bio-techne®

Application Note

Enhance Your TIL Expansion with ExCellerate™ T Cell Media

Tumor infiltrating lymphocytes (TILs) are a heterogeneous population of lymphocytes that have migrated into a tumor. Largely comprised of T cells, TILs are actively engaged within the tumor microenvironment. Their functional impacts are wide ranging due to the immune system complexities within tumors,[1,2] and TILs can either suppress or activate immune responses. In addition, TIL subsets highly expressing CD3 and either CD4 or CD8 [3-6] can exert anti-tumor and anti-proliferative effects in solid tumors, and their presence is associated with improved clinical outcome.[2,7] These encouraging findings have propelled the development of TIL therapy for multiple cancers in recent years.

TIL therapy is an adoptive cell therapy that utilizes TILs from a patient's own tumor. Biopsy-derived TILs are adapted to infiltrate and survive in the patient's tumor, an important capability for immune cell therapies. In TIL therapy, these cells are expanded to therapeutic scale *ex vivo* and delivered back into the patient.[8] TIL therapy has shown significant promise against a wide variety of solid tumors including melanoma, head and neck, colorectal, and early stage lung cancers.[5,6,9-12]

ExCellerate Media for TIL and Organoid Culture

ExCellerate™ Human T Cell Expansion Media is optimized for the *ex vivo* culture of human T lymphocytes in preclinical research. ExCellerate media is xeno-free which means that it is devoid of non-human animal-derived products and therefore provides a more controlled and stable culture environment for T cell expansion.

Organoid culture, pioneered by Hans Clevers and Toshi Sato at the Hubrecht Institute in the Netherlands, is an *in vitro* model system that is valuable for evaluating TIL-tumor cell interactions. The interactions of TILs with tumor organoids requires the generation of large numbers of TILs in a robust and reproducible process. Commonly used methods of TIL expansion rely on the use of human serum with conditioned media containing high-dose IL-2, a time-consuming process that results in significant experimental variability.

In order to develop a more reproducible method for expanding TIL cultures, Rosemary Millen, a previous post-doctoral researcher in the Clevers lab, carried out a media comparison to understand the impact ExCellerate T Cell Media has on the cultures. This comparison showed a 15% - 30% increase in $CD3^+$ T cells cultured in ExCellerate media compared with the conditioned media (Figure 1). These findings are consistent with studies on PBMCs performed at Bio-Techne (Figures 2 and 3).

Learn more about ExCellerate

TILs Grown in ExCellerate Media Show Higher Proportion of Viable CD3⁺ T Cells

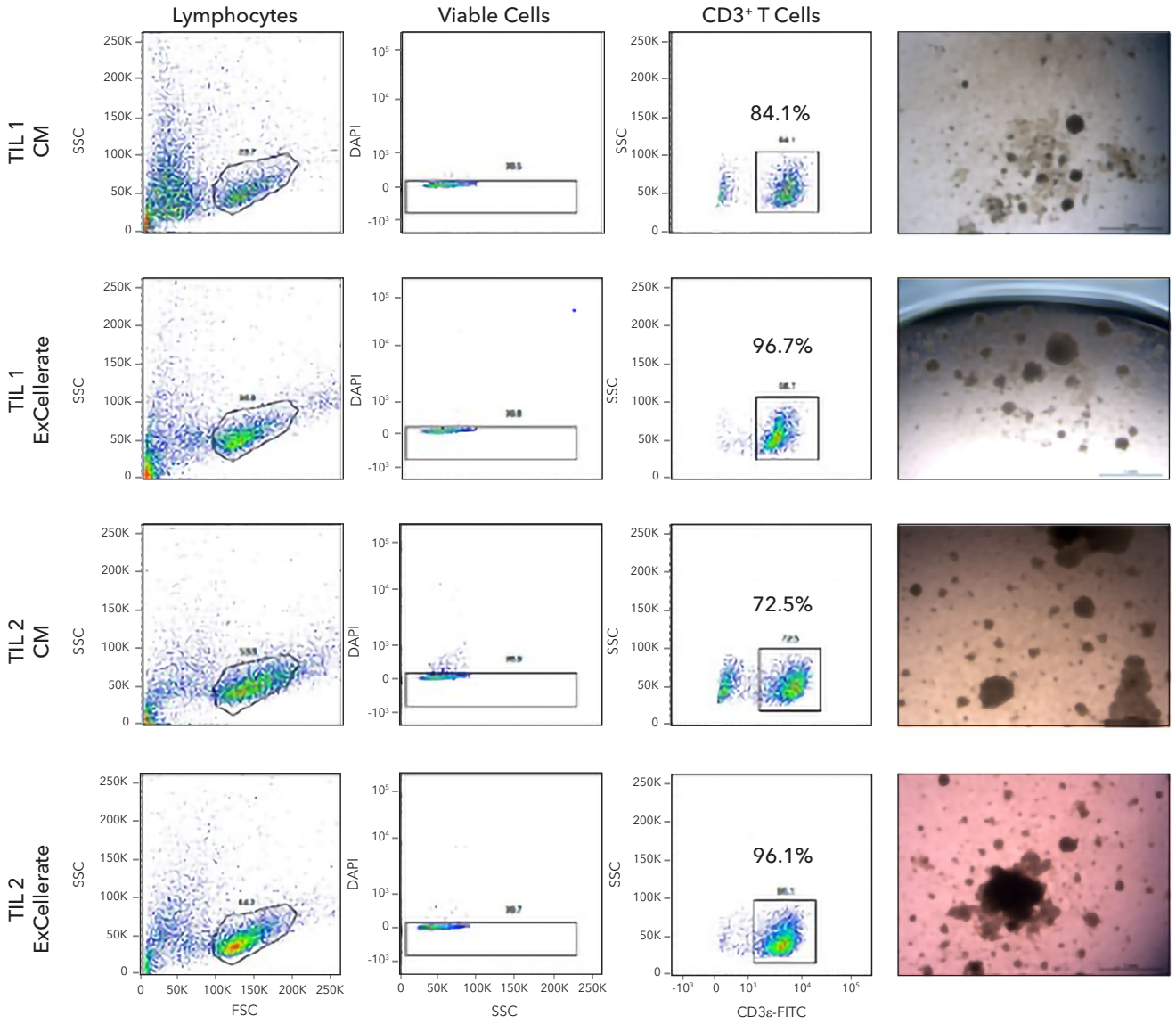

Figure 1. Comparison of ExCellerate Human T Cell Expansion Media and conditioned media (CM). TILs were cultured from two separate patient biopsies (TIL1 and TIL2) for two weeks in CM or ExCellerate media in the presence of recombinant human IL-2 (6000 IU/mL). CD3⁺ T cell expansion is shown by flow cytometry and microscopy images. Data provided by Rosmary Millen.

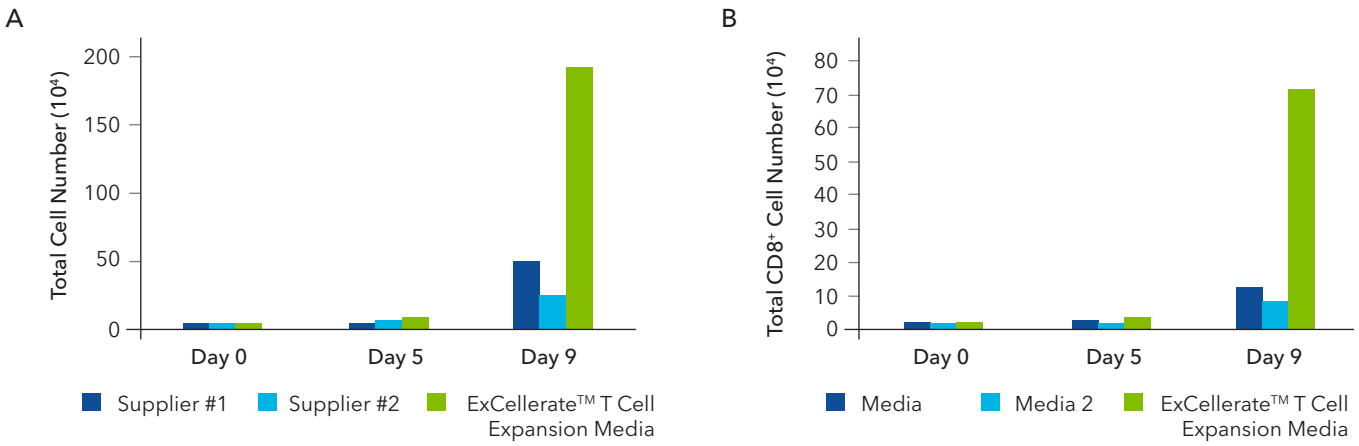

Figure 2. ExCellerate Human T Cell Expansion Media supports greater T cell expansion compared to other commercial T cell media. 2.5 x 10^6 PBMCs were cultured for 9 days using ExCellerate media or other commercially available media **(Supplier #1 or #2)**, in combination with GMP-grade Recombinant Human IL-2, IL-7, and IL-15. The numbers of total T cells **(A)** and $CD8^+$ T cells **(B)** were determined at Days 0, 5, and 9 of culture.

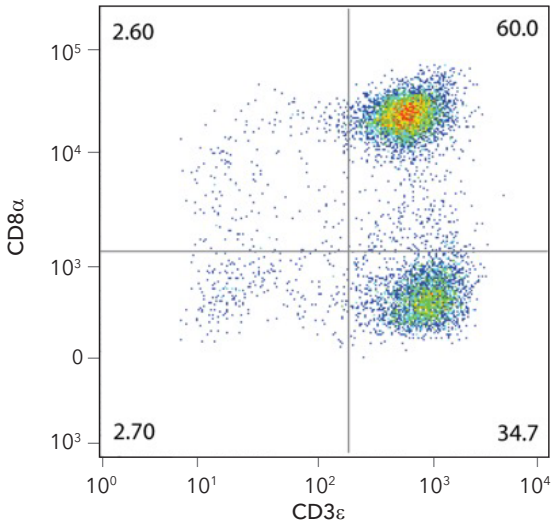

Figure 3. Phenotypic analysis of human T cells expanded in ExCellerate Human T Cell Expansion Media. Human PBMCs were cultured for 9 days in ExCellerate media with Recombinant Human IL-2. $CD8^+$ T cells were enriched during the culture as shown by flow cytometry with Mouse Anti-Human CD3 epsilon APC-conjugated Antibody and with Mouse Anti-Human CD8 alpha PE-conjugated Antibody.

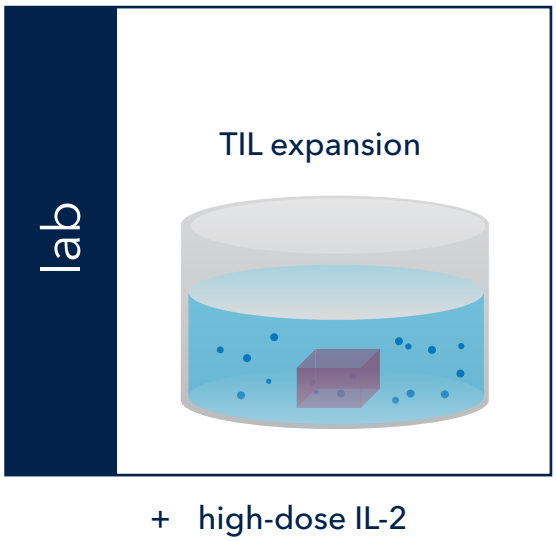

Figure 4. Expansion of TILs from fresh tissue specimens. Biopsy or surgical resection from patients are divided into small pieces and placed into a cell culture dish with conditioned media supplemented with recombinant human IL-2.

Moving Forward

As you advance your TIL program towards clinical studies, it is important to develop TIL expansion and coculture processes that are as robust as possible. Adopting xeno-free and serum-free ExCellerate media will eliminate the risk of contamination with mammalian pathogens, reduce manufacturing risk by reducing batch failure, and eliminate variability due to trace animal components. Better expansion and greater consistency in your TIL cultures will accelerate your progress in ongoing studies and enable your TIL therapy to reach the patients who need it.

References

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Additional Resources for TIL Expansion

- ExCellerate™ Cell Expansion Media
- Serum-Free and Animal-Free Cell Culture
- Transitioning to Animal-Free and GMP
- T Cell Manufacturing for Cell Therapy
- T Cell-Based Therapies eBook