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New paste prevents scarring caused by radiation therapy for cancer

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An antiscarring paste when applied to the skin of mice halts fibrosis caused by the radiation used in cancer therapy. That is according to a study led by researchers at Laura and Isaac Perlmutter Cancer Center to be published tomorrow in the January edition of the *Journal of the Federation of American Societies for Experimental Biology*.

Scarring occurs as key cells lay down tough connective tissue to provide a framework for healing after injury. Fibrosis is a related process that creates connective tissue in the wrong context, often interfering with the architecture or function of tissues as part of disease.

The current study addressed a type of fibrosis called radiation dermatitis, which is a side effect experienced by as many as 95 percent of patients undergoing initial radiation treatment. Radiation applied to the skin causes the buildup of fibrotic tissue and skin thickening, with the effects severe enough in some patients to stop treatment.

The NYU Langone research team says they mimicked the development of radiation dermatitis by exposing the mice's skin to a single dose of 40 Grays, a similar amount of radiation to what patients undergoing anti-cancer radiation typically receive over five weeks. Some of the irradiated animals were normal mice, while others were genetically engineered to lack a specific protein receptor, known as the adenosine A2A receptor. Signaling molecules fit into certain receptors on cells, like keys into locks, to pass on messages, and the A2A receptor does so in pathways related to fibrosis.

Half of the irradiated mice were then treated daily with a topical paste made with the research team's patented A2A receptor blocker. The paste contains 2.5 milligrams of active ingredient per milliliter of 3 percent carboxymethyl cellulose, a gum 'binder' used to make drugs and other products. The rest of the mice received a placebo.

A month after exposure, normal mice that got the placebo showed a nearly two-fold increase in the amount of collagen, skin thickness, and fibrosis. Those treated with the A2A receptor-blocking paste accumulated only 10 percent more skin-thickening collagen. Mice genetically engineered to lack the A2A receptor developed no skin reaction at all to the radiation.

"Our latest study is the first to demonstrate that blocking or deleting the A2A receptor can be useful in reducing radiation-induced scarring in skin," says senior study investigator and rheumatologist Bruce Cronstein, MD, director of NYU Langone's Clinical and Translational Science Institute. "The study also suggests that adenosine A2A receptor antagonists may have broad applications as drug therapies for preventing fibrosis and scarring, not just in the liver but also in the skin."

If further experiments on animals and eventually people prove successful, Cronstein says, clinicians treating early-stage cancers with radiation could eventually prescribe an A2A inhibitor paste to prevent fibrosis. He adds that the team's findings suggest that A2A antagonist drugs could also be used in treating other diseases involving changes in the structure of collagen, a major component of skin and connective tissues, such as scleroderma and interstitial pulmonary fibrosis.

Cronstein, the Dr. Paul R. Esserman Professor of Medicine, and a professor in the departments of Pathology, Biochemistry and Molecular Pharmacology at NYU Langone, says such therapies are badly needed because very few drugs are currently available to treat fibrosis and those

that are on the market are not very effective. Moreover, he says, using a topical formulation like the one his team tested is advantageous because it can be applied directly to affected tissues and patients do not have to worry about any adverse systemic reaction as in oral drugs.

Cronstein says his team next plans to study the mechanism underlying the A2A receptor's role in fibrosis.

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