Abstract ID# 5022: Association of Adaptive Immunity/Inflammatory Genes with Survival in Prostate Cancer

Austin Hopper1, Harris Krause2, Andrew Elliott3, Alex Farrell4, Leisa Sutton5, Pablo Tamayo6, Hannah Carter7, Ahmed Shabaik8, Andrew Sharabi8, Peter Kuhn9, Emmanuel S. Antonarakis10, Chadi Nabhan11, Napoleone Ferrara12, Fotis Asimakopoulos13, Ida Deichaite14, UC San Diego, 2Caris Life Sciences, 3USC, 4Karmanos Cancer Institute, 5University of Minnesota

Background

• Advances in immunotherapy have had little impact on prostate cancer (PCa) treatment outcomes.
• We have previously examined the immune microenvironment in both localized and metastatic PCa and found that primary PCa shows local inflammation/adaptive immunity whereas metastatic disease shows a shift towards immune suppression (Deichhaite, 2022).
• Herein, we examine immune remodeling in PCa by evaluating changes in gene expression between localized and metastatic disease with heterogeneous treatment patterns in both primary and metastatic samples.

Methods

• Tumors from PCA (N = 5,419) were tested at Caris sequencing (592-gene or whole exome) and RNA (whole transcriptome).
• Samples collected from the prostate gland (N = 3,284) or metastatic sites (N = 2,135) were analyzed.
• The Mann-Whitney U test was applied as an appropriate, with P-values adjusted for multiple comparisons (q < .05).
• Real-world overall survival (OS) data was obtained from insurance claims and Kaplan-Meier estimates were calculated for molecularly defined subpopulations. Survival for tumors with high (+) and low (-) expression of genes of interest, defined as top and bottom quartile of expression (transcripts per million, TPM) across all tumors, was investigated.

Results

1. Expression of immune related genes between primary and metastatic sites

We examined differences in expression of genes associated with immune regulation between primary and metastatic sites. This suggests that site-based differences influence immune signaling.

2. Correlation between FOSS and upstream genes

A weak relationship between TNFα and FOSS was observed regardless of site. SELE and IL6 genes had a stronger association with FOSS in tumors biopsied from the primary as opposed to the metastatic site.

3. Correlation between TNFα and immune checkpoint genes

A strong correlation is observed between immune checkpoint genes and TNFα ligand across tumors biopsied at either a primary or metastatic site.

4. Outcomes data in primary vs metastatic sites

High expression of ADAMTS4 is associated with better overall survival (OS) in the primary site but is associated with worse OS in the metastatic site. A similar trend is observed for IL2 and CEBPD gene expression.

Conclusions

• We identified significant differences in the expression of inflammatory regulators and cytokines between localized and metastatic PCa tumors, which correlate with OS.
• These changes in the immune microenvironment can be leveraged for rational immunotherapy development and better targeted approaches.