DEVELOPING AN EFFECTIVE SCALE-DOWN MODEL FOR A SUSPENSION ADAPTED HEK293T-DERIVED LENTIVIRAL VECTOR STABLE PRODUCER CELL LINE

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Lentiviral vectors (LVV) represent an important tool for cell and gene therapy applications. However, inefficiencies in LVV manufacturing processes, such as the inability to achieve high cell densities with HEK293T cell lines in a fed batch process, have resulted in poor upstream yields. Optimisation of cell culture conditions is needed to improve upstream yields, which can be expedited by high-throughput screening (HTP). In this work, we describe the use of the 24 deep square well (24-DSW) microwell platform to develop a scale-down mimic of GSK's established stable suspension LVV production process model at 2 L bioreactor scale. We found that matched mixing time was an effective basis for scale-translation between the stirred tank reactor (STR) and microwells. The growth kinetics and LVV productivity profile in the microwell were reproducible and comparable to the 2 L bioreactor process model. In both vessels, a 6-fold increase in cell density was achieved at the harvest time point and high cell viability (i.e. > 90 %) was also maintained throughout the entirety of the cultures. The 24-DSW model, therefore, is an effective scale-down model for larger-scale stirred-tank bioreactor culture and provides an important tool for rapid, high-throughput optimization of the LVV production process.