DXB11/TAUT HOST CELL ENGINEERING STRATEGY ENABLING THE ESTABLISHMENT OF STRAINS PRODUCING THE HIGHEST YIELD OF ADVANCED RECYCLING ANTIBODIES

Hisahiro Tabuchi, Chugai Pharmaceutical Co., LTD. API Process Development Dept. (Bio Technology), Japan
tabuchihsh@chugai-pharm.co.jp
Masaki Yamaguchi, Chugai Pharmaceutical Co., LTD.
Tao Jialin, Chugai Pharmaceutical Co., LTD.
Hirokatsu Makitsubo, Chugai Pharmaceutical Co., LTD.

Key Words: rcAb, CLD, TAUT, overexpression, Super CHO

Innovation in monoclonal antibody (mAb) production for clinical use continues to be driven by cell engineering strategies to increase mAb yield and to control the complexity of advanced recycling antibodies (rcAbs). rcAbs offer significant advantages for efficacy by dissociating the antigens in endosomes and recycling free antibodies back to plasma. We were able to reduce the instability in an rcAb-producing CHO cell line whereby mAb titer during the stage of cell line development (CLD) was decreased and improve cell culture optimization.

In this study, we used a chemically defined medium (CDM) and CDM-adapted transporter-overexpressing DXB11 host cells for CLD of two different types of rcAb (rcAb-1, rcAb-2). These not only have pH-dependent antigen-binding but also a distinct mechanism of mAb uptake into cells. As described before, taurine transporter (TAUT) overexpression was able to improve DXB11 cell performance. DXB11/TAUT host cells were further developed with CDM, and these enabled the establishment of strains that produced higher yields of rcAb than did DXB11 parent cells.

Yields of these DXB11/TAUT/rcAb-1 strains increased up to 7.0 g/L/17 days under 1-L bioreactor fed-batch conditions. In contrast, the mAb yields of DXB11/rcAb-1 were up to 3.5 g/L/17 days. In addition, the mAb properties of DXB11/TAUT/rcAb-1 were comparable to those of DXB11/rcAb-1. These results suggest that our TAUT overexpression strategy has a unique potential for improvement of DXB11 host cells and is useful for the CLD of advanced antibodies with increased complexity. Since our CLD of DXB11/TAUT/rcAb-2 also shows significant promise, we plan to adopt the DXB11/TAUT host cell as our Super CHO cell for future development of advanced antibody drugs.