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An Addition of Lithium Chloride Improves the Transient Gene Expression Yield in CHO cells

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Abstract

As hundreds of new recombinant therapeutic proteins enter into development each year, a cost-effective transient gene expression (TGE) system is required to assess these proteins at an early phase as a more rapid alternative to a stable gene expression system. While several strategies, such as genetic manipulation and environmental modification, have been attempted in TGE systems to improve the overall yield in Chinese hamster ovary (CHO) cells, chemical supplementation is often employed in industrial processes owing to its simplicity and effectiveness. Lithium chloride (LiCl), which is known to induce G2/M-phase cell cycle arrest, was found to be an attractive chemical additive to enhance recombinant protein production in CHO cells in a previous study by the authors. In the present study, we demonstrate that LiCl can be used as both a transfection facilitator and a production enhancer to enhance the TGE yield in CHO cells. In order to verify the effect of an addition of LiCl on transfection efficiency and episomal DNA stability in the TGE system, green fluorescent protein (GFP) was transiently transfected onto CHO cells in the absence or presence of LiCl and the fluorescence was measured by flow cytometry. At four hours post-transfection, the fluorescence signal was increased in a dose-dependent manner and was prolonged for 72 hours compared to non-added cultures, which showed weaker signals as time passed. For the TGE of monoclonal antibodies (mAb), an addition of 10mM LiCl along with DNA/PEI complexes also showed approximately a 1.3-fold increase in the final mAb concentration compared to non-added cultures. On the other hand, an addition of LiCl at various concentrations to four-hour post-transfected cultures increased the final mAb concentration to more than 3.5-fold compared to control cultures by inducing the G2/M-phase of cell cycle arrest. Taken together, the data obtained here demonstrate that LiCl is a potentially useful additive to improve TGE systems in CHO cells.