UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: Debbie Bolles
214-648-3404
debbie.bolles@utsouthwestern.edu

EMBARGOED UNTIL 11 A.M. CDT, THURSDAY, MAY 5, 2011

UT Southwestern research reveals how cancer-driving enzyme works

DALLAS – May 5, 2011 – Cancer researchers at UT Southwestern Medical Center are helping unlock the cellular-level function of the telomerase enzyme, which is linked to the disease's growth.

Their latest findings, to be published May 6 in *Molecular Cell*, demonstrate that telomerase repairs chromosomes in one of two ways – depending on whether a cell is dividing normally or if the cell is under stress from enzyme inhibition – and could lead to new or improved cancer-fighting therapies that promote inhibition of this enzyme.

"It's a significant advance in our understanding of how telomerase works," said Dr. Woodring Wright, professor of cell biology and senior author of the study. "Our goal is to identify new targets for inhibiting telomerase."

The number of times a cell divides is determined by telomeres, protective caps on the ends of chromosomes that indicate cell age. Every time a cell divides, the telomeres shorten. When telomeres shrink to a certain length, the cell either dies or stops dividing. In cancer cells, the enzyme telomerase keeps rebuilding the telomeres, so the cell never receives the cue to stop dividing.

Although telomerase was discovered in 1985, exactly how this enzyme repairs telomeres to enable cancer cells to divide and grow was largely unknown. Until now, researchers didn't know how many telomerase molecules went into action at the telomeres and under what conditions.

"It's a single molecule under normal cancer growth conditions, but if you shorten telomeres artificially by inhibiting telomerase, now it's more than one molecule acting on the ends of the telomeres," Dr. Wright said of the study's findings.

When acting as a single molecule at the telomeres, telomerase adds about 60 nucleotide molecules "in one fell swoop to the end of the chromosome," Dr. Wright said.

Researchers also discovered that structures in cells called Cajal bodies help process telomerase during chromosome-repair activity. Cajal bodies assemble ribonucleic acid (RNA) within proteins.

"Telomerase uses this RNA in order to add the sequences onto the end, and this complex is assembled or modified in some way in these Cajal bodies," Dr. Wright said.

(MORE)

Cancer-driving enzyme – 2

UT Southwestern scientists next will work to pinpoint the precise molecules that bring telomerase to telomeres for potential development of inhibitors that would be new cancer drugs.

"We now need to find the molecules that are doing that as targets for additional inhibitors," Dr. Wright said. "We have identified the step, but we haven't yet identified the molecules involved."

One drug that blocks telomerase, Imetelstat or GRN163L, was developed by the biotechnology company Geron with help from Drs. Wright and Jerry Shay, professor of cell biology. That drug, tested at UT Southwestern, is currently in clinical trials for treatment of several types of cancer.

Other UT Southwestern researchers involved in this study were lead author and assistant instructor Dr. Yong Zhao; Dr. Jinyong Kim and Dr. Guido Stadler, both postdoctoral fellows in cell biology; Ugur Eskiocak, a student research assistant in cell biology; and Dr. Shay. Biochemistry and molecular biology and genetics researchers at the University of Georgia also participated.

The work was supported by grants from the National Institute on Aging, National Cancer Institute, American Federation for Aging Research and the National Institutes of Health.

Visit www.utsouthwestern.org/cancer to learn more about UT Southwestern's clinical services in cancer.

###