

Fully closed automated CAR-T cells culture system including real-time and sampling-less quality controls: a first demonstrator

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The work presented here concerns the monitoring and quality control required during the expansion phase of CAR-T cell production. During this delicate production stage, quality controls require numerous samples of the bioreactor content, which can themselves be sources of contamination, the most feared cause of losing the entire production. This conference presents the first demonstration of an automated, fully closed T-cell culture system incorporating sampling-free, real-time quality controls. Measurements are based on white light spectroscopy using a cell suspension in a recirculating closed loop which ensure sterile environment.

The cell suspension is set in motion (peristaltic pump) through a circulation loop, which includes a quartz spectroscopy cuvette for spectral measurements. This involves acquiring white light absorption spectra while the suspensions are flowing through the cuvette. These contactless acquisitions can be made at any desired measurement frequency during the expansion phase. The spectra are then numerically processed to determine cell concentration and viability, and to detect whether production can continue or must be stopped early in case of a problem. These controls are performed in real time, without the need to sample the bioreactor's contents. Two situations that would result in production being stopped are considered: the appearance of contamination or an abnormal reduction in cell viability. In both cases, a 'warning value' is derived from the shape of the absorption spectra, and an alarm can be triggered as soon as a problem is detected during the expansion phase. The device also includes an automated system for adding culture medium to maintain suspensions at an optimum cell concentration.

In this presentation, we demonstrate how white light spectroscopy can be used for real-time, sample-free quality control. We will also present the device's architecture, its driving algorithms, and its human-machine interface. Real-time records of T-cell circulation monitoring, observation of SDS-induced T-cell death and automated culture medium addition will be displayed. Real-time measurements of T-cell concentrations, suspension viability and warning values are demonstrated in all examples. Note that this device can be used for sampling-free, real-time monitoring of any suspension cell culture.