Cells 2025 Conference

The 3rd International Online Conference on Cells

25–27 March 2025 | Online

MDPI

Assessment of a gene signature deriving from prostate cancer-associated fibroblasts (CAFs)

Zicarelli A[1], Talia M[1], Cesario E[2], Cirillo F[1], Scordamaglia D[1], Mondino AA[1], Di Dio M[1], De Rosis S[1], Di Dio M[3], Miglietta AM[4], Maggiolini M[1], Lappano R[1]

UNIVERSITÀ DELLA CALABRIA

[1]Department of Pharmacy, Health and Nutritional Sciences, University of Calabria, Rende, Italy; [2]Department of Cultures, Education and Society Department, University of Calabria, Rende, Italy; [3]Division of Urology, Department of Surgery, Annunziata Hospital, Cosenza, Italy; [4]Breast and General Surgery Unit, Annunziata Hospital Cosenza, Cosenza, Italy

INTRODUCTION & AIM

The tumor microenvironment plays a pivotal role in shaping tumor aggressiveness and driving disease progression. In this context, the identification of gene signatures characterizing cancer-associated fibroblasts (CAFs) obtained from one of the most frequently diagnosed cancer worldwide, such as prostate tumor, may improve outcome prediction and therapeutic strategies for patients.

METHOD

The transcriptomes of CAFs isolated from breast and prostate cancer tumor specimens were analyzed using RNA sequencing. Data from The Cancer Genome Atlas (TCGA) were used to compare the gene expression profiles of CAFs of breast and prostate cancer patients. The cluster profiler package was employed to perform pathway enrichment analysis, while the gene signature associated with prostate CAFs was identified applying K-means clustering. Kaplan-Meier curves and log-rank tests were used to assess the prognostic significance of the signature in prostate cancer patients. A decision-tree classification approach validated the clustering results and the prognostic relevance of the gene signature.

RESULTS & DISCUSSION

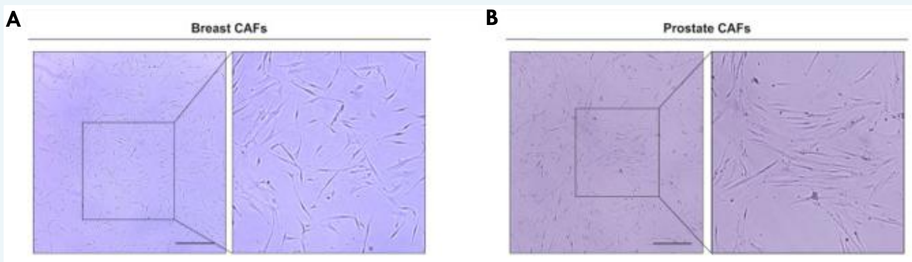

Figure 1. Phase-contrast microscopy images depicting the morphological appearance of breast (A) and prostate (B) CAFs. Scale bar: 100 µm.

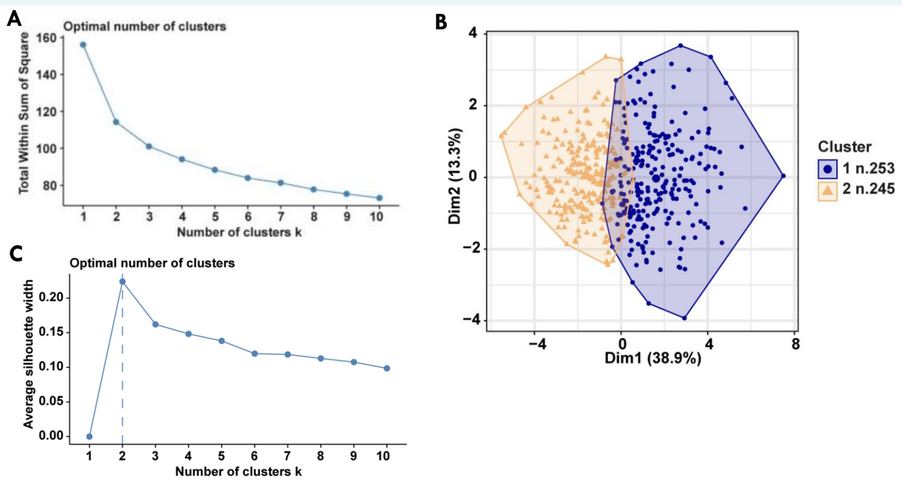

Figure 4. Survival analysis of prostate cancer patients clustered from the TCGA dataset, grouped by cytokine-cytokine receptor interaction pathway gene expression levels. The optimal k-means clusters were determined using within-cluster sums of squares (A) and average silhouette (B) methods. (C) Principal component plot shows patient partitioning by cluster, with counts indicated. (D) Multiple Boxplots showing differential expression of 11 genes between clusters. Disease-free (E) and progression-free intervals (F) for patients in cluster 1 and cluster 2 are shown. (****) indicates $p < 0.0001$.

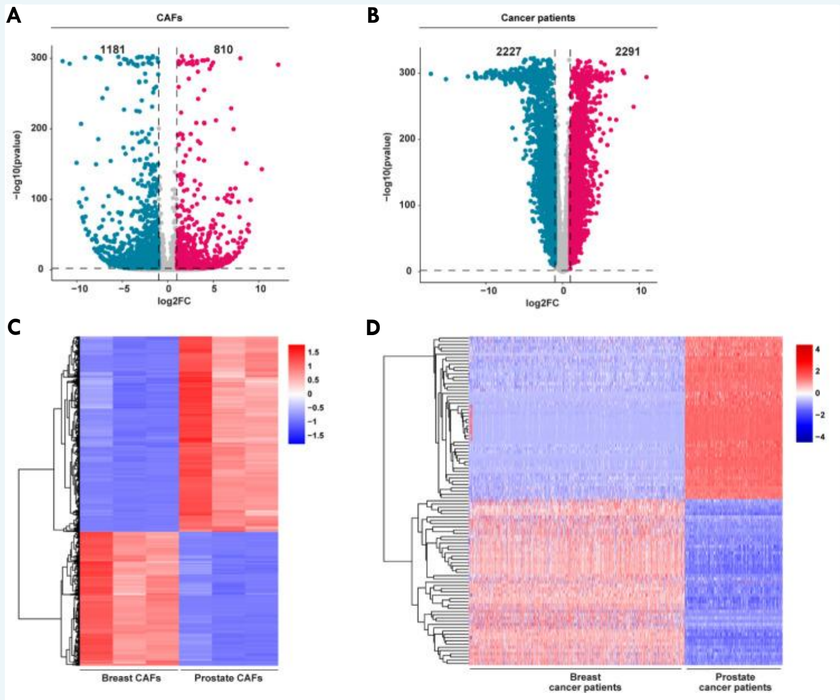

Figure 2. Venn diagram (A), and heat map (C) showing the DEGs in breast and prostate CAFs. Venn diagram (B), and heat map (D) showing the DEGs in breast and prostate cancer patients of the TCGA dataset.

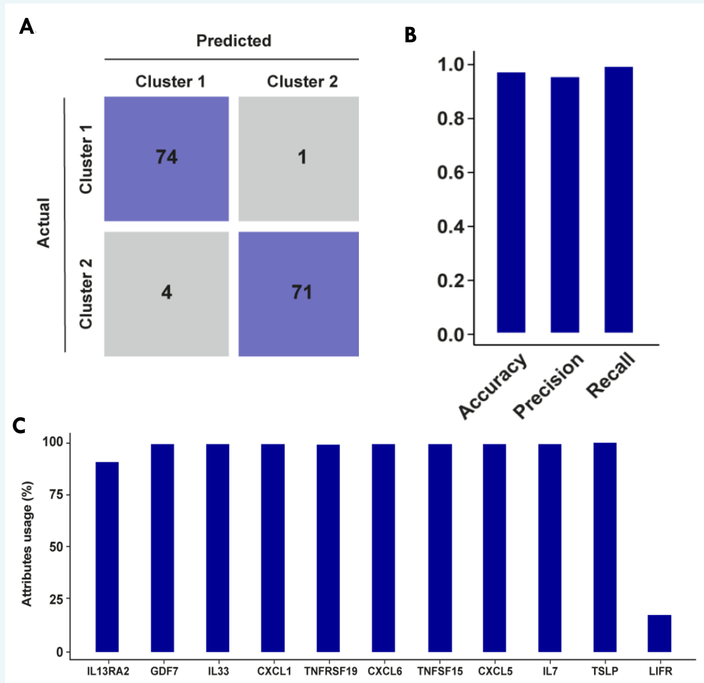

Figure 5. (A) Confusion matrix illustrating model performance on the TCGA dataset, with rows for actual classes and columns for predicted classes. (B) Histogram displaying accuracy, recall, and precision of the model. (C) Percentage usage of 11 genes from the boosting algorithm on the training dataset (25 trials).

Figure 3. (A) The Venn diagram shows the overlap of genes up-regulated in both prostate CAFs and the TCGA cohort of prostate cancer patients. (B) KEGG pathway analysis of 217 common up-regulated genes from both sources, with the X-axis indicating the number of genes in each pathway and the Y-axis listing the KEGG terms ($p < 0.05$).

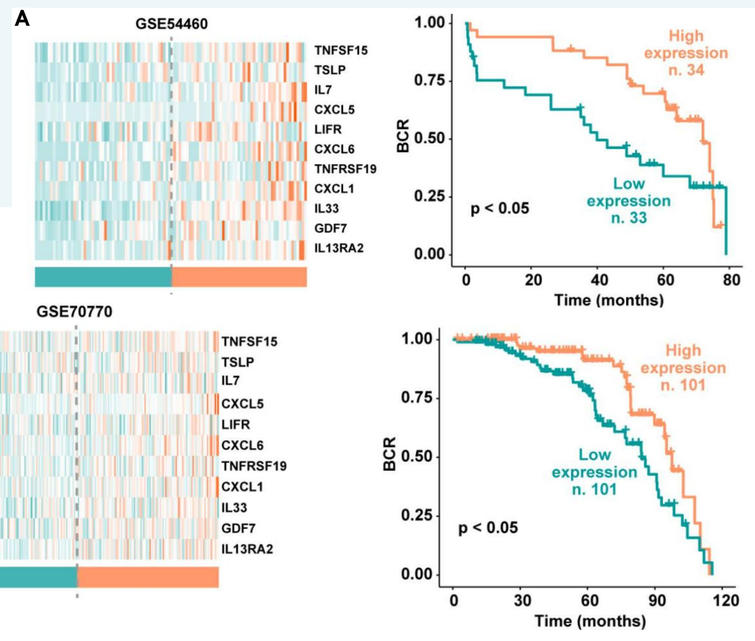

Figure 6. Prostate cancer recurrence is associated with the cumulative levels of genes involved in the cytokine-cytokine receptor interaction pathway. Kaplan-Meier curves illustrate the relationship between high or low expression of these genes and biochemical recurrence (BCR) in prostate cancer patients from the GSE54460 (A) and GSE70770 (B) datasets.

REFERENCES

1) Schwartz SM Clin Chem. 2024; 2) Chen Y et al., Nat Rev Clin Oncol. 2021; 3) Bonollo F et al., Cancers. 2020; 4) ChallaSivaKanaka S et al., Cancer Lett. 2022; 5) Chen H et al., Front Cell Dev Biol. 2024; 6) Martin-Caraballo M et al., Int J Mol Sci. 2024; 7) Talia M. et al., JTM 2024.

CONCLUSION

The prostate CAFs-related gene signature identified might serve as a novel biomarkers for improving the management of prostate cancer patients.