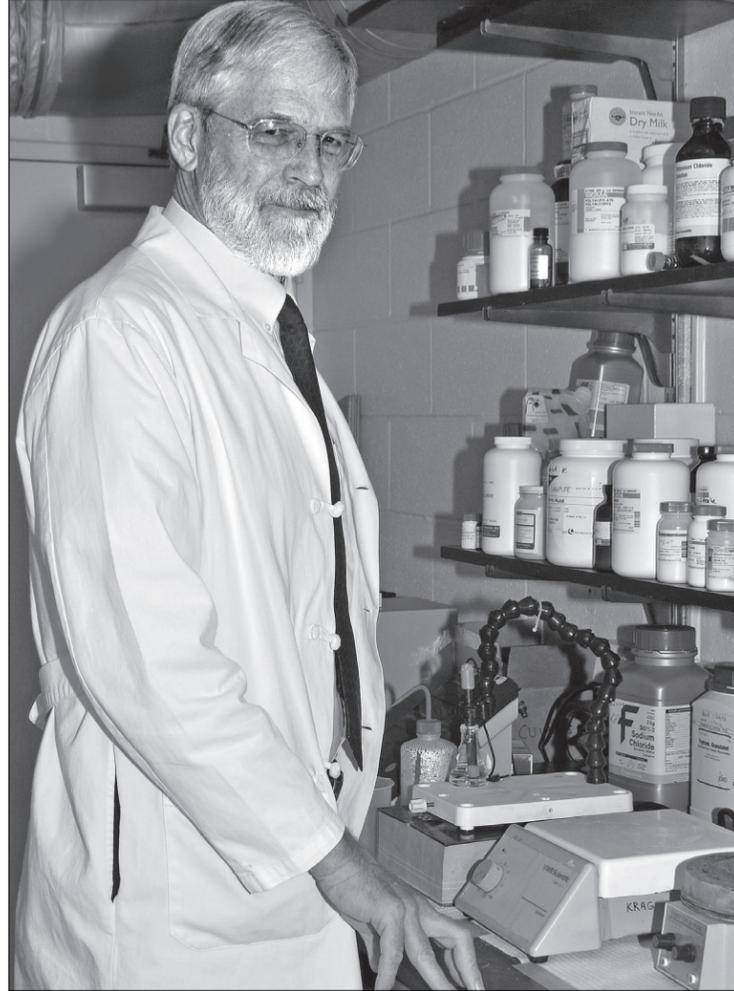


photo: Jan Doerler

Dr. David N. Krag at work in his laboratory at UVM College of Medicine.

act on these messages and tell the immune system to ramp up again.

Some patients have responded dramatically to these immune-activating drugs; others less so or not at all. Great efforts are underway to try and sort this

out. It appears that the best immune response occurs when the immune cells target mutated cancer cell parts. This is where things get very interesting.

What are mutated cancer cell parts? Cancer cells arise because of changes

in the cell genetic code, which leads to its uncontrolled growth. Today, technology enables us to read the genetic code of cancer cells. Computer programs can analyze the human genetic code of about three billion DNA "letters" and find the spots where the code has changed or mutated. Bad genetic code produces bad cells. Mutations are very common in cancer cells and may total several hundred. Since these mutations occur somewhat randomly, the mutations in one person's cancer are very different from those in another.

The genetic code is the template or instruction manual for making cell parts. All cells are constantly replacing and adding to cell parts. When the instructions for making a cell part are from a mutated genetic code, that cell part becomes abnormal. Cancer cells are physically different and are made up of potentially hundreds of cell parts that are different from a normal cell. In fact, the mutated cell parts made from the mutated template are frequently different from any other cell part anywhere in the body.

Our immune system is exquisitely designed to discriminate normal cell parts from abnormal parts. From the perspective of the immune system, the mutated cell part is foreign. Let's circle back to the immunotherapy drugs that activate the immune system. Mutated tumor parts are good targets. If the immune system has figured out how to target these parts, the response may be better. In general, tumors with a larger number of mutations respond better to this type of immune therapy. This makes sense.

Developing Immune-Activating Vaccines

Our lab at the University of Vermont is trying to control the immune response in favor of making the cancer go away. We want an immune response to the mutated tumor parts. We figured out how to make a vaccine composed of mutated cell parts. In mice we have demonstrated that there is a very nice immune response to the mutated cell part. The mouse generates antibodies specifically against these mutated cell parts.

The problem with vaccines is that everyone reacts differently to them. We want to control the response, so we are doing things a bit differently. The injected vaccine travels to a lymph node, where the immune cells reside that respond to the vaccine. In the lymph node are special cells called B cells that are in charge of making antibodies. About two weeks after the vaccine is injected, many B cells in the lymph node develop the ability to make antibodies that specifically target the mutated cell part. This is really good.

We have recently figured out how to isolate these B cells in such a manner that we can produce antibodies in the lab. Now we have the ability to make as much of the antibody as we want. Our story pauses here because that is as far as we have gotten. The next chapter will be to make lots of these antibodies and use them to make cancers go away.

We have a ways to go, but we have a strategy that does not depend upon a single drug. We have, instead, a process. Here is a summary of this complicated sequence:

- Remove a malignant tumor from a patient.
- Read the cancer's genetic code and identify the mutations.
- Make multiple vaccines that each target a mutated cancer cell part.
- Inject this customized vaccine into the same patient.
- Perform a biopsy of the lymph node responding to the vaccine.
- Identify the B cells making antibodies against the abnormal tumor parts.
- Make lots of these anticancer antibodies in the lab. Infuse these anticancer antibodies into the same patient.

Whew! No one said it would be easy. □

FINANCE

Financial Thoughts to Ponder—and 5 Tips as I Go

by C.D. Moriarty

Editor's note: For over 12 years, C.D. Moriarty has provided financial advice to readers of Vermont Woman. This will be her last column. We wish her well.

For over a dozen years, I have joined you in each issue of *Vermont Woman*. I have loved and valued your feedback as we connected in person and via e-mail or phone. Thank you for reading. As this is my last column, I wanted to share with you all that I have learned as a Certified Financial Planner. I will continue to share my work in the world through teaching and writing on platforms near and far. I hope our paths cross and your abundance grows.

Here is a lifetime of experience from where I sit as a coach, financial expert, and lifelong learner and teacher about money. Remember, there is more to money than the simple facts or how much you have.

We are all motivated by something different. So though many of us say we want to retire, educate our children, or buy a house, for each one of us, those goals will look different. Emotions, lifestyle, and understanding impact our money. Despite the differences, there are some basics we all must know.

1. The rules matter: so learn the rules. Each game has rules. There are rules of the road if you drive—and so with money. We all know about fil-

ing income taxes by April 15 and paying taxes through payroll deduction. And you likely know that if you do not file your tax forms on time, there is an added fee. Likewise, in other areas, not knowing the rules can cost you money.

Estate planning laws vary by state. As do divorce laws. Knowing where you live and what impact the laws have on you will make any transition easier. On the investing and savings side, understand compounding. Appreciate how money can grow and

work for you over time. From a debt perspective, you must understand what it means to sign for a car loan, school loan, or mortgage. Think twice before you cosign a loan because this means you are on the hook for the money.

A little education goes a long way. Go online; take a class; read a book. Listen to a radio show or podcast. Your money is your responsibility.

2. Do not make long-term financial decisions when upset or under pressure. When we are emotional, we all make bad decisions. This is why the basic advice to those who have lost a spouse has always been "Do not do anything for a year." This well-known fact is also why salespeople of all types, including those trying

to sell you a financial product, try to get you to spring for a deal that "is only available today!" They know that while under pressure, you are more likely to go for the deal. Away from the situation, you will respond more logically, and they will lose a sale.

3. Build your savings for self-reliance. There is no a better way of ensuring that you can take care of yourself and your family than by having a savings account at a local bank. With money nearby, you can weather any

disaster and save yourself the stress of borrowing at an inopportune time or making a bad decision under pressure (see number 2).

4. Be aware of your monthly payments and keep them low for self-sustainability. In other words, change your spending, change your life. With all the autopays, bank debits, credit card payments, and monthly memberships, we can easily lose sight of where our money goes. Then, when we want to make a change or save money, we become overwhelmed with the details. Many times, as a result, we do not make a change.

The true way to manage money is to be conscious and decisive with your payments. Understanding where your money is going each

month and taking action allows you to make changes. With a living-in-the-present approach to your money, you can be responsive to your immediate needs—rather than playing catch up because every payment is automatic and you forgot to stop the gym or the music subscription you never use.

Take the time to work on your cash flow, which is simply where your money goes in and out of your checkbook. The investment of time *now* makes for financial flexibility later.

5. Your money is your responsibility. Everyone is seeking the perfect advice. Many investment professionals say they can beat the market, do better than others, or serve you better. Remember: No one knows the future. Do not pass on your financial responsibility just because someone is managing your investments or it is all in your retirement at work. Learn. Ask questions. Get second opinions. Find out how much the fees are. Understand what is happening with your money. You deserve to know.

Money is about personal choices. Make your choices well. That will gain you a lifetime of peace of mind, financial health, and self-responsibility.

Wishing you peace and prosperity.

C.D. Moriarty can be found at www.MoneyPeace.com or on Facebook. Listen to her Mondays, 9 a.m.–11 a.m., on WDEV radio 96.1 FM and follow her on Twitter. Stay in touch. □