

Spring 5-10-2016

CHO cell culture process impacts monoclonal antibody trisulfide modification and sulfhydryl-drug conjugation

Michael Hippach
Agensys

Follow this and additional works at: http://dc.engconfintl.org/cellculture_xv



Part of the [Biomedical Engineering and Bioengineering Commons](#)

Recommended Citation

Michael Hippach, "CHO cell culture process impacts monoclonal antibody trisulfide modification and sulfhydryl-drug conjugation" in "Cell Culture Engineering XV", Robert Kiss, Genentech Sarah Harcum, Clemson University Jeff Chalmers, Ohio State University Eds, ECI Symposium Series, (2016). http://dc.engconfintl.org/cellculture_xv/102

This Abstract is brought to you for free and open access by the Proceedings at ECI Digital Archives. It has been accepted for inclusion in Cell Culture Engineering XV by an authorized administrator of ECI Digital Archives. For more information, please contact franco@bepress.com.

Conference:

Cell Culture Engineering XV

May 08-13, 2016. Palm Springs, CA

Title:

CHO cell culture process impacts monoclonal antibody trisulfide modification and sulfhydryl-drug conjugation

Lead Author and Presenter:

Mr. Michael Hippach

Group Leader- Cell Culture Process Development & Manufacturing

Agensys, Inc. 1800 Stewart St. Santa Monica CA 90404

Abstract:

During the production of monoclonal antibodies using a CHO cell culture process, important parameters are generally controlled by a feedback mechanism (PID) in order to ensure consistency in both productivity and product quality. These parameters typically include pH, dissolved oxygen, and temperature. While most of these parameters are controlled very well within their specific dead band range, dissolved oxygen at times can be a little more difficult to control. Oscillations in dissolved oxygen concentration are not uncommon and these fluctuations can sometime be exacerbated when using an aeration strategy with a high mass transfer rate.

Recently, we observed a cell line that becomes lactogenic accompanied by a drop in product titer due to extreme fluctuations in dissolved oxygen concentration. It was also observed that the antibody lots with higher lactate production correlated with increase trisulfide formation between heavy-light chains. Consequently, the elevated trisulfide levels correlate to changes in the drug-to-antibody ratio (DAR), when used in sulfhydryl-targeted maleimide conjugation.

Experiments were conducted to determine if lactogenicity is triggered by low concentrations of dissolved oxygen or by fluctuations in dissolved oxygen concentration during the cell cultivation process. Further experiments were performed to evaluate if the elevated trisulfide is associated with the lactogenic status of the cells or any particular nutrient/metabolite. Results from these experiments will be presented and strategies for better control of the cell culture process and the product quality of antibody-drug conjugates will be discussed.