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CHO-K1 host cell engineering strategy enabling the establishment of strains producing higher yields of recycling antibodies

Hisahiro Tabuchi
Chugai Pharmaceutical Co, tabuchihsh@chugai-pharm.co.jp

Ikumi Murakami
Chugai Pharmaceutical Co

Masaki Yamaguchi
Chugai Pharmaceutical Co

CHO-K1 HOST CELL ENGINEERING STRATEGY ENABLING THE ESTABLISHMENT OF STRAINS PRODUCING HIGHER YIELDS OF RECYCLING ANTIBODIES

Hisahiro Tabuchi, Chugai Pharmaceutical Co., LTD.
API Process Development Dept. (Bio Technology), 5-5-1, Ukima, Kitaku, Tokyo, 115-8543 Japan
tabuchihsh@chugai-pharm.co.jp
Ikumi Murakami, Chugai Pharmaceutical Co., LTD.
Masaki Yamaguchi, Chugai Pharmaceutical Co., LTD.

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As described elsewhere (Biotechnol Bioeng 2010, 2013), our DXB11 ($dhfr^-$) host cell engineering strategy achieved high cell viability for a prolonged period (more than 1 month) and enhanced mAb productivity (>100 pg/cell/day) by nutritional control. Introduction of taurine transporter (TAUT) into DXB11 parent cells increased glutamine uptake and accelerated glutathione metabolism. By forcing the overexpression of TAUT, we were able to control DXB11 host cell functions and thereby increase the monoclonal antibody (mAb) titer up to 8.1 g/L/31 days under conventional 1-L bioreactor fed-batch conditions. Furthermore, the mAb produced by the DXB11/TAUT cells was comparable in quality to the mAb produced by the parent cells.

In this study, we used CHO-K1 host cells and a chemically defined medium (CDM) for the development of cell lines producing recycling antibodies (rcAb). CDM adaptation and TAUT overexpression improved CHO-K1 cell performance. Rapid-growth CHO-K1/TAUT cells were developed, and these enabled the establishment of strains that produced higher yields of rcAb than did CHO-K1 parent cell ($p < 0.05$). Viable cell density of these CHO-K1/TAUT/rcAb strains increased not only under shaker passage culture conditions ($p < 0.01$) but also under shaker fed-batch culture conditions ($p < 0.01$).

These results suggest that our TAUT overexpression strategy also has a unique potential for the improvement of CHO-K1 host cells as well as DXB11 host cells.