SCALE-OUT OF MASSIVELY PARALLEL PATIENT-SPECIFIC CELL CULTURES WITH A MODIFIED TRANSPORTABLE CONDITIONED CELL CULTURE CHAMBER

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Barrier Isolators, which separate the cell culture processing atmosphere from the bioburden of personnel, are the best means to reduce contamination risks. These isolators are currently being used for cGMP-compliant clinical trials[1, 2]. Scaling cell production processes presents non-obvious restrictions to most people. Compared to open processing, modular Cytocentric isolators can be replicated to scale proportionately with each stage in cell processing until all steps are accommodated maximally. This allows a process to efficiently and quickly scale with operations from pre-clinical through clinical studies[3]. However, for processing of massively parallel patient-specific cell cultures, incubation capacity in a barrier isolator, unlike in the open room, can be a bottleneck. Inexpensive and infinitely elastic incubation capacity can be provided by existing external incubators if cultures can be safely transported to and from the isolator for processing. We tested a modified transportable conditioned cell culture chamber (TC4) designed to enclose cell cultures inside the exterior incubator and fit through the airlocks of the barrier isolator to safely deliver cells to the interior for processing. We have previously published on good cell growth using this processing system to expand K562 cells, a hematopoietic stem cell-like cell line that has been used as a surrogate for CAR-T cell processing. In this study, we addressed sterility concerns by running mock production runs with a highly permissive color-changing bacterial broth. We ran three production runs, moving mock cultures between the barrier isolator and the external incubator with the TC4 transport chamber. We took samples of the final mock cell product, sealed them into sterile vials, and incubated them long-term, monitoring for bacterial growth. We also performed environmental monitoring of the barrier isolator processing chamber with an air sampler and contact plates. Positive control samples were all yellow and turbid. Negative samples and all test materials were negative for microbial growth. We concluded that this transport chamber could help safely alleviate the bottleneck in cell production presented by the unique needs of massively-parallel patient specific cell incubation.

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