Do No Harm: Counteracting Side Effects of Cancer Therapies

Side effects from cancer therapies are a price that many patients have willingly paid for hope in the face of life-threatening disease. But the impact of aggressive therapies can be far from negligible, affecting quality of life and compromising health. As our ability to treat and even cure cancers has improved, we have the luxury of shifting some focus away from the front lines of cancer defense to include greater consideration of collateral damage. CCR investigators are actively pursuing strategies to improve not only antitumor efficacy, but also quality of life for patients treated with necessarily harsh chemotherapeutics, radiation therapies, and immunotherapies.

Ten years ago, CCR initiated a program to address chronic Graft versus Host Disease (cGvHD). As Steven Pavletic, M.D., M.S., explains in "Treating the Cure: Grappling with cGvHD after Hematopoietic Stem Cell Transplants," the fact that these transplants have been so successful has led to an increase in the number of patients who experience cGvHD, a multispectrum disorder around which the medical community found it difficult to organize systematic support. CCR created both a clinical program and convened a worldwide consensus project to establish guidelines and criteria for clinical research. This effort has helped to set the stage for testing drugs to counteract cGvHD.

CCR has played a pivotal role in the development of several drugs approved by the U.S. Food and Drug Administration. Among them, the enzyme glucarpidase has recently been approved to treat rare cases of potentially lethal toxicity caused by accumulation of the first-line chemotherapeutic agent, methotrexate. As explained in "Epic Journeys from Bench to Bedside," Brigitte Widemann, M.D., has shown that the drug can prevent acute kidney dysfunction when administered to patients with high plasma concentrations of methotrexate.

As we learn in "Curing Lymphomas, One Subtype at a Time," Wyndham Wilson, M.D., Ph.D., and Kieron Dunleavy, M.D., have not only focused on efficacy, but also on minimizing toxicity from radiation and chemotherapeutic agents. They have recently been able to dramatically lower the aggressiveness of treatment for Burkitt lymphoma while achieving better therapeutic outcomes.

Over time, an additional hope for more effective therapies with fewer side effects lies in precision medicine—in which cancer cells are targeted at a molecular level, sparing even closely surrounding healthy tissues—and in immunotherapeutic approaches which target cancer antigens. As we learn in "The Complex, Inner Life of T cells," Larry Samelson, M.D., Ph.D., has been instrumental in laying the groundwork to understand T-cell receptor function, and is now bringing that depth of knowledge to the development of more effective immunotherapies.

(Photo: R. Baer)

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Of course, the ultimate safeguard against therapeutic side effects is prevention. John Schiller, Ph.D., and Douglas Lowy, M.D., were recently recognized with the National Medal of Technology and Innovation for their work in creating vaccines against the human papilloma virus (HPV), which are now available for the prevention of HPV-associated cancers (see "CCR Researchers Awarded the National Medal of Technology and Innovation," *CCR connections* Vol. 8, No. 2). We are starting to not only defeat cancers, but defeat them on our own terms, without harm.

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