Study finds way to protect healthy cells from radiation damage

21 October 2009

Researchers at the University of Pittsburgh School of Medicine and the National Cancer Institute (NCI), part of the National Institutes of Health, may be hot on the heels of a Holy Grail of cancer therapy: They have found a way to not only protect healthy tissue from the toxic effects of radiation treatment, but also increase tumor death. The findings appear today in *Science Translational Medicine*.

More than half of all cancer patients are treated at least in part with radiation, said study co-author Jeff S. Isenberg, M.D., M.P.H., associate professor, Division of Pulmonary, Allergy, and Critical Care Medicine, Pitt School of Medicine. But the same radiation that kills cancer cells can also destroy healthy ones, causing side effects such as nausea and vomiting, skin sores and rashes, and weakness and fatigue. Long-term radiation exposure can lead to the scarring and death of normal tissue.

He and his NCI colleagues have identified a biochemical signaling pathway that can profoundly influence what happens to both cancerous and healthy cells when they are exposed to radiation. In mouse experiments, they found that blocking a molecule called thrombospondin-1 from binding to its cell surface receptor, called CD47, affords normal tissues nearly complete protection from both standard and very high doses of radiation.

"We almost couldn't believe what we were seeing," Dr. Isenberg said. "This dramatic protective effect occurred in skin, muscle and bone marrow cells, which is very encouraging. Cells that might have died of radiation exposure remained viable and functional when pre-treated with agents that interfere with the thrombospondin-1/CD47 pathway."

There have been concerns that approaches to spare healthy cells will risk inadvertently protecting tumor cells, noted senior author David D. Roberts, Ph.D., of the NCI's Center for Cancer Research. But, he added, "in our experiments, suppression of CD47 robustly delayed the regrowth of tumors in radiation-treated mice."

It's not yet clear why disrupting the CD47 signaling pathway leads to these effects, the researchers said. It's possible that radiation impairs the immune response to tumors even while killing tumor cells, but suppression of CD47 keeps the immune cells safe. Decreasing CD47 levels on tumor cells also could make them more sensitive to attack by the patient's immune system after treatment. Or, suppression of injury to vascular cells might improve blood flow to allow naturally occurring anti-tumor immunity to reach cancer cells more easily.

The researchers are already exploring the signaling pathway's role in several other domains, noted Mark Gladwin, M.D., chief of Pitt's Division of Pulmonary, Allergy, and Critical Care Medicine and director of the Vascular Medicine Institute, where Dr. Isenberg is a principal investigator.

"Dr. Isenberg and his team are examining multiple disease treatment strategies for pulmonary hypertension, wound healing, sickle cell disease and heart attacks, based on the blockade of the thrombospondin-1/CD47 pathway," he said.

Source: University of Pittsburgh