New tumor analysis method identifies high-risk prostate cancer

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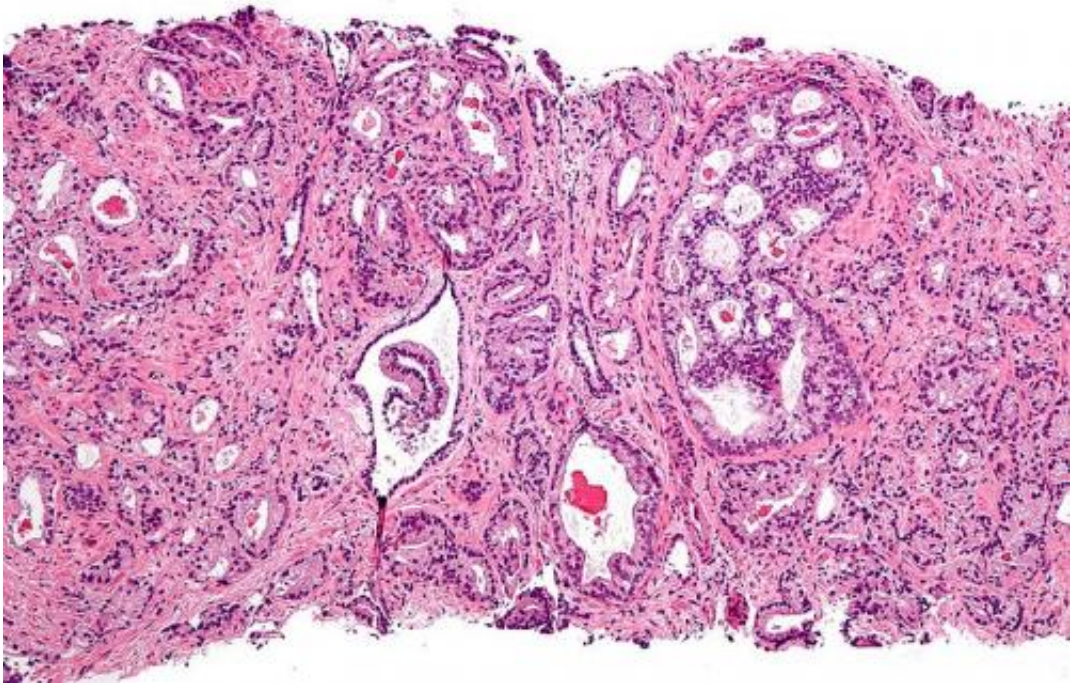

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, CC BY-SA 3.0

Scientists at Cedars-Sinai have developed a new way to identify which prostate cancer patients are likely to develop aggressive types of the disease even if their tumors at first appear to be lower risk. The new findings could help physicians prescribe the most effective treatments for each patient based on how genes are activated in the individual tumor.

"These findings raise the possibility that by determining the gene expression profile of a patient's tumor, physicians may be able to identify aggressive disease at the outset of diagnosis and start treatment earlier," said Sungyong You, PhD, an instructor in the Cedars-Sinai Department of Surgery and the first author of the study.

Although other studies have used genetic data to identify subtypes of prostate cancer, this is the first large-scale study to link clinical outcomes to subtypes based on the processes by which genes are turned on and off in the cancer cells. The study was published in the journal *Cancer Research* by the American Association for Cancer Research.

Prostate cancer affects about 1 in 7 men during their lifetimes and is the second-leading cause of cancer deaths among U.S. men, according to the American Cancer Society. Most tumors grow slowly and are not life threatening, but certain types of prostate cancer can spread to other organs and be fatal.

The new findings divide prostate tumors into three subtypes based on each tumor's gene activation pathways. When the researchers matched this data with clinical outcomes for more than 4,600 patient specimens in medical databases, they found these subtypes were associated with different levels of disease progression.

The study's conclusions address a major challenge in current standards of care for prostate cancer: Without knowing a tumor's underlying biology, physicians cannot reliably predict which of their patients will develop dangerous forms of the disease.

"About 60 percent of prostate cancer patients we treat won't progress to aggressive cancer. The problem was that we didn't have a way of knowing which patients fall into that 60 percent," said Michael Freeman, PhD, director of Cancer Biology and Therapeutics Research in the

Cedars-Sinai Department of Biomedical Sciences and the study's principal investigator. "We hope our findings help physicians provide more patients with optimal treatments, resulting in healthier outcomes."

The new research could lead to a change in the way treatment decisions are made for prostate cancer patients. Currently, physicians rely heavily on a scale called the Gleason grade. The Gleason grade ranks the cancer cells, found by surgical biopsies of the tumor, from 2 to 10 based on how closely the cancerous cells resemble normal prostate cells. The lower the grade, the lower the risk the cancer is judged to pose.

But the Cedars-Sinai research suggests that some prostate cancer patients may not receive needed treatments in a timely way. Others may receive unnecessary treatments, with significant side effects. Among the commonly prescribed therapies are radiation, hormone therapy and surgical removal of the prostate.

Currently, patients with low-grade tumors often receive no treatment and instead are closely monitored, under a strategy known as active surveillance. The new study indicates active surveillance may not be enough for some of these patients.

The study showed that one of the three subtypes of prostate cancer the researchers identified, which they called PCS1, was generally aggressive. In the patients they studied, this subtype showed a high likelihood of spreading and progressing to poor clinical outcomes, including fatalities. Patients experienced poor outcomes even when the tumors had been assigned low Gleason grades. The two other subtypes, PCS2 and PCS3, progressed more slowly.

An additional advantage to the new subtyping is that it can be performed on tumor cells circulating in the blood. This finding has the potential to improve real-time monitoring of tumor evolution during treatment, You

said.

Provided by Cedars-Sinai Medical Center