DNA methylation biomarker for prostate cancer shows promise for accurately determining patient risk

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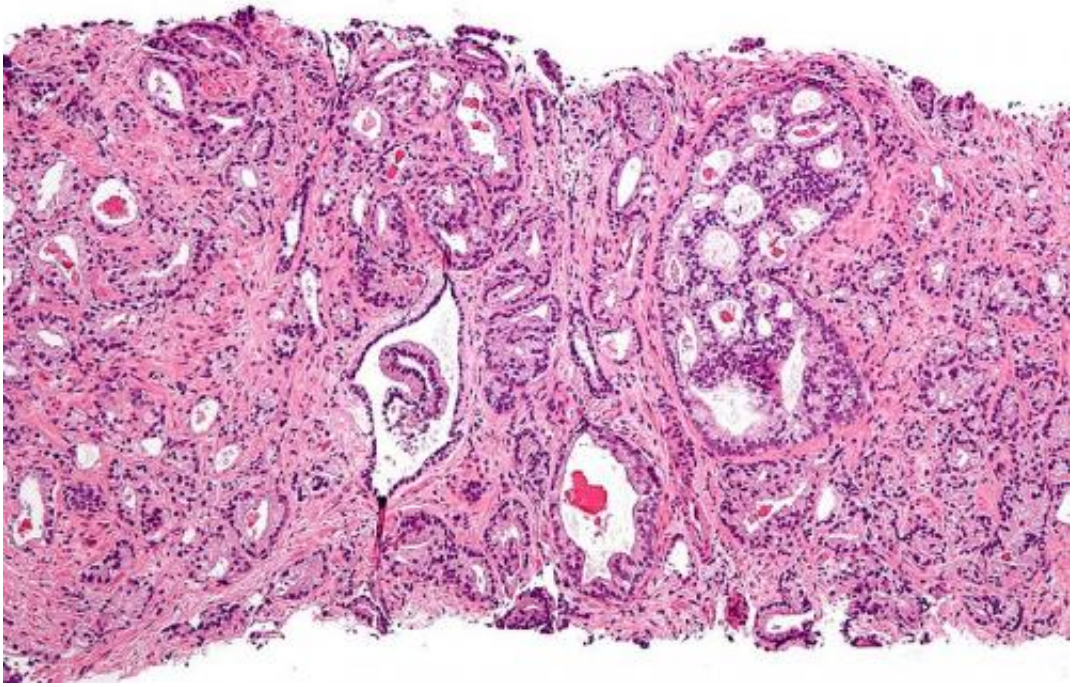

Micrograph showing prostatic acinar adenocarcinoma (the most common form of prostate cancer) Credit: Wikipedia, CC BY-SA 3.0

Prostate-specific antigen (PSA) and other biomarkers are essential tools for diagnosing and monitoring prostate cancer. However, biomarkers to selectively identify patients with high risk of recurrence, those who might benefit from intervention, and those who can safely choose active

surveillance, are lacking. A report in *The Journal of Molecular Diagnostics* describes a biomarker, PITX2 DNA methylation, which is capable of distinguishing cancerous tissue from non-cancerous tissue and predicting the risk of cancer recurrence using only small amounts of tissue obtained from core needle biopsies.

"Previous studies have shown that aberrant PITX2 methylation is a strong prognostic marker for disease progression in breast and lung cancer. In prostate cancer, several studies have demonstrated that PITX2 hypermethylation is an independent prognosticator of biochemical recurrence following radical prostatectomy. However, none of these studies were conducted on presurgical biopsies," explained Glen Kristiansen, MD, of the Institute of Pathology at the University Hospital Bonn (Germany). This is the first study to determine whether PITX2 methylation can be used for individualized risk assessment of prostate cancer using core biopsy tissue.

Investigators measured PITX2 methylation biomarker levels using a quantitative real-time PCR assay in 24 tumor samples, 24 normal adjacent prostate tissue, and 22 samples with benign prostatic hyperplasia. PITX2 promoter methylation was found to be significantly higher in cancer samples compared to matched normal and benign prostatic hypertrophy tissues. "These findings demonstrate that the PITX2 biomarker discriminates between prostate cancer and non-cancerous tissue," noted Dr. Kristiansen.

Researchers then examined whether PITX2 methylation could predict biochemical recurrence (two consecutive rises of serum PSA > 0.2 ng/mL) within a group of 300 prostate cancer patients who had undergone radical prostatectomy. They found that patients with high PITX2 methylation were at significantly increased risk for recurrence.

Subsequently, the biomarker was applied to the core biopsies of 32

patients with prostate cancer and 31 patients with benign prostatic disease. The core needle biopsy, the most common type of prostate biopsy, is performed by inserting a needle into the prostate to remove a small cylinder of tissue. Investigators found that 95% of 753 biopsy cores from 63 patients could be analyzed. PITX2 methylation was significantly higher in tumor-positive biopsies and strongly correlated with prostate cancer severity as indicated by the International Society of Urological Pathology grading system.

Whether a patient with prostate cancer detected by elevated PSA should be treated pharmacologically, radiotherapeutically, or surgically is controversial, especially because of concerns about side effects and in light of recent data that intervention may not affect mortality within the first ten years. "This study not only confirms the prognostic value of PITX2 methylation in prostate cancer, but it also demonstrates its applicability to prostate biopsies. This enables us to plan further studies that may finally translate this biomarker into clinical practice with the aim of further individualizing treatment strategies," commented Dr. Kristiansen.

More information: *The Journal of Molecular Diagnostics*, DOI: 10.1016/j.jmoldx.2016.08.008

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