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CPDR Publishes New Data on
New Strategies for Improving Prostate Cancer Detection

By Justine A. Cowan
Technical Writer – CPDR

The DoD Center for Prostate Disease Research (CPDR) in Rockville, Maryland is proud to announce the publication of two novel and groundbreaking manuscripts which show novel strategies having potential to improve prostate cancer diagnosis in the future. The two recent papers are "Diagnostic Potential of Serum Proteomic Patterns in Prostate Cancer" by Banez et al. (*Journal of Urology,* 170, 42-446, 2003) and "Diagnostic Potential of Prostate-specific Antigen Expressing Epithelial Cells in Blood of Prostate Cancer Patients" by Gao et al. (*Clinical Cancer Research*, 9, 2545-2550, 2003).

The prostate-specific antigen (PSA) test has become a widely used screening test in prostate cancer. It has been attributed to high detection rates leading to prompt medical intervention and lower patient mortality. However, the PSA test has limitations including low specificity (only 25% of patients with high PSA have cancer) and many false-positive and false-negative results. These results have led to other diagnostic measures, including biopsies and anxiety on the part of patients. The serum PSA test is also lacking in that is not an effective marker for disease progression, namely it cannot serve as a predictor of cancer-specific death in afflicted men. Clearly, the development of more accurate diagnostic and prognostic methods of prostate cancer detection is needed. The fields of genomics and proteomics, newer scientific realms, are revolutionizing the cancer research field and providing further possibilities of translational research from the laboratory to the clinical setting.

Two such state-of–the art technologies being evaluated at the DoD Center for Prostate Disease Research (CPDR) include serum proteomic profiling using surface enhanced laser desorption/ionization (SELDI) and detection of circulating prostate epithelial cells (CPECS) in the peripheral blood of patients.

Proteomics is the study of proteins and their interactions in the cells. Samples that can be tested in this way include serum, semen, urine and plasma.

SELDI is a method in which proteins are selectively bound to a chemically-modified solid surface, or "chip", unbound proteins are removed by washing, an energy-absorbing matrix is applied, and the proteins are identified by a mass spectrometer. This ProteinChip system can analyze trace amounts of native proteins in their natural state. This requires only one drop of blood. Through bioinformatic analysis, hidden patterns in the serum proteomic profiles of know prostate cancer patients and healthy males can provide algorithms that can predict the disease status of serum samples with fairly high accuracy (85% specificity/sensitivity).

Through this method, CPDR scientists report promising results with great potential in terms of clinical value in being able to distinguish between patients with prostate cancer and patients with conditions such as BPH or other prostate disease, which PSA is unable to do. Further development of this technology is in progress at CPDR.

Another breakthrough, the detection of circulating prostate epithelial cells (CPECS) in the peripheral blood and bone marrow of prostate cancer patients, shows great diagnostic and prognostic potential. These circulating cells can be isolated from the blood and detected as they travel from the prostate cancer to the rest of the patient's body. These cells are identified by the presence of genes that are selectively expressed in the prostate such as PSA. It turns out that CPECS are in prostate cancer patients and are mostly detected and rarely present in normal controls. Detection of CPECS from prostate cancer patients has been successfully performed in the CPDR laboratory by sensitive methods which involve PCR amplification, or production of large amounts of DNA and then detection of a very specific DNA (in this case prostate related). The specificity and sensitivity of this method is very high - greater than 85% in these initial experiments.

While CPECS could provide more methods of CaP detection, quantitative measurement of CPECS may have prognostic utility. For example, patients with increased number of CPECS may suggest for more advanced stage of the disease than anticipated by current diagnostic modalities. Research along these lines is in progress.

Dr. Shiv Srivastava, CPDR Scientific Director, is very encouraged by these results. "Our group has continued to develop these molecular approaches, which have been in the works in the prostate cancer field for a number of years. PSA has been a great marker but has limitations. Now, we feel that these new methods may provide more specific methods to detect CaP" said Srivastava. "These two new experimental strategies are minimally invasive. They only involve blood tests which are routinely performed, and have potential for providing better care for the patient in the future" he concluded.

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