PRELIMINARY METABOLIC SCREENING METHOD FOR CLONE SELECTION IN THE AMBR®15

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Due to the need to establish and optimize a high-throughput screening model for cell line and clone selection, a scaled down model (SDM) for perfusion mimic in the ambr®15 was developed. A consistent perfusion culture production requires reliable cell retention device(s) and robust controls of the feed and bleed rates. As an alternative to implementing a cell sedimentation process to model cell retention, an approach to model perfusion in the ambr®15 was designed. The developed perfusion mimic model relied on daily viable cell density (VCD) and a target cell specific perfusion rate (CSPR). The design involved a constant CSPR dosing regimen for each vessel, where the perfusion feeding strategy was automatically adjusted based on the growth rate, projected VCD, vessel volume, and integral viable cell concentration (IVCC). In this study, different CSPR targets and concentration of feeds were tested on the same cell host. While the VCD in the study did not reach the density of that at a bench or large scale bioreactor, it was able to reach a viable density of approximately 25 x 10^6 cells/mL with a bleed rate. Subsequently, the true CSPR of each vessel was calculated with the actual IVCC the following day. The correlation between the target and actual CSPRs of each vessel was fairly comparable during the entire production stage. Additionally, this SDM for perfusion mimic can also be used to model the toxic metabolites produced, expelled, and retained within the reactor. Having the toxic metabolite model available can aide in the further understanding of whether the perfusion rate is sufficient to support and maintain the culture density in a continuous process. Insight will be given into whether the perfusion rate can be lowered or increased. This can also shed light on whether the media needs further optimization. Overall, the use of cell specific perfusion rates in ambr15 provided insight for controlling and modeling for cell line and clone selection with a perfusion mimic approach.