Reduced Temperature Production of Recombinant Proteins to Increase Productivity in Mammalian Cell Culture

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***Abstract*—The production of recombinant proteins from an industrial perspective has one of its main goals is to increase the product concentration whether in batch, fed-batch or continuous perfusion bioreactor systems. However, a major problem trying to achieve high product concentration over pro-longed cultivation is the loss of cell viability leading to reduced production rate and lower product quality. One possible means to achieve high product concentration and main high cell viability is to perform the bioreactor operations at a reduced temperature than that traditional used for mammalian cell cultivation.**

A collaborative research project between MIT and the Bioprocessing Technology Institute (BTI) was established where the MIT Ph.D. candidate (S.R. Fox) performed his research in Singapore with the assistances of BTI personnel. The goal of this project was the production of recombinant gamma interferon (γ-IFN) in Chinese Hamster Ovary (CHO) cells by operating the bioreactor at 32^{o} C in contrast to cultivating the CHO cells at the traditional temperature of 37^{o} C. By reducing the cultivation temperature to 32^{o} C, we have found that the specific γ-IFN productivity can be increased to 400% as compared to the higher temperature (37^{o}). This increase was the result of two factors. First the cell death was reduced at the lower temperature and second, the mRNA for the γ-IFN gene was greater (presumably through decreased mRNA degradation).

However, at the reduced temperature, the cell's specific growth was also impaired. Mutation and selection for higher growth rate strain at the reduced temperature was successful but we are concerned with the genetic stability of such mutants. Therefore a new collaborative project has been initiated using molecular genetics to engineer new CHO strains with higher growth rate at the reduced temperatures. The preliminary findings from this new project will be presented as a poster in this Symposium by Mr. Hong Kiat Tan.

[Full Text Not Available]