Lactate reduction in CHO cell cultures through metabolic analysis

Monge, Ivan Martinez; Hefzi, Hooman; Sanchez, Pere Comas; Marín de Mas, Igor Batolomé; Decker, Marianne; Lecina, Martí; Cairó, Jordi Joan; Lewis, Nathan; Nielsen, Lars Keld

Publication date: 2020

Document Version
Publisher's PDF, also known as Version of record

Link back to DTU Orbit

Citation (APA):
Lactate reduction in CHO cell cultures through metabolic analysis

Iván Martínez-Monge*, Hooman Hefzi†, Pere Comas‡, Igor Marin de Mas‡, Marianne Decker†, Martí Lecina†, Jordi Joan Cairó‡, Nathan Lewis§ and Lars Keld Nielsen†

† The Novo Nordisk Foundation Center for Biosustainability, Technical University of Denmark, 2800 Kongens Lyngby, Denmark
‡Chemical, Biological and Environmental Engineering Department, Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain.
§Department of Bioengineering, University of California, San Diego, La Jolla, CA 92093, USA
*Bioengineering Department, IGS-Universitat Ramon Llull, 08017 Barcelona, Spain

1. Lactate generation in CHO cell cultures

CHO cells display Warburg metabolism characterized by high lactate production, which ultimately inhibits cell growth in culture. The current study explored through metabolic flux analysis both process and cell engineering approaches to avoid lactate accumulation, with potential implications in the industry of bioproducts.

2. Background and Experimental Data

The metabolic profile of CHO cells was investigated in batch bioreactor cultures performed under three conditions.

3. Experimental Overview and Results

CHO genome-scale metabolic model

Conventional metabolism

Bioprocess Engineering

Cell engineering

Transcriptomics

Proteomics

Metabolomics

ICHO Genome-Scale Metabolic Model

CHO WT

Non pH-controlled CHO WT

pH-controlled CHO WT

CHO-S

Phase 1

Phase 2

CHO-ZeLa

Constrained-Based Modelling

Dynamic Flux Balance Analysis

Exo-Metabolomics

Flux Balance Analysis

13C Data Integration

Acknowledgements: