BITT
Boston Immune
Technologies & Therapeutics

TNFR2 Antagonists for Treatment of Cancer

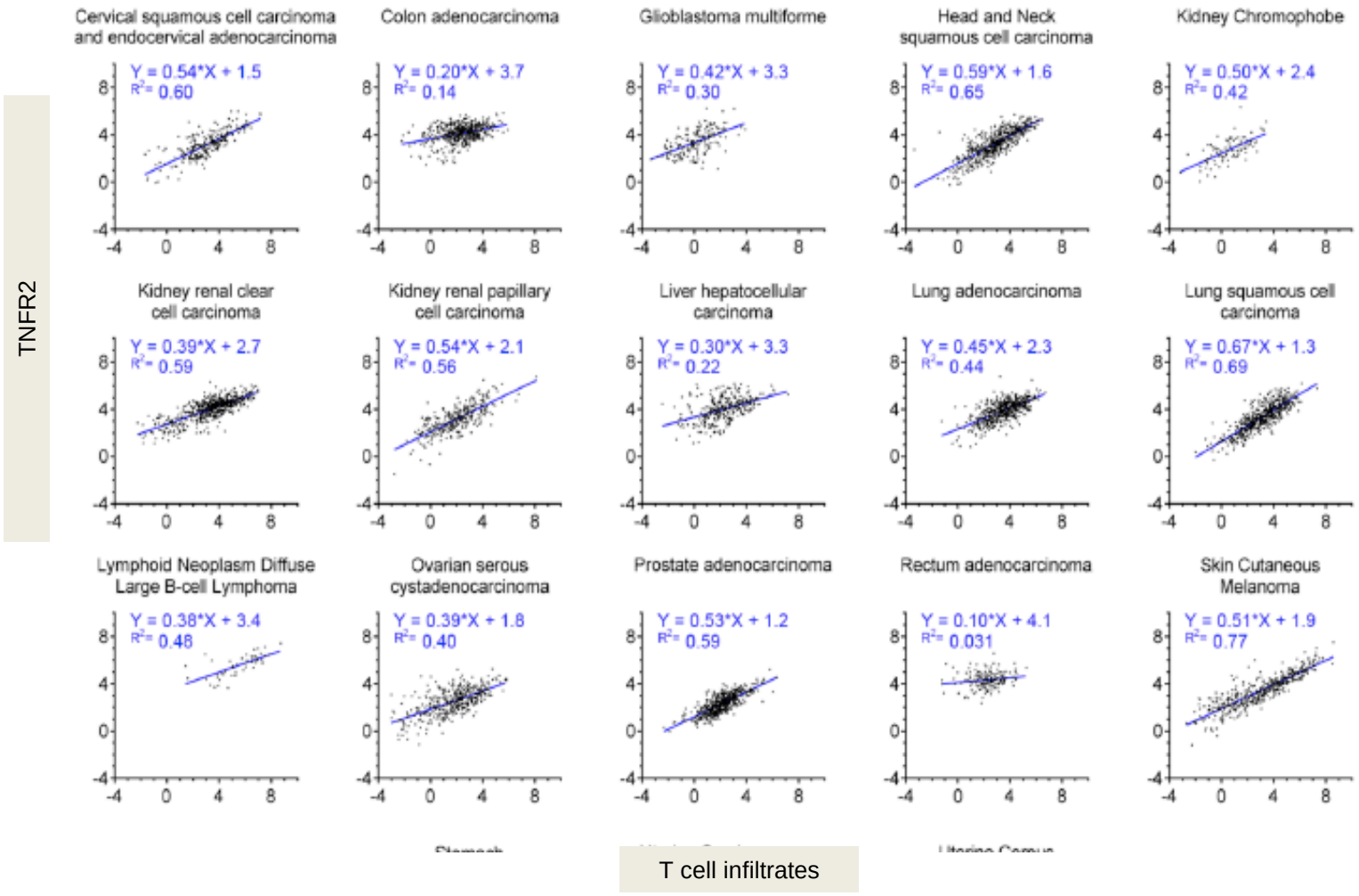
Novel Cancer Immunotherapy

Cancer Progress Mach 7, 2016

BITT and TNFR2 (TNFRSF1B)

- **BITT** has a patent portfolio on and multiple lead antibody candidates that target TNRFR2
  - **TNFR2** is a marker and signaling pathway for expansion of the most potent and abundant Tregs of the cancer micro-environment
  - **TNFR2** is a broadly expressed surface oncogene for aiding human cancer cell growth
- **BITT** is the leader in TNFR2 for cancer, a field that is growing rapidly:
  - Recent TNFR2 papers by:
    - Stanford University (*Nature Genetics*)
    - Broad Institute (*Science*)
    - Medimmune/Astra Zeneca (*Oncotarget*)
  - Collaborations with:
    - Dana Farber Cancer Institute (Colon cancer)
    - University of Pennsylvania (Metastatic melanoma)
    - Stanford University (Cutaneous T cell lymphoma)
    - Harvard/MGH (Ovarian cancer)

Diverse human tumors have high TNFR2 expression associated with T cell infiltrates



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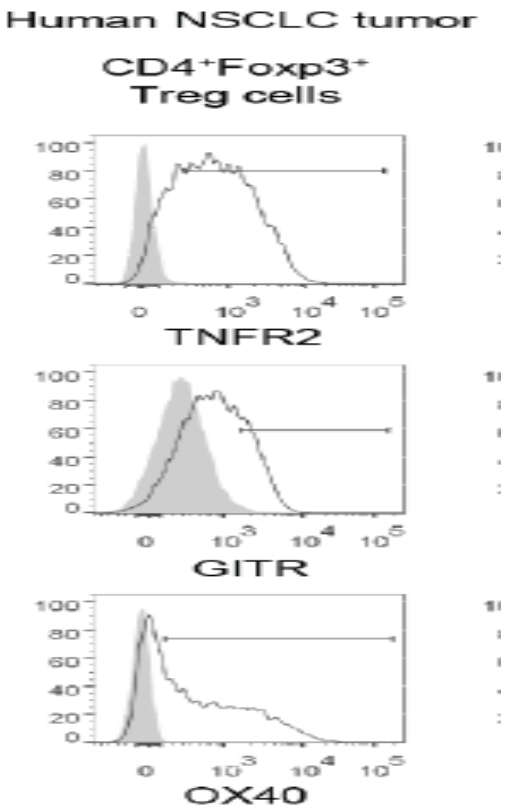
Oncotarget 2016, Medimmune/AstraZeneca

The Cancer Genome Atlas

TNFR2 Tregs Compared to Popular Targets

- TNFR2 compared to other targets in the infiltrate
  - GITR and OX40
  - Tregs expressing each of the targets
  - TNFR2 has more expression in the tumor microenvironment
- TNFR2 is the dominant protein expressed in the tumor microenvironment



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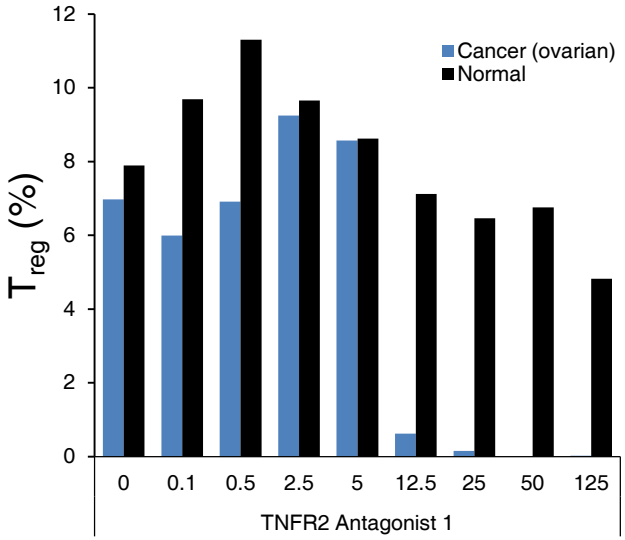
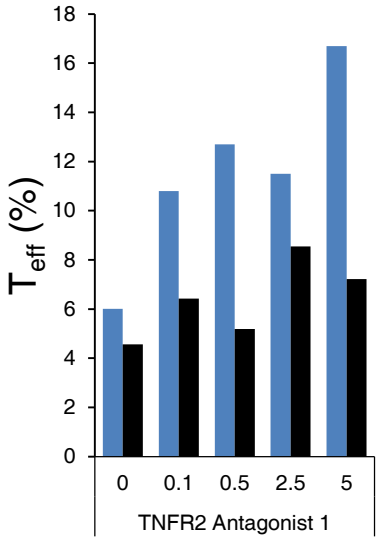
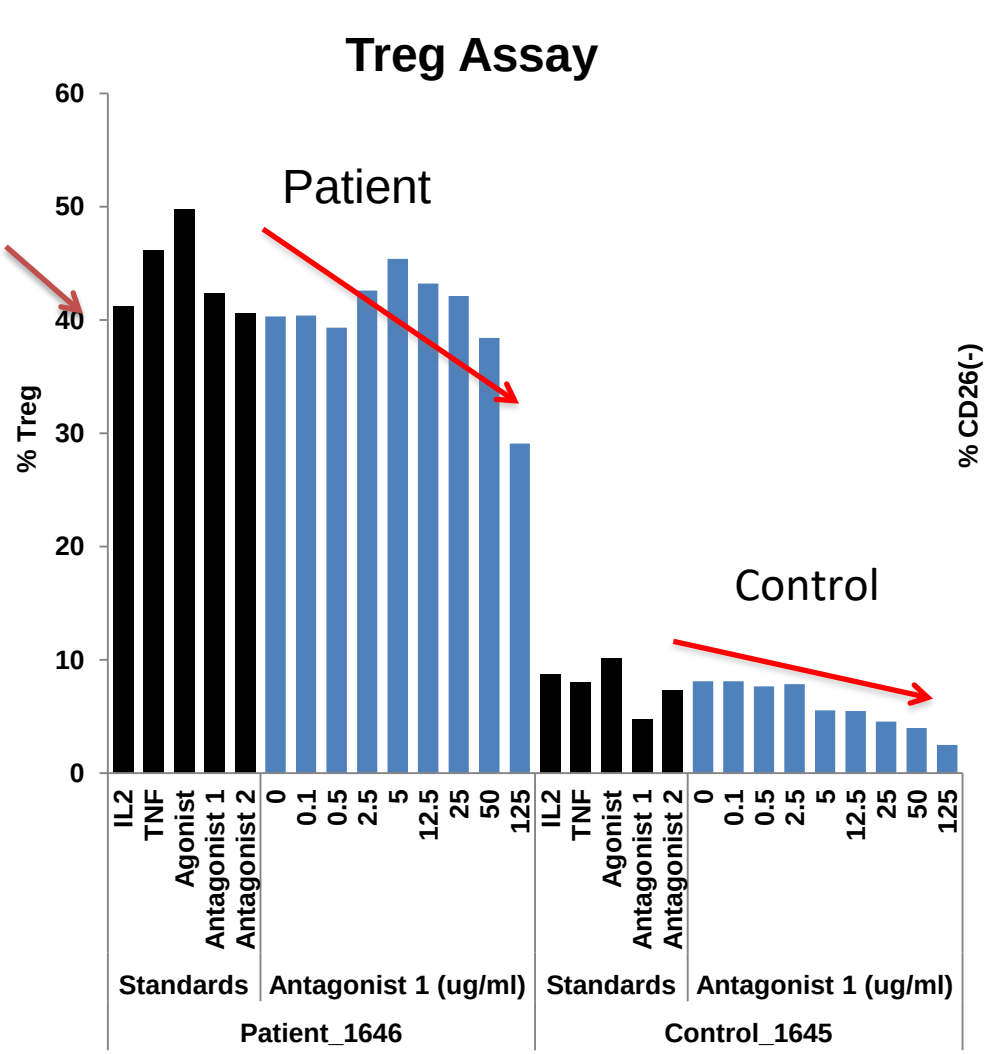
Antagonist antibodies have specificity for the Tregs of the human tumor micro-environment

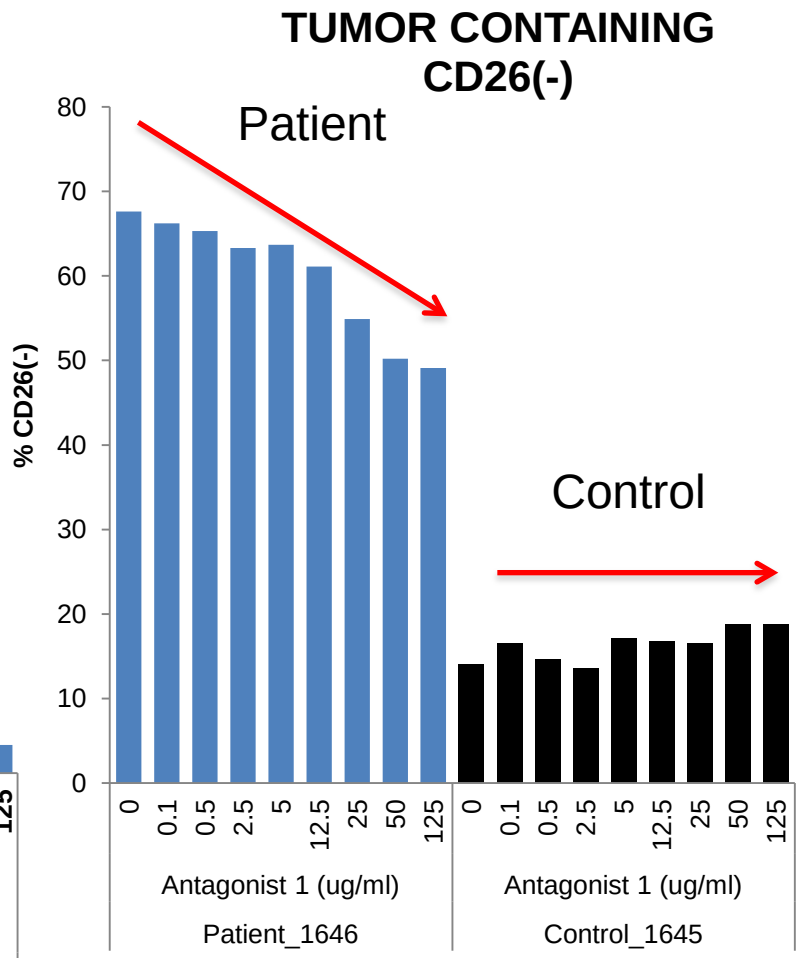
- Ovarian cancer ascites Tregs (untreated subject)





Impact of TNFR2 Antagonists on CTL





Conclusions: TNFR2 antagonist targets Tregs directly and tumor directly
Normal CD26- T cells resistant to TNFR2 antagonist