CONTROL STRATEGIES FOR THE REGULATION OF PROTEASE CLIPPING DURING MAB PRODUCTION IN CHO CELLS

Daniel Blackstock, Vaccine Production Lab, Vaccine Research Center, NIAID, NIH, USA
daniel.blackstock@nih.gov
Peyi Runsewe, NIH, USA
Wei Cheng, NIH, USA
Joe Horwitz, NIH, USA
Frank Arnold, NIH, USA

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In cell culture based protein production, host cell proteases have the potential to cause unwelcome proteolytic cleavage against a product of interest. This cleavage can be hard to predict and avoid during product development and may even result in development termination if significant proteolytic clipping is identified. Thus, in an effort to overcome the limitations that protease cleavage poses on protein production, we propose, test, and evaluate cell culture methods which can reduce or eliminate unwanted protease activity.

In this work, we evaluate three methods for the regulation of proteolytic clipping profiles of a protease susceptible broadly neutralizing HIV mAb product (CAP256-VRC26.25) [1] in CHO cells. Two culture methods aim to reduce the product residence time inside the bioreactor for reduced contact time with the host protease. These methods include using a (fed-batch) draw/fill strategy and a (continuous) perfusion approach. The third method entails the use of inhibitor molecules during culture to regulate proteolytic activity inside the bioreactor. Each method has been shown to be effective in reducing product clipping, and we further asses the approaches based on cell growth, cell productivity/titer, process feasibility, and level of clipping elimination. This work demonstrates the suitability of using specialized culturing options and offers potential solutions when faced with proteolytic problems.

References:
[1] – Ivleva, V., Lei, P., Cheng, K.C., Arnold, F., Investigating product quality of HIV monoclonal antibody CAP256 by LC-MS analysis. In preparation