DESIGNING A HIGHLY PRODUCTIVE NEXT GENERATION CHO FED BATCH PLATFORM

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Decreasing cost of sales by increasing manufacturing productivity and lowering raw material cost is key to meeting rising clinical demands and an important goal for Operations at Amgen. To achieve this goal, a next generation fed-batch platform process was developed which included developing a new host cell line and a cell culture process. The new CHO host cell line attained robust growth and high cell culture viabilities while allowing for the expression of diverse proteins from mAbs to multispecifics, to meet our multi-modality pipeline needs. In addition to our cell line efforts, our process development team designed a novel CHO fed-batch platform process that produced a two-fold titer increase through media and process optimization. Initially, our current in-house media formulations were used to identify the most favorable metabolic profiles and media types. After identifying the ideal backbone media formulation, further experiments were conducted to optimize energy metabolism and amino acid concentrations in the production bioreactor. Stoichiometric relationships, spent media analyses, and design of experiments were used to rebalance media components and make several major improvements to our media formulations. Furthermore, the team explored process control strategies which complemented the media changes and resulted in improved titer and metabolic profiles while minimizing high CO_2 demand in the production bioreactor. Additionally, this process was designed to fit into our existing manufacturing network without major equipment modifications to avoid significant capital costs. Overall, the new cell line, media formulations, and process control strategy resulted in a fed batch process that delivered a high cell specific productivity of 60 picogram/cell-day. These process modifications will be leveraged as Amgen's next generation CHO fed-batch platform capable of delivering diverse modalities, scales, and plant designs to meet patients' needs.