UT SOUTHWESTERN MEDICAL CENTER NEWS

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Single gene mutation induces endometrial cancer, UT Southwestern researchers find

DALLAS – Feb. 10, 2010 – A mutation in a single gene can cause endometrial cancer that is responsive to a specific drug therapy, researchers at UT Southwestern Medical Center have found in an animal study.

The finding suggests that eventually it might be possible to screen women with endometrial cancer to see if they have that mutation and use the drug as targeted therapy, the researchers said.

"Our data suggest that deficiency of this gene can indicate both how aggressive an endometrial tumor will be and how well it might respond to a specific class of drugs," said Dr. Diego Castrillon, assistant professor of pathology at UT Southwestern and senior author of the paper, which appears in the March/April issue of *Disease Models and Mechanisms.*

"Some early clinical trials have shown that about one-fifth of women with endometrial cancers respond to a group of drugs called 'rapalogs,'" Dr. Castrillon said. "Unfortunately, it is not currently possible to predict which women these are."

Endometrial cancer affects the lining of the uterus. This cancer is the most common cancer of the female reproductive tract and is usually detected when a woman complains of excessive bleeding. About one-third of ovarian cancer cases are believed to begin as endometrial cancer, Dr. Castrillon said. The median survival of women with advanced endometrial cancer is one year.

The researchers focused the gene *Lkb1*, which is known to suppress other types of cancers. Mutations in *Lkb1* disrupt its "braking" action on cancer and contribute to the disease in lungs, skin and other tissues.

In the current study, the researchers genetically engineered mice to inactive *Lkb1* only in the endometrium. Without *Lkb1*, the entire endometrium became cancerous early and rapidly, they found.

The researchers found that treating the cancerous mice with the anti-cancer drug rapamycin slowed the progression of the cancers and dramatically shrank existing tumors.

"We hope that someday a test based on this gene or others like it might pinpoint which

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women would respond best to treatment with 'rapalogs,'" Dr. Castrillon said. "Such personalized medicine could spare other women from unnecessary chemotherapy if their tumors are unresponsive to the drugs."

Other UT Southwestern researchers participating in the study were graduate students Cristina Contreras and Esra Akbay; senior research scientist Teresa Gallardo; research assistant Marshall Haynie; Dr. Masaya Takahashi, associate professor in UT Southwestern's Advanced Imaging Research Center; and Dr. Osamu Togao, postdoctoral research fellow in the Advanced Imaging Research Center.

Researchers at Harvard Medical School also participated in the study.

The research was supported by the National Cancer Institute, a Translational Science Award from the Sidney Kimmel Foundation for Cancer Research, the American Cancer Society, and the Harold C. Simmons Comprehensive Cancer Center at UT Southwestern.

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