Common pain relief medication may influence cancer growth

November 18, 2009

Although morphine has been the gold-standard treatment for postoperative and chronic cancer pain for two centuries, a growing body of evidence is showing that opiate-based painkillers can stimulate the growth and spread of cancer cells. Two new studies advance that argument and demonstrate how shielding lung cancer cells from opiates reduces cell proliferation, invasion and migration in both cell-culture and mouse models.

The reports--to be presented November 18, 2009, at "Molecular Targets and Cancer Therapeutics," a joint meeting in Boston of the American Association for Cancer Research, the National Cancer Institute, and the European Organization for Research and Treatment of Cancer--highlight the mu opiate receptor, where morphine works, as a potential therapeutic target.

"If confirmed clinically, this could change how we do surgical anesthesia for our cancer patients," said Patrick A. Singleton, PhD, assistant professor of medicine at the University of Chicago Medical Center and principal author of both studies. "It also suggests potential new applications for this novel class of drugs which should be explored."

The proposition that opiates influence cancer recurrence, prompted by several unrelated clinical and laboratory studies, has gradually gained support. It started with a 2002 palliative-care trial in which patients who received spinal rather than systemic pain relief survived longer. Soon after that, Singleton's colleague, anesthesiologist Jonathan Moss, noticed that several cancer patients receiving a selective opiate blocker in a compassionate-use protocol lived longer than expected. Two recent retrospective studies found that breast and prostate cancer patients who received regional rather than general anesthesia had fewer recurrences. In February, 2009, the Anesthesia Patient Safety Foundation highlighted the issue.

Moss's palliative-care patients were taking methylnaltrexone (MNTX), developed in the 1980s for opiate-induced constipation by the late University of Chicago pharmacologist Leon Goldberg. Goldberg modified an established drug that blocks morphine so that it could no longer cross the protective barrier that surrounds the brain. So MNTX blocks morphine's peripheral side effects but does not interfere with its effect on pain, which is centered in the brain. It won FDA approval in 2008.

"These were patients with advanced cancer and a life expectancy of one to two months," Moss recalled, "yet several lived for another five or six. It made us wonder whether this was just a consequence of better GI function or could there possibly be an effect on the tumors."

So Singleton, Moss and colleagues, including Joe G.N. Garcia, MD, professor of medicine at the University of Chicago, began a series of studies looking at the many peripheral effects of opiates and the potential benefits of blocking those effects.

In laboratory studies, morphine can directly boost tumor-cell proliferation and inhibit the immune response. The researchers found that opiates also promote angiogenesis, the growth of new blood vessels, and decrease barrier function--effects that may exacerbate diseases involving vascular leakiness including acute lung injury in experimental models. In a surgical setting, decreased barrier function may make it easier for tumors to invade tissue and spread to distant sites. Increased angiogenesis helps cancers thrive in a new site.

In the studies to be presented Nov. 18, Singleton and colleagues focus on the mu opiate receptor as a regulator of tumor growth and metastasis and examine the ability of methylnaltrexone to attenuate these effects.

Using two different models of non-small cell lung cancer, the research teams showed that

MEDIA CONTACT

John Easton
773.702.6241
john.easton@uchospitals.edu

RECENT NEWS

UChicago computer programming team again advances to world finals

Political views may skew perception of skin tone, new study finds

UChicago Awards $419,000 to Argonne-University collaborators

University seed grants spur collaboration with Argonne and Fermilab, spark DOE support

UChicago graduates win Rhodes, Marshall Scholarships

Event highlights growth of human rights programs in liberal arts education

Human capital central to emerging economic analysis of education

MNTX inhibited the tumor-promoting effects of opiates. In one study, using bronchioloalveolar carcinoma cells, MNTX blocked oncogenic signaling and prevented tumor-cell proliferation and migration.

In the other study, using Lewis lung carcinoma cells, mice without the mu opiate receptor did not develop the tumors that normal mice did when injected with cancer cells. The researchers further showed that MNTX reduced proliferation of cancer cells by 90 percent in normal mice. It also prevented invasion in cell culture and tumor growth and metastasis in mice.

The opioid receptor promotes Lewis lung cancer tumor growth, angiogenesis and metastasis, the authors conclude in a summary of the second study. "Methylnaltrexone attenuates these oncogenic effects."

"In conjunction with previous studies on opiate-induced angiogenesis by our laboratory and others, these experimental data suggest a plausible explanation for the epidemiologic observations," notes Moss, professor of anesthesiology and critical care at the University of Chicago. "If these laboratory studies are confirmed clinically, the selection of anesthetic technique used during the operative procedure and the possible use of opiate antagonists in the perioperative period may be important."

Additional contributors to the project include Frances Lennon, PhD, Biji Mathew, PhD, and Ravi Salgia, MD, all of the University of Chicago.