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Towards Metabolic Optimization of CHO Cells: In Silico Improvement of Culture Medium, pp. 217-218

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The emergence of “omics” tools and bioinformatics potentiated the development of new strategies to optimize several expression platforms, in particular mammalian cell lines, being CHO cells one of the most commonly used cell line for the production of recombinant proteins. Foremost, computational modelling combined with CHO cell omics data can help optimizing growth parameters, as well as improving the final product yield. In this context, CHO genome scale metabolic model (GSSM) was used in order to study the metabolic behavior of the cells in response to variations in environmental constraints, such as amino acids levels, targeting the development of a novel chemically defined culture medium formulation for CHO cells. To study this influence, GSSM combined with an in-house developed algorithm was employed to determine the minimal medium formulation to sustain growth for non-recombinant as well as for recombinant CHO cells lines. Optflux tool was used to predict metabolic behavior of the cells in response to the environmental constraints tested. Based on in silico predictions, growth yield value was improved 2.8 times and 1.8 times, respectively, for non-recombinant and recombinant CHO cells lines comparing to previously reported data. Furthermore, toxic by-products such as ammonium were decreased to their lowest levels. In silico-based approaches for medium optimization are powerful tools for predicting the metabolic interconnexion in the cell

and for selecting potential experimental conditions for further validation in bioreactor systems.