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Novel, efficient scale-up of inclined settlers for perfusion bioreactor cultures

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NOVEL, EFFICIENT SCALE-UP OF INCLINED SETTLERS FOR PERFUSION BIOREACTOR CULTURES

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Inclined settler has been introduced as a unique cell retention device for perfusion bioreactor cultures over 25 years ago by these authors (Batt et al, 1990; Searles et al. 1994) to selectively remove dead cells and cell debris, while the live and productive cells are recycled back to bioreactor. This device has been scaled up successfully as lamellar settlers and utilized to achieve high cell densities and productivities in production-scale perfusion bioreactors by a number of biotechnology manufacturers, such as Bayer, Biomarin, Eli Lilly, Roche, etc. (Shen and Yanagimachi, 2011; Pohlscheidt, et al., 2013). However, the rectilinear scale up of inclined settlers into lamellar settlers is not very efficient and creates a large footprint. Further, this powerful cell retention technology has not so far been demonstrated or applied successfully for retention of microbial cells to our knowledge.

We have recently developed novel more efficiently scaled up compact cell settlers in cylindrical, spiral and conical geometries (patent-pending). These novel settlers use the three-dimensional space more efficiently to maximize the cell settling efficiencies within smaller footprint and can be used to achieve high cell retention in microbial perfusion cultures as well as mammalian cell cultures. We have first demonstrated the increased cell retention capabilities of these novel cell settlers with the smaller (hence more demanding) microbial yeast cell cultures, achieving high cell densities and viabilities through selective removal of dead cells and cell debris. Now we are demonstrating the effectiveness of these more efficiently scalable cell settlers for perfusion cultures of mammalian cells.

CHO cells cultured in a 5 liter Celligen bioreactor are pumped into the compact cell settlers, in which the larger live cells settle and are recycled to the bioreactors, while the smaller dead cells and cell debris are selectively removed from the top outlet of the settlers, as demonstrated initially by us over twenty five years ago. However the size of the settlers required for the same bioreactor is significantly smaller with reduced footprint, compared to the results obtained with the traditional rectilinear inclined settlers. Latest results from these on-going high cell density perfusion bioreactors with CHO cells will be presented, along with the scale-up considerations for duplicating these successful results at larger production-scale bioreactors

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