DESIGNING A CHO PROTEIN PRODUCTION PLATFORM USING MULTI-OMICS TECHNOLOGY

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Over the last two decades, Chinese Hamster Ovary (CHO) cell line development has continued to push traditional cell density and titer boundaries while improving protein quality. Fed-batch cultures that exceed 60 million cells/mL and 5-10 g/L protein titers are not uncommon. Media and feed systems are necessary and critical to support these demanding cell line requirements. Chemically defined media and feeds that can enhance protein titer in a broad range of cell lines while maintaining protein quality are ideal for industrial applications. Applicability across different clones and cell lines poses developmental challenges that include analysis of metabolic pathways involved in cell growth and protein production to determine nutritional requirements of the cells. We have taken a multi-omics and bioinformatics modeling approach, and incorporated Design of Experiment in developing a novel CHO-based medium and feed system with improved protein quality for multiple CHO cell lines. We evaluated the performance of different CHO cell lines in benchtop bioreactors and analyzed protein glycosylation. Our newly developed medium and feed system supported high titer protein production and increased cell specific productivity compared to other commercially available media. Compared to a competitive fed-batch bioreactor process, the medium and feed system enhanced protein titers by 20-70% with CHO-K1, CHO-K1 GS, DG44, and CHO-S cell lines. For both CHO-S and CHO-K1 cell lines, protein aggregation profiles were comparable, and glycan profiles as well as charge variant profiles were improved when compared to commercially available media and feeds.