Optimized Process Operations Reduce Product Retention and Column Clogging in ATF-based Perfusion Cell Cultures

Yuning Su[1], Zhaohui Wei[1], Yana Miao[1], Liuliu Sun[1], Yina Shen[1], Ziran Tang[1], Le Li[1], Yufen Quan[1], Haiyang Yu[1], Wei-Chun Wang[1], Weichang Zhou[1], and Jun Tian[1]

[1]WuXi Biologicals

March 07, 2024

Abstract

Product retention in the hollow fibers is a common issue in ATF-based cell culture system. In this study, the effects of four major process factors on product (therapeutic antibody/recombinant protein) retention were investigated using Chinese hamster ovary cell. Hollow fibers made of polysulfone presented a product retention rate from 15% ± 8% to 43% ± 18% higher than those made of polyether sulfone varying with specific processes. Higher harvest flowrate and ATF exchange rate increased product retention by 13% ± 10% and up to 31% ± 13%, respectively. Hollow fibers with larger pore sizes (0.65 μm) appeared to have increased product retention by 38% ± 7% compared with smaller ones (0.2 μm) in this study. Further investigation revealed that the effects of pore size on retention could be correlated to the particle size distribution in the cell culture broth. A hollow fiber with a larger pore size (>0.5 μm) may reduce protein retention when small particles (approximately 0.01-0.2 μm in diameter) are dominant in the culture. However, if majority of the particles are larger than 0.2 μm in diameter, hollow fiber with smaller pore sizes (0.2 μm) could be a solution to reducing product retention. Alternatively, process optimization may modulate particle size distribution towards reduced production retention with selected ATF hollow fibers. This study for the first time highlights the importance of matching proper pore sizes of hollow fibers with the cell culture particles distribution and offers methods to reducing product retention and ATF column clogging in perfusion cell cultures.

Hosted file

`Optimized Process Operations Reduce Product Retention and Column Cloggin... all in one.docx` available at https://authorea.com/users/730786/articles/710259-optimized-process-operations-reduce-product-retention-and-column-clogging-in-atf-based-perfusion-cell-cultures