SOUTHWESTERN NEWS

Media contact: Heather Stieglitz
214-648-3404
heather.stieglitz@email.swmed.edu

SCIENTISTS LINK FRUIT FLY COUNTERPART OF HUMAN TUMOR SUPPRESSOR TO ACTIVATOR OF CELL DEATH

DALLAS – March 31, 2000 – Scientists at UT Southwestern Medical Center at Dallas and the University of California, Berkeley, have isolated the fruit fly counterpart of one of the most important human genes involved in tumor formation. Their work provides a model for testing and understanding how this gene works and could lead to new ways of treating human cancer.

Dr. John Abrams, UT Southwestern assistant professor of cell biology, and colleagues describe their research on the fly *Drosophila melanogaster's p53* gene – a cancer gene known as the guardian of the genome – in the March 31 issue of *Cell*. Mutations in *p53* are associated with 50 percent to 80 percent of human cancers.

The normal human *p53* gene is thought to prevent tumor formation by halting damaged cells – cells that sustain cancer-causing or oncogenic changes – from reproducing and by causing the death of those cells in a process called apoptosis, or programmed cell death. Mutations in *p53* lead to the inactivation of this normal cell-death response to damage and allow cells with oncogenic changes to proliferate into tumors.

"Induction of p53 activity by various stress signals is a critical means of limiting cancer development," said Abrams. "But how the p53 protein elicits cell death is not well understood."

The investigators isolated the fly *p53* gene by looking for DNA sequences that were similar to those of the human *p53* gene. They then demonstrated that the fly gene, whose sequence is remarkably similar to that of the human gene, functions in a comparable manner.

"The Drosophila *p53* gene, like its human counterpart, is involved in damage-inducible cell death," said Abrams. "In this animal model, we have linked *p53* to a global activator of cell suicide called *reaper*. The work implies that human *p53* may similarly function through a *reaper*-like gene."

The authors believe that genetic analysis of *p53* in Drosophila -- a well-studied genetic

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organism due to its short life cycle, well-characterized DNA and reproductive capacity -- will offer powerful clues to the molecular function of human *p53*.

UT Southwestern cell and molecular biology graduate student William Nordstrom was a co-author on the paper along with collaborators Dr. Michael Brodsky, Garson Tsang, Elaine Kwan and Dr. Gerald Rubin from the Howard Hughes Medical Institute and Department of Molecular and Cell Biology of the University of California, Berkeley.

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