SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS LOCATE TUMOR-SUPPRESSOR GENE IN FRUIT FLIES THAT CONTROLS CELL PRODUCTION, DEATH

DALLAS – July 16, 2003 – UT Southwestern Medical Center at Dallas researchers have discovered a tumor-suppressor gene that, in fruit flies, simultaneously restricts cell proliferation and promotes cell death, a process that may also play an important role in the genesis of cancer in humans.

Removal of the gene, *hippo*, resulted in tumor formation in every organ of the fruit fly. The findings, which are currently online, will appear in an upcoming issue of *Cell*.

"This is one of the few genes that has been discovered that directly controls two pathways, cell proliferation and cell apoptosis, or cell death," said Dr. Duojia Pan, assistant professor of physiology and senior author of the study. "Sustained growth of cancer cells requires activation of the cell proliferation machinery and suppression of a system called the apoptotic failsafe mechanism. The combination of suppressed cell death and deregulated cell production is likely a key element in cancer."

The researchers identified *hippo* by screening the fruit fly, or drosophila, genome for mutations that promoted abnormal tissue growth.

To determine the relationship between *hippo* and a similar protein found in humans, the researchers replaced the tumor-suppressor gene in fruit flies with a protein in humans called MST2. This resulted in the reduction of tumors in the fruit flies, leading researchers to hypothesize that MST2 plays a similar role in human-tumor suppression.

"We hypothesize that this protein (MST2) may be inactivated in some humans, causing the onset of tumor growth. Tumor suppression is important in humans because it is required to restrict abnormal growth of tissues," said Dr. Pan, the Virginia Murchison Linthicum Scholar in Medical Research.

The researchers report also that *hippo* is linked to two other tumor-suppressing genes, *salvador* and *warts*.

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"These three tumor-suppression genes may define a tumor suppression pathway that coordinately regulates cell proliferation and apoptosis," Dr. Pan said. "This pathway may also be involved in the formation of tumors in mammals."

Current research suggests that the human counterpart of *salvador* is mutated in several cancer-cell lines.

"Our findings will stimulate investigations of this tumor suppression pathway in human cancers," Pan added.

By studying fruit flies, scientists have the ability to perform more experiments than in human studies because the fruit fly genome is easily mutated. Fruit flies carry approximately 70 percent of the same disease genes as humans.

Dr. Pan is currently studying three other tumor-suppressor genes, including *PTEN, Tuberous Sclerosis 1(TSC1)* and *Tuberous Sclerosis 2 (TSC2)*. These genes have previously been identified as tumor-suppressor genes in humans.

Other researchers on the study were Drs. Jixin Dong, Jianbin Huang, and Shian Wu, all postdoctoral researchers in physiology.

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