James P. Allison is the chairman of the immunology department at the
University of Texas M.D. Anderson Cancer Center in Houston. His seminal
research opened up a new field in cancer treatment: immunotherapy. Instead
of poisoning a tumor or destroying it with radiation, Dr. Allison has pioneered
ways to unleash the immune system to destroy a cancer.

Two years ago, Science magazine anointed immunotherapy as the
“Breakthrough of the Year.” More recently, Dr. Allison, 66, won the Louisa
Gross Horwitz Prize, often a precursor to a Nobel. Our conversation has been
edited and condensed.

Q. The class of drugs you’ve helped invent has been hailed as
one of the first truly new cancer treatments in decades. What
makes it so different?

A. It’s a bit counterintuitive. Till now, most cancer treatments —
radiation, surgery, chemotherapy — attacked tumors directly, with the goal of
killing them.

In the 1980s, my laboratory did work on how the T-cells of the immune
system, which are the attack cells, latch onto the cells infected with viruses and
bacteria and ultimately kill them. That research lead me to think that the
immune system could be unleashed to kill cancers.

Basically, I proposed that we should stop worrying about directly killing
cancer cells and develop drugs to release those T-cells.
Looking to the immune system for a cancer therapy isn’t a new idea, is it?

No. There was a surgeon named William Coley in the 19th century who’d noticed that cancer patients who’d gotten infections after surgeries tended to have fewer reoccurrences than those who hadn’t. He thought that there was something in bacteria that provoked the body to do something therapeutic, and he tried to develop treatments based on that.

Coley had some success. His ideas disappeared with the advent of radiotherapy, which became the acceptable treatment.

In the mid- and late 20th century, particularly with the war on cancer, you had multiple attempts to develop therapeutic anticancer vaccines. There were literally hundreds of trials. Nothing really worked. The tumor seemed to thwart the immune system’s ability to attack. Eventually, the whole idea of using immunity to stop cancer became discredited. No one understood why immunity didn’t work.

But your laboratory came up with an answer. What did you discover?

My lab has done a lot of basic research on how T-cells find and mark viruses, bacteria and defective cells. In the 1990s, my team and another group showed that there was a molecule on T-cells that actually acts like an off switch or a brake pedal when T-cells encounter an infected cell.

Instead of attacking the cell, this molecule puts a kind of brake on the immune response. We call it a checkpoint, and it may be why many of those therapeutic anticancer vaccines couldn’t work. We think the immune system may have multiple checkpoints.

I wondered whether we could block this off switch to keep the T-cells turned on. And that’s what we did. We developed an antibody to plug this off-switch. It worked great in mouse models of many types of cancer.

More importantly, it worked for some people with skin cancer. The first drug developed out of this was Yervoy, which was approved by the F.D.A. in 2011 against metastatic and inoperable advanced melanomas.

Long-term follow up of 5,000 melanoma patients who received it found
that 22 percent survived for at least 10 years, some longer.

**Is that a good number?**

Oh, yeah. These were patients with usually seven months, maybe a year, to live.

A woman in Santa Monica was one of the first people to get the drug. She had two kids in high school. She’d failed at everything.

And so Dr. Antoni Ribas at U.C.L.A. said: “Well, we’ve got this experimental thing. We don’t know if it will work. It may be toxic.” She said, “I’ll do anything if I can just live a few more months to see my son graduate high school.” And so they treated her. And her tumors went away within about four months.

I met her 10 years later. She said, “You know, my kids are through school, married, starting families.”

There are a lot of stories like that.

**Are you one of these people who always wanted to be a researcher?**

I’m one of those people who has always wanted to solve puzzles. As a kid, I wanted to be the first to know something that no one else did. I think that’s true of a lot of scientists.

I grew up in Alice, Tex. It’s a really small town. My dad was a country doctor. I was really interested in animals, biology. The high school had some good science teachers, but not in biology, because these people were religious, and biology involved teaching evolution.

Teaching biology without Darwin is like giving a physics course without Newton. I refused to take those classes, and that got me into trouble with those teachers who didn’t like anyone bucking the system.

Eventually, a compromise was worked out where I could take a correspondence course where I got sent these books and this box, and I did these experiments at home with the stuff they sent. It was a lot of fun. But I had to teach everything to myself. So I got a lot of experience in solving puzzles — alone.

**There’s a lot of cancer in your own family, isn’t there?**
My mother died of lymphoma when I was 12. An uncle died of melanoma, another of lung cancer. Both my brothers had prostate cancer — one died from it.

I was diagnosed with it, too. It was caught early. I had a prostatectomy. After seeing how fast it progressed on my brother and how gruesome it was, I said: “I’m not taking any chances. I’ll risk the side effects. Just get it out now.”

It got to the point with my brother where you felt, “Just let it go.” But you know, the body hangs on. It was excruciating.

**Does it give you satisfaction that you’ve dealt a blow to something that’s caused your family such devastation?**

Absolutely. I didn’t set out exclusively to do that. But I’ve thought about it, and I think my mother and brother would be proud. Just the other day, I was with a leukemia and lymphoma research group at M.D. Anderson. They’re starting a big program with drugs of this particular type that I helped invent.

Since Yervoy, there’ve been two other drugs of this type to win F.D.A. approval. And there have been trials with other cancers using Yervoy. It hasn’t been approved yet, but there have been responses with clinical benefits for prostate, kidney and bladder cancers.

At this moment, just about every pharmaceutical company working the cancer space is working on immunotherapy drugs. Not all cancers will respond as well as melanoma. But there’s no reason why they can’t figure out other things to make them as effective.

**On a less serious subject, is it true you once sang with Willie Nelson?**

Only once. I was a postdoc in La Jolla, Calif., and I had this little band that played local bars. He came by and we sang “Blue Eyes Crying in the Rain.” Seeing someone survive cancer because of something I’ve been part of is about as good it gets. But at that time, singing with Willie was big.