

Mechanistic understanding of CHO cell culture improvement by rosmarinic acid through multi-omics analysis

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Abstract

The use of antioxidants in Chinese hamster ovary (CHO) cell cultures to improve monoclonal antibody production has been a topic of great interest. Nevertheless, the mechanisms by which antioxidant pathways are regulated in CHO cells and their effect on metabolism are not fully understood. In this work, we investigated how treatment with the antioxidant rosmarinic acid (RA) improved viable cell density and titer in CHO cell cultures, and attempted to explore the underlying mechanism(s) using transcriptomics and metabolomics. In particular, transcriptomics analysis indicated that RA treatment modified gene expression and strongly affected the MAPK and Akt signaling pathways which regulate cell survival and cell death. Moreover, we observed that these effects did not appear related to an intracellular metabolism change. In summary, this integrated ‘omics analysis has important implications for the role of the antioxidant RA in industrial cell culture processes. The current study also represents an example in the industry of how multi-omics can be applied to gain an in-depth understanding of CHO cell biology and to identify critical pathways that can contribute to cell culture process improvement and cell line engineering.

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