Title: Identification of genes with aberrant expression in metastatic prostate cancer

Authors:
Mina Sattari, Hanna Rauhala, Leena Latonen, G. Steven Bova, Juha Kesseli, Tapio Visakorpi

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Abstract

Prostate cancer significantly impacts male mortality in developed countries, mainly due to the lethal nature of metastases. Understanding the metastatic potential of tumors is crucial for therapeutic strategies. This study focused on a cohort of individuals with samples from metastases of castration-resistant prostate cancer (mCRPC) and their corresponding localized tumors, providing a comprehensive framework to explore disease progression and genetic foundations.

RNA sequencing (RNA-seq) was used to quantify gene expression levels and identify differentially expressed genes. A stringent filtering process was applied to exclude tissue-specific genes. ChIP-seq and ATAC-seq data revealed the presence of transcription factors such as AR, FOXA1, and HOXB13 in regulatory regions of key genes.

Kaplan–Meier survival analysis on 81 patients who underwent prostatectomy assessed the prognostic significance of differentially expressed genes. A Cox proportional hazards model analyzed the association between progression-free survival and factors like age at diagnosis, PSA levels, Gleason score, and pathologic T status.

The study identified 85 protein-coding genes differentially expressed in mCRPC, with 63 upregulated and 22 downregulated. Transcription factor enrichment revealed AR, FOXA1, HOXB13, and other key regulators, suggesting potential therapeutic targets. Progression-free survival analysis identified 16 genes, including FRMPD1, TMEM18, and ZNHIT3, as independent predictors of biochemical recurrence. TMEM18's sensitivity to androgen regulation underscores its impact on prostate cancer progression.

This study highlights potential genes contributing to prostate cancer progression and serving as biomarkers. Further research is necessary to evaluate their mechanistic and prognostic significance.