New accurate epigenetic test could eliminate unnecessary repeat biopsies for prostate cancer

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More than one million prostate biopsies are performed each year in the U.S. alone, including many repeat biopsies for fear of cancer missed. Therefore there is a need to develop diagnostic tests that will help avoid unnecessary repeat biopsies. Two independent trials have now validated the performance of an epigenetic test that could provide physicians with a better tool to help eliminate unnecessary repeat prostate biopsies, report investigators in *The Journal of Urology*.

In the previously reported independent MATLOC (Methylation Analysis To Locate Occult Cancer) trial, a multiplex epigenetic assay (ConfirmMDx for Prostate Cancer) profiling the APC, GSTP1 and RASSF1 genes demonstrated a negative predictive value of 90%. GSTP1 methylation is a specific biomarker for (prostate) cancer and this gene is methylated in up to 90% of prostate cancer cases. Additionally, APC and RASSF1 are important field effect markers and increase the diagnostic sensitivity of the assay.

A second multicenter study, DOCUMENT (Detection Of Cancer Using Methylated Events in Negative Tissue), has validated the performance of the epigenetic assay used in the MATLOC trial as an independent predictor of prostate cancer risk to guide decision making for repeat biopsy. In the DOCUMENT study patients with a negative biopsy were evaluated to identify those at low risk for harboring cancer missed, through biopsy sampling error, who could forego an unnecessary repeat

biopsy. The validation study resulted in a negative predictive value of 88%.

"This epigenetic assay is a significant, independent predictor and has been shown to be the most valuable diagnostic aid of all evaluated risk factors in two independent trials," comments Alan W. Partin, MD, PhD, of the James Buchanan Brady Urological Institute, The Johns Hopkins University School of Medicine, Baltimore, Maryland. "Negative findings of this assay could be used to reduce concern over unsampled cancer and effectively avoid unnecessary repeat biopsies."

A total of 350 patients were enrolled in the DOCUMENT trial from five geographically dispersed medical centers: Cleveland Clinic, Eastern Virginia Medical School, Lahey Hospital & Medical Center, Johns Hopkins University, and University of California Los Angeles. Patients were grouped into those with two consecutive negative biopsies (controls) and those with a negative biopsy followed by a positive biopsy within 24 months. The initial archived, negative for cancer, prostate biopsy core tissue samples were evaluated. All of the men underwent a repeat biopsy on average one year after the initial biopsy.

Only biopsies with a minimum of eight cores per biopsy, collected no earlier than 2007, were included in the study, while initial biopsies with atypical cells suspicious for cancer, i.e. atypical small acinar proliferation by the sites' pathologists, were excluded, since this would have triggered a repeat biopsy based upon histopathology alone.

After correcting for age, prostate specific antigen (PSA), digital rectal exam, histopathological characteristics of the first biopsy, and race, this epigenetic test proved to be the most significant, independent, and strongest predictor of patient outcome with an odds ratio of 2.69 as well as the most valuable diagnostic aid of all evaluated risk factors. The slightly decreased sensitivity of the DOCUMENT trial compared to the

MATLOC trial is most likely associated with a higher PSA screening prevalence in the DOCUMENT cohort.

More information: "Clinical Validation of an Epigenetic Assay to Predict Negative Histopathological Results in Repeat Prostate Biopsies," by Alan W. Partin, Leander Van Neste, Eric A. Klein, Leonard S. Marks, Jason R. Gee, Dean A. Troyer, Kimberly Rieger-Christ, J. Stephen Jones, Cristina Magi-Galluzzi, Leslie A. Mangold, Bruce J. Trock, Raymond S. Lance, Joseph W. Bigley, Wim Van Criekinge, and Jonathan I. Epstein. dx.doi.org/10.1016/j.juro.2014.04.013.

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