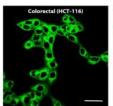
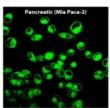
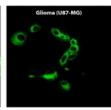


New tumor-targeting agent images and treats wide variety of cancers

11 June 2014







Preferential cancer cell uptake of CLR1501. Fluorescence confocal microscopy illustrates that the fluorescent CLR1404 analogue, CLR1501, is selectively retained in three additional cancer types at 24 hours post treatment. Credit: Weichert et al., Science Translational Medicine 2014

Scientists at the University of Wisconsin Carbone Cancer Center (UWCCC) report that a new class of tumor-targeting agents can seek out and find dozens of solid tumors, even illuminating brain cancer stem cells that resist current treatments.

What's more, years of animal studies and early human clinical trials show that this tumor-targeting, alkylphosphocholine (APC) molecule can deliver two types of "payloads" directly to cancer cells: a radioactive or fluorescent imaging label, or a radioactive medicine that binds and kills cancer cells.

The results are reported in today's issue of the journal *Science Translational Medicine*, and featured in the journal's cover illustration and podcast.

The APC targeting platform is a synthetic molecule that exploits a weakness common to cancers as diverse as breast, lung, brain and melanoma. These cancer cells lack the enzymes to metabolize phospholipid ethers, a cell membrane component that is easily cleared by normal cells. When given in an intravenous solution, APC goes throughout

the body—even across the blood-brain barrier—and sticks to the membrane of cancer cells. The cancer cells take up the APC and the imaging or treatment medication riding on the molecular platform, and retain it for days to weeks, resulting in direct cancer cell imaging or treatment.

The APC analogs were able to tag 55 of 57 different cancers. This large study had multiple stages, including testing in cancer cell lines, in rodents and rodents infected with human and rodent cancers, and in human patients with different cancers such as breast, lung, colorectal and glioblastoma (brain cancer).

"I was a skeptic; it's almost too good to be true," says co-lead author Dr. John S. Kuo, associate professor of neurosurgery and director of the comprehensive brain tumor program at the UW School of Medicine and Public Health. "It is a very broad cancer-targeting agent in terms of the many different cancers that tested positive. The APC analogs even sometimes revealed other sites of cancer in patients that were small, asymptomatic and previously undetected by physicians."

Kuo specializes in the treatment of brain tumors, and also leads the UWCCC CNS Tumors group running many clinical trials for glioma, a brain cancer that is incurable because current treatments leave behind cancer stem cells that can seed and regrow the cancer. He says it was encouraging that the APC analogs also picked up cancer stem cells and will also likely target them for further treatment.

"It's also potentially superior to current imaging methods because the standard clinical MR or PET imaging may give false-positive results due to surgical scars, post-treatment effects, inflammation, or even infection, making it difficult to know if the cancer has truly returned," he says.

Kuo says the fluorescent intraoperative APC imaging might help make cancer surgeries more



effective and safer; any cancer cells that cannot be safely removed can be targeted afterwards with radioactive APC therapy. In addition, APC imaging might avoid the "false positive" results of current imaging, so cancer patients can stay on effective therapies and likely avoid the risks and costs of "second look" surgeries.

The large multidisciplinary study team is also led by co-lead author Dr. Jamey P. Weichert, associate professor of radiology, who cofounded and serves as chief scientific officer of Cellectar Biosciences, Inc., the Madison-based company developing the APC analog platform for <u>cancer</u> imaging and therapy.

More information: "Alkylphosphocholine Analogs for Broad-Spectrum Cancer Imaging and Therapy," by J.P. Weichert et al. *Science Translational Medicine*, 2014. scitranslmed.3007646

Provided by University of Wisconsin-Madison APA citation: New tumor-targeting agent images and treats wide variety of cancers (2014, June 11) retrieved 21 August 2022 from https://medicalxpress.com/news/2014-06-tumor-targeting-agent-images-wide-variety.html

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