acid and MTOR metabolic pathways as a potential novel therapeutic targets for complementary therapy to restore immune function in melanoma and SCC patients.

Ethics Approval This study was performed under an IRB approved protocol.

### Checkpoint blockade therapy

#### P854 CONSTRUCTION OF THE IMMUNE LANDSCAPE OF DURABLE RESPONSE TO CHECKPOINT BLOCKADE THERAPY BY INTEGRATING PUBLICLY AVAILABLE DATASETS


#### Background

Immune checkpoint blockade (ICB) has greatly advanced the treatment of melanoma. A key component of ICB is the stimulation of CD8+ T cells in the tumor. However, ICB therapy only benefits a subset of patients and a reliable prediction method that does not require invasive biopsies is still a major challenge in the field.

#### Methods

We conducted a set of comprehensive single-cell transcriptomic analyses of CD8+ T cells in the peripheral blood (mPBL) and tumors (mTIL) from 8 patients with metastatic melanoma.

#### Results

Compared to circulating CD8+ T cells from healthy donors (hPBL), mPBLs contained subsets resembling certain features of mTIL. More importantly, three clusters (2, 6 and 15) were represented in both mPBL and mTIL. Cluster 2 was the major subset of the majority of hPBL, which phenocopied hallmark parameters of resting T cells. Cluster 6 and 15 were uniquely presented in melanoma patients. Cluster 15 had the highest PD-1 levels, with elevated markers of both activation and dysfunction/exhaustion; while Cluster 6 was enriched for dormant phenotypes (cluster 6) that are unique to tumor bearing conditions. Based on these high-resolution analyses, we developed original algorithms to build a novel ICB response predictive model using immune-blockade co-expression gene patterns. The model was trained and tested using previously published GEO datasets containing CD8 T cells from anti-PD-1 treated patients and presented an AUC of 0.82, with 92% and 89% accuracy of ICB response in the two datasets.

#### Conclusions

We identified and analyzed unique populations of CD8+ T cells in circulation and tumor using high-resolution single-cell transcriptomics to define the landscape of CD8+ T cell states, revealing critical subsets with shared features in PBLs and TILs. Most importantly, we established an innovative model for ICB response prediction by using peripheral blood lymphocytes.

Ethics Approval This study was performed under an IRB approved protocol.