[S3-3] [4/19/2002(Fri) 10:50-11:15/Hall A]

Enhancement of Erythropoietin Production in CHO Cell by Introducing Urea Cycle Enzymes

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Recombinant human EPO (Erythropoietin) has been developed and used for clinical treatment of the anemia associated with chronic renal failure as well as normal anemia induced by HIV infection, cancer chemotheraphy and bone marrow transplantation, etc. The efficient EPO-expression system in mammalian cells is required for massive production for therapeutic use. Ammonium ion is a toxic waste which inhibits cell growth and productivity of recombinant proteins. To reduce the ammonium ion accumulated in mammalian cell culture, CHO cell line (CHO-OTC-A19) expressing the first two enzymes of urea cycle, carbamoyl phosphate synthetase (CPS) and ornithine transcarbamoylase (OTC) was already developed. This cell line showed lower ammonia concentration per cell in culture and higher growth than the vector controlled CHO cells (CHO-neo-5). The purpose of this study was to develop efficient EPO expression system by introducing the enzymes of urea cycle. CPS and OTC were introduced IBE cell which produces high level of EPO by encoding amplifiable selection gene, *dhfr* (dihydrofolate reductase) linked to human EPO gene. IBE expressing CPSI and OTC (CO5) was 15-25% higher cell viability and 15-20% ammonia removal activity per cell than the parental cell line, IBE after 96hr culture. Also, CO5 showed 2-2.5 times higher productivity of EPO as compared with the control, IBE. These results confirmed that improvement of higher ammonia removal activity in CHO cell by introducing urea cycle enzymes led to enhancement of recombinant human EPO productivity with higher cell viability.