Investigational urine test can predict high-risk prostate cancer in men who chose 'watchful waiting'

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Initial results of a multicenter study coordinated by researchers at Fred Hutchinson Cancer Research Center indicates that two investigational urine-based biomarkers are associated with prostate cancers that are likely to be aggressive and potentially life-threatening among men who take a "watchful waiting," or active-surveillance approach to manage their disease. Ultimately, these markers may lead to the development of a urine test that could complement prostate biopsy for predicting disease aggressiveness and progression.

Study principal investigator Daniel Lin, M.D., an associate member of the Hutchinson Center's Public Health Sciences Division, will present these findings today at the 2012 Genitourinary Cancers Symposium of the American Society of Clinical Oncology in San Francisco.

"Prostate biopsies are invasive and don't always pick up all of the cancer. Post-digital-rectal exam urine collection is much less invasive. If a urine-based diagnostic test could be developed that could help predict aggressive disease or disease progression, that would be ideal," said Lin, who is also an associate professor and chief of urologic oncology at the University of Washington Department of Urology.

Lin leads a nationwide consortium of eight institutions called the Canary Prostate Active Surveillance Study, an endeavor dedicated to identifying and validating biomarkers of high-risk prostate cancer.

Because many prostate cancers are slow growing and never become life threatening, many men with early stage prostate cancer choose active surveillance – delaying treatment while closely monitoring to see whether the cancer progresses.

Two urine-based biomarkers were found to correlate with indicators of aggressive disease: tumor volume (the number of biopsy samples that contain cancer) and Gleason score (predicting the aggressiveness of cancer by how it looks under a microscope). The markers that mirrored these correlates of disease aggressiveness were:

- PCA3 – a non-coding RNA that is found at high levels in prostate cancer relative to benign prostate cells; and
- TMPRSS2-ERG – the fusion of TMPRSS2, a gene that is regulated by androgens, with ERG, an oncogene. These genetic rearrangements are found in about half of all prostate cancers and are thought to play a role in prostate cancer development.

The findings were based on an interim analysis of data collected from 401 men who opted for active surveillance of their cancer. The study compared biomarker performance to clinical data collected at the time of study entry. Ultimately, the study aims to enroll 1,000 men and follow them for at least five years.

"The ultimate goal is that men on active surveillance could use a test based on these biomarkers or others to complement biopsy and PSA data to indicate or rule out the presence of an undetected aggressive cancer or future development of aggressive cancer," said Lin, who cautioned that these initial results, while promising, need to be confirmed in a larger study that would evaluate changes in these urine biomarkers over time, along with correlation to disease progression during active surveillance. Lin further noted that neither PCA3 nor TMPRSS2-ERG are FDA-

approved for prostate cancer detection and that their use in active surveillance is investigational.

Provided by Fred Hutchinson Cancer Research Center