Boosting treatments for metastatic melanoma

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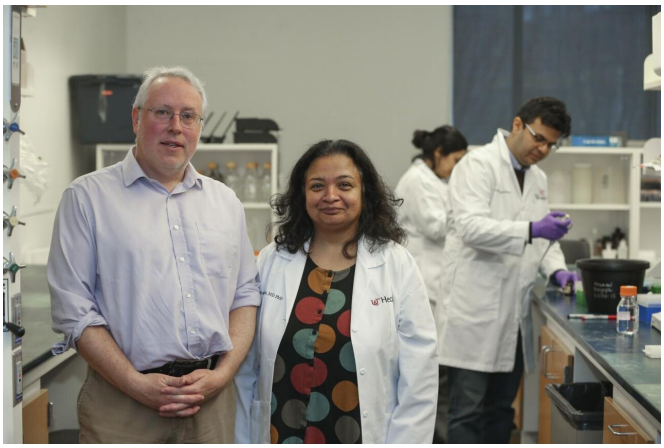

Soma Sengupta, MD, PhD, and Daniel Pomeranz Krummel, PhD, pictured here in their lab in the Vontz, say they might have identified a treatment-boosting drug to enhance effectiveness of therapies for metastatic melanoma. Credit: UC Creative + Brand

University of Cincinnati clinician-scientist Soma Sengupta, MD, Ph.D., says that new findings from her and Daniel Pomeranz Krummel's, Ph.D., team might have identified a treatment-boosting drug to enhance effectiveness of therapies for metastatic cancer and make them less toxic, giving patients a fighting chance at survival and improved quality of life.

"Melanoma is a serious skin cancer that evolves from the pigment cells of the skin and eyes," says Sengupta, associate professor of neurology at UC, UC Health neuro-oncologist and co-director of the UC Gardner Neuroscience Institute's Brain Tumor Center. "There are millions of people in the U.S. living with this type of cancer, and the incidence is projected to increase.

"While physicians can often quickly find and treat melanoma of the skin, metastatic melanoma, or melanoma that has spread to other parts of the body, often the brain, is a lethal cancer. Often, patients who receive immunotherapy, which uses the patient's own immune system to treat the condition, do not have good responses. They also experience many uncomfortable side effects that impact their quality of life."

Sengupta says that her team, including colleagues at Emory University, Columbia University, and University of Wisconsin, recently published results in the *International Journal of Radiation Oncology * Biology * Physics* that show by targeting a particular neurotransmitter receptor through the use of a new class of sedatives, related to Valium or Xanax, cancer treatments like radiation and immunotherapy could be boosted to better fight cancer in patients with reduced toxic side effects. These studies were conducted in animal models but the hope is to soon study outcomes in patients with metastatic cancer.

Researchers found by adding this particular study drug, infiltration of immune cells to the tumor was greatly improved, enhancing the efficacy of the treatment and allowing them to combat melanoma; tumors shrunk and, in some cases, completely disappeared.

"Our long-term goal is to add this new class of drugs to a patient's radiation and immunotherapy treatment," says Sengupta, who is a corresponding author on the paper. They are collaborating with investigators from UC who are helping to formulate the lead compound, including Pankaj Desai, Ph.D., with the James L. Winkle College of Pharmacy, as well as with Mohammad Khan, Ph.D., of Emory University, who will test this approach via clinical trial once Sengupta has approval from the FDA to test this drug in humans.

"We hope this will help patients avoid side effects, and that by adding this drug to the regimens, we will reduce costs, since we think the treatments will become more effective, and in turn, doses of

standard treatments can be lowered. More studies are needed, but this is a promising new approach using a non-toxic drug from a class of compounds that have already been approved for anxiety, but now used for a serious condition that claims lives every day."

When researchers were preparing this study to report their team's findings, they asked a senior colleague and UC cancer researcher Peter Stambrook, Ph.D., to read it and provide feedback. Sadly, Stambrook passed away from melanoma before their work was published.

"Peter died as a result of his melanoma," says Daniel Pomeranz Krummel, Ph.D., research associate professor of neurology and lead author on this study. "He was an outstanding scientist and was incredibly supportive of our research. We feel more driven than ever to push forward with our research and to honor Peter in this way."

More information: Daniel A. Pomeranz Krummel et al, Melanoma cell intrinsic GABAA receptor enhancement potentiates radiation and immune checkpoint inhibitor response by promoting direct and T cell-mediated anti-tumor activity, *International Journal of Radiation Oncology*Biology*Physics* (2020). DOI: 10.1016/j.ijrobp.2020.10.025

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