CD38, immunosenscence and inflammaging in prostate cancer

Author: Goncharov Aviv Philip
Supervisor: MUDr. Gvantsa Kharaishvili, PhD.
[1] Laboratory of Molecular Pathology and Department of Clinical and Molecular Pathology, Palacky University, Olomouc, Czech Republic

FAKULTNÍ NEMOCNICE OLOMOUC

Faculty of Medicine and Dentistry
Palacký University Olomouc

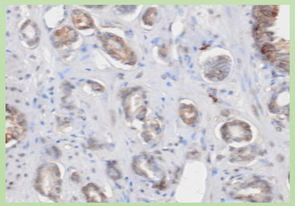
Introduction

Prostate cancer is considered the second most common tumor in men and the second leading cause of death. The PSA used today, is sensitive, but not specific enough and there is not significant correlation between the stage of the tumor and PSA levels. Prostate cancer is an age related disease. low-grade, chronic, sterile inflammation, named “inflammaging,” is a steadfast phenomenon in elderly patients. Immune changes with aging are known as immunosenescence. Both events stimulate CD38 expression, which is implicated in tumorigenesis and tumor progression by modulating immune regulation, metabolism, calcium-mediated signal transduction, cell adhesion, and migration.

Aim of Study

Our aim is to study the role of CD38 in prostate cancer and find associations with pathological parameters, to study the correlation between chronic inflammatory state and prostate cancer.

Fig. 1. Immunohistochemical expression of CD38 (A) and P16(B) in prostate cancer tissue sample.



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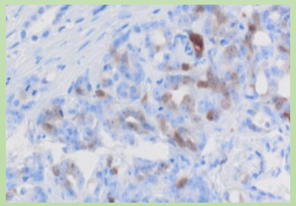

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Methods

In this study we included 47 prostate cancer samples, after assessment of Gleason score and stage, we stained the formalin fixed paraffin embedded tissues with CD38, CD163, H2AX, p16 and CD 68 antibodies by immunohistochemistry and evaluated using light microscopy. Gene Set Enrichment analysis (GSEA) was done for identification of hallmark genes and pathways associated with prostate cancer expressing CD38 and CD274.

Results

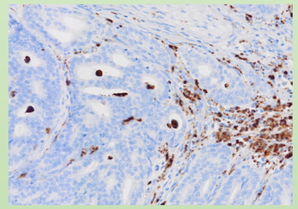
In CD38, positivity in benign prostate epithelial tissue correlates positively with CD38 in malignant prostate epithelial tissue (Rs=0,527, p=0,017) and also positively correlates with CD38 in stromal fibroblasts (Rs=0,419, p=0,033). We didn’t find correlation between the expression of CD38 and the stage of the tumor. Interestingly, other markers as P16 (p=0,007) and H2AX (p=0,019), showed correlation between the expression in stromal fibroblast cells and the stage of the tumor. GSEA identified significant upregulation of genes involved in fatty acid metabolism, protein secretion, reactive oxygen species pathway and more.

Fig. 2. GSEA enrichment plots of hallmark pathways associated with prostate cancer with elevated expression of CD38.

Conclusion

We didn‘t find the correlation between the expression of CD38 and the stage of cancer. It can be explained by the fact that the marker was widely expressed both in malignant cells and benign cells. On the other hand, we found out that H2AX and P16 expressed in stromal fibroblast cells may indicate that major environmental events associated with immunosenescence and inflammaging relate to cancer associated fibroblasts. CD38 was identified in many hallmark pathways associated with prostate cancer, thus, further functional studies are required to establish the possible uses of these hallmarks in prostate cancer.

Fig. 3. Immunohistochemical expression of CD68 (A), H2AX(B), CD163 (C) and CD38 (D) in prostate cancer tissue sample.



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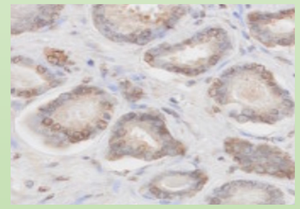

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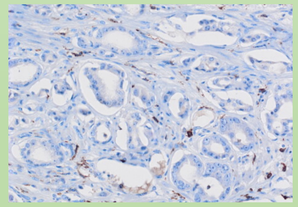

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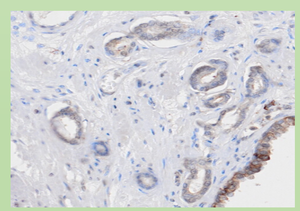

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