Medical Xpress

Study identifying alteration in gene associated with uterine cancer

May 23 2007

Researchers at the Translational Genomics Research Institute (TGen) today announced the discovery of previously unrecognized alterations in a gene called FGFR2 in a subset of endometrial cancers, the most common gynecologic cancer in the United States. The mutations in FGFR2 result in uncontrolled cell division, a hallmark of cancer.

The findings, reported by TGen and research colleagues at Washington University School of Medicine in St. Louis, the Wellcome Trust Sanger Institute, which is part of Cambridge University, and New York University School of Medicine, could accelerate the development of new treatments for endometrial cancer because there are drugs already in clinical trials that inhibit FGFR2 function. The study appears in the May 21, 2007 online version of the journal *Oncogene*.

Nearly 40,000 women are diagnosed with endometrial cancer each year, making it the fourth most common cancer found in women, following breast cancer, lung cancer and colon cancer. Endometrial cancer usually begins in the lining of the uterus and is most commonly found in women between the ages of 60 and 70. If discovered early, this slow-growing cancer can be successfully treated by surgical removal of the uterus. However, about 7,000 women die each year from the more aggressive form of endometrial cancer.

Researchers at TGen used the latest genome-scanning technology to sequence 187 endometrial tumor samples. The research team identified mutations in FGFR2 in 16% of tumors that represented a specific subset

of endometrial cancer. The other types of endometrial cancer did not have these mutations. The FGFR2 gene encodes a protein that plays a critical role in cell growth. In patients with FGFR2 mutations, the tumors were caused by the receptor for this protein being permanently stuck in the "on" position.

"Mutations in several genes have previously been identified in Endometrial cancer, however they have not been druggable targets," said Dr. Pamela Pollock, Head of TGen[1]s Melanoma Research Unit, who spent several years studying the FGFR2 gene in melanoma. "We are excited about this discovery in that the testing of drugs designed to inhibit this gene in early clinical trials means that we are one step closer to personalized medicine for women with endometrial cancer driven by an altered FGFR2 gene."

Dr. Paul Goodfellow, an expert in endometrial cancer and a professor within the departments of surgery, genetics and obstetrics and gynecology at Washington University School of Medicine, and Dr. Pollock are planning additional studies to investigate whether two drugs currently in Phase I trials for other cancers inhibit endometrial cell growth in the laboratory. Future studies include testing these drugs in mouse models of endometrial cancer before being tested in humans.

"We are planning to investigate FGFR2 in tumors from a much larger group of patients to determine whether mutations in the gene lead to aggressive cancers and poor outcome. Given how frequent mutations are in endometrial cancers, we are hopeful we will be able to initiate a Phase II trial treating patients with an FGFR2 inhibitor within the next two to three years," said Dr. Goodfellow, also co-director of the Hereditary Cancer Core at the Siteman Cancer Center at Washington University School of Medicine and Barnes-Jewish Hospital in St. Louis.

"This study illustrates the power of systematic searches for mutations in

cancer genomes in identifying the abnormal genes responsible for driving cancers and providing new therapeutic avenues," said Dr. Michael Stratton, who along with Dr. Andrew Futreal, co-leads the Cancer Genome Project at the Wellcome Trust Sanger Institute.

The identification of the FGFR2 gene and its role in the development of endometrial cancer is a great example of scientific collaboration. Dr. Pollock has studied the FGFR2 gene in melanoma for more than three years. The team headed by Drs. Stratton and Futreal at the Cancer Genome Project at the Wellcome Trust Sanger Institute found preliminary data hinting that FGFR2 might play an important role in endometrial cancer. Dr. Pollock then established a collaboration with Dr. Goodfellow, who provided tumor samples representative of the different types of uterine cancers, as well as a wealth of expertise on endometrial cancer.

"This partnership between researchers at TGen and Washington University School of Medicine combined with previous work in endometrial cancer performed at Cambridge University opened the door for new discoveries to be made," said Dr. Jeffrey Trent, Scientific Director of TGen.

Source: The Translational Genomics Research Institute