PD-1 blockade induces responses by inhibiting adaptive immune resistance


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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
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®
2. Anti-PD-1 therapy
3. Biopsy → gDNA → immunoSEQ

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

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