ENHANCING CRISPR-MEDIATED CHO CELL ANTIBODY PRODUCTIVITY THROUGH CONCENTRATED FED-BATCH OR CONTINUOUS PERFUSION

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Integrated continuous bioprocessing technology has high productivity and cost saving benefit, which combines the upstream (Cell culture) and downstream (Purification) processing. The continuous bioprocessing based biopharmaceutical manufacturing is more profitable than traditional batch/fed-batch processing in increasing quality and quantity. The goal of this study focuses on the upstream continuous process development with crispr-mediated targeted gene integration CHO cell line producing monoclonal antibody. In the upstream processing, we developed concentrated fed-batch culture (CFB) and high density perfusion culture in 2-5 L bioreactor with a cell retention device (alternating tangential flow, ATF). With our concentrated fed-batch culture system, the VCD achieved $8.4x10^7$ cells/m in 11days operation with 1VVD producing antibody 3.3-fold that of fed-batch culture system; in the high density perfusion culture system, the VCD achieved $5x10^7$ cells/ml in 28 days operation with 1 VVD producing antibody greater than 1g/L/day with on the Day10 and keep the cell density, viability and productivity more than 1 month.