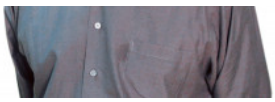
vaccine might be more effective than previous therapies at inducing immune cells to destroy tumors. The research, conducted in mouse models of cancer, was reported in the journal *Cancer Research* on October 1 by James P. Allison, Chair of Sloan Kettering Institute's Immunology Program, and research fellow Michael Curran. [PubMed Abstract]



James Allison

In the 1990s, Dr. Allison discovered that a molecule called CTLA-4 prevents the immune system from attacking the body's own tissues. This inhibitory effect has thwarted many attempts to harness the immune system to fight cancer, but Dr. Allison eventually identified and learned to produce antibodies that can block CTLA-4.

Over the past decade, researchers have investigated giving anti-CTLA-4 antibodies in tandem with a vaccine called Gvax, made up of irradiated tumor cells secreting a signaling molecule called GM-CSF, which enhances the immune response to the dying tumor cells. Although Gvax induces an immune response, it also indirectly causes an increase in the number of regulatory T cells, which suppress immune activation and undermine the strength of the response. "This limitation, among others, led us to look for a vaccine substitute for GM-CSF that would lack its inhibitory effect," Dr. Allison said.

He and Dr. Curran tested a vaccine called Fl3vax — which uses a different signaling molecule, Flt3 ligand — in combination with anti-CTLA-4 to see whether this would generate a more robust immune response. The researchers implanted melanoma tumors in the mice, waited three days, and then gave them Fl3vax and anti-CTLA-4 at the site of the tumor. This treatment induced the immune cells to destroy the tumors in 75 percent of the mice, whereas Gvax was ineffective in the same setting.

"Fl3vax prompted a much higher number of CD8+ T cells, which directly destroy foreign cells, to activate and infiltrate the tumor site, along with creating more dendritic cells, which prime additional T cells to attack," Dr. Curran said. "Fl3vax surpassed Gvax at mobilizing the types of immune cells that you want for an effective response."

The researchers achieved similar results testing Fl3vax with CTLA-4 blockade in mouse models for prostate cancer, suggesting

Fl3vax could be a broadly useful vaccine against many kinds of cancer.