Immunotherapy is counterintelligence against cancer

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*Immunotherapy* is a buzzword currently resounding in research centres and universities alike. It refers to a treatment that lets us tear away the disguise cancer cells use to hide from our bodies’ natural defences, and then to use the immune system to heal ourselves. One way to think of it is as a counterintelligence operation in our bodies, where we unmask and eliminate the enemies in our midst.

Oncologists have already been deploying new treatments along these lines in recent years. A new class of immunotherapy agents called programmed cell death protein-1 inhibitors (PD-1 inhibitors), is of particular interest.

In the mid-1990s, I, along with two of my colleagues at Singapore General Hospital, began some new research by asking whether cancer occurred in patients because their immune system was impaired. We found that there was no difference, in this regard, between healthy people and those who had developed cancer, so we then wondered how it was that these cancer cells could escape detection by our body’s immune system.

Our theory was that cancer cells could camouflage themselves somehow. They must have been able to hide so that the immune system could not detect and destroy them.

To test the hypothesis, we asked patients with superficial, easily accessible tumours for consent to inject foreign genetic material directly into their cancers. This genetic material was meant to let the tumours present themselves as foreign to the immune system—as coming from outside the patient’s body. And much to our delight, we saw some of these tumours shrink and even disappear.

This made us more certain that cancers did not flourish because of a deficiency in the immune system, but rather because they could hide or protect themselves from competent immunity.

Now fast-forward to the present decade. Researchers have found that the T-cells in our immune system have a surface receptor called programmed cell death protein-1 (PD-1). Many cancer cells can produce a protein, called a ligand, that blocks this receptor and stops the T-cells from attacking and killing them. Two pharmaceutical companies have now come up with antibodies that prevent this blockage, freeing the activated T-cells to do their job of killing the cancer cells. The two currently available immunotherapy drugs based on this principle are pembrolizumab (Keytruda) and nivolumab (Opdivo).
The results of studies using immunotherapy have been nothing short of amazing. In one study, code-named CheckMate-057, advanced lung cancer patients who had been previously treated with first-line chemotherapy were randomly assigned to either a control group that would receive a standard chemotherapy, docetaxel, or to an experimental group that would be treated with nivolumab, an immunotherapy.

Patients who received nivolumab lived longer than those in the control group, seeing their risk of death fall. One-year odds of survival were 51% for the nivolumab group, compared to 39% for the docetaxel group. Such novel agents have also been shown to be effective in treating melanoma, colon cancer and malignant lymphoma.

Excitement over the use of immunotherapy remains high. The recent announcement that former United States president Jimmy Carter achieved cancer remission after treatment with pembrolizumab has heightened interest.

In his last state of the Union Address, the current president, Barack Obama, has declared an American commitment to end cancer “once and for all”. There are now more resources and people committed to cancer research than ever before. But the promises that come with new discoveries must be tempered with caution: disappointingly, treatments that are successful in clinical trials may show different results in the real world.

Nonetheless, we are discovering more and more that immunotherapy can help the body heal itself, and that is a great cause for hope.