One compound detects and treats malignant tumors, certain cancer stem cells

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(Medical Xpress) -- More than a decade of laboratory research at the University of Wisconsin has proven that a single chemical compound may both detect and treat malignant tumors and certain cancer stem cells.

In three posters presented at the annual meeting of the American Association for Cancer Research (AACR) in Chicago, March 31-April 4, UW-Madison researchers describe exciting advances involving CLR1404, described as a "diapeutic" agent that can both image and destroy a wide range of malignant tumors and the one type of cancer stem cells examined so far.

The presentations are based on basic research in the lab of Dr. Jamey Weichert, associate professor of radiology at the UW School of Medicine and Public Health (SMPH) and a member of the UW Carbone Cancer Center (CCC).

Clinicians at the UW School of Medicine and Public Health and elsewhere are interested in assessing CLR1404's potential. Several clinical trials evaluating both the cancer imaging and therapeutic capabilities of CLR1404 are under way at the Carbone Cancer Center, with more scheduled to begin soon.

Dr. John Kuo, director of the Comprehensive Brain Tumor Program at UW Hospital and Clinics and a cancer stem-cell scientist at the School of Medicine and Public Health, is studying the possibility of using

CLR1404 to treat glioblastoma multiforme (GBM), a deadly form of brain cancer, by targeting GBM stem cells.

In one of the American Association for Cancer Research posters (#3495), Kuo and Weichert describe how CLR1404 decreases glioblastoma stem cell activity, suppresses GBM growth and improves animal survival.

Another poster (#5740) shows that the PET imaging version of CLR1404, which contains iodine-124, dramatically and selectively illuminates malignant tumors in mice. The poster details how the compound does this.

The third poster (#3831) explains how CLR1404 labeled instead with iodine-131 works as a radiotherapy agent to shrink tumors and extend life in more than 10 animal models of human cancer.

With one injection, iodine-124-containing CLR1404 enters the bloodstream and selectively penetrates and is retained by malignant tumors rather than normal tissues. After 10 days, the compound clears the body but remains in malignant tumor cells. CLR1404 accumulates in both primary malignant tumors and metastases, but not in benign tumors.

"We have found that CLR1404 is taken up by cancer cells through lipid rafts, which are much more abundant in cancer cells compared to normal cells," says Weichert.

Replacing iodine-124 with iodine-131 generates the radiotherapeutic version of CLR1404, which also selectively targets cancer cells. After a single injection, cancer cells are exposed to sustained lethal radiation from inside the cell, while normal tissues are relatively unharmed.

Weichert's team has tested the treatment in many different malignancies,

including cancers of the lung, kidney, colon, ovary, uterus, pancreas, prostate, brain and breast, including the most difficult to treat, triple negative breast cancer. A single intravenous injection significantly suppressed tumor growth and extended the life of animals with these cancers.

In a collaborative effort between their two laboratories, Kuo and Weichert found that CLR1404 also targets and cripples cancer stem cells.

"Like most stem cells, GBM stem cells typically resist therapy, and we think they may cause tumors to recur in the brain," says Kuo, assistant professor of neurological surgery and human oncology at the School of Medicine and Public Health, and chair of the brain tumor group at the Carbone Cancer Center. "Targeting of GBM stem cells is probably critical for improving patient outcome."

Kuo implanted glioma stem cells from patients with GBM into mice - and tumors grew in their brains. When he injected another diagnostic form of the agent, CLR1501, it entered the stem cells and illuminated them. Even after the tumors were removed from the mice and the stem cells were isolated again, the pluripotent cells still glowed, indicating extended retention of the agent.

"This unique prolonged retention of the compound in malignant tumors and cancer stem cells is central to the diagnostic and therapeutic actions of CLR1404," says Weichert.

Kuo's team then treated the stem cells in culture with CLR1404 and found greatly reduced cell proliferation and survival. When the treated stem cells were implanted in animals, tumor growth was suppressed and animal survival increased.

"Infiltration of cancer cells into adjacent normal brain limits the efficacy of the surgery, radiation and chemotherapy we currently use to treat GBM," Kuo says. "Specific retention of CLR1404-related agents in cancer cells suggests its potential use as an anti-cancer therapy on the cellular level - especially for the invading cells that escape current therapies - while minimizing damage to normal brain cells."

Weichert commercialized CLR1404 in 2003 in a company called Cellectar, based in Madison, which merged with Novelos Therapeutics a year ago. Novelos, now based in Madison, is developing five compounds based on the CLR1404 platform.

Provided by University of Wisconsin-Madison