THE EPI-® TECHNOLOGY PRODUCES A POLYCLONAL TIL PRODUCT (LYL845) WITH DIVERSE TUMOR-REACTIVE CLONES THAT HAVE STEM-LIKE QUALITIES AND ANTI-TUMOR FUNCTION

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**Background**

Adoptive cell therapy using tumor-infiltrating lymphocytes (TIL) is a promising method for cancer treatment. Unlike other cell therapies that engineer the tumor-targeting receptor into the T cells, TIL therapy preserves and expands tumor-reactive T-cell clones from surgically resected tumors. TIL products that are highly enriched with tumor-reactive T-cell clones have been shown to mediate responses to treatment. Additionally, stem-like qualities of T cells have been associated with improved outcomes in patients treated with cellular therapies, including TIL. Therefore, a polyclonal TIL product containing diverse, potent tumor-targeting clones with stem-like qualities is vital for improving clinical outcomes in TIL therapy. LYL845 is an autologous TIL product produced with our proprietary Epi-R® epigenetic reprogramming protocol, which was developed to preserve polyclonality and tumor-reactive clones with enhanced stem-like qualities and anti-tumor function.

**Methods**

LYL845 was generated using Epi-R technology and compared with TIL product generated by a standard protocol (as control). To identify tumor-reactive clones, we primarily rely on surrogate measures of clonal frequency and clonal phenotype, but also used tumor co-culture assays to directly measure tumor-reactivity. Using bulk TCR sequencing and CITE-seq + scTCR-seq, LYL845 was assessed for retention of tumor-reactive clones.

**Results**

We observed that both the research and large-scale TIL products expanded from multiple tumor types (melanoma, lung, colon) using Epi-R technology were highly polyclonal. Furthermore, putative tumor-reactive clones identified from initial tumor samples were preserved in LYL845, both at research (n=13) and large-scale (n=3). Using tumor co-culture assays, we confirmed that our approach for identifying putative-tumor reactive clones is a good surrogate for true tumor reactivity. The cells from putative tumor-reactive clones (and true tumor-reactive clones defined from co-culture assays) in LYL845 demonstrate more stem-like and effector function and less exhaustion than the putative tumor-reactive clones in the control products. In tumor co-culture assays, LYL845 demonstrates potent antitumor function, including dose-dependent cytolytic activities and cytokine secretion (figure 1).

**Conclusions**

Preclinical data show that LYL845 is an expanded TIL product that preserves tumor-reactive clones with stem-like qualities. Based on these promising preclinical data, we plan to evaluate LYL845 for safety, tolerability, and anti-tumor activity in an upcoming first-in-human Phase 1 clinical trial.

**Acknowledgements**

We thank members of Lyell Immunopharma’s flow cytometry core (Andrew Jimena, Elizabeth Pedrosa, Ken Xiong), process development team (Merixell Galindo Casas, Carson Harms, Melissa DeFrancesco) and Queenie Vong for their experimental contributions.

**REFERENCES**


**Ethics Approval**

Research was performed with tissues obtained from patients through a procurement protocol approved by WCG IRB, tracking number 20210857.