Dissecting the significance of ACP1 gene alterations in prostate cancer (PCa)

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Abstract

Background:
- The acid phosphatase 1 (ACP1) gene encodes low molecular weight protein tyrosine phosphatase (LMPTP), which is overexpressed in PCa.
- Previous studies demonstrate that LMPTP plays a critical role in PCA growth and metastasis and is evolving as a potential therapeutic target.
- Thus, we analyzed ACP1 expression in primary and metastatic PCa samples and the association of ACP1 with molecular profiles and clinical outcomes.

Methods:
- NextGen sequencing of DNA [592-gene/whole exome] and RNA [whole transcriptome] was performed for PCa specimens (n=5028) submitted to Caris Life Sciences.
- DNA mutational profiles were analyzed for ACP1
- Gene set enrichment analysis was used to assess the Hallmark collection of cancer pathways.
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- Gene set enrichment analysis of the Hallmark collection of gene sets (MSigDB).

Results

Figure 1. Transcriptional expression of ACP1 in prostate cancer across tumor biopsy sites. (A) Differential expression of ACP1 across tumor biopsy sites. (B) Sample size noted in parentheses for each tumor site. (C) Volcano plot of differentially expressed genes in ACP1-High vs. ACP1-Low samples across tumor sites. (D) Gene set enrichment analysis of the Hallmark collection of gene sets (MSigDB).

Figure 2. Genomic landscape associated with ACP1 expression in prostate cancer by tumor site. (A) Oncoprint of recurrent alterations occurring in ≥3% of the overall study among prostate (A), lymph node (B), metastases subpopulations (C) stratified by ACP1 expression. *p<0.05, ***p<0.001, ****p<0.0001.

Figure 3. 3D expression is associated with changes in cell cycle and metabolic pathways. (A-C) Volcano plot of differentially expressed genes in ACP1-High vs. ACP1-Low samples across tumor sites. (D) Gene set enrichment analysis of the Hallmark collection of gene sets (MSigDB).

Conclusions
- In the largest study investigating the significance of ACP1 expression in PCa, we demonstrate that ACP1-high tumors exhibit a distinct molecular profile enriched for TP53 alterations and associated with a ‘cold’ TME.
- Our findings may provide a rationale for novel therapeutic targeting of ACP1-high tumors.

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