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Imaging agents offer new view of inflammation, cancer

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A series of novel imaging agents could make it possible to "see" tumors in their earliest stages, before they turn deadly.

The compounds, derived from inhibitors of the enzyme cyclooxygenase-2 (COX-2) and detectable by positron emission tomography (PET) imaging, may have broad applications for cancer detection, diagnosis and treatment.

Vanderbilt University investigators describe the new imaging agents in a paper featured on the cover of the October issue of Cancer Prevention Research.

"This is the first COX-2-targeted PET imaging agent validated for use in animal models of inflammation and cancer," said Lawrence Marnett, Ph.D., director of the Vanderbilt Institute of Chemical Biology and leader of the team that developed the compounds.

COX-2 is an attractive target for molecular imaging. It's not found in most normal tissues, and then it is "turned on" in inflammatory lesions and tumors, Marnett explained.

"As a tumor grows and becomes increasingly malignant, COX-2 levels go up," Marnett said.

To develop compounds that target COX-2 and can be detected by PET imaging, Jashim Uddin, Ph.D., research assistant professor of

Biochemistry, started with the "core" chemical structures of the anti-inflammatory medicines indomethacin and celecoxib and modified them to add the element fluorine in various chemical configurations.

After demonstrating that the fluorinated compounds were selective inhibitors of COX-2, the investigators incorporated radioactive fluorine (18-F) into the most promising compound. Intravenous injection of this 18-F compound into animal models provided sufficient signal for PET imaging.

The researchers demonstrated the potential of this 18-F compound for in vivo PET imaging in two animal models: irritant-induced inflammation in the rat footpad and human tumors grafted into mice.

They showed that the 18-F compound accumulated in the inflamed foot, but not the non-inflamed foot, and that pre-treatment of the animals with celecoxib blocked the signal. In mice bearing both COX-2-positive and COX-2-negative human tumors, the 18-F compound accumulated only in the COX-2-positive tumor.

The studies support further development of these agents as probes for early detection of cancer and for evaluation of the COX-2 status of pre-malignant and malignant tumors.

"Because COX-2 levels increase during cancer progression in virtually all solid tumors, we think these imaging tools will have many, many different applications," Marnett said.

Provided by Vanderbilt University Medical Center

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