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HIGH TITER TRANSIENT GENE EXPRESSION PLATFORM BASED ON GS CHO CELL LINE – RAPID PROTEIN EXPRESSION TOOL FOR PRECLINICAL DRUG DEVELOPMENT

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Most of the high yielding transient gene expression (TGE) methods for CHO cells reported in the literature involve extensive cell line engineering and plasmid vector optimization in addition to long fed batch cultures lasting up to 21 days. However, this is a laborious, time intensive process and also requires specific vector engineering for transient expression. Here, we present results from development of a high titer TGE process based on GS-CHO cells without resorting to host cell line engineering or TGE specific vector engineering. This was achieved by optimization of direct addition of DNA and PEI, use of DMA to enhance transgene mRNA levels and addition of a proprietary feeds. Protein titers of up to 0.35 g/L or 1 g/L were reached in a 7 day or a 16 day bioprocess respectively. Robustness and reproducibility of this method was demonstrated at scales ranging from 2 ml to 2 L. Moreover, these transfections could be performed in a high throughput manner in 24 deep well plates. Taking advantage of this, we coupled this high throughput transfection process to a high-throughput semi-automated Protein A purification process capable of purifying up to 72 unique mAbs simultaneously. We designed a variable volume elution strategy based on supernatant titer and were able to obtain protein yields of 0.25 mg to 1 mg at concentration >0.5 mg/ml. In efforts to further increase protein expression levels, we tested co-transfection of proteins involved in the unfolded protein response with the goal to enhance secretion capabilities of the transfected cell population. We identified that co-transfection of plasmid DNA encoding XBP1S increased protein expression by 15% to 80%. We also present case studies comparing product quality attributes from transient HEK293, transient CHO and stable CHO pool. Overall, our results demonstrate that a high yielding and representative transient CHO process can be developed while maintaining the speed and simplicity of a TGE process.