PET Visualizes Antitumor Immune Response

Researchers at the University of California at Los Angeles (UCLA) Jonsson Cancer Center reported in November on a noninvasive, quantitative approach to visualize primary antitumor immune response using PET imaging. The study, which appeared in the November 29 issue of the *Proceedings of the National Academy of Sciences* (2005;102:17412–17417), was widely covered in both the scientific and popular media as a breakthrough in the ability to observe in real time "how the immune system initially recognizes cancer and mobilizes to fight the disease."

The researchers, led by first author Chengyi J. Shu, from Microbiology, Immunology, and Molecular Genetics at the Johnsson Center, began by generating a line of bone marrow chimeric mice with multimodality reporter genes. After confirmation of reporter gene expression, mice were challenged with the Moloney murine sarcoma and leukemia virus complex (M-MSV/M-MuLV), and the induced immune response was monitored by microPET imaging. ^{18}F-FDG was used to monitor tumor progression, and ^{18}F-fluoro-3-hydroxymethylbutylguanine (^{18}F-FHBG) was used to image transduced immune cells localized at the tumor and draining lymph nodes (DLNs).

"This study is teaching us about how the immune system recognizes cancer. That's something we couldn't see before," said the study's senior author Owen Witte, MD, Jonsson Cancer Center researcher and a professor of microbiology, immunology, and molecular genetics, who also serves as director of the UCLA Institute for Stem Cell Biology and Medicine and is a Howard Hughes Medical Institute investigator. "We were able to watch the primary immune response, the very first reaction of the immune system to the presence of cancer in body. This gives us a new tool that will allow us to evaluate novel ways to help the immune system become better at finding and eliminating cancer as well as studying autoimmune and immune deficiency disorders."

The researchers treated the M-MSV/M-MuLV-challenged mice with the immunosuppressive drug dexamethasone. ^{18}F-FDG PET imaging was used to measure lymphocyte activation, and by day 21 could no longer detect activation and expansion of immune cell populations in the DLNs. "We were able to observe the moment that the immune system sees the foreign antigens of the cancer in the body and its response, which starts in the local draining lymph nodes," Witte said. "We saw an increased number of lymphocytes and myeloid cells in those lymph nodes, then saw them migrating to the tumor in an attempt to kill the cancer."

Current methodologies that monitor responses to immune-based therapies, including radioimmunotherapies, most often rely on invasive techniques that sample tissues at a given point in time. Using the team's new technique, "we could see much sooner if the therapy was effective, without the need for a biopsy," Witte said. "We would also know very rapidly, within a week or 2. Prior to this, we had to wait many months to find out if a therapy was working."

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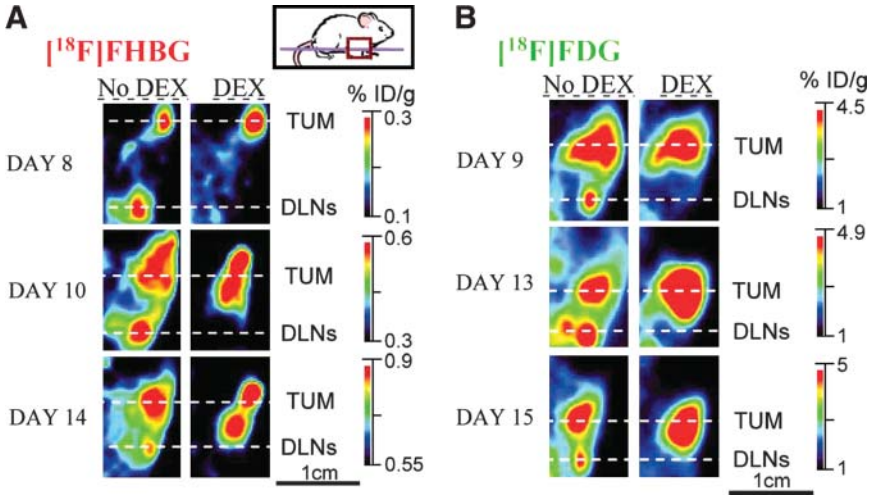

Changes in immune cell localization and activation with or without dexamethasone treatment as detected by ^{18}F-FHBG (A) and ^{18}F-FDG (B) PET. Days represent time after tracer injection. These images are representative of a total of 10 mice imaged in 3 separate experiments. TUM = tumor; DLN = draining lymph nodes.

Images courtesy of Jonsson Cancer Center