



Clinical Proteomics of Genitourinary Cancer for the Development of Biomarkers

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Short Communication

Prostate, bladder, and kidney cancer are the three most common types of genitourinary cancer worldwide. According to the estimated number of new cancer cases among males, these cancers rank within the top ten types, with especially high occurrence in developed countries. In addition, prostate and bladder cancer are ranked in the top ten causes of death according to the number of estimated deaths among males [1]. Prostate cancer is estimated to be the second leading cause of cancer death among men worldwide and the leading cause of cancer death in developed countries. According to most recent estimates of the American Cancer Society, 62,700, 76,960, and 180,890 new cases of kidney, bladder, and prostate cancer, respectively, were observed in the United States in 2016; also that year, the estimated number of respective deaths were 14,240, 16,390, and 26,120 [2]. Considering the high morbidity and mortality of these cancers, their diagnosis and treatment is an important issue for improved clinical practice.

The mechanisms of cancer development and progression are very complicated. Even though considerable effort was expended to sequence and map all genes in the Human Genome Project, cancer formation cannot be understood only through genomic data. In cells, proteins are translated by the nucleotide sequence of their genes and play major function in the physical characteristics of cells. Therefore, proteomic technology is a powerful tool for cancer research. Monitoring changes in the expression of specific proteins during cancer development and progression, through the profiling of functional proteins and the detection of their expression in clinical specimens, is helpful. Proteomic technology is also a useful tool for uncovering potential biomarker candidates for cancer diagnosis, treatment, and other clinical applications.

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In protein biomarker discovery projects, body fluids and/or tissues are usually first used to generate lists of biomarker candidates, classically through comparisons of case and control samples and more recently through longitudinal studies, in which each case is its own control. To refine the list of putative biomarkers, a verification step is then performed using targeted approaches in an increasing number of body fluid specimens (typically tens to hundreds). Ultimately, the clinical validation of these candidates in body fluids is performed in large cohorts to demonstrate the utility, specificity, and sensitivity of a biomarker or a panel of biomarkers and to reveal their clinical relevance as prognostic or diagnostic tools. The verification and validation steps often require the development of assays, such as Enzyme-Linked Immunosorbent Assays (ELISA) and Selected-Reaction Monitoring (SRM) Mass-Spectrometry (MS)-based assays, which require time, investment, and expertise for execution and, possibly, also upstream development [3]. The opportunity to perform first-stage screening in a high number of samples may increase the statistical significance of findings and reduce the number of “pilot” assays to be developed, which require substantial resources. The analytical throughput of the proteomic discovery workflow is also an important aspect to be considered [4].

The final performance of a biomarker or panel of biomarkers is eventually assessed through cost-effectiveness studies of several population-based cancer programs wherein the biomarker is used to solve a real-world clinical problem. The impact of cost-effectiveness in using a biomarker strategy is evaluated using the increase or decrease in total costs, including those of the biomarker tests, infrastructure resources, and avoided or replaced medical events [5]. The economic value is also affected by the assay’s sensitivity and specificity, the cancer’s prevalence rate in the population, and the acceptance of the assay by clinicians and patients. Biomarkers are expected to be cost-effective for identification among high-risk patients with a disease history or risk of recurrence or metastasis

of cancer who require monitoring. A relatively low-cost biomarker assay is required to screen target individuals with no or minor illness symptoms [6]. A multiplex assay may become cost-effective when the costs are lowered through population-wide screening and can alter the non-cost-effective results originally derived in a smaller number of subjects [7]. Using bladder cancer as an example, a diagnostic assay with superior diagnostic sensitivity and similar specificity to cystoscopy will enable a reduction in the number of required cystoscopy procedures by at least 50% during the primary diagnosis of bladder cancer as well as during follow-up monitoring. If the pricing of the biomarker assay is not higher than 50% of the cost of cystoscopy, using a biomarker for bladder cancer detection is cost-effective [8,9]. However, the absolute risk reduction is very small, and using prostate-specific antigen testing for the screening of prostate cancer was found to not significantly affect all-cause mortality; hence, the conclusion remains debatable [10-12]. The clinical effectiveness and cost-effectiveness of photodynamic diagnostic methods have also been compared with white-light cystoscopy as well as urine biomarkers and cytology for the detection and follow-up of bladder cancer. The clinical effectiveness and extra cost of societal acceptance for replacing white-light cystoscopy with photodynamic diagnostic methods are not clear [13]. For many novel protein biomarker candidates discovered using proteomic techniques, additional studies to evaluate the comparative effectiveness and cost-effectiveness in a collaborative manner would be beneficial because the availability of such data is limited for genitourinary cancer.

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