An innovative fixed bed bioreactor platform for linearly scalable, biomass predictable, single-use adherent cell biomanufacturing

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Abstract

Scalable single use adherent cell-based biomanufacturing platforms are part of solutions to realize the full potential of cell and gene therapies. Here, we reported the development of an innovative fixed bed bioreactor platform for the scale-up of adherent cell culture. The bioreactor platform is centered on a packed bed of woven polyethylene terephthalate mesh discs that are vertically stacked and sandwiched between two fluid guide plates. Computational fluid dynamics modeling was used to direct the design and development of bioreactor series, targeting uniform flow with minimal shear stress. Residence time distribution measurements revealed that a pulse injected dye tracer solution passed through the bioreactors with great uniformity and narrow distribution of residence time, mimicking plug flow. Periodic media sampling with an offline analyzer showed that there was minimal gradient of four important metabolites (glucose, glutamine, lactate, and ammonia) across the bioreactor throughout cell growth. The bioreactor platform was further validated in automated cell harvesting with ~96% efficiency and ~98% viability, as well as linear scalability, in terms of both operational parameters and performance, for cell culture and adeno-associated virus vector production. Finally, mathematic models based on oxygen uptake rates were developed and proven effective to model cell growth curves and estimate biomass in real-time. This study shows that this innovative fixed bed bioreactor platform enables linearly scalable adherent cell-based biomanufacturing with high productivity.

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