UT SOUTHWESTERN MEDICAL CENTER NEWS

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Arsenic aids tumor imaging when joined to cancer-homing drug, UT Southwestern researchers find

DALLAS – March 1, 2008 – Arsenic linked to a drug that binds to the blood vessels of cancerous tumors provides a powerful imaging agent that could one day allow physicians to detect hard-to-find tumors and more closely monitor cancer's response to therapy, researchers at UT Southwestern Medical Center have found.

The findings, based on animal studies and appearing in today's issue of *Clinical Cancer Research*, mark the first time arsenic has been used to label antibodies for the detection of tumors.

Dr. Philip Thorpe, professor of pharmacology at UT Southwestern and senior author of the study, created the cancer drug called bavituximab, an antibody that homes in on the blood vessels that feed tumors. Bavituximab is being tested in clinical trials in the U.S. and India for its ability to treat solid-tumor cancers by destroying their blood vessels.

"Arsenic has been used as a poison for centuries," Dr. Thorpe said. "Arsenic-labeled bavituximab is, however, safe. The dose of arsenic needed for imaging tumors is about one-millionth of that needed to cause toxicity."

In the study, Dr. Thorpe and his colleagues injected radioarsenic-labeled bavituximab into rats with prostate tumors. When the bavituximab bound to the tumor blood vessels, the tag-along arsenic created a "hot spot" of radioactivity that the researchers then imaged using positron emission tomography methods. The radioactivity levels produced by the arsenic are comparable to those used in standard imaging procedures in humans. The technique allowed them to locate and capture unusually clear images of the tumors. They also discovered that there was little or no detectable uptake of bavituximab by normal organs, including the liver, a common site where drugs become entrapped.

"We hope to use this technique to detect early tumor deposits that are not visible using other imaging techniques," said Dr. Thorpe. "The images we obtain are so clear that we may be able to see secondary tumors that have spread from the original tumor mass and lodged in distant organs."

The forms of arsenic used in the experiments are called radionuclides, which are radioactive versions, or isotopes, of the element. Several radionuclides currently are used in imaging, but many of

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the isotopes decay, or breakdown, before they reach the target in the body. The slow rate of decay of arsenic isotopes, together with their stable chemistry, allowed the researchers to couple arsenic to bavituximab and obtain images of the tumors for several days after the drug was given. Optimal tumor imaging in humans is often achieved three days or more after a radio-labeled antibody is administered.

"Long neglected as an awkward Cinderella, arsenic has great potential for new imaging agents and therapeutics based on multiple isotopes with diverse useful characteristics," said Dr. Ralph Mason, professor of radiology, director of the UT Southwestern Cancer Imaging Program and one of the study's authors.

Dr. Mason recently received a grant from the Department of Defense Breast Cancer Initiative to investigate whether arsenic could be used to image breast tumors. The next step in Dr. Thorpe's research will be to test the imaging technique in clinical trials.

In addition to Drs. Thorpe and Mason, other investigators in UT Southwestern's Harold C. Simmons Comprehensive Cancer Center carried out the research in collaboration with colleagues from UT Austin, Johannes Gutenberg University of Mainz in Germany and the University of Brussels in Belgium. The collaboration included pharmacologists, physicists and chemists.

Other UT Southwestern scientists involved in the study were Dr. Matthew Lewis, assistant professor of radiology; Dr. Dawen Zhao, assistant professor of radiology; Dr. Edward Tsyganov, clinical assistant professor of radiology; Dr. Nikolai Slavine, assistant professor of radiology; Linda Watkins, research scientist in pharmacology; Dr. Vikram Kodibagkar, assistant professor of radiology; and Dr. Peter Antich, professor of radiology.

The research was funded by Gillson Longenbaugh Foundation, National Cancer Institute, Peregrine Pharmaceuticals Inc., Deutsche Forschungsgemeinschaft and the Department of Defense.

Peregrine has exclusively licensed bavituximab from UT Southwestern and has a sponsored research agreement to further explore clinical uses of the drug. Dr. Thorpe is a consultant to and has an equity interest in the company.

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