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UTILIZING RNA-SEQ TECHNIQUE TO IMPROVE MOLECULAR UNDERSTANDING OF CHINESE HAMSTER OVARY (CHO) CELL BIOPROCESSING

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Chinese Hamster Ovary (CHO) cells are an important biopharmaceutical cell line, accounting for the production of over 70% of the approved protein therapeutics. However several limitations exist with the use of CHO cell lines including low product titers. Understanding of CHO cells in bioprocessing has up until now relied heavily on empirical results with a limited knowledge of the intracellular dynamics. With the recent establishment of both Chinese hamster and CHO-K1 cell line genome assemblies, it is now possible to leverage the genomic resources to better understand and further improve CHO cell bioprocessing. In this study, RNA-Seq, next-generation transcriptome sequencing, was used to characterize the gene expression profile of three different CHO cell lines under several industrially relevant conditions including low culture temperature and pH. Each culture condition sample was sequenced by HiSeq 2000 and contained over 15 million short reads, which were assembled using the Chinese hamster reference genome (v1.01). Differential gene expression between conditions was statistically quantified based on generalized linear models using edgeR software for the replicate samples. One of the applications of the RNA-Seq analysis method, in this study, was to observe and understand the impact of low culture temperature on CHO gene expression behavior. In a CHO-K1 cell line adapted to protein-free medium, the cultures grown at 33°C had higher expression of 251 genes and lower expression of 15 genes (filter criteria were a minimum of two-fold expression change and FDR ≤ 0.05) compared to cultures grown at 37°C. These genes could be utilized as potential targets for cellular and metabolic engineering to further improve CHO cell lines. The current investigation presents the potential of next-generation sequencing techniques for advanced characterization of CHO cell bioprocessing.