SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS FIND TELOMERASE INHIBITORS MAY HELP PREVENT BREAST CANCER

DALLAS – Jan. 3, 2001 – Cell biology researchers at UT Southwestern Medical Center at Dallas have found that attacking an enzyme called telomerase, which promotes indefinite cell growth, could prove helpful in preventing breast cancer. Their research is the first to demonstrate that telomerase is not only a target for cancer therapy but also for cancer prevention.

Dr. Brittney-Shea Herbert, working with Drs. Jerry Shay and Woodring Wright, professors of cell biology at UT Southwestern, and scientists from the National Cancer Institute, treated noncancerous breast cells for three months with chemopreventive and anti-telomerase agents. They reported in the January issue of the *Journal of the National Cancer Institute* that almost none of the cells began the infinite division process that signals the onset of cancer. By contrast, untreated cells in a control group began the "immortalization" or continuous cell-division process.

"This confirms the potential of anti-telomerase agents as a means of preventing cancer," said Herbert, a postdoctoral researcher in cell biology.

Normal, healthy cells have a finite capacity for growth and eventually experience an aging process. With each division, the chromosomes progressively shorten their telomeres, which are the distal extremities of chromosomal arms. Cancerous cells, however, grow and divide indefinitely and are said to be immortal. Cellular immortality is thought to occur when normal shortening of telomeres is prevented by the activation of telomerase. In fact, telomerase activity has been detected in greater than 90 percent of all cancer cells tested but not in adjacent normal tissues.

Herbert and her colleagues hypothesized that telomerase could provide a target for cancer prevention. They focused on breast cancer because telomerase activation occurs early in breast-cancer patients. Noncancerous, pre-immortal breast epithelial cells were derived from a 31-year-

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old woman with Li-Fraumeni syndrome, a genetic condition with a predisposition toward immortalization, a critical step in breast-cancer progression. The cells were treated in cell culture for three months with four different chemopreventive agents and two different telomerase inhibitors.

The results were dramatic and offer a new approach for the development of rational chemoprevention strategies for women with a genetic predisposition to breast cancer, the researchers said. The prevention of immortalization described in this work also offers a new intermediate endpoint for validating novel chemopreventive agents.

Shay and Wright in 1998 broke new ground in the research of aging by finding that telomerase causes the immortalization of cells. In 1999, Shay and Dr. David Corey, a UT Southwestern assistant professor of pharmacology, developed synthetic telomerase inhibitors that cause progressive telomere shortening and eventually the death of cancer cells.

The research was funded by the Division of Cancer Prevention of the National Cancer Institute, a component of the National Institutes of Health. Herbert's postdoctoral fellowship is funded by the Susan G. Komen Foundation.

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