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Enhancing recombinant glycoprotein yield and quality using gene targeted CHO cells lines

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Background

It has been widely reported that CHO cells undergo apoptosis in culture, despite nutrient supplementation through fed-batch strategies. An understanding of apoptosis signaling can thus enable the identification of key genetic targets for the engineering of cell lines that could prolong culture viability and attain higher cell densities to effectively improve recombinant glycoprotein yield and quality.

Results

Transcriptional profiling using microarray technology, which allowed for the expression profiling of thousands of distinct genes simultaneously, has been adopted for the analysis of apoptosis signaling in a CHO cell fed-batch culture system. The subsequent analysis has allowed for the identification of early apoptosis signaling genes, which were significantly up- or down-regulated as the culture transited from the exponential to the stationary phase. Novel gene targeted CHO cell lines were developed by targeting the following anti- and pro-apoptosis genes, either individually or in combination: *Fadd*, *Faim*, *Alg-2*, *Requiem* and *Molecular Chaperones*. Comparison of these engineered CHO cell lines with the parental CHO in terms of recombinant glycoprotein yield and glycosylation profiles will be presented. As hypothesized, the gene targeted CHO cell lines exhibited improved resistance to apoptosis, resulting in prolonged culture viability and more importantly concurrent improvement in recombinant protein yield for fed-batch cultures.

Conclusion

This study showed that by harnessing the information from gene expression analyses, a rational approach to the development of robust CHO cell lines possessing the desired culture characteristics to enhance recombinant protein yields and quality can be achieved.