Discovery of PTN as a serum-based early biomarker for poor prognosis prostate cancer

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Abstract

Background: Prostate cancer is the most common non-cutaneous cancer and the second leading cause of cancer-associated deaths in men in the US and UK. One of the major clinical challenges in prostate cancer is distinguishing clinically significant from indolent disease. Here, we utilized a targeted human protein biomarker discovery approach and identified pleiotrophin (PTN) as a potential prognostic serum and tissue biomarker for clinically significant prostate cancer.

Methods: Serum samples from 4 different groups: 1) cancer-free group, 2) Cambridge Prognostic Group 1 (CPG1) disease with 97% 10 year survival, 3) Cambridge Prognostic Group 5 (CPG5) disease with 50% 10 year survival, and 4) men with metastatic disease at diagnosis were analyzed using high-multiplex immunoassays from Olink Proteomics (n=20 samples per group). PTN was selected for further validation by sandwich ELISA in the discovery cohort and immunohistochemical analysis in a validation cohort.

Results: We discovered that nine out of 174 proteins are significantly elevated in metastatic prostate cancer patients when compared to all other groups. PTN levels are significantly increased in CPG5 and metastatic prostate cancer serum samples in comparison to those from cancer-free and CPG1 groups. Moreover, high levels of PTN in localized prostate cancer tissues are predictive for biochemical recurrence ($p<0.05$) and correlate with pre-operative serum prostate specific antigen levels ($p=0.003$), pathological tumor stage ($p=0.0083$), and biopsy Gleason Score ($p=0.0012$). High tissue PTN level was an independent predictor of biochemical recurrence in patients with low pathological Gleason Grades ($p<0.05$).

Conclusions: Serum PTN expression may be specific for the presence of poor prognosis local and metastatic disease. PTN may also serve as a predictor of disease progression. Our data justifies its further evaluation as a potential early detection biomarker of lethal disease.