SOUTHWESTERN NEWS

Media contact: Heather Stieglitz
(214) 648-3404
heather.stieglitz@email.swmed.edu

SCIENTISTS UNCOVER HOW A COLON-CANCER PREVENTION DRUG WORKS

DALLAS – September 16, 1999 – Researchers at UT Southwestern Medical Center at Dallas have discovered how a drug known to help prevent colon cancer inhibits cell growth and prevents inflammation, a discovery that could lead to the design of new cancer pharmaceuticals.

Dr. Richard Gaynor, director of the Harold C. Simmons Comprehensive Cancer Center and colleagues describe their research on the molecular mechanism of the nonsteroidal anti-inflammatory drug sulindac and its breakdown products in the Sept. 17 issue of the *Journal of Biological Chemistry*.

Sulindac has been shown to cause the regression of benign colon polyps, thereby helping to prevent development of colon cancer. The drug inhibits the growth of laboratory-grown cancer cells that do not express cyclooxygenase, which synthesizes inflammatory mediators known as prostaglandins

Gaynor and collaborators believe sulindac and its breakdown products inhibit cell growth by promoting programmed cell death – a mechanism by which potentially cancerous cells commit suicide. They found that sulindac prevented the activation of the cellular regulatory protein NF-κB. It is known that NF-κB is critical in regulating cellular growth and stimulating the inflammatory response. High levels of NF-κB have been found in the nucleus of some types of tumor cells, implicating a role for NF-κB in the stimulation of cancer-cell growth.

"We found that sulindac inhibits a kinase (an enzyme that adds phosphate onto its target), which in turn prevents the activation of NF-κB," Gaynor said. "This kinase should be an excellent target not only for the development of novel anti-inflammatory agents but also for the development of agents to inhibit the growth of cancer cells."

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Other UT Southwestern co-authors were internal medicine research assistant Yumi Yamamoto, instructor of internal medicine Dr. Keng-Mean Lin and former internal medicine research fellow Min-Jean Yin. Gaynor is chief of hematology/oncology at UT Southwestern.

This research was supported by grants from the National Institutes of Health, the Council for Tobacco Research and the Department of Veterans Affairs.

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