RNA-seq DATA REVEALS METABOLIC REGULATION IN CHINESE HAMSTER OVARY CELL CULTURE

Sha Sha, University of Massachusetts Lowell, MA 01854
Sha_sha@student.uml.edu
Seongkyu Yoon, University of Massachusetts Lowell, MA 01854

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Mammalian cells have been known to be undergoing amount of physiological alterations during culture. This is a result of cell responses to extrinsic and intrinsic changes from culture environment. Understanding the alteration from intracellular context is an important way to decipher cell regulations and omics’ approaches have become to be the main way to gain insights beyond the traditional investigation of extracellular culture parameters only. Metabolic flux studies from literature had extensively discussed cellular changes overtime in culture. However, studies of gene expression changes during culture are lacked. An aspect of gene regulation in culture is important because genes become the targets of cell line engineering. In this study, RNAseq was used to carry out a comprehensive examination of the transcriptomic changes of Chinese hamster ovary (CHO) cells across the time progression in batch culture. Genes associated with energy pathway, carbohydrate distribution, oxidative stress, apoptosis and glycosylation related pathways were investigated. From the results, the genes catalyzing energy pathways showed overall decrease during culture. This result complies with the understanding from many metabolic flux analyses. A very distinct characteristic of transcriptome was found at the point when lactate started to be consumed in culture. From a wide range of transcriptome, a series of alteration in the genes associated with stress and glycosylation, as well regulation to the energy pathways was concurrently found. This study provides a view of cellular activity comprehensively progressing in culture; and reveals possible intrinsic correlation between veracious cellular activities. Three CHO cell lines producing different monoclonal antibodies were included in the study. The results showed a good extent of similarity from the results of the three cell lines.