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NOVEMBER 9–14
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Society for Immunotherapy of Cancer

Impact of EphB4 and PD-1 targeting on immune infiltrate in advanced bladder cancer

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Disclosures

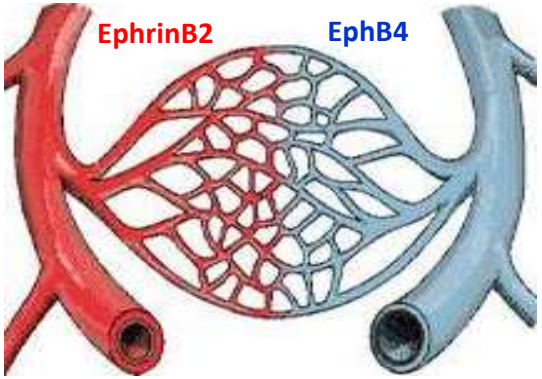
Research funding from:

- Merck, Pfizer

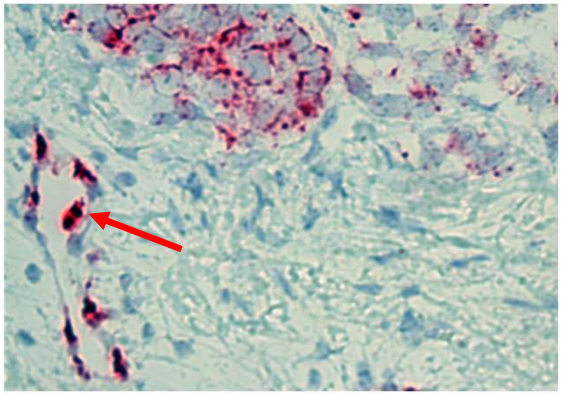
Advisory Board:

- Pfizer, Tempus, Janssen, Seagen

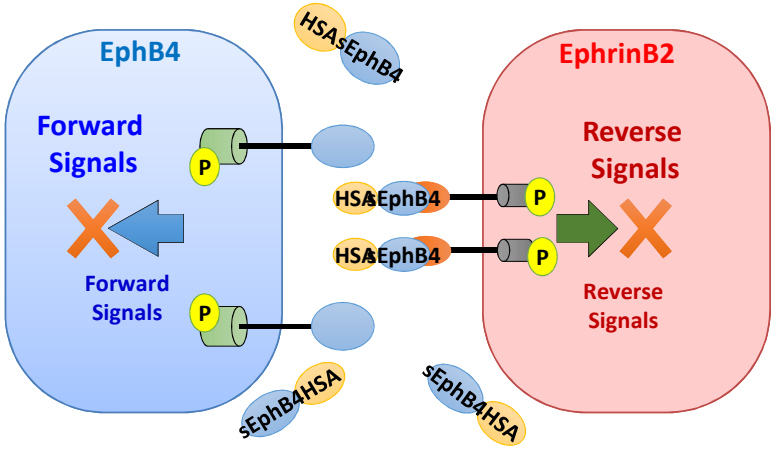
Aim: Analyze alteration in tumor immune markers in paired human tumors following treatment with sEphB4 or sEphB4 plus PD-1 antibody in spatial temporal context using GeoMx technology

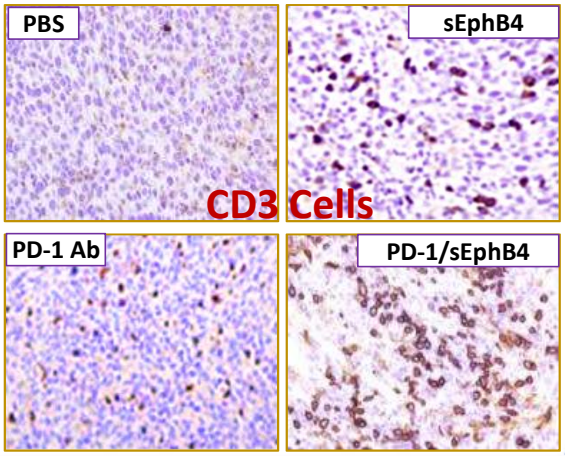


Embryonic Vessel Maturation



EphrinB2 re-induction in human tumor

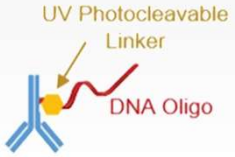




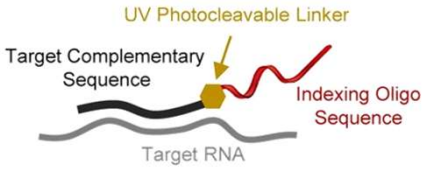
GeoMx® DSP Enables Spatial, High-Plex Protein & RNA Profiling

High-Plex Mixtures of Proprietary Reagents

Protein reagents
Oligo-labeled antibodies



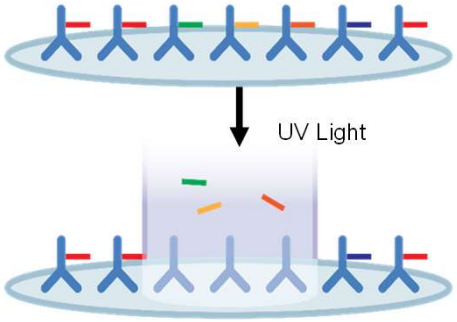
RNA reagents
Oligo-labeled probe



Profile Regions of Interest on FFPE slide

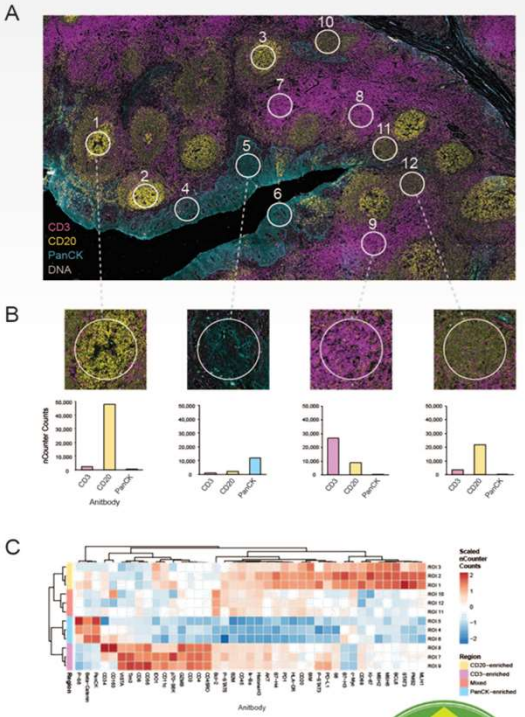
GeoMx™ Digital Spatial Profiler

Label FFPE Slide with Probe Mix



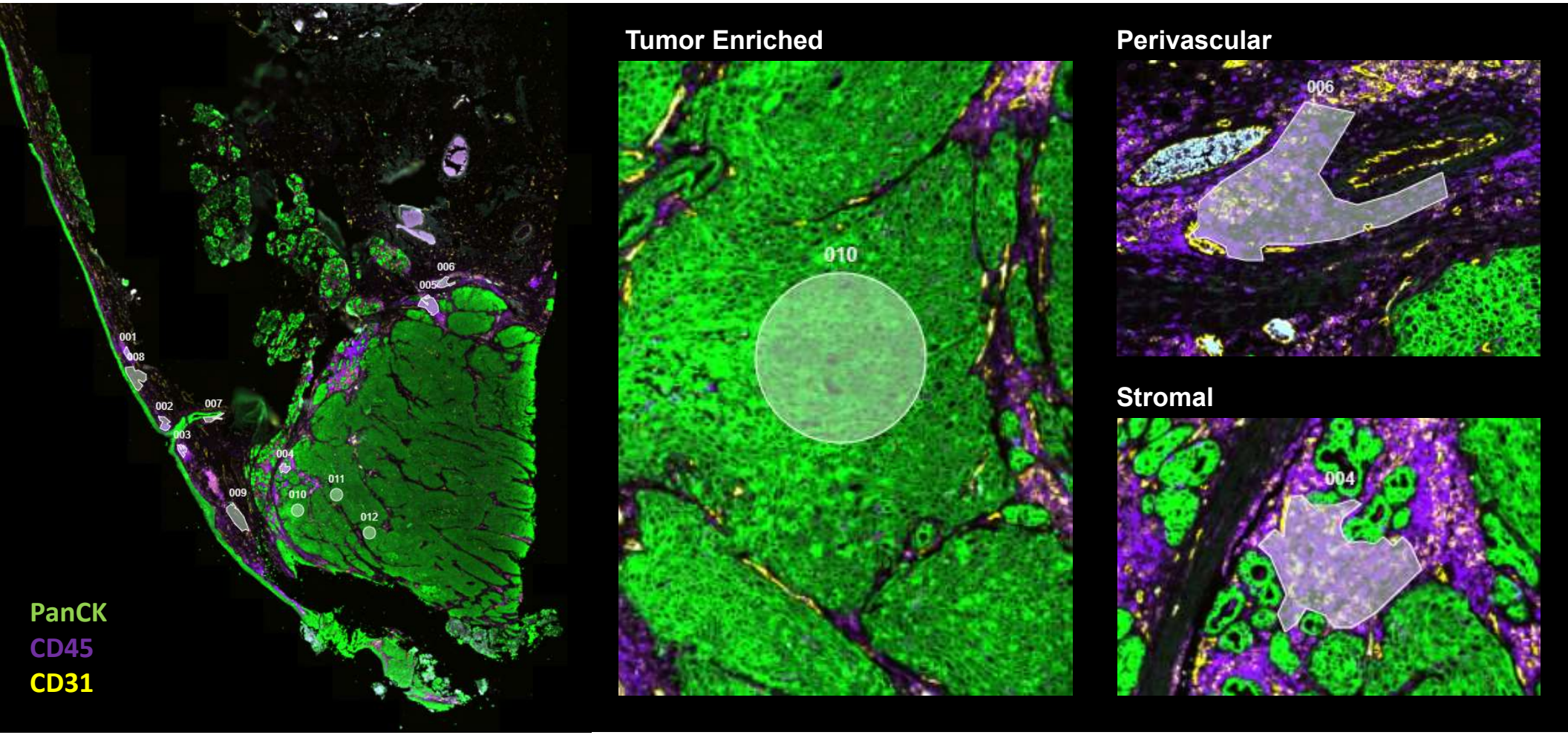
Illuminate Region of Interest, as Small as a Single Cell

Rich Data Sets of Biology, Region by Region

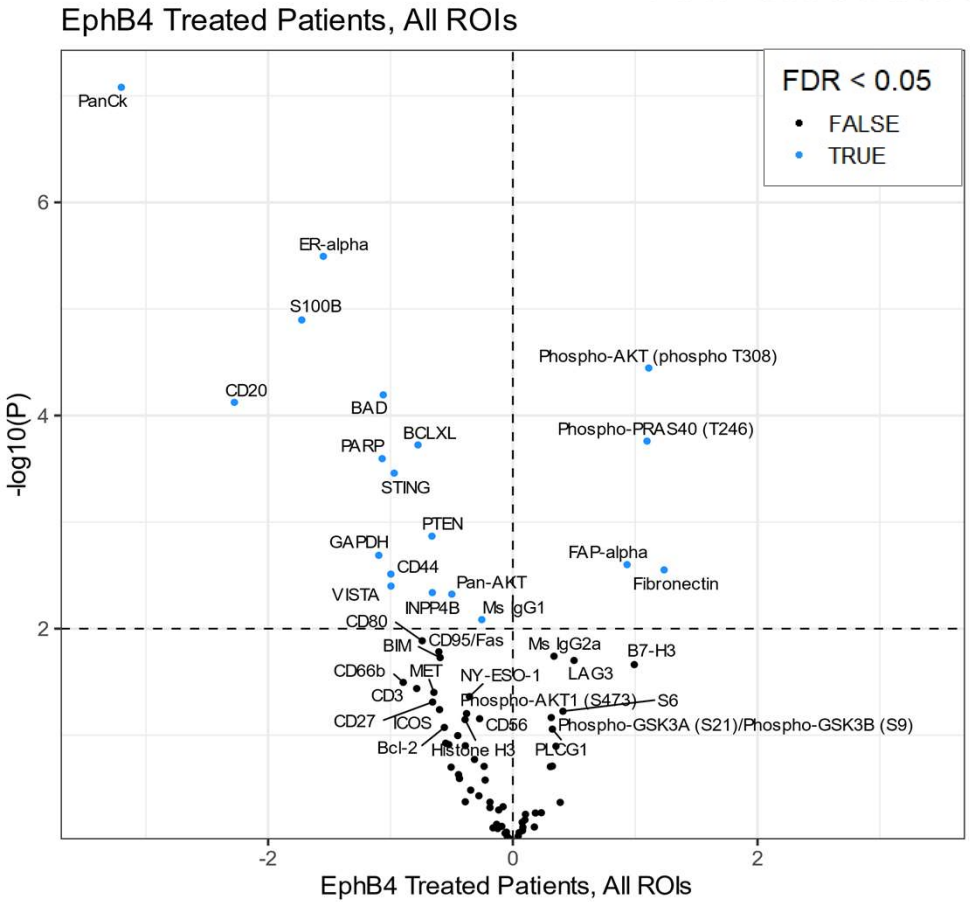


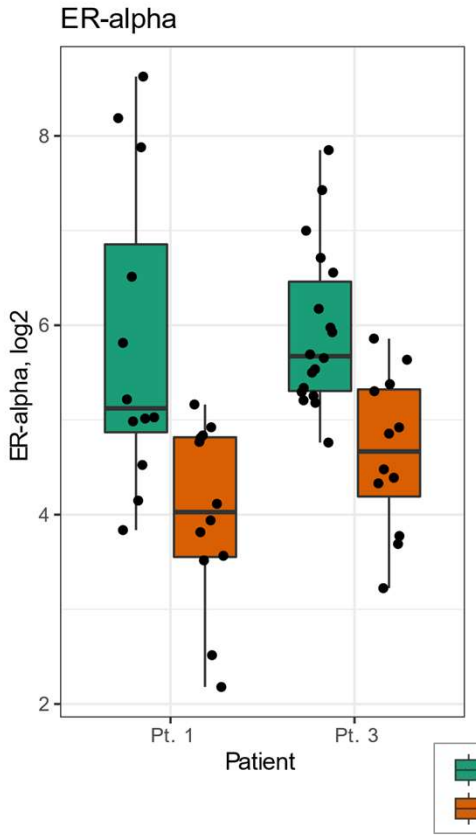
ROI selection strategy: Enriching for functional areas of tumor biology modulated by EphB4

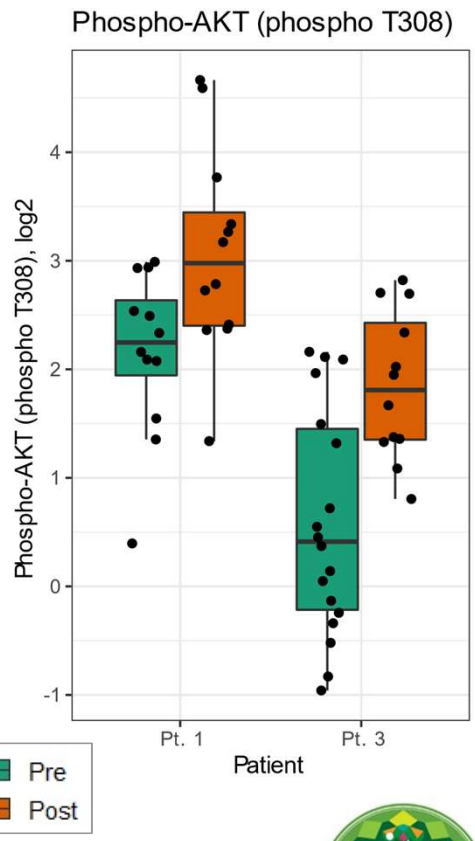
Pre-treatment EphB4 patient sample



Protein profiling: soluble EphB4 patients show differentiation based on estrogen-induced and AKT-associated cell proliferation

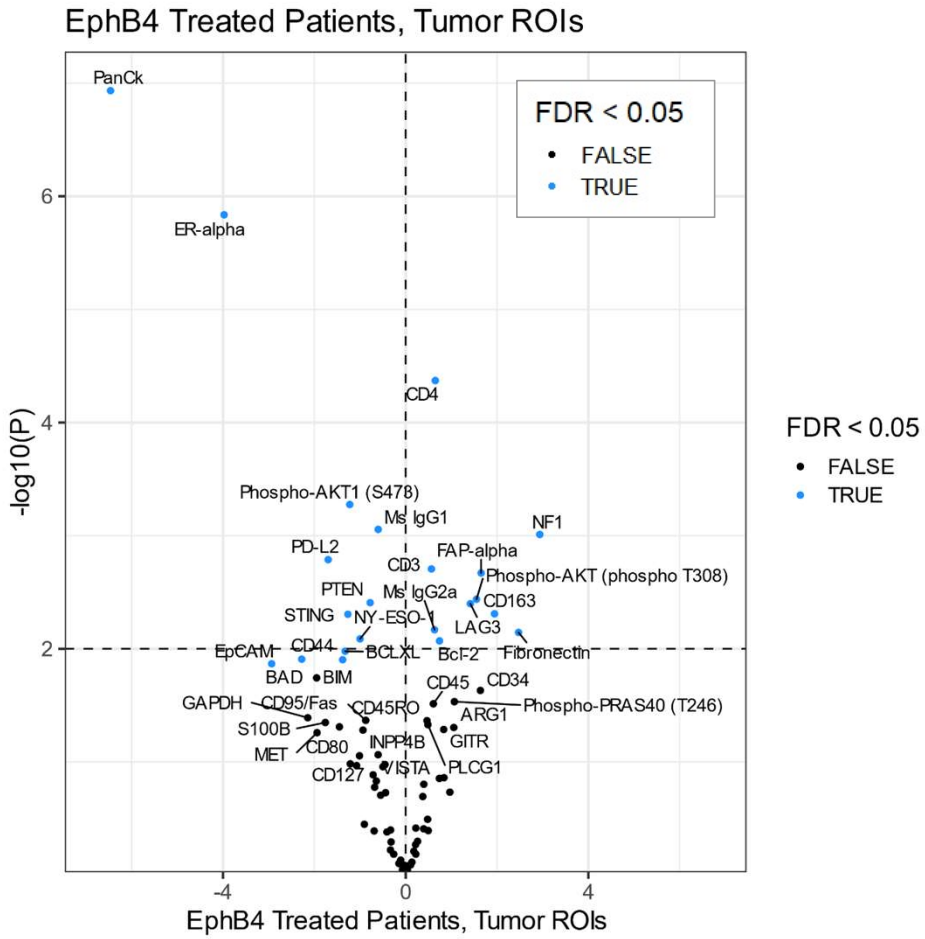


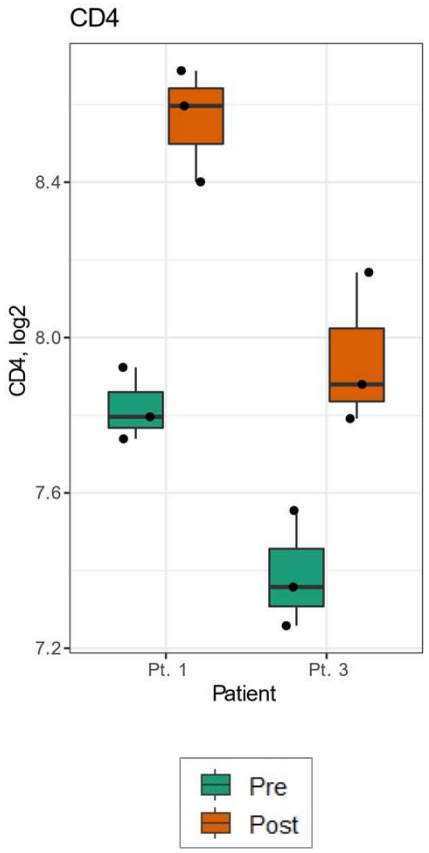




Pre-Treatment ← Enrichment, Log2(FC) → Post-Treatment

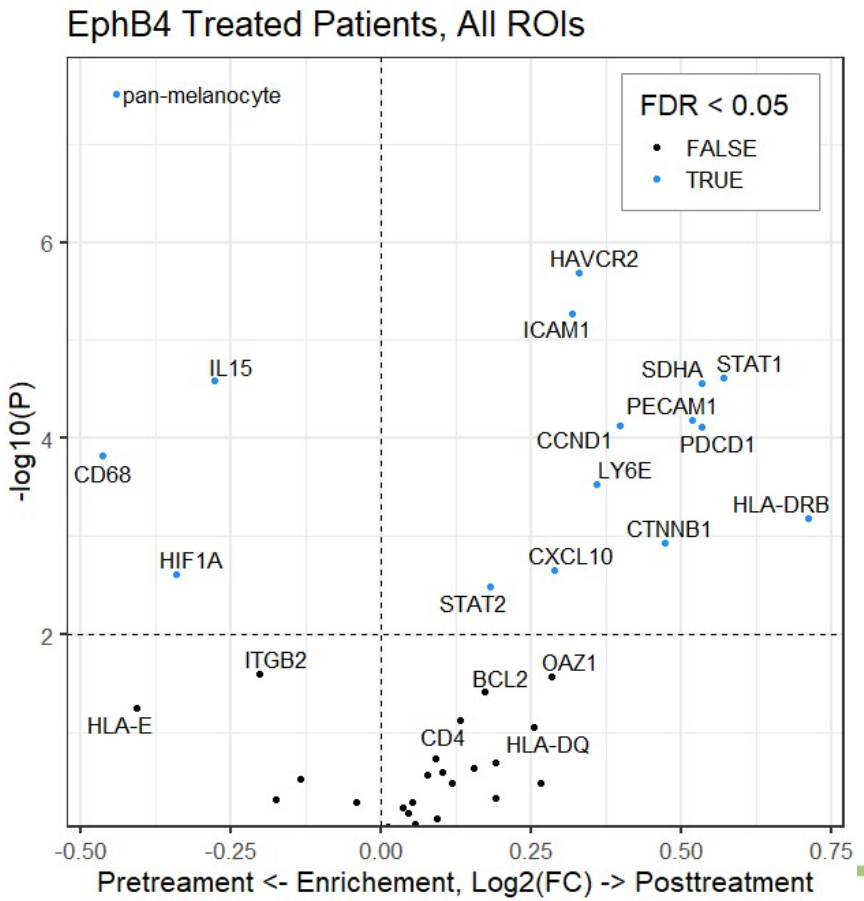
macrophages, T-cells and checkpoint regulators (LAG3) are increased post-treatment

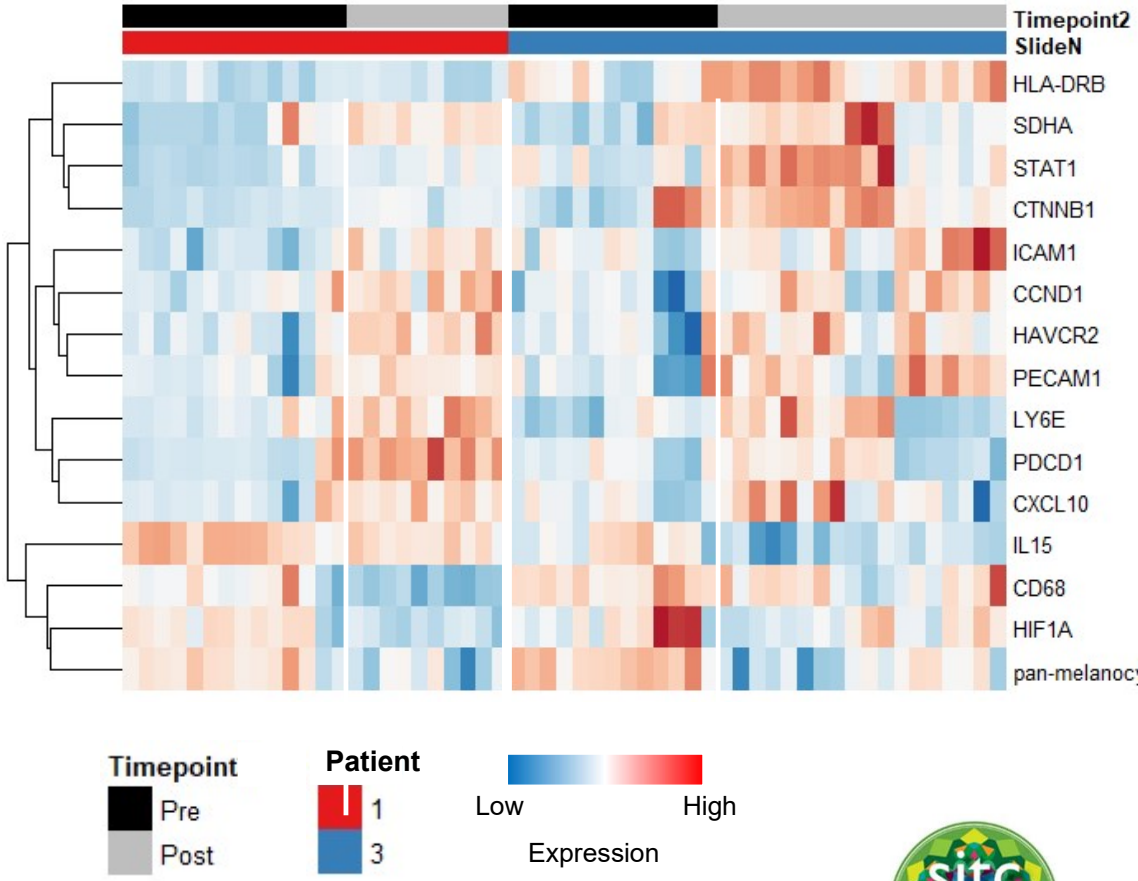




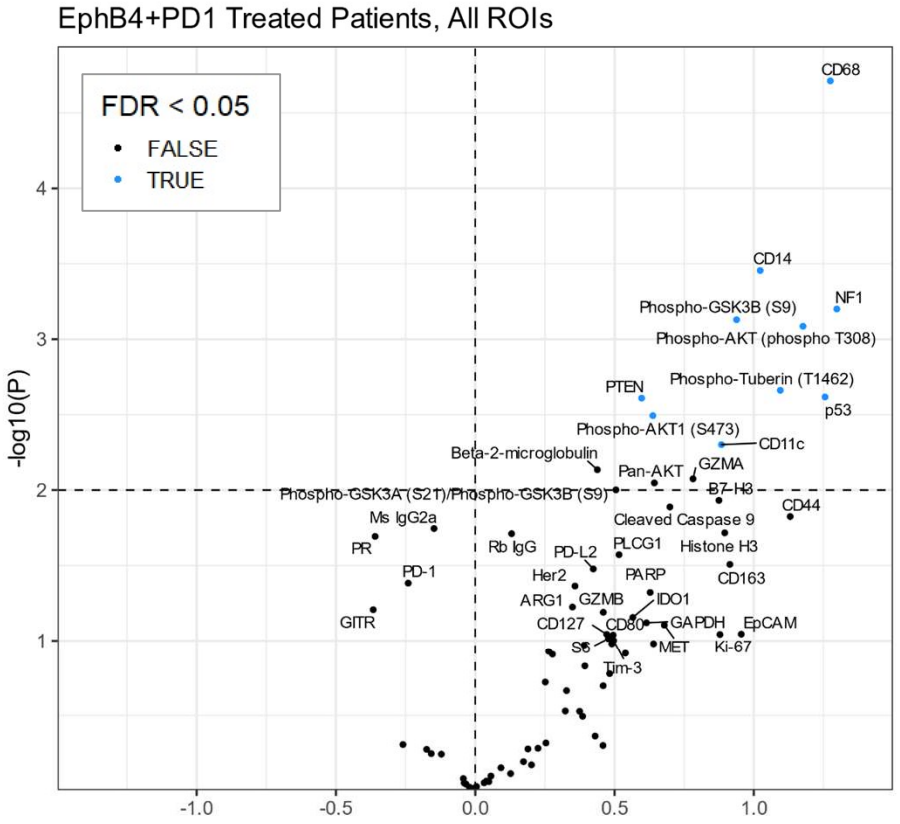
Pre-Treatment ← Enrichment, Log2(FC) → Post-Treatment

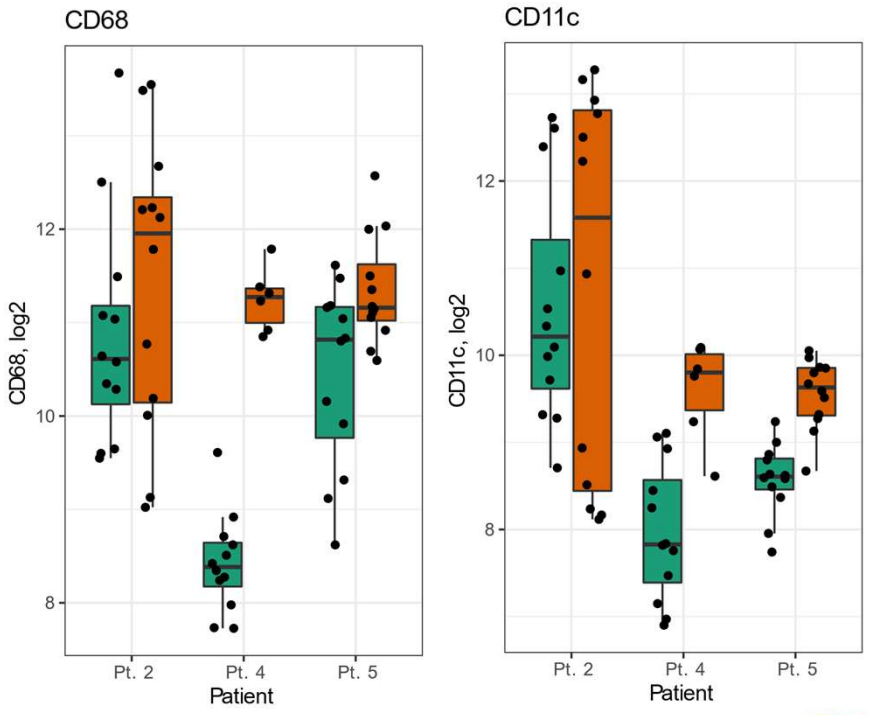
RNA profiling: soluble EphB4 patients show induction of inflammatory signaling





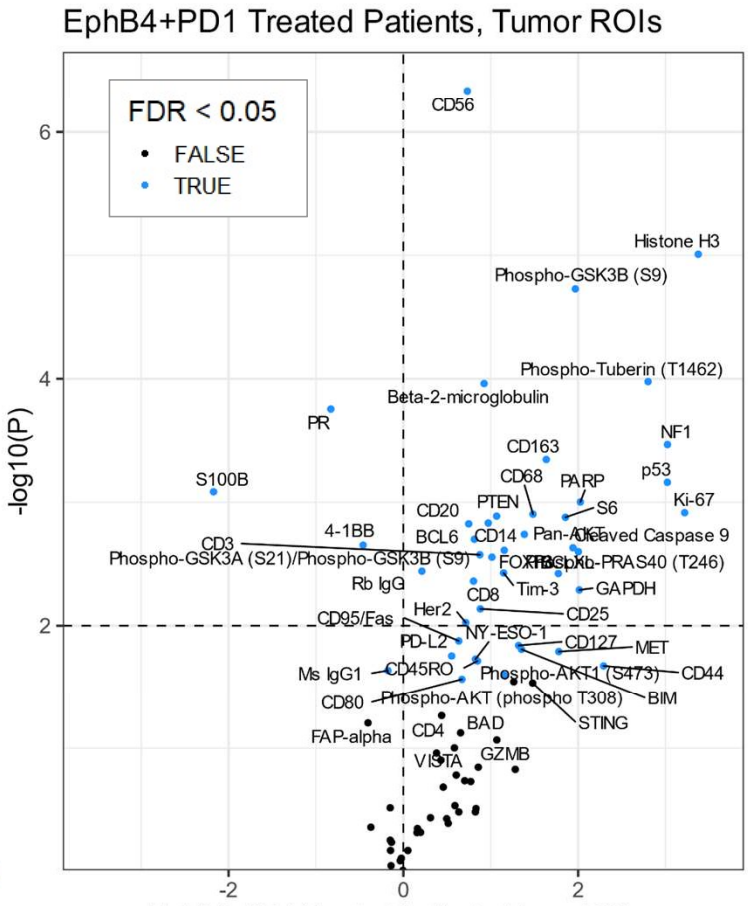
Protein profiling: soluble EphB4+PD1 patients show enrichment in CD68 (*esp* Pt. 4) and dendritic cells across all ROIs

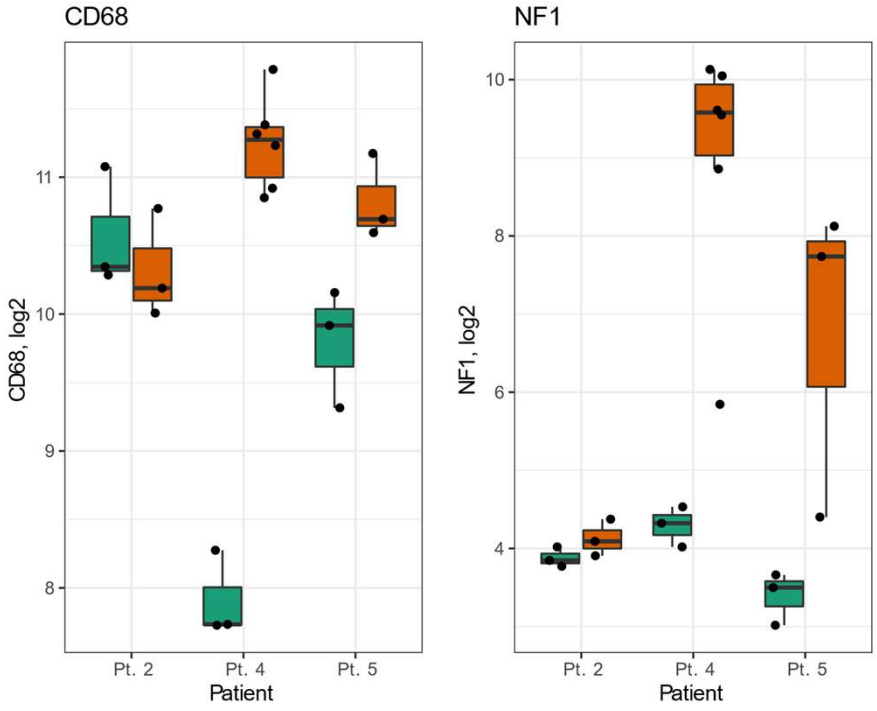




Pre-Treatment ← Enrichment, Log2(FC) → Post-Treatment

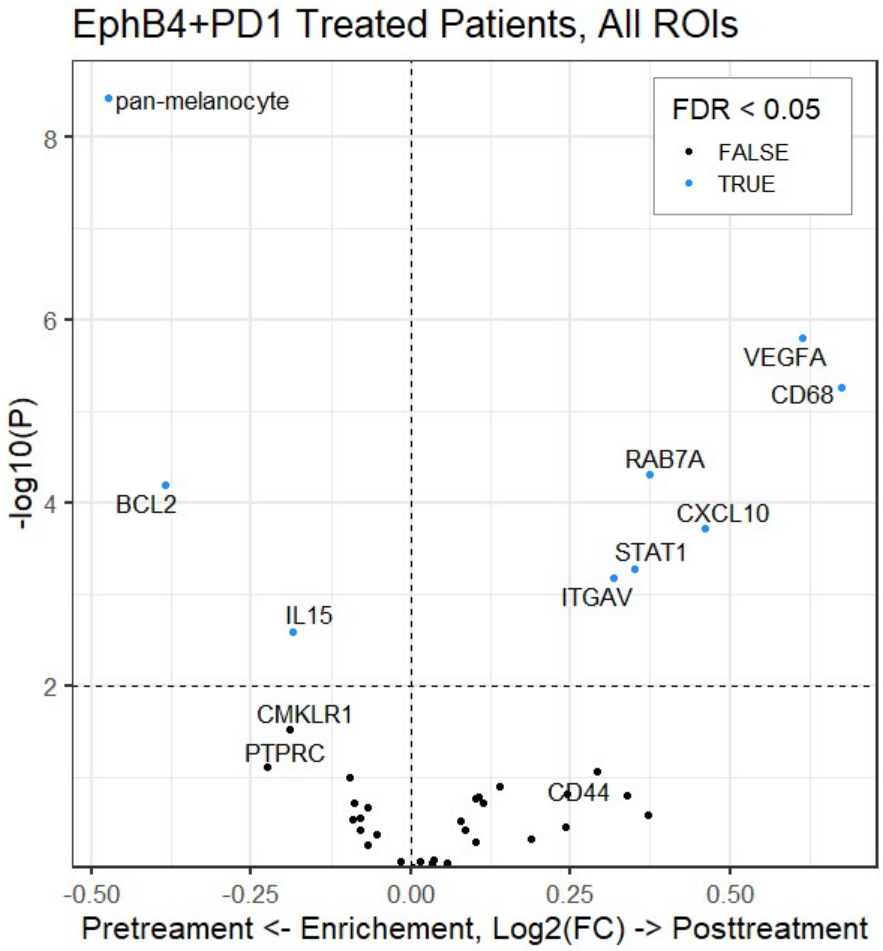
Protein profiling: Within Tumor, macrophages show inter-patient variation and NF1 shows similar pattern as seen in monotherapy

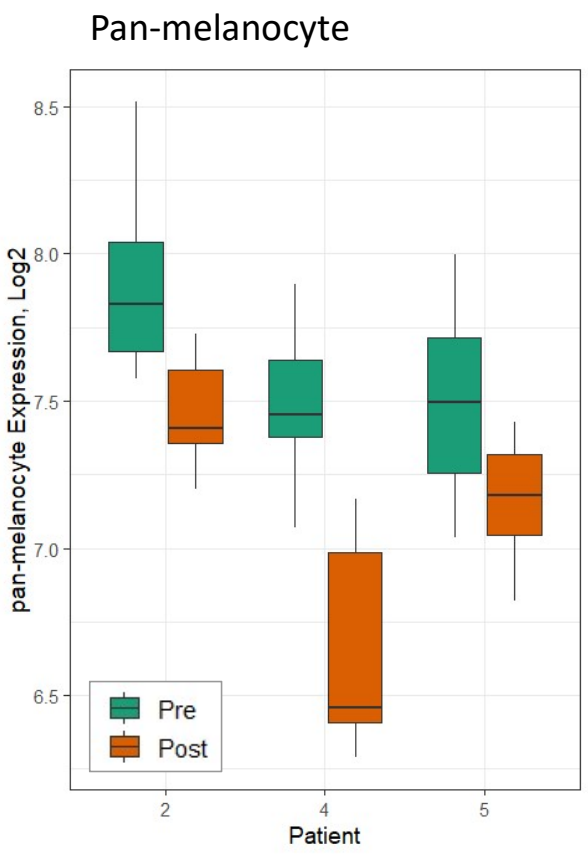


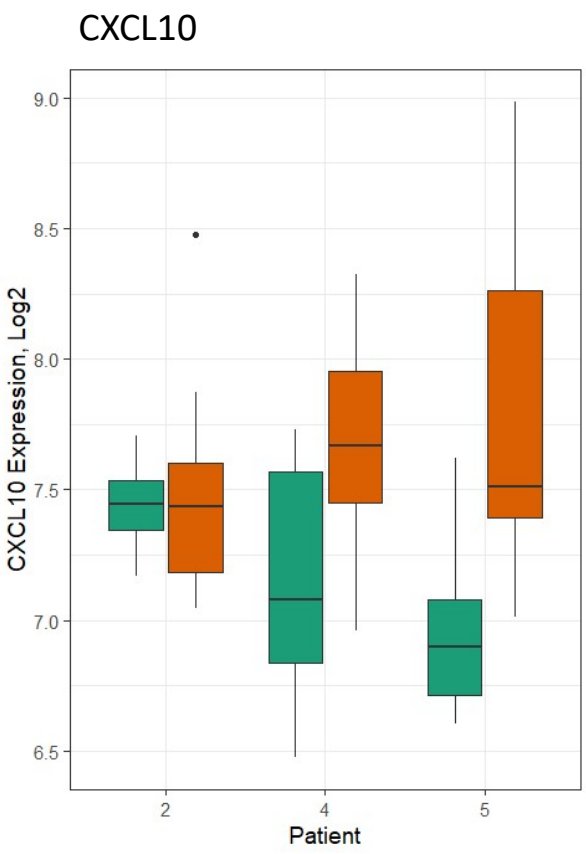


Pre-Treatment ← Enrichment, Log2(FC) → Post-Treatment

RNA profiling: EphB4 patients show induction of inflammatory signaling







Conclusions:

These discoveries provide insights into the mechanism of action of soluble EphB4 combination therapy in bladder cancer, providing support for a role of soluble EphB4 acting as an adjuvant for PD1 therapy.

Our results highlight the ability of soluble EphB4 to activate the immune system in key structures within the tumor microenvironment during combination therapy.

acknowledgement

USC - Norris Cancer Center

Troy McEachron
John Carpton
Imran Siddiqi
Alexandra Jackovich
Binyun Ma
Gangning Liang
Parkash Gill

Nanostring Technologies

Sarah E Warren
Jason Reeves
Tyler Hether
Jason Yeon
Richard Mangio
Jason W Reeves
Yan Liang