Anti-cancer drug protects normal cells from radiation damage, increases effectiveness of radiation therapy

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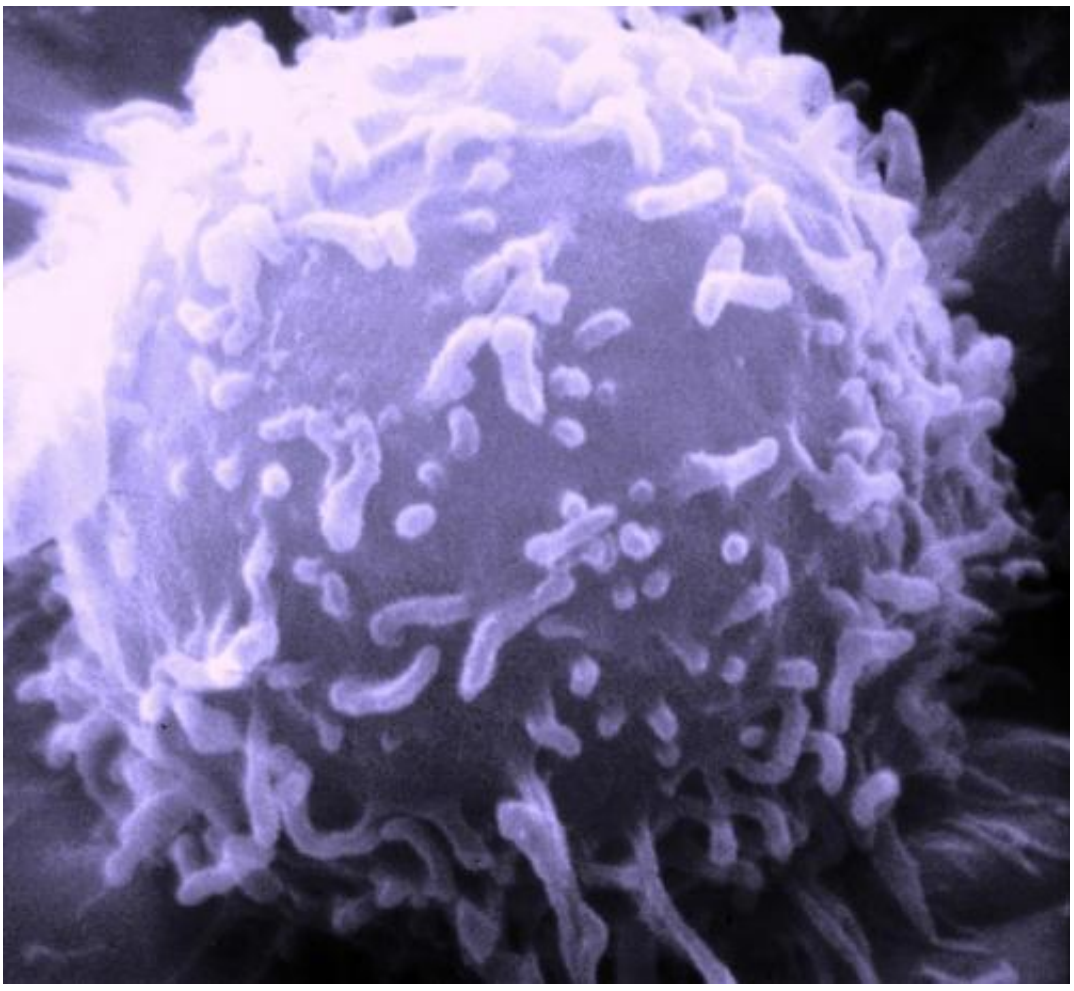

Electron microscopic image of a single human lymphocyte. Credit: Dr. Triche National Cancer Institute

Although radiation treatments have become much more refined in recent years, it remains a challenge to both sufficiently dose the tumor while sparing the surrounding tissue. A new anti-cancer drug, already in clinical development, may help address this issue by protecting normal cells - but not the cancer - from the effects of radiation. The research, published November 14th in *Molecular Cancer Therapeutics*, further suggests this drug may also be useful in treating accidental exposure to radiation.

"It was a stroke of luck that the drug that most effectively protected normal cells and tissues against radiation also has anti-cancer properties, thus potentially increasing the therapeutic index of radiation therapy," says Ulrich Rodeck, M.D., Ph.D., Professor of Dermatology and Cutaneous Biology and Radiation Oncology at Thomas Jefferson University, and senior author on the study.

Together with first author Vitali Alexeev, Ph.D., Assistant Professor, Dermatology and Cutaneous Biology, Dr. Rodeck and colleagues tested five compounds that were shown to have radiation-protective properties in earlier studies. The researchers gave the mice one of the five compounds a day before and for several days after radiation treatment. A compound called RTA 408 emerged from this screen as a robust radiation protector and its effect was comparable to the only drug currently approved by the FDA for that purpose. (The approved drug, called amifostine, however, has a number side effects including severe nausea or vomiting that make it an unappealing choice for clinicians.) Sites that are usually most susceptible to radiation damage including the gut and blood cells in the bone marrow were both protected in mice treated with RTA 408.

Using human prostate cancer cells growing in mice, the researchers also showed that RTA 408 did not confer radiation protection to the cancer cells. In fact, when RTA 408 was given alone, without radiation, it also

slowed the growth of human prostate cancer transplants in mice. In combination, it further amplified the tumor growth inhibitory effects of radiation.

"It was really exciting to see," says Dr. Rodeck, "that combining radiation and RTA-408 more effectively inhibited tumor growth compared to using either one or the other as single treatment modalities."

Dr. Rodeck and colleagues plan to continue to unravel the molecular underpinnings of these radiation-protective effects in order to understand how exactly this compound works and how its mechanism of action might be improved for clinical applications.

RTS 408 is currently being developed by REATA pharmaceuticals for a number of clinical applications, including a trial currently enrolling patients for a topical form of the drug applied to patients who experience radiation dermatitis.

More information: V. Alexeev, et al., "Radiation protection of the gastrointestinal tract and growth inhibition of prostate cancer xenografts by a single compound," *Molecular Cancer Therapeutics*, DOI: 10.1158/1535-7163.MCT-14-0354, 2014

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