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Poster Presentation

Transcriptional profiling of recombinant CHO cells by a novel inter-species analysis strategy

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Background

Despite the widespread use of CHO cells for the production of many industrially relevant biopharmaceuticals, this system is poorly understood on the genetic level and mainly relies on empirical procedures, due to the lack of adequate sequence information. In order to advance its overall performance, we successfully tested the applicability of a cross-species microarray approach, for investigating CHO specific transcription profiles [1]. In the present study we show expression signatures of individual recombinant CHO clones which correlate with their associated phenotype.

Results

Clones were cultivated in repeated batch mode (5 batches) in Sixfors bioreactors. Several CHO model clones were analyzed on an Agilent genomics platform using 60-mer oligonucleotide mouse microarrays. We could detect distinctive target genes between different model clones, all characterized by high production levels of the recombinant protein. What we also found were commonly enriched Gene Ontology (GO) categories present in all the clones with this particular property. In addition, a group of similar clones with improved sialylation capabilities was studied, since the protein used in these experiments is heavily glycosilated, and found to share common signature genes and enriched GO terms. In a further model we tried to identify predictive genes for stress susceptibility under bioreactor conditions. We compared a resistant and a susceptible clone in spinner cultures and during bioreactor cultivation. There was a striking similarity both in the expression profile and the level of expression when early and late growth stages of this clone were compared. Hence, these prognostic signatures could be used as a selection tool and further help to understand some of the factors involved in stress response under altered growth conditions.

Conclusion

Transcriptome analysis has the potential to efficiently identify parameters for cell line improvement. In particular, cross-species analysis can be a useful tool to study gene expression profiles of related organisms for which species-specific microarrays are not available. The signature genes we were able to detect correlated with the phenotypic properties of the investigated clones, like high production levels, improved capabilities of product glycosilation, and stress resistance under bioreactor growth conditions. This knowledge could be helpful in understanding cellular mechanisms and could further serve to develop a robust host cell line for effective process performance.

References

1. Ernst W, Trummer E, Mead J, Bessant C, Strelec H, Katinger H, Hesse F: **Evaluation of a Genomics Platform for Cross-Species Transcriptome Analysis of Recombinant CHO Cells.** *Biotechnol J* 2006, **1**:639-650.