SOUTHWESTERN NEWS

Media Contact: Scott Maier
214-648-3404
scott.maier@utsouthwestern.edu

EMBARGOED UNTIL 11:01 P.M. CDT SUNDAY, SEPT. 14, 2003

UT SOUTHWESTERN RESEARCHERS LEARN CERTAIN ENZYME INHIBITORS MAY HELP IN CANCER THERAPY FOLLOWING INITIAL PROCEDURES

DALLAS – Sept. 15, 2003 – Certain enzyme inhibitors may slow tumor formation within weeks and could lead to treatments that retard or prevent recurrences of cancers, researchers at UT Southwestern Medical Center at Dallas have discovered.

Their findings appear in the current issue of the journal *Cancer Research.*

The researchers sought to inhibit telomerase, an enzyme that maintains telomeres – repeating sequences of DNA at the end of each chromosome that are believed to function as a counting mechanism for cellular aging. Telomerase prevents the shortening of the sequences of DNA that occurs in normal cells as they age. The enzyme is found in most types of tumor cells but not healthy cells, indicating telomerase inhibitors may be a powerful new approach to chemotherapy.

Telomerase inhibition, however, has posed challenges for therapy. In earlier studies, scientists have found that months of treatment with an inhibitor are required before tumor growth could be expected to significantly slow.

The UT Southwestern researchers treated cultured human tumor cells with a unique compound that blocks telomerase activity, and the cell proliferation slowed substantially after just a few weeks.

Further, prostate cancer cells treated with the inhibitor barely formed tumors in mice and yielded very low levels of prostate specific antigen (PSA), a marker associated with malignancy. Cells treated with a similar compound that was not a telomerase inhibitor formed large tumors with high PSA levels.

"Telomerase is widely appreciated as a promising target for therapy," said Dr. David Corey, professor of pharmacology and biochemistry and the study's senior author. "Our results

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suggest that if you can inhibit telomerase in tumor cells and shorten telomeres, you will slow the growth of tumors."

The researchers also discovered that when the telomerase inhibitor is combined with standard cancer therapeutic agents carboplatin and cisplatin, there are additional antiproliferative effects. Dr. Corey said these results suggest a relatively small amount of telomere shortening is sufficient to slow tumor growth, and telomerase inhibitors are a useful therapeutic option, especially in combination with agents already being used to treat patients.

"No one is suggesting telomerase inhibitors alone would cure cancer, but in conjunction with standard therapy, they might help to slow or prevent the recurrence of tumors after the initial cancer has been removed through surgery, radiation or chemotherapy," Dr. Corey said. "Since most patients die from the recurrence of cancer, effective telomerase inhibitors could have a large impact on the treatment of many different types of cancer."

A similar telomerase inhibitor currently is in advanced preclinical trials with the Geron Corp. These new findings are likely to influence how clinical trials are designed and interpreted and to provide more support for pushing them forward, Dr. Corey said.

Dr. Zhi Chen, pharmacology postdoctoral researcher, and Dr. Kenneth Koeneman, assistant professor of urology, also contributed to the study. The research was supported by the National Institutes of Health and the Department of Defense Prostate Cancer Research Program.

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