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Topical therapy for radiation-induced skin damage shows promising results

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A team of University of Pittsburgh researchers has demonstrated that a newly developed topical therapy applied before or after radiation exposure prevents skin damage in both animal and human models.

The results, published online in the *Journal of Investigative Dermatology*, are expected to accelerate efforts that will lead to clinical studies and licensing of the technology, said Louis Falo, M.D., chairman of the Department of Dermatology at the Pitt School of Medicine and corresponding author for the study.

The skin is the largest human organ and protects the body from physical, chemical and environmental exposures. Radiation-induced skin damage ranges from photo-aging and ultraviolet sun exposure to radiation dermatitis, a treatment-limiting condition caused by radiation therapy; and skin radiation syndrome, a frequently fatal consequence of exposures from nuclear accidents.

Dr. Falo teamed with Joel Greenberger, M.D., professor and chair of the Department of Radiation Oncology, and Peter Wipf, Ph.D., Distinguished University Professor of Chemistry, in 2008. Drs. Greenberger and Wipf were exploring treatments to mitigate radiation poisoning caused by an accident at a nuclear power facility or from a so-called "dirty bomb" device. Together, they determined that the approaches being developed and investigated at Pitt could potentially benefit the approximately 1 million people annually in the U.S. who undergo radiation therapy to the skin for breast, head and neck, and

other cancers.

"During the course of radiation therapy, patients can develop irritating and painful skin burns that can lead to dangerous infections and diminished quality of life," Dr. Falo said. "Sometimes the burns are so severe that patients must stop their treatment regimen. Our results show that topical treatment with this therapeutic agent prevents skin damage at the source."

Dr. Wipf's lab developed the molecule that targets the formation of oxidative free radicals in the cell's mitochondria, thereby preventing inflammation and cell death.

"This provides for potentially improved treatment options for patients undergoing radiation therapy with the prospect for more simplified treatment regimens and reduced concern about quality of life post-treatment," he said. Dr. Wipf's former student, Joshua Pierce, Ph.D., who now operates his own lab at North Carolina State University, is credited with synthesizing the molecule, named JP4-039.

Dr. Falo said he is optimistic about the therapy's performance in clinical trials because the treatment appears to be effective in a model that uses human skin obtained from cosmetic procedures.

Looking beyond treating radiation therapy, he and his team are pursuing further studies of the molecule's ability to reduce skin damage from sun exposure, including sunburns and the molecular changes that lead to skin cancer, as well as cosmetic applications to prevent skin changes caused by the oxidative stress that is associated with normal skin aging.

More information: Rhonda M. Brand et al. A Topical Mitochondria-Targeted Redox Cycling Nitroxide Mitigates Oxidative Stress Induced Skin Damage, *Journal of Investigative Dermatology* (2016). DOI:

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