J Cancer Sci Ther 2015, 7:5
http://dx.doi.org/10.4172/1948-5956.S1.045

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International Conference on Prostate Cancer

June 22-24, 2015 Florida, USA

The epigenetics revolution: How epigenetics has changed our understanding of prostate cancer and can be applied to improve patient management

Leander Van Neste
University of Maastricht, Belgium

Besides being the most common cancer in men, prostate cancer is heavily debated because of patient management issues. Since the adoption of PSA testing for routine screening and diagnostic purposes, many men have been diagnosed through the use of this molecular marker, however, at the cost of over-diagnosis and over-treatment. Recent reports of the PLCO (US) and ERSPC (Europe) trials indicate that prostate cancer screening by means of PSA has only a modest effect on mortality. However, men in the control group could still have undergone a PSA test that eventually led to the prostate cancer diagnosis. Strikingly, but not unexpected, over 75% of all the biopsies were false positive and of those men that were identified with prostate cancer, the majority were early stage (I or II) and low Gleason score (6). Epigenetics in general and DNA methylation in particular has been shown to play a crucial role in the onset and progression of cancer. DNA-methylation biomarkers are actively used to improve patient management and avoid unnecessary repeat biopsies and potential over-treatment of patients. The utility of DNA-methylation markers goes much further and could eventually find application in predicting which men are at increased risk of harboring occult cancer whether a man has aggressive cancer or whether he could go on to active surveillance or such markers could be used for early stage screening purposes in non-invasive sources. A single marker or set of markers is unlikely to result in an absolutely correct prediction. Hence, the most optimal solution would be to combine the strengths of different types of markers and to strive for the largest complementarity and synergy. The relative weight of the markers can be done based on their individual and proven value as interpreted by experts or this could be mathematically modeled leading to a more uniform decision making process and better patient management.

leander.vanneste@mdxhealth.com

Circulating tumor cells: A possible biomarker for diagnosis and therapies of prostate cancer

Pravin D Potdar
Jaslok Hospital and Research Centre, India

Prostate cancer is the most common cancer among men in all over the world. In 1980s, US Food and Drug Administration (FDA) approved the serum Prostate-Specific Antigen (PSA) test as a screening test to detect asymptomatic and early-stage prostate cancer. However, PSA is a relatively poor, nonspecific test, which results in false-positive and false-negative results. Several cellular and molecular bio-markers are established by several investigators. However so far, there is no specific biomarker has been approved by US FDA as a prognostic and predictive marker for prostate cancer. As cancer is a multi-step process there is a possibility to use this property of cancer for identification of specific cell type or a bio-marker for early detection and management of prostate cancer. A number of molecular events and cytogenetic markers are gaining attention as the potential prognostic indicators for prostate cancer. In the current era of genomic medicine, evaluating genetic variants of Prostate cancer cells is considered as a cutting-edge technology to resolve this problem. The purpose of this study is to search for reliable molecular markers of prostate cancer cells that can accurately stratify patients for their risk in developing prostate cancer. Circulating Tumor Cells (CTCs) are rare cells that are shed from primary and metastatic tumor and circulated into the peripheral blood of patients thus represent a simple way of performing non-invasive tumor cells testing for prostate cancer patients. Enumeration of CTCs burden and its molecular profiling before and after therapy will certainly help in monitoring and predicting response to therapy in these patients. My laboratory is presently working on development of methodology to isolate and identify circulating tumor cells from various cancers such as breast, colon, lung, and ovarian and prostate cancer. Using the cell based technology we have identified circulating tumor cells from prostate cancer patients and studied their morphological features by Light and Phase Contrast Microscopy. These circulating tumor cells from prostate cancer patients will be further confirmed for their epithelial and metastatic properties by using epithelial and several cancer metastatic markers by RT/PCR and Immunofluorescence microscopy. The presentation is basically the overview of the importance of established bio-markers for diagnosis and therapies of prostate cancer along with latest advancement in isolation and molecular characterization of CTCs in diagnosis and therapies of prostate cancer.

ppotdar@jaslokhospital.net, ppravin012@gmail.com