Adaptive T cell therapy (ACT) with autologous tumor-infiltrating lymphocytes (TIL) has demonstrated high response rates in patients with metastatic melanoma. TIL products recognize tissue-specific antigens, neoantigens, and non-cancer related antigens. Neoadjuvant TILs are considered the main contributors to the anti-tumor activity of TILs. Strategies enriching TILs for the neoadjuvant TILs are expected to yield more potent therapeutic products, especially in epithelial cancers which contain a high proportion of non-cancer specific T cells. Several studies have demonstrated that expression of PD1 on TIL identifies the neoadjuvant-specific T cells. 

The expanded PD1+ TILs are functional as determined by IFNγ secretion and CD107a mobilization in response to non-specific stimulation.

**REFERENCES**

2. Physick E, et al., Durvalumab in patients with PD-L1-positive urothelial carcinoma combined with platinum doublet chemotherapy (NCT02315419).

**MATERIALS & METHODS**

- **PD1-positive (PD1⁺) cells** were sorted via flow cytometry directly from fresh tumor digests and expanded in vitro.
- **Samples** from six melanomas, three sarcomas, six breast cancers, and eight lung cancers were evaluated.
- **3 populations were studied:**
  - **PD1⁺ sorted TIL**
  - **PD1⁺ sorted TIL**
  - **Expanded PD1⁺ TIL**
- **TIL were evaluated for yield (cell count), phenotype (flow cytometry), TCR V family repertoire (RNA-sequencing), non-specific functionality (anti-CD3 and PMA), and tumor reactivity and killing (co-culture assays).**

**RESULTS**

**Expanded PD1+ TIL are functional as determined by IFNγ secretion and CD107a mobilization in response to non-specific stimulation.**

**DISCUSSION & FUTURE STUDY:**

- **Expanded PD1⁺ TIL demonstrate oligoclonality, compared to PD1⁺ TIL and bulk TIL, a sign of antigen-driven clonal expansion at the tumor site.**
- **Preliminary data demonstrate autologous tumor cell killing by PD1⁺ but not PD1⁻ TIL.**
- **Functionality of the expanded PD1⁺ TIL was confirmed by robust IFNγ and CD107a expression in response to non-specific stimulation.**
- **Importantly, in vitro expansion of PD1⁺ TIL resulted in products phenotypically comparable with bulk TIL, indicating a strong therapeutic potential.**
- **T cell makers regulated at the surface of expanded PD1⁺ TIL relative to pre-sort TIL included CD1 and CD25 and suggest a high activation level.**
- **We intend to investigate this TIL product in clinic.**