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Development of hyper osmotic resistant CHO host cells

Yasuharu Kamachi

Abstract

We have developed a cell culture platform for monoclonal antibody (IgG) production by Chinese Hamster Ovary (CHO) cells. The platform feed used the continuous feeding method. This platform can maintain high cell density and produce high antibody titer. However because operation of continuous feed is complex, contract manufacturing organization (CMO) that can perform continuous feed is limited. Therefore, we tried to change the feeding method from continuous feed to bolus feed. However the previous studies showed that the rapid changes of osmolality by bolus feed and the hyper osmolality repressed the cell culture growth and the final titer.

In this study, we developed hyper osmotic resistant CHO-S host cell A (resistant to 450mOsm). To establish osmotic resistant CHO-S host cells, original CHO-S cells were passaged on a hyper osmotic basal media with repetition for about 100 days. We demonstrated that there were obviously differences in the cell growth under osmotic pressure of iso- (328 mOsm) and hyper- (450 mOsm) osmolality between the two host cells. Metabolic analysis of cell culture supernatant on CHO-S host cell A and CHO-S host cells with/ without osmotic stress performed. Compared to original CHO-S host cells, the osmotic resistant CHO-S host cell A has a greater capacity to generate osmolytes (sorbitol and erthritol) and decreased level of oxidized glutathione (GSSG), which suggests the osmotic resistant CHO-S host cells A handles osmotic stress better. Moreover, the characteristic of osmotic resistant on hyper osmotic resistant CHO-S host cell A was maintained even after 7 passages on a basal medium (330 mOsm). We will establish hyper osmotic resistant antibody production CHO cell line by using the CHO-S host cell A.