diagnose endometrial cancer and choose treatments that will target genomic mutations in women with endometrioid and uterine serous adenocarcinomas, the two most common types of endometrial cancer. The findings could also guide clinical trials and the development of new drugs.

“These findings have an immediate therapeutic application, as patients with endometrial cancer can be tested routinely to see whether they qualify for a targeted therapy clinical trial,” said Memorial Sloan Kettering gynecologic oncologist Douglas A. Levine, MD, corresponding author on the study, principal investigator of Memorial Sloan Kettering’s TCGA Tissue Source Site, and Co-Chair of TCGA’s Endometrial Working Group. “The current landscape of treatment for endometrial cancer is quite chaotic, and this research may provide order to that landscape, especially for more-aggressive endometrial cancers.”

Endometrial cancer, which forms in the tissues lining the uterus, is the fourth leading type of cancer among women and the eighth leading cause of cancer death. Endometrioid tumors are usually less aggressive, while uterine serous tumors are more aggressive.

There has been little agreement among doctors over the best treatment approach following surgery for

patients with a high risk of recurrence, with decisions relying largely on a tumor's pathology. However, it is difficult for pathologists to reliably differentiate high-grade endometrioid tumors from uterine serous tumors.

According to Dr. Levine, incorporating new genomic information into treatment planning could be a great leap forward, helping to make certain that additional therapies are used effectively and only when necessary.

The analysis of 373 endometrial tumors showed that approximately a quarter of high-grade endometrioid tumors have certain types of genomic alterations also found in uterine serous tumors. This suggests that a significant portion of endometrioid tumors should be treated more aggressively after surgery.

Many of the tumors analyzed had mutations in important cancer-related genes and pathways for which targeted therapies are already being tested in clinical trials for other cancers. For example, 84 percent of the tumors have some alteration in the PI3 kinase pathway, which is implicated in many cancers. Additionally, genomic alterations in uterine serous tumors share many features with ovarian serous and triple-negative breast cancers, suggesting opportunity for shared treatments.

Investigators at Memorial Sloan Kettering are now translating these findings into clinically useful tests that may be applied to ongoing and planned clinical trials.

A project jointly funded by the National Cancer Institute and the National Human Genome Research Institute, TCGA is one of the most comprehensive national efforts to collect and analyze the largest set of tumor samples to date using state-of-the-art genomic and molecular techniques. Memorial Sloan Kettering currently houses one of TCGA's Genome Data Analysis Centers, led by computational biologist Chris Sander, PhD, biocomputing manager Nikolaus Schultz, PhD, and molecular pathologist Marc Ladanyi, MD. For the endometrial cancer study, Memorial Sloan Kettering contributed more than 10 percent of all tissue samples analyzed.

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