MedicalXpress

Study adds to cancer-fighting promise of combined immunotherapy-radiation treatment

September 15 2014

A study in mice implanted with breast and melanoma cancers adds to a growing body of evidence that highly focused radiation – long thought to suppress immunity – can actually help boost the immune system's fight against cancer when combined with a new kind of immune-enhancing drug.

The study, led by Johns Hopkins Kimmel Cancer Center researchers, shows how in principle, radiation may specifically activate immune system cells responsible for attacking cancer cells, leading immune cells to "remember" how to fight cancer long after the cancer is gone.

Andrew Sharabi, M.D., Ph.D., a resident in the Department of Radiation Oncology and Molecular Radiation Science at Johns Hopkins, is expected to present details of the study at the 2014 annual meeting of the American Society of Radiation Oncology (ASTRO) in San Francisco Sept. 15. Sharabi's report is believed to be among only a few animal studies selected for presentation at the meeting's plenary sessions.

The study made use of a relatively new class of anticancer agent that interferes with a tumor's ability to dampen the immune system's cancer recognition process. With the U.S. Food and Drug Administration's recent approval of one such "checkpoint inhibitor" (pembrolizumab) and more in the pipeline, Sharabi says, tumors once hidden from the immune system may now be found and destroyed. But scientists, he added, have

only begun to explore how standard therapies like radiation could be combined with the new immunotherapies.

"The immune system has powerful brakes, and removing those brakes with checkpoint inhibitors may be key to unleashing the full potential of the immune system against cancer," says Sharabi. "Adding radiation therapy to this mix may provide an additional boost by increasing tumor cell death and releasing targets for the immune system."

"We found that focused radiation therapy, once thought to suppress the immune system, actually increases specific, antitumor responses from the immune system," says Sharabi.

For the study, the Johns Hopkins team delivered stereotactic image-guided radiation therapy to melanoma and breast cancer cells implanted in mice on both of their flanks. One flank was radiated; the other side was shielded. Before, during and after radiation, the researchers injected the mice with a checkpoint inhibitor that targets the PD-1 pathway, which is used by tumors to suppress an immune response. The combined radiation-checkpoint inhibitor treatment shrunk the tumors by up to six times more than either therapy alone. The combination also increased the generation of other antitumor molecules (antibodies) that help the immune system recognize and attack cancer cells. In addition, the scientists found an increased number and activation of cancer-fighting T-cells in lymph nodes near the tumor.

"The increased immune cell division in lymph nodes suggests that radiating the tumor seems to activate immune cells in the surrounding lymph nodes, not just the tumor," says Charles Drake, M.D., Ph.D., associate professor of oncology and medical oncologist at the Johns Hopkins University School of Medicine and the Kimmel Cancer Center. The investigators also observed increases in memory T-cells, the type that retain memory of the tumor, in mice treated with the combination

radiation and checkpoint blockade drug. Sharabi says, "This may help stem recurrence of cancer."

To provide evidence for the memory making, Sharabi transferred immune cells taken from mice treated with the combination therapy into normal mice, and then implanted new tumors under the skin of these mice. "The transferred immune cells inhibited growth of the tumors, suggesting that the immune cells can travel throughout the body and attack sites outside of the radiation field," says Sharabi.

The scientists also provided a possible mechanism for how radiation awakens the immune system. "Radiation causes damage to cancer cells, and the cells produce molecules called chemokines that can help to recruit an immune response," says Sharabi.

The Johns Hopkins team is conducting further studies to determine the optimal radiation dose and timing needed to trigger the best immune response.

Provided by Johns Hopkins University School of Medicine