

## **ADVANCING THE ROBUST MANUFACTURE OF T-CELL THERAPIES THROUGH THE APPLICATION OF STIRRED TANK BIOREACTORS**

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A growing pool of efficacy has ballooned the landscape of engineered T-cell therapy clinical trials to over 90 active trials in the United States with many more in pre-clinical phases. This group of therapies consisting of Chimeric Antigen Receptor T-cells (CAR-T), T-cell Receptors (TCRs), Regulatory T-cells (T-regs), and Tumor Infiltrating Lymphocytes (TILs) could provide a breadth of solutions in the oncologic space and elsewhere, however a robust manufacturing process is required to realize these solutions in the clinic. A main hurdle in establishing a robust manufacturing process for these therapies is that a lengthy expansion period is typically necessary to reach a therapeutic dose of cells. The issues with current culture methods present in the forms of a high cost of goods, increased production timelines, and highly variant expansion rates.

At Hitachi Chemical Advanced Therapeutic Solutions, we have investigated stirred tank bioreactors as an alternative to the standard static and rocking motion culture methods using the ambr15 microbioreactor system. Stirred tank bioreactors pose a unique solution for the manufacture of both autologous and allogeneic T-cell therapies with high rates of mass and gas transfer and established process control methods. Given these advantages, a comparison study of T-cells expanded in the ambr15 microbioreactor system and batch fed static cultures resulted in a three-fold increase in total cell number with the bioreactors. Further development of stirred tank culture methods has demonstrated 64-fold expansion over an eight-day culture period. These outcomes indicate a T-cell expansion method that could expand the potential of the revolutionary therapies through reduced media requirements, shortened culture periods, and high yields. By further utilizing established techniques in cell culture, T-cell therapies become increasingly viable treatments for a range of indications.