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Commentary

Inflammation: An Important Parameter in Prostate Cancer Biomarkers

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DESCRIPTION

A more specific and early diagnostics for prostate cancer (PCa) is highly desirable. In this study, being inflammation the focus of our effort, serum protein profiles were analyzed in order to investigate if this parameter could interfere with the search of discriminating proteins between PCa and benign prostatic hyperplasia (BPH).

Patients with clinical suspect of PCa and candidates for trans-rectal ultrasound guided prostate biopsy (TRUS) were enrolled. Histological specimens were examined in order to grade and classify the tumor, identify BPH and detect inflammation. Surface Enhanced Laser Desorption/Ionization-Time of Flight-Mass Spectrometry (SELDI-ToF-MS) and two-dimensional gel electrophoresis (2-DE) coupled with Liquid Chromatography-MS/MS (LC-MS/MS) were used to analyze immuno-depleted serum samples from patients with PCa and BPH. The comparison between PCa (with and without inflammation) and BPH (with and without inflammation) serum samples by SELDI-ToF-MS analysis did not show differences in protein expression, while changes were only observed when the concomitant presence of inflammation was taken into consideration. In fact, when samples with histological sign of inflammation were excluded, 20 significantly different protein peaks were detected. Subsequent comparisons (PCa with inflammation vs PCa without inflammation, and BPH with inflammation vs BPH without inflammation) showed that 16 proteins appeared to be modified in the presence of inflammation, while 4 protein peaks were not modified.

With 2-DE analysis, comparing PCa without inflammation vs PCa with inflammation, and BPH without inflammation vs the same condition in the presence of inflammation, were identified 29 and 25 differentially expressed protein spots, respectively. Excluding samples with inflammation the comparison between PCa vs BPH showed 9 unique PCa proteins, 4 of which overlapped with those previously identified in the presence of inflammation, while other 2 were new proteins, not identified in our previous comparisons.

Despite the improvements in clinical and surgical practice, prostate cancer (PCa) remains one of the most widespread cancers in males, with an unchanged mortality rate.

Furthermore, benign conditions such as prostatitis and benign prostatic hyperplasia (BPH) can lead to an increase in PSA levels causing false positive. With the aim of improving accuracy in the detection, monitoring and distinction between benign conditions and PCa, it is imperative to identify new and reliable molecular targets.

In recent years, proteomic techniques have achieved a rapid evolution, due to innovative experimental approaches and improvements in sensitivity, resolution and accuracy of the mass analysers. Several proteomic studies have been carried out on serum, urine, biopsy tissue and cell lines, with the purpose of identifying promising targets for the early detection of PCa. Unfortunately, the majority of the candidate biomarkers are still awaiting validation. Other studies have been performed in the attempt to discriminate PCa from BPH. Adam and co-workers used the protein profiling technology approach coupled with an artificial intelligence data analysis algorithm to distinguish PCa from non-cancer forms. More recently, the examined biopsy samples from BPH and PCa patients using two-dimensional gel electrophoresis (2-DE) followed by Matrix Assisted Laser Desorption/Ionization-Time of Flight-Mass Spectrometry analysis (MALDI-ToF-MS), to identify potential biomarkers that might differentiate the two clinical events. In order to identify distinctive protein profiles able to unquestionably discriminate patients with a benign prostate condition from those with a malignant situation, the serum protein expression of PCa and BPH was investigated by proteomics. Differently from previous publications, the benign states were considered vs the pathological ones focusing on the co-existence of inflammation, since emergent research underline a tight link between chronic inflammation and endothelial activation in both PCa and BPH. Cancer and inflammation are closely linked, so much that cancer patients show both local and systemic changes in inflammatory parameters.

In some cancer types, inflammatory conditions are present before a malignant change occurs; otherwise, in different type of cancer, an oncogenic alteration generates an inflammatory microenvironment that induces the development of tumor.

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