Identification of Novel Stromal Biomarkers for Prostate Cancer Progression

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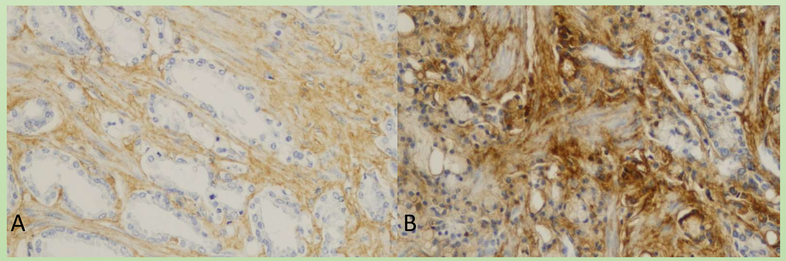
Introduction

Prostate cancer is the second most common cancer and the fifth most deadly cancer worldwide in men. Prostate cancer initiation and progression is a complex process largely dependent on tumor microenvironment, its cellular and noncellular components such as extracellular matrix proteins that could serve as a stromal markers for disease prognosis and prediction. In this regard, periostin (POSTN) and versican (VCAN) seem promising.

Aim of Study

To study extracellular matrix proteins/genes periostin (POSTN) and versican (VCAN) as stromal biomarkers in the progression of prostate cancer.

Fig. 1. Immunohistochemical expression of Periostin (A) and Versican (B) in prostate cancer tissue sample.



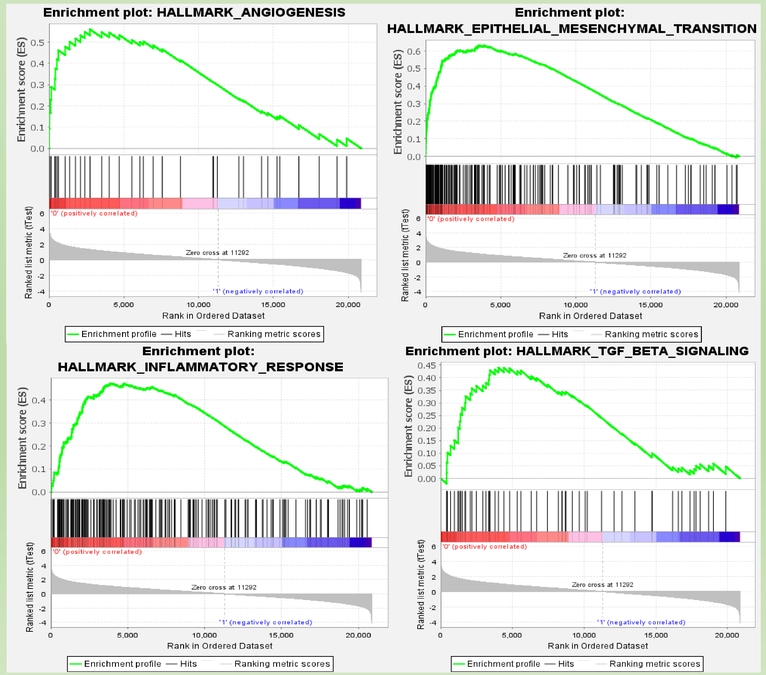
Methods

101 formalin fixed paraffin embedded prostate cancer tissue samples were studied immunohistochemically for periostin and versican protein expression. Using the Cancer Genome Atlas (TCGA) and Gene Expression Omnibus (GEO) data that were processed by Gene set enrichment analysis (GSEA), we aimed to identify hallmark genes/pathways associated with prostate cancer with elevated expression of periostin and versican. Associations with clinical and pathological variables were also studied.

Results

POSTN and VCAN were upregulated in various tumors in comparison to normal tissues. Immunohistochemically, periostin stromal positivity correlated with versican stromal expression (Rs 0.368, p<0.001). Periostin stromal expression positively correlated with tertiary Gleason and Gleason grade group ((Rs 0.276 and 0.269, both p=0.008). Periostin was involved in prediction of metastatic progression (p<0.01.)High versican stromal expression was independent predictor for high Gleason grade group. GSEA analysis showed enrichment of genes involved in angiogenesis, epithelial-mesenchymal transition, inflammatory response and TGF-beta signaling in VCAN high group, while genes involved in cell cycle regulation, MYC-targets, IL6-JAK-STAT3 signaling and epithelial mesenchymal transition were enriched in POSTN high group.

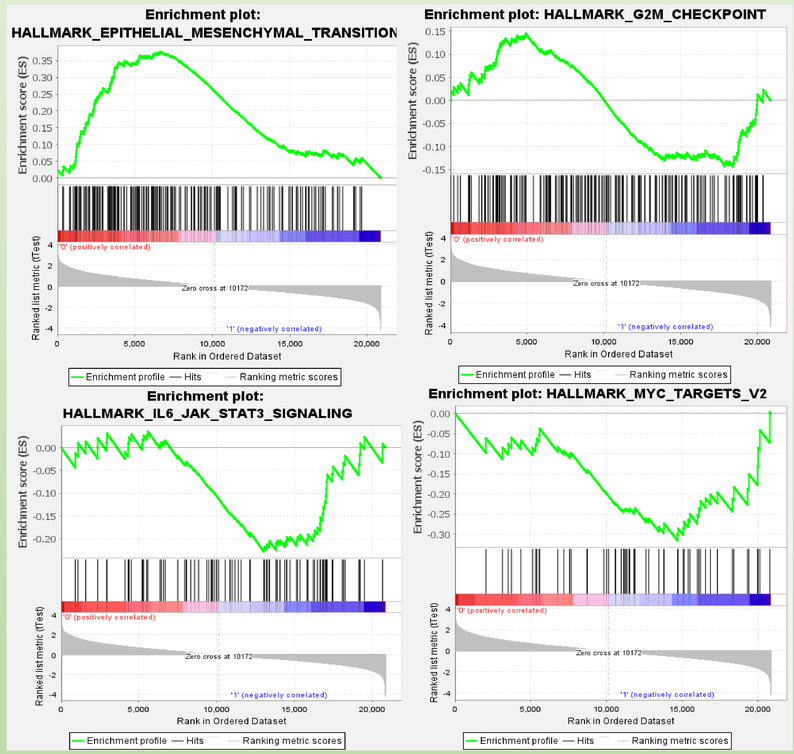
Fig. 2. Gene Enrichment Analysis of prostate cancer samples with high POSTN levels.



Conclusion

We showed for the first time the association between periostin and versican with pathological parameters of advanced prostate cancer and revealed associated gene groups and signalling pathways that can serve as potential anticancer targets.

Fig. 3. Gene Enrichment Analysis of prostate cancer samples with high VCAN levels.



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4. Cattrini C, Barboro P, Rubagotti A, et al. Integrative Analysis of Periostin in Primary and Advanced Prostate Cancer. *Transl Oncol*. 2020;13(7):100789.