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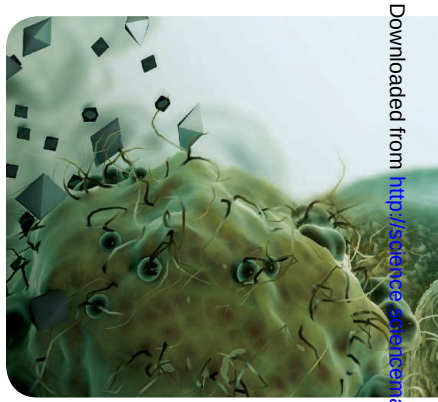
Cancer Immunotherapy

THE WAR ON CANCER BEGAN A LITTLE MORE THAN 40 YEARS AGO AS A NATIONAL RESEARCH PROGRAM to radically improve the survival of patients with cancer, a leading cause of death in the United States and worldwide. The main weapons deployed have been surgery, radiation, and chemotherapy, treatments that often carry risks and/or cause adverse side effects. Although some forms of cancer yield to these therapies, not all do, and thus mortality remains high.

To that list we now add a fourth weapon, cancer immunotherapy. Constructed over decades, it has begun to demonstrate such promising results in cancer patients that we have selected it as the Breakthrough of the Year for 2013. The choice of a topic that is clinical in nature is something of a departure for *Science*. But we believe that 2013 marks a significant moment in cancer history, and today's achievements merit recognition and celebration, even if uncertainties remain. With more people now living well beyond age 65, the incidence of cancer is projected to rise steeply in the coming years. Thus, the population who might benefit from immunotherapy is potentially quite large.



Cancer immunotherapy aims to harness the body's own immune system to fight cancer. Today's successes are rooted in fundamental research beginning in the late 1980s in the labs of James Allison and others to decipher protein receptors that put the brakes on T cells (see the News story on p. 1432). Cancer researchers hypothesized that if these receptors could be blocked, the immune system might attack cancerous cells. At least in principle, such immune-based therapies would offer two advantages over other cancer drugs: These therapies could be applied to a diverse range of tumor types, and patients would not be expected to develop resistance to them.

Research ultimately led to the development of several antibody therapies, one of which is now on the market. Meanwhile, on another front, researchers are genetically engineering T cells to target tumor cells. Although dozens of clinical trials are still under way, the results are encouraging: Some patients with end-stage metastatic disease that had not responded to other aggressive therapies are surviving for much longer than doctors would predict. A paper published in July* reported that among 52 people with advanced melanoma, tumors shrank in 21 of those receiving a combination of two antibodies. More recent findings presented at meetings this fall suggest that immunotherapy's promise is holding up, although there are many uncertainties and side effects from some of the treatments.

Certainly we have a long way to go. Some patients who initially do well later see their cancer progress and die from it. Many questions remain as to why others do not respond to immunotherapy at all. In the long run, there is always the risk that the strategy will prove disappointing for any number of reasons. The responses may not persist over the long term, and unexpected side effects may become evident as a larger number of patients receive these new treatments. Laboratory scientists are already hard at work designing new ways to make these therapies safer and more effective, as illustrated in a paper published in *Science Translational Medicine* last week.†

As Pearl Harbor was reeling from the Japanese attack of 7 December 1941, my father dropped out of his freshman year at Harvard, waived exemption for a heart murmur, and enlisted in the U.S. infantry. With free cigarettes in his rations from the government, thus began his long relationship with tobacco that ended just a few years before his death from lung cancer in 2001. Breakthroughs in cancer immunotherapy may have arrived too late for my father, but there are many cancer patients around the world whose lives could potentially be extended as we learn more about this promising new approach.

– Marcia McNutt

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*J. D. Wolchok *et al*., *N. Engl. J. Med*. **369**, 122 (2013). †V. D. Fedorov, M. Themeli, M. Sadelain, *Sci. Transl. Med*. **5**, 215ra172 (2013).

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