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Future of Urological Diagnosis Using Proteomics: A Review of Literature

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Abstract

Proteomics is a large-scale study of proteins. Several technologies are used to isolate and identify proteins of various spectra, which is useful in differentiating complexity of proteins. Critical role of proteomics can be applied to the field of urology, as a means of noninvasive biomarkers to diagnose patients with benign and malignant nephro-urological diseases. The accuracy of proteomic analysis findings in predicting specific clinical pathologies continues to draw controversy, thus further studies are necessary to confirm the diagnosis. Future of diagnosis in urology is expected to be done by proteomic urinalysis.

Keywords: Proteomics; Mass spectrometry; Congenital urinary tract obstruction; Partial bladder outlet obstruction; Prostate cancer

Introduction

Proteomics is a large-scale study of proteins, which can be used in the identification of complications and diseases that develop in various organs and tissues. With the advancements in technology, so has the understanding of protein expression, function, and detection. Due to the complexity of proteomes, it is critical to separate proteins or peptides based on the physical and chemical properties for more accurate identification (**Tables 1 and 2**). Proteomics is widely used in oncology using serum to determine up-regulated proteins specific to cancers [1-3].

The complexity of the protein is greater than that of the genome because of many disparities due to post-translational modifications (e.g. phosphorylation, glycosylation, acetylation, and methylation), RNA splicing, chemical damages (e.g. glycation, oxidation, and nitration), and a single gene coding for more than one protein [4,5]. These post-translational modifications are exponential due to a multitude of environmental effects spanning different individuals [6]. Magnitudes of proteomes span over 8-10 orders, whereas

current mass spectrometer can only analyze up to 4 orders, add a challenge to this study [7].

New areas of medicine are being enriched with ongoing advances in the field of proteomics. This review article in particular focuses on the impact of proteomics in the field of urology.

Table 1 Methods of protein/peptide separation.

Sodium Dodecyl Sulfate-PolyAcrylamide Gel Electrophoresis [8]
Two-Dimensional-Differential In-Gel Electrophoresis [8]
Multi-Dimensional Protein Identification Technology [9-11]
Ultracentrifugation [12]

Table 2 Technologies used for proteomics: Protein identification.

Mass Spectrometry [13]
Electrospray Ionization [14]
Matrix-Assisted Laser Desorption Ionization [15]
Tandem Mass Spectrometry [16]
Surface Enhanced Laser Desorption Ionization - Time of Flight Mass Spectrometry [15]

Proteomics in Urology

Urine is an ideal medium for proteomic analysis because it is readily and noninvasively available. Urine is a proximal fluid to the majority of organs and diseases that present in the urogenital tract [17,18]. Though an excellent tool for diagnosis, analysis can be very challenging because the amount of protein found in urine can vary and contains excreted compounds [18]. Spectrometric datasets have identified 2217 ureter proteins; 751 of these proteins are detected in urine, which originate via glomerular filtration and interact with the urinary tract [19]. Magdeldin et al. speculates that these proteins can be biomarkers for many diseases regarding the ureter [19].

A few urological studies have used proteomics to diagnose using analysis of urinary proteome. Chevalier et al. discussed

how congenital urinary tract obstruction may be the cause of chronic kidney disease. Without any etiologies, the discovery of congenital urinary tract obstruction is possible by determining the presence of hydronephrosis using prenatal ultrasonography. With the present advancements in proteomics, biomarkers for congenital urinary tract obstruction allow much quicker diagnosis, further safe guarding the patients from development of chronic kidney disease, and improve the quality of life in patients [20]. Alsaikhan et al. used proteomics with an animal study to describe the molecular change due to partial bladder outlet obstruction, which is a common issue in urology. This method paves the way to use proteomics for prevention and treatment options of partial bladder outlet obstruction [21]. Urine proteomics can also identify IgA nephropathy, diabetic nephropathy, nephrotic syndrome (focal-segmental glomerulosclerosis), ureteropelvic junction obstruction, urosepsis, preeclampsia, and many other nephro-urological disorders [22-28].

Along with benign urological complications, many malignant diseases may arise. Adeola et al. determined potential biomarkers that can be used for the identification of prostate cancer. Of the 12 potential biomarkers found, several were found in the urine of both normal patients and patients with prostate cancer, insinuating that proteomic urinalysis is not infallible. The protein HPR is more commonly found in the urine of patients with prostate cancer, though it has been found in one healthy individual in the study [29]. In another study, conducted by Percy et al. described that 136 proteins, of greater than five order of magnitude, found in urine can be applied to prostate cancer samples, a possible means of diagnosis [30]. Bernardo et al. further used the proteomic studies to gain insight on the pathogenesis of bladder cancer due to *Schistosoma haematobium*, which can also be used for early detection of urogenital schistosomiasis-induced bladder cancer [31]. Proteomics can aid in diagnosing patients with clear cell renal cell carcinoma using urine analysis as stated by Sandim et al. who found 49 up-secreted proteins in patients with clear cell renal cell carcinoma, which included apolipoprotein A, fibrinogen, and haptoglobin [32]. Though proteomics can be useful in determining the presence of neoplasm without invasive procedures, it is not without certainty as the biomarkers can potentially be found in both healthy patients and patients with neoplasms. Lastly, the sample size in these studies was limited, eliciting additional information for a confirmed diagnosis.

Conclusion

Proteomics is a rapidly developing discipline. It can provide a great deal of insight into diseases of the urogenital tract and assist with proper diagnosis and prevention options. Despite controversies proteomic urinalysis can potentially pave the way for future diagnostic studies, early detection, and fair prognosis. Further studies are essential to strengthen the evidence from the finds of urinalysis using proteomics. With continuing advancements in technology for the studying

proteins, proteomics can prove to be a staple in the clinical examination to diagnose patients.

Compliance with Ethical Standards

The authors declare they have no conflict of interest.

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