Novel Associations Between the Immune Landscape of Prostate Cancer and Postoperative Radiation Response


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Background

• Role of immunotherapy in prostate cancer is not well defined
• Sipuleucel-T: first FDA approved cellular therapy shown to improve OS (Kantoff et al. NEJM 2010)
• Negative randomized trials for ipilimumab (CTLA-4) for primary endpoint OS (Beer et al. JCO 2017; Kwon et al. Lancet Onc 2014)
  • Improved PSA response suggesting therapeutic effect in subset
• Understanding immune infiltrate may be critical to predict response to various therapeutic strategies
• Difficult to histologically assess intra-tumoral immune infiltrate directly
Purpose

Leverage high throughput transcriptomic profiling and computational methods to characterize the immune landscape of localized prostate cancer.
Methods

• Retrospective (N=1567) and prospective (N=7826) radical prostatectomy samples on a clinical grade microarray platform
  • Clinical outcomes available on retrospective data only
• Immune Content Score derived from immune cell specific genes in the literature
• Relative fractions of immune cells estimated using Cibersort
Immune Pathways Cluster in Prostate Cancer

Tumor samples
N=9393
Immune Content Score May Predict Response to Post-op RT

Multivariate (adjusting for clinicopathologic variables and ADT use) interaction: $P$-value $= 0.017$
PD-L2

PDL1

PDL2

Log$_2$ Intensity

p=0.013, HR=1.17 [1.03-1.33]
p=0.014, HR=1.25 [1.05-1.49]
p=0.0033, HR=1.45 [1.13-1.86]
Conclusions

• Computationally estimated the immune infiltrate in 9393 localized prostate cancer samples and identified a potentially high-immune subset
• Immune content appears to be prognostic as well as predict response to post-op radiotherapy
• First report of PD-L2 as a potential novel target for checkpoint inhibition in prostate cancer