
Study Finds Low Dose Radiation More Effective at Killing Cancer Cells than Higher Doses

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A new study shows that lower doses of radiation elude a damage detection "radar" in DNA and actually kill more cancer cells than high-dose radiation. With these findings, scientists believe they can design therapy to dismantle this "radar" sensor allowing more radiation to evade detection and destroy even greater numbers of cancer cells.

Researchers at the Johns Hopkins Kimmel Cancer Center tested the low-dose radiation strategy on cultured prostate and colon cancer cell lines and found that it killed up to twice as many cells as high-dose radiation. The extra lethality of the low-dose regimen was found to result from suppression of a protein, called ATM (ataxia telangiectasia mutated) which works like a radar to detect DNA damage and begin repair.

Theodore DeWeese, MD, who led the study, speculates that cells hit with small amounts of radiation fail to switch on the ATM radar, which prevents an error-prone repair process. DeWeese, chairman of the Department of Radiation Oncology and Molecular Radiation Sciences at Johns Hopkins, presented his evidence at the annual meeting of the American Society for Therapeutic Radiology and Oncology (ASTRO) on October 5 in Atlanta.

"DNA repair is not foolproof—it can lead to mistakes or mutations that are passed down to other generations of cells," DeWeese explained. "A dead cell is better than a mutant cell, so if the damage is mild, cells die instead of risking repair."

Higher doses of radiation cause extreme DNA damage and widespread cell death, so the ATM damage sensor is activated to preserve as many cells as possible, protecting, ironically, the cancer cells targeted for destruction by the radiation.

While the low-dose regimen works in cultured cells, it has not proved successful in humans. This has led to effort by Hopkins scientists to study ways to use viruses that can deliver ATM-blocking drugs to the cells. Tests in animals are expected to begin soon.

In the current study, colon and prostate cancer cell lines were treated with either high levels of radiation or small amounts spread over many days. Low-level radiation is defined as 10 times more stronger than normal background

exposure, while high doses are 1,000 times stronger. Approximately 35 percent of colon cancer cells survived low-dose radiation as compared to 60 percent receiving high-dose. In prostate cancer cell lines, half of the cells survived low-dose radiation, while 65 percent survived higher doses.

In the low-dose group, ATM activation was reduced by 40 to 50 percent. The researchers proved ATM inactivation was the culprit since low-dose irradiated cells fared better after ATM was reactivated with chloroquine, best known as a treatment for malaria.

"Tricking cancer cells into ignoring the damage signals that appear on its radar could succeed in making radiation more effective in wiping out the disease," says DeWeese.

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Research participants from Johns Hopkins include Spencer Collis, Julie Schwaninger, Alfred Ntambi, Thomas Keller, Larry Dillehay, and William Nelson.

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