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The Understanding of Prostatitis and Biomarker Research

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Prostatitis is the most common urologic diseases and the third most common urologic diagnosis in men after Benign Prostate Hyperplasia (BPH) and prostate cancer [1,2]. The National Institutes of Health (NIH) consensus classification of the prostatitis syndromes released in 1995 categorized prostatitis into four clinical entities: I, acute bacterial prostatitis; II, chronic bacterial prostatitis; III, Chronic Prostatitis/ Chronic Pelvic Pain Syndrome (CP/CPPS); and IV, asymptomatic inflammatory prostatitis [3]. It has been estimated that only 5% to 10% of prostatitis patients have acute or chronic bacterial infection, whereas the majority of men with prostatitis (about 90%–95%) experience chronic pelvic pain without any evidence of infection (category III). CP/CPPS is an important public health problem.

Furthermore, unlike BPH, which is more prevalent among elderly men, chronic prostatitis affects men of all ages and ethnicities. CP/ CPPS is a poorly understood entity characterized by pelvic or perineal pain, irritative voiding symptoms, and sexual dysfunction, and, from a clinical point of view, is truly lacking a cause that would allow a more rational-driven therapy [4].

While various mechanisms including immunological dysfunction, infection, neurological dysfunction, psychosocial factors and endocrine abnormalities have been cited in the development of the CP/CPPS, the etiology and pathogenesis of CP/CPPS is poorly understood [5]. So the treatment for prostatitis lacking enough specificity is far from satisfactory. The relapse rate is quite high in patients. In order to explore the pathogenesis and screen effective drugs, reliable experimental animal models of human diseases are critically important for the discovery of molecular pathways, genetic influences, environmental factors, and successful management strategies for humans. At present, there are mainly several experimental animal models including spontaneous prostatitis models, infectious prostatitis models, immune-induced prostatitis models, hormone-associated prostatitis models and miscellaneous prostatitis models [6].

As a common genitourinary disease of adult male, diagnosis, treatments and prognostic monitoring of prostatitis have always been the focus of clinical attention, as a result of its setbacks, such as complex pathogenesis and clinical symptoms, lacking specificity in medication and its high rate of recurrence and so on. Currently, there isn't a "golden standard" in diagnosis of prostatitis, while the detection of biomarkers can be helpful for the diagnosis, treatment and prognostic monitoring of prostatitis. Following significant improvements of the methods of detection in biological fluids, a number of prostate inflammation biomarkers were identified and quantified, in peripheral blood, urine and seminal plasma [7].

In fact, White Blood Cells (WBC) count in expressed prostatic secretions (EPS) has long been considered as the marker of prostatitis. However, it does not appear to be the optimal marker of inflammation and the current categorization of chronic prostatitis/chronic pelvic pain syndrome III B and asymptomatic inflammatory prostatitis as inflammatory or non-inflammatory based on WBC count appears to offer little clinically useful information [8,9]. And whilst WBC can be found in the prostatic fluid or seminal plasma of asymptomatic men as well as in that of men with pelvic pain. Also, the measures of the NIH-CP Symptom Index in symptomatic men show no correlation with WBC in EPS or seminal plasma.

As the prostatitis biomarkers, cytokines/chemokine may have high sensitivity and good specificity. Cytokines are regulatory proteins released by various cellular subtypes that promote intercellular communication and immune responses. Chemokines are a subset of cytokines that recruit and activate immune cells to sites of inflammation.

Interleukin 8 (IL-8) is a pro-inflammatory cytokine and plays an important role in different inflammatory diseases, such as rheumatoid arthritis, abdominal aortic aneurysms, gastritis, inflammatory bowel disease, atherosclerosis, and inflammatory lung disease [10,11]. Significant correlations between IL-8 levels and symptom score results (P<0.001) were found. IL-8 values strongly correlated with CP/CPPS (P<0.001). Moreover, the patients with higher levels of IL-8 reported the worst symptoms [10]. The study of Penna et al. has shown that IL-8 was significantly elevated compared to controls in patients with CP/ CPPS IIIA, CP/CPPS IIIB and benign prostatic hyperplasia (BPH). IL-8 is a reliable biomarker in seminal plasma for chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), and for BPH, and also the IL-8 levels were correlated with symptom scores and serum PSA values, increasing its value as a biomarker for prostate inflammation [12].

Monocyte chemoattractant protein 1 (MCP-1) and macrophage inflammatory protein-1α (MIP-1α) recruit monocytes and macrophages via their release from fibroblasts and macrophages in joints of patients with rheumatoid arthritis and perpetuate the inflammatory process. For MCP-1 and MIP-1α, chronic pelvic pain syndrome subtypes had statistically higher levels than the control group and patients with benign prostatic hyperplasia. Receiver operating curves using MCP-1 levels greater than 704 pg/ml and MIP-1αgreater than 146 pg/ml identified patients with chronic pelvic pain syndrome with an accuracy of 90% from control patients. MIP-1αlevels (p=0.0007) correlated with the pain subscore of the chronic prostatitis symptom index while MCP-1 (p=0.71) did not. MCP-1 and MIP-1α within the prostatic fluid in both chronic pelvic pain syndrome subtypes provide candidate future biomarkers for chronic pelvic pain syndrome [13]. In addition, macrophage inflammatory protein-1α increase in expressed prostatic secretions provides a new marker for clinical pain in chronic pelvic pain syndrome patients [14]. Given these findings prostatic dysfunction likely has a role in the pathophysiology of this syndrome.

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