BiP Inducer X: An ER Stress Inhibitor for Enhancing Recombinant Antibody Production in CHO Cell Culture - DTU Orbit (25/07/2019)

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Prolonged endoplasmic reticulum (ER) stress reduces protein synthesis and induces apoptosis in mammalian cells. When dimethyl sulfoxide (DMSO), a specific monoclonal antibody productivity (qmAb) -enhancing reagent, is added to recombinant Chinese hamster ovary (rCHO) cell cultures (GSR cell line), it induces ER stress and apoptosis in a dose-dependent manner. To determine an effective ER stress inhibitor, three ER stress inhibitors (BiP inducer X [BIX], tauroursodeoxycholic acid, and carbazole) are examined and BIX shows the best production performance. Coaddition of BIX (50μm) with DMSO extends the culture longevity and enhances qmAb. As a result, the maximum mAb concentration is significantly increased with improved galactosylation. Coaddition of BIX significantly increases the expression level of binding immunoglobulin protein (BiP) followed by increased expression of chaperones (calnexin and GRP94) and galactosyltransferase. Furthermore, the expression levels of CHOP, a well-known ER stress marker, and cleaved caspase-3 are significantly reduced, suggesting that BIX addition reduces ER stress-induced cell death by relieving ER stress. The beneficial effect of BIX on mAb production is also demonstrated with another qmAb -enhancing reagent (sodium butyrate) and a different rCHO cell line (CS13-1.00). Taken together, BiX is an effective ER stress inhibitor that can be used to increase mAb production in rCHO cells.

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