Radiology-2013

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference on
Radiology and Imaging

August 14-16, 2013 Chicago, USA

Fluorocoxib C: A long-lived near-infrared COX-2 probe enabling selective visualization of inflammation and cancer *in vivo*

Md. Jashim Uddin

Vanderbilt University School of Medicine, USA

Abstract

Optical imaging with near-infrared (NIR) contrast agents is a sensitive technique for detection of lesions in deep tissues because NIR light (approximately 690–890 nm) can penetrate several centimeters below the skin surface. However, non-specific biodistribution and clearance of probes from non-targeted organs are obstacles to achieve high signal-to-noise. So, there is a considerable need for probes that are targeted to specific lesions. As an imaging target, cyclooxygenase-2 (COX-2) is attractive, because it is an inducible enzyme and expressed in inflammation and various cancers in high levels. In inflammatory lesions, inducible COX-2 modulates edema and pain, and in tumor tissues it promotes growth and metastatic potential of cancer cells. We synthesized a series of fluorescent compounds by the attachment of near-infrared fluorophores through different tethers to indomethacin or celecoxib, etc. Compounds were evaluated for COX-2 inhibitory activity against purified enzyme, macrophages, and tumor cells. The most effective compound was a conjugate of indomethacin and NIR664 linked through an *n*-butylenediamide tether, called fluorocoxib C. This NIR probe exhibited a high level of selectivity and potency for COX-2 inhibition over COX-1. Introduction of this probe by intraperitoneal or intravenous injection into Sprague-Dawley rats or C57BL/6 mice provided sufficient signal for *in vivo* fluorescence imaging and high levels of accumulation in inflamed compared to non-inflamed tissue. Experiments with animals bearing COX-2-positive or COX-2-negative tumors verified that selective accumulation in COX-2-positive tumors was due to binding to COX-2. Non-specific fluorescent signals were also detected around the peritoneal cavity 4 h post-injection of fluorocoxib C. The fluorescence in the peritoneal cavity completely cleared with time so that by 7 d post-injection, the fluorescence of fluorocoxib C was only detectable in the tumor. We validated the COX-2-targeted delivery by pre-dosing the animals with celecoxib, which blocked the probe uptake into both inflamed and cancerous tissues. The *in vitro* and *in vivo* properties of fluorocoxib C suggest it will be useful as a long-lived COX-2 probe for detection of cancer by delayed NIR imaging. This work was supported by grants from the National Cancer Institute (CA136465 and CA89450).

Biography

Md. Jashim Uddin has completed his Ph.D. at the age of 32 years from Shinshu University and postdoctoral studies from University of Alberta. He is a ‘Research Assistant Professor’ of Biochemistry at the Vanderbilt University School of Medicine. He has developed new drug design concepts for cyclooxygenase-2 (COX-2) inhibition. Also, he has contributed significantly in the development of cyclooxygenase-2 (COX-2) targeted imaging agents for early detection of cancer. He has developed Fluorocoxib A that has been marketed for pre-clinical applications. He has published more than 30 scientific publications in the world’s leading organic, bioorganic, medicinal chemistry, and cancer research journals.