SOUTHWESTERN NEWS

Contact: Morgan Lyons
(214) 648-3404

UT SOUTHWESTERN RESEARCHERS FIND LINK TO MOST CANCERS

DALLAS — December 23, 1994 — The discovery of inappropriate telomerase activity, which appears in nearly 90 percent of cancers, is a significant "marker" that may help physicians diagnose and treat the disease more effectively, say researchers at UT Southwestern Medical Center at Dallas and Geron Corporation of Menlo Park, California.

"In the 12 types of tumors we studied, we found inappropriate telomerase expression 90 out of 101 times," said Dr. Jerry Shay, professor of cell biology and neuroscience at UT Southwestern. Almost all established tumor cell lines have telomerase activity. The enzyme telomerase modifies the ends of the chromosomes and allows cells to reproduce indefinitely. This unlimited proliferation of cells may contribute to cancer.

The study, published in the Dec. 23 issue of *Science*, examined several major types of human cancer, including breast, lung, colon and prostate, as well as pediatric and adult leukemia.

Shay and UT Southwestern collaborator Dr. Woodring Wright, a professor of cell biology and neuroscience, explained that telomeres (the DNA — deoxyribonucleic acid — at the ends of chromosomes) work like a cellular clock. Under normal conditions, they shorten as the cell ages. Each chromosome loses a certain number of telomeres each time the cell divides. This information gives researchers information about the development or maturity of the cell. Eventually the telomeres get so short that normal cells stop dividing.

Cancer cells, on the other hand, turn on telomerase, which adds DNA to the telomeres. The cells continue growing long after their telomeres should have shortened and made them stop dividing. In other words, telomerase keeps the telomeres "on" and makes the affected cells "immortal."

"This alteration in telemorase activity is the highest marker of cancer established by researchers," Shay said. "The next closest marker is the altered p53 gene, a tumor suppressor gene, that has been found to be involved

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in about 50 percent of human cancers."

The study also determined that immortal cells are almost always required to maintain tumor growth.

Researchers at UT Southwestern and Geron developed a highly sensitive test to measure telomerase activity, which indicates the presence of cancer more than 90 percent of the time. This test eventually will give physicians an important new diagnostic tool. "This test will tell us if a cell is truly immortal and may tell us if the cancer cells are going to continue growing once they have metastasized or moved within the body," Shay said.

The investigators believe their discovery also will have applications for cancer therapy in the future. They foresee the development of drugs that would not only inhibit telomerase activity but also be more effective and have fewer side effects.

Before that happens, Shay and Wright say more study is needed to further clarify the link between telomerase activity and specific types of cancer. Researchers also must gain a more complete understanding of the regulation of telomerase. "We know cells need telomerase to become immortal," Wright said. "Our next step is to determine what causes the immortalization process to begin."

Research collaborators and co-authors of the study were Dr. Mieczyslaw Piatyszek, a research fellow in cell biology and neuroscience at UT Southwestern, and Drs. Nam Kim, Karen Prowse, Calvin Harley, Michael West, Peter L.C. Ho, Gina Coviello and Scott Weinrich from Geron Corporation.

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