http://popularmechanics.com FEBRUARY 2003

Popular Mechanics

SCIENCE

Attacking Cancer

BY JIM WILSON

Jefferies's cancer vaccine turns the body's natural defenses against tumors.

BIOLOGY

Every army has a doctrine, a core belief that guides the way everyone from generals down to privates fights. In World War II that doctrine was unconditional surrender. During the Cold War it was containing communism. The war on cancer also has a doctrine. It is the belief that cancer is not one disease but a family of diseases, each demanding a unique treatment. Waging the war disease by disease has produced impressive results. Childhood leukemia is no longer a death sentence. And specialized drugs have proved almost magically effective in shrinking rare tumors. Encouraging though these victories may be, the big picture is bleak. Cancer is chiefly a disease of old age, and the baby boomer generation is getting older. Today, cancer is the No. 2 killer after heart disease. Within about four years it will be No. 1, killing upward of 730,000 Americans annually, according to the National Cancer Institute. It is against this dark statistic that a discovery by a University of British Columbia scientist shines like the proverbial light at the end of the tunnel. It turns out that cancer tumors share a

common weak link: the inability to tell the body's immune system that they need to be destroyed. Wilfred Jefferies has found a way to reverse that defect, and turn the body's natural defense into a powerful ally.

Stimulating TAP

Think of a cell as a small engine. It burns fuel and oxygen, and gives off exhaust. Looking at exhaust tells you a lot about the condition of a vehicle's engine. The same holds true for a cell. When something goes wrong inside it, a cell sends out the biochemical equivalent of a puff of black smoke. Specialized white blood cells tag the offenders. Other cells—the immune system's hit men—move in for the kill.

Among the white blood cells is a group called T cells, so named because they originate in the thymus gland. "A subset of T cells are responsible for killing virus-infected cells and cancer cells," Jefferies tells POPULAR MECHANICS. Unless they are suffering from an immune system disorder, most people can rapidly produce massive numbers of T cells to fight invaders. The problem is that in many cancer cells the ability to emit a warning signal ("destroy me"), in the form of a compound called tumor antigen peptide, is missing. "This hides the cancer cells from the immune system, and they grow into tumors that eventually kill the person."

Several years ago, Jefferies, who is a professor of medical genetics, microbiology and immunology, tracked down the root of the problem. Cancer cells were producing a warning signal, but it was not being pumped to the surface. Closer investigation revealed that the gene that told the cell to produce a protein called TAP (transporter associated with antigen processing) was disabled. "Loss of TAP expression in tumors is highly correlated with disease progression and survival rates in humans," Jefferies says. "The 5-year survival rate for patients whose tumors [are] positive for the TAP protein is nearly 90 percent. All of those [negative for TAP] were dead within four years."

Jefferies reasoned that the problem could be reversed by infecting tumors with a virus that contained a working copy of the damaged gene. To test his theory, he gave laboratory mice small-cell lung cancer, followed by his TAP technology cancer vaccine. Seventy percent of the mice survived.

In the past, attempts to marshal the immune system to fight cancer have fallen short. Although about 20 immune system-activating drugs have been licensed or are in clinical trials, none is targeting as broad a spectrum of cancers as TAP technology.

"TAP technology is a method of restoring the ability of the body's immune system to recognize the cancer cells as foreign, thereby boosting the natural process for destroying the cancerous cells," says Jefferies. He expects it also would be used in conjunction with existing cancer treatments, such as chemotherapy.

Last year, Jefferies received a U.S. patent for applying the TAP technology to all solid tumors. In addition to his university position, he became chief scientific officer for GeneMax of Blaine, Wash., a company that will commercialize the drug. Clinical trials should be under way within about a year. If it proves as effective in humans as in lab animals, the critical battle in the war on cancer may have begun at last. **PM**