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The potential of small molecules to modulate glycosylation by media design

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The Potential of Small Molecules to Modulate Glycosylation by Media Design

Background and novelty

A large number of recent publications demonstrate the effect of cell culture media on post-translational modifications of recombinant proteins[1]. This study aims to extend the toolbox of media design beyond the commonly known media components. We identified and tested a large variety of cell culture compatible chemical components such as pigments and sugar derivatives in industrial relevant Chinese hamster ovary cell lines (CHO) expressing recombinant antibodies.

Experimental approach

The cells were cultivated in fed-batch mode cultures using shaking 96-deepwell plates, and process performance such as viable cell density, viability and product titer were monitored. Supernatants of each culture were purified and N-glycan analysis was performed by CGE-LIF. The findings were confirmed in 30 mL fed-batch shake tube cultures and/or 15 mL micro-scale bioreactors (ambr15^{TM} system) operated at controlled pH and pCO_2.

Results and discussion

The addition of the components at the beginning of the culture exhibited significant changes of the glycosylation profile of the expressed protein. Furthermore, strategies such as the adjustment of the levels and the supplement addition in the feed instead of the media and maintaining constant media osmolality while increasing the supplement concentration allowed to fine-tune the effect of the components on glycosylation profile and to improve the culture performance. Finally, the use of some of the tested supplements increased peak cell density to levels above 20 mio viable cells/mL and product titer up to 1.5-fold, while maintaining high viability throughout the culture. These results show that media design alone is sufficient to specifically modulate some of the essential protein quality attributes and to increase productivity, which circumvents the need of modifying the gene expression of the cell line.

[1] Brühlmann D, Jordan M, Hemberger J, Sauer M, Stettler M and Broly H, Tailoring Recombinant Protein Quality by Rational Media Design, Biotechnol Progress 2015, **31**:615–629.