immunoSEQ®

HEMATOLOGY/ONCOLOGY

CASE STUDY

PD-1 blockade induces responses by inhibiting adaptive immune resistance

Tumeh PC, *et al.* (2014) *Nature* 515(7528):568–71
NOVEMBER 2014

WHY IMMUNOSEQ?

The immunoSEQ Assay enables the monitoring of treatment effects on tumor infiltrating lymphocytes (TILs)

immunoSEQ metrics such as clonality and proportion of T-cell infiltrates have predictive value in evaluating response to anti-PD-1 therapy

amplify **discovery**™

CASE STUDY: PD-1 blockade induces responses by inhibiting adaptive immune resistance — Tumeh PC, *et al.* (2014) *Nature* 515(7528):568–71

BACKGROUND

- Therapies targeting the programmed death-1 (PD-1) receptor have shown unprecedented rates of durable clinical responses in patients with various cancer types
- In a Phase 1a clinical trial evaluating the safety and efficacy of the anti-PD-1 monoclonal antibody pembrolizumab (MK-3475) in advanced melanoma, tumor infiltrating lymphocytes were analyzed and correlated with outcomes

AIM

To determine whether pre-existing tumor-infiltrating $CD8^+$ T cells (TILs) inhibited by PD-1/PD-1 ligand (PD-L1) engagement represent key factors in determining clinical response to PD-1 blocking therapy

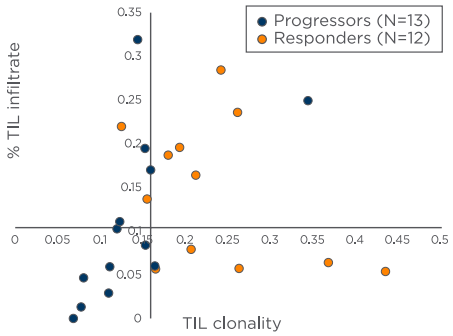
METHODS

Serial biopsies in 25 melanoma patients

1. Biopsy → gDNA → **immunoSEQ® (TCRB)**
2. **Anti-PD-1 therapy**
3. Biopsy → gDNA → **immunoSEQ (TCRB)**

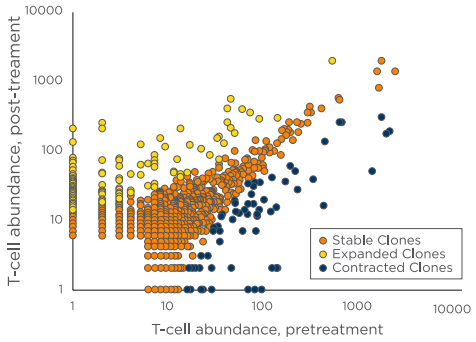
RESULTS

Quantitative sequencing of T-cell receptor beta (TCRB) in patients with melanoma

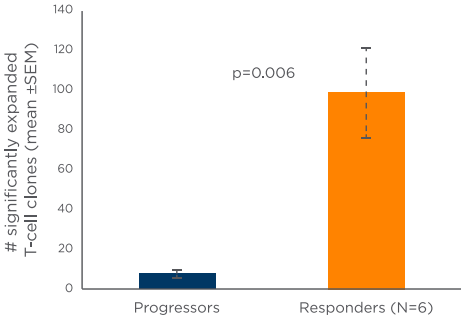


Progressors were associated with lower levels of TILs and lower TIL clonality

Measurement of drug effect in the tumor



Representative scatterplot of clones from a responding tumor



Clonal expansion in terms of clinical response

CONCLUSIONS

- Responding patients showed significant proliferation of pre-existing clones post-treatment
- Pretreatment samples from patients responding to anti-PD-1 therapy showed a higher proportion of TILs and more clonality, while samples from progressors showed lower levels of TILs and greater diversity

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