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Illuminating Tumor Cells

Diagnostics: Fluorescent agents target enzyme in cancer cells

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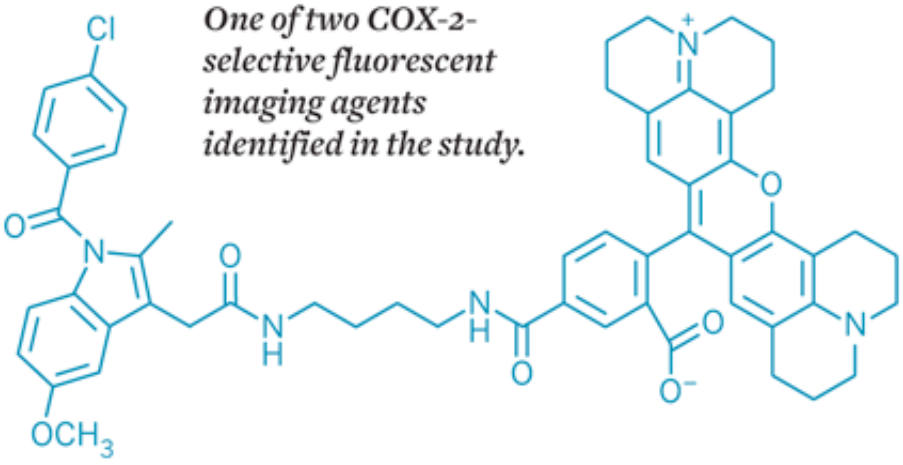

A new way to light up tumor cells could make it possible to diagnose cancer more easily on the skin and in the gastrointestinal tract. The approach uses fluorescent imaging agents to signal the presence of cyclooxygenase-2 (COX-2), an enzyme produced at much higher levels in premalignant and malignant tumors than in normal tissues.

Cancer researcher and chemical biologist Lawrence J. Marnett of Vanderbilt University School of Medicine, in Nashville, and coworkers developed the new imaging compounds, which they call "fluorocoxibs" (*Cancer Res.* **2010,** *70,* 3618).

"Because of their high specificity, contrast, and detectability, these fluorocoxibs are ideal candidates for detection of inflammatory lesions or early-stage COX-2-expressing human cancers, such as those in the esophagus, [upper airway], and colon," the researchers write.

"This is breakthrough research in the imaging area," comments J. S. Dileep Kumar, a positron emission tomography (PET) imaging specialist at Columbia University College of Physicians & Surgeons, in New York City. "It's the first paper reporting selective imaging agents for COX-2. The developed imaging probes might be good biomarkers for early diagnosis, monitoring of disease progression, and indicating effective treatments."

COX-2 is expressed at high levels in precancerous cells, and its expression increases as tumors develop and mature. Marnett and coworkers set out to develop agents that would mark such cells by targeting COX-2 selectively. They made many fluorescent analogs of the COX-2-selective drugs celecoxib and indomethacin and found two that had optimal properties. When administered by injection to cultured cells and animals, they are stable, selective for COX-2, bind to it for a long time, and fluoresce strongly. COX-2-targeted imaging agents developed earlier for PET and single-photon-

emission computed tomography often have had problems with nonselective binding and/or have not been shown to work in vivo.

The need for improved diagnostics for colon, esophageal, and skin cancer is significant. Detecting raised cancerous polyps in the colon "is very straightforward with standard colonoscopy," but detecting flat cancerous lesions in the colon and precancerous esophageal lesions is difficult, Marnett says. "These may be lit up by our fluorocoxibs." And although it's currently easy to spot skin cancer, "it is not easy to detect transformed cells that are early cancers or precursor lesions," he says, "and we feel our compounds may be useful in this setting as well."

Marnett notes that the group plans to test the agents' diagnostic capabilities in human clinical trials and to investigate fluorocoxib-drug conjugates that might target therapeutics selectively to COX-2-expressing cells.

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