spERt TECHNOLOGY: A NOVEL STRATEGY TO IMPROVE PRODUCTIVITY THROUGH ENHANCED POLYRIBOSOME ASSEMBLY ON THE ENDOPLASMIC RETICULUM IN CHO CELLS

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In cell line development process, it is frequently observed that increased mRNA levels do not always correlate with protein expression levels in CHO cells. In line with this gap, the endoplasmic reticulum (ER) in CHO cells is much less proliferated as compared with that in terminally differentiated (*i.e.,* professional) secretory cells, suggesting that there is still room to improve their specific productivity if translational efficiency on the ER can be up-regulated. Here we present a novel engineering approach (spERt Technology) to improve specific production rates by mimicking the ER translational apparatus of professional secretory cells.

In spERt Technology, we exploit the unique factors that are required for translationally active polyribosome formation on the ER to directly enhance the translational efficiency (1, 2). A high antibody (Ab) producing clone generated by a novel screen using flow cytometry (3) was used as a model cell line. The factors were introduced into the high producer and a series of the spERt Technology - introduced cell lines were generated Among these cell lines, we selected one of the best clones (spERt-f9) having stable and high productivity. Polyribosome analysis of these cell lines revealed that enhanced assembly of the ER polyribosomes as expected (1). Consistent with the highly developed polyribosomes, the spERt-introduced cell lines produced higher levels of Ab than that of parental cells, and showed prominent increase of specific production rates. Further optimization of feeding process resulted in remarkable increase of productivity in spERt-f9 cells: Ab titers of 7.6 g/L and 9.5 g/L on day 14 and 17, respectively, were achieved in shake flask fed-batch cultures by using chemically defined media. Importantly, high cell viabilities were maintained in spERt-f9 cells throughout the culture periods. In addition, lower glucose consumption and reduced accumulation of ammonia were observed. Product quality in these cells were analyzed and compared with that in the parental cells.
In conclusion, spERt Technology enables to improve productivity of high Ab producers, associated with reduced accumulation of waste metabolites and high cell viabilities.

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