Predicting prostate cancer: Test identifies new methods for treatment

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A genetic discovery out of the University of Pittsburgh School of Medicine is leading to a highly accurate test for aggressive prostate cancer and identifies new avenues for treatment.

The analysis, published today in the *American Journal of Pathology*, found that prostate cancer patients who carry certain genetic mutations have a 91 percent chance of their cancer recurring. This research was funded by the National Institutes of Health (NIH), American Cancer Society and University of Pittsburgh Cancer Institute (UPCI).

"Being able to say, with such certainty, that a patient is nearly guaranteed to see a recurrence of his prostate cancer means that doctors and patients can elect to be more aggressive in treating the cancer, knowing that the benefits likely outweigh the risks," said Jian-Hua Luo, M.D., Ph.D., professor of pathology, Pitt School of Medicine and member of UPCI. "Eventually, this could lead to a cure for prostate cancer through genetic therapy. With this discovery, we're at the tip of the iceberg in terms of possibilities for improving patient outcomes."

Prostate cancer is the second most common cancer among men (behind skin cancer), with one in seven men diagnosed with prostate cancer in their lifetime. The American Cancer Society estimates that this year in the U.S., about 233,000 new cases of prostate cancer will be diagnosed, and 29,480 men will die of prostate cancer.

Despite the high incidence rate, only a fraction of men diagnosed with prostate cancer develop metastases, and even fewer die from the disease.

"In some cases, this can make the treatment more dangerous than the disease, so doctors need more accurate tests to tell them which patients would most benefit from aggressive therapies, such as surgery, radiation and chemotherapy," said Dr. Luo.

Dr. Luo and his team sequenced the entire genome of prostate tissue samples from five prostate cancer patients who experienced aggressive recurrence of their cancer and compared them to normal tissue samples from men without cancer.

In the patients with prostate cancer recurrence, they identified 76 genetic fusion transcripts, which are hybrid genes formed from two previously separate genes and often are associated with cancer. After further testing, eight of the genetic fusion transcripts were found to be strongly associated with prostate cancer.

The researchers then screened for the eight fusion transcripts in 127 samples from patients with aggressive prostate cancer recurrence, 106 samples from prostate cancer patients with no recurrence at least five years after surgery, and 46 samples from prostate cancer patients with no recurrence less than five years after surgery. The samples came from UPMC, Stanford University Medical Center and University of Wisconsin Madison Medical Center.

In those samples, 91 percent with aggressive recurrence of their prostate cancer were positive for at least one of the fusion transcripts. Two of the fusion transcripts in particular were strongly associated with poor outcomes—none of the patients whose samples contained them survived to five years.

In contrast, 68 percent of patients whose samples did not contain at least one of the transcripts remained cancer-free.

Dr. Luo said if continued clinical trials of the test do well, it could be available to all prostate cancer patients in a few years.

In addition, studies are being developed to further investigate the genetic fusion transcripts most strongly associated with aggressive prostate cancer

. Drugs and therapies could be developed to correct or stop the mutations, thereby halting the cancer progression, Dr. Luo explained.

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