

Computer-aided growth medium design for optimal growth of Chinese hamster ovary cells

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Systems biology and metabolic engineering tools hold a tremendous promise in improving biomanufacturing attributes since they represent one of the auspicious modern biomanufacturing optimization approaches. The emergence of “omics” tools and bioinformatics enables the development of new strategies to optimize expression platforms in general and Chinese hamster ovary (CHO) cell lines in particular, which are the most commonly used cell lines for the production of recombinant proteins. Computational modelling combined with CHO cell omics data can help optimizing growth parameters, as well as improving the final product yield. Here we use a genome-scale metabolic model (GSMM) of CHO to study the growth and metabolic behavior of CHO cells in response to environmental stimuli, such as changing amino acids levels. To study this influence, GSMM combined with an in-house developed algorithm was employed to determine the minimal medium formulation to sustain optimal 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 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.