PRODUCTION OF GYPCHEK IN THE WAVE® CELL CULTURE BIOREACTOR: COMPARISON TO PRODUCTION IN A STIRRED TANK BIOREACTOR

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ABSTRACT

A bioreactor with a completely novel design has become the bioreactor of choice by pharmaceutical companies using insect cell lines to produce proteins. This bioreactor, termed the Wave bioreactor, has several advantages compared to a stirred tank bioreactor. Methods to produce Gypchek in the Wave bioreactor were developed at 5 and 10 liter scales. Using the revertant Ld652Y cell line (described below), polyhedra production levels of approximately 4 x 10^{10} polyhedra per liter were found in both the 5 and 10 liter bags. This result indicates that production of virus in the Wave bioreactor will be scaleable to larger bags without a change in polyhedra production levels. A comparison of polyhedra production in the Wave vs. stirred tank bioreactors was made using the current revertant Ld652Y cell line. For these comparisons, cells from the same seed flasks were used to charge the bioreactors with cells. Consequently, the only difference in these studies was in the bioreactor used. Polyhedra production in the Wave bioreactor was found to yield higher amounts of polyhedra in all studies compared to production in the stirred tank bioreactor. Production of polyhedra in the Wave bioreactor yielded twofold more polyhedra compared to the stirred tank bioreactor. As a consequence of these results, further studies will focus on virus production in the Wave bioreactor.

During the course of our recent studies in the Wave and stirred tank bioreactors, we observed a steady significant decline in polyhedra production that stabilized at a level of about tenfold less than earlier production levels. Studies on this decline revealed that the maximum achievable cell densities in the bioreactors declined from 8 x 10^6 cells/ml to only 2 x 10^6 cells/ml, which is the reason for the drop in polyhedra production. During these studies the morphology of the Ld652Y mixed cell line changed from being primarily fibroblast-like to spherical. The new cell line became adapted to growth in suspension culture conditions and is termed suspensionLd652Y (SLd652Y). The SLd652Y cell line performs well in suspension conditions; however, it cannot achieve the necessary cell densities for economical polyhedra production. To solve this problem we are regenerating an Ld652Y cell line that is adapted for static cell growth through continuous propagation in static T-flasks. At this date, the cells have been subcultured 60 times in T-flasks, and the cell population is reverting to the original fibroblast cell line. This process is not yet complete; however, significant increases in polyhedra production have been achieved. Increases in polyhedra production of 3.5-fold and 4.0-fold have been achieved in the stirred tank and Wave bioreactors, respectively. However, for bioreactor production of virus to become operational, it is necessary to generate and use clonal cell lines that will give consistent production levels. Efforts are in progress to generate clonal *L. dispar* cell lines from available *L. dispar* cell line mixtures.