USING NEXT-GENERATION SEQUENCING TECHNOLOGY, RNA-SEQ, TO UNDERSTAND THE CHINESE HAMSTER OVARY (CHO) CELL TRANSCRIPTOME UNDER INDUSTRIALLY RELEVANT CONDITIONS

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Chinese hamster ovary (CHO) cell lines are the current gold standard mammalian cell line used for production of recombinant protein therapeutics due to ease of culturing, low risk for viral contamination, and favorable post-translational modifications that mimic those of human proteins; yet protein yields are only 5-10 g/L, leading to high market prices. Improving product yields and quality in the bioprocessing industry has heavily relied on empirical characterization with a limited knowledge of internal molecular dynamics. Transcriptomics is one such medium through which cellular mechanisms could be better understood by measuring gene expression. The information obtained from comprehensive transcriptome analysis can be leveraged to engineer CHO cells with desired phenotypes including high protein titers and used to control the bioreactor environment to reduce waste production. In this work, the next-generation sequencing technique, RNA-seq, was harnessed to quantify the transcriptome changes in CHO cells under several industrially relevant treatments, particularly to observe genotypic changes due to the adaptation of CHO cells to serum-free media, low temperature, low pH, and medium glucose concentration across three different CHO cell lineages (Figure 1). In this global study, statistically enriched and bioprocess-relevant genes, gene sets, and pathways were investigated across all studies to gain potential cell line engineering targets to further improve production processes.

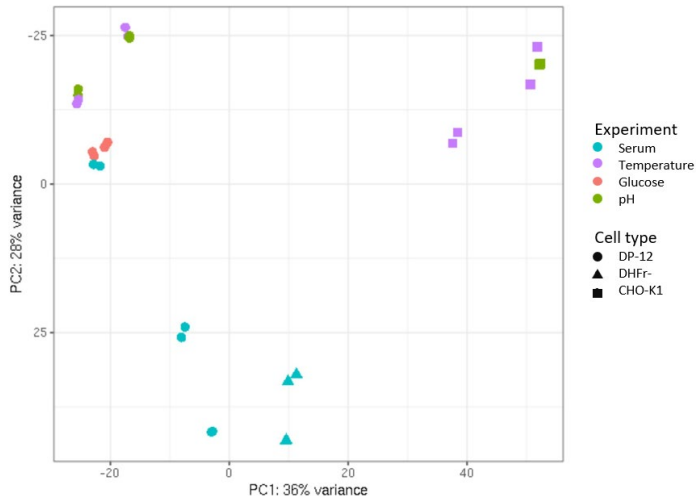

Figure 1 – Principal component analysis (PCA) of all 13,413 differentially expressed genes.