

Successful Expansion and Characterization of Tumor Infiltrating Lymphocytes (TILs) from Non-melanoma Tumors

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Abstract

Background

Adoptive cell therapy (ACT) has shown promise in comparison to other methods of cancer immunotherapy that rely on the active development of anti-tumor T-cells *in vivo* to mediate cancer regression¹. Administration of autologous TILs in melanoma patients have shown an overall response of 56% at NCI and variable response rates at multiple sites¹. The durable responses observed in melanoma and cervical patients using ACT has encouraged us to explore broadening their utility in multiple solid tumor settings. Here, we demonstrate the feasibility of growing TILs and to develop TIL therapies for other solid tumors.

Results

To date, we have been able to successfully culture TILs from tumors obtained from bladder, cervical, head and neck, lung, and Triple Negative Breast Cancer (TNBC). The average yield of TILs from pre-REP is listed in **Table 1**. Phenotypic characterization of TILs from bladder, cervical, and lung cancer were >60-70% CD8+ T-cells whereas TILs from head and neck demonstrated variable distribution of CD8+ and CD4+ T-cells. TILs propagated from TNBC were >80% CD4+ T-cells. Regardless of the tumors, most cultures had <20% CD56+ NK-cells.

Table 1. Average yield of TILs obtained from pre-REP in non-melanoma tumors

Tumor	Number of patient tumors	Average yield (and range) of TILs from pre-REP (10 ⁶)
Bladder	2	290 (97-600)
Cervical	4	360 (147-800)
H&N	7	539 (132-738)
Lung	8	688 (50-915)
TNBC	13	429 (81-665)

Methods

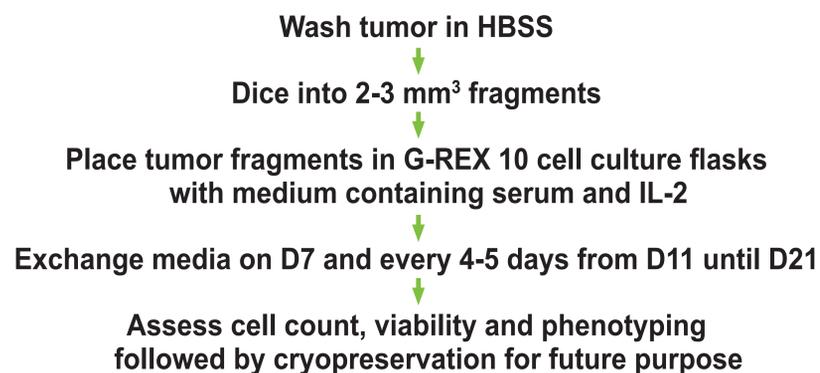


Figure 1. Successful expansion of TILs from non-melanoma tumors

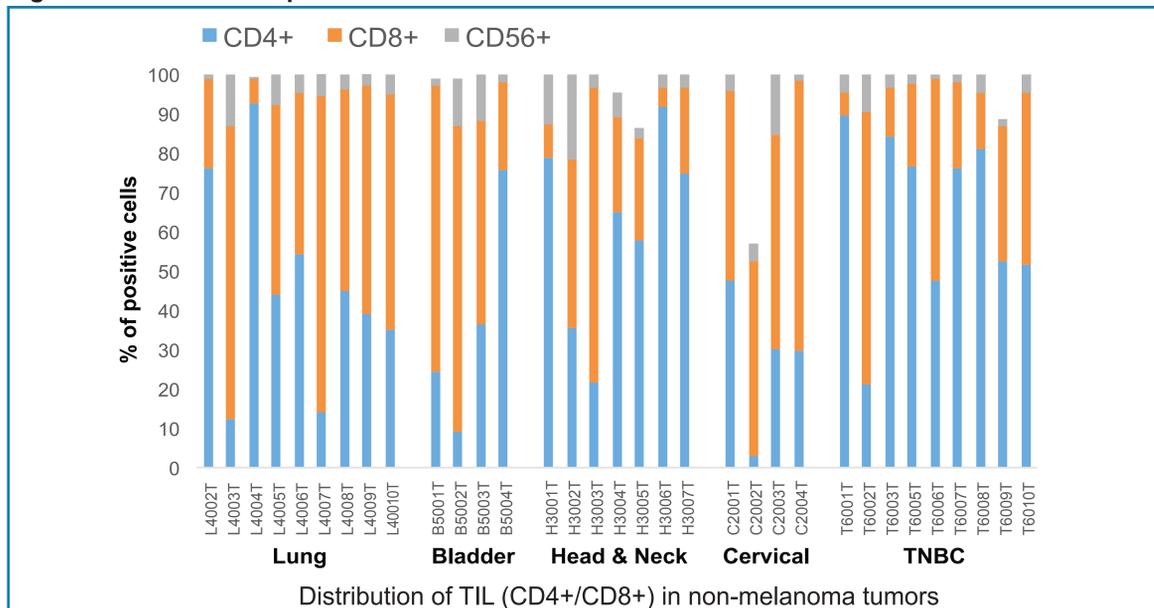


Figure 2. Non-melanoma TILs expressed CD27 and CD28, consistent with young TILs

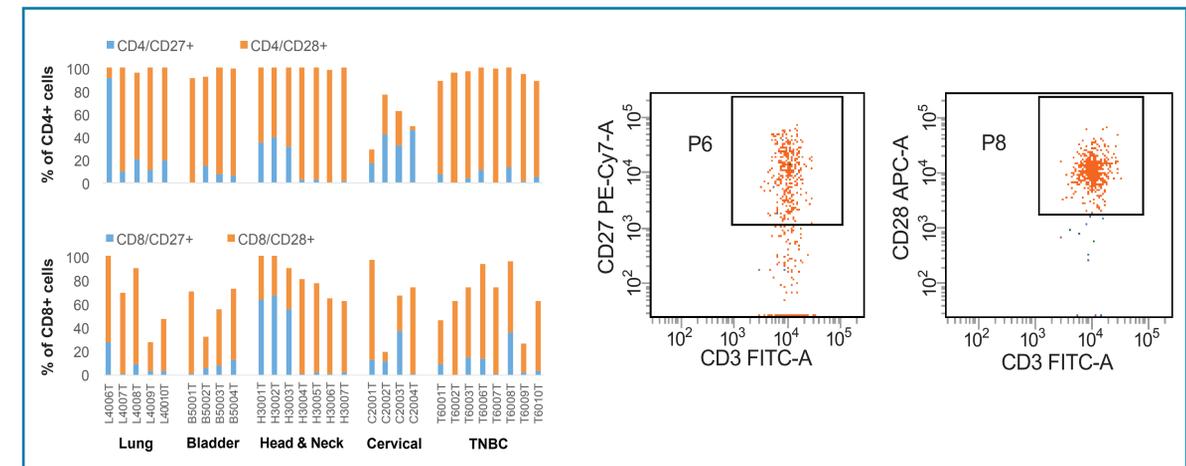
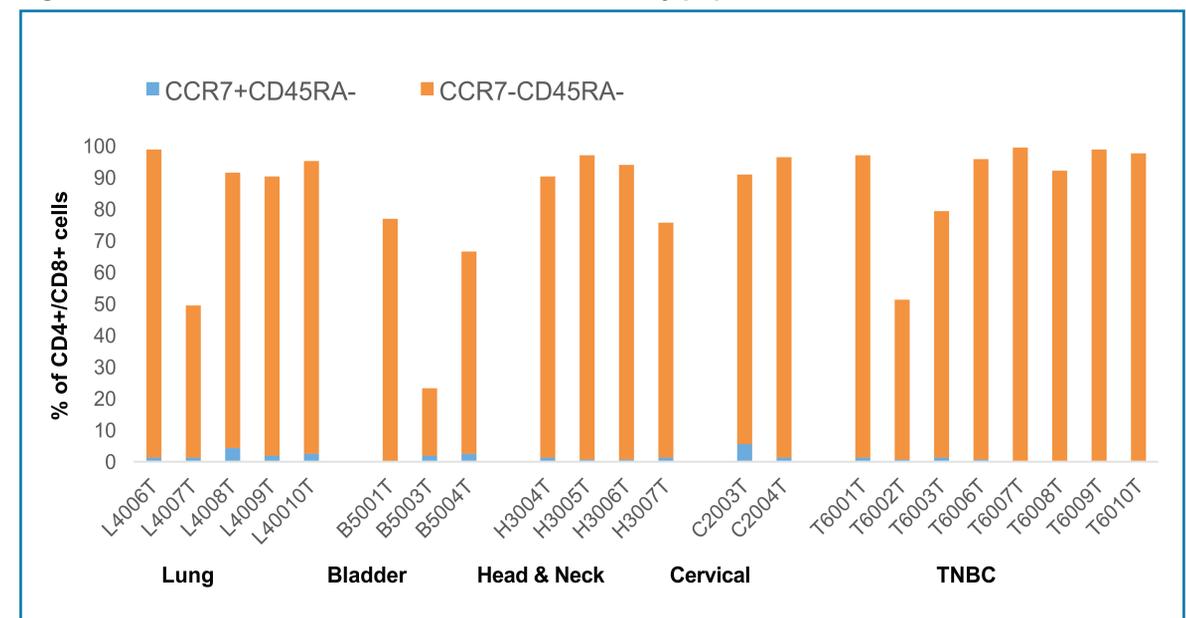


Figure 3. Activated TILs skew towards effector memory population



Conclusions

- We have been able to successfully grow TILs from lung, bladder, head and neck, cervical, and TNBC patient tumors.
- Lung, bladder, and cervical tumors showed greater proportion of CD8+ TILs, whereas head and neck and TNBC tumors were mostly CD4+ TILs.
- Further characterization of CD4+ and CD8+ TILs demonstrated effector memory phenotypic cells that were also CD27+ and CD28+.

Reference

1. Rosenberg SA and Restifo NP: Adoptive cell transfer as personalized immunotherapy for human cancer. *Science*. 2015, 348:62-8.

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