

Technical University of Denmark



CHO On A Detox: Removing By-Product Formation Through Cell Engineering

Pereira, Sara; Kildegaard, Helene Fastrup; Andersen, Mikael Rørdam

Publication date:
2016

Document Version
Peer reviewed version

[Link back to DTU Orbit](#)

Citation (APA):

Pereira, S., Kildegaard, H. F., & Andersen, M. R. (2016). CHO On A Detox: Removing By-Product Formation Through Cell Engineering. Abstract from 1st ESACT Frontiers Retreat, Lyon, France.

DTU Library

Technical Information Center of Denmark

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

P16 - CHO ON A DETOX: REMOVING BY-PRODUCT FORMATION THROUGH CELL ENGINEERING

Sara Pereira¹, Helene F. Kildegaard¹, Mikael R. Andersen¹

1) *Technical University of Denmark / DTU Biosustain*

Chinese Hamster Ovary (CHO) cells are the preferred hosts for the production of therapeutic glycoproteins. However, there is a need for improvement of the bioprocesses towards increased cell growth and higher productivities without compromising the product quality. Efforts to obtain tailor-made products with the desired properties that meet the requirements of regulatory authorities are continuously being made. Of equal relevance is to develop methods to engineer cell lines with improved by-product metabolism.

CHO cells are not efficient at converting substrate into product or biomass. At the moment, up to 50% of the carbon fed to the cells is wasted in toxic non-productive by-products, like lactate and ammonium that accumulate throughout the culture time in mammalian cells, that reduce the potential cell growth rate and protein productivity.

As genome sequences of CHO cell lines and draft genome of *Cricetulus griseus* (Chinese Hamster), alongside genome editing tools like CRISPR/Cas9 are recently available, an “omics” approach for studying the CHO metabolism is now possible. This allows for reengineering cell lines towards a more efficient metabolism and higher cell densities.

The methodology includes reviewing the literature in search of potential targets affecting cell growth and productivity, using CRISPR/Cas9 for genome engineering to knock-out and/or knock-in target genes in order to produce cell lines with improved phenotypes. In addition, for assessment of the genome engineering, DNA-seq, RNA-seq and proteomics are also used. Moreover, the phenotypes of the different clones are characterized in batch and bioreactor cultivations.

The effects of genome engineering of candidate genes are being assessed alongside data on specific rates for uptake and formation of nutrients, metabolites and by-products. Based on these, enhanced CHO cell lines potentially producing reduced amounts of by-products will confirm the success of the cell line engineering strategy.