UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: Aline McKenzie
214-648-3404
aline.mckenzie@utsouthwestern.edu

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DNA end caps may lead to cancer treatments, UT Southwestern researchers report

DALLAS – Feb. 2, 2006 – The two ends of human DNA have different structures that are treated differently as a cell divides, UT Southwestern Medical Center researchers have found in a study that could help lead to cancer therapies.

The study – published in the Feb. 3 issue of the journal *Molecular Cell* – focuses on the ends of DNA, which are capped by segments called telomeres. Each time the cell divides, the telomeres shorten. When they become too short, the aging cell can no longer divide. But in most cancer cells, an enzyme called telomerase keeps the telomeres from shortening, making the cells immortal and potentially malignant.

"Drugs that influence these mechanisms might be used to slow replicative aging in normal cells and increase the efficacy of telomerase-inhibition therapies for cancer," said Dr. Woodring Wright, professor of cell biology.

In human cells, every chromosome has a telomere at each end, and each telomere ends in a single-stranded overhang. (DNA is normally double-stranded.) The overhang at one end of the chromosome is longer than at the other.

"Understanding the structure of the overhang is clearly very important for our ultimate ability to understand and manipulate these things for a variety of purposes," Dr. Wright said.

The researchers believe that the rate of shortening is influenced by the length of the overhang – more DNA is lost from ends that have longer overhangs. Telomerase also changed the relative size of the two tails.

"We need to understand how this size is regulated, since we would like to be able to manipulate it for therapeutic purposes," he said.

Dr. Wright and his collaborator, Dr. Jerry Shay, professor of cell biology, are world-renowned for their work on telomeres and telomerase. They helped develop an anti-telomerase drug that helps

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slow the spread of lung cancer cells in mice. The drug is being tested in humans to see if it's safe.

The researchers say that any anti-telomerase drug would not be used alone to treat cancer. Rather, it would be used in conjunction with more traditional treatments, such as surgery or chemotherapy, to ensure that any cells not killed by those treatments don't spread to other tissues.

Other UT Southwestern researchers involved in the study were Dr. Weihang Chai, instructor of cell biology, and former senior research associate Qun Du, now with Cumbre Inc.

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