

A NOVEL SCALABLE MANUFACTURING PLATFORM FOR T-CELL ACTIVATION AND EXPANSION IN ADOPTIVE T-CELL THERAPY

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Adoptive T cell therapy (ACT) is growing rapidly, representing the revolution in cancer treatment. However, the current manufacturing platforms are largely based on magnetic microbeads surface coated with agonist antibodies to T-cell receptors CD3 and CD28. These manufacturing platforms use expensive reagents including the viral transduction vectors, and also require multiple discrete stages and open processes with significant human interaction, contributing to the high-cost for cGMP manufacturing of these therapies.

We developed a single-use, beads-free bioreactor system (*Figure 1a*), which provides a closed-loop T-cell activation and expansion. The perfusion-based platform also facilitates the development of the bioreactor system into a fully automated, turn-key system used in both centralized and decentralized (e.g., hospitals) manufacturing settings.

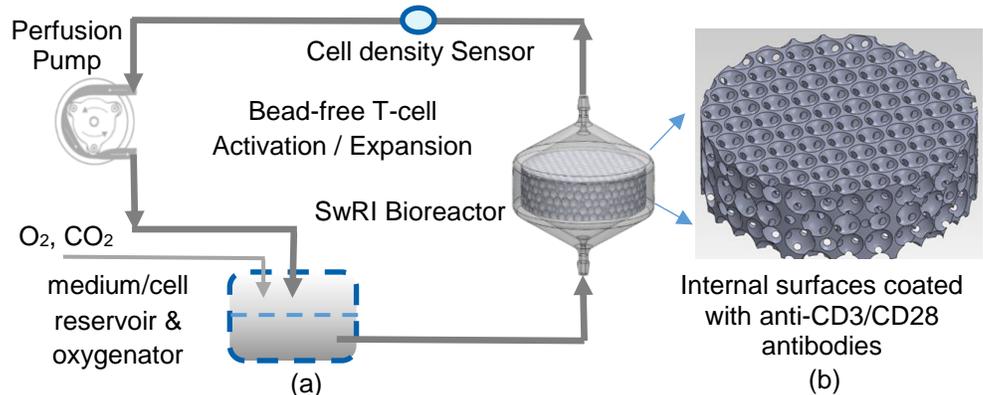


Figure 1: (a) Bioreactor for T-cell expansion; (b) internal structure of the bioreactor.

The bioreactor has a unique internal structure (*Figure 1b*), formed by a large number of interconnected hollow spheres tightly packed in a 3D space, which yields large surface areas to increase the reactivity between the bioreactor and the T cells flowing through the bioreactor. The surfaces of the bioreactor are coated with anti-CD3 and CD28 antibodies to mimic the antigens for T activation and expansion. The feasibility of using the perfusion-based bioreactor for T-cell activation and expansion is demonstrated in *Figure 2*. Briefly, 20×10^6 PBMCs were seeded into the bioreactor system and perfused for two days during the T-cell activation phase, with the medium containing no cytokine IL2. After two-day of activation, human IL-2 was added to the system so that the total IL-2 concentration was 20 IU/mL. Then the T-cell expansion phase was carried out for three-days. On Day 5, T cells were achieved a three-time expansion after activation, which is similar to the magnetic beads-based system. However, the perfusion based bioreactor has the potential to offer multiple advantages over the current beads-based system as discussed above.

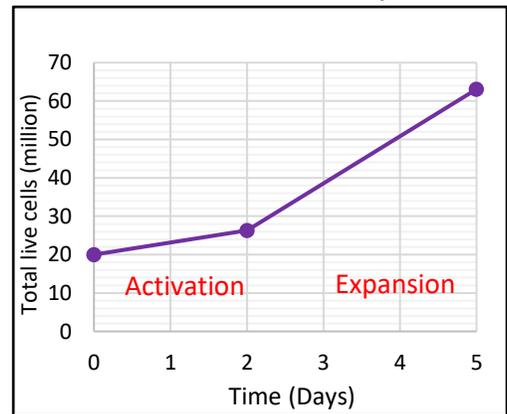


Figure 2: T-cell expansion in the perfusion bioreactor.