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Original article

Protein regulator of cytokinesis 1 overexpression predicts biochemical recurrence in men with prostate cancer

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ABSTRACT

Background: Protein regulator of cytokinesis 1 (PRC1) has been reported to be implicated into the completion of cytokinesis and is dys-regulated in a cancer-specific manner. However, it roles in human prostate cancer (PCa) remain unclear. In the current study, we aimed to investigate the expression pattern of PRC1 and its clinical significance in this malignancy.
Materials and methods: PRC1 protein expression in human PCa and non-cancerous prostate tissues was detected by immunohistochemistry, which was validated by microarray-based Taylor data at mRNA level. Then, the associations of PRC1 expression with clinicopathological features and clinical outcome of PCa patients were statistically analyzed.
Results: PRC1 expression in PCa tissues, at both mRNA and protein levels, were significantly higher than those in non-cancerous prostate tissues. In addition, the PCa patients with PRC1 overexpression more frequently had high Gleason score, advanced pathological stage, positive metastasis, short overall survival time and positive PSA failure than those with low Gleason score, early pathological stage, negative metastasis, long overall survival time and negative PSA failure (all $P<0.05$). Moreover, PRC1 expression was identified as an unfavorable prognostic factor of biochemical recurrence-free survival in PCa patients ($P<0.001$).
Conclusion: These findings suggest that the aberrant expression of PRC1 may predict biochemical recurrence in men with PCa highlighting its potential as a prognostic marker of this malignancy.

1. Introduction

As one of the frequently diagnosed solid malignancy in men, prostate cancer (PCa) has become the second leading cause of male cancer death in the developed countries [1]. The incidence of this cancer has been increasing over the past two decades, because of the improved overall longevity of the population worldwide and the more widespread use of prostate-specific antigen (PSA) testing [2]. PCa is a multi-focal, field-type disease which forms solid tumors of glandular origin [3]. Since androgens are involved into the differentiation, development and normal functioning of the prostate, it has been reported to play a role in prostate carcinogenesis. Conventional treatment based on the deprivation of androgens to the developing tumor produces a high rate of cure for patients with localized disease, but there is no cure once the disease has been at advanced stages and spread beyond the prostate due to the acquisition of androgen independence in PCa cells [4]. Recent studies have identified several molecular alterations involved in prostate carcinogenesis, progression and recurrence [5,6]. However, the precise mechanisms underlying this malignancy has not been fully elucidated. Thus, it is of great clinical significance to identify novel and efficient markers for better

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understanding the biology of PCa, and for improving the diagnostic and prognostic levels of this cancer.

Although radical prostatectomy (RP) is the most appropriate treatment for patients with localized PCa, the risk of biochemical recurrence (BCR) of these patients is about 25% [7]. The cell cycle progression (CCP) score, an emerging and promising tool as an RNA expression signature based on the average expression level of 31 CCP genes, has been shown to predict BCR after prostatectomy [8]. The prognostic value of the CCP score have been confirmed for both newly diagnosed patients and patients who have undergone prostatectomy but are at risk of disease recurrence [9]. Among 31 CCP genes, protein regulator of cytokinesis 1 (PRC1) encodes a protein that is present at high levels during the S and G2/M phases of mitosis and involved in cytokinesis [10]. It is located in the nucleus during interphase and associates with the mitotic spindle in a highly dynamic manner during mitosis, and localizes to the cell

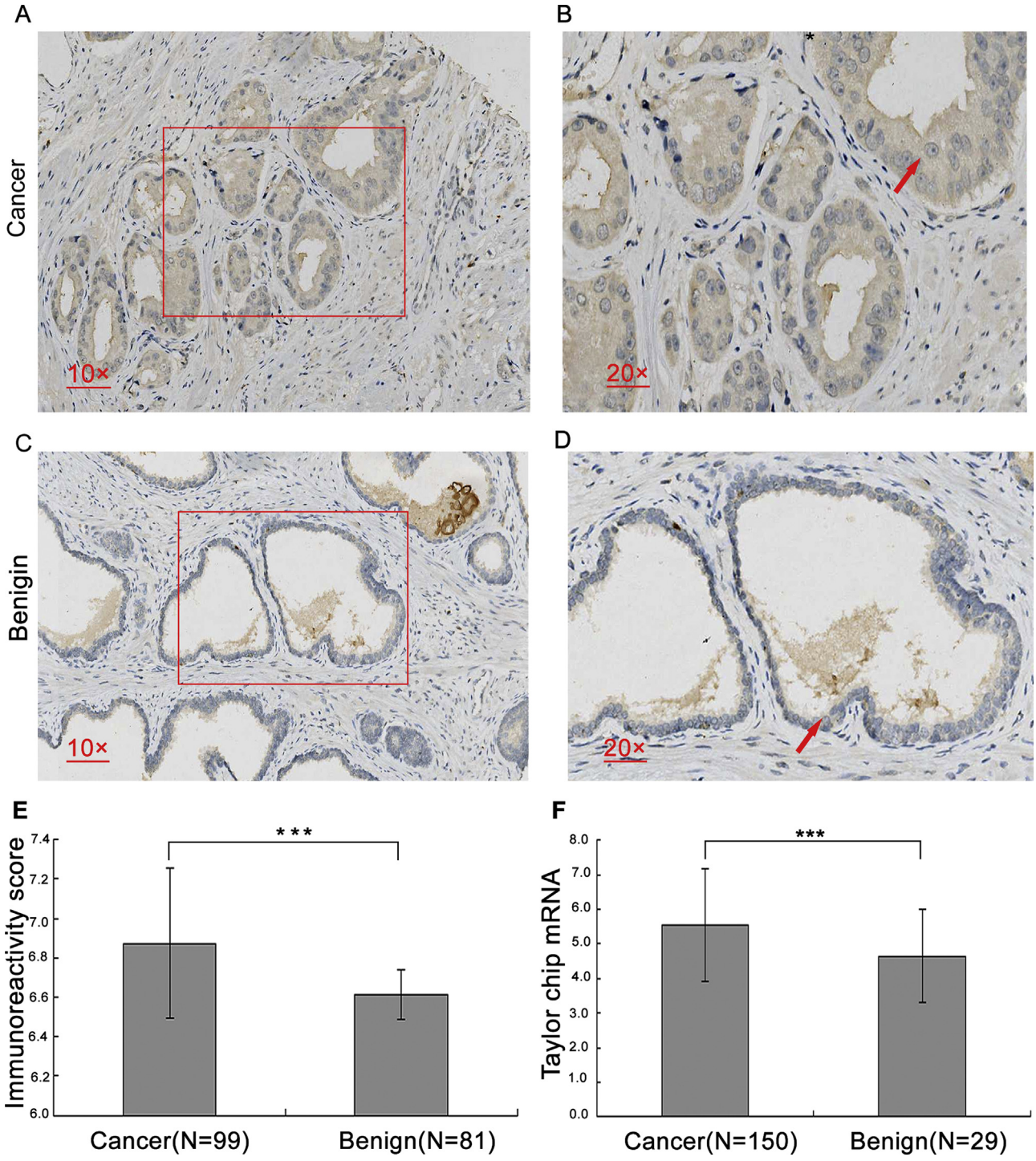

Fig. 1. Overexpression of PRC1 in human PCa tissues. (A and B) Immunostainings of PRC1 protein were predominantly localized in the cytoplasm of PCa cells; (C and D) PRC1 protein was weakly or negatively expressed in normal prostate gland cells in adjacent non-cancerous prostate tissues; (E) statistical analysis found that the expression levels of PRC1 protein in PCa tissues were significantly higher than those in adjacent noncancerous prostate tissues (IRS: PCa = 5.56 ± 1.62 vs. Benign = 4.65 ± 1.35, $P < 0.001$); (F) the expression levels of PRC1 mRNA in PCa tissues was significantly higher than that in adjacent non-cancerous prostate tissues significantly (PCa = 6.87 ± 0.38 vs. Benign = 6.61 ± 0.12, $P < 0.001$). '***' $P < 0.001$, the comparison between PCa tissues vs. adjacent non-cancerous prostate tissues.